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NEW OBSERVATIONS ON OCULAR ONCHOCERCIASIS

Related Pathological Methods and the Pathogenesis of the Various Eye Lesions

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SYNOPSIS

The records of 2000 blind or partially blind persons in the onchocerciasis areas of West Africa provided the background information for this report.

The author has grouped his material in three sections. The first of these deals with diagnostic methods, and contains the results of skin and conjunctival biopsies, as well as a description of onchocercomas and an estimate of the life-span of *Onchocerca* adults.

Next, the pathogenesis of ocular lesions is discussed in the light of evidence obtained from a series of animal experiments designed to test two theories—namely, the existence of an allergic state and damage by toxins.

In the last section, which is devoted to clinical observations, the author demonstrates the existence of a relationship between the posterior segmental lesion and vitamin A deficiency, and shows that punctate corneal opacities result more often from certain virus diseases and malaria than from onchocerciasis. A description follows of various degenerations due to a local nutritional disorder combined with vitamin A deficiency in onchocercal limbitis and anterior uveitis.

The observations reported in the present paper are based on material collected and studied during the West African Survey, sponsored by the British Empire Society for the Blind, which started in 1952 in Ghana (then the Gold Coast) and later moved to Nigeria and the Cameroons. The information on which our conclusions are based was taken from the records of 2000 blind or partially blind West Africans examined in onchocerciasis areas, almost half of whom were given more than usually stringent examinations—physical, ocular and pathological—up to the end of 1954.

The observations presented here are related to various points brought out in the first report of the WHO Expert Committee on Onchocerciasis.[1]

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which met in Mexico in 1953, and are grouped under the following headings to facilitate reference to that report:

(1) Observations related to diagnostic methods

(2) Observations on the pathogenesis of the ocular lesions of onchocerciasis

(3) Clinical observations.

I. OBSERVATIONS RELATED TO DIAGNOSTIC METHODS

Biopsies

It is considered that a suspected case of onchocerciasis should not be dismissed until the following minimal diagnostic requirements have been fulfilled: right and left conjunctival biopsies (where the eye is acutely inflamed the skin of the lids is a very good substitute for the conjunctiva), and skin biopsies taken from the neck, chest, thigh and calf; if found negative these latter should be repeated until a total of 16 skin biopsies has been taken. Positive biopsies should be stained and the microfilariae identified. There is always the possibility that the microfilarial species observed is *Acanthocheilonema perstans*, which is very widespread in the north of the area surveyed. The stain we prefer is our own simple modification of Mayer's haemalum.

In the tropics blood should not be drawn when skin biopsies are taken; but when the shade temperature falls below 65°F (about 18°C) we have found it wise to take the biopsy deeper. In 12 cases with ocular manifestations characteristic of the disease, but with a negative skin series, deep biopsies were carried out and blood was drawn. All were found to be positive, and the microfilariae recovered were identified after staining as *Onchocerca volvulus*. These interesting results were obtained among the people of the high plateau of north Nigeria during the rains, when the temperature stood at one time at 58°F (14.5°C), and the patients had been waiting in an almost naked state exposed to a cold, wet wind.

Of the conjunctival biopsies taken from our Ghana cases 44% were positive. In one-third the invasion of this tissue was unilateral; 9, including 5 children, of the 900 cases given the full examination showed positive conjunctivae in the absence of a positive skin series. The size of the conjunctival biopsy does not seem to matter. In 100 people in a village on the Red Volta the piece of conjunctiva removed from the left eye was three times as large as the piece from the right eye. Sixty from the right eye and 57 from the left were positive. This village was in an area of high endemicity, where the skin infectivity rate in persons over the age of 20 was 100%, and the average rate for all age-groups was 87%. But in less heavily infected areas the practice of taking a small biopsy might falsify the results. Nevertheless, the smaller the wound the quicker it heals.

The portion of skin least commonly infested is that at the junction of the base of the neck with the shoulder. Only 36% of the biopsies taken from this region were positive. The chest, thigh and calf seem to be equally heavily infected; and in the series of 900 subjects examined the figures were 60%, 57% and 53% respectively. It appeared that the skin over the ribs had a slightly higher infectivity rate in the cases examined during our survey.

Intraocular microfilariae were found to be much less common than we had been given to expect. The rate of infestation was under 15% in the aqueous humour. In only two instances was a microfilaria seen in the vitreous; in both cases the lenses were dislocated below the pupil, and as a result of the alteration in the optical system the magnification was increased, and the parasites could be seen with great ease pushing their way through a partially fluid vitreous. As intraocular microfilariae are seen readily, it is difficult to explain the low figure.

Nodules

Nodules (onchocercomas) may occur anywhere in the body; areas where they are frequently missed are the sacrum and the head. Head nodules tend to be small in West Africa and are usually hard and tightly adherent to the underlying bony fascia. At first several were removed to settle our doubts; in every case they proved to contain live *Onchocerca* adults. They were more common on the heads of children.[a] The most common site, however, is undoubtedly around the pelvis, especially in the region of the trochanters and iliac crests. In this our findings agree with those of Van den Berghe, published in the second of his well-known papers on this subject.[10] We never permit ourselves to diagnose the presence of an onchocercoma in the groin by palpation. As nodule puncture, if negative, is completely unreliable, excision alone can decide.

Small hard onchocercomas we found to be nearly always active; a large soft cystic one on the other hand is frequently negative, containing dead adults; nevertheless the microfilariae present in the fluid of such nodules appear to live there for a very long time. Onchocercomas are often found in aggregations of three or four in cases in North Ghana; the number obviously varies with the degree of infectivity. It is usual to find two or three together, the superficial nodule riding free in the tissue, but at a greater depth there will be a hard solid onchocercoma bound tightly to the fascial sheaths.

It has often been said that the life-cycle of the adult worms is unknown; a rough estimate may be obtained by excising nodules in cases in an endemic area, preferably one with not too heavy an infectivity rate. In such an area 15% of the children under 10 years of age and 75% of the adults between the ages of 20 and 30 were infected. None of the children under 10 had

[a] Of children in the under-10 age-group, 9% had palpable nodules; 58% of these were on the head.

soft onchocercomas, and when the hard nodules were excised they revealed live adult worms. Among the men over 20, on the other hand, soft necrotic onchocercomas were a commonplace. These findings may not be comprehensive, but we believe that they provide a basis for the assumption that the life of the adult *Onchocerca* is about 10-15 years. At the least, we can be sure that the disease is self-limiting. There is evidence that this factor is related to the habits of the human host. For example, the Mohammedan covers his body, except when he farms. When he farms he is bitten and infected many times. If he becomes blind, he farms no more, but sits in his white doti on the thoroughfares. He is not bitten or infected so readily under these circumstances. Several such cases in the 20-30 age-group have been noted in our records as being free of *O. volvulus* and having only old degenerate nodules. The practice of carrying babies bound to the mothers' backs by cloths so that only the infants' heads are exposed almost certainly explains the high prevalence of head nodules in children. That these nodules disappear as the child grows into a man indirectly supports our estimate of 10-15 years as the life-span of *Onchocerca* adults.

The occasional absence of palpable onchocercomas does not surprise those with experience of the disease. In areas of high endemicity we have found onchocercomas in only 77% of cases, whereas the skin infectivity rate was 98%. On the periphery of the endemic area, where the latter rate was 16%, only 10% of cases revealed nodules, despite intensive palpation.

II. OBSERVATIONS ON THE PATHOGENESIS OF THE OCULAR LESIONS OF ONCHOCERCIASIS

Ever since the pioneer work of Hissette [2] a state of allergy induced by the microfilariae has been put forward as an explanation of the inflammatory phases of onchocerciasis in the skin. Recently Toulant (in a personal communication) suggested the possibility that this might also apply to the eye.

The popular view of the pathogenesis is that the lesions are caused by toxins released as the dead microfilariae disintegrate. Ridley [4] says that all lesions are caused by this process. Sarkies [8] postulates an allied vitamin deficiency as the primary cause of the posterior lesion, and selects riboflavin, although the clinical trials proved unconvincing.

The theory that allergy is the *modus operandi* will be difficult to disprove, for our knowledge in this field is still far from complete, and such information as is available is frequently contradictory. The scientist will maintain that the existence of an allergic state requires a single sensitizing dose of antigen, and that the shocking dose will only be effective when given after at least 14 days. Doses of antigen given at periods of less than a week after the initial sensitizing dose are more likely to desensitize. On the other hand those who have studied the clinical characteristics of allergy in the eye will claim that the greatest sensitivity arises from repeated assaults of

antigen or from the maintenance of a tiny focus of infection over a long time. Of the two views the latter seems better to fit the clinical picture of onchocerciasis.

Of course it might happen that the eye itself becomes sensitized locally when the first microfilaria invades it, but the allergic attack will not occur until the next parasite enters the hypersensitive zone. When we consider the allergic state induced in the skin by filaricides, it is difficult to explain why no reaction ever occurs in the eye, even if invaded, for ocular symptoms in our opinion do not invariably accompany skin allergy. If allergy occurs always in the skin, why does it not occur always in the eye?

Clinically, the fact that an acute onchocercal eye is greatly alleviated by the intravenous injection of a foreign protein favours the theory that an allergic quality exists; nor is there anything in the pathology of the onchocercal eye to exclude this possibility—on the contrary it tends to strengthen it. Despite these conflicting arguments we decided to carry out several experiments on rabbits and guinea-pigs, a description of which is given below.

Experiments

Our first object was to demonstrate passively transferable allergic antibodies in the serum of heavily infected human subjects. Such antibodies are usually more easily detected by passive transfer tests in animals than by sensitivity tests in human beings.

Tests were carried out with the blood sera of patients with detectable microfilariae in skin biopsies. Those with very heavy infections were chosen. Small samples of serum (0.05 ml) were mixed with an equal volume of antigen preparation, being injected intradermally in one guinea-pig series, and instilled into the conjunctiva of a second series. The treated parts were inspected over a period of an hour for local signs of hyperaemia and oedema. The preparations and results were as follows:

(1) A supernatant was prepared from nodule fluid. No reaction was observed.

(2) Microfilariae were extracted from the skin by standing the samples in warm Ringer-Locke, and subsequently centrifuging at 5000 r.p.m.; the supernatant contained 90 microfilariae per ml. No reaction was observed.

(3) The conditions were the same as in (2), only the supernatant was subjected to supersonic waves (frequency, 1 megacycle; power output, 6 watts; cell diameter, 4 cm). No reaction was observed.

(4) The supernatant was treated by heating to 100°C for 30 minutes. No reaction was observed.

(5) The supernatant was treated by the addition of an equal volume of acetone, and left to stand for 30 minutes at 4°C; the acetone was then removed by evaporation in vacuo. No reaction was observed.

(6) The supernatant was treated with 3% trichloracetic acid, allowed to stand for 30 minutes at 40°C, and then neutralized by sodium hydroxide. No reaction was observed.

Although we were unable to demonstrate the presence of antibodies by these experiments in the guinea-pig, the possibility that they are produced in man is not of course excluded.

Active immunization experiments were also undertaken. Ten ml of antigen prepared by the trichloracetic acid method were injected subcutaneously into a series of rabbits; in another series, the antigen was repeatedly instilled into the subconjunctiva, with a view to reproducing a possible local allergic state. After a period of 15 days the shocking dose was placed in the fornix. Animals which did not receive the sensitizing dose served as controls. Negative results were again obtained. Guinea-pigs sensitized by antigens prepared by each of our experimental methods also failed to exhibit hypersensitivity in these tests. In short, the bulk of our evidence to date fails to support the allergic theory.

The second theory—damage by toxins—was then investigated. Four possibilities exist here:

(1) Excretory products of living microfilariae may act as toxins to the eye, although it is felt that they are unlikely to attain a sufficiently high titre in the general circulation to accomplish this.

(2) Products formed locally by the decomposition of the dead organisms may enter the general circulation and act as toxins.

(3) Excretory or degenerative products may act as vitamin analogues, and in this way affect the sensitive posterior coats of the eye.

(4) Some essential ocular nutrient or nutrients, such as vitamin A, may be preferentially assimilated by the products of microfilarial decomposition and excretion, or by the live parasites, either microfilarial or adult. As a result the use of this essential nutrient may be blocked at some stage in its metabolic cycle.

The involvement of vitamin A was suggested by the constant occurrence of night blindness as a presenting sign of the posterior lesion. Although the following experiments were carried out, much work remains to be done.

(1) Living microfilariae were injected subconjunctivally into rabbits—perhaps for the first time. The suspension contained only 18 microfilariae per ml and 10 organisms were injected. Two days later a piece of conjunctiva was taken, but no microfilariae were recovered. The result was a slight but definite hyperaemia of the conjunctival vessels after 36 hours, increasing in intensity over three days. At its height it led to the infiltration of the adjacent crescent of the cornea by leucocytes (limbitis).

(2) Subconjunctival injection of dead microfilariae produced a reaction within a few minutes. This lasted longer and was more intense. The antigen

used was derived from the previous extract by centrifuging and bombardment. The reaction consisted of a violent hyperaemia of the conjunctival and limbal vessels; neovascularization of the neighbouring cornea had occurred within 24 hours (the invasion seen by optic section was between Bowman's membrane and the epithelium) and a crescent-shaped "snow-storm" effect in the corneal epithelium was produced—probably by an invasion of leucocytes. In all these operations full aseptic precautions were taken. The results show that dead or dying microfilariae can produce a reaction in all ways similar to the limbitis so characteristic of ocular onchocerciasis.

These experiments have been described in the present paper, despite the fact that they are still only in the developmental stage, in order to illustrate their great potential value. One concludes from them that it is the dead rather than the living microfilariae which act as toxins, and that the reaction is a primary (toxic) one. Several antigens also act in this way, however, so it may well be that the hypersensitive state which was lacking in guinea-pigs and rabbits is in fact produced in man. Our future work may reveal this.

III. CLINICAL OBSERVATIONS

The Posterior Segmental Lesion

Clinically, it is far more probable that the posterior lesion is due to an intoxication than that it is caused by a state of allergy. It must be remembered that there is no treatment for this manifestation of ocular onchocerciasis; in no recorded case has an improvement ever been noted. The condition usually progresses to blindness; it is always bilateral and often equally severe. The fundal appearance described by Ridley [4] is not always the characteristic one—as many other workers have remarked—although it may well be that here we are dealing with more than one lesion. But this paper does not intend to give a general account of the disease; rather it will confine itself to observations on some of the accepted characteristics.

First, the belief that the sheathing of the vessels, originally described by Ridley,[4] is evidence of the filarial origin of the disease is very questionable. Sarkies [8] states that the sheathing of veins and arteries is consistent with the diagnosis, claiming, in fact, that it is specific. We cannot agree. The sheathing is a parallel sheathing, seldom extending more than 5 mm from the papilla. In a few cases only was it seen that a vessel (always an artery) had been converted into a fibrous cord; the latter invariably ran into a dense area of aggregated pigment and oedema, leaving one with the impression that the artery was compressed mechanically by the focal reaction. Parallel sheathing of blood vessels within a few millimetres of the optic nerve-head is, however, a commonplace in the African eye, whether or not it is associated with a defect in vision. It is not very uncommon in

Europe in young healthy eyes. The cause is said to be a congenital thickening of the adventitial layers (in which there is a marked neuroglial component).

The second observation stems from the pathological reports on four eyeballs that we obtained. No microfilariae were found in the choroid or retina of any one of them. Hissette [2] and Hughes [3] have demonstrated the parasites in the choroid. It is always possible of course that a high titre of toxin will be produced in the root of the iris and the ciliary body during an acute iridocyclitis and will reach the veins; but although there was an indication in one of these four cases that the anterior uvea had been affected, the clinical evidence of such a condition is usually only slight—if it exists at all. In addition, in cases treated with Hetrazan—and we have treated several—where the microfilariae are rapidly destroyed *in situ*, if the posterior lesion is due to the presence of dead organisms, one would expect a loss of acuity. In none of our cases was there any change—for worse or for better. These findings encouraged us to look for another factor. Since we arrived in Nigeria 19 cases have been taken into the ward of the Survey Research Centre; of these 19, 8 had a moderately severe onchocerciasis, 7 had a very slight infection, and 2 showed neither microfilariae nor onchocercomas, despite the fact that 16 skin biopsies were taken. This does not necessarily signify that adult filariae are not present free in the tissues, of course. Such information as was sought could not be elicited in North Ghana, where the infectivity rate is much higher than it is in the Jos area of Nigeria, from where these people came. The average rate in the Plateau Province of Nigeria (over 2000 feet (610 metres) above sea level) is, according to our figures to date, about 10%. The figure does not matter; the fact that such cases were found with slight infection, or without apparent infection, does. In view of the fact that night blindness is the presenting sign, we decided to make every effort to combat vitamin A deficiency. A few cases with positive WR tests were subsequently excluded, and a few others failed to present themselves for further investigation. The rest—8 in all—were typical examples of the posterior lesion. Five of the 8 cases had a secondary optic atrophy, and 3 had normal discs. As usual, the degree of optic atrophy bore no relationship to the degree of visual defect. In 4 cases there was evidence of infection with *A. perstans* microfilariae, in addition to onchocerciasis; yet another had microfilariae of *W. bancrofti* in his night blood. Each subject was given 165 000 I.U. of vitamin A daily. Improvement in the visual acuity of 4 of them occurred at the end of the first week, and at the end of a month they could see to move about. The quick and early response to this massive vitamin A intake appears to be important in the prognosis. The recorded acuities are as follows:

Case 1: Visibility of hand movements improved to 6/36 in the right eye and to 6/12 in the left.

Case 2: Vision in both eyes improved from 6/24 to 6/12.

Case 3: Perception of light only in both eyes improved to about 6/36; this case had a nuclear sclerosis, otherwise the improvement would have been much more marked.

Case 4: Visibility of hand movements improved to 6/12 in both eyes.

Vitamin A therapy was continued for another two to three weeks, but no further improvement occurred. A course of Hetrazan was then administered, but the vision remained unchanged. (The dosage that we recommend is one of 12 g of Hetrazan over 13 days.) It must be stressed here, as it was at the WHO Conference on Onchocerciasis in Africa, that our work is still incomplete, but from what we have said it must be obvious that doubt has been raised as to the exact relationship of onchocerciasis to the posterior lesion, although the existence of some sort of connexion between the two has not been dismissed out of hand. The optic atrophy which so frequently accompanies the posterior lesion may also have a nutritional element, for nutritional deficiencies in Africa are usually multiple. Earlier studies [6, 7] have shown that a deficiency in thiamin, especially if coupled with a riboflavin deficiency, can lead to optic atrophy in rats. An analysis of 238 nutritional amblyopias in prisoners-of-war strengthens this belief.[5]

Corneal Opacities

If we are still not sure whether the posterior lesion is a manifestation of onchocerciasis, there should no longer be any doubt that as a general rule the corneal opacity when present in an otherwise healthy eye is not related to the disease. Theoretically, of course, such infiltrations can form around a dead microfilaria. But it should be emphasized that there is a better explanation of it in the case of the African cornea. There are signs already that in an area of endemicity every single case in which a corneal opacity is found in association with microfilariae in the skin is designated ocular onchocerciasis.

What are these opacities? They are made up of a collocation of faintly grey flecks, the centres of which are either clear or dense, or outlined with a white line. The size of the opacities varies considerably. They may be single or multiple; some lie entirely in the epithelium; most involve the anterior margin of Bowman's zone; a few are interstitial; several are saucer-shaped, but as they are filled with epithelium the convexity of the cornea is maintained. The frequent accompaniment of other opacities, which are not round, has received little mention, although their presence is highly significant.

Ridley [4] described the death of a microfilaria in the cornea, observing that 7 days later it was encompassed by a corneal opacity of the type just described. Several living microfilariae were observed in the cornea in the

course of this survey. Yet no corneal opacity answering to the classic description was produced as a result of their passage through the eye, even after a week had elapsed. Moreover we excised from the human eye quite a few of these characteristic opacities, staining and examining them under the microscope, but never saw any sign of anything resembling a microfilaria. Of course the parasite body may be absorbed quickly. In two instances living microfilariae were seen in the cornea, and the slice containing them was cut out with a Graefe knife. The parasites were observed crawling between the basal epithelium and Bowman's membrane. This is probably the only place where microfilaria are visible with the slit lamp. We have never been able to see them in the stroma, although we know that they occur there from examination of eyes that have been sectioned. The microfilariae found it difficult to force a passage through the cornea, and the course taken was very tortuous. This must also be true when they push through the corneal stroma, for although the protoplasmic arms of the cellular syncytium of the cornea run parallel in one meridian, in all others they intersect in an intricate network. These findings are mentioned because it has been stated that the " pathways " taken by the microfilaria in the cornea can be seen, and that these " pathways " lead to the ultimate burial ground of the parasites—the opacity. Thus one misinterpretation leads to another, for the " pathways " described were said to be straight. We have argued that this is most unlikely. I have described these observations at length, for each of them supports our own contention—namely, that the corneal opacities frequently manifest a herpes corneae, nearly always following malaria, the initial vesicular stage of which either does not occur, or, if it does, lasts only a matter of hours.

In a group of African youths (average age 17 years) attending a Teacher's Training College, and therefore with sufficient education to enable them to answer straightforward questions fairly accurately, 41 were found to have corneal opacities of the type under discussion. None of them had onchocerciasis. Of those with opacities 60% had had an attack of malaria within the last month, and 88% within the last two months. This is just the type of history one would expect in cases of herpes simplex. Only 38% and 40% respectively of those without opacities gave such a history. The average period since the last attack was 38 days in those with opacities, and 69 in those without.

Corneal opacities may be induced by protein shock, if the temperature rises well. It is as untrue to say that the opacities occur in every case of fever as it is to say that every corneal opacity is due to malaria. Fuchs' corneal opacities—clinically known as epidemic keratoconjunctivitis—are also found from time to time. We have recorded cases of herpes zoster, the first signs of which are identical. The opacities in leprous keratitis, too, are not dissimilar. But there is other evidence to support the thesis. The polyhedral opacities referred to earlier are characteristic of the dendritic

form of herpes simplex; the greater prevalence of the nummular form in Africa is no more surprising than the predominance of the papillary over the follicular form of trachoma, for that occurs nowhere else in the world. Hypoaesthesia of the cornea was found to exist in just under one-half of all our cases of corneal opacities; since this was restricted to the region of the opacities, stimulation by quadrants is essential if records are to be kept. Keratitis metaherpetica disciformis is fairly common.

Finally, in one-third of the 379 cases on our records enlargement of the multi-fibre corneal nerve bundles, a frequent accompaniment of herpes, was noted; these may be the microfilarial " pathways " already referred to. Malaria is such a commonplace in the tropics that it is easy to lose sight of the fact that despite his degree of immunity the African suffers many attacks. The answers to a questionnaire issued to the entire community of the Training College in Toro, Nigeria, showed that on the average a young African will have from two to three attacks of fever every year. In view of the recrudescences of herpes febrilis and the many attacks of fever to which the African is subject, the high prevalence of corneal opacities in African communities is not surprising.

All these facts provide enough evidence to refute the statement that the corneal opacity is sufficiently typical to be diagnostic of ocular onchocerciasis.

Degenerations of the Anterior Segment of the Eye arising out of Local or Systemic Nutritional Factors

The bulk of the evidence strongly suggests that an inflammation of the iris results from the direct invasion of this very sensitive tissue by microfilariae. In several of our cases histological examination revealed many microfilariae in the iridal tissues; pieces of iris removed through a keratome incision in an acute onchocercal iritis were teased under the microscope, and live microfilariae emerged as from a skin biopsy. They were identified as *O. volvulus.* Bung-eye is not always associated with acute iritis; when it is, it coincides with a heavy infection of the skin and deeper tissues of the lids; in several cases sent for biopsy, the eyelid was found to contain a lipoma. However, our observations on the keratitis and anterior uveitis of onchocerciasis—the common lesions—are not yet ready for presentation. The matter is brought up because both symptoms, especially the latter, initiate a whole series of conditions arising primarily from interference with the nutrition of the lens and cornea. In people whose diet is already deficient in vitamin A it is not surprising that this leads to trouble.

Xerosis corneae is a common complication of long-standing keratouveitis of onchocercal origin. Irregular grey or white patches or crescents, frequently confluent, form on the surface of the cornea or run parallel with the limbus. They are usually covered by the epithelium. If the epithelium

is broached pigmentation follows. Pigmentation and rucking of the lower bulbar conjunctiva is a common accompaniment of chronic onchocercal limbitis; here too, one should suspect vitamin A deficiency as playing a part. In time these conditions, if they do not progress to keratomalacia, lead to the total metaplasia of both cornea and conjunctiva, so that their external appearance becomes identical. The metaplasia is followed by keratinization and deep pigmentation. The epithelium is papillated; it includes many fine granules of melanin. Connective-tissue cells are also present. The epithelium is vascular, bleeding readily when excised, and oedematous, but no cellular infiltration exists. We have never found microfilariae present is such end-membranes. Elastin is found in the deeper layers, and an excess of subepithelial reticular and collagen fibres. Where keratomalacia is superadded, the cornea ruptures. This is a common end-picture of onchocercal keratitis.

There are many other types of degeneration that follow repeated attacks of ocular onchocerciasis. They all distort and disguise the front of the eyeball, but with patience and care even a dense leucomatous phthisical eye can be interpreted. The more interesting conditions include band-shaped opacity, Fuchs' *Dellen* or dimples, Coats' white rings, lipin degeneration, as well as the more common hyalinization, calcareous degeneration, epithelial bullae, honeycomb excrescences, changes in the corneal thickness, fragmentation and calcification of Bowman's membrane, and thickening of Descemet's membrane. They do not all occur in old opaque corneae, but sometimes result only from a limbitis. In most instances, however, there is a coexisting anterior uveitis, usually quiescent. The systemic deficiency completes the picture, wherever the lesion exists.

Lastly, there is the question of the involvement of the crystalline lens. It was stated during the WHO Expert Committee meeting in Mexico [11] that it was not certain if onchocerciasis led to cataract. Appelmans [1] could find no evidence of microfilarial invasion of the lens—but is that necessarily a prerequisite? Scott [9] reported the presence of a dead microfilaria stuck to the anterior capsule (epithelium?) and observed the subject in question over a period of 8 months. No cataract resulted. No reaction whatsoever occurred in the eye.

If the lens is not directly attacked, it is most assuredly indirectly affected. Fine exudates in the retrolental and vitreous spaces, and cyclitic membranes behind, and fibrous occluding membranes in front involving the anterior capsule epithelium have been found in 7 of 16 eyeballs that we have excised. It is not surprising that in the midst of such devastation the lens should suffer. The opacification is cortical; the epithelium may be grossly proliferated. The suspensory ligament in turn becomes degenerate, and as a result the cataractous lens at first becomes tremulous, then subluxates, and finally dislocates. This is the picture of what is in fact an onchocercal endophthalmitis.

In association with the same plastic exudation that surrounds the lens, blockage of the canals of Schlemm occurs. Of our 16 cases examined pathologically, 5 showed deep secondary glaucomatous cupping. Unless we can find a rapid way of controlling the acute onchocercal kerato-uveitis, even if we cure the disease, such irreversible degenerative processes will already have been set in train.

RÉSUMÉ

Les observations rapportées dans cet article ont été réunies au cours de l'enquête poursuivie dès 1952 en Afrique occidentale (Côte de l'Or, Nigeria, Cameroun britannique) sous les auspices de la British Empire Society for the Blind (Société de l'Empire britannique pour les aveugles). Cette enquête a porté sur 2000 sujets atteints de cécité totale ou partielle dans des zones infestées par l'onchocercose.

Après avoir décrit et discuté les méthodes d'examen clinique et histopathologique appliquées au diagnostic de cette filariose, l'auteur aborde la question de la pathogenèse des lésions oculaires. On a supposé que les lésions qui entraînaient la cécité pouvaient être dues à des phénomènes d'allergie ou bien à des toxines mises en liberté par la décomposition des filaires mortes, cette intoxication étant aggravée par une carence en vitamine A. L'auteur rend compte d'expériences sur le lapin et le cobaye, effectuées en vue de préciser l'origine de ces lésions. Aucun résultat positif ne permet de considérer qu'un phénomène allergique soit la cause de troubles oculaires chez ces animaux. Qu'il puisse en être autrement chez l'homme n'est évidemment pas exclu. En revanche, l'inoculation à l'animal de produits toxiques (injection subconjonctivale de microfilaires mortes ou de microfilaires vivantes) produit une réaction ressemblant beaucoup à l'inflammation du limbe caractéristique de l'onchocercose oculaire. Ces essais, quoique préliminaires encore, semblent indiquer que la lésion peut être la conséquence de phénomènes toxiques, produits par la désintégration des microfilaires mortes. Les constatations cliniques des lésions de la partie postérieure de l'œil, chez l'homme, sont en meilleur accord avec la théorie toxique qu'avec la théorie allergique. Toutefois, il n'a pas été possible encore d'élucider l'origine des troubles, toujours bilatéraux, qui conduisent presque fatalement à la cécité. L'administration de vitamine A à des sujets présentant des troubles d'origine filarienne a amélioré la vision chez quelques-uns d'entre eux. Il est possible que l'atrophie optique qui accompagne souvent les lésions postérieures soit favorisée par l'une des carences alimentaires si fréquentes en Afrique.

L'opacité cornéenne, dans un œil par ailleurs sain, n'est pas forcément en relation avec l'onchocercose. Une enquête auprès de jeunes Africains, par exemple, montra que les 41 d'entre eux qui étaient atteints d'opacité cornéenne ne présentaient pas de signes d'onchocercose, mais que 60% avaient eu un accès de paludisme le mois précédent et 88% au cours des deux derniers mois. D'autres affections, en particulier celles qui sont accompagnées de manifestations fébriles, fréquentes en Afrique, pourraient expliquer en partie l'incidence élevée des opacités cornéennes.

Parmi les lésions de la partie antérieure de l'œil, l'inflammation de l'iris semble due à l'invasion directe de ce tissu, très sensible, par les microfilaires. Plusieurs types de manifestations dégénératives sont la conséquence d'attaques répétées d'onchocercose oculaire.

Quant au cristallin, s'il n'est pas directement attaqué, il est indirectement affecté par les lésions des tissus voisins. Il s'opacifie et, en raison de la dégénérescence des ligaments, peut finalement se disloquer. C'est ainsi que progresse ce que l'on peut appeler l'endophtalmie onchocercosienne.

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