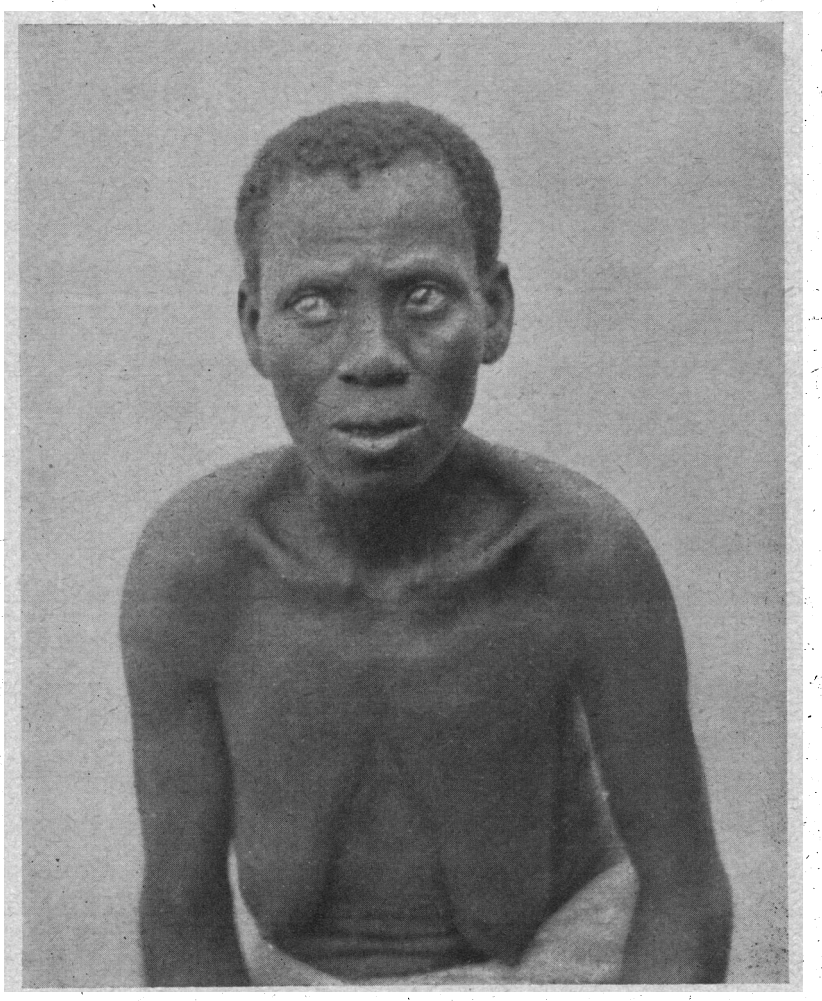

Blind woman.

OCULAR ONCHOCERCIASIS*

Including an Investigation in the Gold Coast

IF every ophthalmic surgeon were asked to record a vote for the worst infection or infestation of the eye there is little doubt that trachoma would head the list by an overwhelming margin, and such a decision would probably be justified by the hundreds of million sufferers of whom a large proportion are blind or whose lives are made a burden by the sequelae. Yet there is another disease perhaps even more terrible in that it affects not only the cornea but practically every part of the eye, and has so far proved completely incurable. Moreover, though not so widespread as trachoma, its victims may well exceed a million if a complete survey could be made. Though onchocerciasis is widely endemic in the major part of the British Colonial Empire it has excited only the barest interest amongst British ophthalmologists. The lack of appreciation of its importance is shown by the absence of any mention of this disease at a discussion on " Important diseases affecting West African troops " held in London in 1944.

Ocular onchocerciasis is a disease caused by infection with the microfilariae of a threadworm, onchocerca, which enter practically all parts of the eye, particularly the cornea, the uveal tract and the optic nerve, leading to blindness from corneal opacities, complicated cataract, choroido-retinal degeneration and optic atrophy. The disease is insidious and chronic without a marked acute stage and has a strong tendency to bilateral symmetry. Infection is carried by a fly, Simulium, which breeds in running water.

Historical.—Onchocerciasis is a disease of comparatively recent recognition. Leuckart (1893) described and named *Onchocerca volvulus* but recognised only the nodules which in themselves are unimportant. O'Neil (1875) had previously found the microfilariae in the skin in " Craw craw." During the next 20 years Kulz, Ouzilleau, Fulleborn, Rodhain and many others working in Africa described the worm and the microfilariae, and reported general effects of the infection, in particular the nodules, skin lesions, elephantiasis and the presence of microfilariae in the skin and lymph glands. In 1915 Robles in Guatemala saw two cases of severe ocular disease associated with nodules and what was known as " Coast Erysipelas " which led him to look for some new disease. He discovered the presence of onchocerciasis in Central

* Received for publication, November 25, 1944.

America, some ocular complications of the disease and even suspected that Simulium was the intermediate host. Nevertheless the precise mechanism of the disease was not understood. Calderon (1919) considered that the eye lesions were the result of toxins from the adult worms entering the blood stream, and though much work was done by Rodhain (1920), Montpellier and Lacroix (1920), Fulleborn (1924), Dyce Sharp (1926) and others, it was left to Ochoterena (1930) to find the microfilariae in the eye, a discovery which led to an understanding of the mechanism of the ocular lesions. Meanwhile Blacklock (1927), working in Sierra Leone, had proved conclusively that Simulium was an intermediate host.

Hisette (1932), in the Belgian Congo, provided the first comprehensive account of the eye lesions, and further work has since been done by many workers, in particular Strong (1931), Hisette (1935), Bryant (1935), Van Den Berghe (1936), and Quevedo (1941). Fulleborn (1931) reported a case in a European and Adams (1938) another seen at Liverpool. In all some 30 European cases have been recorded.

While the early descriptions of the parasite and the general lesions came from Africa, those of the ocular complications came from Central America, in particular Guatemala, where the worm was named *Onchocerca caecutiens,* Brumpt 1919, " the blinding filaria."

The African variety, *o. volvulus,* Leuckart 1893 was said by Muhlens (1932) to differ in not affecting the eyes, a view also held at that time by Strong and Blacklock. This view was, however, completely disproved by Hisette (1932). Ouzilleau (1923) had previously mentioned that a number of patients in the Belgian Congo suffering from onchocercal elephantiasis also had disease of the eyes but did not definitely associate the two conditions. It now appears that the differences between the two species of *onchocerca* are very slight and probably non-existent, and it would seem possible that the disease is primarily African and was carried to the Americas by the slave trade.

Geographical.—Human onchocerciasis is widely endemic in Tropical Africa and in Tropical America, but so far as is known does not occur in the corresponding latitudes of Asia and the East Indies. About 5 million square miles of the earth's surface with a population of roughly 100 millions are involved.

The infection rate varies considerably according to the height above sea level, the annual rainfall and geological structure of the country as well as the latitude, factors which affect the breeding of the insect carrier. Robles (1916) found hyperendemicity in one village in Guatemala while its nearest neighbour only a few miles away was free from the disease. The localised endemicity therefore precludes any infection index for countries

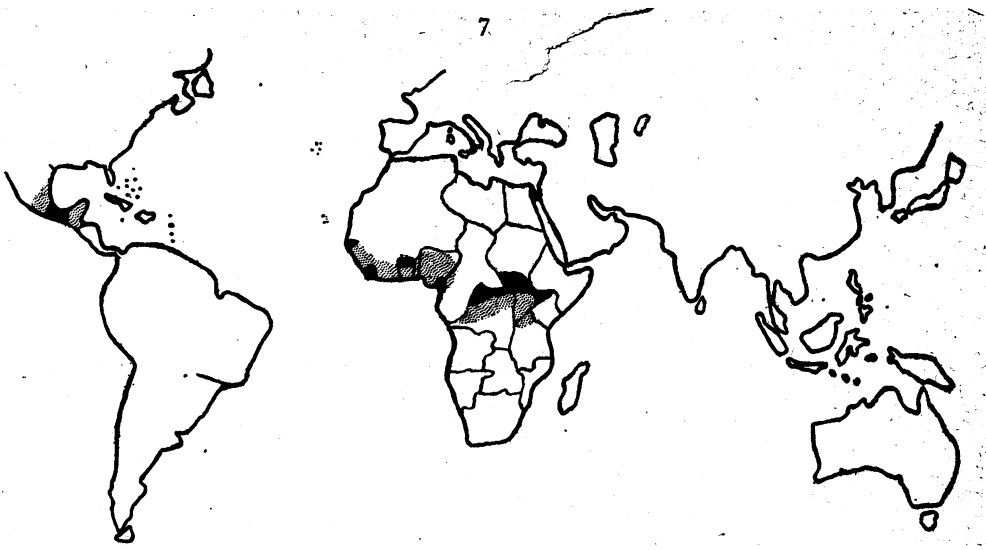

FIG. 1.

Map of the World, showing the areas in which onchocerciasis has so far been reported. Hyperendemic areas in black.

which have not as yet been completely surveyed, and a further difficulty has been that in many cases the equipment for the investigation has been sadly deficient. Nevertheless reported infection rates are not without interest and onchocerciasis has so far been reported from the following countries:—

Country	First report traced	Highest recorded infection in endemic locality
Guatemala	Robles (1916)	60 per cent. Munoz Ochoa (1934)
Mexico	Hoffman (1930)	100 per cent. Nettel (1941)
Belgian Congo	Dubois (1916)	90 per cent. Rodhain (1942)
Cameroons	Kulz (1914)	95 per cent. Dyce Sharp (1928)
Fernando Po	Najera Angelo (1935)	
Gold Coast	Fulleborn and Simon (1914)	34 per cent. Macfie and Corson (1922)
Ivory Coast	Clapier (1917)	34 per cent. Richet (1939)
Kenya	Dupuy (1924)	60 per cent. Macmahon (1940)
Nigeria	Leiper (1913)	55 per cent. Dyce Sharp (1927)
Nyasaland	Gopsil (1939)	1 per cent. Gopsill (1939)
Rhodesia	Messer (1942)	
Senegal	Lecomte (1915)	45 per cent. Laigret (1930)
Sierra Leone	Blacklock (1926)	45 per cent. Blacklock (1927)
Tanganyika	Fischer (1932)	4 per cent. Hawking (1940)
Tunis	Anderson and Lehucher (1940)	
Uganda	Gibbins and Lowenthal (1933)	

The high infection rates recorded refer to selected districts which are not representative of the country as a whole, and are based on the finding of *o. volvulus* or its microfilaria in samples of the local population.

The incidence of ocular as opposed to generalised onchocerciasis has not been fully investigated and there appear to be wide variations in the frequency of eye complications in different endemic districts. Blacklock (1926) reported that the eyes were not affected in the onchocerciasis patients at Konno, Sierra Leone, but this statement has proved to be unfounded, as one soldier seen at Accra and who came from Konno was found to have microfilariae in the aqueous and nummular corneal opacities. Similarly eye complications are said to be rare on the Congo below Leopoldville though nodules are common there.

In the Gold Coast, the territory with which this report is chiefly concerned, though the occurrence of onchocerciasis had long been known, its importance as a source of blindness remained unrecognised in the medical centres until the end of 1943.

Enquiries in the middle of that year disclosed that no case of ocular onchocerciasis had been diagnosed in Accra. For this the lack of modern apparatus was undoubtedly largely responsible. In 1936, however, Dr. G. Saunders, the Senior Medical Officer in charge of the trypanosomiasis campaign, surveyed a wide area in the Northern Territories investigating avitaminosis to which condition he at first attributed the prevalent eye lesions. On reading the report of Hisette (1932) he realised the true nature of the trouble and was able while on a later survey to confirm onchocerciasis by excision of nodules and by microscopy of conjunctival snips. Unfortunately his reports were unpublished. Dr. Saunders kindly informed the writer of several endemic areas and did everything in his power to promote and assist an expedition by an ophthalmologist. His knowledge of the country and the inhabitants proved extremely valuable.

Highly endemic areas occur throughout the granite country, particularly between Wa and Navrongo and around Bawku, but there are other areas of high infectivity in the country adjoining the large rivers. It was not, however, realised that sporadic cases at least occur in widely scattered districts, some not far from the coast. The map indicates places from which patients with onchocerciasis have been seen. No doubt many others would be revealed by a more complete survey. The main investigation reported below was performed at Funsi, a village in the West of the Northern Territories about 500 miles from the coast.

Other forms of onchocerciasis affecting particularly horses, dogs and cattle are very widespread. In Queensland *o. gibsoni* is a serious problem in cattle, rendering the carcases unfit for human consumption.

The danger of spread to other countries would appear to be very real, especially since the onchocerca may not be very particular about its intermediate host. African troops, many of whom

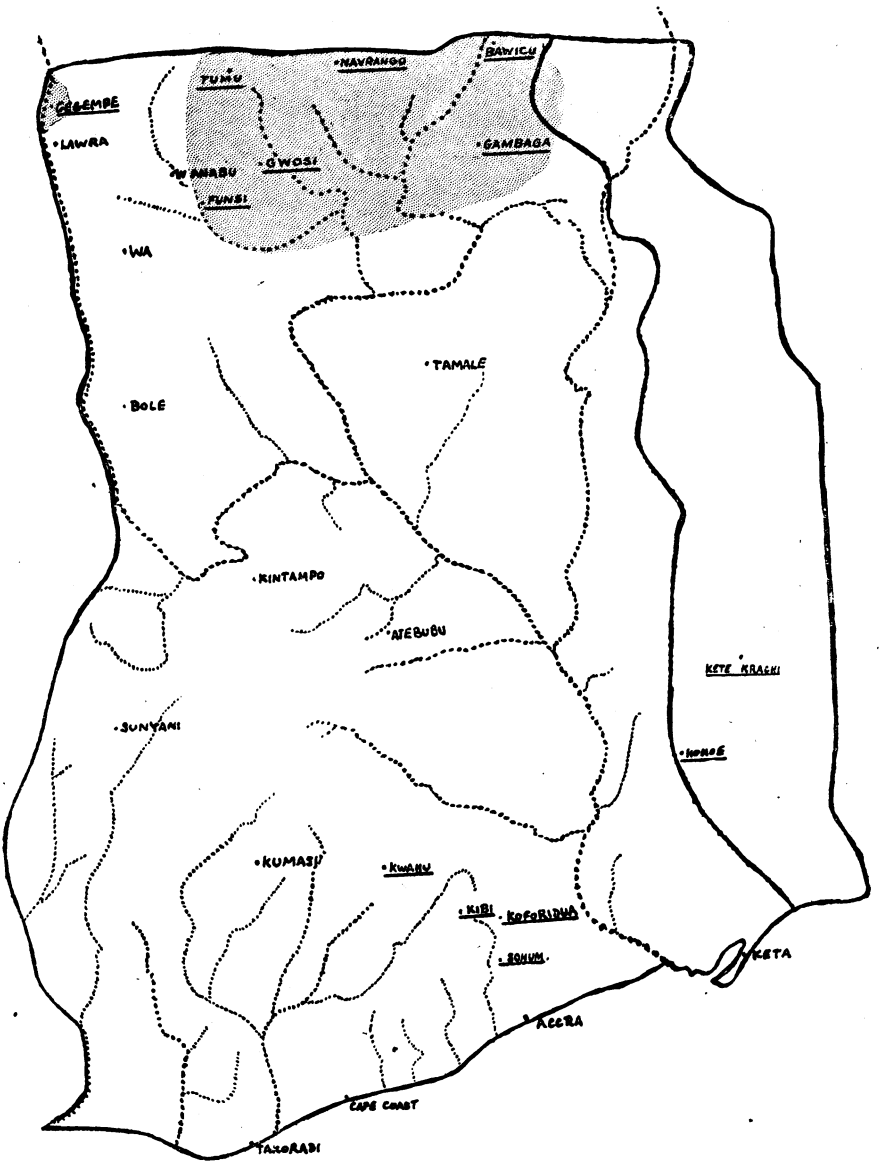

FIG. 2.

Map of the Gold Coast and British mandated Togoland. Onchocerciasis endemic in shaded areas. Sporadic cases have been seen from districts underlined.

are infected, may well carry the disease to South East Asia and the East Indies, and the danger of spread by air lines has been commented on by Dampf (1943) in Mexico. It is not inconceivable that the disease may spread to temperate climates, and in this connection the single case of a boy aged 15 in Le Goulette who had never left Tunisia (Anderson and Lehucher, 1940) where *Simulium damnosum* is unknown, is of great interest. Onchocerca may well prove adaptable to climatic changes and the disease is known to occur from sea level to 4,500 feet. Johnstone and Larsen (1933) have reported a definite northward spread of Simulium in the western states of the U.S.A. Hardwicke (1928) was able to trace onchocerciasis over the Sierra Madres mountains and suggested that the disease entered Mexico from Guatemala.

Racial.—Though the vast majority of sufferers are Africans or Central Americans there seems little evidence to postulate a partial immunity for Europeans though so far surprisingly few eye cases have been reported, even though District Commissioners and others who live in endemic areas are only too well acquainted with the bites of Simulium. Twenty-nine cases of onchocerciasis in Europeans have been recorded, but only 4 with ocular lesions.* Semadini (1943) reported a very severe case in a Swiss geologist who died in a mountaineering accident and whose eyes were sectioned post-mortem. Adams (1938) also reported a typical case in Liverpool in an Englishman who had for some time " lived native " in the Belgian Congo. Personal precautions including adequate clothing doubtless play a part, and it is possible that prolonged residence in a danger area is necessary before the probability of infection becomes evident. If this is not so it may well be that after the War some of those serving in the British Army in Africa may demonstrate the disease at home.

Onchocerca

The various species of *onchocerca,* Diesing 1841, belong to the phylum *nematoda* and the family *filaroidea* all members of which are ovo-viviparous threadworms. Of the several species of onchocerca only two, which are probably the same are known to affect man. These are *o. volvulus,* Leuckart 1893, the African, and *o. caecutiens,* Brumpt 1913, the American variety. Brumpt supported his claim for a separate species on account of differences in the size and number of the genital papillae, though he admitted that these were inconstant. Calderon (1919) also described minor differences, but Fulleborn (1924) insisted that they were morphologically indistinguishable, an opinion which is

*The case reported by Levy (1939) must be regarded as unproved in the absence of the discovery of nodules or microfilariae.

generally held to be correct. Other species of onchocerca are common parasites of lower animals, *o. gibsoni* in cattle and *o. reticulate* and *o. cervicalis* in horses. *Filaria repens* and *dirofilaria immitis* are common parasites in dogs. It is probable that certain animals, in particular the eland and the buffalo form a reservoir for *o. volvulus,* a circumstance rendering eradication of the disease impracticable in Africa where herds of game abound. Africans say that they have seen nodules in domestic goats, on which Simulium is known to feed, but there is as yet no proof that these are caused by the human species of worm. It may well be that onchocerciasis is primarily a disease of animals comparatively recently acquired by man.

The life history comprises four main stages :—

1. Adult, found in man the true host.
2. Egg, found in man.
3. Microfilaria, found in man.
4. Larva, various forms found in insects, usually Simulium, the intermediate host.

N.B.—Microfilariae have in many instances been referred to as larvae, but as the two stages of development are quite separate it is important to distinguish between them. In this paper the word larva refers exclusively to the stage described under that heading below, *i.e.*, a stage of development in the insect host.

Onchocerca Volvulus

1. Adult.—Adult male and female worms are found usually, though not always, in subcutaneous nodules or cysts. Generally nodules contain more than one pair and there are usually more males than females. Some of the smaller nodules contain immature adults showing no signs of reproduction. They are coiled up in endothelial-lined channels, probably derived from lymph vessels and it is impossible to dissect them out whole, though if a freshly removed nodule is slightly incised and placed in warm normal saline a worm will sometimes emerge and its removal may be assisted with forceps. The method whereby the nodule is partly digested by the gastric juice of a dog is unnecessary. The question of whether the adults ever leave the nodules or can live in the tissues is of great practical importance. Hisette (1932) said that in 1,000 cysts he had seen one only in which the worm was not completely enclosed, but in the series of cases reported below a portion of worm was found protruding on many occasions. Several cases too have been recorded wherein the adult was found loose in the tissues unassociated with reticulo-endothelial reaction. Dyce-Sharp (1927) found one in an amputation stump, Van Den Berghe (1936 and 1941) reported 5 cases, 2 of which were subcutaneous in the trochanter region, and Nettel (1941) published a

microphotograph of one lying loose among muscle fibres. Moreover not all cases with positive skin snips have nodules. Dyce-Sharp (1936) found 55 per cent. and Strong (1934), 91 per cent. without nodules.

Adult *o. volvulus* is distinguished from other thread worms affecting man in having annular, very slightly oblique cuticular striations. *Wucheraria bancrofti* has a smooth cuticle without appendages at the head, *acanthocheilonema perstans* a similar cuticle with head appendages whilst *filaria loa* has rounded cuticular bosses. The adult form of *agamofilaria streptocerca* which might be confused with *o. volvulus* having also intracutaneous microfilariae is at present unknown.

The male measures some 20-40 mm. x 0·2 mm. and is a white threadworm with a slightly spiral tail, bulbous at the tip. There are two pairs of preanal, postanal, and intermediate papillae and two unequal spicules. The female is much larger, sometimes as much as 300 mm. x 0·5 mm. but the cuticular striations are less marked and the head is rounded.

The duration of life of *o. volvulus* is unknown, but there is reason to believe that it is very long, possibly even as long as that of the host. Adult *f. loa* have on many occasions been removed from the conjunctiva 15 or more years after the host has left the tropics. The writer has seen one case in London of 12 years duration, and in the case of onchocerciasis the patient's history frequently indicates that nodules have been present for 20 years. Moreover it is observed that head nodules are often relatively as well as actually larger than in children. Hisette (1932) reported that when the worms were killed by injection of toxic substances into or incision of the nodule the lump disappeared " like snow." When nodules are present the existence of living threadworms may be assumed, though a certain number of cystic nodules have been found to contain dead and degenerating worms.

2. Egg.—Reproduction is ovo-viviparous. Inside and around the gravid females within the nodules can be seen large numbers of thin transparent envelopes, oval with a point at each end, containing a coiled up microfilaria. The chitinous shell is striated and measures about 50 μ. x 40μ. (46-61 x 30-51, Strong). The contained embryo measures 260-290 μ. and appears fully developed.

3. Microfilaria.—The microfilariae of *o. volvulus* and *o. caecutiens* are indistinguishable. They are found chiefly in the skin, mammary gland, eye and lymph glands, and rarely (Rodhain and Gabrilov 1935) in the spleen and kidney and in the perilobular connective tissue of the liver. They are found only occasionally in the blood and in the cerebro-spinal fluid (Hisette 1932 and Van Den Berghe 1941), where their presence may be

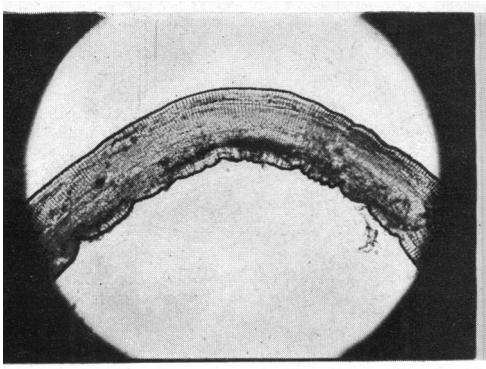

FIG. 3.

Adult onchocerca volvulus showing cuticular striations.

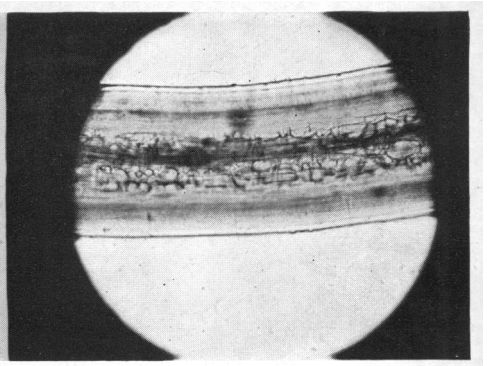

FIG. 4.

Adult Loa loa, showing cuticular bosses.

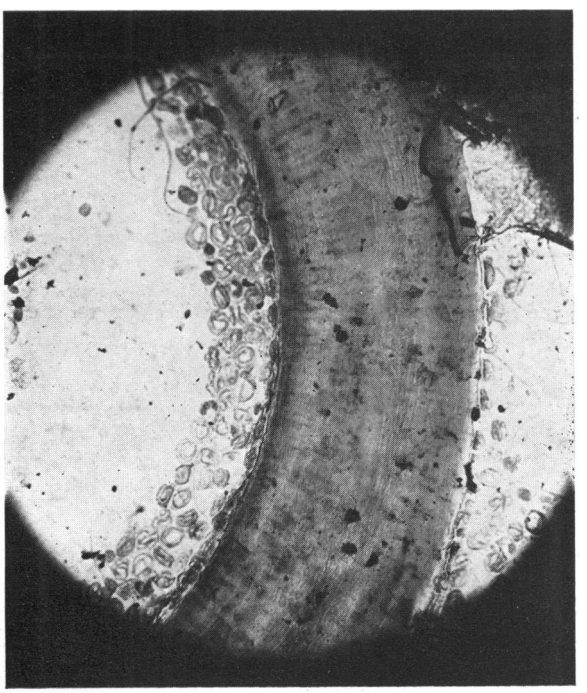

FIG. 5.

Microphotograph of scraping of nodule contents, showing adult female with masses of eggs.

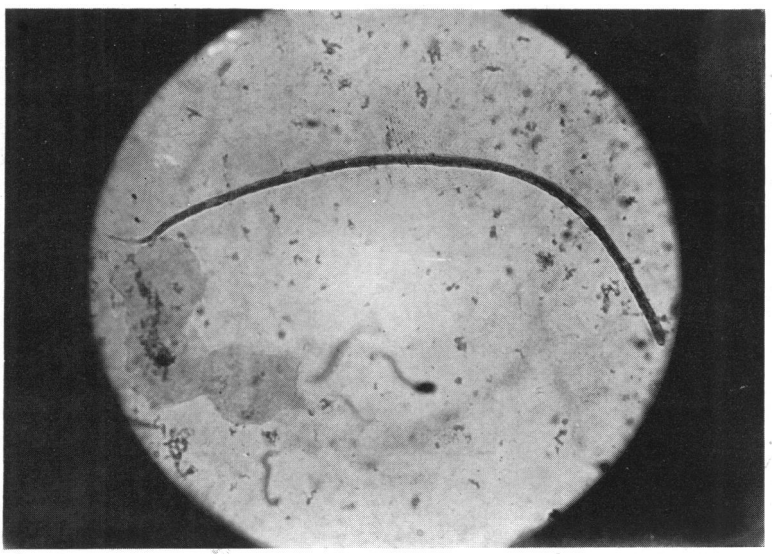

FIG. 6.

Microfilaria volvulus from anterior chamber of eye. Shows clear areas at head, end of anterior quarter and tail. Note characteristic attitude in death and the absence of sheath.

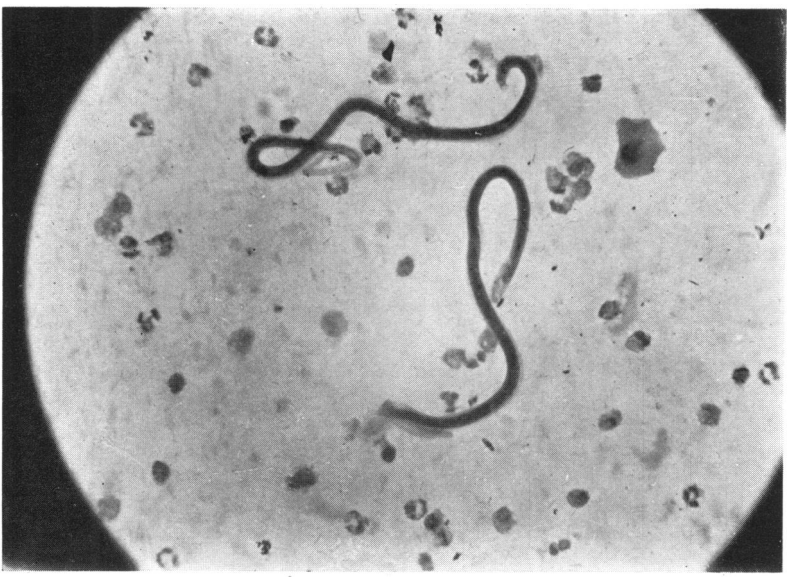

FIG. 7.

Microfilararia loa, from blood. (Same magnification as above). To show sheaths.

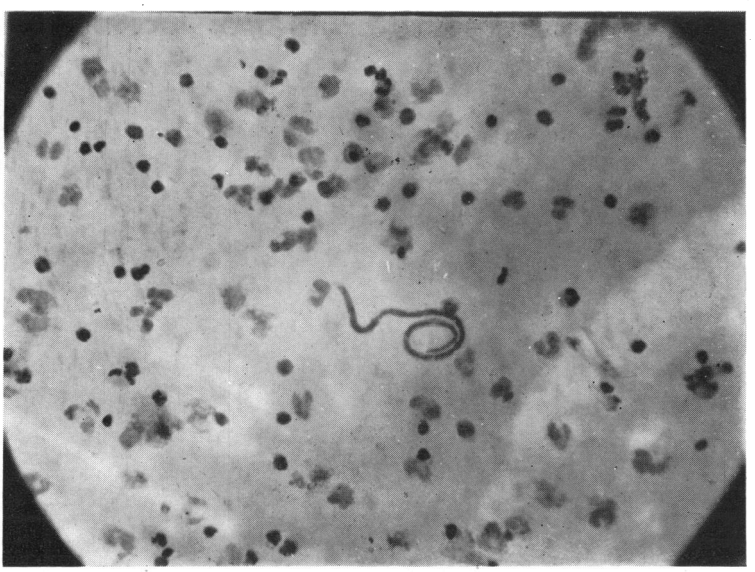

FIG. 8.

Microfilararia perstans from blood to show characteristic attitude in death, small size and absence of sheath.

a contamination due to the passage of the needle through infected skin. Microfilariae live within the tissues but are also endolymphatic passing along the lymph channels and resting in the lymph nodes of which the inguinal are commonly and the others rarely enlarged. They are definitely dermotropic. There is some doubt as to whether they are positively (Hisette 1932), or negatively (Torres Estrada 1942), phototropic. Experiments at Accra suggest that, if anything, the worms dislike light. When placed in normal saline on a slide from which all light except that passing through the microscope has been excluded some reduction in the number of microfilariae in the field was noted. Similarly if a slide is flooded with saline and one half exposed to daylight and the other half shaded more worms are to be found in the shaded area. While living they cause no tissue reaction but when dead excite a considerable but localised inflammation.

Microfilariae of onchocerca are most readily obtained by teasing with a needle a small snip of skin or conjunctiva, or by aspiration of an inguinal lymph gland. They are seen to be unsheathed and with a nuclear column, the remnants of an intestine, stretching from near the tip of the slightly bulbous head to within 15 μ. of the tip of the pointed tail. The size is approximately 300 μ. x 8 μ. and there are three clear areas free from nuclei, at the tip the head, at the end of the anterior quarter and at the tip of the tail.

Differentiation from other microfilariae is relatively simple. The lack of a sheath immediately distinguishes it from *mf. bancrofti* and *mf. loa*. *Mf. perstans* is unsheathed but much smaller and the nuclear column reaches to the tip of the rather blunter tail. *Mf. streptocerca* is most likely to be confused since it too is found in the skin and is unsheathed though considerably smaller. *Mf. ozzardi* and *mf. malayi* are unlikely to be confused with *mf. volvulus*. The attitude in death is generally characteristic, unless the worm has died in a viscid medium such as hydrocele fluid, (Holden 1944). *Mf. volvulus* lies in a gentle curve with a bend at the tail, *mf. loa* and *mf. bancrofti* assuming several somewhat angular curves and *mf. perstans* being more or less coiled up. *Mf. streptocerca* when dead is straight with a crook at the tail looking like a walking stick.

Fulleborn and Simon (1913) give the following measurements. Total length alive 298 μ., when fixed 269·2 μ. Width 0·8 μ. In percentages of length the nerve ring is at 24·2 per cent., the genital cell at 69·51 per cent. and the last tail cell at 95·61 per cent. The corresponding figures for *mf. bancrofti* are 19·6 per cent., 70·6 per cent. and 95·1 per cent.; and for *mf. loa* 21·6 per cent., 68·6 per cent. and 99-100 per cent. *Mf. perstans* and *mf. streptocerca* are much smaller, the latter measuring only 180-240 μ. x 3 μ., Macfie and Corson (1922). Ochoterena (1930) gives the following percentages for *mf. volvulus*, non-nucleated 5·11 per

cent., prenervous 24·2 per cent., excretory pore 34·5 per cent., cells of Rodenwalt 63 per cent., anal pore 90 per cent., and end of nuclear column 95 per cent.

The duration of life is unknown but is probably considerable. Personal observation has shown them in the anterior chamber 8 months after removal of all discovered nodules. Microfilariae which live in the blood are more convenient for experiment. Fulleborn injected intravenously a normal dog with *mf. repens* and found the microfilariae present $2\frac{3}{4}$ years later, and Gonnert (1942) injected himself with blood infected with *mf. loa* and *mf. perstans* and found *mf. perstans* present in small numbers 3 years later, though *mf. loa* persisted only 5 days.

4. Larva.—The life history of *o. volvulus* in *simulium damnosum* has been investigated very completely by Blacklock (1926) and confirmed by Van Den Berghe (1941) and Vargas (1942). Microfilariae are ingested as the fly bites through the skin to suck blood, and there is evidence that the worms are attracted to the site. They enter the alimentary canal and pass out, probably through the oesophageal diverticulum, to the thoracic muscles where they are found within 20 hours. Any microfilariae which fail to leave the stomach within 24 hours are digested. Development occurs in the thoracic muscles, the larva first becoming a somewhat immobile sausage-shaped body with a caudal spine. At this stage it measures 166-425 μ. x 18-43 μ. Several ecdyses occur and the larva becomes longer and thinner, develops an intestine and measures at this stage 350-450 μ. x 17 μ. It is now capable of development to maturity and makes its way to the proboscis to await an opportunity for entering a warm-blooded animal. While in the proboscis the size may be up to 560-660 μ. x 18-28 μ. As many as 236 larvae have been found in a single fly, though a heavy infection usually kills the insect. Larvae are found in the mouth-parts of Simulium only when the temperature is between 88° and 49° F. (Blacklock 1926).

Nothing is at present known of the development of the worm in man before full maturity is reached.

The Intermediate Host

Various species of Simulidae are known to carry onchocerca, and since an essential stage of development occurs in the insects they are hosts, not merely vectors. Direct infection from man to man is therefore impossible. Man, in whom the sexual stage occurs, is the true host and the fly the intermediate.

The following species of Simulium, or more correctly Eusimulium, are known carriers of human onchocerciasis :—

In America. *S. ochraceum*, Walker 1861. *S. metallicum* (=*s. avidum*), Ballardi 1857. *S. callidum* (=*s. mooseri*), Dyar

and Shannon 1927. In addition *s. emboni* and *s. dinelli* were suggested by Robles in 1916.

In Africa. *S. damnosum. S. neavei. S. adersi.* Possibly also *s. reptans* and *s. lineatum.*

S. reptans occurs in Europe, especially Spain and Italy and even in England, and there are other European species, including *s. columbac zense,* the Golubacser fly. This is at times a scourge of cattle in the Danube valley, maddening them by their painful bites and causing them to rush into the river and drown, or causing death by the toxins of the bite. On one occasion in 1923, 16,474 domestic animals died from this cause, not from filariasis, though there were no human deaths possibly on account of the protection of clothing.

Intermediate hosts other than Simulium are possible, though not so far proved. Species of *culicoides* carry *mf. perstans* in man, and *o. gibsoni* in cattle, and *culex nebeculosus* transmits *o. cervicalis* in the horse. Strong (1926) found small numbers of *mf. volvulus* in *glossina palpalis,* the tsetse fly. No *mf. volvulus* have been found in anopheles mosquitoes after they have bitten infected skin, but they have been found in the gut of certain other insects in similar circumstances though no developmental stages have been discovered. Rodhain and Van Den Branden (1916), found *o. volvulus* in *aedes aegypti* and *cimex rotundus* 4 days after feeding, and Blanchard and Laigret (1924) found it in ticks, *ornithodorus moubata.* Vargas (1941) discovered the worm in certain arthropods in the following percentages, *ornithodorus turicata* 44 per cent., *triatoma picturata* 8·3 per cent., *pediculus* 4 per cent., and *cimex* 1·8 per cent.

Undoubtedly the main carriers are, in America *Simulium ochraceum,* Ochoterena (1930) which is particularly attracted to man for blood, Guiaquinto Mira (1937), and in Africa *S. damnosum,* Blacklock (1926). The infectivity rates naturally vary widely according to place and time, Blacklock (1926) found 2·5 per cent, in Sierra Leone, McMahon (1940) 9 per cent., all *s. neavei* in Kenya, and Van Den Berghe (1941) 33·3 per cent. in the Kasai district of the Belgian Congo.

Simulium Damnosum

S. damnosum, also known as the " Buffalo gnat " on account of its hump-backed appearance, has several local names, the " Kilteb " or " Kunteb " fly in the Sudan, the " Jinja " fly in Kenya, " Mbwa " in Uganda and " Mooli " in Sierra Leone, but in the Gold Coast it has no native name, being regarded simply as a form of day-biting mosquito.

It is a small black, or rather very dark brown dipterous insect about 6 mm. in length, and armed with short strong jaws with

which it bites through the skin. The blood-sucking apparatus is less highly developed than in the mosquito. Only the female sucks blood, and the size of the ovaries is proportional to the quantity ingested. The bite is usually on the leg especially around the ankles and is very painful, a wheal with a diameter of 5-8 mm. and a central red spot develops, and sometimes a trickle of blood runs down from it.

The saliva of Simulium contains an anti-coagulin like that of viperine snakes; many haemorrhages were found in the viscera of animals killed by *s. columbaczense*. The American varieties differ in that they bite about 5 feet from the ground and therefore more commonly on the head, probably on account of the shade in the coffee plantations and partly perhaps because of the better clothing of the people. *S. reptans* also bites on the head. Van Den Berghe (1941) found that Africans standing on a table were not bitten by *s. damnosum* though those standing on the neighbouring ground received many bites. Normally the fly does not travel far from the river of its origin, but is found in large quantities within 5 yards of the stream, though in dull weather and after rain it may travel 500 to 700 yards. Bryant (1935) reported that it occasionally becomes domesticated living in native huts but not in the surrounding country. It dislikes sunlight and usually shelters in the long grass and does not appear to search for its prey but waits until the grass is touched. Unlike the mosquito it feeds by day, particularly during the shade of early morning and late evening, but not as a rule during or immediately after heavy rain. Blacklock (1923-25) made very complete investigations in Sierra Leone. He performed experiments on himself and other volunteers and found that *s. damnosum* remained on the skin for an appreciable time before making its bite felt and filling with blood, indicating that considerable trauma is needed to reach a blood vessel. The victim feels a vague scratching for one minute following by pricking and finally intense irritation persisting for some 10 minutes. Scratching somewhat relieves the irritation. The fly sucks blood for 1½ to 5 minutes, and though spray will normally drive it away even gentle immersion in water does not stop it feeding when it has begun to suck blood. It can live under water for 5 minutes by means of air bubbles attached to it, and having finished the meal rises to the surface and flies away. It was found possible to infect 80 per cent. of the flies if the bite was near a nodule as opposed to only 17 per cent. if the fly was allowed to bite where it wished. Strong (1931) found that the bite of Simulium attracted microfilariae to the area. The duration of life in captivity is usually 3 or 4 days, though some lived as long as 10, and it is probable that in natural conditions a greater span is normal for the larval stage of *o. volvlus* lasts 7 to 10 days.

The female Simulium in due course lays her eggs in a gelatinous

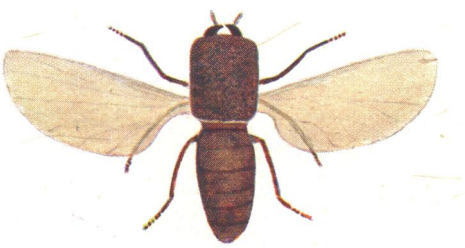

PLATE I.

Sketch of Simulium Damnosum (after Austen).

mass of about 500 on a stone or plant-stem in running water. In 2 to 3 weeks a larva hatches and attaches itself by its posterior sucker to a stone to avoid being washed away by the stream. It has external rectal blood-gills and can live only in highly oxygenated water. Bequaert (1934) found that the optimum rate of flow was 4·5 k.p.m. with extremes of 1·1 and 30 k.p.m., and that the temperature could vary from just above freezing point to 30·6° C. The danger areas where highly oxygenated water occurs are around rippling brooks in the rainy season and near the large rivers whose rocks are exposed in the dry weather. Between two such areas of distinct seasonal endemicity there is often a portion of country where onchocerciasis is uncommon. The larvae seem to prefer an area where the stream is shaded. In due course pupation occurs and the cocoon also is attached to stones. The adults on hatching may become infected by biting a man or animal visiting the stream for water or obtaining food from the fertile ground beside the watercourse.

Clinical Manifestations of Onchocerciasis in Man

Symptoms.—Accurate histories, and even an estimate of age are difficult to obtain and frequently inaccurate when dealing with a backward and illiterate people. The most reliable information is in respect of the duration of blindness and inability to work. Skin nodules are the first lesions to be noticed followed by irritation of the skin, known in Africa as "Craw craw," and this is usually most troublesome at night. In many cases no doubt diseases such as scabies are complications. Ocular complications probably do not occur for some years (Hoffmann (1930) 5 years) but the interval varies with the distance of the nearest nodule from the eyes and probably too with the age and general health of the patient. A chronic conjunctivitis with subacute exacerbations is the first ocular complaint to which is added a degree of photophobia when corneal complications begin. Meanwhile there may be some oedema of the eye-lids as well as in other parts of the body, the face and ear mainly in the American type and the genital area in the African. Lesions of the anterior segment of the eye are insidious, giving rise to little except very slow but steady deterioration of sight, but those of the retina cause entoptic phenomena particularly "fiery serpents," Hisette (1932), presumably due to direct retinal stimulation. Though the course is usually prolonged, Bryant (1935), reports that in "Sudan Blindness" retinal degeneration is often complete within 2 to 5 months of the onset of symptoms. Hemeralopia is a frequent complaint and one which would be expected from the nature of the retinal lesions. Unfortunately the majority of patients reported below who complained of this symptom had severe ocular lesions and it is difficult to assess

how much of the night blindness was due to general visual deterioration, or to deficiency of vitamin A.

The occurrence of more rapid progress is suggested by the finding of established ocular changes in a child aged 4 years. Robles (1919) states that a case has been reported in a child of 2 months who had a nodule and eye trouble, and this suggests the possibility of a congenital origin. In general the finding of the more advanced ocular lesions in those over middle age shows that chronicity is the rule, and it is probable that the disease generally runs some 10 years before producing complete blindness. There is little to indicate that the disease is self limiting, and the prognosis must be regarded as thoroughly bad.

The Nodules.—These are the most obvious, commonest and by themselves least important manifestations of the disease. They are lumps beneath but not attached to the skin and vary in size

FIG. 9.

Excised nodules, including pedunculated scalp protuberance.

from that of a pea to an inch or more in diameter. They feel like rubber and are free from pain or tenderness. They may be globular or lobulated and frequently several are found close together, some perhaps being so small as to escape palpation. A peculiar and striking feature is that the site of predilection is over a bony

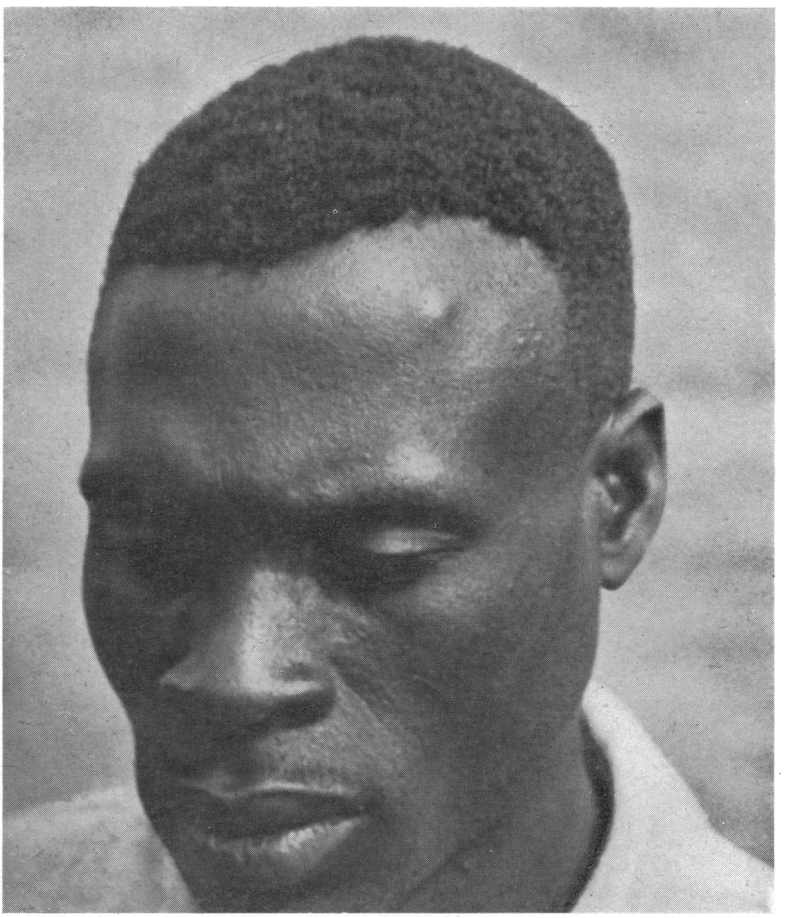

FIG. 10.

Frontal nodule, typical small nodule.

area and the mass being attached to the deep fascia or to the periosteum. Cases have been reported in which the cranial bones have been eroded and even perforated (Robles 1919). In one case at Funsi several nodules were found contained in a pedunculated extension of the scalp, the whole mass feeling like a bag of cherries. Quite frequently the nodule is cystic containing sterile detritus, and rarely they become infected. Barlovatz (1940) reports inflammation in the nodules in the prodromal stages of typhoid and typhus. The number of nodules varies widely, being smaller in the American type. In Africa, Strong (1937), examined a man with 150 nodules though the largest number he saw in Guatemala was 19, and Hisette (1932) records that Mutonji removed 126 before further operation was refused. In the cases reported in this series the largest number of nodules discovered was 16. Bilateral symmetry was strikingly common not only as regards the situation but also the number of nodules on the two sides.

The site of the nodules is of importance, for the nearer they are to the eye the more probable are ocular complications; the eyes are

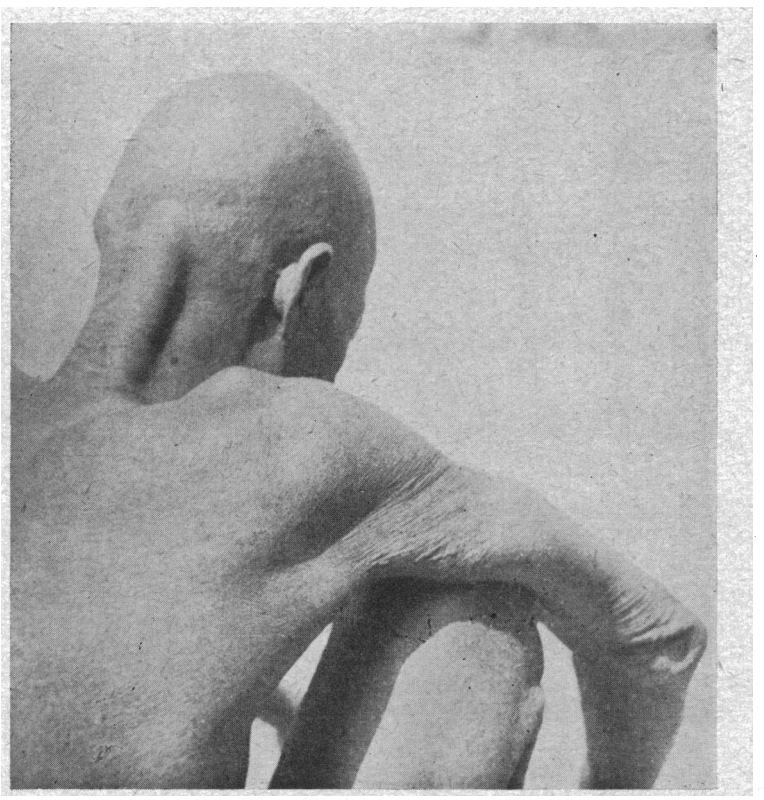

FIG. 11.

Parieto-occipital nodule. Note also "elephant skin" on arm.

almost invariably involved when the nodules are present on the scalp. In America it is reported that all or nearly all (Nettel, 1941) are on the head, and particularly around the ear or even in the meatus. This, however, is not the case in Africa and was one factor which led early observers to believe that eye lesions did not occur. In Africa, for the most part, nodules are found on the ribs

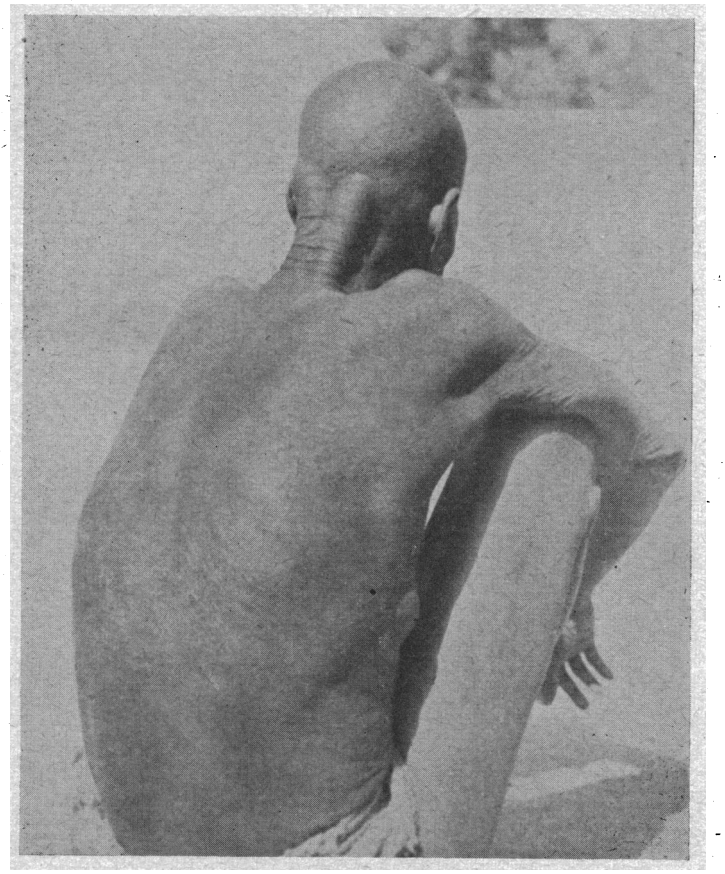

FIG. 12.

Chest nodule (also shows skin changes).

(in the series reported usually on about the 8th rib in the mid-axillary line), the anterior and lateral aspects of the iliac crests and the trochanters; less commonly on the joints especially the knee, and over the spine and sacrum. Head nodules were found at Funsi in 50 per cent. of the eye cases and 20 per cent. of the total, and preponderated in children. The absence of nodules from the sternum, clavicle and other anterior bones was noted.

The site of the nodule can be only vaguely connected with that of the bite. It is true that the frequency of head nodules in America is associated with the habit of the American Simulidae of biting several feet from the ground in the shade of the coffee plantations, but in Africa most bites occur on the legs and the commonness of certain situations precludes the possibility of the site of the bite being the same as of the nodule. Local bruising,

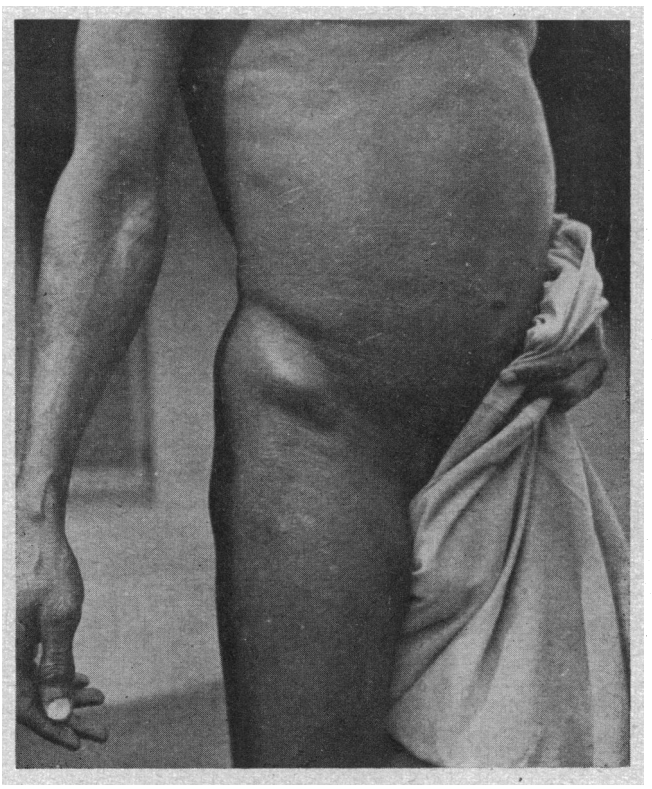

FIG. 13.

Bilateral symmetrical iliac nodules (one side excised).

such as on the hips and trochanters during sleep on the ground, may encourage the worms to choose certain sites, and Van Den Berghe (1941) suggests that the constriction of a hat band may have some bearing on the formation of periauricular nodules.

The irritation caused by the quiver strap commonly worn may account for the frequency of nodules on the side of the chest at Funsi, for elsewhere the iliac crests were the commonest situation. Head nodules may be common in children because they are short and the fly bites relatively higher up the body. It is difficult to

explain the marked tendency to bilateral symmetry. Excision is generally easy under local anaesthesia, but nodules attached to the bones of the skull may present a little difficulty.

Complications other than ocular.—Between the date of discovery of the nodules (1893) and that of the eye lesions (1915) a number of reports appeared relating to elephantiasis associated with the finding of *microfilaria volvulus* in the lymph glands draining the affected part. The degree of oedema seems always to be less than

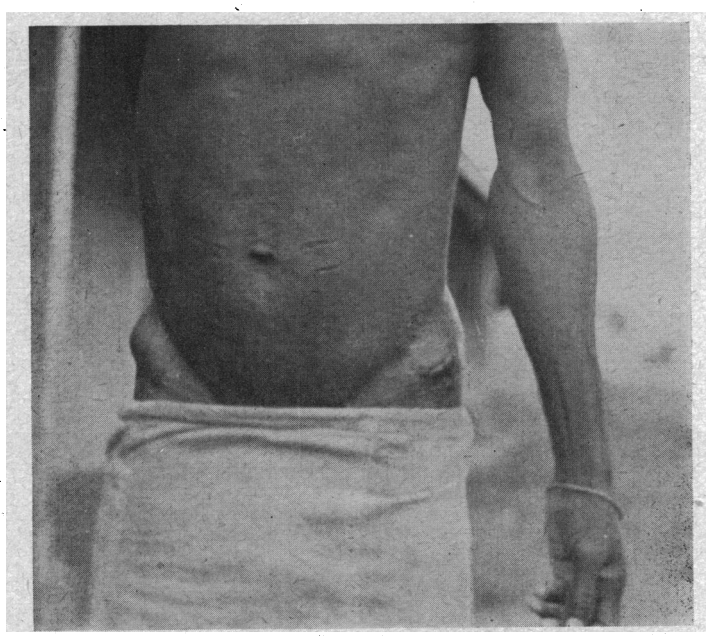

FIG. 14.

Bilateral symmetrical iliac nodules (one side excised).

that caused by *filaria bancrofti* and in Africa affects chiefly the genital area and sometimes the lower extremity giving rise to oedema of the leg or a synovial effusion in the knee. Besides the oedematous swellings hydrocele is common and typical mf. volvulus can be found after centrifuging the fluid. Accurate identification of the worm is necessary for African patients are frequently found to have more than one form of filaria. Rodhain (1931) suggested that the oedema was due to a secondary infection, usually streptococcal, but in view of the proved changes elsewhere caused by dead microfilariae and since the oedema is often transient this hypothesis does not seem proved. In America a somewhat different condition is found, for the swellings are chiefly on the face and ears and give rise to " Coast Erysipelas " which may assume

an acute form with a red shiny skin and increased temperature, or a chronic hard oedema in which the skin is a livid green and the pinna may be twice the normal size (Robles 1916). Doubtless the site of the oedema is associated with the position of the nodules and to some extent with that of the bite.

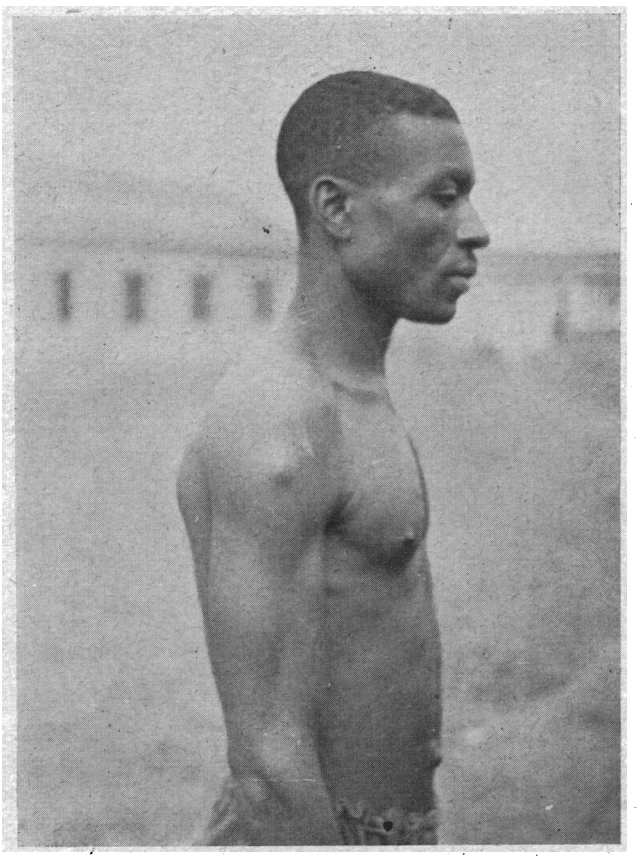

FIG. 15.

Lipoma simulating nodule.

Skin lesions are common and have been called scleroderma, lizard-skin, pseudo-ichthyosis and lichenisation by various authorities, but the native name of " elephant skin " is perhaps as descriptive as any. The dry wrinkled skin frequently causes the patient to look far older than his years. The native word " craw craw " refers to any irritative dermatitis, usually scabies. Other factors, such as avitaminosis, must be taken into account in the production of crazy pavement skin on the legs and thighs, but

there seems every reason for regarding the prevalent skin lesions as filarial. Even in the African variety there is sometimes thickening of the skin of the face and ear leading to a degree of onchocercal facies, which must be distinguished from leprotic thickening. *Mf. volvulus* is not found in the blood except on very rare occasions, but an eosinophilia is constant, reports averaging about 30 per cent., though sometimes being as high as 70 per cent. (Montpellier, Lacroix and Boutin 1921). In the cases seen at Accra the average was 38 per cent. with a maximum of 55 per cent. It was impracticable to perform blood counts in the Bush. Some degree of eosinophilia is almost universal in Africans for nearly all suffer from systemic or intestinal helminthiasis. Gutierrey (1931) and Stephanopoulo (1940) have described complement fixation tests but their reliability is uncertain and in any case more accurate checks on diagnosis are readily available. Antigen can be prepared from dessicated adult worms but at Accra they sometimes gave a positive reaction in controls indicating lack of specificity. Van Hoof (1934) reported moreover that intradermal antigen failed to give a positive skin reaction in 12·5 per cent. of proved cases. The degree of antibody reaction which the body may produce appears insufficient to prevent further infections, judging by the number of nodules which may occur in a single patient. Infection confers no immunity.

The microfilariae reported on rare occasions in the cerebro-spinal fluid are probably contaminations from the skin.

Ocular Lesions

The lids and orbit.—For the most part there is little sign of abnormality in these structures, though sometimes a temporary oedema of the lids may occur and is in some cases accompanied by proptosis. Two such cases were seen at Accra in the middle of 1943 in which the structures returned to normal in a few days. In one instance there had been a previous attack. The rapid and complete resolution and a high blood eosinophilia accompanied by the absence of microfilariae in the blood suggested onchocerciasis, but at that time the importance of taking skin snips to confirm the diagnosis had not been appreciated. Scott (1944) has reported similar cases. Examination of a skin snip for *mf. volvulus* is always indicated in Africans with proptosis of obscure origin.

The conjunctiva.—Conjunctivitis is not a marked feature of the disease, unless accompanied by trachoma or some pyogenic infection. The eye is usually white and free from vascular congestion though increased lacrimation and some photophobia occur when, as is usually the case, the cornea becomes involved. In the later stages the conjunctiva becomes thickened and pigmented and has

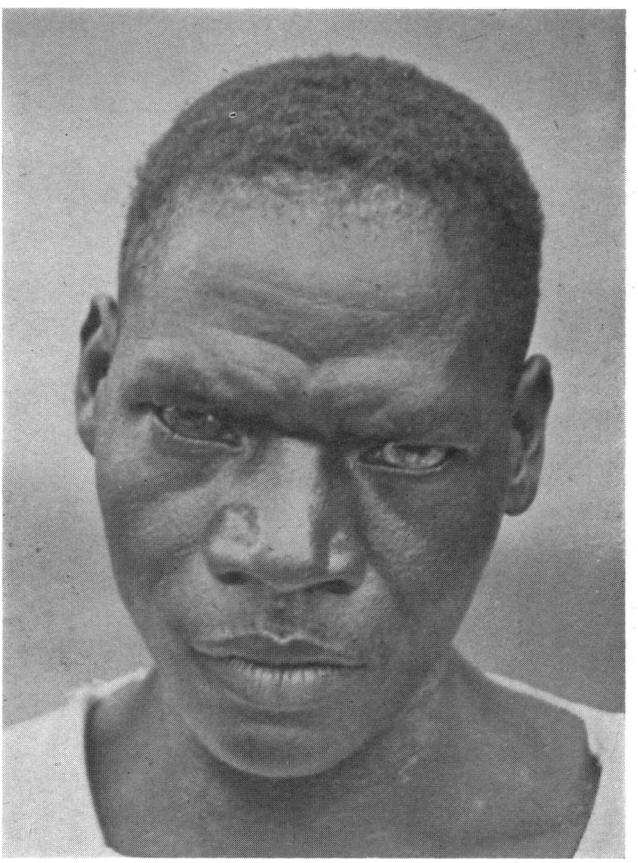

FIG. 16.

Blind patient showing corneal opacities (choroido retinal degeneration also present).

a marbled appearance. No microfilariae have been seen in the conjunctiva with the corneal microscope, though their presence in the majority of cases is proved by examination of snips. This indeed is one of the most satisfactory methods of establishing or confirming the diagnosis of ocular onchocerciasis. Under cocaine anaesthesia a small piece of bulbar conjunctiva is seized with toothed forceps and abscised with scissors. No stitch is necessary for repair and patients do not resent this procedure. Captain Holden found that the simplest and quickest method was to examine with the low power of the microscope a fresh unstained specimen in which movement of the worm attracts immediate attention. This is done by placing the snipping in a drop of normal saline on a slide and after slight finger pressure on the coverslip the worms can be seen, usually at the cut edge of the tissue as though trying to escape into the fluid. A permanent stained specimen may be made, and in all cases in this series the worm was proved to be *mf. volvulus*.

The cornea.—The cornea is involved in nearly, though not quite every case in which the eyes are affected. The typical appearance is of grey nummular opacities in the stroma. Though found most commonly in the inter-palpebral area, especially on the nasal side, they may occur anywhere in the lower two-thirds including the pupillary area though not it seems in the region usually associated with trachomatous pannus. The opacities vary little in size and when fully developed measure about 0·6 mm. in diameter, the edges are ill-defined and within recent lesions the dead body of a microfilaria may be seen lying straightened out usually in a horizontal direction. It has been noted that *in vitro* the dying worm assumes the same attitude. The appearances of the two corneae are usually strikingly similar. On one occasion only in more than 1,000 examinations the writer had the good fortune actually to see a living microfilaria struggling in the corneal stroma. It caused no visible reaction but on the next day it was dead and around the corpse the typical opacity developed being fully formed in about one week. It was thought by earlier writers that the microfilariae entered between Bowman's membrane and the epithelium, but in the present series of cases no worms were seen in this situation. In the early stages, before the epithelium becomes involved, corneal sensation is normal and vascularisation absent. The typical corneal lesion therefore is an avascular nummular interstitial keratitis affecting the interpalpebral area.

As the disease progresses the nummular opacities increase in number and may become confluent, giving rise to a frosted glass appearance in the lowest third of the cornea. In this stage the epithelium degenerates and superficial vessels appear producing a form of pannus. Corneal vascularisation, however, is usually very

slight. Sometimes calcification follows leading to dehiscence of the abnormal epithelium though true ulceration does not occur in the absence of secondary infection. The epithelial changes seem to be secondary to those in the substantia propria and are probably caused by a disturbance of corneal nutrition. Marked folding of Descemet's membrane may occur producing in some cases the appearance of a fan at the back of the cornea due no doubt to the greater degree of inflammation and contracture below.

In advanced cases the inferior portion of the cornea becomes a mass of chronically inflamed tissue. Ciliary injection previously absent may appear, and the corneal sensation, normal in the early stages is now diminished.

Nummular interstitial opacities unassociated with epithelial degeneration may resolve completely in the course of two or three months if further microfilariae can be discouraged from entering the cornea. Formation of scar tissue is not inevitable.

It is assumed that the portal of entry is from the conjunctiva via the sclera. Though microfilariae are frequently seen close to the endothelium it is unlikely that they penetrate the extremely resistant Descemet's membrane, and certainly nothing seen with the corneal microscope indicates a perforation of this water-proof structure.

Lesions of the cornea were by far the commonest in the Funsi series, 45 of the 51 cases being affected.

The anterior chamber.—Microfilariae are very commonly seen, sometimes in large numbers, swimming vigorously in the aqueous. The focal beam of the slit-lamp is ideal, almost essential for demonstrating them and they assume the form of a golden wriggling thread. Frequently several join together resembling an octopus and sometimes they attach themselves to a strand of pupillary membrane which is almost invariably found in African eyes. When illuminated they are usually found to be moving upwards against the convection current in the corneal portion of the aqueous. The best place to begin to search for them is in the infero-nasal quadrant just behind the cornea. The microfilariae are not always seen even in eyes known to be infected, and a few minutes in the beam of the slit-lamp makes them difficult to find though they appear again after a short exposure to subdued daylight. They are at least as numerous and active at midnight as at noon. The living worms seem quite harmless and so far as can be ascertained cause no photopsiae when crossing the pupil. When dead, however, they fall to the bottom of the anterior chamber forming a grey-brown mass and are associated with changes described under irits. Microfilariae can be aspirated from the aqueous for identification. If a hollow needle is employed it must be of wide bore for it is unlikely that a worm 0·3 mm. long will be sucked in head on. Such an

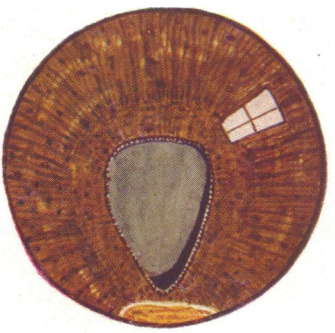

PLATE II.

Sketch to show the pear-shaped pupil and the mass at the base of the anterior chamber in Onchocerciasis.

operation, however, seems to carry an unduly high risk in the case of Africans who, in addition to having difficulty in understanding what is required of them, are often frightened and liable to make unexpected movements. It seems a safer procedure to make a valvular incision with a small keratome and to aspirate the aqueous through an anterior chamber irrigation nozzle attached to a small syringe, or even to depress the lip of the wound and catch the flow in a small hollowed instrument. The risk of direct aspiration in relatively undamaged eyes simply as a confirmation of the diagnosis seems unjustifiable especially since other simpler methods are available.

After aspiration some weeks elapse before many microfilariae are to be seen in the anterior chamber, an indication that worms do not readily enter and leave the aqueous.

The iris.—Iritis of the usual plastic type with posterior synechiae is not a common feature of the disease though it occurs occasionally. Rather more common are small star-shaped patches of connective tissue in the stroma causing some local contracture, but by far the most frequent abnormality is a generalised atrophy of the iris pigment. This produces a spongy appearance well described by Ochoterena (1930) as " pumice-stone iris." Small particles of iris pigment are found on the corneal endothelium, and these also account for the brown colour of the mass seen in the lower part of the anterior chamber. This mass, light brown in colour, is caused by dead worms in the aqueous and the resulting inflammatory reaction leads to downward and forward traction of the iris causing an inverted pear-shaped pupil which is one of the characteristic signs of the disease. The appearance of a downdrawn distorted pupil with an iris attached to a mass in contact with the cornea at first sight suggests the effects of a perforating corneal ulcer. In spite of the gross distortion the slit-lamp reveals a remarkable absence of inflammation in the iris except perhaps in the immediate vicinity of the mass, neither are there signs of irritation such as may occur with incarceration of the iris in a wound. There may well be some atrophy of the iris muscle for the pupils seldom dilate well even after the instillation of several doses of atropine; this is, however, to some extent the case with normal African eyes, probably on account of their habitual exposure to bright sunlight or to the fact that the stroma is heavily stuffed with pigment.

In short, iritis is of a relatively mild type and not of itself a cause of blindness.

The characteristic distorted pupil was present in 9 out of the 51 Funsi cases.

The ciliary body.—Cyclitis, indicated by the presence of keratic precipitates, is found more frequently than iritis. It is non-specific and of a mild serous type with few inflammatory cells in the

aqueous though the K.P. may be large. Though in most cases microfilariae are seen in the anterior chamber and the cornea it is by no means certain that the portal of entry whereby the worms enter the ciliary body is by the conjunctiva, though they are known to prefer the superficial layers of the body. It may well be that entry is by the ciliary vessels, long or anterior, or by the muscle insertions.

The importance of cyclitis lies chiefly in its complications, secondary cataract and glaucoma. Hisette (1932) found secondary glaucoma an important source of blindness and for this performed several corneo-scleral trephines, but at Funsi phthisis bulbi appeared to be equally common due presumably to degeneration of the ciliary body. Hisette also suggested that certain interstitial corneal lesions might be due to damage to the ciliary vessels, but for this there seems little satisfactory evidence for the upper portion of the cornea is usually normal.

Cyclitis occurred in 20 of the 51 Funsi cases.

The lens.—The lens, with the exception of the retina, is the only structure in the eye wherein no microfilariae have been seen or so far reported. Nevertheless cataract is an important source of blindness, and is considered to be due to deficient or abnormal nourishment caused by degeneration of the ciliary body.

Cataract was found in 20 of the 51 Funsi cases.

The vitreous.—In the series of cases reported below no microfilariae were seen in the vitreous in spite of careful search limited in some instances by lack of co-operation and defective mydriasis. In the absence of iridocyclitis clarity of the vitreous seems to be the rule even with marked choroido-retinal lesions though a few opacities such as are of very general occurrence were seen. There were two cases, however, in which vitreous degeneration of the " asteroid hyalitis " type was present, Silva (1925) saw microfilariae in the vitreous, using a plane mirror and with a Gullstrand ophthalmoscope. Both Hisette (1932) and Appelmans (1935) reported their occasional presence. Torres Estrada (1942) records seeing worms swimming freely in the vitreous, using a slit-lamp with a Koeppe mirror and with an electric ophthalmoscope and a plus 20 or plus 40 lens. He asserts that they are commoner here than in the aqueous, being present in all his 11 cases of which only 4 had microfilariae in the aqueous and 6 keratitis. While the possibility of confusing the situation or nature of the opaque bodies must be considered it seems highly probable that infestation of the vitreous may on occasions occur. Semadini (1943) in his sections of a severely affected eye failed to find worms in the vitreous though they were present in most other structures in the eye.

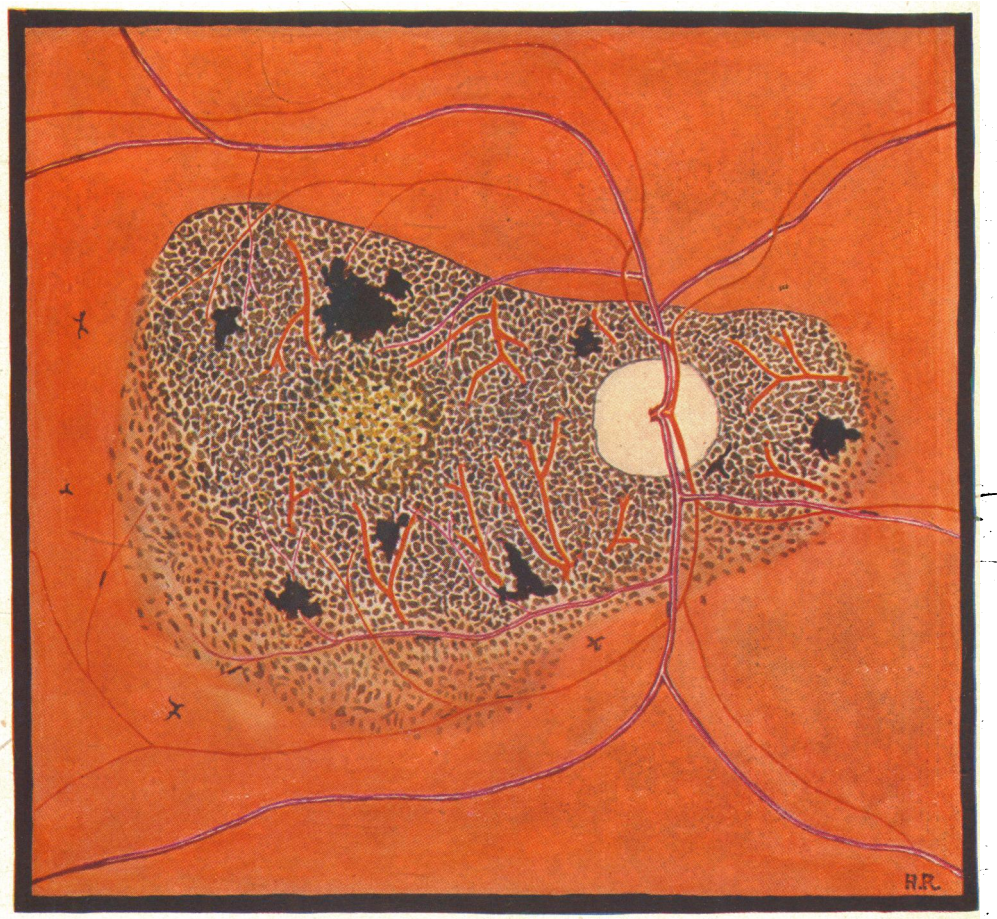

PLATE III.

Fundus oculi in Onchocerciasis, from a sketch of a case at Funsi. February, 1944.

The retina and choroid.—The fundus changes are the most striking and in many ways the most important though fortunately not the most common lesions. Having once seen a typical case it should be possible to diagnose others on sight, for the appearance is quite distinctive and unlike anything else, the nearest approach being perhaps a hypothetical combination of choroidal sclerosis with retinitis pigmentosa.

Typically there are one or more large and approximately circular areas of tapeto-retinal degeneration many disc-diameters in size situated posterior to the equator and generally extending to the disc margin. The edge is often sharply demarcated from normal areas though in most parts a gradual transition occurs. The retina is abnormally transparent and its pigment heaped into one or more masses. Nothing suggesting a dead microfilaria has been seen in the pigment aggregations. In addition to the absence of the hexagonal epithelium the choriocapillaris and the layer of medium choroidal vessels disappear exposing a dark brown background, presumably the lamina fusca, across which run large choroidal vessels which look a bright orange in colour. In the pigmented background are white streaks due to the sclera showing through the spaces occupied by choroidal vessels now occluded or by their thin atrophic walls. The background may well be described as resembling cracked sunbaked mud such as is seen on the floor of a dried-up watercourse. In surrounding areas of otherwise normal retina a few small " bone corpuscle " aggregations of retinal pigment may be present. The condition seems typically to be bilateral, though one eye may be more advanced than the other. Probably an acute stage occurs at first analagous to that in the cornea though the writer did not have the good fortune to observe this.

Hisette (1932) gave an account of the fundus changes, and Bryant (1935) described a typical case under the diagnosis of " Sudan Blindness," a condition quite common in that country causing blindness in 2 to 5 months in persons, usually men, between the ages of 7 and 70.

It is notable that in a few eyes with advanced choroido-retinal lesions the anterior segment was normal except for the presence of microfilariae in the aqueous. This suggests that the worms may enter the eye from behind, probably along the posterior ciliary vessels.

A remarkable case was reported by Wilson (1933) in which it appears that an adult *o. volvulus,* recognised by the cuticular striations was seen attached to the macula. The surrounding retina showed mild inflammation and when the worm disappeared 15 days later an area of retinal atrophy remained.

Choroido-retinal changes were found in 12 of the 51 Funsi cases, though the proportion might have been higher had not opacities in the media in some instances prevented detailed examination.

Optic nerve.—Optic atrophy of some degree and generally of the consecutive type was seen in all cases with gross choroido-retinal lesions. The disc margins were quite well defined and there was little evidence that atrophy had been preceded by more than a slight degree of swelling of the papilla. Diminution of calibre of the retinal vessels, particularly the arteries was general and perivascular sheathing chiefly around the veins was frequent. In two cases optic atrophy with marked vascular constriction occurred in the absence of other fundus lesions suggesting a direct involvement of the nerve or its vessels. Three other similar cases were seen in which the diagnosis of onchocerciasis could not be confirmed but these have not been included in the series.

Optic atrophy was seen to be present in 14 of the 51 Funsi cases.

Pathology

It was found impossible at Funsi to persuade any patient with a blind eye to have it enucleated and much of the histopathology reported below is taken from material published in earlier papers. It appears that material everywhere is difficult to obtain for pain even in the advanced stages is not excruciating. So far very few eyes have been available for microscopical examination.

The earlier observers, Calderon (1920) and others, thought that the ocular lesions were caused by toxins liberated by the adult worms into the blood stream. Ochoterena (1930), however, proved the presence of microfilariae in the cornea but it was still doubtful whether or not the lesions of the posterior segment were of the same nature. There is now no doubt that all lesions are caused by toxins released locally by dead microfilariae; the microfilariae while living appear to set up no tissue reaction. The living adults, however, do stimulate a reticulo-endothelial reaction leading to the formation of the fibrous nodule. Presumably this is a defence mechanism on the part of the host like that which occurs around a retained foreign body.

The skin.—The skin even in advanced cases may show relatively normal histology. The epidermis is normal but microfilariae occur in large numbers in the dermis sometimes lying between normal connective tissue fibres without reaction, but elsewhere surrounded by inflammatory cells. Presumably the former are worms living at the time of excision and the latter those which had died shortly before.

The nodules.—The structure of nodules varies considerably, marked degeneration being found in old ones. The capsule consists of concentrically arranged collagenous and elastic fibres many of which have undergone hyaline degeneration. Within the capsule and between the spaces in which the adult worms lie are masses of loose connective tissue and inflammatory cells, mostly mononuclear and of which a large proportion are eosinophils and plasma cells. Some of the stroma is composed of large cells, roughly square in shape with small central nuclei and cytoplasm containing very fine granules. An occasional giant cell may be seen. There are very few blood vessels.

The tortuous channels containing the adult worms are bounded by a condensation of the connective tissue and appear in some places to be lined by poorly developed endothelium. Microfilariae may be seen within the nodule, generally only in certain regions particularly around the female adults. In other cases no microfilariae are present and absence of degenerate cells suggests that the nodule is of recent formation. On the other hand the nodule may be cystic, the contents being decomposing worms, inflammatory cells and degenerative connective tissue, a form of cold abscess. Some of the smallest nodules such as are commonly found on the scalp may contain mature adults and many microfilariae.

The conjunctiva.—Living microfilariae are often seen in this structure in large numbers. Sections of early cases show little surrounding inflammation but the mild chronic conjunctivitis is probably caused by worms recently dead. In advanced cases the conjunctiva becomes thickened and irregular patches of pigment may appear.

The cornea.—The corneal microscope used on the living eye demonstrates most of the changes. The living worm has been seen moving in normal substantia propria without any sign of inflammatory reaction, and dead worms can be watched as they produce an opacity which reaches its full dimensions in some 7 to 10 days. Sections show an infiltration with chronic inflammatory cells, chiefly lymphocytes and plasma cells, but in early stages there is no destruction of the corneal lamellae so that complete resolution is possible and does indeed occur in favourable cases. At this stage the epithelium is quite normal, but when Bowman's membrane becomes eroded (Hisette, 1932) or the interstitial nummular opacities become numerous and confluent epithelial degeneration and vascularisation begin. Eventually hyaline and calcareous degeneration may supervene as in many other forms of chronic keratitis.

Folding of Descemet's membrane is due either to increased cellular or fluid content of the substantia propria or to the fibrosis

resulting therefrom. The endothelium becomes abnormal by the deposit of keratic precipitates from cyclitis and by the adherence of pigment granules from degeneration of the iris.

The sclera.—Microfilariae have been found in sections of the sclera, and Hisette (1932) demonstrated two in trephine discs.

The anterior chamber.—The light brown mass at the bottom of the anterior chamber is composed of dead microfilariae and chronic inflammatory cells. Occlusion of the filtration angle by mechanical and inflammatory obstruction gives rise to glaucoma. The local decrease in depth of the anterior chamber due to forward traction of the iris probably plays but a small part.

The iris.—Hisette (1932) published microphotographs of microfilariae in otherwise normal iris tissue. Iritis is usually confined to the lower portion where this structure is in apposition with bodies of dead worms in the angle of the anterior chamber. Distortion of the pupil is accompanied by remarkably little frank iritis and toxins liberated into the aqueous by worms recently dead must reach such a low concentration that little generalised iritis results.

Posterior synechiae and occlusion do, however, sometimes occur and in such cases the aqueous has been found to be swarming with microfilariae.

The ciliary body.—Large numbers of microfilariae have been reported in this structure by Hisette (1932) and Semadini (1943). When dead they are surrounded by a chronic inflammatory reaction sometimes ending in gross destruction of ciliary tissue leading to secondary cataract. The keratic precipitates may be large, though much exudation into the vitreous is uncommon.

The lens.—So far no microfilariae have been demonstrated in the lens.

The vitreous.—Sections have not revealed the presence of microfilariae, though their presence has been postulated on clinical grounds. Degeneration of the "asteroid hyalitis" type has already been referred to though confirmed only with the corneal microscope.

The retina and choroid.—The disturbances here are of peculiar interest and have been studied by Hisette (1932), Bryant (1935) and Semadini (1934). Microfilariae have been demonstrated in the choroid and when dead producing a reaction with mononuclear inflammatory cells and occlusion of the smaller blood vessels. As a result the outer layers of the hexagonal epithelium become heaped into masses. Though microfilariae have not been

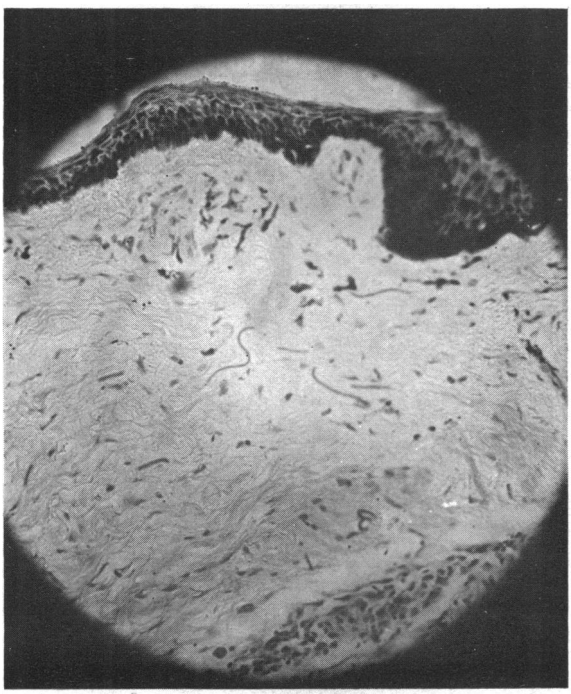

FIG. 17.

Microphotograph of section of skin. (Note the absence of inflammatory reaction around microfilariae near surface and the round cell infiltration around dead microfilaria in deeper layer).

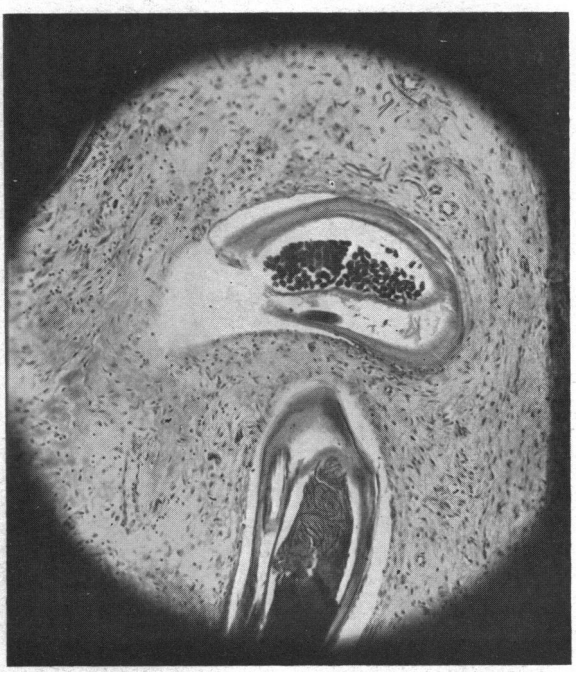

FIG. 18.

Section of nodule showing eggs and microfilariae in adult worm.

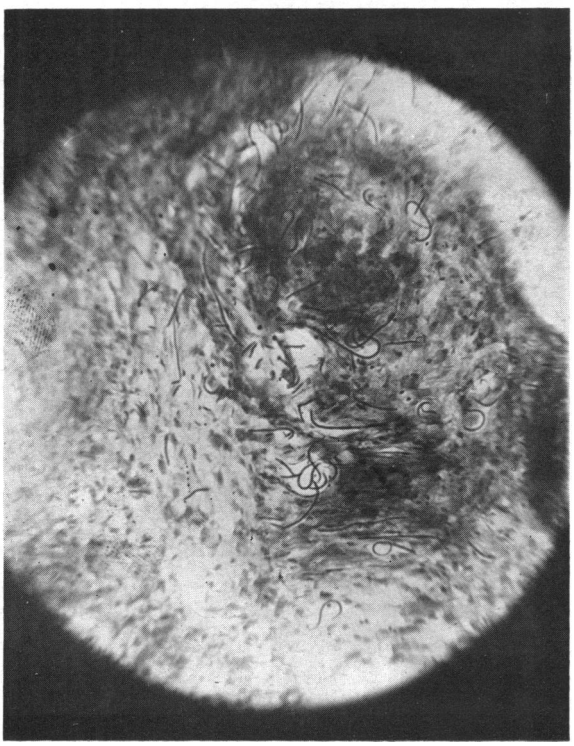

FIG. 19.

Section of mature nodule containing many microfilariae.

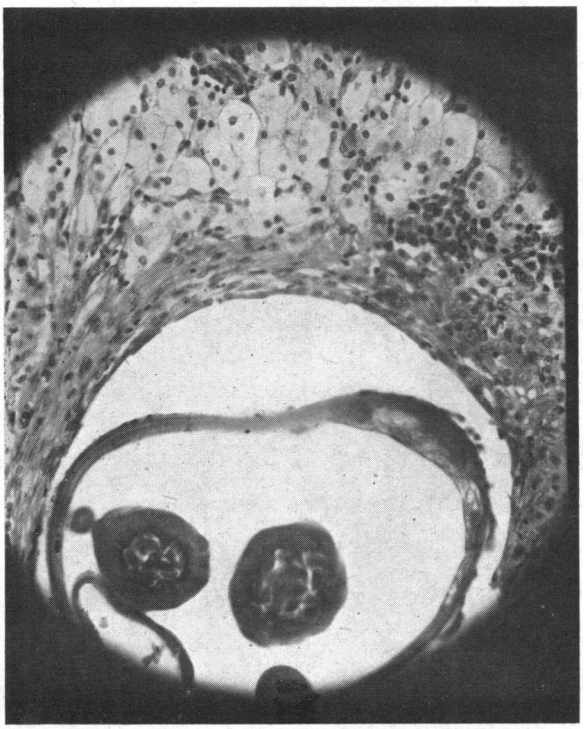

FIG. 20.

Immature nodule showing characteristic cells with small nucleus and finely granular cytoplasm.

demonstrated in the retina, degenerative pathological changes are marked. Hisette (1932) found haemorrhages in the ganglion cell layer. In the later stages the changes are those of atrophy, inflammatory cells having disappeared. In view of the extensive area usually involved and the frequency of lesions around the posterior pole of the eye it seems probable that perivascular infiltration and endothelial proliferation of the short ciliary vessels may be additional, perhaps the main, factors in the production of diffuse choroido-retinal degeneration.

The optic nerve.—Microfilariae were demonstrated in the optic nerve by Ochoterena (1928), Hisette (1932) and Mira (1934). The worms are found in the perivascular spaces setting up an inflammatory reaction and also causing an endothelial proliferation. Optic atrophy is doubtless due to vascular occlusion, the slight glial proliferation being secondary. The outer layers of the nerve are reported to be normal.

Similar vascular changes were found in the orbit (Hisette, 1932).

Account of an Investigation in the Gold Coast

Application for permission to arrange a research expedition was made in July, 1943, but owing to the exigencies of the service a start was not possible until seven months later when leave became available. Meanwhile a few cases of ocular onchocerciasis had been discovered in soldiers not all of whom had inhabited or visited recognised endemic districts.

In February, 1944, largely owing to the good offices of Brigadier G. M. Findlay, Consulting Physic n to the West African Force, a party consisting of the writer, Captain J. R. Holden, as pathologist, and Pte. Kofi Nartey, an African Nursing Orderly as ophthalmic assistant, left Accra for the Northern Territories. One steward boy knew the Wala language and it was hoped would be useful as an interpreter, though as it turned out his knowledge was of little value. Very complete ophthalmic equipment was kindly lent by the Army Medical Services, and included a slit-lamp run off two 6-volt car batteries, a projection lamp, an operating chair and instruments for ophthalmic surgery. It is believed that no slit-lamp had ever previously been taken on such an expedition and its value was unquestionable. It was necessary also to take food, drinking water and camp equipment, and it is a tribute to the country that the only firearm was a 12 bore sporting gun. Transport was provided by a 3-5 ton desert lorry.

In due course Wa, some 500 miles inland was reached, not without delays due to road blocks caused by fallen trees and broken culverts. Dr. Maurice Browne, the Colonial Medical Service

Officer, entertained the party and put at its disposal his local knowledge which was of the greatest value since those on the expedition had but slight knowledge of local bush conditions. At the time he was strenuously engaged with an epidemic of cerebro-spinal meningitis in addition to the usual diseases such as trypanosomiasis, malaria, yaws, schistosomiasis, and dracontiasis, all of which are very common. Captain Holden was able to assist in controlling an outbreak of anthrax.

It was soon decided that though the main roads were just passable to a loaded 3 ton lorry there was no chance of negotiating bush roads, the surface of which is at the best laterite and the width sometimes only the bare track of a car and bordered by a deep ditch to provide drainage in the heavy rains. Such roads are impassable to all wheeled traffic during the rainy season. Every few hundred yards there are culverts composed only of bush sticks covered with laterite, never very strong structures and towards the end of the dry season so weakened by white ants that they frequently give way beneath the weight of a car; dozens indeed did so. In view of transport difficulties a search was made in relatively accessible villages near the Black Volta but no onchocerciasis was found although trachoma and pterygium were common. It was decided therefore to adhere to the original idea of visiting Funsi, some 40 miles direct, but 64 by road from Wa. At the last moment Dr. Browne most kindly offered to convey the party with minimal equipment to Wahabu on the river Kulpwan whence a trek of some 12 miles would lead to Funsi. In actual fact despite difficulties it was found possible to drive right through, crossing the river by ford. On the return journey, however, the car ran off the road owing to a collapsing culvert, breaking a spring and damaging the steering. To save weight, much equipment was left behind at Wa. Only one steward boy was taken on and the medical equipment reduced to the slit-lamp, the projection lamp, a few operating instruments and essential drugs. Food consisted of five small loaves and a few tins of canned food. Twelve petrol tins of drinking water were carried and were just sufficient with care to last a week. The whole made up 14 headloads varying from 20 to 68 lbs. each. The 12 bore and a borrowed express rifle were relied upon to augment the food supply for little, if anything, could be obtained from the villagers who had nothing to spare.

It is evident that for a complete survey a far more elaborate expedition is required. Further medical assistance as well as the services of an entomologist and a skilled photographer would have been of great value and the shortage of time imposed severe limitations. A highly organised and costly expedition of this type would require adequate transport and a regular supply of fresh

food, and, most important of all, water. It is to be hoped that at some future date the subject of onchocerciasis in Africa will attract the attention of a research organisation.

Conditions at Funsi.—1. The country and the people. The village stands on high ground in savannah country outwardly resembling Dartmoor in August; scorched grassland with granite outcrops and few trees except beside the watercourses. The harmattan, the hot arid wind from the Sahara was in season and the small streams were completely dried up.

The village is composed of mud huts and the people are said to number 500-700. The nearest inhabited area is some 15 miles away, Wahabu having been deserted for some reason not ascertained. The inhabitants are Sissalas, members of a small tribe with a language of its own. They are exceedingly poor for the

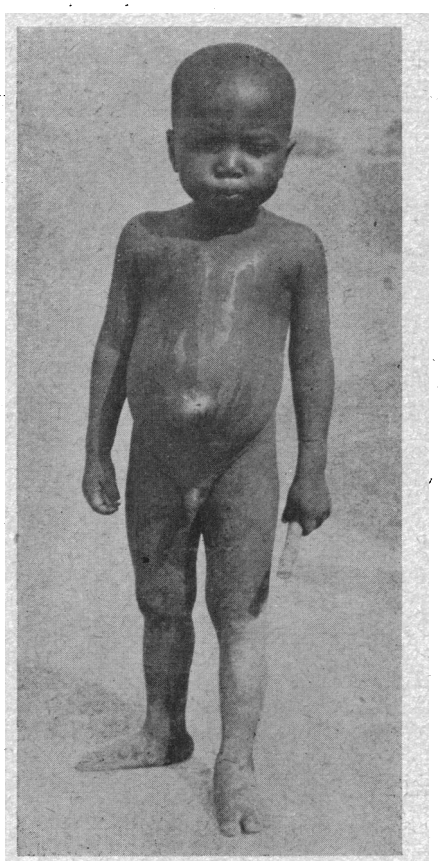

FIG. 21.

Child aged four years with ocular onchocerciasis.

land is infertile, producing little except guinea corn and yams and those in very moderate quantities. These products together with shea butter made from the nut of a local tree, a certain amount of game and a little river fish comprise the food supply. Game is hunted with bows and arrows, and fish caught with hook and line or by poisoning pools in the dry season with a cultivated plant

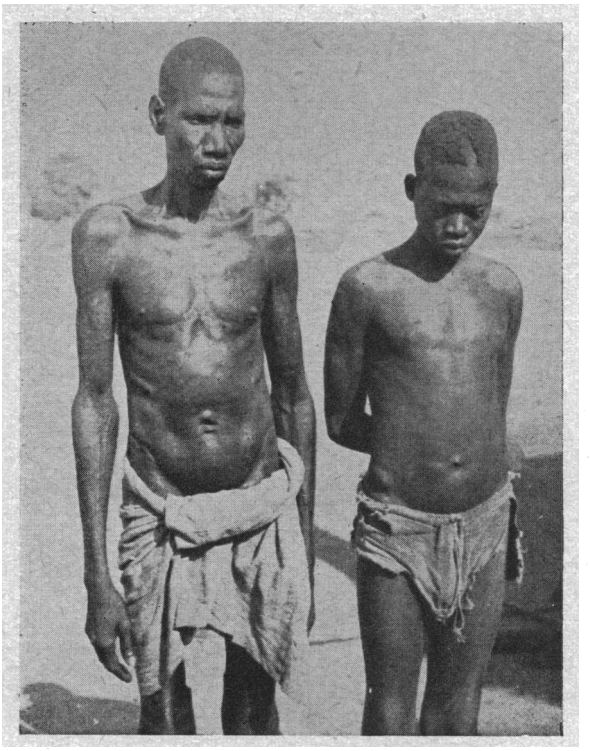

FIG. 22.

Two blind men.

called " biel." The appearance of the inhabitants suggested considerable malnutrition; the last harvest had been poor and there was undoubtedly a deficiency of vitamin A which is practically absent from shea butter. The only iron implements are knives and arrow heads. The women's clothing consists of a tail of leaves fore and aft attached to a girdle round the waist and the men wear a sort of triangle of hide and a leather sling over the shoulder to carry a quiver. The chief and some of the wealthier people have cotton clothes. The heads of both sexes are completely shaved, a custom which rendered examination for head nodules simple. The women are degraded and of lower mentality than the men but

their duties require little intelligence; they are the "hewers of wood and drawers of water," carrying large calabashes on their heads from surface wells or sometimes from the big river 5 or 6 miles away. Tiny children are usually strapped to the backs of the women so that even in infancy there is risk of infection with the onchocerca. Marriage seldom occurs before the age of 20, but morality is of a high standard, venereal disease being very rare though exceedingly prevalent in more civilised areas. There is good reason to believe that syphilis is unknown. Polygamy is, however, the custom, the chief having 9 wives. Infant mortality is around 15 per cent. compared with 50 per cent. further south. Trypanosomiasis and malaria were said to be relatively uncommon and were it not for the eye disease the district might be relatively healthy.

Despite their many hardships the Sissalas are nature's gentlemen. The chief was most friendly and helpful and never failed to pay an official call with his retinue at the end of the day to render thanks for work done. His people were happy, agreeable and honest. Instruments, medicines, clothing and even guns could not be guarded constantly yet not a single article was lost, though the average income must have been a few shillings per annum and the present of even an empty sardine tin was received with grateful thanks. The chief refunded the money paid for the one purchase of yams and provided eggs when he had any, and the larger of two fish caught was offered as a present. Though food is nearly always scarce no one starves for they help each other. Were it not for this there would be little hope for the blind who are an economic loss to the community. Surely such people deserve assistance to rid them of blindness, their chief scourge.

On departure, with mutual regret, presents were exchanged and bearers provided to carry the equipment to Wahabu. Some were surprised by the weight of the accumulators but the 12 miles were covered in 3 hours. The man with the slit-lamp weighing 68 lbs. never left the party by 10 yards, he had been warned of its value and evidently attributed much " ju-ju " to it. Electric light, of course, had never been seen before and, indeed, years may pass without the visit of a single white man. Fortunately two Sissalas spoke English and were invaluable as interpreters. They were intelligent men and explained the local customs and conditions. They said that the people recognised the importance of head nodules, which they called " Nukoli," as a cause of blindness but attributed no harm to " Sangeli " nodules on the trunk. Two persons had visited a native surgeon at Belepong, the next village, to have head nodules excised, but most feared the native doctor.

2. Medical examination of the people. A dark room was set up in a mud hut, the small windows of which were darkened by

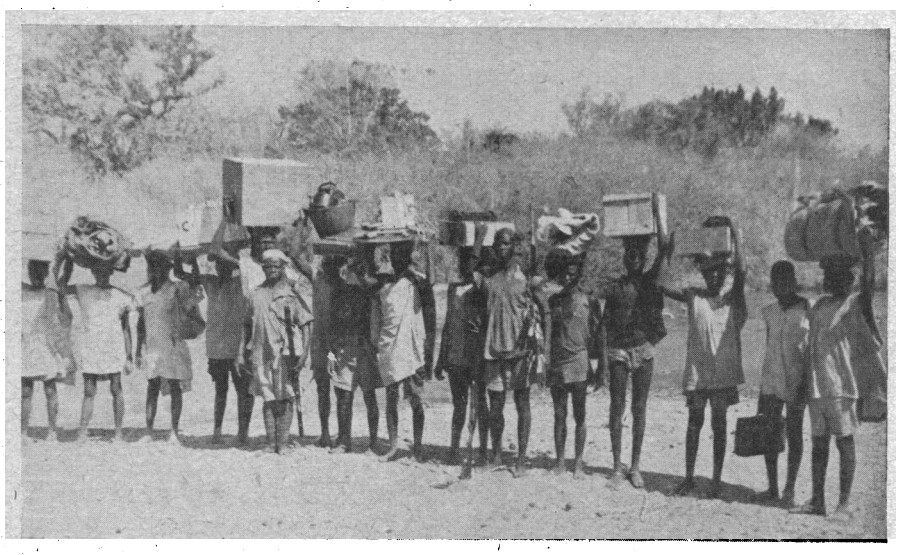

FIG. 23.

Carriers on trek.

FIG. 24.

Carriers on trek.

interested spectators, and after demonstrations on Europeans followed by the chief and other influential persons the populace readily submitted to examination. It was hoped that the entire population would be examined but limitations of time prevented this and only some 300 were seen, a number comprising perhaps

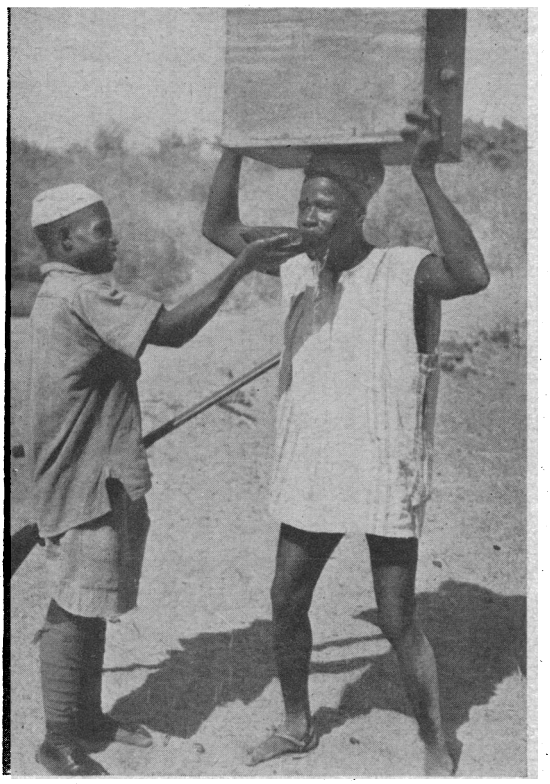

FIG. 25.

The man carrying possibly the first slit-lamp to be taken into the Bush.

an unduly high proportion of eye cases. A higher proportion of those with poor sight attended on the first days but on the other hand women generally failed to appear owing to fear or to engagement with domestic duties, and it was said that there were several aged and infirm blind persons who could not easily be moved. It is possible therefore that the figures for the proportion of the population with defective sight may be more accurate than are claimed. One hundred and thirty-one persons were examined with the slit-lamp and ophthalmoscope, and of these 61 had serious

eye disease, 51 ocular onchocerciasis including 22 who were below British blind certification standards, and 11 trachoma. Signs of vitamin A deficiency were practically universal. These figures compare with those of Larumbe (1928) who reported from Mexico 800 eye patients, including 100 blind amongst 4,000 persons with onchocerca nodules. Hisette (1931) at Sankuru in the Belgian Congo found that 50 per cent. of those with nodules had eye

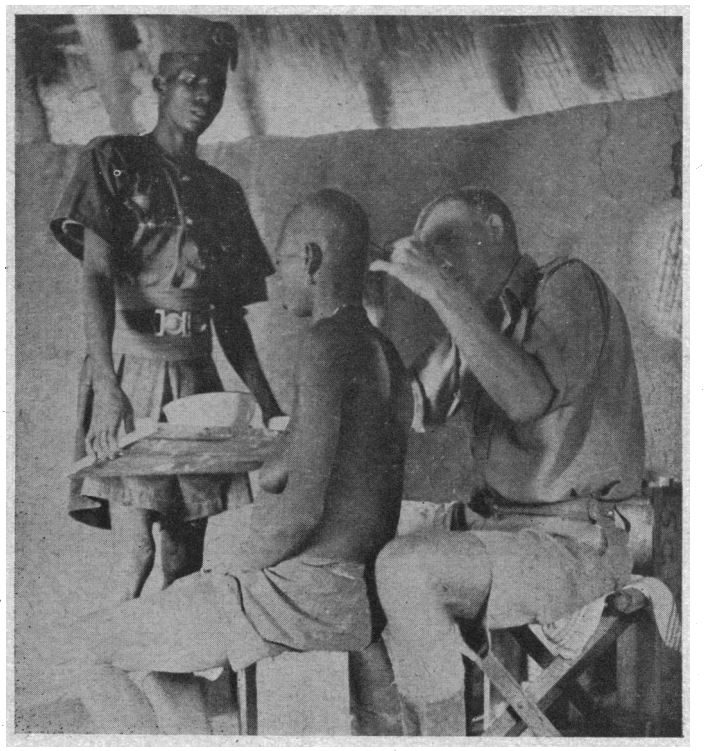

FIG. 26.

Bush surgery.

lesions, 10 per cent. being blind; Strong (1931) in Guatemala 54 per cent., and Hawking (1939) at Kakamega in Kenya 34 per cent.

At Funsi many factors rendered ophthalmic examination difficult, particularly with the slit-lamp, and doubtless some points escaped notice which would have been apparent in normal circumstances. In one important respect the expedition was a failure, for no blind eye was excised. The disease though painful in the later stages is not excruciating and the Native Administration

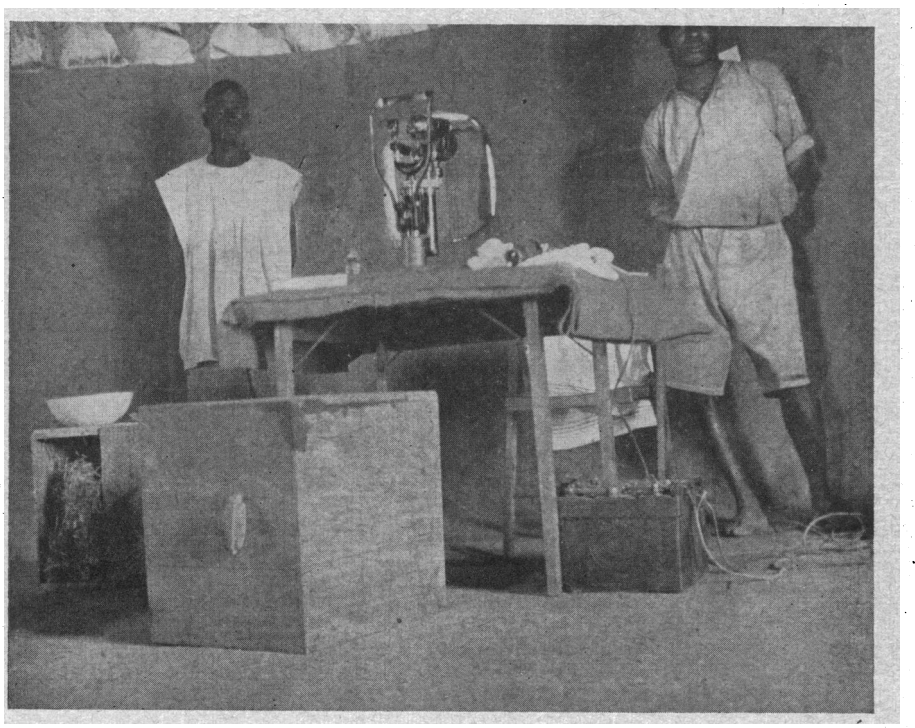

FIG. 27.

The mud hut used for examinations.

Clerk said that it was believed that if an eye was taken from a man his soul passed to the recipient so that even a post-mortem would be refused. The offer of a glass eye or the writer's own spectacles failed to overcome the tribal beliefs. Hisette (1932) encountered similar difficulty. The lack of pathological material imposes a severe limitation on this investigation. Captain Holden did much to augment the popularity of the visit by excising 40 nodules, chiefly from children, under local anaesthesia. He also confirmed the diagnosis in doubtful cases by finding microfilariae in conjunctival snips, and made several permanent microscopical specimens.

TABLE I.—*Summary of 51 cases of ocular onchocerciasis examined at Funsi in the Northern Territories of the Gold Coast in February, 1944.*

Case No.	Sex and Age.	Microfilariae seen.			Conj.: Snip.	Cornea.	Corneal opacities.	Mass in Anterior Chamber.	K.P.	Distorted Pupil.	Choroido-Retinal Degeneration.	Optic Atrophy.	Remarks.
		Nodules.	Vision.	Aqueous.									
5	M.50	Chest	Blind	+	—	—	+++	—	++	—	L+++	+	R. Cataract, Fundus obscured.
12	M.50	Chest	Bad	+	—	—	+++	+++	+	+	—	—	R. marked folding of Descemet membrane Tension—1.
14	M.35	Chest	Blind	—	—	—	—	—	—	—	+++	L+ R—	Typical fundus.
16	M.30	Chest	Blind	—	—	—	++	+++	—	++	—	—	Lens opacities obscured fundi. Tension—1.
20	M.30	Chest	Fair	+	+	—	++	—	++	—	R— L+	R— L+	
21	M.70	Knee	Bad	+	+	+	+	—	+	—	+++	++	
24	M.70	Chest, etc.	Blind	—	—	+	+	—	+	—	+++	++	
27	M.68	None found	Bad	—	+	—	+	—	—	—	+++	++	
28	M.20	None found	Good	—	+	—	+	—	—	—	—	+	R. Secondary glaucoma tension +2.
29	M.60	Chest	Blind	+++	+++	—	—	—	+	Inactive	+++	+++	Tension—1.
38	M.24	Chest	Good	+	†	+	++	—	—	—	—	—	
39	M.19	Ilium	Good	+	†	+	+	—	—	—	—	—	
40	M.70	Chest, etc.	Good	+	†	—	+	—	—	—	—	—	
41	F.18	Head	Good	—	†	+	+	—	+	—	—	—	
42	F.14	Head	Good	+	†	+	+	—	—	—	—	—	
49	M.30	Head, etc.	Bad	++	†	+	++	+	+	+	—	—	Fundi obscured.
52	M.70	Head, etc.	Blind	—	+++	—	+++	+	++	+	—	—	Fundi obscured.
56	M.22	Head	Blind	—	+++	—	+++			—	—	—	Fundi, etc., obscured.
57	M.12	None found	Blind	—	+	—	—	+	+++	—	—	—	Malnutrition and avitaminosis.
59	M.10	Head, etc.	Good	—	—	+	+	—	—	—	—	—	
63	M.25	Chest	Bad	—	+	—	+++	—	+++	—	L—	L—	E. Fundus obscured.
64	M.50	Head, etc.	Blind	—	+	—	+++	†	†	†	†	†	Internal Structures obscured.
65	M.45	Chest	Blind	—	—	+	+++	†	†	—	†	†	Internal structures obscured. Tension +1.

† No examination under the appropriate heading was performed.

TABLE I—*continued.*

Case No.	Sex and Age.	Microfilariae seen.			Conj.: Snip.	Cornea.	Corneal opacities.	Mass in Anterior Chamber.	K.P.	Distorted Pupil.	Choroido-Retinal Degeneration.	Optic Atrophy.	Remarks.
		Nodules.	Vision.	Aqueous.									
69	M.25	Head	Good	+	†	—	+	—	++	—	—	—	
71	M.25	Chest	Good	—	†	+	+		+	—	—	—	
73	F.50	Chest	Blind	—	—	—	+++	+	+	+	+++	++	
75	F.50	Chest	Blind	+	†	+	+	—	+	R— L—	+++	++	
79	F.30	Ilium	Fair	—	—	+	++	—	+	—	†	†	Fundi obscured.
81	F.30	Head, etc.	Good	+	†	—	++	—	+	—	—	—	
82	F.10	Head	Good	—	†	+	+	—	—	—	—	—	
84	M.14	None found.	Good	—	—	+	+	—	—	—	—	—	Possibly arrested by excision of head nodules.
85	M.12	Head	Good	—	†	+	++	—	—	—	—	—	
86	M.25	Head	Good	+	†	+	++	—	—	—	—	—	
87	M.16	Ilium, etc.	Fair	+	†	—	+	—	—	—	—	—	Trachoma present.
90	F.8	Head	Good	—	†	+	+	—	—	—	—	—	
91	M.7	Head	Fair	—	†	+	++	—	—	—	—	—	Gross epithelial pigmentation.
92	M.6	Head	Good	—	†	+	+	—	—	—	—	—	
95	M.22	Head	Bad	+	†	+	+	—	—	—	—	++	
97	M.45	Head	Good	+	†	+	+	—	—	—	—	—	
99	M.30	Head, etc.	Fair	—	+	—	++	—	—	—	—	—	
100	M.25	Knee	Blind	+++		+	+	—	++	—	++	+	
103	F.45	Head, etc.	Fair	—	+	—	+++	+	+	+	—	—	Fundi obscured.
104	M.8	Head	Good	—	†	+	+	—	—	—	—	—	
105	F.30	Scapula	Fair	++	†	—	++	—	—	—	—	—	Trachoma present.
108	M.12	Head	Fair	—	+	—	++	—	—	+	—	—	
115	M.35	Chest	Good	+	†	—	—	—	—	—	—	—	
118	M.30	Chest	Bad	+	†	+	+	—	+	—	++	++	
119	M.19	Chest	Blind	—	+	—	+++	—	—	—	—	—	Fundi obscured. Trachoma present.
120	F.16	Head	Good	—	—	+	+	—	—	—	—	—	Trachoma present.
121	M.4	Head	Fair	—	+	+	++	—	—	—	—	—	
131	M.29	None found.	Bad	—	+	—		—	—	—	+	+	

† No examination under the appropriate heading was performed.

ANALYSIS OF FUNSI CASES

Persons examined for nodules	approx.	300
Patients with onchocerciasis nodules		131
Ophthalmic examinations		141
Severe eye disease present in		61
Ocular Onchocerciasis		51
Microfilariae seen in eye or conjunctiva ...	45	
Microfilariae not seen, but clinically typical...	6	
(Probable but unproved cases not included 3)		
Blind	14	22
Below British blind certification standard but able to walk unaided	8	
Fair sight	9	
Good sight	20	
Youngest patient ... ..., ...	4 years	
Youngest blind patient	12 years	
Patients with head nodules	25	
Patients with nodules on trunk only... ...	21	
Patients without discoverable nodules ...	5	
Corneal opacities	45	
Mass in anterior chamber	7 and ? 3 (view obscured)	
Iridocyclitis	20 and ? 3 (view obscured)	
Choroido-retinal degeneration	12 and ? 11 (view obscured)	
Optic atrophy	14 and ? 11 (view obscured)	

Other eye diseases	
Trachoma	8
Optic atrophy, unknown cause	3
Ophthalmia neonatorum	1
Iridocyclitis, non-specific	1
Gross avitaminosis, probable	1
Pterygium	very common
Corneal epithelial pigmentation probably vitamin A deficiency	almost universal

Case Reports of Patients with Gross Visual Impairment

Cases number 5, 29, 52, 73, 75, and 100 and 118 may be regarded as typical.

CASE 5.—Kumpe. Male, aged 50 years. Blind. Two multilobular nodules on chest wall, present for more than 10 years. Slight conjunctivitis, microfilariae not seen in snip. Corneae: superficial and deep opacity affecting entire lower half, but sparing relatively the pupillary area. Right and left corneae almost symmetrical, dead white appearance suggests calcification; superficial vascularisation. Microfilariae seen in aqueous. Large old K.P. and some exudate on left anterior capsule but no posterior synechiae or distortion of pupils. Considerable opacity in right lens. Fundi: left only visible, marked choroido-retinal atrophy affecting a wide area around posterior pole; some large masses of retinal pigment and some of "bone corpuscle" type. Optic nerve: moderate degree of atrophy; with some constriction of retinal vessels. Tension normal.

CASE 12.—Daibikpa. Male, aged about 50 years. Almost blind. Nodules on chest. Slight conjunctivitis, no microfilariae seen in snip. Corneae: Gross scarring affecting substantia propria and epithelium in interpalpebral periphery and lower quarters; right more advanced than left, and also shows well-marked folding of Descemet's membrane giving appearance of a fan or of out-stretched fingers pointing upwards; a few superficial vessels. Microfilariae seen in aqueous. Anterior chambers: grey-brown mass at base. Irides: drawn downwards and forwards to corneae below causing inverted pear-shaped pupils; no posterior synechiae and upper halves of irides show no sign of inflammation; "pumice stone" atrophy of anterior stroma. Fundi normal. Tension: R. normal, L. −1.

CASE 14.—Bajinhilia. Male, aged about 30 years. Blind. Small nodule on right 7th rib in mid-axillary line. No conjunctivitis, no microfilariae seen in snip. Corneae: normal. No microfilariae seen in aqueous. Irides: normal, pupils circular. Lens and vitreous: clear. Fundi: R. considerable pigmentary disturbance on temporal side of optic disc. L. Gross and typical choroido-retinal degeneration very diffuse and even though least marked in superior nasal quadrant large choroidal vessels exposed and appear bright orange on the dark brown background. Optic discs: R. normal vessels normal; L. lower half only pale, vessels normal calibre. Tension normal.

CASE 16.—Duma. Male, aged about 30 years. Blind. Several nodules on chest for more than ten years. Head nodule removed in childhood by native doctor. Has been blind for ten years. Marked conjunctivitis, no snip examined. Corneae: Dense opacity of lower halves with calcification and vascularisation at periphery: calcified epithelium flaking off; right more affected than left. No microfilariae seen in aqueous. No K.P. Anterior chambers: Grey brown mass at base. Irides: drawn downwards and forwards to mass in anterior chamber; inverted pear-shaped pupils; atrophy of pigment frill and "pumice stone" appearance but no sign of past iritis. Lens: R. hypermature cataract; L. vacuoles in anterior and opacity in posterior cortex. Fundi obscured. Tension: R. & L. −1.

CASE 21.—Fundi. Male, aged about 70 years. Almost blind. Nodule on right knee. Cannot see in dim light and complains of entoptic vision of a worm. No conjunctivitis, no snip examined. Corneae: a few nummular opacities. Microfilariae seen in aqueous. Anterior chamber: normal. A few old K.P. Irides: normal, pupils circular. Lens and vitreous clear. Fundi: typical choroido-retinal degeneration affecting a large area, outlines sharply defined, large aggregations of retinal pigment especially temporal to discs; large orange choroidal vessels running over brown "cracked mud" background. Optic nerves: Atrophy of consecutive type with marked diminution of retinal vessels. Tension: normal.

CASE 24.—Adoma. Male, aged about 70 years. Blind. Nodules on chest, back and iliac crests. Could not see in dim light before sight finally failed. No conjunctivitis, microfilariae not seen in snip. Corneae: a few nummular opacities. Microfilariae not seen in aqueous. A few old K.P. Anterior chambers: normal. Irides: normal, pupils circular. Fundi: gross and typical choroido-retinal disturbance with large aggregations of retinal pigment. Optic discs: Atrophy with constriction of vessels. Tension: Normal.

CASE 27. Musa. Male, aged about 70 years. Almost blind. No nodule discovered but reported to have had one which burst spontaneously 10 years before. Cannot see in dim light. No conjunctivitis, microfilariae seen in snip.

Corneae: Some keratitis with large superficial vessels, not typical of onchocerciasis, much epithelial pigmentation. No microfilariae seen in aqueous. Irides: normal, pupils circular. Lens and vitreous clear. Fundi: generalised choroido-retinal degeneration with aggregations of retinal pigment chiefly of the "bone corpuscle" type; L. Gross and typical changes above and around disc and in temporal half of retina, large masses of pigment near periphery of affected area. Optic discs: Atrophic with narrow vessels. Tension: normal.

CASE 29.—Sedigi. Male, aged about 60 years. Blind. One nodule on right side of chest. No conjunctivitis, many microfilariae seen in snip. Corneae: normal. Many microfilariae seen in aqueous. Anterior chambers normal. Irides: R. signs of slight past iridocyclitis; L. normal. Lens: R. slightly hazy due to deposit on anterior capsule; L. normal. Vitreous: clear. Fundi: Gross choroido-retinal degeneration of typical pattern, retinal pigment heaped into large masses and also into "bone corpuscle" figures; large orange choroidal vessels seen lying on dark brown "cracked mud" background. Optic discs: White, completely atrophic; retinal vessels minute in R. and grossly constricted in L. Tension: R. −1, L. normal.

CASE 49. Mama. Male, aged about 30 years. Almost blind. Nodules on occiput forehead and chest. General appearance of man of 50 years. Cannot see in dim light and sight has been bad for 5 years. Marked conjunctivitis, trichiasis, no snip examined. Corneae: well marked nummular opacities with some localised epthelial degeneration and superficial vascularisation. Many microfilariae seen in aqueous. Anterior chambers: grey brown mass at base. Irides: "pumice stone" appearance but no signs of past inflammation; pupils slightly distorted and drawn downwards. Fundi: not well seen owing to opacities in cornea but appear normal. Tension: normal.

CASE 52. Duma. Male, aged about 70 years. Blind. Nodules on occiput and chest for 20 years. Blind for 3 years. Moderate conjunctivitis, many microfilariae seen in snip. Corneae: gross keratitis affecting all layers causing dense opacity, superficial vascularisation. No microfilariae seen in aqueous. Anterior chamber: grey-brown mass at base. Large K.P. Irides: considerable chronic iridocyclitis; R. pupil drawn slightly downwards and forwards; on surface of R. iris are three grey masses, suggestive of fibrosis around bodies of dead microfilariae, causing local contraction. Lens: some opacity. Fundi: reflexes only visible. Tension: normal.

CASE 56.—Kwasi. Male, aged about 22 years. Blind. Nodule the size of a split pea on L. forehead, also in both mastoid areas. Has been blind for one year. Moderate conjunctivitis, many microfilariae seen in snip. Corneae: Several typical nummular opacities in addition to general frosting of lower 2/3 particularly below, epithelium oedematous as well as pigmented near periphery. Anterior chambers: deep; no mass seen. Fundi: obscured. Tension: +2.

CASE 57.—Mpara. Male, aged 12 years. Almost blind. No nodules discovered. Looks starved. Probably avitaminosis (Holden). No conjunctivitis, microfilariae seen in snip. Corneae: Marked epithelial pigmentation but no nummular opacities. Anterior chambers: Mass at base. Large K.P. Irides: severe iridocyclitis. Fundi: obscured. Tension: normal.

CASE 63.—Kampa. Male, aged about 25 years. Almost blind. Nodule on left side of chest in mid-axillary line. Moderate conjunctivitis, microfilariae seen in snip. Corneae: R. completely opaque below and severely affected above; L. similar though less severe. Irides: R. obscured; L. advanced iridocyclitis with large K.P. Fundus: L. appears normal.

CASE 64.—Bowa. Male, aged about 50 years. Blind. Nodule on head and others on both sides of the chest. Visual deterioration for 10 years and blindness for 3 years. Slight conjunctivitis, microfilariae seen in snip. Corneae: R. completely opaque, gross epithelial degeneration and vascularisation; L. similar though upper portion less affected. Intra-ocular structures obscured.

CASE 65.—Vienwa. Male, aged about 45 years. Blind. Nodule on chest. Blind for many years. Slight conjunctivitis, microfilariae not seen in snip. Corneae: R. typical nummular opacities with much epithelial degeneration, and pigmentation; L. ground glass cornea. Intra-ocular structures obscured. Tension: R. and L. +1.

CASE 73.—Haduma. Female, aged about 50 years. Blind. Nodules on right chest in mid-axillary line. Slight conjunctivitis, microfilariae not seen in snip.

Corneae: Dense opacity of lower halves with epithelial degeneration and vascularisation. No microfilariae seen in aqueous. Anterior chambers: No mass visible at base. Irides: Typical inverted pear-shaped pupils, irides drawn downwards and forwards, upper halves show no sign of inflammation but some "pumice stone" atrophy of stroma. Lens: Some deposit on anterior capsules. Fundi: Gross and typical choroido-retinal degeneration around posterior pole with large aggregations of retinal pigment; large orange choroidal vessels clearly visible on dark brown "cracked mud" background. Optic discs: consecutive atrophy with diminution of calibre of retinal vessels. Tension: normal.

CASE 75.—Haduma. Female, aged about 50 years. Blind. Nodule on chest since childhood. Blind for five years but could not see in dim light before. No conjunctivitis, no snip examined. Corneae: well developed nummular opacities. Microfilariae seen in aqueous. Anterior chambers: R. small mass at base; L. normal. Irides: R. some distortion downwards. Lens: R. some deposit on anterior capsule. Fundi: Well developed and typical choroido-retinal degeneration with aggregations of retinal pigment and exposure of large orange choroidal vessels on dark brown "cracked mud" background. Optic discs: consecutive atrophy with constriction of retinal vessels.

CASE 95.—Jabagargardi. Male, aged about 22 years. Almost blind. Nodule on right chest for 6 years. No conjunctivitis, no snip examined. Corneae: a few nummular opacities only seen in each. Microfilariae seen in aqueous. Iris, lens, vitreous, retina and choroid normal. Optic discs: Gross pallor with marked constriction of retinal vessels with perivascular sheathing. Tension: normal.

CABE 100.—Wiayuga. Male, aged about 25 years. Blind. Nodule on right knee for years. Blind for 4 years, previously vision defective in dim light. No conjunctivitis, no snip examined. Corneae: nummular opacities confined to interpalpebral periphery. K.P. present. Many microfilariae seen in aqueous. Irides: R. normal; L. marked iridocyclitis with posterior synechiae. Lens and vitreous clear. Fundi: Gross and typical choroido-retinal atrophy in extensive sharply delimited areas around posterior pole; massive aggregations of retinal pigment and in addition white plaques suggestive of fibrosis; Large orange choroidal vessels exposed lying on dark brown "cracked mud" background. Optic discs: consecutive atrophy with only slight narrowing of retinal vessels and no sheathing. Tension: normal.

CASE 118.—Jaya. Male, aged about 25 years. Almost blind. Nodule on left chest. Sees normally in dim light. No conjunctivitis, no snip examined. Corneae: a few typical nummular opacities. Microfilariae seen in the aqueous. Anterior chambers: No mass at base. Irides: R. slight iridocyclitis with atrophy of pigment frill and "pumice-stone" appearance of stroma, pupil not distorted; L. normal. Fundi: typical choroido-retinal degeneration; besides pigment masses there are discrete white spots around optic disc; R. more affected than L. Optic discs; well developed atrophy; retinal vessels much reduced in calibre and sheathed. Tension: normal.

CASE 119.—Niemuny. Male, aged 19 years. Blind. Nodule on right chest. Looks about 14 years old. Starved appearance. Marked conjunctivitis, microfilariae seen in snip; active trachoma. Corneae: Gross scarring below complicated by trachomatous pannus above. Intra-ocular structures obscured. Tension: normal.

CASE 131.—Duma. Male, aged 29 years. Almost blind. No nodule discovered. No conjunctivitis, microfilariae seen in snip. Corneae: a few typical nummular opacities. Irides: normal, pupils circular. Fundi: diffuse choroido-retinal degeneration though area not sharply limited and pigmentary disturbance and atrophy less marked than in other cases. Optic discs: some abnormal pallor. Tension: normal.

Other Cases of Ocular Onchocerciasis

In addition to those at Funsi 20 other cases proved by the finding of *mf. volvulus* have been seen at Accra, 16 African soldiers and 4 civilians. As would be expected the eye lesions in the soldiers were in a relatively early stage though two of the civilians

were virtually blind. Not all the Gold Coast soldiers had lived in or visited districts recognised as endemic. Others came from Nigeria, Sierra Leone, French Togoland and Liberia. All 20 cases had microfilariae in the aqueous; 18 had keratitis, 6 iridocyclitis, 6 choroido-retinal degeneration and 6 optic atrophy. One had synovitis of the knee and 2 oedema of the leg, manifestations which tended to resolve and relapse, and 2 had hydrocele and a slight degree of elephantiasis. Other cases of onchocerciasis uncomplicated by eye lesions were also seen and among these were 2 more with hydrocele. It is unnecessary to record all these cases in detail, but some points deserve mention. Though 5 of the soldiers had choroido-retinal degeneration, in some cases extensive, none showed the fully developed picture. One of these who complained of night blindness and had only white spots scattered over the fundi had been misdiagnosed by the writer six months before as a case of retinitis punctata albescens. Another was complicated by very severe trypanosomiasis. One with bilateral oedema of the lids and *mf. volvulus* in the skin had also acute iridocyclitis but in spite of the presence of proved onchocerciasis it did not appear that the eye lesions were due to the worm, for the inflammation was more severe than in the other cases and no microfilariae were discovered in the conjunctiva or aqueous. The Kahn test proved to be positive and antisyphilitic treatment produced rapid improvement. This case may be regarded as a warning against too enthusiastic diagnosis of ocular onchocerciasis. On these cases it was possible to perform blood and cerebro-spinal fluid examinations, investigations which were impracticable in the Bush.

In addition one case of absolutely typical choroido-retinal degeneration was seen at Wa during the examination of a routine trypanosomiasis clinic, though unfortunately apparatus for demonstrating microfilariae was not available at the time. Another, equally typical, was later seen in the trypanosomiasis clinic at Kintampo together with three other cases of unsuspected ocular onchocerciasis. The diagnosis was confirmed with the slit-lamp in all four.

Differential Diagnosis

The diagnosis may be established with a high degree of certainty by the finding of microfilariae in the aqueous or conjunctiva and by staining those aspirated from nodules, or better those from the anterior chamber. It is said that *mf. loa* and *mf. bancrofti* (McMullen, 1939) also enter the aqueous though the writer has so far never succeeded in finding other than *mf. volvulus* in spite of repeated examinations of several cases of proved loa and perstans infections. Intra-ocular microfilariae in the absence of apparent

onchocerciasis would certainly call for paracentesis of the anterior chamber and detailed examination of the worms removed. Microfilariae of onchocerca appear to be the only ones which cause damage to the eye, though the adults of other filariae enter the conjunctival vessels and occasionally also the globe.

There is no doubt that many ocular lesions have been attributed to other diseases because the possibility of onchocerciasis has not been considered. It may well be wondered what proportion of cases of keratitis, iritis and choroido-retinitis attributed to trypanosomiasis may in fact be filarial, for the two diseases often occur in the same district and may well be concurrent, and the lethargy produced by trypanosomiasis predisposes to the bites of Simulium. In just over 100 cases of trypanosomiasis personal observation has revealed no ocular complications other than a mild papilloedema, such as may occur in any lymphocytic meningitis, in the absence of infection with Onchocerca. Keratitis and uveal complications, however, are common when the two diseases coexist.

Nodules situated over bony points are easily diagnosed, but might be mistaken for fibromata, lipomata or the juxta-articular nodes of yaws.

In the cornea the nummular opacities are very typical, particularly if the dead worm can be seen, but might be confused with the nummular keratitis of Dimmer (1905) or with a fairly common nodular interstitial keratitis probably of virus origin which runs a more acute course and causes irregularity of the endothelium by swelling. The later stages of onchocercal keratitis may resemble any form of sclerosing keratitis, particularly keratitis e lagophthalmo and leprosy. In the past diagnoses of avitaminosis, trachoma and even pterygium have been made.

Iridocyclitis should present little difficulty if the characteristic inverted pear-shaped pupil and the mass at the bottom of the anterior chamber are present, but other cases may be indistinguishable from those of non-specific origin.

Choroido-retinal changes may resemble non-specific forms when only of a mild atypical degree. The fully developed picture is pathognomonic.

Optic atrophy may occur with many diseases, and in particular one or more, common in Africa, which are so far unidentified. Avitaminosis, especially lack of vitamin B complex has been blamed (Fitzgerald Moore, 1930-39, and others), but this awaits further investigation.

Other eye diseases may, of course, coexist and possibly play a part in reducing the resistance of the organ to the toxins of the dead microfilariae. Lack of vitamin A, the effect of which on the cornea and retina is well known, may well be an adjuvant. At Funsi practically everyone had pigment not only at the limbus

but also spreading over a considerable area of corneal epithelium, the abnormal area tapering into a sinuous line. Trachoma seems to have no influence on the onset or course of ocular onchocerciasis.

Treatment

It must be confessed that so far there is no effective treatment, for no drug is known which will kill any form of microfilaria without endangering the life of the host. This is somewhat remarkable considering the relatively high degree of specialisation of the parasite. The adult form of onchocerca also is resistant to systemic chemotherapy though local injection of toxic substances into the nodules is often effective, gentian violet in 42 per cent. of cases and hexyl resorcinol in 26 per cent. (Strong, 1937).

It would seem that there are three methods by which cure or improvement might be attained if the diagnosis is established in time.

1. Destruction of the microfilariae.
2. Destruction or sterilisation of the adults.
3. Prevention or discouragement of the microfilariae entering the eye.

The first two methods appear the most logical, though there would seem to be some danger of a severe general reaction if many or all the microfilariae were destroyed at the same time. The risk, however, is not so great as in the case of those species of microfilariae which circulate in the blood, which when killed have been found to cause infarcts. Experiments are best performed on dogs with *dirofilaria immitis* or *filaria repens* or on cattle or horses with *onchocerca cervicalis* or *o. reticulata*. A great number of drugs have been tried and the results reported by many writers (O'Connor, 1923, Findlay, 1939, and others), gentian violet, trypan blue, plasmoquin, bismuth, gold preparations, various arsenic compounds, thymol, oil of chenopodium, hexyl resorcinol, mercurochrome, emetine and many preparations of antimony, the results being almost uniformly disappointing.

Rather more promising results were reported by Khaw and Chew (1936) who injected dogs with antimosan and fouadin (stibophen), a tervalent antimony preparation, and succeeded in killing some adult worms and sterilising the remainder, though thromboses and infarcts caused by the bodies of the dead microfilariae were frequent and the drugs themselves caused considerable fatty degeneration. They found fouadin without effect, however, on 11 human subjects. Wright and Underwood (1936) restored to usefulness 90·3 per cent. of 997 dogs with fouadin but the mortality was 4·9 per cent. Gulati (1934) reports the cure of cattle filariasis with 100 c.c. of 1 per cent. potassium antimonyl tartrate.

Brown and Sheldon (1941) cured 5 out of 6 dogs suffering from *dirofilaria immitis* with sulphanilamide by the mouth and stibophen intramuscularly for 10 days. Stibophen alone for 10 days cured 2 out of 4 dogs.

In man, Rao (1926) claimed clinical improvement with sodium antimony tartrate, and Harris (1940) using the same drug claimed success in 12 out of 16 cases after excision of nodules, judged by the disappearance of microfilariae from the skin and the decrease of eosinophilia. Adams (1938) stated that neostibosan two years before had produced great improvement in his European case. Sharp (1927) had one successful case with a gold preparation, B. 1916. Enzer (1942) found good results with euflavine, tryparsamide and Bayer 205 but only when combined with shock therapy. Chopra and Rao treated patients with soamin (atoxyl). Strong (1931) found no benefit from antiserum produced from rabbits into which microfilariae had been injected. In a case of loa infection Gordon and O'Connor (1934) claimed some improvement from the use of X-rays applied to the kidney area.

Excision of the nodules was naturally one of the first lines of treatment adopted, and at first was hailed as a cure when the theory that the eye lesions were caused by toxins from the adult worms was thought to be correct. Larumbe (1928), however, reported that improvement lasted only a few days and, in 1930, that the treatment was without hope, a view supported by Fulleborn (1926) and others. There is no doubt that adult worms may live outside nodules and that some nodules may escape detection being very small or situated perhaps in some inaccessible region of the body. Moreover microfilariae may persist in the eye long after excision of all known nodules, eight months at least in one of the cases at Accra. Nevertheless excision of all discoverable nodules seems essentially a helpful measure reducing, at the very least, the source of supply of microfilariae, and this would remain an important part of the treatment even when a drug lethal to microfilariae is discovered. Local injection of toxic substances is much less reliable.

As regards driving the worms from the eye, prospects of benefit apply only to the anterior segment. There is reason to think that the main portal of entry is by the skin and conjunctiva though fundus changes are caused by microfilariae entering along the paths of the orbital vessels and nerves. It was considered possible that frequent application of some noxious drug might kill or drive away microfilariae lurking in the conjunctiva. With this in mind mercury perchloride 1/5,000 has been used as a lotion 4-hourly. It is impossible to make definite claims without extensive trials including adequate controls, but there is some evidence that further corneal lesions are prevented and those already present are

given an opportunity to resolve, even though microfilariae persisted in the aqueous.

Silva (1932) injected plasmoquin into the anterior chamber and saw the worms die, but this procedure is not without risk and simple drainage and irrigation removes the microfilariae as effectively without leaving behind the bodies to set up inflammation. Moreover this appears to be effective in clearing the aqueous for some weeks at least and there is little contra-indication to repetition every few months if necessary.

Experiments have been made on microfilariae *in vitro*. Suspensions in normal saline are made from scrapings of the contents of a recently excised nodule. By this means it is possible to concentrate 20-40 microfilariae in a single drop and they remain alive and motile for many hours at room temperature. As might be expected any protoplasmic poison kills them when in suitable concentration. The first experiments were made with mercury salts because this metal is readily absorbed through the skin in which, as has already been shown most microfilariae are found. Furthermore inunctions could be applied by simple people without the need for very close supervision. Mercury collyria too are in very general use and it was hoped that a larvicidal concentration might be attained in the aqueous. Experiments indicate that mercury perchloride 1/2,000, a drop of 1/1,000 solution mixed with a drop of the suspension, is lethal in a few seconds and that the minimal effective dilution is 1/10,000 in which the worms can live for nearly one hour. No external application has yet been found to kill microfilariae in the anterior chamber.

Destruction of microfilariae *in vivo* is a much more difficult problem for high concentrations of filaricides are very toxic. The administration of various drugs has been tried at Accra, mercury inunctions, gentian violet, mepacrine, quinque- and ter-valent arsenic, sulphonamides, shock therapy, antimony preparations and others. Observation has been maintained on the number of worms in the aqueous supplemented on occasions by examination of skin snips. In one case under treatment with tervalent antimony half the nodules were excised before the course and the other half after. It was considered that there were more dead adults and fewer microfilariae in the second group of nodules, though confirmation of this impression must be awaited. It appeared too that there were fewer worms in the anterior chamber though the aqueous infestation in this case was never high.

At present treatment is most unsatisfactory, but pending further knowledge the following measures are employed :—

1. Excision of all discoverable nodules.
2. Drainage and irrigation of the anterior chamber.

3. Conjunctival irrigation with 1/5,000 perchloride of mercury, 4-hourly.

4. One or more course of stibophen.

Stibophen is a tervalent preparation of antimony containing 15·8 per cent. of the metal. It is used in 6·3 per cent. solution and after preliminary doses of 1·5 c.c. and 3·5 c.c. eleven intramuscular injections of 5 c.c. are given during 14 days, making a total of 60 c.c. The course may be repeated.

There is no doubt that patients treated in hospital on these lines improved at least to some extent, especially as regards the corneal lesions. It is possible that factors other than the drugs administered were partly responsible, such as freedom from malnutrition, particularly deficiency of vitamin A and protection from the irritant effects of glare and dust.

Prevention

Eradication of the disease is clearly the ideal to be attained, but the problem is truly formidable and indeed in present circumstances almost insuperable when vast areas of such undeveloped country as have been described have to be considered. It would seem possible, however, to clear a relatively small area, say 10 square miles, if for instance a gold mine were discovered in a hyperendemic district. The co-operation of the entomologist, the sanitary engineer and administrative services would be required.

It is necessary to break the chain by which the disease is perpetuated in either man and animals or in the insect. Protective clothing particularly boots and long trousers would go far to prevent Simulium biting in the usual area below the knee, and it has been noted by Blacklock (1926) as well as at Funsi that the wealthier people who are better clothed have a lower infection rate, though perhaps this is partly because they do less work on the farms where flies abound. Repellant cream which usually contains Pyrethrum, Dimethyl phthalate, Rutgers 612 or Indalone could be used to protect exposed areas of skin, though the substances so far produced are effective for only a limited time being washed away by sweat. Perhaps the more persistent D.D.T., Dichloro-diphenyl-trichlorethane may have possibilities. Excision of nodules around which microfilariae are most numerous is of value not only to the patient himself but also because it lessens his danger to others. Strong (1934) working in Central America found that by excising all nodules from 1,000 persons the infection rate was reduced from 40 per cent. to 4·5 per cent. in the following year and that there was a 50 per cent. reduction in the fly infectivity. In some cases it might be necessary to transfer infected persons to another district, clearly one in which Simulium is

proved to be absent for fear of spreading the disease, and animal carriers such as goats would need to be excluded and herds of game driven away. Such methods would not only protect the individual directly but would also reduce the chances of Simulium ingesting the worm.

Elimination of Simulium is by far the most important measure, especially since the bites are a nuisance as well as a danger. Since breeding takes place in running water, and even little streams so extensive in the rainy season are sufficient, considerable surface drainage would be required. The aims would seem to be to decrease oxygenation of the water by slowing the current by means of locks or dams, and by clearing away vegetation and rocks over which the water ripples and on which the fly lays her eggs. Slowing and deepening the streams would also augment the effect of chemical poisons introduced into the water. O'Kane, quoted by Strong (1937) found Phinotas oil a fairly effective larvicide, and Dampf (1942) used Creolin, one drop per second for 24 hours repeated every 15 days. Certain small fish are known to feed on mosquito larvae and these might also be used with success against Simulium, though measures would be required to keep them alive in the dry season.

The provision of an adequate water supply by the drilling of wells or if necessary by pipe lines would lessen the need for persons to frequent the streams.

Clearing the long grass especially where shaded by trees would reduce the harbourage of adult flies, and spraying with D.D.T. the vegetation in the danger area near the streams clearly has possibilities. Low-flying aircraft employed for this purpose could cover a wide expanse of country.

Future Prospects

It would be long before such measures as these could stamp out this terrible disease and it is to be expected that medical science will in time devise more efficient methods. The effects of treatment may be tried on animals, either dogs suffering from other forms of *filariasis* or on cattle or horses with *onchocerca gibsoni* or *o. cervicalis*. For this there should be plenty of material in Queensland. If goats are proved to suffer from the human type of the disease, as seems probable, they should prove suitable experimental animals. Attempts are now in progress to transmit the disease to monkeys.

The effect of treatment may be assessed by the reduction of microfilariae in the aqueous, by the increase in the proportion of dead adults in the nodules and dead microfilariae in the skin, and to some extent by the fall in the eosinophil count.

The most promising drugs to date are organic preparations of metals, especially antimony and arsenic. Since the worms do not live in the blood some cumulative drug appears desirable in order to obtain sufficient tissue concentration. Many preparations already produced await trial and it is inconceivable that in the end science will be defeated by a filaria.

Acknowledgments.—My thanks for assistance in this investigation are due to many. To Brigadier G. M. Findlay, Consulting Physician, West African Force, without whose help the tour of investigation might never have been possible and whose interest and advice have been of the greatest value. To the Army Medical Services for the loan of instruments and the provision of transport. To Captain J. R. Holden, R.A.M.C., not only for his excellent professional work but also for his assistance and comradeship on tour. To the Colonial Medical Service in the Gold Coast for the use of the library and the microphotographic apparatus, and to several of its officers and in particular Dr. G. Saunders and Dr. Maurice Browne whose help has already been recorded. To Major K. R. Hill, R.A.M.C., and others of my colleagues for preparing some of the specimens, and to the Ministry of Information for developing and printing the photographs.

REFERENCES

ADAMS, A. R. D. (1938).—*Lancet*, p. 545.
ANDERSON, C. and LEHUCHER, P. (1940).—*Arch. Inst. Pasteur de Tunis*, Vol. XXIX, p. 1.
APPELMANS, M. (1935).—*Rev. Belge Sci. Med.*, Vol. VII, p. 525.
AUSTEN, E. E. (1909).—" African Bloodsucking flies other than Mosquitoes and Tsetse flies," London.
BARLOVATZ, A. (1940).—*Ann. Soc. Belge de Med. Trop.*, Vol XX, p. 149.
BEQUAERT, J. C. (1934).—*Contrib. from Dept. of Trop. Med. and Inst. for Trop. Biol. and Med.*, Cambridge, Mass.
BLACKLOCK, D. B. (1926).—*Ann. Trop. Med. and Parasit.*, Vol. XX, pp. 1 and 203.
——— (1927).—*Brit. Med. Jl.*, January 22nd, p. 129.
BLACKLOCK, D. B. and SOUTHWELL, T. (1938).—" A guide to Human Parasitology for Medical Practitioners," 3rd Edition.
BLAMCHARD, M. and LAIGRET, J. (1924).—*Bull. Soc. Path. Exot.*, Vol. XVII, p. 409.
BOASE, A. J. (1935).—*East African Med. Jl.*, Vol. XI, p. 326.
BROWN, H. W. and SHELDON, A. J. (1941).—*Jl. Amer. Vet. Med. Assoc.*, Vol. LXXXXVIII, p. 47.
BRUMPT, E. (1919).—*Bull. Soc. Path. Exot.*, Vol. XII, p. 464.
——— *Ibid*, Vol. XIII, p. 535.
BRYANT, J. (1935).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXVIII, p. 52.
CALDERON, V. M. (1917).—*Juventud Medica.*, Vol. XVII, p. 97.
——— (1919).—Doctorate Thesis, Guatemala, June, 1920.
CASTELLANI, A. (1925).—*Jl. Trop. Med. and Hyg.*, Vol. XXVIII, p. 1.
CHOPRA, R. N. and RAO (1939).—*Ind. Jl. Med. Sci.*, Vol. XXVII, p. 549.
CLAPIER (1917).—*Bull. Soc. Path. Exot.*, Vol. X, p. 150.
CORSON, J. F. (1922).—*Ann. Trop. Med. and Parasit.*, Vol. XVI, p. 407.
COUTELEN, F. (1935).—*Bull. Soc. Path. Exot.*, Vol. XXVIII, p. 126.
CRUIKSHANK, A. (1938).—*East African Med. Jl.*, Vol. XIII, p. 172.
DAMPF, A. (1942).—*Bol. Oficina Sanitaria Panamericane*, Vol. XXI, p. 753.
DARRIBA, A. R. (1935).—*Medicina Paises Calidos*, Vol. XII, p. 561.

DEJOU, L. (1938).—*Bull. Soc. Path. Exot.*, Vol. XXXI, p. 720.
DE LA TORRE, I. (1931).—*Bull. Office Internat. d'Hyg.*, Publique, Vol. II, p. 201.
DESOIL, P. and BENOIT (1920).—*C.R. Soc. Biol.*, Vol. LXXXIII, p. 682.
D'HOOGHE, M. (1934).—*Ann. Soc. Belge Med. Trop.*, Vol. XIV, p. 153.
——— (1935).—*Ibid.* Vol. XV, p. 159.
DUBOIS, A. (1916).—*Bull. Soc. Path. Exot.*, Vol. IX, p. 305.
——— (1917).—*Ibid.* Vol. X, p. 365.
DUBOIS, A. and VITALE, S. (1938).—*Ann. Soc. Belge Trop. Med.*, Vol. XVIII, p. 553.
DUPUY (1924).—*Bull. Med. du Katanga*, Vol. 1, p. 258.
DYCE SHARP, N. A. (1926).—*Trans. Roy. Soc. Trop Med. and Hyg.*, Vol. XIX, p. 3.
——— (1927).—*Proc. Roy. Soc. Med.*, Vol. XX, p. 927.
——— (1927).—*Lancet*, December 17, p. 1290.
——— (1928).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXI, p. 3.
ENZER, J. (1942).—*East African Med. Jl.*, Vol. XIX, p. 134.
FINDLAY, G. M. (1939).—" Recent Advances in Chemotherapy," 2nd Edition, London.
FISCHER, O. (1932).—*Arch. f. Schiffs-u. Trop. Hyg.*, Vol. XXXVI, p. 1.
FUCHS, V. F. (1938).—*Geographical Jl.*, Vol. LXXXXIV, p. 318.
FULLEBORN, F. (1923).—*Arch. f. Schiffs-u. Trop. Hyg.*, Vol. XXVII, p. 386.
——— (1924).—*Proc. Internat. Conference on Health Probl. in Trop. America*, p. 241.
——— (1926).—*Arch. f. Schiffs-u. Trop. Hyg.*, Vol. XXX, p. 189.
——— (1931).—*Arch. f. Dermat. u. Syph.*, Vol. CLXIV, p. 216.
FULLEBORN, F. and SIMON (1913).—*Arch. f. Schiffs-u. Trop. Hyg.*, Vol. XVII, p. 8.
——— *Idem.*, Beihefte, p. 5.
GIAQUINTA MIRA, M. (1937).—*Ann. d'Igiene*, Vol. XXXXVII, p. 109.
GIBBINS, E. G. and LOEWENTHAL, L. J. A. (1933).—*Ann. Trop. Med. and Parasit.*, Vol. II, p. 48.
GOPSILL, W. L. (1939).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXXII, p. 55.
GORDON, R. and O'CONNOR, F. W. (1934).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, p. 385.
GONNERT, R. (1942).—*Zentralb. f. Bakt.*, Vol. CIL, p. 75.
GOVANNES, ALVAREZ, J. (1933).—*Trabajos*, Vol. II, p. 41.
GUERRERO, P., RETI, A., MORA, C. F. and SAENZ, C. F. (1922).—*La Juventud Medici* (Guatemala), Vol. XIX, p. 460.
GULATI, R. L. (1934).—*Indian Vet. Jl.*, Vol. XI, p. 32.
GUTIERREY, V. L. (1931).—*Rev. Mexicana de Biol.*, Vol. XI, p. 1.
HARDWICKE, C. (1928).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXI, p. 495.
HARLEY-MASON, R. J. (1939).—*East African Med. Jl.*, Vol. XV, p. 363.
HARRIS, B. P. (1940).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXXIV, p. 233.
HAWKING, F. (1939).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXXIII, p. 95.
HEYDON, J. M. (1927).—*Austral. Jl. Experiment. Biol. and Med. Sci.*, p. 61.
HISETTE, J. (1931).—*Ann. Soc. Belge Med. Trop.*, Vol. XI, p. 45.
——— (1932).—*Ibid.* Vol. XII, p. 433.
——— (1933).—*Bull. Med. du Katanga*, Vol. X, p. 61.
——— (1938).—*Supp. to Amer. Jl. Trop. Med.*, Vol. XVIII, p. 58.
HOFFMANN, C. C. (1930).—*Ann. Inst. Biol. Univ, Nac. Mexico*, Vol. 1, p. 5.
——— (1930).—*Arch. f. Schiffs-u. Trop. Hyg.*, Vol. XXXIV, p. 461.
HOLDEN, J. R. (1944).—Personal Communications.
JOHNSTONE, H. G. and LARSEN, A. E. (1935).—*California and Western Med.*, Vol. XXXVIII, p. 000.
JOYEUX, C. L., SODAN, J. and ESMENARD, J. (1935).—*Bull. Soc. Path. Exot.*, Vol. XXVIII, p. 435.
KHAW, O. K. and CHEW, S. H. (1936).—*Chin. Med. Jl. Supp. No.* 1, p. 402.
KULZ, L. (1914).—*Arch. f. Sc.*, Vol. XVIII, p. 164.
KULZ, L. and BACH, F. W. (1913).—*Centralbl. f. Bakt.*, Vol. LXX, p. 321.
LAIGRET, J. (1922).—*Bull. Soc. Path. Exot.*, Vol. XV, p. 303.
——— (1930).—*Ibid.* Vol. XXII, p. 497.
LARUMBE, J. E. (1930).—*Ann. Soc. Mexicana de Oftalmologia y oto-rhino-laringoliga*, Vol. VIII, p. 16.
LECOMTE, A. (1915).—*Bull. Soc. Path. Exot.*, Vol. VIII, p. 655.
LEIPER, R. T. (1913).—Report of the Advisory Committee of the Tropical Diseases Research Fund. Colonial Office, May, 1913.
LEVY, A. H. (1939).—*Proc. Roy. Soc. Med.*, Vol. XXXII, p. 1620.
LOWENTHAL, L. J. A. (1943).—*Ann. Trop. Med. and Parasit.*, Vol. XXXVII, p. 147

MacFie, J. W. S. and Corson, J. F. (1922).—*Ann. Trop. Med. and Parasit.*, Vol. XVI, pp. 439 and 465.
McMahon, J. P. (1940).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXXIV, p. 65.
McMullen, W. H. (1939).—*Trans. Ophth. Soc. U.K.*, Vol. LIX, p. 587.
Marbaix and Appelmans, M. (1937).—*Arch. d'Ophtalmologie*, Vol. I, p. 978.
Martinez-Baëz, M. (1935).—*Ann. Parasit. Humaine et Comparee*, Vol. XIII, p. 207.
Messer, C. C. V. (1942).—*Proc. Rhod. Sci. Assoc.*, Vol. XXXIX, p. 28.
Mira, M. G. (1934).—*Riforma Med.*, Vol. L, p. 858.
Mohammed, A. S. (1931).—*Ann. Trop. Med. and Parasit.*, Vol. XXV, pp. 215 and 509.
Mora, C. F. (1922).—*La Juventud Medica*, Vol. XIX, p. 460.
Montpellier, J. and Lacroix, A. (1920).—*Presse Med.*, Vol. XXVIII, p. 207.
——— (1922).—*Bull. Soc. Path. Exot.*, Vol. XV, p. 815.
——— (1921).—*Bruxelles-Medical*, Vol. V, p. 140.
Montpellier, J., Lacroix A. and Boutin, P. (1921).—*Bull. Soc. Path. Exot.*, Vol. XIV, p. 653.
Munoz Ochoa, M. (1934).—*Contrib. from Dept. of Trop. Med. and Inst. for Trop. Biol. and Med.*, Cambridge, Mass.
Muhlens, P. (1932).—*Arch. f. Schiffs-u. Trop. Med.*, Vol. XXXVI, p. 287.
——— (1936).—*Ibid.* Vol. XL, p. 28.
——— (1937).—*Ibid.* Vol. XLI, p. 430.
Nettel, R. (1941).—*Medicana, Mexico*, Vol. XXI, p. 409.
——— (1943).—*Ibid.* Vol. XXIII, p. 368.
Ochoterena, I. (1927).—*Rev. Mexicana de Biol.*, Vol. VII, p. 55.
——— (1928).—*Arb. u. Tropenkran*, Fests. Schr. N. Nocht., p. 386.
——— (1930).—*Ann. Inst. Biol. Mexico*, Vol. I, pp. 77, 307 and 309.
——— (1931).—*Ibid.* Vol. II, p. 109.
O'Connor, F. W. (1922).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XVI, p. 28.
O'Neil (1875).—*Lancet*, p. 265.
Ouzilleau, F. (1913).—*Bull. Soc. Path. Exot.*, Vol. VII, p. 80.
——— (1923).—*Presse Med.*, Vol. XXXI, p. 617.
Ouzilleau, F., Laigret, J., and Lefrou (1921).—*Bull. Soc. Path. Exot.*, Vol. XIV, p. 717.
Pacheco-Luna, R. (1918).—*Amer. Jl. Ophthal.*, Vol. I, p. 122.
——— (1919).—*Ibid.* Vol. II, p. 793.
——— (1920).—*Revista Cubana d'Oftalmologia*, Vol. II, p. 80.
——— (1921).—*Amer. Jl. Ophthal.*, Vol. IV, p. 175.
Pittaluga, G. and Goyanese, J. (1932).—*Medicana Paises Calidos*, Vol. V, p. 124.
Preston, P. G. (1935).—*Jl. Trop. Med. and Hyg.*, Vol. XXXVIII, p. 81.
Quevedo, A. (1941).—*Amer. Jl. Ophthal.*, Vol. XXIV, p. 1185.
Raynal, J. (1931).—*Marseille-Med.*, Vol. LXVIII, p. 821.
Reti, A. (1922).—*La Juventud Medica*, Vol. XIX, p. 471.
Richet, P. (1938).—*Bull. Soc. Path. Exot.*, Vol. XXXII, p. 341.
Rodenwalt, E. (1914).—*Arch. f. Schiffs-u. Trop. Hyg.*, Vol. XVIII, p. 1.
Robles, R., quoted by Calderon (1916).—*La Juventud Medica*, 1917, Vol. XVII, p. 97.
——— (1919).—*Bull. Soc. Path. Exot.*, Vol. XII, p. 442.
Rodhain, J. (1915).—*Bull. Soc. Path. Exot.*, Vol. VIII, p. 734.
——— (1920).—*Ibid.* Vol. XIII, p. 848.
——— (1931).—*Ibid.* Vol. XXIV, p. 882.
——— (1942).—*Ann. Soc. Belge de Med. Trop.*, Vol. XXII, p. 11.
Rodhain, J. and Dubois, A. (1931).—*Ann. Soc. Belge de Med. Trop.*, Vol. III, p. 613.
Rodhain, J. and Gabrilov, W. (1935).—*Ann. Soc. Belge de Med. Trop.*, Vol. XV, p. 551.
Rodhain, J. and Van den Branden (1916).—*Bull. Soc. Path. Exot.*, Vol. IX, p. 186.
Rodhain, J. and Valcke, G. (1935).—*Ann. Soc. Belge de Med. Trop.*, Vol. XV, p. 361.
Roubaud, E. and Jamot, E. (1920).—*Bull. Soc. Path. Exot.*, Vol. XIII, p. 232.
Saenz, C. F. (1922).—*La Juventud Medica*, Vol. XIX, p. 460.
Sandground, J. H. (1934).—*Contrib. from Depart. of Trop. Med. and Inst. for Trop. Biol. and Med.*, Cambridge, Mass.
——— (1938).—*Supp. to Amer. Jl. Trop. Med.*, Vol. XVIII, p. 91.
Saunders, G. (1929).—Annual Report, Gold Coast Med. Dept.
——— (1936).—*Ibid.* (unpublished).
——— (1943).—Personal communications.

SCHWETZ, J. (1930).—*Ann. Soc. Belge de Med. Trop.*, Vol. X, p. 385.
SCOTT, J. G. (1944).—*Brit. Med. Jl.*, April 22, p. 553.
SEMADINI, B. (1943).—*Schweiz. Med. Woch.*, Vol. LXXIII, p. 75.
SILVA, R. (1932).—*Southern Med. Jl.*, Vol. XXV, p. 113.
STEPHANOPOULO, G. (1942).—*Bull. Soc. Path. Exot.*, Vol. XXXV, p. 157.
STRONG, R. P. (1931).—*New Eng. Jl. of Med.*, Vol. CCIV, p. 916.
——— (1931).—*Science*, Vol. LXXIII, p. 593.
——— (1934).—*Contrib. from Depart. of Trop. Med. and Inst. for Trop. Biol. and Med.*, Cambridge, Mass.
——— (1937).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXX, p. 489.
——— (1938).—*Supp. to Amer. Jl. Trop. Med.*, Vol. XVIII, p. 1.
TORRES ESTRADA, A. (1942).—*Amer. Jl. Ophthal.*, Vol. XXV, p. 1445.
VAN DEN BERGHE, L. (1936).—*Ann. Soc. Belge de Med. Trop.*, Vol. XVI, p. 519.
——— (1941).—*Ibid.* Vol. XXI, pp. 63, 167 and 261.
VAN HOOF, L. (1934).—*Trans. Roy. Soc. Trop. Med. and Hyg.*, Vol. XXVII, p. 607.
VARGAS, L. (1941).—*Rev. Inst. Salubridad y Enfermedades Trop.*, Vol. II, p. 365.
——— (1942).—*Ibid.* Vol. III, p. 57.
VOGEL, H. (1931).—*Med. Welt.*, Vol. 25.
WILSON, R. P. (1933).—*Eighth Ann. Rep. Giza Memorial Ophth. Lab.*, Vol. LXXXV.
WRIGHT, W. H. and UNDERWOOD, P. C. (1936).—*N. Amer. Vet. Jl.*, Vol. XVII, p. 39.