CHRONIC SPLENOMEGALY IN WEST AFRICA (WITH SPECIAL REFERENCE TO NIGERIA): AN ENQUIRY INTO THE CONTRIBUTION OF SYPHILIS AS A FACTOR IN ITS CAUSATION; WITH SOME OBSERVATIONS ON THE COMMONER SIGNS OF THIS DISEASE AMONG WEST AFRICAN NEGROES.

Being

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By

SAMUEL LAYINKA AYODEJI MANUWA

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TABLE OF CONTENTS

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This thesis is composed entirely by myself and is based on clinical data which have been collected and analysed by me while acting as Resident Medical Officer at the African Hospital, Calabar, Nigeria, West Africa. The Sachs-Georgi reactions and blood and stools examinations described therein were done as part of the routine laboratory work by G. W. St.C. RAMSAY, Esq., M.D., F.R.F.P.S. Glas., D.T.M.& H. Eng., Pathologist attached to the hospital.

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A. A. Manuwa.

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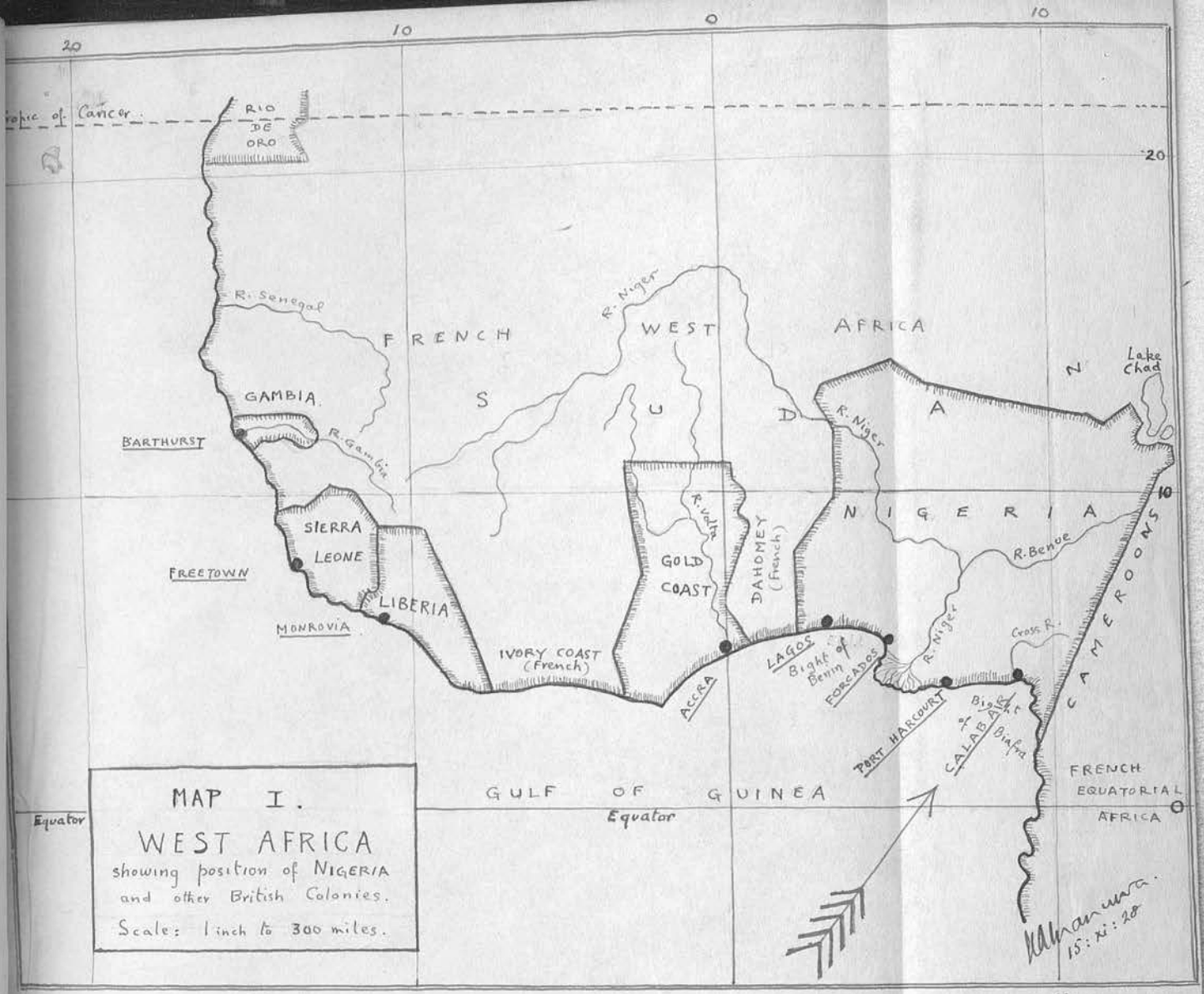
PART 1.

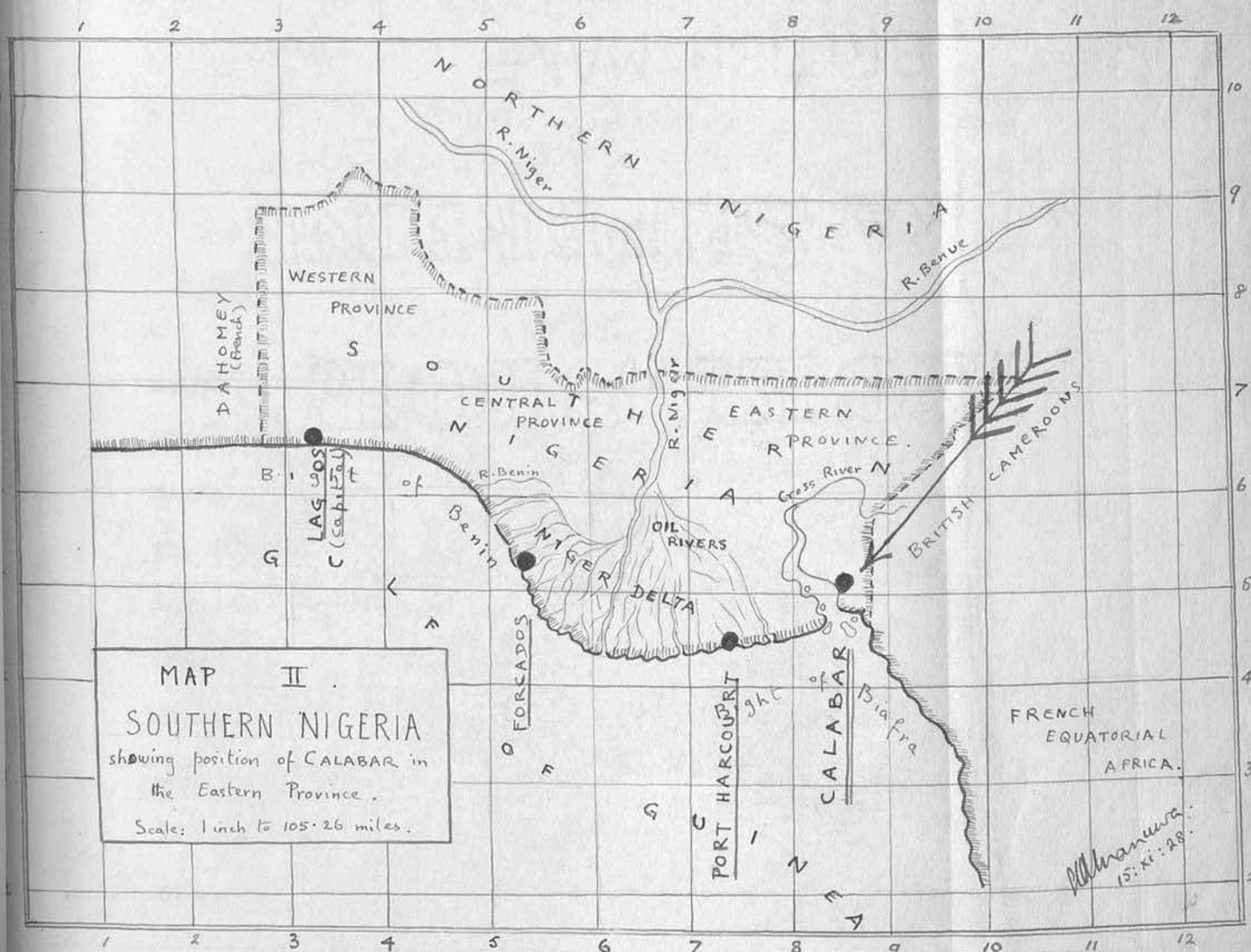


MAP I.

WEST AFRICA

showing position of NIGERIA and other British Colonies.

Scale: 1 inch to 300 miles.



MAP II.

SOUTHERN NIGERIA

showing position of CALABAR in the Eastern Province.

Scale: 1 inch to 105·26 miles.

INTRODUCTORY - The Geography of Nigeria.

The work described in this thesis was done in CALABAR, which is one of the sea-coast towns of Southern Nigeria. A brief sketch of the position, extent, population, topographical features, and climatology of the country may therefore serve as an introduction.

Position and extent. Nigeria is situated in West Africa (Map 1) on the north-eastern coast of the Gulf of Guinea, some 5 degrees north of the equator. The position of the country is particularly well defined, on account of its being intersected by two great rivers, the Niger and the Benue, which divide it into three parts, and which have converging courses bearing a strong resemblance to the letter Y. (see Maps 1 & 11). The territory is washed on one side by the sea and extends from the Bight of Benin, on the Gulf of Guinea, to Lake Chad, bordering on Central Africa; and from the Bight of Biafra, also on the Gulf of Guinea, to the confines of the French possessions on the Middle Niger. Its greatest length from east to west is 700 miles, and its greatest breadth, 600 miles. The upper regions of the country which are situated roughly above the northern banks of the Rivers Niger and Benue before the junction of these two rivers are called Northern Nigeria. They lie well within the western portion of the Sudan, which is an enormous tract of desert or semi-desert ~~and~~ land stretching eastward as far as the River Nile. The regions which lie below the confluence of the rivers are called Southern Nigeria, and would be enclosed roughly by a line drawn parallel to the coast-line 160 miles north of it. The area of Nigeria is approximately 336,000 square miles,

of

of which Southern Nigeria is 80,000. Nigeria therefore is about 1/33 the size of the whole African Continent, and ¾ that of the entire British possessions in West Africa. It is larger than any British Dependency other than Tanganyika (East Africa), India, and the self-governing Dominions, and is more than 3 times the size of the United Kingdom. The calculation given does not include the neighbouring area of the mandated territory of the Cameroons, which is administratively part of Nigeria, and is about 30,000 square miles.

Topographical and Geological features. The chief topographical feature is the River Niger, from which the country derives its name. It bisects Southern Nigeria into 2, and, as it nears the coast, breaks up into a wonderful network of waterways and lagoons which form a delta that subtends over 150 miles of coast line.

Along the entire littoral of Nigeria runs a flat, low-lying belt of dense mangrove forest and swamp, from 10 to 60 miles in width. This belt is intersected by branches of the Niger delta and other rivers - The Oil Rivers - which are connected with one another by innumerable creeks. The whole thus constitutes a continuous inland waterway from beyond the western boundary of Nigeria almost to the Cameroons. Behind this belt lies a thickly populated, dense bush country. Further inland, the forests become thinner and are succeeded by open, undulating grass-land. The extreme north contains very little vegetation, and a good portion of it is desert land. Mountains in the southern territories of Nigeria are very few, except along the eastern portion bounding on the Cameroons; but, north and east of the confluence of

confluence of the Rivers Niger and Benue, there is a large plateau from 2,000 to 6,000 feet in height. Except in the mountainous and plateau regions, no part of the country exceeds an altitude of much over 200 feet. The country, especially the southern portion, is very well watered by rivers. Besides the great Niger and Benue, there are a number of important rivers of which Cross River, on which the port of Calabar stands, is the largest. Lake Chad on the extreme north-east frontier is the only large lake.

Population. The population of Nigeria (1921) is approximately 18½ millions. Of these, about 8½ millions inhabit the Southern territories, giving and average density of 101 to the square mile. The native inhabitants are of pure Negro race, and, in Southern Nigeria, comprise a large number of tribes of which the chief and most numerous are the Yorubas, the Ibos, the Ibibios, and the Efiks. The first inhabit the western province, which is half of that part of the country west of the Niger and its delta; while the latter three occupy the central province, which is the other half, the Niger delta itself, the Oil Rivers area, and the eastern province, to the east of the Niger (see Map 11). The people along the coast areas are educated and civilised; but many in the interior are still "bush-people" and semi-savage.

Climate and Rainfall. The climate of the whole of Nigeria is divided into two seasons - the "dry" season (October to March) and the "Rainy" season (April to September). The "Harmattan", a cold north-east wind which brings with it a thick haze composed of minute particles of sand from the Sahara Desert, blows from November to February. During this season, frost often occurs in the highland plateaus. The average maximum shade temperature for the whole country

country is about 92°, the average minimum varying from 64.5° in the Southern, to 70° in the Northern provinces. The Southern provinces, especially the districts near the sea or the River Niger, are very humid.

The amount of rainfall varies considerably in different parts. In the sea-coast regions, the rainfall in the west is about 72 inches in the year, whilst in the east, it reaches as high as 245 inches. Northwards over the whole country the rainfall varies from 30 inches to 60 inches.

The Chief industries are mainly agricultural and are connected mostly with palm produce, mahogany, rubber, and cocoa: the first especially.

The Chief Towns are the sea-ports and these are, from west to east, Lagos (capital), Forcados, Port-Harcourt, and Calabar.

CALABAR (from which the names "Calabar bean" and "Calabar swelling" are derived) is the most easterly port of Southern Nigeria. It is in the eastern province, and is situated on the Bight of Biafra approximately at 5° north latitude by 8½° east longitude. It lies on the Calabar River, about 35 miles from the broad estuary of the Cross River, to which the Calabar River is the largest tributary. It is the chief port of the eastern province, as it taps much of the palm-oil and rubber belt of country around the Niger delta and Cross River territories. The general topographical features of the town and the surrounding district resemble in all respects those of other sea-coast towns of Nigeria and West Africa. It is low-lying and flat. The average annual rainfall (1927) is 190, and the absolute temperature (1927) varies from a minimum of 66° to a maximum of 89°, with an average of

of 71° and 87° respectively. It has a population (1927) of 55,236.

The Calabar Hospital, at which the data for the present enquiry were collected, is the headquarters hospital for the whole of the eastern province of the country, as well as for the mandated territory of the Cameroons which adjoins it. It therefore draws its materials from fully half of Southern Nigeria, serving a population of over 4 millions which comprise chiefly the Ibos, Ibibios, and Efiks. The conclusions arrived at can therefore be considered as applicable to Southern Nigeria as a whole and also to the coastal belt, at least, of the whole of West Africa.

PART II

CHRONIC SPLENOMEGALY IN WEST AFRICA (WITH SPECIAL REFERENCE TO NIGERIA): AN ENQUIRY INTO THE CONTRIBUTION OF SYPHILIS AS A FACTOR IN ITS CAUSATION; WITH SOME OBSERVATIONS ON THE COMMONER SIGNS OF THIS DISEASE AMONG WEST AFRICAN NEGROES.

THE GENESIS OF THE ENQUIRY.

The differential diagnosis between the various pathological conditions which are accompanied with chronic enlargement of the spleen occurring either alone, or in association with enlargement of the liver, is still one of the great difficulties of tropical medicine. Although many are the conditions which cause the spleen to enlarge, yet, as BALFOUR (1927 and 1928) recently pointed out, we still know so few of them that further research on splenic pathology is indicated. For example STRONG, SHATTUCK, BEQUAERT, and WHEELER (1926) have only recently described a peculiar and ~~a~~ new form of tropical splenomegaly occurring in the Amazon*. More recently still, PROCTER (1927) described another hitherto unknown type which affects Kikuyu children in Kenya. PINOY and NANTA (1927), EMILE-WEIL, GRÉGOIRE, and FLANDRIN (1927) gave an account of a mycotic variety from Algeria. It was only lately that BLEYER (1926) noted even ordinary measles as a cause of enlarged spleen.

Malaria, splenic anaemia, and "idiopathic splenomegaly" still remain diagnostic "rag-bags" into which spleens enlarged from an unknown cause are too often apt to be relegated in tropical practice. It is true that many brilliant researches, especially from the therapeutic stand-point, have been done in the past

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* BOYD (1927) does not agree that these observers have excluded malaria as a causal factor.

past for example with regard to the effect of drugs other than quinine on the size of presumably "malarial" spleens. BARLOW (1916) has recorded a more rapid reduction in the size of chronic "malarial" spleens with intravenous injections of mercuric chloride (combined with oral quinine) than he obtained with quinine alone. His results were later confirmed in India by GREIG and RITCHIE (1917). MONTEL (1915) in Indo-China has reduced an enormous spleen of six years' standing to its normal size with injections of neosalvarsan alone in two months. Similar results have been recorded in South Bulgaria by SEYFARTH (1918) and others. No attempt, however, seems to have been made by these observers to correlate therapeutic findings with etiological factors. There is no conclusive proof that their cases did not have an etiological element other than malaria. Malaria, indeed, is so firmly established in traditional respectability as a cause of splenic enlargement that its role, though important in this connexion, is often very apt to be exaggerated. That malaria is a most frequent cause of many of the enlarged spleens is a fact that cannot of course be doubted. However, it seems remarkable that though most of the people in a tropical community have at one time or other in their life been infected with malaria, yet not all of those so infected, even in highly malarious regions, develop chronically enlarged spleens. Indeed, ROSS (1910) was among the first to suggest that splenomegaly in this disease depends in any given two equally infected communities on various factors, and that the spleen rate constitutes a very inexact guide to the prevalence of malaria as such in such two communities. It is not an uncommon phenomenon in tropical practice to find that no splenic enlargement occurs in non-natives who have had repeated attacks of undoubted malarial fever. There must be some factor in the native, therefore, which causes the spleen

to enlarge in one case of malaria and not in another.

During my very early days of tropical practice in Calabar, I was struck with the frequency with which chronic splenomegaly in many adults and children was associated with very few, if any, of the signs of chronic malarial infection. Fever, very severe anaemia, and cachexia, were often absent. Parasites, as has often been observed in most cases of chronic malaria, were generally not to be found in the peripheral blood. Many patients had enlarged livers as well, associated in a few cases with a variable degree of ascites. The significant point, however, was that many of the cases gave a strong positive Sachs-Georgi reaction, and shewed one or other clinical manifestations of syphilis; and syphilis is one of the diseases which produce enlargement of the spleen. In Calabar, mosquitoes of course exist, but attention has sometimes been called to the comparative small numbers of the anopheline variety. Besides, the inhabitants have known the benefits of quinine as a prophylactic and cure for malaria for many years. The spleen rate therefore probably gives a higher indication of malaria than really does exist in this community. Syphilis, however, is rife, and has been present untreated, for generations. It has been pointed out* that syphilis of the spleen even in the acquired form of the disease is not so rare as supposed. TIMBAL (1922) and LACROIX (1927) have recently independently described some cases of this type. The disease, then, either alone or in association with malaria as a factor in the causation of chronic splenomegaly, would

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* Med: Sci: Abs: Rev. 7-3. 12.22. p.206. Reference supplied by Dr. A. Balfour, London.

would seem to be one to be seriously taken into account. I therefore considered that it would be of some interest if some data were collected and analysed, and therapeutic tests carried out, so far as circumstances allowed, in order to find out what part syphilis plays in chronic splenomegaly in West Africa.

Unfortunately, two chief difficulties were foreseen at the very beginning of the investigation. Firstly, yaws is a disease that is endemic to some extent throughout this colony. Like syphilis, it gives a positive Wassermann or Sachs-Georgi reaction, and its tertiary signs are difficult and very often impossible to distinguish from the tertiary lesions of that disease. It will be realised, therefore, that the assessment of the value of data regarding clinical manifestations of syphilis or regarding serological reactions would be attended with great difficulty and might indeed considerably detract from the scientific validity of any specific conclusions that might be drawn from the investigation of a series of cases. Secondly, it was to be expected that the average duration of the stay in hospital of each case would not be long enough to permit of adequate facts being collected for an investigation of this kind, especially with regard to its therapeutic portion. However, such an investigation would be of some value if the data were collected with a reasonable degree of care.

* * * * *

Yaws, syphilis, and malaria, then, are the three diseases that will require to be considered, and, for their investigation, certain criteria are necessary.

CRITERIA FOR AN ENQUIRY INTO ONE OR MORE OF THE FACTORS WHICH PRODUCE ENLARGED SPLEEN IN THE TROPICS.

Such investigation must cover the following grounds:-

(1) The cases collected must be consecutive, must be unselected, and must be representative.

(2) They must be sufficiently numerous to warrant inferences of any scientific value being drawn at the

conclusion of the investigation.

(3). They must be kept under prolonged observation.

(4). In addition to cases showing splenic enlargement, those who show hepatic enlargement with or without any enlarged spleen should also be investigated.

(5). The analysis of the cases should be done in age groups, a sufficient number being collected for each group to make comparison with other groups of any value. Particular attention should be paid to the children.

(6). All observations must be duplicated on a larger number of cases who do not present enlarged spleen or liver, so as to act as controls.

(7). The enquiry would be largely statistical in nature; but clinical details should weigh more considerably than statistical data only, in the inferences drawn.

(8). The essential points to be embodied in the clinical data should be, with regard to each case,-

i. an accurate history;

ii. a careful and complete ordinary clinical examination;

iii. special methods of investigation which should comprise the following, viz., examination of the stools and blood for parasites, accurate actual and differential blood counts, qualitative haemocytological examination, the Wassermann reaction, and the van den Bergh and other serological or biochemical reactions that might be indicated.

iv. Splenic, liver, and gland punctures for parasites;

v. therapeutic tests of the effect of drugs.

vi. the post-mortem finding in fatal cases.

COMPARATIVE

COMPARATIVE INCIDENCE OF YAWS, SYPHILIS, AND MALARIA IN CALABAR AND NIGERIA.

It may be convenient here to discuss the comparative incidence of the three diseases which, as previously stated, have an important bearing on the question as it affects this country, namely, yaws and syphilis on one hand, and malaria on the other.

According to the Nigerian Annual Medical Report of 1927 (Chart No.3. facing p.20), of the total number of "infective diseases" treated in the whole colony, syphilis accounted for 13.01 per cent, malaria 22.00 per cent, and yaws 25.58 per cent. In Calabar here, during 1926, the total number of the three diseases as treated in the African Hospital was 1426, of which 277 were yaws, 358 syphilis, and 791 malaria, i.e. a proportion of 1 : 1.3 : 2.8. In both series of figures, the incidence of malaria is probably too high, as it includes many cases of fever which were not microscopically proved to be definitely due to that disease. On the other hand, the figures for syphilis are undoubtedly too low, because many cases of undoubtedly syphilitic origin, such as aneurysms, paralysis, and so on, are put down under separate headings and are not included in the syphilis returns as syphilis; and the number of such lesions is not inconsiderable. Further, it must be remembered that the diagnosis of a tertiary lesion as yaws or syphilis often depends to some extent on the bias of the examining officer in favour of one or other disease. Attention to this fact has been drawn by STANNUS (1926). Now, the figures from Uganda, a colony whose state of civilisation and development closely approximates Nigeria and in which the question of syphilis is closely investigated through numerous special venereal clinics, are of

more

more significance. Of the total "epidemic, endemic, and infectious diseases" treated in the whole of that colony in 1926 (Uganda Annual Med. & Sany: Report, 1926, Chart No.3 facing p.8), syphilis topped the list with 35.73 per cent, malaria 26.39 per cent, and yaws 10.88 per cent. Most medical officers working in Southern Nigeria are agreed that syphilis is rife among the native population. This is in complete agreement with the observations of most workers among natives in most parts of tropical Africa. For instance, according to NOGUE (1924), 52.77 per cent of the natives of Senegal (French West Africa) are syphilitic, while NAGELSBACH (1926) gives a per-centage of 40 among the natives of West Abyssinia.

It is to be noted that in Calabar, yaws is not as common as syphilis, and that malaria is the commonest of the three diseases.

P A R T 111

Age period.	Total examined
0 - 10	166
11 - 20	258
21 - 30	201
31 - 40	117
41 - 50	129
51 - 60	129
Total	1000

THE PRESENT ENQUIRY.

Total Number examined.

The present enquiry was done on 1,000 consecutive unselected persons who were treated at Calabar Hospital. The ages of the patients varied from a few months to 60 years. It might be pointed out that assessment of age of individuals among primitive peoples is to be regarded as only approximate, because most are illiterate and cannot tell their age. The assessment of the ages in this series was done in consultation with a hospital dispenser who was formerly a schoolmaster. The age-incidence of the cases arranged in decennial periods is indicated in Table 1.

TABLE 1.

Age Incidence

Age period.	Total examined
0 - 10	148
11 - 20	268
21 - 30	201
31 - 40	151
41 - 50	129
51 - 60	103
Total	1000

1.- INCIDENCE OF SPLENIC AND HEPATIC ENLARGEMENT.

The spleen and liver index was determined by ordinary palpation and percussion. A spleen was deemed to be enlarged if it was palpable at or extended beyond the subcostal region, with the patient lying in the recumbent position with the knees drawn up. It was not found convenient or necessary

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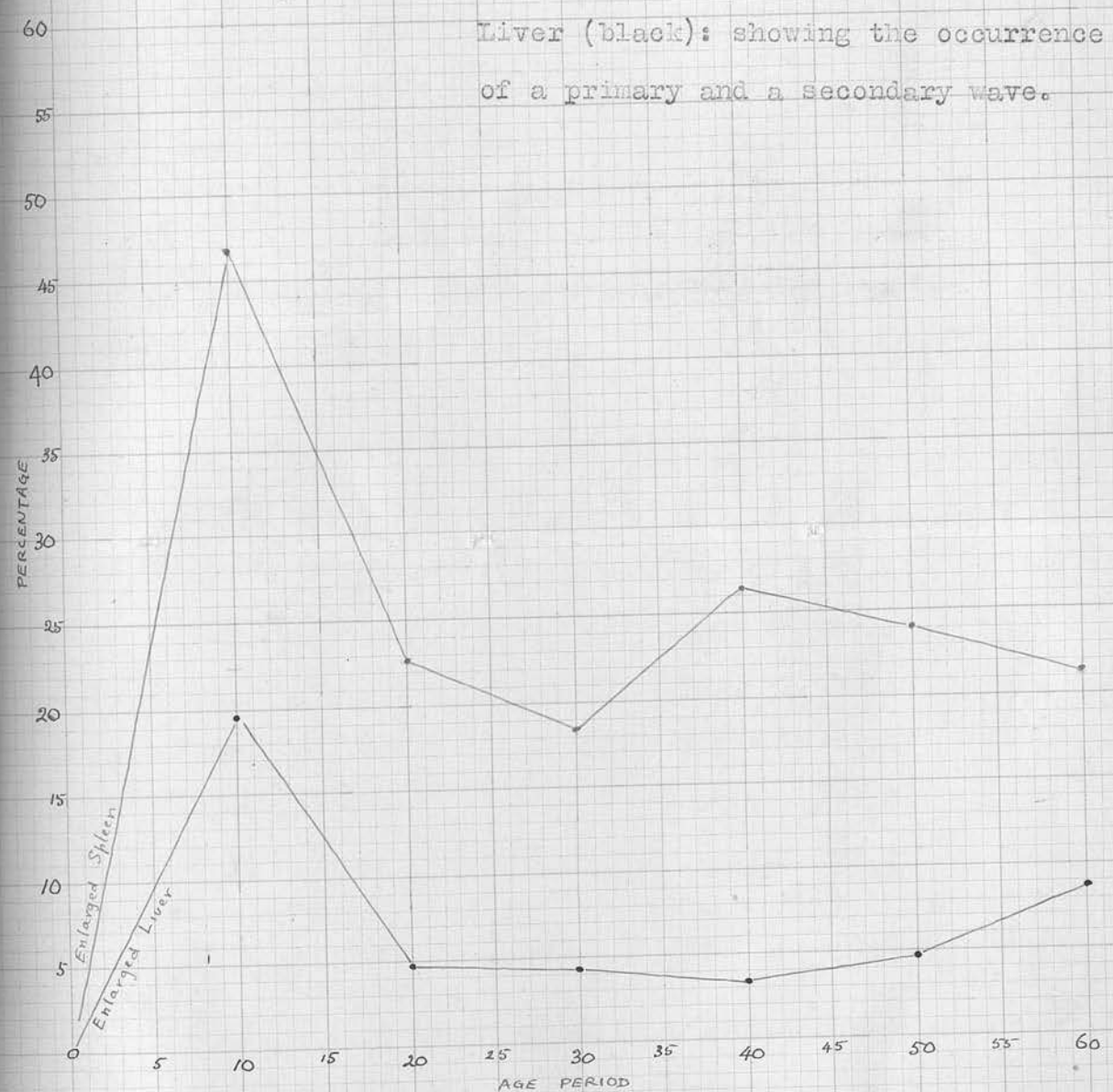
CHART I

Incidence of Enlarged Spleen (red) and Liver (black): showing the occurrence of a primary and a secondary wave.



necessary to employ CHRISTOPHER'S (1924) more exact anthropometric method. The liver was considered enlarged if it could be palpated at the costal margin and roughly if it extended in the middle line beyond the patient's hand's-breadth placed below the xiphisternum. Care was taken to exclude cases which were not true enlargements, for example, spleens or livers enlarged as a result of general visceroptosis. All the cases were those of chronic enlargement. Table II and Chart I show the results obtained arranged in decennial periods.

TABLE II

Incidence of Splenic and Hepatic enlargement.

Age period.	Total examined.	Total of enlarged spleens.	% per total examined in age group.	Total not showing splenic enlargement.	% per total examined in age group	Total of enlarged livers.	% per total examined in age group.
0 - 10	148	69	46.6	79	53.4	29	19.5
11 - 20	268	61	22.7	207	77.3	13	4.8
21 - 30	201	37	18.4	164	81.6	9	4.4
31 - 40	151	40	26.4	111	73.6	5	3.3
41 - 50	129	31	24.0	98	76.0	6	4.6
51 - 60	103	22	21.3	81	78.7	9	8.7
TOTAL	1000	260	26.0	740	74.0	71	7.1

It will be observed that 260 persons showed chronically enlarged spleens, leaving a total of 740 in whom the spleen was not enlarged. These latter were used as controls throughout the enquiry in all examinations carried out. The highest incidence was in children up to the age of 10, who gave a percentage of 46.6. A rapid decline to 22.7 per-cent and then to 18.4 per-cent between the ages 11-30 was then noted to occur, followed by a secondary wave to 26.4 per cent at 31-40,

and

and then a slight decline to 21.3 per cent at 51-60. These figures are interesting in that they show the occurrence of two distinct waves in the spleen rate. The rapid rise noted in children 0-10 years old is in accordance with the finding of many observers in the tropics, and the sharp decline which follows after that age is usually explained as being due to a rapidly acquired immunity to malaria. However, the secondary rise which occurs after the age of 30 cannot be admitted to be due to the "wearing off" of this immunity, inasmuch as infection and re-infection with malaria is of perennial occurrence. What, then, is the significance of this secondary wave ? What also is the significance of the fact that not all the spleens enlarged up to the age of 10 years resolve after that age, though all have presumably acquired a partial immunity ?

The liver was enlarged in 71 cases. Of these, 67 occurred along with the splenic enlargement. The high incidence of 19.5 per cent noted in children up to 10 is in general accord with the common finding in healthy persons of that age, and is perhaps not of much significance. A sharp decline to 4.8 per cent was noted between the ages 11 and 20. Of more significance however is the fact that, as in the case of the "spleens", a secondary rise from 3.3 to 8.7 per cent occurred, between the ages 41 to 60. The question therefore arises as to whether the enlarged spleen is ~~as~~ an essential part of the same disease as that which caused the enlargement of the liver, or ~~is~~ an independent, autonomous enlargement. We may note here at once that CASTELLANI and CHALMERS (1919) are sceptical about malaria causing enlargement of the liver and are of opinion that this factor is "less frequent than is admitted by many authors."

General Clinical Features. 207 of the cases in this series were warded in the hospital. The remainder were out-patients. The diagnosis of the primary disease for which the in-patients were admitted were recorded according to the form officially prescribed, and are set forth in Table III.

TABLE III.

Diseases for which 207 Spleen Cases were admitted.

Disease.	Number.
I. Epidemic, Endemic, & Infectious Diseases:	
Paratyphoid fever	1
Malarial fever	12
Influenza	4
Dysentery, diarrhoea	5
Yaws (secondary)	2
Tuberculosis	4
Syphilis	18
*Acute gonorrhoea	8
II. General Diseases:	
Carcinoma of the breast, with secondary metastases in the liver.	1
Debility	1
von Jaksch's anaemia	1
III. Affections of the Nervous system and Organs of the Senses:	
Locomotor ataxia	1
Paresis	1
Cerebral softening	1
Neuralgia	2
Cataract	1

* The figures for acute gonorrhoea are few, because the native regards the disease as trifling and therefore does not often come for treatment. Over 70% of all patients treated in this hospital have signs of chronic gonorrhoeal infection.

Disease.	Number.
Iritis	1
Keratitis	1
IV. Affections of the Circulatory System:	
Mitral incompetence: chronic heart failure with backward pressure.	3
Aortitis and Aortic dilatation or obstruction.	5
Myocarditis	2
Angina pectoris	1
V. Diseases of the Lymphatic System:	
Suppurative lymphadenitis	13
VI. Affections of the Respiratory System:	
Laryngitis	1
Bronchitis	7
Pneumonia (including broncho-pneumonia)	6
VII. Diseases of the Digestive System:	
Ancylostomiasis	1
Hernia	14
Haemorrhoids	1
Fistula-in-ano	1
Cirrhosis of the liver	1
Gumma of the liver	1
Jaundice	5
VIII. Non-venereal diseases of the Genito-urinary System:	
Chronic Nephritis	2
Schistosomiasis	1
Urethral stricture	3
Epididymitis	2
Salpingitis	2
Uterine fibroid	1
Abortion	1
IX. Affections of the Skin & Cellular Tissues:	
Impetigo	3
Mastitis	1
Abscess	4

Ulcers

Disease.	Number.
Ulcers	39
Elephantiasis	3
Juxto-articular nodules	1
Ganglion	1
Lipoma	1
Ulcerating granuloma	1
X. Diseases of the Bones & Organs of Locomotion:	
Osteitis	3
Synovitis	2
Arthritis	1
Fracture	1
XI. Affections produced by external causes:	
Wounds, burns &c.	6
XII. Miscellaneous:	
Gondou	1
TOTAL	207

It will be observed from this list that only few of the cases were admitted for conditions pointing directly to the spleen or liver. Among the diseases which may be associated with splenic enlargement, the following occurred.

TABLE IV.

Total number of cases (In-patients)	207

Disease present	Number of cases.	Per-centage.
Syphilis	18	8.7
Malaria	12	5.8
Tuberculosis	4	1.9
Chronic heart failure with backward pressure.	3	1.4
Yaws	2	0.96
von Jaksch's anaemia	1	0.5
Paratyphoid fever	1	0.5
Cirrhosis of the liver	1	0.5
Gumma of the liver	1	0.5
Ancylostomiasis	1	0.5
Schistosomiasis	1	0.5
Acholuric jaundice	1	0.5
TOTAL	46	22.2

It will be seen that syphilis was the disease noted in the largest number of the cases. It must be pointed out however that the figures given are much too low, and in this respect illustrate in detail what would appear to be the fallacy of the present system of classification, to which reference has already been made. The obvious affection that the patient presents on admission is that recorded for ordinary registration purposes. Lesions such as chancre, secondary eruptions, and obvious superficial gummata are of course set down as syphilis, but undoubtedly syphilitic lesions such as aortitis, locomotor ataxia, some cases of hemiplegia, iritis, keratitis, chronic ulcers, and osteitis would be filled in under separate headings, and not as syphilis. It is to be noted that 39 cases were admitted for various kinds of ulcerations, of whom over 75 per cent gave a positive serum reaction. Some were of the tropical phagedaena type, but many were certainly syphilitic though they were often recorded simply as "ulcers". No person of course can be put down under more than one diagnosis. Thus a person admitted for a local injury was recorded under that heading alone even if routine examination later revealed that he was a subject of tertiary syphilis. The fallacy of this method of classification has been pointed out by STANNUS (1926a) with special reference to the figures for syphilis. The real incidence of this disease will be referred to in more detail later, when it will be seen that there is a great discrepancy between the above figures and the actual figures. Malaria accounted for 12 cases. Yaws was observed in only 2 cases, both of them children, who showed the typical secondary eruption of the disease. One case each of gondou and juxto-articular

nodules

nodules was noted. Most observers are now agreed that these latter two diseases are tertiary manifestations of yaws. Enlargement of the liver and spleen are said to occurs in children with yaws, but CASTELLANI and CHALMERS (1919a) are of opinion that this is probably due to preceding or concomitant malaria infection. Tuberculosis occurred in 4 cases. They were all cases of phthisis, showed no miliary involvement, and cannot be regarded as causing the enlargement noted. Mitral incompetence accounted for 3 cases. The case of von Jaksch's anaemia occurred in a child aged 2, who showed the typical blood picture of this disease and died some months later of cancrum oris. The diagnosis of the paratyphoid case was serologically established. The case of cirrhosis was of the atrophic type, was accompanied with ascites, and was fatal. Gumma of the liver accounted for one case. Ancylostomiasis is listed by some authors as one of the diseases that may cause enlargement of the spleen; but, according to CASTELLANI and CHALMERS (1919b), the spleen in this disease is often shrunken. Ancylostome ova were present in the stools of a large number of the cases, as will be shown later; but in only one case were the clinical signs and symptoms so typical and the ova so numerous as to make the diagnosis of ancylostomiasis admissible. It occurred in a child aged 5 years. The one case of schistosomiasis noted was of the urinary (S. haematobium) type, and showed enlargement of the spleen only. Acholuric jaundice accounted for 1 case in a child age 12. It is to be noted that many of the commoner diseases associated with splenic enlargement, such as leukemia, lymphadenoma, splenic anaemia, Banti's disease, pernicious anaemia, malignant endocarditis, rickets etc., were not noted. Blood diseases apart from secondary

anaemia

anaemia are rare in Nigeria. For example, only 35, 11, and 2 cases of pernicious anaemia, leukaemia and lymphadenoma respectively were reported in the whole country during 1927. Rickets is very uncommon, only 45 Nigerian cases being reported during the same year. The absence from the present series of protozoal infections such as leishmaniasis, trypanosomiasis, and relapsing fever must be noted. The 9 cases of leishmaniasis reported for the whole country during 1927 were of the cutaneous type and occurred in the northern provinces near the Sudan. Trypanosomiasis is confined almost entirely to the upper regions of Northern Nigeria.

A moderate degree of anaemia was present in many of the cases seen. It was accompanied in the majority with a chronic low fever usually referred to by the patients as "evening fever". Ascites was noted in 5 cases of whom 1 died. In 2 cases, the ascites was so considerable that nearly 2 gallons were removed at one tapping. The jaundice cases numbered 5, and will be referred to later in connexion with the van den Bergh reaction. They all occurred in cases showing both enlarged liver and spleen.

11. - INCIDENCE OF BLOOD PARASITES.

(i) Malaria and Microfilaria.

The blood of all the patients was examined microscopically for the presence of parasites. In each case, the examination was carried out by the thin film and thick drop method, the blood being obtained from a prick in the finger. The films were allowed to dry in the air, and, without previous fixation, were stained in dilute Giemsa solution. The results obtained among the "Spleens", i.e. those showing enlargement of the spleen, and the "Others" i.e. the controls showing no enlargement, were as follows:

follows:

TABLE V.

Malaria and Microfilaria Incidence.

Age period.	Spleens.					Others.				
	Total examined.	Malaria positive.	%	Microfilaria. positive.	%	Total examined.	Malaria positive.	%	Microfilaria positive.	%
0-10	69	17	24.6			79	15	18.9		
11-20	61	10	16.3			207	23	11.1	149	
21-30	37	3	8.1	55		164	12	7.1	"	
31-40	40	1	2.5	"	21.1	111	6	5.4	Total	20.1
41-50	31	1	3.2	Total		98	3	3.0		
51-60	22	0	0.0			81	1	1.2		
TOTAL	260	32	12.3			740	60	8.1		

Most of the malaria parasites found were of the subtertian variety, and Mf. perstans formed the majority of cases of microfilaria. The following Table shows the findings with regard to the species of parasite.

T A B L E VI.

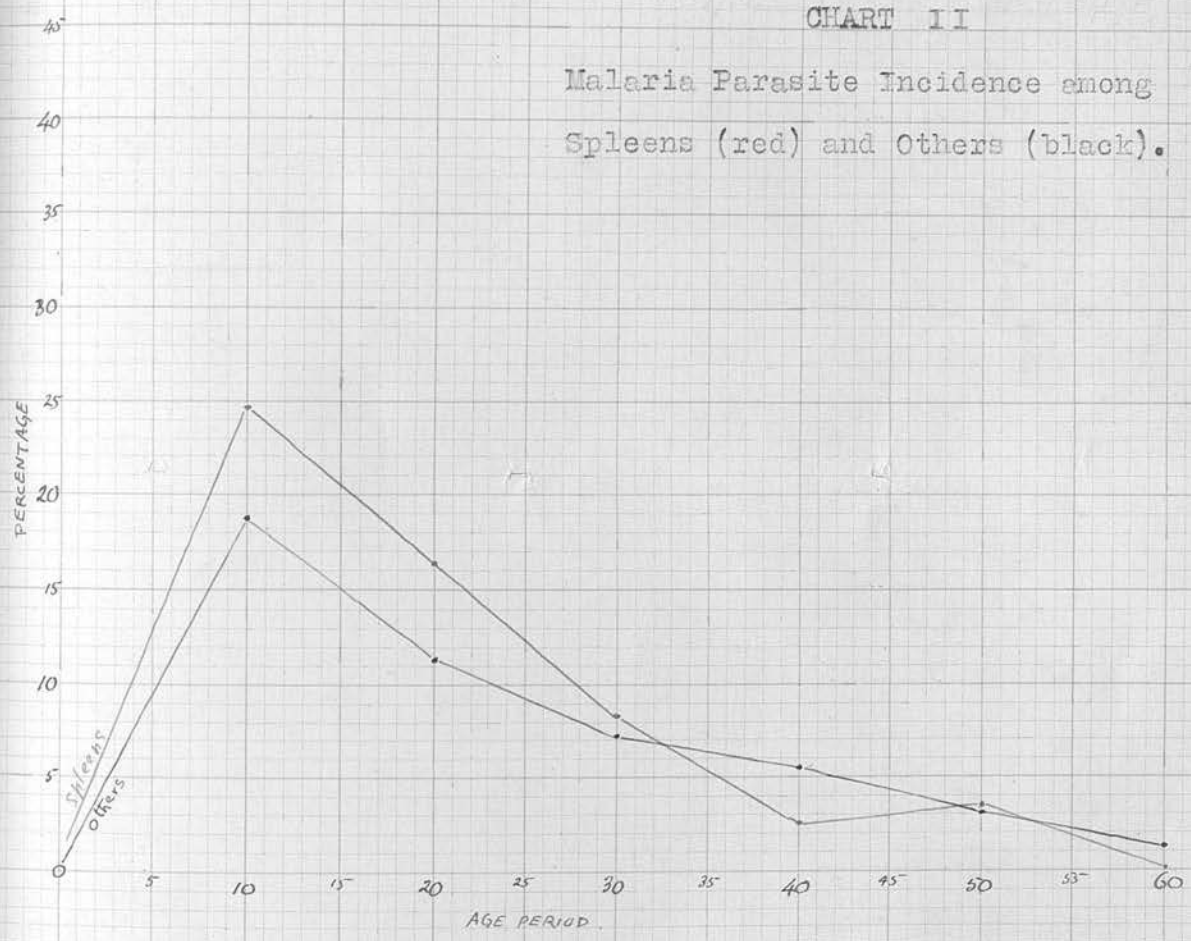
Species of Malaria and Microfilaria found.

Class	Malaria						Microfilaria.					
	Total number of patients.	Simple tertian	Subtertian	Quartan	Total	%	M. perstans.	M. loa	M. bancrofti.	A. Streptocerca.	Total	%
Spleens	260	-	28	4	32	12.3	51	4	-	-	55	21.1
Others	740	-	59	1	60	8.1	125	18	2	4	149	20.1
TOTAL	1000	-	87	5	92	9.2	176	22	2	4	204	20.4

It is not suggested that the results obtained represent the real proportion of individuals harbouring malaria or microfilaria. A single examination of a drop of blood necessarily gives a low indication of the numbers infected, and in order to obtain reasonably accurate figures,

CHART II

Malaria Parasite Incidence among Spleens (red) and Others (black).



figures, repeated examinations are necessary. With regard to malaria, the prevalence of the habit of taking quinine whenever feeling out of sorts often makes the microscopic confirmation of a clinical diagnosis of this disease a difficult and in many cases an impossible task. It may be emphasised, however, that the standard employed among the "spleens" and "others" with regard to the factors of the time of day, length, method, and number of examination was exactly the same. Further, the seasonal factor was constant for both groups of cases. The figures given may therefore be accepted as correct for the purpose of comparison between the two.

Malaria Parasite Incidence. The incidence of malaria parasite among all the patients cannot be said to be very high. 92 persons altogether were found to harbour parasites, giving a per centage of 9.2. The proportion who showed parasites among the enlarged spleen cases was observed to be about 4 per cent higher than among those whose spleens were not enlarged. Had observation been also made with reference to the presence of pigmented leucocytes, it is quite probable that the spleens would have shown a still higher degree of past malarial infection. This is as might be expected, because it must necessarily be assumed that the degree of enlargement of the spleen in malaria possibly corresponds directly to the severity or number of infection, or, inversely to the strength of acquired immunity present in the person infected. It may be remarked here that in only few instances among the cases could parasites be made to appear in the peripheral blood by means of provocative injections of adrenalin, strychnine, or novarsenobillon in cases where they were previously absent. Chart II shows graphically the results obtained among both classes. It was

observed

observed in both that the higher the age, the less likelihood was there of finding malaria parasite in the peripheral blood. This is a common observation in malariology, and has been repeatedly demonstrated by many observers like REICHENOW (1917) in Northern Nigeria, and others. A comparison of the curves of the "spleens" and "others" in Chart II shows that, as a whole, and for all age periods excepting those of 31-40 and 51-60, the malaria incidence in the former is higher than in the latter. There is a primary rise in both classes during the age period 0-10 years, corresponding to the primary wave in the enlarged spleen incidence.* With the exception of a very slight rise among the "spleens" between 41-50 due probably to the small number of cases seen in the age group, both show a steady decline in malaria incidence from the age of 11 to 60, the decline being to zero at 60 years in the case of the "spleens". The well-marked secondary wave at 31 to 60 which is observed in the curve for spleen enlargement has no counter-part in the curve for the malaria incidence. This must therefore be of some significance, the probable nature of which will be discused later. The common observation that malaria may exist without splenomegaly is illustrated by the figures here, which show that of a total of 92 persons who were proved to harbour parasites in their blood, only 32, i.e. barely ~~half~~ one-third, showed any demonstrable enlargement of the spleen. The question therefore arises as to

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* The figure obtained for the parasite incidence among the "spleens" of age 0-10, i.e., 24.6 per cent, closely corresponds to that of MAXCY and COOGLE (1923) who found that out of those who had enlarged spleen among 2,330 children, only 20 per-cent showed parasites in their blood.

to whether some other factor or possibly disease must be super-added to malaria before a chronic, permanent enlargement could result.

It must again be emphasised that it is by no means suggested that the figures given for the incidence of Parasites represent the total number of persons who can be said to be subjects of chronic malaria. It is a well established fact that chronic malaria often exists without parasites in the peripheral blood. The figures obtained from an investigation of histories of one or more attacks of malarial fever during at least the previous 12 months might perhaps have furnished more accurate figures. Histories, however, are very seldom of any help among native patients and are often entirely misleading. No trouble was therefore taken in this respect as regards previous attacks of malarial fever. Indeed, the average native cannot differentiate between malarial or any other kind of fever. Previous infection of most inhabitants in Calabar with malaria can however be reasonably assumed, despite the universal habit of quinine taking, and the comparatively small numbers of anophelines.

Microfilaria. The incidence of this parasite among both the "spleems" and "others" was observed to be nearly equal(Tables V & VI). The parasite cannot therefore be regarded as factor in the production of splenomegaly.

(ii). Other blood parasites.

The presence of other blood parasites such as trypanosomes and spirochaetes (e.g. of relapsing fever) was looked for as a routine in every case, more especially where indicated by clinical symptoms. In no case were such organisms found.

III.- HELMINTHS

A single examination only of the stools of all the

the patients was made for the presence of ova. The results obtained were possibly too low, in view of the fact that no concentration technique was attempted. They were as follows:

TABLE V11

Incidence of Intestinal Parasites

Parasite	Spleens (260)		Others (740)	
	No.	%	No	%
Negative	29	11.1	97	13.1
Ascaris	136	52.3	316	42.7
Ancylostome	123	47.3	369	49.8
Trichuris trichiura.	57	21.9	192	25.9
Strongyloides	14	5.3	21	2.8
Tape Worm	-	-	-	-
E. histolytica	3	1.1	21	2.8

All the stool examinations in the two groups of cases were carried out before any anthelmnintic medicine was given. The results obtained among both groups did not differ in any degree likely to justify the inference that the presence of helminths was a predisposing factor in the production of splenomegaly. Indeed, cases who showed splenic enlargement gave a slightly lower percentage of "negatives" than those in whom no enlargement occurred. It will be observed that the "spleens" gave a lower incidence of ancylostomes than the "others". Ancylostomes cannot therefore be considered to exert ~~any~~ to any appreciable degree any special influence in the production of the condition.

IV.- ACTUAL AND DIFFERENTIAL BLOOD COUNTS.

Actual and differential blood counts were done on 33 of the spleen cases. In each case, 300 cells were counted. The results are tabulated in Table V111.

TABLE VIII.

Actual & differential blood counts on 33 spleen cases.

Register number.	Age.	Total red cells.	Total white cells.	Polymorphs.	Eosinophiles.	Lymphocytes.	Large mononuclears.	Basophiles.	Transitionals.	Myelocytes.	Nucleated red cells.	Remarks
435/27	16	3,850,000	14,800	64.6	5.3	23.0	6.0	-	1.0	-	-	5-finger spleen. Count done before splenectomy.
545/27	13	2,320,000	20,400	24.0	17.0	56.5	1.0	-	1.5	-	present	Acholuric jaundice
560/27	40	4,200,000	9,400	21.3	14.6	60.0	3.3	-	0.6	-	-	Cerebral softening: syphilitic. Blood & cerebrospinal fluid positive for S.G.
565/27	36	2,560,000	7,600	63.0	2.0	30.0	2.6	-	2.0	-	-	Carcimona of breast with liver metastases.
600/27	30	3,100,000	6,500	24.0	0.6	66.6	4.6	-	4.0	-	-	Syphilitic (Gummatous) ulcer.
649/27	30	4,990,000	8,800	70.0	9.0	17.0	2.3	-	1.6	-	-	Elephantiasis of scrotum.
682/27	33	4,720,000	9,400	40.0	12.0	40.3	2.6	2.0	2.6	-	-	6-finger spleen. Count done after splenectomy.
684/27	26	1,050,000	17,800	59.3	7.3	24.6	4.6	-	0.6	3.3	-	P.U.O. S.G. positive. No malaria parasites or pigmented leucocytes.
695/27	32	3,120,000	11,600	47.6	15.3	35.0	1.3	-	0.6	-	-	Hernia.
706/27	40	4,040,000	11,400	73.6	1.3	20.0	1.3	-	0.3	3.3	-	Aortic dilatation.
6/28	34	3,360,000	25,000	84.0	-	14. 0	0.6	-	0.6	-	-	Pneumonia, Chronic heart failure with backward pressure, & suppurative inguinal lymphadentis.
8/28	2	1,960,000	49,500	21.6	20.3	52.6	1.3	-	1.3	2.6	present	von Jaksch's anaemia.

TABLE VIII (Contd.)

Actual & differential blood counts on 33 spleen cases.

Register number.	Age.	Total red cells.	Total white cells.	Polymorphs.	Eosinophiles.	Lymphocytes.	Large Mononuclears.	Basophiles.	Transitionals.	Myelocytes.	Nucleated red cells.	Remarks.
50/28	36	3,830,000	6,600	61.6	5.6	26.0	6.0	-	0.6	-	-	Chancre.
74/28	46	3,320,000	5,400	72.0	2.0	23.3	1.3	-	0.8	-	-	Locomotor ataxia.
81/28	26	2,260,000	10,600	47.3	17.3	20.6	2.6	-	12.0	-	-	Ulcerating granuloma of groin.
87/28	25	3,680,000	8,400	40.6	16.0	39.6	2.3	-	1.3	-	-	Suppurating inguinal adenitis.
93/28	17	5,000,000	8,200	30.0	9.3	57.3	1.3	-	2.0	-	-	Inherited syphilis.
108/28	15	3,840,000	7,600	54.6	20.6	16.6	4.6	-	3.3	-	-	Phagedaenic ulcer.
116/28	42	2,920,000	8,400	23.3	14.6	57.3	2.6	0.6	1.3	-	-	Syphilitic (gummatous) ulcer.
123/28	25	2,540,000	7,400	50.0	10.0	31.3	4.0	-	4.0	-	-	Aortitis
130/28	12	3,890,000	7,200	43.0	20.6	33.3	2.3	0.3	0.3	-	-	Inherited syphilis.
136/28	15	4,380,000	7,600	41.3	28.0	22.6	2.6	2.6	2.6	-	-	Ganglion. M. loa & perstans. Heavy ascaris infection.
160/28	32	3,920,000	6,400	34.6	10.0	52.0	3.3	-	-	-	-	Arthritis.
170/28	6	2,330,000	10,400	84.0	0.6	13.0	1.3	-	-	-	-	Bronchitis
226/28	35	2,720,000	9,600	68.6	10.6	18.0	-	-	2.0	-	-	Cirrhosis of liver. S.G. positive.

TABLE VIII (contd.)

Actual & differential blood counts on 33 spleen cases.

Register number.	Age.	Total red cells.	Total white cells.	Polymorphs.	Eosinophiles.	Lymphocytes.	Large Mononuclears.	Basophiles.	Transitionals.	Myelocytes.	Nucleated red cells.	Remarks.
292/28	36	3,520,000	6,400	32.6	12.0	27.3	24.6	-	1.3	2.0	-	Syphilitic ulcer and Subtertian Malaria Parasites & pigmented leucocytes.
301/28	45	2,740,000	9,700	78.0	1.3	18.0	1.3	-	1.3	-	-	Aortic dilatation.
302/28	36	3,680,000	7,200	33.3	9.3	28.6	28.0	-	-	0.6	-	Gumma.
318/28	17	2,720,000	5,100	35.0	17.6	35.0	12.3	-	-	-	-	Subtertian Malaria parasites.
334/28	30	2,780,000	6,400	76.0	1.3	20.0	1.3	-	1.3	-	-	Anaemia and Chronic debility. ? Malarial in origin. Pigmented leucocytes.
400/28	30	3,040,000	8,000	30.0	12.5	32.5	22.0	-	2.5	-	-	Chancre.
621/28	53	2,400,000	12,000	84.0	-	16.0	-	-	-	-	-	Broncho-pneumonia. Chronic heart failure with backward pressure.
635/28	19	2,440,000	11,200	66.0	0.3	30.6	2.6	-	-	-	-	Chronic polyorrhomenitis.
AVERAGE.	27.8	3,246,060	10,969	52.9	9.8	29.7	4.8	0.2	1.6	0.3	-	Average of total number of cases, i.e., 33.

The Table shows that hardly any of the cases had a total or differential count of the normal orthodox formula. It may be pointed out that many of them did not present any abnormality which was likely to produce much deviation of the blood count from the "normal", the exception perhaps being the few in whom a high degree of leucocytosis was found. It would appear that the estimated number of leucocytes stereotyped in text-books of medicine is too low and applies only to natives of temperate climates. None of the usual text-books on tropical medicine gives indication of what the normal count in the tropics is. FISCHER and TSUNG (1919) have pointed out that the average leucocyte count in the healthy Chinese adult differs greatly from the standard European count especially in the number of lymphocytes, which are more numerous in the Chinese. According to McCAY, the Bengalis of India have a red and white cell count of 5,300,000 and 9,000 respectively. DE LANGEN and LICHTENSTEIN (1923) in Java have demonstrated that the normal total and differential counts differ among various races and found that the average total count in healthy Europeans, Chinese, and Javanese was 7,300, 8,000, and 9,300 respectively. MORRISON (1927) has observed that a "normal" differential count among the natives of Northern Nigeria is a rarity and is of opinion that, in the tropics, a blood count is hardly of any value and becomes merely a factor of interest when other clinical examinations have been made. A few examinations were made at the beginning of the present investigation to find out what was the normal count among healthy Calabar natives. It was found that it varied within such wide limits even among the small number examined that the examinations were abandoned. The blood of some of the cases in the present series who had no enlargement of the spleen was also examined in order to act as controls.

As

As it was found that these showed no striking difference to those with uncomplicated splenomegaly, it was not considered necessary to continue them.

The following features were observed in the 33 spleen cases examined:-

Age. This varied from 2 to 53 years, with an average of 27.8 years.

Sex. One was female (Case 435/27). The rest were males.

Total red cells. Varied from 1,050,000 to 5,000,000; average 3,246,060.

Haemoglobin per-centage. The estimations are not recorded in the Table. Only the Tallquist's haemoglobinometer was available and the figures given by this method were not found to be very reliable. It will be seen from the figures for red cells that almost all had some degree of anaemia. In no case was the haemoglobin estimation higher that 70 per cent or the colour index above unity.

Total white cells. Minimum of 5,100 to maximum of 49,500 (case of von Jaksch's anaemia), with an average of 10,969. It will be observed that only a few cases of leucopenia were noted.

Polymorphs. 21.3 per cent to 84.0 per cent. Average, 52.9 per cent.

Eosinophiles. Varied from 0.0 per cent to 28.0 per cent, with an average of 9.8 per cent. This high percentage is largely accounted for by the presence of intestinal parasites in the majority of the cases, and of microfilariae in many.

Lymphocytes. Usually increased at the expense of the polymorphs. Varied from 13.0 per cent to 66.6 per cent, with an average of 29.7 per cent. This increase hardly constitutes any great deviation from the Nigerian "normal", MORRISON (1927) having demonstrated that 75-80 per cent of his Northern Nigeria cases gave a per-centage of over 30. It is of interest to note that BUTLER (1927) in Lagos has observed that lymphocytosis in Nigerian children often occurs "in

more

more than the usual frequency."

Large Mononuclears. Increased; varied from 0.0 per cent to 28.0 per cent, with an average of 4.8 per cent.

Basophiles. 0.0 per cent to 2.6 per cent, with an average of 0.2 per cent.

Transitionals. Varied from 0.0. per cent to 12.0 per cent, with an average of 1.6 per cent.

Myelocytes. 0.0 per cent to 3.3 per cent. Average, 0.3 per cent. The highest figures were in cases of undoubted syphilis. According to DA COSTA, myelocytes are found in subtertian malaria infection up to 0.51 per cent. One such case in this series gave a per-centage of 2; but it was complicated by a syphilitic ulcer.

Nucleated red cells. Noted in the case of von Jaksch's anaemia and of acholuric jaundice.

Apart from the high degree of leucocytosis observed in the case of von Jaksch's anaemia and certain of the febrile conditions, these figures hardly present any special feature. Many of the cases including the 5- & 6-finger spleens did not show the leucopenia which occurs in chronic malaria and splenic anaemia. Increase in the lymphocytic and mononuclear counts often occurs in malaria, syphilis, and many protozoal infections. The figures obtained cannot therefore be held to have any special differential diagnostic connexion with the first two diseases as being the cause of most of the enlarged spleens that were noted. They are of value however in showing that no case of those blood dyscrasias which are accompanied with splenic enlargement occurred, except the case of von Jaksch's anaemia.

The Arneth count was not done, as it was not considered likely to shed much light on the problem.

V.- SPLEEN, LIVER AND GLAND PUNCTURE.

V.- SPLEEN, LIVER, AND GLAND PUNCTURE.

The well-known danger of splenic and liver puncture prevented its being used more frequently in many of the cases than was done. In none of them however was it strictly necessary as a means of diagnosis. In those punctures that were made, neither malaria nor leishmania bodies nor any other parasite was recovered. Some of the punctures were made after death in cases where a complete post-mortem examination had been refused by the relatives, as is usually the case among natives. One case in whom a complete necropsy was done showed malaria parasites in the splenic smear.

VI.- VAN DEN BERGH'S TEST.

Lack of materials did not permit of the test being carried out as might have been correct to do on all the cases irrespective of whether they had jaundice or not. It is well known that, by means of this test, it is possible to recognise latent jaundice when the hyperbilirubinaemia is not of a sufficient degree to produce colouration of the conjunctivae or urine. Addison's anaemia (except in the acute haemolytic crises) and a very slight degree of biliary obstruction such as may occur in diffuse cirrhosis of the liver are types of this condition (PRICE). The sclerae of most natives are seldom clear and often present such varied tints of yellowish-white that it is sometimes difficult to say whether a slight degree of jaundice is present or not. Many may possibly be examples of latent jaundice, especially in view of the fact that BUTLER (1926a) has observed in a long series of post-mortem examinations that cirrhosis of the liver is very common in Nigerian natives. It therefore follows that the number of positive van den Bergh tests given here is not a true index of the

incidence

incidence of hepatic damage among the cases examined, because the test was done only on cases of undoubted jaundice in which definite jaundice colouration of the selerae was indisputable and was accompanied by that of the palate and presence of bile in the urine. The 5 cases of jaundice presented the following features:

(1) Case 441/27. J., male aet.26. Case of malaria fever complicated by jaundice. Spleen and liver slightly enlarged. Blood: contained subtertian malaria parasites. S.G. positive; denied syphilis and never had yaws. van den Bergh reaction biphasic. Urine: bile present but no albumen. Stools: ascaris and trichuris ova. Course of illness. Fever subsided promptly with intramuscular quinine. Patient discharged 7 days after admission with jaundice cleared and urine free from bile.

(2) Case 545/27. B.V., male aet.13. Admitted 5/10/27 with complaint of enlargement of the abdomen and jaundice for past 7 years. He had otherwise always enjoyed very good health. Previous and family history: nothing to note. Said none of his family had had jaundice to his knowledge. Condition on admission: Sclerae jaundiced. Basal haemic murmurs over heart. Spleen slightly tender and enlarged to 2-fingers below the umbilicus crossing over to right of middle line. The liver was slightly enlarged downwards but not tender. The were no signs of congenital syphilis. Urine: No albumen or bile. Blood. Microfilaria perstans. Actual and differential counts: R.B.C.: 2,320,000 with many nucleated reds, W. B. C.: 20,400. Polymorphs 24.0, eosinophiles 17.0, lymphocytes 56.5, large mononuclears, 1.0, transitionals 1.5. There was increased fragility of the cells. The S.G. and van den Bergh reactions were negative. Stools: ancylostome and ascaris ova. Course of illness. Ran a low form of fever during the first 3 weeks of stay in hospital. The jaundice was a little less six weeks after admission, when the patient was discharged to go to his district in order to get his parents' permission for splenectomy. His treatment consisted of a bicarbonate mixture, iron, and quinine, and of inunction of iodine ointment over the spleen area. No decrease in the size of the organ occurred.

(3) Case 275/28. S.K., male aet.33. Sergeant, Nigeria Regiment. Present illness: Admitted on 13/4/28 with fever, jaundice, slight pain in the epigastrium and lower half of left chest, occasional vomiting, loss of appetite, and a slight cough - all during the past 4 days. Abdominal pain had no special relation to food or to any kind of food, was localised to the epigastrium and was relieved by vomiting - the vomit being bile-coloured. The jaundice and epigastric pain started simultaneously. Past illnesses: Had never had any attack of biliary colic or jaundice. Had a splenectomy done for a 6-finger spleen 4 months previously (case 682/27). Examination of the excised spleen on that occasion revealed the presence of much peri-splenitis, fibrosis, deposit of pigment, but no parasites. The liver at operation was slightly enlarged. His S. G.

was

was positive and the blood was negative for parasites or pigmented leucocytes. The blood count before splenectomy was as follows:- R.B.C.: 3,520,000. W.B.C.: 10,200. Polymorphs 44.6, eosinophiles 20.0, lymphocytes 30.0, large mononuclears 2.6, basophiles 1.3, transitionals 1.3. On discharge 2 months later, the count was R.B.C.: 4,720,000. W.B.C.: 9,400. Polymorphs 40.0, eosinophiles 12.0, lymphocytes 40.3, large mononuclears 2.6, basophiles 2.0, transitionals 2.6. He gave no history of dysentery or of yaws but admitted syphilis acquired 4 years previously. Was not alcoholic. Condition on admission. Temp.102.2, resp.22, pulse 120, full and regular. Sclerae and palate jaundiced. Pupils normal. Slight pleural friction and occasional crepitations over base of the left lung, but no dulness. Heart normal. Hyperalgesia, tenderness on pressure and slight rigidity over epigastrium and right hypochondrium. Murphy's sign not elicited. Liver slightly enlarged downwards. Scar on penis and of old bubo in right inguinal region. Inguinal and epitrochlear glands enlarged. The ankle jerk was absent but all the other deep reflexes were present though sluggish. The plantar response was flexor in both feet. Scars and periosteal nodes were present over both tibiae. Urine: slight albumen and bile; no casts; threads present. Blood: negative for parasites on 3 examinations. S.G. positive. van den Bergh reaction biphasic. Actual and differential counts: R.B.C.: 3,050,000. W.B.C.: 17,800. Polymorphs 59.3, eosinophiles 7.3, lymphocytes 24.6, large mononuclears 4.6, transitionals 0.6, myelocytes 3.3. Stools: ancylostomes and trichuris ova. Course of illness. Ran an irregular temperature for first 6 days after admission. Jaundice, fever and other symptoms disappeared by the 10th day with antisyphilitic treatment, and he was discharged a fortnight after admission.

(4) Case 521/28. A.E., male aet.33. Admitted 16/6/28 with jaundice of one week's duration. Abdomen nil, except for slight enlargement of the spleen. 2nd aortic sound accentuated. Scar on penis and in right groin. Blood: S. G. positive, van den Bergh reaction immediate direct. No parasites. Urine: bile and slight albumen. Stools: negative for ova and E. histolytica. Had no temperature during whole of stay in hospital. Discharged on 9th day at own request before the effect of antisyphilitic remedies on the progress of the disease could be watched.

(5) Case 619/28 J.D., male aet.27. Case of jaundice complicating lobar pneumonia. S.G. negative; van den Bergh reaction biphasic. No parasites in blood. Ascaris ova in stools.

Comments. Case 441/27 was a case of malarial jaundice. Case 545/27 was a clear one of acholuric jaundice. No family history was obtained; but the disease was probably of the familial or hereditary type. No signs of congenital syphilis were noted, and the S.G. was negative. No opportunity was afforded for watching the effect of splenectomy on his condition. Case 275/28 has been described in some detail in order to illustrate

illustrate what may happen after a case of splenectomy in a syphilitic native. His original condition on his first admission was certainly not due to splenic anaemia, because the leucopenia which usually accompanies this disease was absent. He showed no evidence of malaria. He was a syphilitic subject and was still sero-positive 4 months after the institution of specific therapy. The fact that his jaundice was of syphilitic origin is suggested by his ready response to antisyphilitic measures. Cases of jaundice responding to such treatment is within my experience in Calabar, and it is of interest to note that BRISCOE (1918) has reported a series of similar cases among Negro labourers in Panama. Case 521/28 was of the catarrhal type, possibly of specific origin.

Vll.- THE YAWS FACTOR.

Reference has been made to the well-known fact that the tertiary lesions of yaws are often indistinguishable from those of syphilis. A positive Wassermann is obtained in both diseases. Hardly any authority now holds the old view that yaws is only a tropical form of syphilis. In the present enquiry, therefore, in order to assess the true incidence of tertiary syphilis in a population among whom ~~where~~ yaws is also endemic, a careful investigation of the history of each case must be made, as it is often only by this means that a differential diagnosis between the two diseases is possible. For instance, a tertiary manifestation in a child who gives a history of yaws is probably yaws, not syphilis. However, the two diseases may and often do co-exist. According to most observers such as SPITTEL (1922), MOSS and BIGELOW (1922), congenital yaws does not exist, as hereditary transmission in this disease does not occur. With

regard

regard to tertiary lesions, it is of great interest to note that POWELL (1923) who had the opportunity of watching the introduction of yaws into India found no instances of tertiary yaws among his cases during a period of 10½ years. RAMSAY (1925) also believes that tertiary lesions are uncommon, while, according to CASTELLANI and CHALMERS (1919c) the disease often terminates in the secondary stage.

The degree of the endemicity of the disease in Nigeria has already been referred to. Its comparatively low rate in Calabar in particular can be inferred from the fact that less than one-tenth of the total number of patients who receive weekly injections of novarsenobillon at the hospital do so for secondary yaws. This fact is of some significance because the value of the injection in this disease is so well known to natives in the remotest bush-districts that they often travel great distances in order to receive it when they or their children contract the disease. The history of yaws was very carefully gone into in every one of the cases in the present investigation. Though the primary and secondary manifestations of the disease are well known to most natives, it was very early observed that some wrongly call by its name certain pustular eruptions which may in reality be pustular syphilides, a form which secondary syphilis very commonly takes in Negroes (BAETZ,1916). A peculiar pleomorphic West African skin disease called "craw-craw" is sometimes wrongly referred to by some natives as yaws. BLACKLOCK (1924) has proved that this disease is none other than scabies. No case therefore was recorded as having had yaws unless he was able to show where on his body the scar of the primary yaws was located, and unless he distinctly remembered having had the typical framboesiform, granulomatous, and decidedly

Figure 1.

Figure 2.

Figure 3.

decidedly itchy eruption of that disease. (Figs. 1, 2, and 3). In the case of children the history was confirmed by questioning the parents and by identifying the usually pigmented marks left by the secondary eruption on the skin. The results obtained among the "spleens" and "others" were as follows:

TABLE IX

Incidence of History of Yaws.

Age period.	Total examined.		Had yaws before.				Never had yaws before.			
	Spleens	Others	Spleens	%	Others	%	Spleens	%	Others	%
0-10	69	79	8	11.5	12	15.1	61	88.4	67	84.8
11-20	61	207	8	13.1	37	17.8	53	86.8	170	82.1
21-30	37	164	3	8.1	17	10.3	34	91.8	147	89.6
31-40	40	111	4	10.0	9	8.1	36	90.0	102	91.8
41-50	31	98	4	12.9	11	11.2	27	87.0	87	88.7
51-60	22	81	2	9.0	8	9.8	20	90.0	73	90.1
TOTAL	260	740	29	11.1	94	12.7	231	88.8	646	87.2

It will be observed that the figures for the incidence of the history of yaws among the "spleens" and the "others" do not materially differ. The incidence is about the same in every age period. The "spleens" show a slightly lower total incidence, so that the disease cannot be said to be of any importance in producing enlargement of the organ.

VIII.- SYPHILIS.

Clinical Manifestations.

The yaws factor having now been eliminated, it becomes less difficult to demonstrate in what degree tertiary signs noted were due to syphilis alone. Table X shows the number in whom clinical signs of syphilis were noted.

TABLE X.

TABLE X

Number in whom signs of syphilis were noted.

Age period.	Total examined		Total showing signs of syphilis.			
	Spleens	Others	Spleens	%	Others	%
0-10	69	79	10	14.4	6	7.5
11-20	61	207	12	19.6	29	14.0
21-30	37	164	28	75.6	101	61.5
31-40	40	111	27	67.5	53	47.7
41-50	31	98	21	67.7	41	41.8
51-60	22	81	15	68.1	34	41.9
TOTAL	260	740	113	43.4	264	35.6
Average = 377 out of 1000 cases = 37.7 per cent						

Emphasis must be laid on the fact that in no case among either group of patients was a diagnosis of syphilis made where the serum reaction was negative and where a history of yaws was obtained in cases with tertiary lesions. Also, in all cases (including children), enlargement of the spleen or liver was not taken as a sign of syphilis, unless other signs were present. The significant fact that emerges from an analysis of the Table is that the "spleens" gave a consistently higher incidence of syphilis for each age period as well as for the totals. The relation of the syphilis to the spleen curve will be discussed later. Table XI. gives in detail the signs of syphilis present. The per-centages are on the number in whom signs of syphilis were noted, and not on the total altogether examined.

TABLE XI.

TABLE XI

Signs of syphilis present among "spleens" and "others"

Group of lesion.	Lesion present	Spleens (113)		Others (264)	
		No.	%	No.	%
1	Bone & joint pains and nocturnal headache.	71	62.8	157	59.4
2	Genito-urinary lesions :-				
	Scar on penis & chancre	65	57.5	156	59.0
	Gumma of testes	1	0.8	-	-
3	Enlarged lymphatic glands:-				
	Inguinal	101	89.3	235	89.0
	Epitrochlear	38	33.3	81	23.1
	Axillary	7	6.1	19	7.1
	Cervical	22	19.4	49	18.5
	Scars of old inguinal bubo	43	38.0	108	40.9
4	Skin lesions:-				
	Skin eruption	1	0.8	3	1.1
	Depigmented skin with scarring	5	4.4	13	4.9
	Gummatous ulcers	23	20.3	31	11.7
	Scars of old ulcers	83	73.4	192	72.7
	Condylomata	-	-	1	0.3
	Rhagades	1	0.8	-	-
	Alopecia	-	-	1	0.3
5	Lesions of mucous membrane:-				
	Snuffles	4	3.5	1	0.3
	Mucous plaques	1	0.8	-	-
	Scarred pharynx	3	2.6	4	1.5
	Gumma of pharynx	-	-	1	0.3
	Hutchison's teeth	1	0.8	-	-
6	Bone & joint lesions :-				
	Arthritis (acute & chronic)	13	11.5	37	14.0
	Periostitis & periosteal nodes	78	69.0	169	64.0
	Sabre tibia	5	4.4	3	1.1
	Saddle nose	61	53.9	117	44.3
	Perforated palate	-	-	1	0.4
	Destroyed nasal septum	2	1.7	5	1.8
7	Cardio-vascular lesions:-				
	Syphilitic myocarditis	2	1.7	-	-
	Syphilitic aortitis and aortic dilatation.	12	10.6	23	8.7
	Arterio-sclerosis	9	7.9	20	7.5
8	Nerve lesions:-				
	Locomotor ataxia	1	0.8	-	-
	Cerebral softening	1	0.8	-	-
	Optic atrophy	1	0.8	1	0.3
	Interstitial keratitis	1	0.8	-	-
	Iritis	-	-	1	0.3
	Hemiparesis	1	0.8	2	0.7
	Hydrocephalus	1	0.9	-	-
9	Visceral infiltrations :-				
	Nephritis	2	1.7	1	0.3
	Cirrhosis of the liver	1	0.8	-	-
	Gumma of the liver	1	0.8	-	-
	Rectal stricture	-	-	1	0.3

For reasons previously stated, certain of the figures do not correspond to those given in Table III. For instance, the figures for aortic lesions in Table XI exceed those in Table III, the excess representing those in whom the lesions were found though they were primarily admitted for some other disease. Further, it will be found that the totals in certain groups of lesions add up to more than the number of patients in whom signs of syphilis were noted. Thus, the group of enlarged lymphatic glands among the "spleens" and "others" totals 211 and 492 respectively, while the numbers of all the syphilitic "spleens" and "others" in whom they were noted are only 113 and 264. This is because more than one sign under the same group may occur in the same person. Thus a person might have enlargement of all the groups of lymphatic glands: he was recorded separately under "inguinal", "epitrochlear", "axillary" and "cervical". It may be added that the fact that tertiary syphilitic lesions are often multiple, pleomorphic, and widely disseminated in Negroes has been repeatedly noted by many observers. Thus, in the present series, each syphilitic individual was found to have an average of 6 signs. These are, in their order of frequency, inguinal adenitis, scars of old ulcers, periostitis and periosteal nodes, scars of old sore on the penis, nocturnal bone and joint pains, and saddle nose. The relative importance of these signs are discussed below under the various groups.

1. Bone and joint pains. This sign of the early tertiary stage has been noted in Negroes in more than its usual frequency by many workers like BAETZ (1916) in America, NOGUE (1924) in Senegal, and WEBB and HOLLIDAY (1927) in Uganda. It was generally worse at night. It was often present in a large

proportion

proportion of those with chronic ulcers, with evidence of past chronic ulceration of the lower extremities, and with periosteal nodes. Usually accompanying it were what the natives call "evening fever" and, among the females, "dark menstrual courses". The combination of these symptoms very seldom failed to give a positive serum reaction. They generally cleared up very rapidly with specific therapy.

2. Genito-urinary lesions. Scars on the penis were the most numerous. A history of previous ulceration of the penis was always obtained in cases where a scar was noted. In only a few cases however was a typical Hunterian chancre seen. Owing to the dirty habits of the average bush-native and the frequent occurrence on his genitals of various itchy skin eruptions, chancres very commonly develop into phagedaenic ulcers which are frequently multiple. When first seen at this stage, it was often impossible to say whether the ulcer originally started as a chancre or a chancroid. It was not always possible therefore to say whether any given scar was the result of a chancre or of the latter condition. In the same way, the cause of an inguinal bubo or its resulting scar was not generally easy to determine. The glans penis is not uncommonly completely ulcerated away.* For example, in one case among the "others", only a stump ¼ of an inch long represented the entire organ. Genital scar or chancre accounted for by far the largest number of those of the age periods 21-40 among both groups of patients. No case of intra-meatal chancre was noted. Chronic ulceration of the vagina was present among many of the female cases. It was sometimes accompanied

* The native name for syphilis among the Yoruba tribe is "Reko-Reko", i,e,, "the disease that eats away the penis."

Figure 4.

Figure 5

Figure 6

accompanied with extensive scar formation which in a few cases produced partial atresia of the passage. A history of previous difficult labour was not often obtained among these cases, so that trauma can be excluded as a factor.

3. Enlarged lymphatic glands cannot be considered as having much specific bearing on the diagnosis of syphilis in West African Negroes. Presence of enlarged inguinal glands is the rule rather than the exception in most natives and is often caused by tinea cruris, "craw-craw", and non-venereal infections of the lower extremities or genital regions. The frequency with which inguinal adenitis becomes suppurative is shown by the high figures in Table XI for scars in the inguinal region. Tinea capitis accounted for most of the cases of enlarged cervical glands, the posterior group of which were those commonly affected. Enlarged epitrochlear glands are perhaps of more diagnostic value. Attention has been called to their comparatively frequent incidence among the black races by VERDELET (1920) and as a sign of syphilis among Haitians by CORDES (1926). It may be pointed out that in only very few instances of enlarged epitrochlear glands among the cases described here were other signs of syphilis wanting or the Sachs-Georgi reaction negative. General adenitis does not occur in yaws unless complicated by syphilis (POWELL, 1923).

4. Skin lesions. Syphilitic ulcers accounted for many of the cases. Small scars and local areas of varying degrees of depigmentation of the skin especially of the lower extremities have been recorded in the figures in the above Table. Both however occur in many natives who are not syphilitic and are probably therefore of little, if any, diagnostic value. The scars in many cases are of traumatic origin, and the depigmentation of the skin, which is often bilateral, is probably a condition of simple leucoderma.

Figure 7.

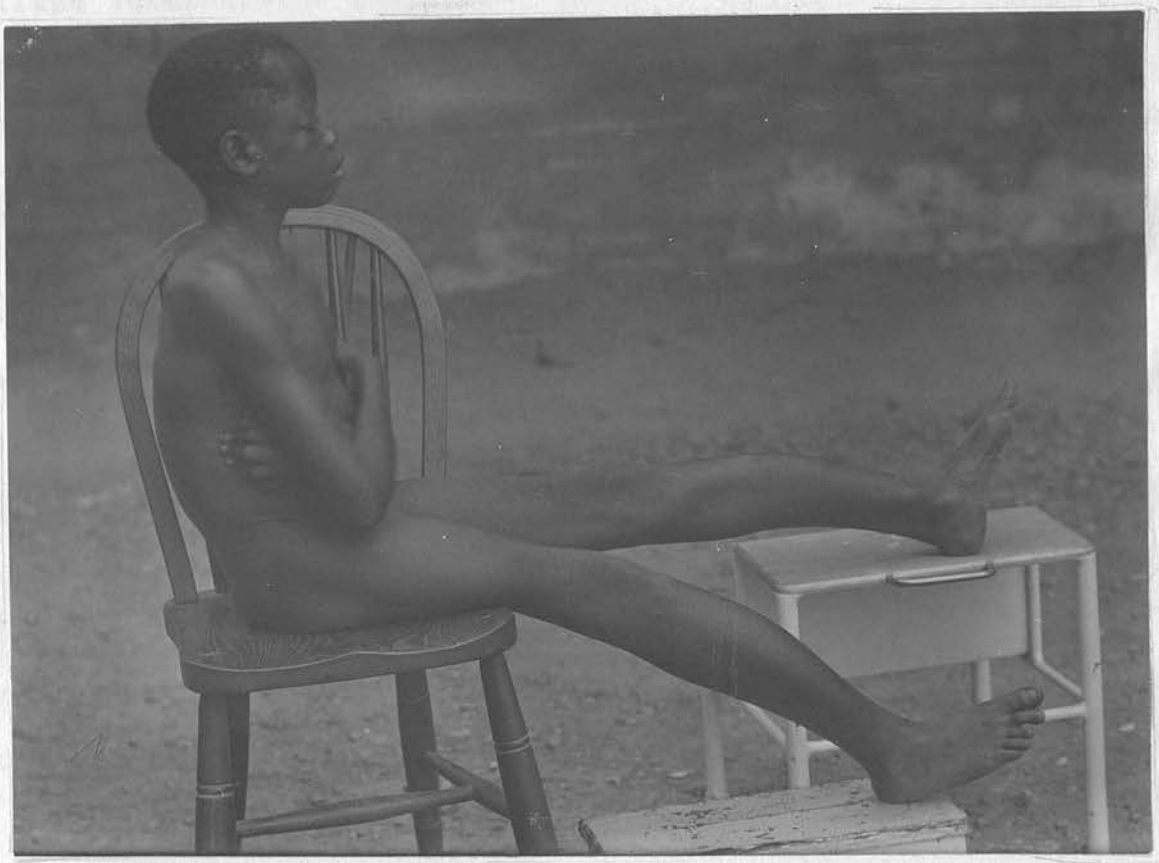

Figure 8.

It gives the skin a very characteristic mottled appearance which arrests the attention especially when the areas involved are extensive. The condition is not due to pinta, and in no case could a fungus be isolated*. Of more significance however are fairly extensive irregularly outlined cicatricial skin lesions covering up to half or more of an extremity or large parts of the trunk (Figs.4,5,and 6). Some degree of contracture was present in a few of the cases, and the condition was sometimes accompanied with the loss of one or more digit (Fig.5). The part affected had an irregular mosaic appearance the patterns of which were usually larger than the ordinary leucodermatous mottling previously mentioned. It usually occurred among persons over 30 years of age. The condition was not of yaws or leprotic origin, and was apparently not identical with the condition described as "melung" by ZIEMANN (1923) in the Cameroons**. The areas were not anaesthetic, and in no case could B.leprae be recovered from a nasal smear or skin puncture. They are probably evidence of healed diffuse subcutaneous gummatous infiltration and are generally sero-positive. Another not uncommonly observed lesion was a fairly extensive scar around the patella which could not be ascribed to yaws or trauma (Fig.7).

Secondary skin eruptions were infrequent, all the cases seen being of the papulo-pustular type. The native does not usually seek treatment for syphilitic skin eruptions unless they cause obvious disfigurement by appearing on the face.

5. Lesions of mucous membrane were uncommon. The rarity of Hutchison's teeth, snuffles, and other signs of congenital syphilis will be referred to later. One case of gummatous ulceration of the pharynx and old scarring of this organ were seen. Only one case of mucous plaque occurred.

6. Bone and joint lesions. These were of very frequent occurrence, periostitis and especially periosteal

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*A few isolated cases of pinta have been recorded from the Gold Coast but none so far from Nigeria.

**Trop. Dis. Bull. Rev. Vol. 23. No. 1. p.10. 1926. Jan.

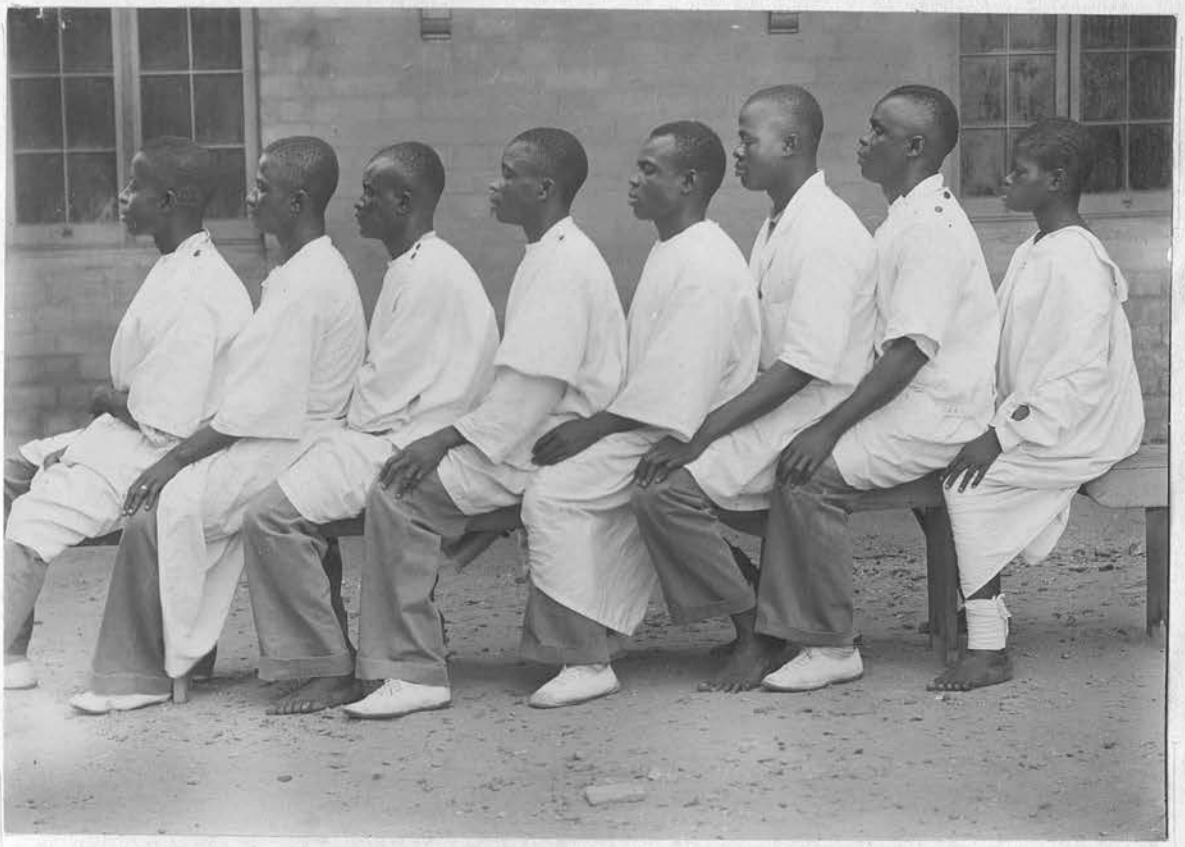

Figure 9.

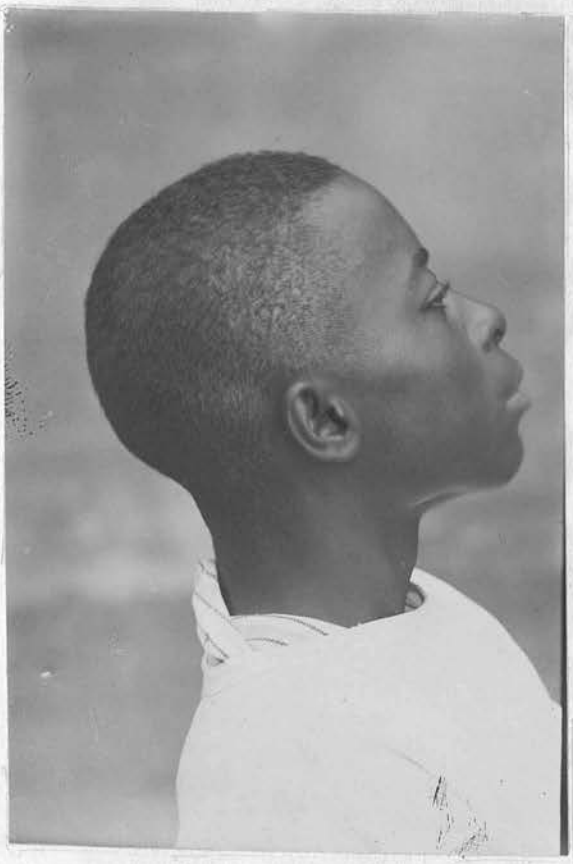

Figure 10.

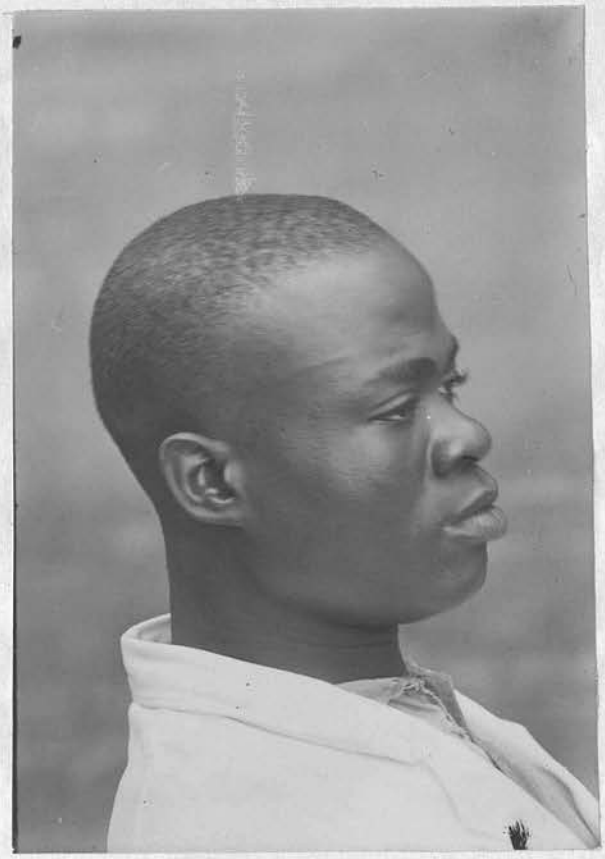

Figure 11.

periosteal nodes being the commonest signs. The latter were more apparent to palpation than inspection, the tibia being the commonest bone involved. These periostitic changes were often accompanied with a diffuse proliferative osteitis of a probably gummatous nature. The same changes however are said to occur in yaws. The presumably yaws cases were eliminated by the history and are not included in the figures in the above Table. It might have been of some interest as a point in differential diagnosis to have made a radiological examination in order to see whether the bone changes were of the osteosclerotic type such as occurs in syphilis, or of the osteo-porotic, such as is associated with yaws. Typical sabre tibia (Fig.8) was not of frequent occurrence. It would appear to be more common as a tertiary manifestation of yaws than as a sign of congenital syphilis. The figures recorded occurred among those in whom no history of yaws was obtained. Various degrees of depression of the nasal bridge is so common among the people of this province, especially among the Ibibios and Cross River tribes, that it might almost be considered a national or tribal characteristic. (Figs.9,11,and 13). It consequently loses much of its value in the diagnosis of congenital syphilis unless it is associated with other signs. The depression is however usually more marked than that of the commonly accepted normal negroid type. Inasmuch therefore as many Negroes exist in whom the nose can be said to conform to normal (Figs.9,10, and 12), it must be supposed that those who show abnormal depression of the root of their noses are the victims of a pathological condition which is probably syphilitic. A point of interest is that persons with such noses frequently give a positive serum reaction.

The

Figure 12

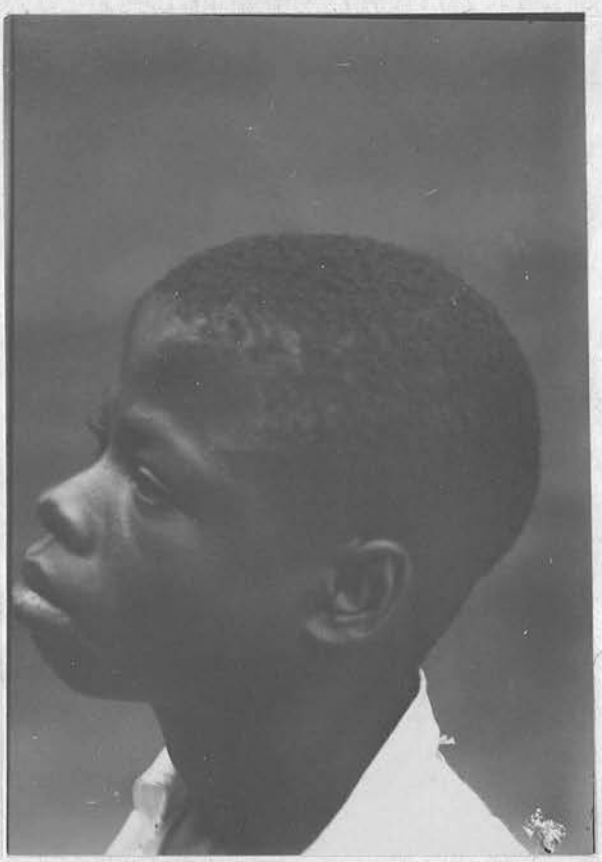

Figure 13

The condition does not occur in yaws. Seven cases of complete destruction and absorption of the nasal septum were seen. They were all of syphilitic origin and in none of them could any other disease like yaws, tubercle, or leprosy be said to be a factor.

7. Among the Cardiovascular lesions, those of the aortic valves were the commonest. This is in accord with previous observations on the effect of syphilis on tropical Negroes. Vague pains in the chest were commonly complained of by many of the patients, and, when not due to mediastinitis, was often associated with signs of chronic aortitis such as marked accentuation of the second aortic sound or a systolic aortic murmur. No case of aneurysm was observed, but aortic dilatation was comparatively common. None of the cases gave a history of rheumatic fever.

8. Nerve lesions and lesions of sense organs among Negroes are admitted by all observers to be rare. The most interesting case was that of cerebral softening which was accompanied with an enlarged spleen and will be described later. The only case in which Argyll-Robertson pupil was noted was that of locomotor ataxia, who presented also the other typical signs of that disease. Purely syphilitic eye lesions were infrequent. Iritis occurs fairly often in many natives, but its common association with chronic gonorrhoea usually makes the differential diagnosis difficult even when others signs are present. Only 1 example of interstitial keratitis was seen: it occurred among the spleens. Many complained of defective vision, but usually no error of refraction could be detected. The optic disc was however

often

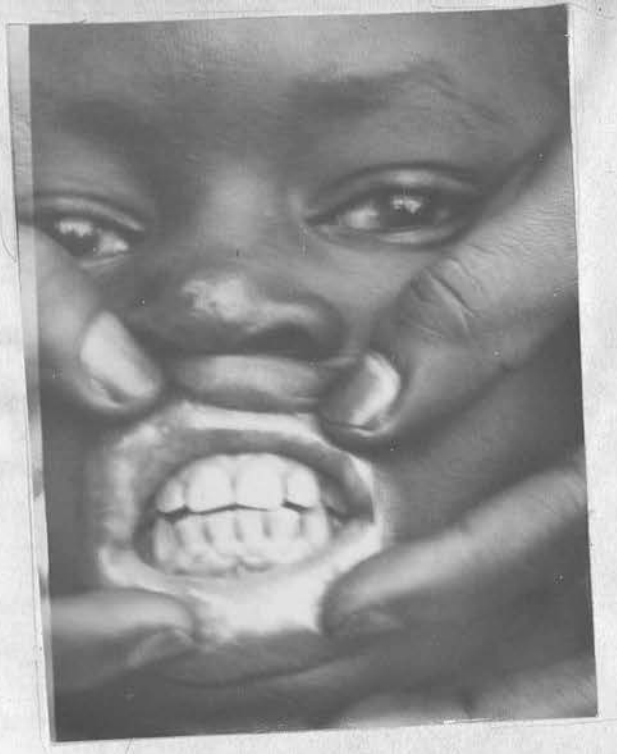

Figure 14

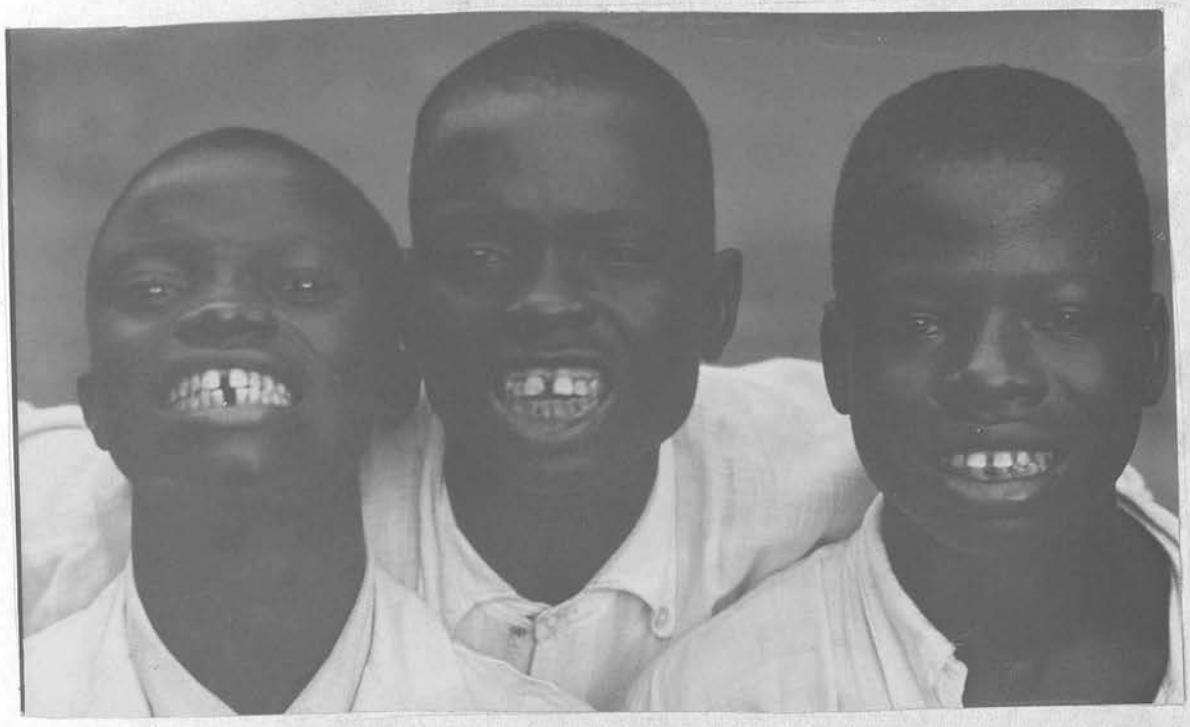

Figure 15

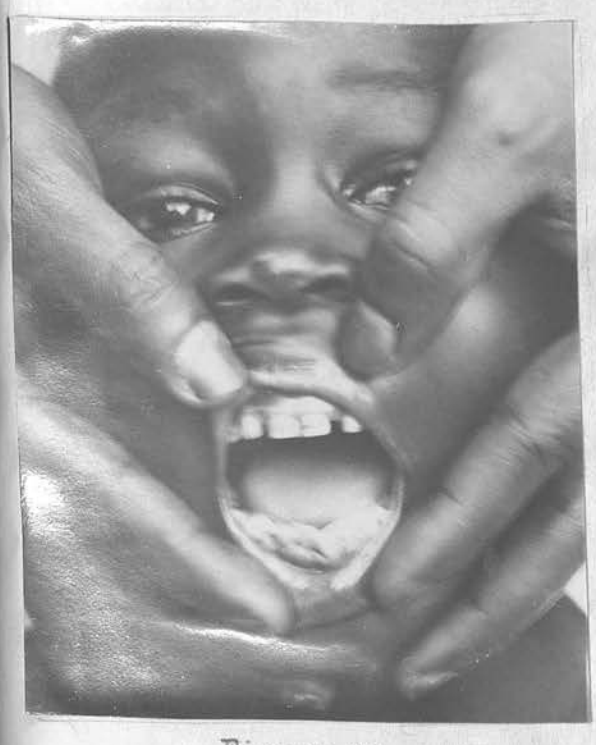

Figure 16

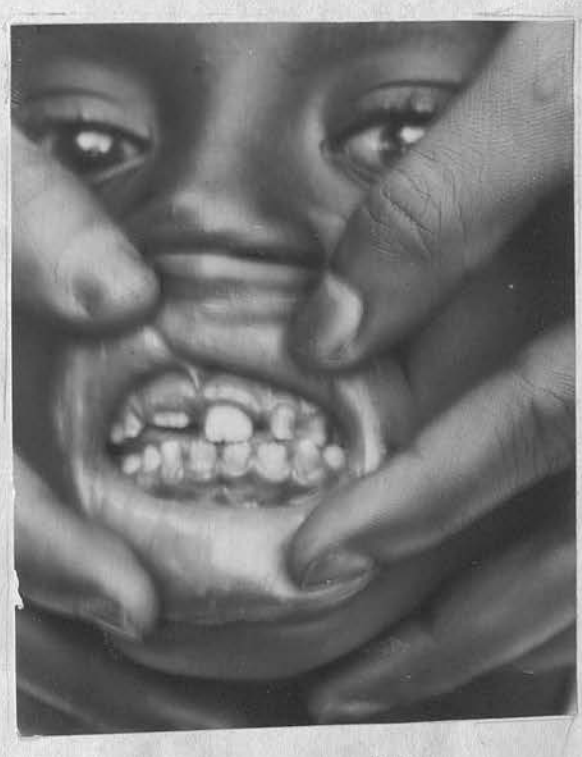

Figure 17

often pale; but it was not usually easy to say whether this was pathological or was a heightening of the normal pallor of the disc compared with the surrounding retina which, in most natives, is very deeply pigmented. Apart from the case of locomotor ataxia, one definite case of optic atrophy was observed.

9. Visceral infiltrations. According to SPITTEL (1922), visceral infiltration in yaws is rare. On the other hand, NOGUE (1924) found visceral syphilis was of common occurrence in Senegal (French West Africa). The diagnosis of the few that were noted in this series was based on clinical findings, with the exception of the case of diffuse cirrhosis of the liver, the syphilitic nature of which was demonstrated beyond doubt post-mortem. The case of gumma of the liver was therapeutically proved, in addition to the physical signs present.

Congenital syphilis. That stigmata for congenital syphilis are surprisingly low among those native races in whom the disease is known to be universal has been repeatedly commented on by most observers like McARTHUR (1923) in Bechuanaland (South Africa), NOGUE (1924) in Senegal, STONES (1925) in Kenya, NAGELSBACH (1926) in Abyssinia, and WEBB and HOLLIDAY (1927) in Uganda. NAGELSBACH has never seen a case of congenital syphilis in Abyssinia, 40 per cent of whose population are, according to him, syphilitic. He alleges that the acquired infection however is very common in infants. McARTHUR in an analysis of 1547 syphilitic cases from his Bechuanaland clinic has observed that "keratitis is only seen occasionally, specific deafness unknown, Hutchison's teeth simply

simply do not exist". According to STONES (1925) writing of Kenya, "Hutchison's teeth, affections of the cranium and interstitial keratitis seem to be rare". The Nigerian figures for 1927 for hereditary syphilis among the total number of 6,653 cases of syphilis recorded was 129, a per centage of 1.9. It will be observed from the Table given that, with the exception of saddle nose, the figures for stigmata are very few. For instance, only 1 case each of Hutchison's teeth and interstitial keratitis was seen. Dental irregularities which do not conform to the classical Hutchisonian type were commonly met with. (Figs.15,16,and 17. Fig.14 shows normal). A good example of keratitis punctata was noted among the "spleens" in a boy of 14 who gave no history of yaws, had a saddle-nose, sabre-tibiae, bossed frontals and a positive Sachs-Georgi. Syphilitic rashes were observed in 2 infants. Hydrocephalus was noted in a boy aged 4 who was a typical idiot. He could neither walk nor speak. He had buphthalmos of the left eye and plexiform neurofibromatosis of the cutaneous branches of the left 5th cranial nerve. His spleen and liver were enlarged, and both diminished in size with specific treatment. He had never had yaws, and his S.G. reaction as well as that of his mother, who was a lunatic, was positive. The rarity of stigmata in tropical natives is astonishing even where the syphilis rate among children is high, as has been pointed out by WEBB and HOLLIDAY (1927) with regard to Uganda. That the syphilis rate was really much higher among the present series than what the figures for stigmata suggest will be demonstrated when the figures for Sachs-Georgi are being discussed. In no single one among the cases of congenital syphilis in children of the age group

0-10 was a history of previous abortion or miscarriage wanting in the mother. Though in no case was the presence of an enlarged spleen taken to indicate syphilis when other signs were wanting, yet it was observed that the incidence of the hereditary disease was about 2 times as great among cases with enlarged spleen than among those without. That the proportion is probably even very much higher will be shown later. NOGUE (1924) who examined 850 school children in Senegal found that the commonest evidence of congenital syphilis among them was enlarged liver and spleen, an observation which confirms LOUY'S (1920) previous one on the Ivory Coast (West Africa). McARTHUR (1923) believes that most of the tertiary signs of syphilis among natives occurring for the first time at later periods of life towards middle age are instances of what he calls "syphilis hereditaria tarda", while MARGERIDON (1926) is of opinion that similar manifestations among adult Central African natives are the result of hereditary disease. The comparative rarity of stigmata is commonly explained as being due to a high death rate among syphilitic infants. Registration of births in Nigeria is not universal, so that no general infantile mortality rate can be cited. The figures for Lagos (capital) where notification of births and deaths is compulsory are undoubtedly lower than those for the whole country, but they are of some interest. During 1927, among a population of 110,000, the birth rate, infant mortality rate, and general death rate were 28.9, 174.9 and 20.2, while the per centage of still-births per total births was 3.2. BUTLER (1927) is of opinion that some factor other than malaria must be responsible for the high infant mortality rate among

among the Lagos children. The early death of the syphilitic infant however does not wholly explain the absence of stigmata in those who survive. However, the fact must not be lost sight of that, owing to primitive habits, the extragenitally acquired disease may be very common among children, and that it may therefore frequently exist in them without showing the usual congenital stigmata. That this is most likely so will be referred to later.

It now remains to see in what degree these observation are supported by serological and therapeutic evidence, viz., (a) the Sachs-Georgi reaction and (b) the effect of specific treatment on the size of the enlarged spleen.

A. SACHS-GEORGI REACTION.

The Sachs-Georgi reaction was carried out in this investigation instead of the Wassermann, because there were no facilities for satisfactorily carrying out the latter test in all its full and exacting details. It is now practically admitted by most authorities that a positive Sachs-Georgi reaction is, for all practical purposes, as valuable and as specific as a positive Wassermann in the serological diagnosis of syphilis. However, so many diseases have been reported as giving a positive reaction in the tropics in the absence of syphilis that the test cannot in these regions have exactly the same value in the diagnosis of the disease as in temperate zones. The results require therefore to be entertained with infinite caution when dealing with the elements of a native populace. The diseases alleged to give a positive reaction include yaws, malaria, relapsing fever, leprosy, and trypanosomiasis. It is doubtful whether leprosy and trypanosomiasis do give rise to a positive S.G. reaction

in

in the absence of syphilis. FAIRLEY (1925) has reported 25 per cent of his cases of relapsing fever as giving a strong positive Wassermann reaction. However, neither this disease nor leprosy nor trypanosomiasis occurred among the cases described here and so may be left out of account. Malaria, yaws, and syphilis, then, are the three diseases which require to be considered.

HAROLD (1922) in a purely immunological study of malaria and syphilis has observed that "in malaria under certain conditions, bodies may appear in serum which belong to the globulin group and react in the same way as the Wassermann bodies". DUBOIS (1922) however, who carefully investigated the serum reactions in a series of tropical diseases in the Congo which included syphilis, yaws, malaria, relapsing fever, trypanosomiasis, leprosy, tropical ulcer, small-pox, and certain pathological conditions of doubtful syphilitic origin, claims that "a definitely positive reaction is not obtained except in syphilis, yaws, and perhaps tick (relapsing) fever". According to MARCIALIS (1924) who investigated a large number of microscopically-proved malaria, an only slightly positive S.G. reaction is occasionally detected during fever, but absolutely none during the apyrexial periods even where there are parasites in the blood. This observation regarding the behaviour of the test during the febrile and non-febrile periods of malaria has been completely confirmed by BUSINCO and FOLTZ (1924), and many other workers. Perhaps the most significant reported case bearing on the question of malaria and positive serum reactions is one described by McCONNEL (1923) in which the Wassermann was plus-4 positive, subtertian malaria was microscopically established, and no clinical evidence

of

of syphilis was noted. Yet the necropsy revealed definite syphilitic lesions of the aorta. None of the S.G. test in the present enquiry was undertaken during any febrile period, so that no fallacy in this respect affects the figures obtained. These figures, further, are those for definitely positive reactions. Malaria therefore may be excluded as a factor likely to influence the results that were obtained. With regard to yaws, CASTELLANI and CHALMERS (1919c) state that "the Wassermann is positive in the great majority of recent cases, but is fairly often negative in old cases"; while, according to MOSS and BIGELOW (1922), negative reactions frequently occur in the late secondary, the tertiary, and the latent stages.

Technique. The technique of the reaction as used throughout this series is that employed by DOCTOR RAMSAY, Government Pathologist, who carried out the test in all cases within 5-8 hours of drawing off the blood. He describes his method as follows:-*

"In all cases, 3-5 c.cm. of blood is with-
"drawn from one of the veins of the forearm into
"a test tube. The serum is allowed to separate
"and is then pippeted off into another test tube,
"after which it is inactivated in a water bath
"for half an hour at 56°C. For the test proper,
"four small Wassermann tubes are used for each
"reaction. Into the first is put 1.6 c.cm of nor-
"mal (0.89 per cent) saline, and 1.0 c.cm. into
"each of the others. To the first tube is added
"0.4 c.cm of the patient's serum and the contents
"mixed. 1.0 c.cm. of this dilution is carried
"over into the next tube and so on. The resulting
"dilutions are 1/5, 1/10, 1/20, and 1/40. The
"antigen used is that put up by Burroughs Wellcome
"& Co. in 1.0 c.cm. ampoules. For use, the antigen
"is diluted to a strength of 1/20 by slowly adding
"normal saline in a test tube or measuring glass.
0.5 c.cm of diluted antigen is added to each dilu-
"tion of the patient's serum. The tubes are then
"placed in a water bath at 37°C.; the water reach-
"ing halfway up the contents of the tubes. They are
"left in the water bath overnight, and next morning
"the readings are taken. Precipitation of the
"colloid antigen in any of the dilutions is read as

* Personal communication from Dr. Ramsay.

"as a positive reaction. Precipitation occasionally "fails to occur in the lower dilutions, but takes "place in the higher ones (1/20, 1/40). This is a "common observation when dealing with colloids and "is known as the 'Zone Phenomenon'. It does not "invalidate the test in any way.

" There are one or two points which require "attention if the test is to be reliable. The serum "must be very free from organisms, or a pseudo-positive "tive reaction will occur. The blood should, therefore, be taken into a sterile test tube and the "test should be done within 24 hours. This is sometimes very hard to carry out in the tropics where "specimens may take 3-4 weeks to reach the laboratory. BUTLER (1926) reports that a very small "quantity of boracic acid prevents serious contamination if added to the serum when it is separated, "and that it does not interfere with the reaction. "It is also important that the antigen should be "diluted very slowly and gently shaken while this is being done. Properly prepared antigen has a peculiar fluorescence due to the cholesterol in the "extract, and if this is not present a pseudo-positive reaction may occur. The Wassermann tubes in "which the actual test is dome must be absolutely "clean. Although in a strong positive serum precipitation may be observed very soon, readings should "not be taken for at least 12 hours."

Yaws and syphilis being the chief diseases with which we have to deal among the cases here with regard to the reaction, it will be necessary to give the figures both before and after eliminating the yaws factor before any accurate data can be arrived at in respect of the syphilis rate. The results obtained among all the patients irrespective of whether they ever had yaws or not were as follows:-

TABLE XII

Combined Syphilis and Yaws rate

Age period.	Spleens			Others.		
	Number examined.	S.G. positive.	%	Number examined.	S.G positive	%
0-10	69	34	49.2	79	27	34.1
11-20	61	35	57.3	207	82	39.6
21-30	37	35	94.5	164	124	75.6
31-40	40	35	87.5	111	67	60.3
41-50	31	28	90.3	98	56	57.1
51-60	22	19	86.3	81	46	56.7
TOTAL	260	186	71.5	740	402	54.3

Average = 588 positive out of total 1000 = 58.8 per cent

All the cases who had had yaws (Table IX) gave a positive serum reaction. The per centage for each of the age periods among the "spleens" between 21 and 60 is rather high, probably because of the smallness of the total number examined in each group. It is of interest to note, however, that the average percentage of serum positives among the total 1,000 altogether examined, viz., 58.8 is only a little higher than the S.G. rate of the general Calabar community. Of 2,531 patients examined as a routine at Calabar hospital, 56.5 per cent gave a positive reaction. Among these was included a series of 600 in-patients of 18 years and upwards, no less than 65 per cent of whom gave a positive S.G. reaction. This per centage is but slightly lower than the combined figure in the present series among both the "spleens" and "others" of the age periods 21-60. These total 584, of whom 410, i.e. 70.2 per cent, gave a positive reaction. The total average figure also approximates closely those that have been obtained in other parts of Nigeria. BUTLER'S (1927) figures for Lagos are 57.0 per cent, while MORRISON (1927) reports that 45.4 per cent of Northern Nigeria natives have a positive reaction. Both observers however do not state whether yaws has been excluded from their figures. Those for Calabar, at least, represent the combined syphilis and yaws rate; and, in order to eliminate the yaws factor, it will be necessary to deduct from the above figures the number of those who have had yaws. This will represent the real syphilis rate as nearly accurately as possible. Table XIII gives the figures so obtained :-

TABLE XIII.

TABLE XIII

Real Syphilis rate.

Age period.	Total examined				Sachs-Georgi reaction			
	Total number examined.		Number who never had yaws.		S.G. positive among those who never had yaws.		% out of total number altogether examined i.e Real Syphilis Rate.	
	Spleens	Others	Spleens	Others	Spleens	Others	Spleens	Others
0-10	69	79	61	67	26	15	37.6	18.9
11-20	61	207	53	170	27	45	44.2	21.7
21-30	37	164	34	147	32	107	86.4	65.2
31-40	40	111	36	102	31	58	77.5	52.2
41-50	31	98	27	87	24	45	77.4	45.9
51-60	22	81	20	73	17	38	77.2	46.9
TOTAL	260	740	231	646	157	308	60.3	41.5

Average = 465 positive out of total 1000 = 46.5 per cent

As might be expected, the above figures are much less among both classes of patients than the combined rate given in Table XII in every age group, for the totals, and for the averages. Here again, the percentage of serum positives in the age periods between 21 and 60 among the "spleens" is rather high, even among a community known to lead a life of unbridled sexuality. The high incidence is probably due to the fact that the total numbers examined in the age groups were small. However, the figures confirm the clinical finding that, as a whole, the "spleens" have a higher incidence of syphilis than the "others". The highest rate among both classes of patients was between 21-30, the age period at which genital infection most commonly takes place.

Comparison between figures for serological and clinical syphilis: Syphilis in Negro children.

If the percentages of serologically established

syphilis

syphilis (Table XIII) are compared with those of the disease as clinically observed (Table X), the following results are arrived at :-

TABLE XIV

Comparative per-centage of serological and clinical syphilis.

Group	Spleens							Others.							
Age period.	0 to 10	11 to 20	21 to 30	31 to 40	41 to 50	51 to 60	To-tal.	0 to 11	11 to 20	21 to 30	31 to 40	41 to 50	51 to 60	To-tal.	Aver-age of 1000 cases exa-mined.
Serolo-gical per cen-tage.	37.6	44.2	86.4	77.5	77.4	77.2	60.3	18.9	21.7	65.2	52.2	45.9	46.9	41.5	46.5
Clini-cal per cen-tage.	14.4	19.6	75.6	67.5	67.7	68.1	43.4	7.5	14.0	61.5	47.7	41.8	41.9	35.6	37.7

Discussion: It will be observed that the figures for positive serum reaction are higher than those for clinically observed syphilis both among the "spleens" and "others" for all age periods and for the totals. Much interest attaches however to the occurrence of a higher Sachs-Georgi rate among the "spleens" because it confirms a finding by MENK (1926) on Negroes in South America. Of those showing enlarged spleen among a series of cases suffering from various diseases, he found 29.0 per cent definitely positive for Wassermann; 51.0 per cent being negative and 20 per cent anticomplementary. He referred to this positive incidence as being "astonishingly high". He also made the significant observation that the larger the spleen, the higher was the incidence of positive Wassermann. Thus, he found that while 25 per cent of 4 to 7-finger spleens gave a positive Wassermann, those

that

that were enlarged to more than 7 fingers gave a per-centage of no less than 41.7. Malaria and yaws were excluded as factors influencing his results. His total positive results are lower than in the present series probably because of the large number who gave an anticomplementary reaction. They however indicate that a high proportion of cases of splenomegaly do give a positive serum reaction in the absence of yaws and malaria. An important point that arises from an analysis of Table XlV is that the disproportion that exists between the serological and clinical figures is more marked in both groups of patients in children of the ages 0-10 and 11-20 than at any other age. This is much more noticeable among the "spleens", in whom the disproportion is over over 30 per cent. One or more of the following reasons may be the explanation of the high disproportion during these two age-periods, especially as regards the spleens.

1. That the serological figures are not correct, i.e., that they are high because the yaws factor has not been completely eliminated and that the clinical figures given represent the only true incidence of congenital syphilis occurring in children. This is not likely, as the yaws history was investigated with some care.

2. That the serological figures are correct as indicating the incidence of congenital syphilis among the children, but that the clinical figures are not high because the disease exists among them without its usual signs. That the serological figures are probably correct is shown by the results of the Sach-Georgi reaction among

among the mothers of the children examined. Of 21 mothers of children with enlarged spleen, 18 (85.7 per cent) were positive, while only 10 (30.3 per cent) were positive out of 33 mothers of children whose spleens were not enlarged. These results are not conclusive in view of the small number of mothers whom it was possible to examine; but they are suggestive. It must seem unlikely, however, that congenital syphilis alone will be so common as to produce such a high Sach-Georgi rate without showing more evidence of its stigmata than was observed.

3. That the serological figures represent not only congenital syphilis but also acquired disease among children. In other words, that the acquired infection in children is most probably common. STANNUS (1924 and 1926b) has called attention to its probably frequent occurrence even in districts where yaws is equally endemic. That this is actually so among natives of tropical Africa has been observed by GILKS (1924), NAGELSBACH (1926) and many others. von DURING (1916) states that child infection occurs also even among the Turks. According to some workers, syphilitic rashes among infants are looked upon by natives as but one of the commoner exanthemata of childhood. Child infection is not within my experience, though it undoubtedly occurs.

4. That enlarged spleen and liver are by far the commonest signs of the congenital or possibly also of the early acquired disease. This is most likely so because in collecting the figures for cases in whom clinical signs of congenital syphilis were noted, no child in whom only enlarged spleen or liver was present was put down as syphilis if other indisputable clinical evidence

was

was wanting, even when the S.G. was positive and a negative history of yaws was obtained. Such cases were not uncommon, and the fact that they were not put down as syphilis is largely responsible for the low "clinical" figures obtained. Now, according to HUTCHISON (1928) "splenomegaly may be the only sign of a syphilitic taint, and it appears again about the age of puberty in association with syphilitic cirrhosis of the liver." Reference has already been made to the observations of LOUYS (1920) and NOGUE (1924) among the children of the Lower Ivory Coast and of Senegal with regard to the relation of enlarged liver and spleen to syphilis. It seems most likely therefore that many of the children in this series in whom only enlarged spleen or liver was present were in reality cases of congenital or early acquired syphilis, even when other signs were not observed besides the enlargement of the spleen or liver. That this condition in adults also is of syphilitic origin is suggested by the figures for the other age periods.

The part played by Malaria and Syphilis in the production of Splenomegaly.

It may be accepted then, that, for the purpose of comparison, the figures given as the real syphilis rate are correct. A comparison of these figures with those for malaria among cases showing enlarged spleen is shown in the following Table. The figures for the incidence of enlarged liver are also shown, separately :-

TABLE XV.

CHART III

Comparative Incidence of Enlarged Spleen (dotted red), Liver (dotted black), Syphilis (red), and Malaria Parasite (black).

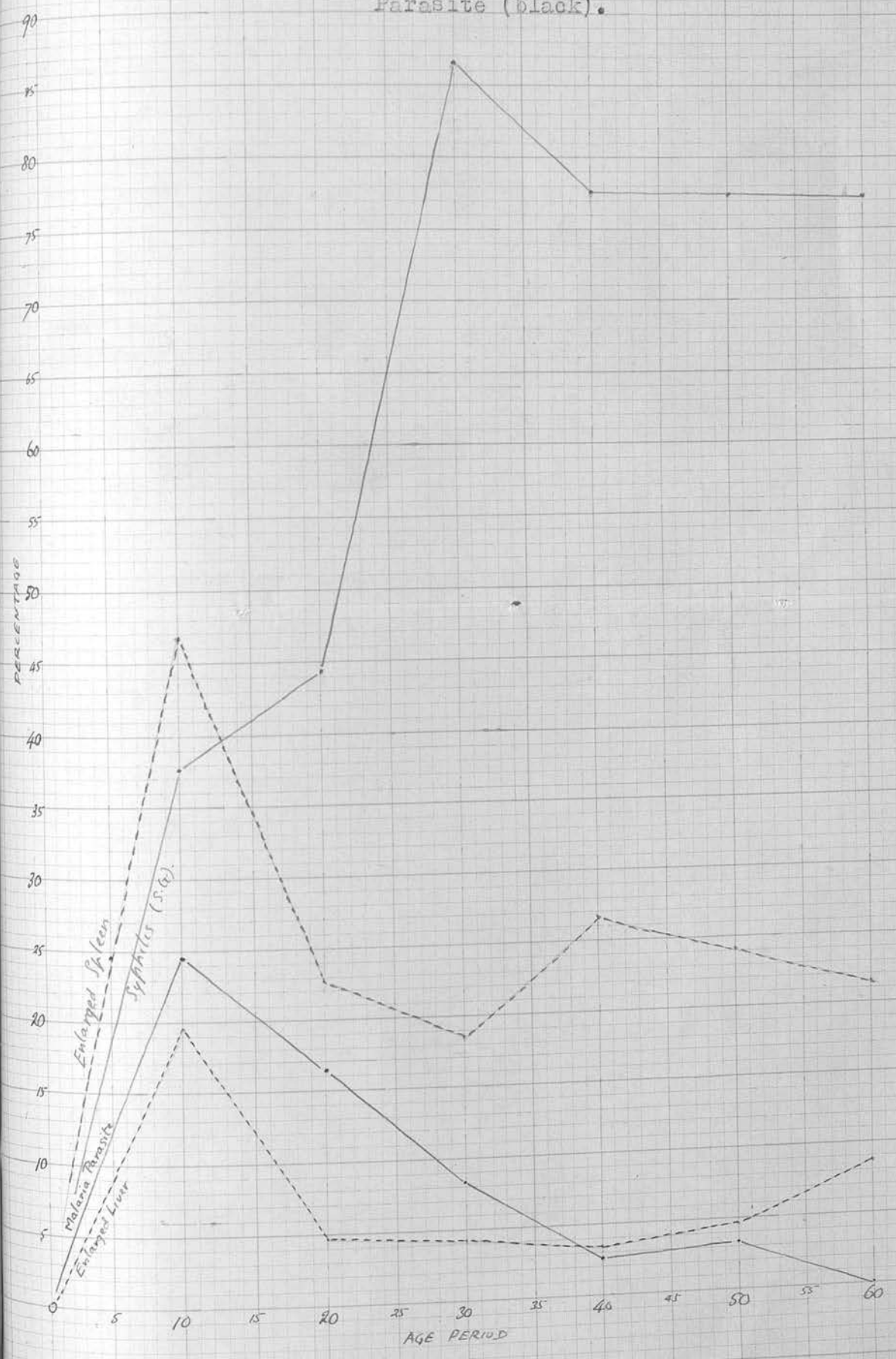

TABLE XV

Comparison of Spleen, Liver, Syphilis, and Malaria Parasite Rates.

Age period.	0 to 10	11 to 20	21 to 30	31 to 40	41 to 50	51 to 60	Total
Enlarged Spleen %	46.6	22.7	18.4	26.4	24.0	21.3	26.0
Enlarged liver %	19.5	4.8	4.4	3.3	4.6	8.7	7.1
Syphilis %	37.6	44.2	86.4	77.5	77.4	77.2	60.3
Malaria parasite %	24.6	16.3	8.1	2.5	3.2	0.0	12.3

These results are graphically represented in Chart 111. The following facts arise from an analysis of the Table and Chart.

(1) All the four groups of per-centages show a primary rise during the age period 0-10.

(2) The liver, spleen, and parasite rates show a sharp partial subsidence during the period 11-30 years while the syphilis rate continues to rise, especially between 21-30.

(3) Both the spleen and liver rates show a secondary rise. The highest point in the secondary wave is reached in the spleen rate during the age period 31-40 followed by only a slight decrease. The liver rate shows a gradual increase between the age of 41 and 60.

(4) With the exception of a slight rise of less than 1 per cent at the age period 41-50, the malaria parasite rate shows a complete subsidence to zero at 60. The syphilis rate shows a slight subsidence after the age of 30.

(5) The four rates stand in numerical order as follows:- syphilis, spleen, liver, malaria parasite.

Discussion:- That malaria causes many of the enlarged spleens and livers particularly among children cannot

cannot be doubted. It would appear from the figures given however that congenital or early acquired syphilis plays at least as big a share in the production of this condition as malaria. Syphilis would appear to be more common than malaria at all age periods, particularly between the ages 0 and 10. The incidence of parasites in the blood at the age group 0-10 can be taken as a fairly accurate index of the malaria rate during that age period and can, as such, be compared with the syphilis rate in order to assess the part which the two diseases play in producing enlarged spleen. This cannot however be admitted to hold good for the later periods, at least after the age of 20, because, as is well recognised, the parasite rate is probably an imperfect index of chronic malaria as it actually exists during these periods. In the present series, the syphilis rate rose considerably from 20 years and upwards. It is not likely however, that acquired syphilis would give rise to much splenic enlargement. Some authorities seem to be agreed that though this condition is frequently met with in the early stages of inherited syphilis, yet it is often not much apparent in the adult congenital syphilitic, at least in Europe. Splenic enlargement often occurs however during the tertiary stages of the acquired disease, with or without syphilitic cirrhosis of the liver, and may be of the cirrhotic or gummatous type. Much significance attaches therefore to the observation in the course of this enquiry that the spleen rate showed a secondary wave during those age periods that tertiary lesions are most apt to manifest themselves. Further, reference has already been made to McARTHUR's

(1923)

(1923) view that tertiary lesions (which must be taken to include splenomegaly) which occur during these periods are evidence of "syphilis hereditaria tarda". It seems therefore reasonable to suppose that syphilis must have a share in producing splenomegaly in adults as it has in children. This may not be in accordance with observations of the disease as it exists in Europe. The fact must not be lost sight of, however, that the disease as it exists among the primitive races of Africa cannot be compared to its condition in Europe. All observers are agreed that it is very widespread throughout tropical Africa. The degree of its prevalence in a particular locality is of course much influenced by the habits and state of civilisation of the people, and, as far as West Africa at least is concerned, its high incidence is in a great measure accounted for by the almost absolute absence of sexual morality. This however is by no means the sole influence. Many natives live an existence that is very communal. Whole families live in filthy, small, one-roomed mud huts, with little or no attention to hygiene. Syphilitics and non-syphilitics often share the same bed, the same pipe, the same eating utensils, and even the same clothing - when any at all exists. Social carelessness in these respects, therefore, together with the habitual exposure of the skin and the frequent occurrence of skin diseases such as "craw-craw" which must constitute foci through which infection more easily gains entrance into the body have combined with ignorance to produce the infection of multitudes who had not been sexually exposed to risk. These factors as well as the absence of any effective native mode of treatment have

have conduced to give to the malady an aspect of general and individual severity which it no longer exhibits in Europe.

A theory; and its application.

It is not proposed to suggest that syphilis, common as it is, produced all the enlarged spleens noted. Though FINDLAY (1928) has suggested that congenital syphilis as a cause of splenomegaly has been overestimated, yet it cannot be doubted that among many native children, the part that syphilis (including the early acquired form) plays in producing the condition is almost as big as that of malaria. Indeed, it has been pointed out that splenic enlargement in malaria among South American children is not as common as supposed*. What it is proposed to suggest here is that the universally prevalent syphilitic taint, acquired and congenital, probably forms a basis on which enlargement of the native spleen develops more easily or in a more exaggerated degree than in an individual whose constitution is not thus burdened. That is to say, that where the splenomegaly is not primarily due to syphilis, the taint of the disease probably destroys or thwarts the development of the resistance of the individual to malaria so that splenic enlargement is then more easily produced: the degree of enlargement being directly proportionate to the degree of weakened resistance. A congenital taint in malaria and yaws can be left out of account, as most authorities are agreed that hereditary transmission in these diseases does not occur.

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*Discussion on paper "Malaria in Infants" by Morgan SMITH (1918), Southern Med. Jl. Mar. Vol 11. No.3 pp.213-214 (vide Trop.Dis.Bull., xii, 40-41)

If this theory is applied to the spleen curve obtained in this series, we arrive at the following conclusions.

i. The enormous rise to 46.6 per cent during the age period 0-10 is due to malaria combined with congenital and early acquired syphilis.

ii. Some of the children by the time they arrive at 20 years of age acquire some immunity to their malaria infection and their spleens as a consequence completely 'go down'. These are presumably normal, non-syphilitic children. The others, however, are burdened with a syphilitic taint, and therefore do not acquire such an immunity. Their spleens therefore persist or continue to enlarge. This phenomenon would explain why the spleens of all children do not completely 'go down' during this age period. It is assumed of course that the degree and frequency of malarial infection among both classes of patients is the same.

iii. A few of those who have not already acquired an immunity to malaria during the preceeding age period succeed in overcoming their infection during the next decennial period. This would explain the slight drop in the curve at this age group.

iv. During the age period 31-60, the tertiary manifestations of syphilis acquired during the period of childhood (extragenitally), adolescence and early manhood (genitally and extragenitally), introduce a new factor which combines with congenital syphilis to weaken or destroy such resistance as might already have existed. The disease acquired in adolescence and early manhood also tends to create a new series of individuals whose spleens in later life become enlarged primarily as an evidence of its "tertiary stage", apart from malaria or any other influence.

influence. That would account for the secondary wave in the incidence of enlarged spleen during this period. That malaria probably has little or nothing to do with this secondary wave is shown by the fact that the malaria parasite incidence shows no corresponding rise during this period. It is suggestive that the incidence of enlarged liver also shows a rise during the latter portion of the period. The syphilis rate among the cases of enlarged liver as a whole was 64.7 per cent.

It is recognised that this would not account for all cases of chronic splenomegaly. For instance, a person subjected to heavy and frequently repeated attacks of malaria must in course of time show some degree of chronic enlargement of the spleen, even if he had no syphilitic taint. The factors concerned are probably multiple. Syphilis, however, probably forms the fundamental basis on which all other factors (including malaria) must be superadded before splenomegaly is permanently produced.

We may now proceed to find out how far this theory is supported by therapeutic test.

B. EFFECT OF TREATMENT ON SIZE OF ENLARGED SPLEEN.

Researches of previous investigators.

Before proceeding to describe the results obtained in the present investigation, it may perhaps be desirable to examine in some detail the effect of various drugs other than quinine which have been used by several observers. Brief reference has already been made to some of these.

According to WILLS (1928), the efficacy of inorganic arsenic in reducing the size of enlarged

spleens

spleens has been known to the Chinese for many centuries. DENNYS (1916) has observed that this drug in combination with iron and quinine was successful in cases of long-persistent attacks of malaria and chronic enlargement and induration of the spleen after all methods of treatment by quinine alone had actually failed. His formula was Arsenious acid gr.1/60, Ferri et Ammon. Cit. gr.3, Quin. Sulphat. gr.1, in a tabloid, one to four daily after meals. He regards the quinine as "a spell rather than a potent ingredient" in the tabloid. Intravenous injection of Mercuric Chloride in doses of gr.1/8 in 10 c.cm. normal saline was found by BARLOW (1916) to have a directly destructive effect on malaria parasites and, in combination with quinine, to produce a strikingly rapid reduction of the size of enlarged spleens. These results were confirmed by GREIG and RITCHIE (1917). These observers employed intravenous injection of 11 c.cm of a 1/1000 solution of mercuric chloride in normal saline every other day for a fortnight, and gr.30 of quinine in tripartite doses daily for that fortnight and the week following. Quinine alone was used in the check series. The total period of observation appears to have been three weeks. They found that the combination of mercuric chloride and quinine was "more effective than simple quinine in reducing an enlarged spleen where the enlargement is considerable and chronic", and that the combined treatment was "more particularly applicable to cases of considerable enlargement where the spleen can be felt 3 fingers to a hand-breadth below the ribs". According to LEVY and

WALL (1918), intravenous injection of 1 to 6 c.cm of 2 per cent solution of tartar emetic given twice weekly has the same result in chronic "malarial" enlargements, though no effect is produced on the parasites. The results of organic compounds of arsenic are perhaps the most interesting. Brilliant results have been noted to follow injections of neosalvarsan alone by MONTEL (1915), who obtained a remarkable amount of shrinkage after only the second injection. Reference has already been made to one of his cases in which an enormously enlarged spleen of six years' standing which extended from the left axilla to the pubis returned to normal size after six injections given at intervals during two months. The dosage was 50 cgm. at the first injection and 90 cgm. at each of the other five. Similar results have been obtained by SEYFARTH (1918) who combined neosalvarsan with quinine. In all these observations, the splenic enlargement was always referred to as being of malarial origin on what would appear to be rather insecure evidence. No proof was adduced that some other factor apart from or in combination with malaria did not enter into the production of the enlargement. No observation for instance seems to have been made with reference to the possibility of syphilis. It is true that STEPHENS, YORKE, BLACKLOCK, and MACFIE (1919), NIEUWENHUYSE (1921) and others have demonstrated that organic derivatives of arsenic have a directly destructive effect on malaria parasites, though we are not told whether these drugs produce this effect by virtue of a specific power on these parasites or whether they act

simply

simply as general protoplasmic poisons*. It must seem remarkable however that arsenic and mercury, both of which are specific antispirochaetal remedies, should produce such a remarkable result in chronic splenomegaly were the condition not to have at least a partial spirochaetal element. In the present investigation, therefore, an attempt has been made to find out the comparative results of these drugs on cases in which there was a probable element of syphilis, and on those in whom such element was known to be absent.

Procedure in present investigation.

It was not found possible to subject every one of the 260 cases of enlarged spleen to the treatment of which the results are indicated below. The difficulty of keeping natives in hospital for the length of time necessary for an investigation of this kind has already been referred to. To this must be added the impossibility of keeping the patients under a sufficiently prolonged observation after they leave hospital. Had it been otherwise, it is quite possible that the results obtained would have been far more striking than they were.

180 cases were subjected to the therapeutic test. The number examined in each age group from the 1st to the 6th decades were 50, 42, 28, 28, 18, and 14 respectively. These numbers comprised

* According to the observers quoted, the parasiticidal effect is most marked on Plasmodium vivax only. The effect is negligible or nil on P. falciparum and P. malariae. Reference has already been made to the fact that the P.falciparum (subtertian) type was by far the most common one met with in the present investigation; it is the most common type in West Africa.

comprised both the presumably syphilitic and those presumably non-syphilitic, based on the results of their serum reactions. They were divided into two equal groups in every age period viz, Group A and Group B. The number in either group was 90 which was made up of 50 syphilitics and 40 non-syphilitics who acted as controls in each group. It may be stated at once that it is recognised that in an experiment of this nature, these non-syphilitic controls ought to have been more numerous than the syphilitics if the results obtained among the latter are to carry much scientific weight. Unfortunately, this could not be done under the circumstances that prevailed. As will be pointed out later, the results obtained can only be regarded as suggestive.

Table XVI shows how the cases are disposed at each age period in either group.

TABLE XVI.

Therapeutic Test - Grouping for.

Age period.	Total examined.	Total in each group.	Composition of each group.	
			Syphilitics.	Non-Syphilitics.
0-10	50	25	11	14
11-20	42	21	11	10
21-30	28	14	10	4
31-40	28	14	9	5
41-50	18	9	5	4
51-60	14	7	4	3
TOTAL	180	90	50	40

The average period during which all the cases were subjected to observation was six weeks. During the first three weeks, each group was given a course of quinine or antisyphilitic therapy alone. Thus those of Group A received

quinine

quinine alone during that period, while those of Group B received antisyphilitic remedies alone for the same length of time. During the next three weeks, the cases in Group A whose spleen did not decrease with quinine were treated with antisyphilitic remedies, while similar cases among Group B received quinine. These resistant cases in both groups are classified as Group C. The quinine was administered by the mouth in liquid form according to the following formula:- ℞ Quin. sulphat. gr.5, Acid. sulphuric dil. m.5, Aq. ad ½oz. The dosage of the quinine sulphate given varied according to age. Children 0-10 years received from gr.½ to 2 t.i.d; 11-20 years, gr.3 to 5 t.i.d; 21 years and upwards gr.5 to 10 t.i.d. Antisyphilitic measures comprised the following:- (a) The oral administration of the following mixture: ℞ Liq. Hydrarg. Perchlor. m.30, Pot. Iodidi gr.5, Tr. Lavandulae Co. m.15. Inf. Gent. Co. ad ½ an ounce t.i.d. The Pot. Iod. was increased to gr.10 during the 2nd week, and gr.15 during the 3rd week. (b) Intravenous (in the case of small children intramuscular) injection of novarsenobillon, the adult dosage being 0.45 gramme, 0.6 gramme and 0.9 gramme during the 1st, 2nd, and 3rd weeks respectively, at weekly intervals. (c) Inunction of iodine ointment over the splenic area b.i.d. The doses of medicines given under (a) and (b) varied proportionately according to the age of the patient.

Diminution to the extent of one finger or more in the size of the enlarged spleen was recorded as a decrease. The results obtained are shown in Table XVII.

TABLE XVII

Therapeutic Test - Results of

(1) Group A.- received quinine alone

Age period.	Total	SYPHILITICS					NON-SYPHILITICS				
		Number treated.	Decrease in size of spleen.	%	No decrease in size of spleen.	%	Number treated	Decrease in size of spleen	%	No decrease in size of spleen	%
0-10	25	11	2	18.2	9	81.8	14	2	14.3	12	85.7
11-20	21	11	-	-	11	100.0	10	1	10.0	9	90.0
21-30	14	10	-	-	10	100.0	4	-	-	4	100.0
31-40	14	9	-	-	9	100.0	5	-	-	5	100.0
41-50	9	5	-	-	5	100.0	4	-	-	4	100.0
51-60	7	4	-	-	4	100.0	3	-	-	3	100.0
TOTAL	90	50	2	4.0	48	96.0	40	3	7.5	37	92.5
(2) Group B. received antisyphilitic therapy alone											
0-10	25	11	2	18.2	9	81.8	14	1	7.1	13	92.9
11-20	21	11	1	9.1	10	90.9	10	1	10.0	9	90.0
21-30	14	10	1	10.0	9	90.0	4	-	-	4	100.0
31-40	14	9	2	22.2	7	77.8	5	-	-	5	100.0
41-50	9	5	2	40.0	3	60.0	4	1	25.0	3	75.0
51-60	7	4	-	-	4	100.0	3	1	33.3	2	66.7
TOTAL	90	50	8	16.0	42	84.0	40	4	10.0	36	90.0
(3) Group C.- Resistant cases who received additional quinine or antisyphilitic therapy.											
0-10	43	18	4	22.2	14	77.8	25	5	20.0	20	80.0
11-20	39	21	4	19.1	17	80.9	18	3	16.7	15	83.3
21-30	27	19	2	10.5	17	89.5	8	-	-	8	100.0
31-40	26	16	3	18.7	13	81.3	10	1	10.0	9	90.0
41-50	15	8	-	-	8	100.0	7	1	14.3	6	85.7
51-60	13	8	1	12.5	7	87.5	5	-	-	5	100.0
TOTAL	163	90	14	15.6	76	84.4	73	10	13.7	63	86.3

41 cases altogether in Groups A, B, and C showed a decrease in the size of the spleen out of the 180 cases treated,, giving a per centage of 22.7. Of these, 24 were syphilitic and 17 non-syphilitic.

Figure 18

The following facts emerge from the above Table.

(1) Group A. Of the syphilitic cases who received quinine, only 4.0 per cent showed any decrease in the size of their spleen. The number among the non-syphilitic class who showed a response was almost double, viz., 7.5 per cent. It is to be noted that among both classes the decrease occurred only among children.

(2) Group B. Of the syphilitic cases who received specific remedies, 16.0 per cent showed a decrease as opposed to 10.0 per cent among the non-syphilitics. The response among both groups occurred throughout nearly ever age period (Fig.18).

(3) Group C. Many of those cases who showed no response to preliminary quinine or specific therapy did so when they were put on the second course of treatment additional to what they had already received. The group can therefore be regarded as having had a combined course of quinine and antisyphilitic treatment, though not simultaneously. The total number in this group who showed a response to the combined treatment was more than those who showed a similar response to the single form of treatment only among the other two groups. The number in whom a decrease was noted was nearly equal among both classes: 15.6 per cent syphilitics and 13.7 per cent non-syphilitics. The highest number showing a decrease occurred in both classes among children 0 to 10 years and 11 to 20 years.

(4) 41 cases out of the total 180 treated showed a decrease in the size of the spleen (22.7 per cent). Of these, 24 were syphilitic and 17 non-syphilitic.

Significance of the results obtained.

In view of the fact that the number on whom these

these tests were carried out was not sufficiently large and that the time (average 6 weeks) for which they were observed was not sufficiently long, it is not proposed to argue any dogmatic conclusions from the observations made. The results are not new and only confirm the more brilliant ones of BARLOW, GREIG, and others. They are however suggestive. The fact that enlarged spleen occurs in a patient who is syphilitic does not of course necessarily mean that his splenomegaly is due to his syphilis. But the observation in the present enquiry that the spleen of those cases who were syphilitic showed a more rapid response to specific measures, than to quinine therapy while a directly opposite result was obtained among the non-syphilitic controls certainly suggests that the splenomegaly of the former had an element of syphilis in it. That a large number of the cases who previously showed a negative result with either form of therapy ultimately responded when the additional form of treatment was instituted showed perhaps that the malaria and syphilis factors were probably both equally operative. It cannot be said however, that the fact that many of the cases showed no response to quinine disproves their malarial origin. It cannot be expected that this drug could have much appreciable effect in resolving advanced fibrosis in a spleen that has been enlarged for many years. It may exert some influence on fibrosis in children but is not likely to do so in adults. Indeed, it may be urged on the contrary that the potassium iodide contained in the antisyphilitic mixture which was administered acted on the cases which responded not because of any specific property but through its power to dissolve fibrous tissue of whatever origin. Large doses of iodides for instance

are

are known to produce considerable reduction in the size of mycotic spleens.

The fact that 22.7 per cent of the total number of cases subjected to treatment for only 6 weeks showed some decrease in the size of their spleen certainly suggests that medical treatment on these lines should be instituted in all cases of chronically enlarged spleens in the tropics before the decision is arrived at to perform splenectomy.

An omission that perhaps detracts somewhat from the value of the findings here is that a second serum test was not always carried out at the end of treatment, especially where there was decrease in the size of the spleen following antisyphilitic therapy. A negative Sachs-Georgi reaction following treatment where the reaction was previously positive would be at least some evidence of an existing spirochaetal infection. It must be remembered however that, according to WEBB (1922) of Uganda, "the Sachs-Georgi reaction shows a very decided tendency to become negative as treatment progresses irrespective of the clinical condition of the patient and the probability of his cure". As a matter of fact, the few cases in which a second Sachs-Georgi reaction was done after specific treatment both in this enquiry and among the general hospital cases did not often give a negative reaction. For various reasons, it was seldom possible to give each adult patient more than a maximum total dose of 2.0 grammes of novarsenobillon, and it is hardly to be expected that so small a dose could render the blood negative in a case of syphilis. Indeed, the observation

observation that only very few of the cases among the present series gave a negative reaction after treatment though the spleen was decreased showed that they were in actual fact syphilitic, because, according to RAMSAY, a Sachs-Georgi reaction that becomes negative after about 1.2 grammes of novarsenobillon is often due to yaws, while, "when the patient has syphilis, however, a negative reaction after so little treatment is a very exceptional occurrence".*

IX.- ABSTRACT OF TEN ILLUSTRATIVE CASE RECORDS.

(1) Case 435/27. E.A., female, aet. 16. Admitted on 18/8/27 with a history of "swollen abdomen" of 1 year's duration.** Condition on admission. Pallor of conjunctivae; tinea capitis, with palpable posterior cervical glands; heart, basal haemic murmurs; lungs, normal; spleen, enlarged to 5 fingers' breadth below costal margin, tender on palpation, with sharp edge; liver, 1 hand's breadth below costal margin, surface smooth and margin regular; slight ascites present; inguinal and left epitrochlear glands enlarged; no tibial nodes or scars; nervous system, normal. Urine: thick albumen but no casts. Stools: ancylostome and ascaris ova. Blood: subtertian rings. S.G. negative. Actual and differential counts: R.B.C. 3,850,000. W.B.C. 14,800. Polymorphs 64.6, eosinophiles 5.3, large mononuclears, 6.0, lymphocytes 23.0 basophiles 0.0, transitionals 1.0 myelocytes 0.0. Spleen and liver puncture: negative. Course of illness. The presence of thick albumen in urine prevented N.A.B. from being given. Quinine administered before splenectomy which was done 4 weeks after admission produced only slight diminution in size of the spleen. Splenectomy was undertaken as the diminution in the size was not considered rapid enough to justify further medical measures.

(2) Case 675/26 and 560/27. E.E., male, aet. 40. Was admitted to hospital on 7/11/26 with a history of enlargement of and periodical pain over the spleen: duration, 12 years. Previous history of gonorrhoea and syphilis, but not of yaws. On admission: Spleen enlarged to about 1 inch below level of umbilicus. Urine: normal. Stools: ancylostome and ascaris ova. Blood: few subtertian malaria rings; haemoglobin 60%; S.G. strong positive. Course of illness. Quinine and antisyphilitic

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* Personal communication from Dr. Ramsay. His researches on this subject are included in a paper entitled "A study of Leprosy in Southern Nigeria" which will be published shortly.

** A detailed history of any value is often very difficult to obtain from uneducated natives.

treatment was at once instituted. He received a total of 1.65 grammes of N.A.B. Twelve days after admission, the spleen was noted to be gradually diminishing in size. He refused a splenectomy and was discharged on 7/1/27 to continue his course of N.A.B. as an out-patient.

The patient was readmitted 10 months later on 11/11/27 with a history of impotence and slight incontinence of urine of one month's duration, as well as repeated, temporary fits of loss of consciousness which were not however preceded by any aura or followed by paralysis or paresis. Had nocturnal bone pains and headache. He was said to sometimes "talk silly", have loss of memory and wander in his speech. Condition on admission: muddy and speckled sclerotics; pupils, sluggish reaction to light, otherwise normal; heart, aortic incompetence, pulsating brachials and thickened radials; lungs, normal; spleen, enlarged to 4 fingers; liver, slightly enlarged; scar on penis; enlarged epitrochlear and inguinal glands; tibial periosteal nodes, with numerous scars; knee-jerk present but very sluggish; ankle jerk and plantar reflex* absent; superficial reflexes sluggish; no tremors or ankle clonus; slight Rombergism. Urine: threads, otherwise normal; no casts. Stools: ascaris ova. Blood: no parasites; S.G. positive. Actual and differential counts: R. B.C. 4,200,000, haemoglobin 70%; W.B.C. 9,400. Polymorphs 21.3, eosinophiles 14.6, lymphocytes 60.0, large mononuclears 3.3, basophiles 0.0, transitionals 0.6. Cerebrospinal fluid: increase in cell count; S.G. positive. Spleen and liver puncture: negative. Course of illness: Ran a low irregular fever for first 10 days of admission. Provocative injections of adrenalin and strychnine failed to produce any parasites in the peripheral blood. Received antisyphilitic treatment. Total dose of N.A.B. given, 2.1 grammes. Discharged in about 1½ months with spleen just palpable subcostally, all the other symptoms improved, and the blood S.G. negative.

(3) Case 623/27. N., male aet. 2 years. Admitted 9/11/27. History of cough for past three days and a big abdomen, more prominent on the left side, since birth. On admission: temperature 99.6°F respiration 26, pulse 104. A marasmic, puny child; depressed bridge of nose and snuffles; rhonchi in both lungs; abdomen distended - spleen tender and enlarged to 4 and liver to 2 fingers' breadth; no ascites or palpable abdominal glands; papular rash all over body; inguinal, epitrochlear, and axillary glands palpable. Urine: normal. Stools: ancylostome and ascaris ova. Blood: subtertian malaria parasites; haemoglobin 40%; S.G. of patient and mother positive. Sputum: negative for T.B. Course of illness. Never ran a temperature of more than 98.4°F to 99°F throughout stay in hospital. Was put on a course of expectorants and quinine. By 24/11/27 the lungs were almost clear but there was no appreciable decrease in the size of the spleen. Antisyphilitic treatment was commenced on both patient and mother and continued as out-patient after he was discharged from hospital on 14/12/27. He was lost sight of after a week, but before then his spleen and liver had begun to decrease, the rashes had disappeared and he was rapidly gaining in

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*The plantar reflex is very difficult to obtain in most uncivilised natives the soles of whose feet are usually very much thickened by reason of the fact that they always walk bare-footed.

in weight and improving generally.

(4) Case 116/28. N.E. male aet.42. Admitted 13/2/28 with a 2 months' history of ulcer of scrotum. Previous illnesses: Sore on penis "several years ago"; right inguinal hernia with herniotomy 2 years ago; several attacks of gonorrhoea - the last one 2 months ago; never suffered from yaws. On admission: Had an ulcer with a thickened, indurated, serpiginous edge and sloughy base on the scrotum, size of about ½ a crown, with much thickening and hyperpigmentation around; enlargement of all superficial groups of glands was present, with scar of old buboes in the groin; aortic systolic murmur; spleen enlarged to 3 fingers; liver, normal; deep scar on penis; tibial nodes and scars over both tibiae - some being fairly recent and hyperpigmented; reflexes sluggish. Urine: normal. Stools: ancylostome and trichuris ova: Blood: Mf. perstans and loa; no malaria parasite; S.G. strong positive. Actual and differential counts: R.B.C. 2,920,000. W.B.C. 8,400. Polymorphs 23.3, eosinophiles 14.6, lymphocytes 57.3, large mononuclears 2.6, basophiles 0.6, transitionals 1.3. Course of illness. Ulcer almost healed and spleen reduced to 2 fingers at end of 5 weeks antisyphilitic treatment, when he was discharged to O.P. Total dose of N.A.B. received = 3.75 grammes. S.G. weak positive on discharge.

(5) Case 179/28. I.A., female, aet.30. Admitted 2/3/28 with history of shortness of breath and pain over the spleen for 5 years, the pain being increased during attacks of what appeared to be malarial fever. Previous history: Nothing to note; had yaws during childhood. Family history: father and mother dead, cause unknown; number of "husbands", 3, all living; 1 child: died shortly after birth, and born after 2 miscarriages* On admission. Pallor of conjunctivae; generalised adenopathy; heart, soft basal haemic murmurs, otherwise normal; lungs normal; spleen, huge, enlarged to 2 fingers below umbilicus, tender and with very hard, sharp margin; downward enlargement of the liver; reflexes present and brisk. Urine: normal. Stools: ancylostome, ascaris, and trichuris ova. Blood: Mf. perstans; negative for malaria. S.G. positive; Course of illness: Quinine and antisyphilitic measures improved the general condition but failed to make any impression on the spleen and liver except the cessation of pain over the former organ. Received a total dose of 1.95 grammes of N.A.B. Discharged 15/4/28.

(6) 257/28. A.A., female, aet.40. Admitted 22/3/28 with history of an ulcer of left ankle of 1 year's duration, nocturnal pains in the bones and headache, dimness of vision, and dark, irregular menstruation. Previous illnesses: nothing to note. Family history: has 5 children, all alive and well; no miscarriage, abortion, or still birth: On admission: had a typical syphilitic gummatous ulceration over the left ankle; scarred pharynx; general adenopathy; heart and lungs normal; spleen enlarged to 2 fingers subcostally; liver normal; recent pigmented scars on both legs; reflexes normal; pallor of optic disc. Urine: normal. Blood: negative for parasites. S.G. positive. Course of

* This is a type of family history which is very common among the women of Calabar.

Course of illness: Ulcer almost healed and spleen not palpable even on deep inspiration on discharge on 23/4/28. Total dose of N.A.B. received was 2.35 grammes. S.G. still positive on discharge.

(7) 292/28. A.A., female, aet.36. Admitted 3/4/28 with a chronic syphilitic ulcer of left leg, duration 4 months; nocturnal bone pains and irregular menstruation for past 6 months. Previous and family history: nothing to note. On admission: In addition to the syphilitic ulcer of the leg, had an anterior staphyloma of right eye; general adenopathy; spleen enlarged to 3 fingers' breadths; liver not enlarged; had scars on legs and around the patella; periosteal nodes; ulceration and scarring of vagina (no history of child birth). Urine: trace of albumen. Stools: ancylostome and trichuris ova; Blood: subtertian malaria parasites and pigmented leucocytes. S.G. strong positive; Actual and differential counts: R.B.C. 3,520,000; haemoglobin 60%. W.B.C. 6,400. Polymorphs 32.6, eosinophiles 12.0, lymphocytes 27.3, large mononuclears 24.6, transitionals 1.3, myelocytes 2.0. Splenic puncture: negative. Progress. 19/4/28: Ulcer healing up but no appreciable decrease in size of spleen: had then had 1.8 grammes N.A.B. 18/5/28 - date of discharge: ulcer healed, spleen decreased to 2 finger-breadths; had then had 4.2 grammes of N.A.B. S.G. negative on discharge. Patient never had any attack of fever during the whole of her stay in hospital though parasites were present in her blood.

(8) 306/28. E.A., male aet.40. Admitted 5/4/28. History of "swollen belly", haemorrhoids, and double reducible inguinal hernia, "for many years". Previous illnesses: no history of yaws, never had hamatemesis or any of the other commoner symptoms which accompany portal obstruction. Family history: nothing to note. Habits: not alcoholic. On admission: in addition to the double hernia had - profoundly anaemic conjunctivae; general glandular enlargement; heart, left ventricle enlarged, with apex in 6th space in anterior axillary line; double aortic murmur; heart sounds slow and heaving, spleen 5 finger-breadths; liver, 3 finger-breadths, hard, irregularly nodular; slight ascites; large scar on penis and chronic urethral discharge; old superficial gummatous infiltration of the legs which had a mottled, scarred appearance; no oedema of extremities; both tibiae showed periosteal nodes; had slight stricture of rectum in addition to piles; reflexes sluggish; peripheral neuritis and other signs of chronic alcoholism were absent. Urine: threads, slight albumen. Stools: ancylostome and ascaris. Blood: negative for parasites. S.G. positive. Progress: Antisyphilitic treatment had no effect on size of spleen or liver. Double herniotomy was done at patient's urgent request on 17/4/28 with gas and oxygen, and, despite the condition of his heart it was entirely successful, the wound healing by first intention. Had a syncopal attack on 2/5/28; began thereafter to run an irregular remittent temperature which could not be controlled with quinine or other measures, progressively collapsed, and died on 10/5/28. Post-mortem. Heart much enlarged, with very much thickened left ventricle; extensive syphilitic atheroma of the aorta, the valves being

sclerosed

sclerosed to a very considerable extent producing stenosis and incompetence; tough pleural adhesions; * lungs normal, with no evidence of T.B.; stomach and intestines normal except for the rectal piles; liver enlarged, with irregular syphilitic scarring, and perihepatitis; spleen enlarged, with perisplenitis; slight ascites; kidneys small, with atrophy of cortex and prominent vessels. Section of spleen and liver showed much fibrosis and deposition of pigment. No malaria or any other parasite was present in the splenic smear. There was no evidence of fungus infection.

(9) Case 550/28. N.U., female, aet.2½. Admitted 15/6/28 with history of typical malarial fever and cough for past 3 days. Previous history of yaws six months before; history of previous malarial attacks. On admission: temperature 103.6°F., respiration 30, pulse 142. Skin hot and covered with profuse sweat; pallor of conjunctiva; heart, rate quickened, otherwise normal; lungs, a few crepitations on both sides but no areas of dulness; spleen tender and considerably enlarged, to 2 fingers' breadth below level of umbilicus, the edge being very sharp; liver enlarged to 3 fingers below rib margin; inguinal glands enlarged. No signs of congenital syphilis were noted. Urine: trace of albumen. Stools: ascaris ova. Blood: subtertian and quartan malaria parasites. S.G. strong positive (taken after subsidence of fever). Course of illness: Temperature subsided to normal immediately on giving gr.2 quinine intramuscularly. A similar dose was continued by the mouth, t.i.d. 22/6/28: spleen reduced to 2 fingers below costal margin and was not then tender; liver still 3 fingers; no malaria parasites now in blood. 27/6/28: patient given 0.2 grammes N.A.B. repeated on 4/7/28, quinine being still continued. 6/7/28; discharged, with spleen just palpable subcostally; liver decreased by 1 finger breadth.

(10) Case 635/28. S.A., male aet.19. Admitted 11/7/28 with a history of cough and debility for 2 months. There had been no loss of weight and the appetite was good. Previous and family history: nothing to note except an attack of yaws in childhood. Condition on admission: pallor of conjunctivae; pleural friction and a few crepitations at base of left lung but no physical signs of T.B. could be made out; haemic murmurs over base of heart; spleen, tender and enlarged to 2 fingers' breadth below level of umbilicus; liver enlarged to 1 finger subcostally; ascites was present; no enlarged abdominal glands could be palpated; the left posterior cervical, left epitrochlear, and inguinal glands on both sides were enlarged; no signs of congenital or acquired syphilis were present. Urine: slight albumen. Stools: ancylostome and ascaris ova. Sputum: negative for T.B. Blood: negative for parasites. S.G. positive. Actual and differential counts: R.B.C. 2,440,000, haemoglobin 40%. W.B.C. 11,200. Polymorphs 66.0, eosinophiles 0.3, lymphocytes 30.6, large mononuclears 2.6, basophiles and transitionals, nil. Progress: general treatment

* Extensive chronic pleural adhesions are frequent finding post mortem on natives and are usually unaccompanied by any other sign of disease of the lungs.

treatment included a course of N.A.B. of which he had 1.2 grammes till 2/8/28 by which time the S.G. was negative, but there was no effect on the size of the spleen or liver. On 11/8/28 he began to run an irregular temperature and was put on gr.10 quinine t.i.d., and inunction of iodine ointment over the spleen area. 10 days after, 21/8/28, there was a slight decrease in the size of the spleen by one finger's breadth, the organ then being less tender, softer, and with less sharp an edge. On 26/8/28, the spleen had decreased to level of umbilicus, but the patient's general condition was worse; he still showed an irregular remittent temperature, with no periodicity, and no parasites could be found in the blood. He died on 3/9/28. Post mortem: The general condition found at post-mortem suggested the condition known to English pathologists as "Chronic Polyorrhomenitis" and called by the Italians "Concato's disease". There was general chronic inflammation of the serous membranes. The heart was flabby, slightly dilated, with chronic pericardial adhesions. The lungs were congested and oedematous; there were extensive, dense pleural adhesions which were separated from the chest wall with difficulty. No signs of tuberculosis were present in the lungs. There was chronic mediastinitis and chronic peritonitis. The liver was enlarged and fatty, with considerable and dense perihepatitis. It was not nodular. The spleen was considerably enlarged, was covered with a much thickened capsule and was very fibrous: smear showed malaria parasites. Ascites was present, but there was no enlargement of the mesentric glands; the omentum was normal. Intestines, normal. Kidneys, congested. There was no evidence of tuberculosis in any organ.

Comments: Some of these cases have been reported mainly to show the type of splenomegaly that might have been diagnosed as being of purely malarial origin owing only to the presence of parasites in the blood. Cases 675/26, 623/27, and 550/28 are examples. It is interesting to observe that the latter 2 cases are both children under 3 years. The response of their enlarged spleen to specific treatment cannot be regarded as conclusive, though it argues at least a partial syphilitic origin. Case 550/28 showed a distinct response to preliminary quinine treatment alone, though the response was more marked when a course of N.A.B. was begun later. She can however be regarded as a typical malarial case, the S.G. positive reaction being due to yaws contracted 6 months before. Case 675/26 and 560/27 was a very interesting patient. I still see him as an out-petient from time to time

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when he attends - rather irregularly - for N.A.B. injections. His mental and general condition has greatly improved. His spleen however shows a tendency to increase somewhat in size during those periods when he omits to come for his injections, while it "goes down" when he starts to receive them regularly again. Cases 116/28, 257/28, and 292/28 illustrate the class of cases in which a syphilitic ulcer and enlarged spleen occurred in the same patient, both lesions improving simultaneously. Case 179/28 is a type which, from the history, is of malarial possibly combined with a syphilitic origin. Her spleen showed no response to quinine or antisyphilitic treatment. Perhaps it represents a type in which the condition of the spleen as regards fibrous tissue formation is too far advanced to be influenced by any form of treatment. 306/28 was a clear case of syphilis from the clinical and post mortem evidence, though his spleen failed to respond to treatment. Case 635/28 was a subject of chronic perihepatitis and splenomegaly occurring as part of a general condition of chronic polyorrhomenitis. He showed no signs of syphilis or tubercle. He was sero-positive, but that might have been due to the yaws he had in childhood. The fact that the spleen responded slightly to quinine perhaps suggests a partly malarial origin. This perihepatic condition has been occasionally met with in some cases on whom splenectomy was performed in this hospital and may therefore not be so very rare. The condition was usually accompanied with a considerable degree of ascites. Its etiology is obscure.

The chief possibilities in the practical diagnosis of Splenomegaly in West Africa.

The chief possibilities in the practical diagnosis of Splenomegaly in West Africa.

Reference has already been made in the earlier part of this thesis to the relative frequency with which the various factors that cause splenic enlargement occur in Nigeria. In the present enquiry the relative importance that these factors carry in the southern half of that colony has been investigated in some detail. It remains therefore to make some practical suggestions with regard to the diagnosis of the causes of splenomegaly as seen in this country. Putting aside the cases of enlarged spleen from acute infective fevers, backward engorgement from valvular disease of the heart, the leukaemias, and the rarer types of chronic splenomegaly, the following short list would cover the usual possibilities regarding enlarged spleen and liver in West Africa, though it is by no means suggested that it is in any way comprehensive:-

(1) Simple malarial enlargement of the spleen, with or without simple enlargement of the liver, also of malarial origin.

(2) Syphilis. In children - of the congenital type. The splenic enlargement is primary and is often accompanied with cirrhotic enlargement of the liver of similar origin. In adults - as a late tertiary manifestation of acquired syphilis or of "syphilis hereditaria tarda". The splenic enlargement may be irregular - due to localised gummata, or uniform and regular - due to diffuse cirrhosis. It may or may not be accompanied with syphilitic enlargement of the liver. Ascites may be present.

(3) Malaria-cum-syphilitic enlargement of the spleen, often with diffuse syphilitic cirrhosis of the liver. Ascites often present in the latter stages.

(4) Splenic enlargement accompanying portal or alcoholic cirrhosis of the liver, in adults. Other signs of alcoholism such as gastritis and peripheral neuritis may be present.*

(5) Leishmaniasis - does not occur in many parts of West Africa, but its possibility is to be kept in mind in parts bordering on the Sudan.

(6) Chronic polyorrhomenitis (Concato's disease).

(7) Splenic anaemia - probably rare in West Africa.

Numbers 1, 2, and 3 are the most common. Syphilis has been given a prominent place in the above list because the results of the present enquiry suggest that its influence ranks probably almost - if not equally - as high as that of malaria in the production of chronic splenomegaly in Nigeria. It must again be emphasised however that the results obtained are only suggestive. No dogmatic conclusions can be drawn from them as to the real part that syphilis plays. Nevertheless, there can be no doubt that as a factor which contributes in no small measure to the production of splenomegaly in West Africa, this disease certainly has to be reckoned with.

As far as I am aware, no publication has as yet been made of the results of observations on

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* Alcoholic cirrhosis of the liver seems to be rare in West Africa, though the gin and palm wine drinking habit is very prevalent. Only 7 cases were reported for the whole of Nigeria during 1927. DUFOUR and BURGEOIS (1928) regard concurrent malaria or syphilis as the dominant factor which produces splenomegaly in this disease. They regard the influence of portal obstruction as only slight and are opinion that "in alcoholic cirrhosis if there is not an obvious co-existing infectious disease, the presence of a large spleen is in favour of concurrent syphilis"

on syphilis as seen among natives of British West Africa on quite as large a series of cases as are recorded here, nor on the relative part that various factors (excepting malaria) play in the production of chronic enlargement of the spleen in that country. The present enquiry therefore may be regarded as an original contribution to our knowledge in these respects in this part of the world.

SUMMARY AND CONCLUSIONS.

1. Of 1000 consecutive cases that were treated at the African Hospital, Calabar, West Africa, 260 had enlarged spleens, and 71, enlarged livers. 67 of the latter were associated with enlarged spleens, leaving 4 which were not so associated. It is considered that the cases are in every way representative of the condition as it occurs in Nigeria and the coastal belt of West Africa.

2. The cases were principally examined in order to find out what part syphilis plays in the production of splenomegaly in West Africa. Those cases who did not show enlarged spleens among the total number examined were used as controls. The various criteria necessary for such an investigation are discussed.

3. The spleen rate was found to show 2 waves: a primary one during the age periods 0 to 20 years, and a secondary wave from 31 to 60 years. The liver rate showed a corresponding primary wave between 0 to 20 years. This was followed by a slight decline from 21 to 40 years, and then a secondary rise from 41 to 60.

4. The general clinical features presented by 207 in-patient cases as a whole are discussed, and a list given of the diseases for which they were

primarily

primarily admitted. Only a few of the cases were admitted for conditions pointing directly to a splenic or hepatic condition.

5. Those diseases which may produce splenic enlargement and which occurred in the series are discussed. Syphilis was the commonest, followed closely by malaria. It is pointed out that owing to the method of classification, the figures for syphilis are too low. For example, many of the cases of chronic ulcerations were of syphilitic origin, though they were often recorded simply as "ulcers".

6. Many of the commoner diseases, especially those of the blood, which cause splenic enlargement did not occur among the series: they are rare in Nigeria.

7. It is pointed out that malaria, yaws, and syphilis are the three diseases to which attention would have to be principally concentrated in the present enquiry. It was recognised that the investigation of the syphilis factor would be attended with some difficulty because many of its tertiary lesions and its serological reactions are identical with those of yaws, a disease which is endemic in Nigeria. The comparative incidence of the three diseases in the country is discussed. Their order of frequency in the area served by the Calabar Hospital is stated to be yaws, syphilis, and malaria in the proportion 1: 1.3 : 2.8. It is considered however that these figures given for malaria are too high while those for syphilis are low.

8. The results of a single examination of the blood for malaria and microfilaria are noted. The malaria parasite rate among cases who showed splenic enlargement (referred to as the "spleens") as well as the controls who showed no such enlargement

enlargement (referred to as the "others") showed a rise between 0 to 10 years of age followed by a steady decline from 11 to 60 years. This rise corresponded to the primary wave of the spleen and liver rates. The secondary wave in the spleen and liver rates however had no counterpart in the malaria parasite rate. The "spleens" showed a higher malaria parasite rate than the "others".

9. It is emphasised that the malaria parasite rate was no indication of chronic malarial infection, the incidence of which could be more accurately assessed by taking into consideration the history of previous attacks among the cases, at least during the last 12 months. It is pointed out however that this could not be done because of the inability of most natives to give accurate history of their illnesses.

10. Filarial and intestinal protozoal infection was not a factor in the cases of splenomegaly examined.

11. Actual and differential blood counts of 33 spleen cases were done and the averages recorded. It was observed that these showed not much difference from what can be regarded as the West African normal and that the only value they have in the present enquiry was to show that only a single case of blood disease (von Jaksch's anaemia) occurred.

12. The examination of spleen, liver, and gland punctures for parasites showed negative results.

13. Five cases of jaundice occurred, of which one at least was of definitely syphilitic origin.

14. In order to eliminated the yaws factor from the figures obtained for clinical syphilis, a careful investigation was made into the history of the former disease in every case. No person was

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regarded as syphilitic where there was any possibility of the yaws factor operating. The number who gave a history of yaws was found to be approximately equal among both the "spleens" and the "others" (controls) i.e., 11.1 and 12.7 per cent respectively. The disease cannot therefore be regarded as being a factor in the production of splenomegaly.

15. The cases who showed physical signs of syphilis among the spleens and controls are recorded. The former showed a consistently higher incidence of the disease as clinically observed at each age period and among the cases as a whole.

16. The commoner signs of the disease as seen among the cases are considered in some detail, their relative diagnostic importance being discussed. Adenopathy was found to be of little or no value. Nocturnal bone and joint aches were one of the commonest symptoms. A peculiar type of depigmentation of the skin of the lower extremities which is sometimes accompanied by loss of one or more digits is described. It is pointed out that this lesion is not of leprotic or yaws, but is most probably of syphilitic origin. Lesions of the nervous system were uncommon.

17. The figures for stigmata of congenital syphilis were low. It is pointed out that this is in accord with similar observations in many parts of Africa where the syphilis rate among the general population is known to be high, and that the probable explanation is that it is due to the high death rate among syphilitic infants.

18. A Sachs-Georgi test was done on all the cases. The technique is described and the value of the test discussed with special reference to yaws, syphilis, and malaria. It is pointed out that the initial

initial figures obtained represented the combined yaws and syphilis rate, and that the correct assessment of the rate for the latter disease was made by eliminating the yaws factor. This was done by finding out the number of serum - positives among those who had never contracted yaws. The "spleens" were found to have a combined yaws and syphilis rate of 71.5 per cent while the real syphilis rate was 60.3 per cent. The corresponding figures among the "others" were lower, being 54.3 and 41.5 per cent respectively. The combined yaws and syphilis rate among the total 1,000 cases examined was 58.8 per cent, while the real syphilis rate was 46.5 per cent. It is pointed out that the former rate approximates those for other parts of Nigeria, and for the general Calabar community.

19. There was a marked disproportion between the serological and clinical figures especially in children of 0 to 10 and 11 to 20 years old among both classes of patients, more particularly among the "spleens". The possible reasons for this are discussed. It is pointed out that the high serological figures during these age periods represent not only the rate of congenital syphilis but also that of the disease acquired very early in childhood. It is further pointed out that the clinical figures among these children are low because in collecting them, several cases in whom the sole lesion observed was enlarged spleen were not included and that many of such cases were possibly congenital syphitics or subjects of the early acquired disease. It is considered therefore that an enlarged spleen may often be the only sign of congenital or early acquired syphilis among West African children.

20. The syphilis and malaria parasite rates

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are compared with the incidence of enlarged spleen and liver in each group. It is shown that enlarged spleen was found to associate more commonly with signs of syphilis than with those of malaria as parasitologically observed during the age period 0 to 10 years. This holds true as an index of chronic malarial infection only for this age period alone, as the figures for malaria parasite at the other age periods are an imperfect guide to the part that this disease plays. Though it is recognised that malaria is a considerable factor in the production of splenomegaly, yet it is suggested that the 2 waves which occurred in the spleen and liver rates during the age period 0 to 20 and 31 to 60 were partly of syphilitic origin: the primary wave being in part due to congenital and possibly early acquired syphilis, and the secondary being in part a tertiary manifestation of the sexually acquired disease or a late manifestation of "syphilis hereditaria tarda".

21. It is pointed out that owing to the primitive state of civilisation, to ignorance regarding the mode of spread and to lack of effective native treatment, syphilis is very prevalent in Africa. The theory is propounded that where the universally prevalent syphilitic taint does not give rise primarily to a syphilitic splenomegaly, its presence probably forms a basis on which enlargement of the native spleen in malaria develops more easily or in a more exaggerated degree than in an individual whose constitution is not originally thus burdened. The incidence of enlarged spleen in each age group among the cases described is analysed in the light of this theory.

22. The effect of quinine and antisyphilitic treatment on the size of the enlarged spleen in

in 180 cases is recorded. These were grouped according as to whether the syphilitic factor was or was not operating in the production of the splenomegaly according to the serum reaction of the cases. The syphilitics showed a readier response to specific treatment than to quinine, while the non-syphilitics were more rapidly influenced with quinine than with antisyphilitic treatment. It is pointed out that, though by reason of the smallness of the numbers examined no dogmatic conclusions can be drawn from the results obtained, yet these results suggest that the syphilitic element was present in an appreciable number of cases. It is urged that as 22.7 per cent of the cases treated showed some response during the short space of 6 weeks to combined quinine and antisyphilitic treatment, cases of chronic splenomegaly should first be given the benefit of such treatment before the decision is arrived at to perform splenectomy.

23. An abstract of 10 cases records is given principally to illustrate the types of splenomegaly that might have been diagnosed as of purely malarial origin while they were really in part syphilitic. The post-mortem notes are given of 2 cases which were fatal and included a case of chronic polyorrhomenitis. It is pointed out that as this condition is sometimes met with in cases on whom splenectomy is performed, it may not be so very rare.

24. A short list of the possibilities in the practical diagnosis of splenomegaly as seen in West Africa is given. Syphilis is given a prominent place because the results of the present investigation suggest that the influence of this disease ranks probably almost as high as that of malaria in

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the production of the condition.

25. The respect in which this work constitutes a contribution to our knowledge is indicated.

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DESCRIPTION OF THE ILLUSTRATIONS.

Figures.1, 2, and 3. Typical eruption of secondary yaws in children.

Figure 4. Various types of depigmentation of the skin of the lower extremities, usually below the knee. Generally bilateral. The depigmentation of the 2 men on the

the 2 men on the right is a simple form of leucoderma and shows no scarring. That of the other 2 on the left is syphilitic and is accompanied with extensive scarring. This is particularly marked in the 2nd man from the left who shows a chronic syphilitic ulcer on the right ankle and loss of the 1st, 2nd, and 5th toes of the right foot. There is much superficial scarring and some degree of contracture of the foot. The 1st man on the left incidentally shows bilateral elephantiasis groin glands. The depigmented areas in all the men are quite sensitive. There are no signs of leprosy. They are not cases of pinta, and no fungus could be isolated from any of the cases. There was no history of yaws.

Figure 5. A closer view of the right foot of the 2nd man from the left in Fig.4.

Figure 6. Depigmentation with much scarring around the right ankle in a syphilitic patient. The mark above the heel is the scar of a recently healed syphilitic ulcer which as well as his enlarged spleen responded to vigorous anti-syphilitic treatment. The foot on standing up is held in the position of pes equinus. Both tibiae are slightly curved. There was no history of yaws.

Figure 7. Syphilitic scarring over right patella. There are scars also on the other leg.

Figure 8. Sabre tibiae in a boy aged about 13 years. A congenital syphilitic. No history of yaws.

Figure 9. Normal and abnormal bridges of nose in the Negro. The 1st 4 from the left show what may be regarded as the normal depression that is commonly present in Negroes. The last 4 show marked depression of the bridge. The depression is a really marked one and is not due to the normal depression being exaggerated by too bulky or widened alae nasi. It is particularly marked in the 2nd and 4th men from the right. This type of nose is very common in the Ibibios and the interior Cross River tribes among whom syphilis is exceedingly common.

Figure 10. A normal Negro type of nose in an adult.

Figure 11. A depressed type in an adult, an Ibibio.

Figure 12. A normal type in a young boy.

Figure 13. A depressed nose in an Ibibio boy who is a congenital syphilitic. Note also the prominent frontals.

Figure 14 A normal set of teeth in a Negro boy.

Figures.15, 16, and 17. Various types of dental irregularities in Negro Boys. Note the gap between the central incisors in Figure 15 - a very common type of irregularity.

Figure 18. A syphilitic subject with enlargement of the spleen and liver, and ascites. To show effect of anti-syphilitic treatment on the size of these organs. The shaded portions of the diagram on his abdomen represent the present size of his spleen

and

and liver below the costal margin, after treatment. The upper line of the shaded areas is the costal margin. The unshaded areas represent the margins of his spleen and liver on admission, i.e., before treatment. Incidentally, he also shows a right inguinal hernia.