tary and more particularly in the posterior lobe. But there are some difficulties that have to be answered before the diagnosis of Fröhlich's syndrome can be accepted. The adiposity is of a very remarkable type. While the condition of the upper limbs is about normal, that of the face and trunk is of excessive obesity, whereas that of the lower limbs is below normal and the buttocks are markedly emaciated. The sexual organs do not come up to the standard, and while the testicles are atrophied and undescended, the penis is about normal. The voice cannot be called distinctly feminine, but it is not masculine, either. Though the patient has some hair on the face and pubis, it is rather scanty and below par. His mental condition accords with Fröhlich's syndrome. A very close parallel distribution of fat in this patient will be found in Case 45 of Harvey Cushing, and in the case shown by Turney.[4] The fat over the spine shows the same creases as the case shown by F. F. Batten.[5] As the adiposity in this case fails to correspond with a case of dystrophia adiposogenitalis of pituitary origin, we have to think of other ductless glands, namely, the adrenals or sexual glands. With adrenal hyperplasia, the adiposity is general and is practically always associated with sexual precocity, of which there has been no indication in this case. Neither did this patient have adrenal tumor or pigmentation, which therefore speaks against adrenal hyperplasia. The scanty hair is not a symptom of adrenal hyperplasia, for in such cases we have increase of hair.

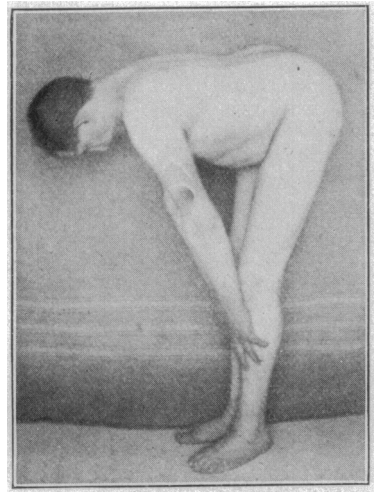

Fig. 3.—Case 2. The patient is bending body at right angle with the hips. Creases in the back entirely absent. The short big toes are easily distinguished.

Turning our attention to the sexual glands, we must recall that atrophy of these glands is always an accompaniment of pituitary diseases. As the testicles never descended, they were probably primarily involved, and the posterior lobe of the pituitary followed secondarily.

The occurrence of short thumbs and shortened big toes of both feet point directly to a disturbance in the secretion of the anterior lobe of the pituitary, which controls growth of bones.

This case is probably one of pituitary sexual gland syndrome, "polyglandular syndrome," the deficiency being mainly in the anterior lobe of the pituitary.[6]

I am greatly indebted to Dr. George R. Elliott for his kind and valued assistance, and to Dr. S. Wachsmann, the medical director of Montefiore Home and Hospital, for permitting me to report the second case.

1210 Tinton Avenue.

4. Turney: Proc. Roy. Soc. Med., Sec. Neurol. and Ophth., 1912-1913, vi, p. lxxi.

5. Batten, F. F.: Case of Hypopituitarism, Dystrophia Adiposogenitalis, Proc. Roy. Soc. Med., Sec. Neurol. and Ophth., 1912-1913, vi, p. xxxi.

6. This patient was shown in 1912 by Dr. G. R. Elliott at a meeting of the orthopedic section of the Academy of Medicine, New York, and various opinions regarding the diagnosis were expressed by the members present. The diagnosis was cleared up only after careful study by Dr. Elliott and myself.

THE INFLUENCE OF HOOKWORM DISEASE ON THE EYES

A STUDY OF FIFTY-THREE CASES *

J. W. JERVEY, M.D.
GREENVILLE, S. C.

Whenever a new disease is discovered or an old one brought into prominence, the students of the various specialties make determined and laudable efforts to establish a serious connection between the disease in question and their particular specialties. The newly found (in America) hookworm disease and the students of ophthalmology may well be expected, therefore, to become involved in some sort of investigation. In this particular case, then, let us assume that the incidence of eye lesions in connection with uncinariasis might be of interest and importance in two ways:

1. Is the hookworm infection a causative factor in the existing eye lesion?

2. If it is a causative factor, is the presenting eye lesion sufficiently distinctive or characteristic to be of diagnostic aid in the clinical recognition of uncinariasis?

Before attempting to answer let us briefly consider some salient facts and some of the observations of others appertaining to the questions before us.

GENERAL CONSIDERATIONS

Uncinariasis, or hookworm disease, belts the earth in a zone about 66 degrees wide, extending from parallel 36 north to parallel 30 south. Practically all countries between these parallels are infected, and these countries contain nearly 60 per cent. of the earth's population.[1] The incidence of the hookworm ranges from 50 to 90 per cent. of the population of many of these countries. Evidently it is a world problem. In the rural districts of our Southern states approximately 40 per cent. of the people are infected with this parasite.[2]

Zoologists state that there are two different species of hookworm, the European and the American. As all are agreed that their effects are the same when infecting the human family we may, in this study, disregard the helminthologic distinction. The general pathology and symptomatology of the disease has been well covered in a somewhat extensive literature, which I have carefully considered,[3] but comparatively little has been done in the direction of any special study of ocular conditions in connection therewith.

EYE LESIONS NOTED IN THE UNITED STATES

Hansell[4] has reported the case of a boy aged 15 infected with hookworm and exhibiting serous and hemorrhagic retinitis with characteristic appearances of retinal anemia.

A. W. Calhoun[5] has reported two cases of uncinariasis exhibiting cataracts in patients aged, respectively, 42 and 14 years.

* Read before the Section on Ophthalmology at the Sixty-Fifth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1914.

1. Hookworm Infection as a World Problem, editorial, THE JOURNAL A. M. A., June 22, 1912, p. 1946.

2. Fourth Annual Report, Rockefeller Sanitary Commission for the Eradication of Hookworm Disease, 1913.

3. The bibliography is well known and easily accessible—especially the Porto Rican studies by Ashford, King and Igaravidez, and the American studies by Stiles.

4. Hansell: Am. Med., 1901, ii, 412.

5. Calhoun, A. W.: Ophth. Rec., 1904, xii, No. 7.

F. P. Calhoun[6] reports four cases of uncinariasis, three of the patients, aged, respectively, 20, 26 and 22 years, exhibiting cataracts, and the fourth showing recurring spontaneous hemorrhage from the upper conjunctival fornix of the right eye.

Mauldin[7] reports a case of hookworm disease showing "iridocyclitis approximating an interstitial keratitis."

Stiles[8] says that in uncinariasis the pupils of the eyes have a decided tendency to dilatation, the patient may show a blank stare, and that night-blindness is reported in a number of cases. In another place Stiles[9] says:

> If the patient is directed to stare intently into the observer's eyes, there will be noticed a symptom which it is difficult to describe, but which I have found more constant than almost any other noticed, namely: After a moment, the length of time apparently varying slightly, according to the degree of the disease, the pupils dilate and the patient's eyes assume a dull, blank, almost fish-like or cadaveric stare very similar to that noticed in cases of extreme alcoholic intoxication.

Dock and Bass,[10] after a brief consideration of eye-lesions reported by foreign authors, say:

> We have often noticed that the pupil dilates readily and usually remains wide, even in the presence of considerable light, but this is a common symptom of all severe anemias.

The authors of this book report no original investigations.

So far as I am aware, these are the only published reports of observations in the United States of eye-lesions in hookworm disease. In the spring of 1910 I reported to the Greenville (S. C.) County Medical Society the cases of two girls, aged 10 and 14 years. Both had interstitial keratitis, and both were typical hookworm cases, easily admitting of snapshot diagnosis. This was verified microscopically and the patients were turned over to a colleague for thymol treatment. It is true that the family history, while not positively indicating it, was not such as to be above a suspicion of hereditary lues; but the improvement in the ocular conditions after two or three thymol treatments was little short of astounding. I thought I had made a very interesting and valuable observation, and so I had; but the most interesting part of it came a year later when both patients died of tuberculosis — one of the commonly accepted causes of keratitis parenchymatosa.

EYE-LESIONS NOTED IN FOREIGN COUNTRIES

The European observations on the incidence of eye-lesions in uncinariasis are somewhat fuller, yet even so the literature on the subject is apparently not extensive.

M. Rampoldi,[11] reporting in 1880, noted that in hookworm patients who complained only of a slight asthenopia, or of the lack of ability to fix objects, he found ophthalmoscopically a whitish retinal reflex, characteristic of edema of this membrane. In some cases visual acuity was diminished. In the case of a woman who died of hydremia he found a true exudative retinitis, which reminded him of Liebreich's cases of splenic leukemia. There were also hemorrhages into the retina, and he found lymphoid elements deposited in great quantity between the retina and the choroid.

Von Nieden[12] notes in these cases a pale conjunctiva and shining sclera. With the ophthalmoscope he observes marked paleness of the blood-current in the contracted arteries, and tortuous veins; sometimes arterial pulsation, porcelain-colored papillae and, above all, characteristic hemorrhages, like those of pernicious anemia, which lie as isolated spots or broad patches on the periphery of the retina and show a tendency to fatty degeneration. There is, he says, sclerosis and fatty degeneration of the vascular endothelium as in the pernicious anemia of *Bothriocephalus latus*. The subjective symptoms he describes as central disturbance of vision with narrowing of the field, anesthesia of the retina, accommodative and muscular asthenopia, with diplopia and a tendency to nystagmus. In spite of this picture, as outlined, von Nieden expresses the belief that the conditions are not due to anemia, but to a toxin. Out of 3,686 cases examined by him he found three cases of bilateral blindness.

Nuel and Leplat[13] say that miners suffering with hookworm frequently show disturbances of vision consisting of fatigue of the eyes without appreciable lesion; a certain amount of hemeralopia, and frequently nystagmus. These authors examined eighty-one cases and found in five the following changes: One showed retinal hemorrhages; another showed numerous retinal hemorrhages in the right eye, especially in the nerve-fiber layer, and a pale papilla in the left eye, with veins somewhat engorged; two other patients showed infiltration of papilla and retina; while the fifth, an albuminuric, had a neuroretinitis.

A. Nieden[14] announces that the hemorrhages of the ocular fundus are characteristic. He says that they occur more in the periphery of the retina, and are frequently in groups, point-shaped and close together, but without merging into each other. They frequently follow the course of the vessels, seeming to lie in the vessel walls, and appear rather like stripe-shaped exudates accompanying the vessels to the papillary area. In addition there are extensive blood-exudates in the retinal tissue, represented as large plaques with ray-formed margins. The microscope discovers sclerotic and fatty degeneration of the endothelium of the blood-vessels. In most cases the patient does not know that his eyes are affected, and he is troubled with scotomas only when the macula is the chief location of the blood-spots. More marked are the weakness of accommodation, asthenopia, fatigue of the eyes and periodic slight pareses of intrinsic and extrinsic muscles with diplopia and vertigo. Among miners there are frequently photophobia and hemeralopia. Also there is often a moderate narrowing of the field. The visual disturbances, he thinks, are caused not so much by the retinal changes as by the general symptoms of the disease. (Compare this description with von Nieden's observations abstracted above.)

Fischer[15] notes that the hookworm itself has never been found in the eye. Birmer asserted that retinal hemorrhage was pathognomonic of the anemia named after him, but this is incorrect, since it is well known, as Fischer observes, that retinal hemorrhages occur in

6. Calhoun, F. Phinizy: Eye Complications Caused by Hookworm Disease, The Journal A. M. A., Sept. 21, 1912, p. 1075.
7. Mauldin: Jour. South Carolina Med. Assn., 1910, vi, 521.
8. Stiles: Osler's Modern Medicine, i, 589.
9. Stiles: Quoted by Ashford and Igaravidez.
10. Dock and Bass: Hookworm Disease, St. Louis, 1910.
11. Rampoldi, M.: Cong. period. internat. d'ophth., 1880, Milan, 1881, vi, 283.
12. Von Nieden: Ophth. Klin., Stuttgart, 1903, vii, 181; Centralbl. f. prakt. Augenh., 1903, xxvii, 207.
13. Nuel and Leplat: Ann. d'Ocul., 1889, lii, 150.
14. Nieden, A.: Wiener med. Presse, 1897, xxxviii, 1094.
15. Fischer: Ber. d. ophthal. Gesellsch., Stuttgart, 1892, xxii, 26; Deutsch. med. Wchnschr., xix, 311.

all forms of anemia, but especially, he thinks, in ankylostomiasis.

Lutz[16] remarks that in ankylostoma infection the vessels of the fundus, especially the arteries, are contracted and the papilla is paler than normal. Lutz has also noted, as a rare sign, chemosis of the bulbopalpebral fold.

R. Rampoldi[17] relates a case of bilateral convergent strabismus, coming on suddenly, and accompanied by homonymous diplopia. Treatment for hookworm was administered and the strabismus disappeared.

Ashford and Igaravidez[18] state that in a series of cases of this disease, 69.5 per cent. had more or less serious disturbances of the eyes. (There seems to be an error in the figures, however, and the percentage should have been put at 34.9.) They go on to say:

> We cannot doubt that much of this was due simply to the degree of anemia, but there remains a considerable percentage . . . with more or less marked visual affections with very little anemia.

They quote Loebker and Bruns as remarking on the pallor of the eye-grounds, pulsation of veins, lowered intra-ocular pressure, venous tortuosity and, commonly, retinal hemorrhages. They note that many authors speak of edema of the papilla. They quote Siccardi as observing nystagmus, diplopia, amblyopia, muscular and accommodative asthenopia and restriction of the field. This author admits the possibility of anemia being the cause of most of the eye symptoms, and that functional visual disturbances may be due to reflex irritation from the intestinal tract, but avers that when we have a retinitis coincident with optic atrophy, the question of the presence of a circulating toxin must be considered. Ashford and Igaravidez emphasize the occurrence of "blurred vision" and night-blindness, and mention the fact that corneal ulcers have been reported, they having seen one case of the latter. They report that Lippitt, with a large experience, states that fully three-fourths of his cataract patients in Porto Rico were anemic.[19]

COMPARATIVE CONSIDERATIONS

Here, then, we have an array of symptoms and pathologic conditions, any of which — with the exception of cataract, noted and discussed below — might be fully expected to appear in the ordinary run of cases of anemia. The lesion most frequently noted and dilated on appears to be retinal hemorrhage, and one or two of the authors referred to above seem to think that the appearance of these hemorrhages in the peripheral area of the retina is more or less characteristic. This is assuredly a mistake, for such lesions commonly occur in other forms of anemia. Some idea of the frequency of retinal hemorrhages in anemia may be had from the figures quoted by Weeks,[20] which recite that of 238 American cases of pernicious anemia, 31 per cent. had retinal hemorrhages, and of 326 foreign cases 72 per cent. exhibited this eye-lesion.

In uncinariasis there is a decrease of the hemoglobin content and of the red blood-corpuscles, and a comparative increase in the leukocyte-count. When Weeks wrote his book, which was published in 1910, he had probably never given a thought to hookworm disease as having any influence on the eyes, nor, I believe, was there any reason why he should have, but the following brief extracts from his discussion of leukocythemic retinitis and the retinitis of pernicious anemia (which he remarks are very similar) make an interesting comparison with Nieden's report abstracted above: In the first-mentioned form of retinitis he says, "The fundus of the eye usually appears lighter in color than normal . . . the arteries are pale, often somewhat reduced in caliber . . . the veins are dilated, broad and tortuous . . . the retina often becomes hazy . . . numerous hemorrhages occur near the periphery of the retina . . . many striped or flame-shaped hemorrhages may occur in the vicinity of the disk," and in the retinitis of pernicious anemia he says, "The nerve-fiber layer of the retina is often edematous . . . in places the fibers are pushed apart by hemorrhages . . . the elements of the deeper layers of the retina are also separated by the constituents of the blood that have escaped from the blood-vessels . . . the escaped blood-corpuscles undergo degenerative changes . . . white corpuscles are found in the clots, and, in addition, small hyaline masses are present." Indeed, in this brief description one can almost see before his mind's eye one of Nieden's "characteristic" hookworm cases.

In reference to the blurring of vision and blindness mentioned as accompanying uncinariasis, it is to be noted that Kurtsinger[21] collected 198 cases of more or less complete blindness due to hemorrhage from remote parts of the body, the bleeding having been either sudden and profuse — a single hemorrhage — or slow and continuous (this is the method of extraction by the hookworm). It is interesting to observe that out of 189 of these cases, seventy-two were from hemorrhage from the stomach and intestine, and that three followed the application of leeches.

Some of the authors quoted above maintain that the presence of the eye-lesions which they have noted must be explained on the theory that there is a specific toxin in hookworm disease. But why should a mere theory be mooted to explain something that is already easily comprehensible and that has been demonstrated time and time again to be based on a well-recognized pathologic principle? Furthermore, if the eye-lesions were caused by a toxin, then those having the heaviest infections should produce the most eye symptoms; but this is not at all the case. It is well to remember that the retinal lesions of anemia are due either to a reduction in the amount of circulating blood, or to a change in the quality of the blood. The hookworm accomplishes both ends, whether or not it is the manufacturer and disseminator of a specific toxin, for it extracts blood in volume, and decreases the hemoglobin and red corpuscle contents. The hookworm, then, causes an anemia, by no means necessarily a toxemia, and any form of anemia may cause the eye symptoms we are discussing — a fact which has been recognized certainly ever since Helmholtz gave us the first ophthalmoscope more than sixty years ago.

In addition to the symptoms mentioned, pallor of the disk, exudative retinitis, retinal edema and vascular tortuosities are more or less common fundus

16. Lutz: Samml. klin. Vortr., Leipsic, 1880-1886, Inn. Med., No. 88.
17. Rampoldi, R.: Ann. di Ottal, Pavia, 1888-1889, xvii, 170.
18. Ashford and Igaravidez: Uncinariasis in Porto Rico, U. S. Senate Document 808, 1911, p. 96.
19. Two Japanese authors have had something to say on this subject, but I was unable to find a translator. The references are: Inoshita, Chingai Iji Shinpo, Tokio, p. 1160. Onishi, idem., xiv, No. 4, p. 2. Hisaki, Chiba Igahuhwai-Zassh, Tokio, 1900, No. 47, p. 1. For these and some other references I am indebted to Dr. Charles Wardell Stiles.
20. Weeks: Diseases of the Eye, 1910, p. 766.
21. Kurtsinger: Quoted by Weeks: Diseases of the Eye, 1910, p. 434.

changes in anemia, and cannot be considered as indicating any specific causation.

Dilatation of the pupil is of such common occurrence (a weakening of the iris constrictor) in the various anemias that it is familiar even to the general practitioner; yet many of such cases may be more fancied than real, since there is no fixed physiologic size for the pupil. In the fifty-three cases which I have tabulated I did not once see a really noticeably dilated pupil; but there were very few severe cases in this series. I failed entirely to elicit Stiles' "fish-like-stare" sign, though I made a number of efforts to do so. Ashford and Igaravidez, with their unlimited field of observation, were unable to recognize it.

Imbalance of the ocular muscles and accommodative weakness are not infrequently seen in anemia. It would be curious, indeed, if, in the general myasthenia, the delicate musculature of the eye should escape involvement.

It is hardly fair to accuse the hookworm in cases of hemeralopia and nystagmus. The authors noting these are foreigners, many of whose cases are in miners, who are, of course, as a class, peculiarly subject to these ocular symptoms.

As to nyctalopia, this is a phenomenon known to exist most frequently in tropical and subtropical countries, and it is therefore easy to understand why the principal references to this symptom come from Ashford and Igaravidez in Porto Rico.

F. P. Calhoun[6] believes and Hansell[22] concurs, that the cataracts which he has observed in hookworm patients were caused by a toxin originating from the parasite, and directs attention to the theory that some forms of cataract may be caused by circulating toxins of various sorts — chemical or biologic. It may well be that the hookworm evolves a toxin; Ashford and Igaravidez and others believe so, as I have already remarked, but it has never been demonstrated; and it is certainly strange, if there is such a toxin and it is a cause of cataract, that only five such cases have been reported in our Southern states, where it has been demonstrated that 40 per cent. of the population of the rural districts are the victims of uncinariasis.

Lippitt,[23] with a large experience, states that fully three-fourths of his cataract patients in Porto Rico were anemic. It is well known that cataract occurs more often among the lower classes and the poorly nourished than among persons in better environments. When, therefore, we consider that 80 per cent. of Porto Rico's population is infected with hook-worm,[24] and are consequently in poor hygienic condition, it is certainly not remarkable that three-fourths of all cataract patients in that island are observed to be anemic. Indeed, it is rather more to be wondered at, in the light of these facts, that the percentage of anemic cases in such a series does not go to a much higher figure.

A TABULATED SERIES OF FIFTY-THREE CASES

Other eye-lesions associated with anemia are some forms of choroiditis, vitreous opacities and palpebral folliculosis. Curiously enough, none of these have been mentioned heretofore in connection with hookworm anemia, yet they must have been present in some of the thousands of cases that have been examined. Doubtless, choroiditis has been overlooked in the frequent retinal involvement, though I saw traces of it in two cases (4 per cent.) of my series tabulated herewith (Cases 1 and 9). Vitreous opacities might, of course, be easily overlooked unless especially sought for. In my series I noted four cases (7.5 per cent.) of folliculosis (Cases 5, 40, 42 and 50).

In the fifty-three cases of my series there were thirty-five males and eighteen females. The ages ranged from 9 to 22 years. The diagnosis of hookworm was made microscopically in every case. Only one patient (Case 27) had been treated previously. Homatropin mydriasis was used in every case for retinoscopy and ophthalmoscopy. It was my impression (without actual timing) that the patients on the whole responded to the mydriatic more quickly than normal persons would have. The refractive errors were found to follow closely the well-known average of persons of like age. The two cases of interstitial keratitis noted have been referred to in the foregoing text. There were no marked eye-symptoms voluntarily referred to by a single patient. In twenty-six of these cases (approximately 50 per cent.) I thought I observed a shallowness of the anterior chamber, one of them (Case 37, a severe case) being especially marked. I cannot insist on this observation, however, since I had no means of accurate measurement, so that the report on this point is but a matter of opinion without substantiation, and I do not, myself, attach any great significance to it. The most common fundus changes were pallor and tortuous vessels, the latter occurring in twelve cases (22.6 per cent.). Retinal hemorrhage had occurred in only two cases (Cases 1 and 9), and then in but slight degree.

CONCLUSIONS

1. The answer to the first question in the opening sentences of this paper is that hookworm disease, by virtue of the qualitative and quantitative anemia and the general systemic ill condition for which it is responsible, is, in this indirect way, and in this way only, a causative factor in the various eye-lesions which have been described as accompanying it.

2. To the second question the answer is that none of the eye-lesions occurring in this disease are in any sense sufficiently distinctive or characteristic to be of diagnostic value.

The evidence, collected from various sources, seems complete enough, and in addition if, in a systematic examination of the eyes of fifty-three consecutive and unselected cases, we find nothing to point us to a specific causative factor for the eye-lesions, and nothing in the clinical ocular pathology that could be regarded as a distinctive diagnostic aid in the recognition of the systemic disease, we may safely conclude that, in the light of our present knowledge, the association of eye-symptoms and uncinariasis must be regarded as purely incidental, or at least that the eye-symptoms occur only as the sequelae of general pathologic conditions, the principles of whose existence have long been recognized.

It need hardly be pointed out that the importance of these conclusions lies, of course, in the fact that many cases of anemia, with or without eye manifestations, occur without an accompanying hookworm infection, and also that many cases of uncinariasis, with or without eye complications, are encountered which are lacking the symptom of anemia. The latter condition is seen in many apparently robust and even

22. Hansell: Discussion on article by Calhoun, Footnote 6.
23. Lippitt: Quoted by Ashford and Igaravidez.
24. Ashford and Igaravidez: Uncinariasis in Porto Rico, 1911, p. 179.

athletic young persons from the rural districts and is especially marked in the negro, who seems more or less immune to the hookworm syndrome, though Burdell[25] has shown that in certain localities in our South 65 per cent. of all negroes are infected with the parasite, and, while acting as intermediary hosts and active carriers of the disease, present no clinical symptoms whatever.

Obviously, it is well to know, when we see the signs of anemia in the eye-grounds, or in the facies for that matter, that we might properly suspect the hookworm of being a possible cause of the anemia; but beyond this our studies of the coincidental eye-lesions in uncinariasis have not yet carried us.

25. Burdell: Jour. South Carolina Med. Assn., 1910, vi, 326.

ABSTRACT OF DISCUSSION

DR. CHARLES W. KOLLOCK, Charleston, S. C.: Dr. Jervey asks: 1. Is the hookworm infection a causative factor in the existing eye-lesion? 2. If it is a causative factor, is the presenting eye-lesion sufficiently distinctive or characteristic to be of diagnostic aid in clinical recognition of uncinariasis?

EYE-SYMPTOMS IN FIFTY-THREE HOOKWORM PATIENTS*

Case No.	Severity of Infection	General Condition	Vision Without Correction		Conjunctiva	Cornea	Anterior Chamber	Retinoscope Refractive Error	Ophthalmoscopic Findings	Remarks
			P.	L.						
1	Light	Fair	15/15	15/15	Normal	Normal	Normal	Comp.hy.astig.	Tortuous vessels. Tiny old hemorrhage and pigment left.	
2	Light	Fair	15/20	15/20	Normal	Normal	Normal	Hy. astig.	Normal	
3	Light	Fair	15/20	15/20	Normal	Normal	Normal	Comp.hy.astig.	Normal	
4	Light	Fair	15/15	15/15	Normal	Normal	Normal	Hy.	Normal	
5	Light	Fair	15/20	15/20	Folliculosis	Normal	Normal	Comp.hy.astig.	Normal	
6	Light	Fair	15/15	15/15	Blepharitis	Normal	Shallow	Hy.	Slight retinal congestion	
7	Light	Fair	15/20	15/20	Normal	Normal	Normal	Comp.hy.astig.	Pale retinas, large veins	
8	Medium	Poor	15/15	15/15	Pale	Normal	Normal	Emmet.	Pale disks, tortuous vessels	
9	Medium	Poor	15/30	15/30	Normal	Normal	Normal	Mixed Astig.	Red disks, tiny hem. and pigment left	Epicanthus
10	Light	Fair	15/15	15/15	Normal	Normal	Normal	Emmet.	Retinas congested, disks indistinct	
11	Light	Fair	Illiterate		Normal	Normal	Shallow	Hy.	Normal	
12	Light	Fair	15/15	15/40	Normal	Normal	Shallow	Hy.	Venous congestion, tortuosities	
13	Light	Fair	15/30	15/30	Normal	Normal	Shallow	Hy.	Pale fundi	
14	Light	Fair	15/20	15/20	Normal	Normal	Shallow	Hy.	Normal	
15	Light	Fair	15/15	15/15	Normal	Normal	Shallow	Hy.	Normal	
16	Light	Fair	15/30	15/30	Normal	Normal	Shallow	Hy.	Normal	
17	Light	Fair	15/15	15/15	Normal	Normal	Normal	Emmet.	Central veins full	
18	Light	Fair	15/15	15/15	Normal	Normal	Normal	Hy.	Veins full and tortuous, disks obscure	
19	Light	Fair	15/30	15/40	Normal	Normal	Shallow	Hy.	Normal	
20	Light	Fair	15/20	15/20	Normal	Normal	Shallow	Hy.	Normal	Epicanthus
21	Light	Fair	15/15	15/15	Normal	Normal	Shallow	Comp.hy.astig.	Tortuous vessels	
22	Light	Fair	15/20	15/20	Normal	Normal	Normal	Comp. My. astig.	Deeply pigmented fundi, tortuous vessels	
23	Light	Fair	Illiterate		Normal	Normal	Normal	Hy.	Normal	
24	Medium	Fair	15/15	15/15	Normal	Normal	Shallow	Hy.	Normal	
25	Medium	Fair	15/15	15/15	Normal	Normal	Shallow	Emmet.	Normal	
26	Medium	Fair	7/70	6/70	Normal	Normal	Normal	Hy.	Deeply pigmented fundus, tortuous vessels	Alternating internal strabismus
27	Severe	Fair	15/15	15/15	Normal	Normal	Shallow	Emmet.	Retinal congestion, disks indistinct, tortuous vessels	Thymol treatment 4 weeks ago. Numerous ova now in feces.
28	Severe	Fair	15/15	15/15	Normal	Normal	Shallow	Emmet.	Right fundus normal, left congested	
29	Light	Fair	Illiterate		Normal	Normal	Normal	Emmet.	Pale fundi	
30	Light	Good	15/15	15/15	Normal	Normal	Shallow	Comp.hy.astig.	Pale disks	
31	Light	Good	15/20	15/20	Normal	Normal	Shallow	Hy.	Normal	
32	Light	Fair	15/20	15/15	Normal	Normal	Shallow	My.	Vessels full and tortuous	
33	Light	Fair	15/15	15/15	Normal	Normal	Normal	Hy.	Normal	
34	Light	Fair	15/20	15/20	Normal	Normal	Normal	Hy.	Pale fundi	
35	Light	Fair	15/20	15/20	Normal	Normal	Normal	Hy. Astig.	Vessels full and tortuous	
36	Light	Fair	15/15	15/15	Normal	Normal	Shallow	.....	.....	
37	Severe	Poor	15/15	15/15	Normal	Normal	Very shallow	Hy.	Pale fundi	
38	Medium	Poor	15/20	15/20	Normal	Normal	Shallow	Emmet.	Pale disks	
39	Medium	Poor	15/20	15/30	Normal	Normal	Shallow	Hy.	Fundi pale, disks hazy	
40	Medium	Poor	15/15	15/15	Folliculosis	Normal	Normal	Hy.	Pale fundi	
41	Light	Good	15/15	15/15	Normal	Normal	Normal	Hy.	Disks pale, vessels tortuous	
42	Light	Good	15/15	15/15	Folliculosis	Normal	Normal	Hy.	Normal	
43	Light	Fair	15/15	15/15	Normal	Normal	Normal	My.	Normal	
44	Light	Fair	15/70	15/70	Chr. congest'n	Normal	Normal	Comp.hy.astig.	Normal	
45	Light	Fair	15/70	15/70	Chr. congest'n	Normal	Normal	Mixed astig.	Normal	
46	Severe	Poor	15/15	15/15	Normal	Normal	Shallow	Emmet.	Fundi pale, vessels tortuous	
47	Light	Good	15/15	15/15	Normal	Normal	Normal	Hy.	Normal	
48	Light	Poor	15/15	15/15	Normal	Normal	Shallow	Hy. astig.	Normal	
49	Light	Fair	15/15	15/15	Normal	Normal	Shallow	Hy.	Normal	
50	Light	Good	15/30	15/20	Folliculosis	Normal	Shallow	Hy.	Normal	
51	Light	Fair	15/15	15/15	Normal	Smoky	Shallow	Hy. astig.	Normal	
52	Severe	Very poor	....	.....	Congested	Normal	Normal	.....	.....	Interstitial keratitis. Died tuberculosis one year later.
53	Severe	Very poor	....	.....	Congested	Smoky	Normal	.....	.....	Interstitial keratitis. Died tuberculosis one year later.

* In all the patients the pupils were normal in size and reaction, and the lenses were normal.

A careful study of the report of his cases leads me to conclude that in no instance is there a lesion or condition which could be ascribed to any particular cause. The only condition which he mentions as being more conspicuous than others occurred in twenty-six of the fifty-three cases reported and was an apparent shallowness of the anterior chamber. This was marked in one, a very severe case, while the general condition of the others in which it was noted was fair. He does not mention an increase of tension; in fact the opposite condition would be more likely observed in this class of cases, as a condition of the vessels and blood which permits the latter to pass through the walls of the former might also exist in and about the cornea and cause increased exosmosis and a temporary shallowness of the anterior chamber. This is, perhaps, theorizing too much, but there is no reason to deem it characteristic of anything more than a weakened general condition.

Calhoun, Hansell, Ashford and Igaravidez suggest that a toxin may originate from the hookworm and be a cause of cataract as other toxins have been supposed to be. Dr. Jervey well says that in the South, where 40 per cent. of the population have the disease, it is strange that only five cases of cataract have been reported. In the number of cases reported he is mistaken, though it will not alter his deductions. I have reported two cases of cataract in children having hookworm and have seen two others who were undoubtedly infected, though at the time nothing was known of the worm. These two had every appearance of the disease and came from a neighborhood where such cases were and still are very numerous. These children were from 8 to 12 years of age and on two I operated successfully for the removal of the cataracts. All were white. The negro is said to be immune to the effects of the worm and it is undoubtedly true that cataract is less frequently seen in the negro than the white child, even the zonular variety which is probably due to congenital causes. I have sometimes thought that the corneal affections, so common in the negro, might be indirectly due to the hookworm, but of this there is no proof and a more likely cause is syphilis. Night-blindness is much more frequent among negroes than whites, especially among children, sometimes in those who appear in fair condition and often among those who suffer from xerosis. Xerosis and night-blindness, which often go hand in hand, are very rare in white children in my part of the country, while uncinariasis is of every-day occurrence. It would be strange, if night-blindness is caused by the worm, that it should occur so frequently in the negro, who is immune, and so seldom in the white child, who offers a fertile soil. The numerous conditions which have been mentioned by writers, such as retinal hemorrhages, pallor and edema of the retina, haziness of the optic disk and weakened accommodation, are all such common associates and followers of the various anemias that it would take a wide stretch of the imagination to class them as pathognomonic of the disease until much more is known about it than now.

My own experience and a digest of the views of others cause me, therefore, to accept the conclusions of Dr. Jervey as correct until, at least, further investigations shall prove to the contrary.

DR. F. PHINIZY CALHOUN, Atlanta, Ga.: My remarks are not a criticism of Dr. Jervey's paper, but a defense of my views presented before this Section in 1911. That ocular changes do occur, no one can deny, and Dr. Jervey's report of fifty-three cases shows a fairly large percentage of eye complications, namely, two cases of retinal hemorrhage and twelve cases in which the retinal veins were congested or tortuous—evidences of circulatory changes. I believe that Dr. Jervey and I agree that eye complications do occur in hookworm disease, and the only real point of difference is whether an anemia or a toxemia is the exciting cause.

Dr. Jervey's views, expressed in the answer to his first question, brings up an old subject in the discussion of hookworm disease, namely, the existence of a toxemia and the cause of the anemia. It was early assumed that the worms attaching themselves to the alimentary wall would lead to hemorrhages and the resulting loss of blood would cause the characteristic anemia. Necropsies have shown only a severe, profuse catarrh of the small intestines and often spots of hemorrhagic infiltration with the worms hanging to it. It does not follow that the worms suck the blood; in fact, Loos insists that their natural food is intestinal epithelium, and although blood is found in the intestines of the worms, the red corpuscles are not digested. These findings led to the belief that hookworm anemia was one of toxemia and not secondary to the loss of blood, and two main theories have been propounded: that the worm directly secretes a toxin, or that this toxin is produced by some extraneous organism, as intestinal bacteria. Numerous attempts have been made to isolate a hemolytic substance, with varying success. As to which theory is correct I do not venture an opinion, but I rely solely on my clinical observations and the words of students of this disease, that a toxin does exist. I, however, have seen cases of great anemia in hookworm disease in which a few worms were found; this is substantiated in one case of hookworm cataract with anemia and few worms. The fact that no specific toxin has yet been positively demonstrated should not lessen our belief that it does exist. Within a few days after the administration of the treatment for the elimination of the worms, the patient's symptoms of malaise and general lassitude disappear, yet it is weeks or months before the corpuscular and hemoglobin elements in the blood approach a normal. Again, chlorosis more nearly than any other chronic ailment approaches hookworm disease in its anemia. In the former, there is the usual development of the genitalia, pubic hair and even a beard, whereas in the latter, all are markedly undeveloped.

We find certain extra-ocular and asthenopic changes associated with disease, many of them present in other serious chronic ailments due to a "systemic ill condition," as Dr. Jervey aptly puts it, but for the more serious intra-ocular findings, such as changes in the retina, choroid and even the lens, I do believe that hookworm disease *per se* is the cause, and not in an indirect way through the anemia, just as circulatory changes of the retina occur in chronic nephritis, diabetes, the cancerous cachexia and even pellagra, analogous diseases in which eye changes, even cataract, have been recorded. Whether we believe in the toxin theory of hookworm disease, or the existence solely of an anemia, lenticular changes in young people can be explained, on account of the anatomic relation of the lens to the ciliary body, iris and humors of the eye which supply its nourishment. Given a hookworm subject who states positively that at one time he saw distinctly and many months after the initial lesion (ground-itch) his sight began to fail, and when extracting a milky-white, soft cataract, there were seen retinal disturbances, such as tortuous vessels and small hemorrhages, which disappeared after the elimination of the worms and health restored, is it not reasonable to suppose that the hookworm was responsible for these changes? Such has been my experience with a case not profoundly anemic.

By no means does it follow that if the eye lesions were caused from a toxin then those patients having the heaviest infection of hookworm should produce the most eye symptoms. I am not sure that the severest cases of anemia, diabetes or nephritis show the most eye changes. I have seen, in a few hookworm patients, eye lesions such as tortuous veins, choroidal changes and spontaneous hemorrhages from the conjunctiva without a profound anemia and the number of worms expelled were in fair quantity.

The existence of any characteristic eye lesion associated with or caused by hookworm disease I myself seriously doubt, but the fact that reports have been made should serve to stimulate certain ophthalmologists and field workers in the disease to the further investigation of the subject and to report their findings. Only from hundreds of such reports can we accurately draw conclusions.

DR. J. W. JERVEY, Greenville, S. C.: I think Dr. Calhoun feels that I have in some way argued against the existence of a toxin in hookworm disease. By no means do I take that stand. There may readily be a toxin. Perhaps there is. I don't know. I know it has never been demonstrated, and that statement was my only reference to toxin. With regard to the other matters, I think the argument is presented in full in the paper.