EYE CHANGES IN EPIDEMIC CEREBROSPINAL MENINGITIS: A CLINICAL AND PATHOLOGIC STUDY OF 200 CASES*

PHILIP M. LEWIS, M.D.
Memphis, Tennessee

Although the literature on the eye changes that take place in cerebrospinal meningitis is quite extensive, no reference to the subject has appeared in the Transactions of the American Ophthalmological Society. For this reason the eye findings in a series of 200 cases are now presented, together with a brief review of the publications bearing on this subject. Certain unusual findings were noted among the author's cases, and a few patients were kept under observation for several years. Bacteriologic studies of the conjunctiva and of the aqueous, together with a report of the pathologic examination of four eyes, increase the scientific value of the data obtained.

The epidemic of cerebrospinal meningitis in Memphis and the surrounding country set in in the late autumn of 1929. Except for a brief recession during the summer months, numerous cases occurred during 1930, 1931, and well into 1932. Even in 1933 the disease was much more frequently observed than before the beginning of the epidemic. Many of the patients came from the surrounding small towns and country, but all were treated in the Isolation Department of the Memphis General Hospital.

The total number of cases from November, 1929, when the epidemic began, until July, 1934, was 452. Of this number the author personally examined the eyes in 200 cases—a few only once, the majority at least twice, and some very often.

* From the Department of Ophthalmology of the University of Tennessee. Candidate's thesis for membership accepted by the Committee on Theses.

A few cases with interesting findings have been under observation for over four years. About 150 patients passed through the hospital before the author began to examine these cases (April, 1930). Between 1930 and 1935 about 100 cases were not examined, due mainly to the fact that death occurred soon after admission.

Historical Review

According to Neal, the first published account of the condition described as epidemic cerebrospinal meningitis, and proved to be authentic, was that of an epidemic in Geneva in 1805. Vieusseaux described the clinical picture, and Matthey reported the postmortem findings. In America the disease first appeared in March, 1806, at Medfield, Massachusetts, and was described by Danielson and Mann.

The earliest ocular complications in epidemic cerebrospinal meningitis appeared in 1842, when Toudes published his observations of the Strasbourg epidemic of 1840 and 1841. He mentioned diplopia, dimness of vision, and several cases of ophthalmia. Schilizzi, in a monograph written the same year, also reported certain eye involvements. Chadouine, in 1844, Companyo, in 1847, and Daga, in 1851, mentioned several ocular complications. Knapp, Kreitmair, Salomon, Jacobi, Hirsch, and Ziemssen and Hess, about 1865, described various eye changes, especially iridochoroiditis. Wilson, in 1867, recorded the eye diseases he had observed about that time in an epidemic of meningitis in Ireland. Jacobi reported that in the Swedish epidemic of 1855–1857 Lindstrom described cloudiness of the cornea, cataract formation, and a purulent inflammation of the entire eye.

Only a few articles on the subject appear to have been written during the next sixteen years—one each by Berthold and Kotsonopulos in 1871, one by Knapp in 1872 (another in 1885), and one by Bull in 1873. Markusy, in 1879, described a case with bilateral panophthalmitis. In 1883 Nettleship reported several cases of destructive ophthalmitis simulating glioma occurring in children having a febrile dis-

ease, and mentioned the possibility of meningitis as the exciting cause. In 1885 he reported another case. In the same year Lichtenstern stressed the frequency of nystagmus. Weeks and Hoffman published reports in 1885 and 1886 respectively. In 1893 Randolph reported a study of 40 cases, in only three of which the eyes were entirely normal. Following this period writings on the subject became so numerous that only the more important reports will be considered under the various subheadings of this paper.

FREQUENCY AND TYPE OF VARIOUS EYE SYMPTOMS

The incidence of various eye lesions and the types of these lesions vary greatly in different epidemics, and even at various times during the same epidemic. This accounts for the fact that some observers—Walravens, for example—considered eye complications as rare, whereas others, such as Randolph, regarded them as exceedingly common. In this series of 200 cases 98, or 49 per cent., showed some deviation from the normal. This is the same percentage that was given in 1931 in the author's report* of 65 cases. When the epidemic reached its peak, involvement of the eyes was actually and relatively more frequent than during the early stages or during the period of abatement. Table 1 shows the frequency of the various eye conditions in this series:

TABLE 1.—EYE FINDINGS IN 200 CASES OF EPIDEMIC CEREBROSPINAL MENINGITIS

Diagnosis	*Number of Complications*	*Percentage*
No ocular complications	102 normal cases	51.0
Subconjunctival hemorrhage	2	1.0
Conjunctivitis	8	4.0
Keratitis	3	1.5
Strabismus	7	3.5
Pupillary abnormalities	12	6.0
Lens abnormalities	3	1.5
Endophthalmitis	15	7.5
Papillitis	12	6.0
Hyperemia of discs and retinas	22	11.0
Simple engorgement of retinal veins	32	16.0
Amaurosis	4	2.0
Orbital cellulitis	2	1.0
Nystagmus	1	0.5

* South. M. J., 1931, xxiv, p. 101.

The apparent mathematical error in the total number of cases and total percentages is due to the fact that several patients presented two or more distinct ocular complications, and hence were recorded more than once in Table 1.

The principal eye findings of observers of several large epidemics of cerebrospinal meningitis appear in Table 2.

TABLE 2.—PRINCIPAL FINDINGS OF OBSERVERS OF LARGE EPIDEMICS OF CEREBROSPINAL MENINGITIS

Physician:	*Randolph*	*Uhthoff*	*Heine*	*Terrien and Boudier*	*Sinclair**	*Rolleston**	*Neal**	*McLean and Caffey**	*Borovsky**	*Lewis*
Year:	*1893*	*1905*	*1905*	*1909*	*1919*	*1919*	*1925*	*1928*	*1930*	*1934*
Number of Cases:	*40*	*110*	*100*	*42*	*128*	*502*	*500*	*136*	*190*	*200*
Diagnosis:										
Conjunctivitis	8	1	..	6	2	28	5	2	0	8
Keratitis	0	3	..	2	1	0	0	0	0	3
Strabismus	8	9	15	8	8	..	30	29	24	7
Pupillary abnormalities	19	8	..	30	..	Frequent	..	12	3	12
Endophthalmitis	0	4	5	0	7	7	10	3	3	15
Papillitis	6	18	10	16	0	..	..	1	..	12
Hyperemia of discs and retinas	19	..	..	7	..	..	..	..	..	22
Nystagmus	1	8	..	0	0	0	0	14	7	1

* Ophthalmoscopic examination not made routinely.

Description of Eye Lesions

1. The Eyelids.—Involvement of the eyelids is evidently rare, since only a few observers have mentioned it. However, Romer stated that "the palpebral fissures gape widely, and winking is diminished in deep stupor, but this lagophthalmos is not the result of a facial paresis, but is due to the stupor of the sensorium." Ballentyne's experience, of seeing 15 of 73 cases with retraction of the eyelids so that the sclera was visible above and below the cornea, was most unusual. McLean and Caffey mentioned staring as being quite noticeable in six of their 136 cases, a symptom that was probably due to this phenomenon. Ballentyne also observed herpes of the eyelid in one patient. According to Wilbrand and Saenger, ptosis occurs rarely. Borovsky reported four cases among 190 patients, and Neal four in 500.

In the author's series of cases no abnormalities of the eyelids occurred except a temporary edema in several patients with endophthalmitis. No instance of staring was noticed. Frequently while a patient was in coma the eyelids were slightly open, but this finding is certainly not restricted to cases of meningitis.

2. THE LACRIMAL APPARATUS.—The writer has found no reference in the literature to involvement of any portion of the lacrimal apparatus in meningococcic meningitis. Even epiphora is rarely mentioned, and was not present in any of his cases unless the eye was acutely inflamed. No lacrimal disturbances were noted in the series of cases here reported.

3. THE CONJUNCTIVA.—According to Parsons, conjunctivitis is regarded by some authors as rare, and by others as common. However, in the reports of all large epidemics of meningitis reviewed by the author this condition was found to be rare. Thus, Neal reported only five among 500 cases of meningitis; Uhthoff one in 110, and Borovsky found none among 190 patients. On the other hand, McKee reported seven cases of epidemic meningitis with ocular complications six of which were conjunctivitis. Meningococci were cultured from the conjunctiva of two of these patients. Shaw found conjunctivitis in 60 per cent. of his cases.

In Rolleston's series of 502 cases, there were 28 patients (5.6 per cent.) with conjunctivitis.

BACTERIOLOGIC EXAMINATION OF THE AUTHOR'S CASES.—The author observed only eight cases of conjunctivitis, or 4 per cent., in his series of 200 cases. All were mild, clearing up in from one to five days with the usual treatment employed for conjunctivitis. The secretion in these cases was not stringy or tenacious, and therefore could very easily be removed from the eye. No chemosis was present, and the palpebral conjunctiva was only slightly thickened. The condition could not be differentiated clinically from conjunctivitis caused by other organisms.

In five of these cases smears were taken and cultures made

in brain broth. No micro-organisms were found in two, the Staphylococcus albus was found in one, and in two cases gram-negative intracellular diplococci, identical morphologically with the organisms from the spinal fluid, were discovered. In both of these cases blood cultures were negative on admission to the hospital. Nevertheless, the infection of the conjunctiva was probably blood-borne, as neither case showed lagophthalmos. Parsons stated: "It [conjunctivitis] is probably sometimes endogenous in origin; in other cases, due to defective closure of the lids." However, the author believes that infection of the conjunctiva with meningococci from the nasal and oral secretions could and does occur, just as it frequently occurs in cases of common cold.

Hemorrhages into and beneath the conjunctiva are quite rare, being present in only two of the patients studied.

4. The Cornea.—The cornea is rarely involved in meningococcic meningitis. Terrien and Boudier's report of two corneal ulcerations in a group of 42 cases appears to give the highest percentage in any large group reported. Uhthoff saw three cases of keratitis in his series of 110; Sinclair observed one case in 128. Pillat reported a case of metastatic keratitis complicating meningococcic meningitis in which the patient recovered with fair vision (6/20). He attributed the good result to an intragluteal injection of milk. In large epidemics most observers have not seen even one case of keratitis. Only three patients in the present series developed keratitis. All were Negro males—two adults and a boy of fourteen. In two the condition was ulcerative and unilateral. One patient had a bilateral involvement of the parenchyma. In none of these cases were smears or cultures from the conjunctiva positive for meningococci.

Corneal Involvement in Author's Cases

Case 1.—In this patient the corneal ulceration was the last of many complications. A report of this case (J. P.) is given under the section on Endophthalmitis. Orbital cellulitis developed on the

twenty-third day of the illness. There was marked proptosis, and the whole cornea ulcerated rapidly and perforated from exposure. The eye was enucleated. A description of the pathologic findings with photomicrographs of sections is given under the head of Endophthalmitis.

CASE 2.—F. P. This man had been ill for two days, and when he was admitted to the hospital he was violently ill. Findings, both clinical and laboratory, were typical of meningitis and included a positive blood culture. His eyes were first examined two days after his admission, serum having been administered intravenously once, and intraspinally three times. The left eye showed a mild conjunctivitis, the smears and cultures from which were negative. Near the limbus, and running entirely around the cornea, was an annular or ring ulcer with grayish infiltration extending through the parenchyma to the central or pupillary area. The pupils had previously been dilated with atropin. Vitreous opacities and the clouding of the cornea made examination of the fundus impossible. The opacities in the vitreous were freely movable, and did not suggest the fixed membrane formation seen in the author's cases of endophthalmitis. Vision was reduced to hand movements. In spite of all treatment, including the cautery, the ulceration spread rapidly over the entire cornea. Seven days after admission perforation occurred near the limbus below. After this the inflammation began to subside. The patient was discharged in fair general condition after only thirty-two days in the hospital. The end-result as regards the eye was a somewhat dense opacity of the entire cornea. Vision was light perception with good projection. Apparently the posterior segment of this eye was not seriously involved. No lagophthalmos was ever observed in this patient. It is, therefore, not unreasonable to assume that the keratitis developed endogenously, as the blood culture was positive for meningococci. However, no culture of any organisms from the cornea or the conjunctiva was made.

CASE 3.—P. S. This man was extremely ill on admission to the hospital and died three days later. The duration of the disease before entering the hospital was unknown. Spinal-fluid and blood cultures were positive for meningococci. When first seen, the cornea of the right eye was infiltrated throughout, and presented a grayish color. The pupil could be only slightly dilated, as there were several posterior synechiae. The cornea of the left eye also showed several spots of deep infiltration; the iris was congested,

and the pupil was only partly dilated. There was no ulceration of either cornea. The vitreous contained a yellowish membrane. No fundus reflex could be obtained in either eye. Permission for enucleation or for autopsy was refused.

In this last case, as well as in the second one, the corneal disease was probably the result of an infection through the blood stream. The first case was an ulceration due to exposure, and was probably not due to infection with meningococci. One other patient (E. H.), on the third day of illness, developed a slight haziness of the cornea associated with iritis, hypopyon, and pus in the vitreous (endophthalmitis). The cornea cleared completely in three days. (See Case 2 under Endophthalmitis.)

5. The Motor Nerves and Extra-Ocular Muscles.—Strabismus was comparatively rare in this series, and occurred in only seven of the 200 cases, or 3.5 per cent. This seems to be the lowest percentage reported by any observer. The average percentage for eight epidemics, studied by different authors, was computed and found to be 11 per cent. in a total of 1,246 cases. The highest frequency of strabismus was 31.2 per cent. in a series of 144 cases reported by Smithburn, Kempf, Zerfas, and Gilman. McLean and Caffey reported 20 per cent. in 136 cases, and considered strabismus the most important ocular symptom in this disease. The nearest approach to the author's low figures for any large epidemics was by Neal and by Sinclair—both about 6 per cent.

Parson's opinion was that in the early stages there is often kinetic strabismus or conjugate lateral deviation of the eyes. Uhthoff observed five conjugate deviations in 110 cases. There is little if any mention made of this condition by most authors. Only one case of conjugate deviation was observed in the series here described and none with kinetic strabismus. These symptoms are due to lesions in the cortex or in the pons.

The strabismus which develops with considerable frequency in epidemic meningitis is of the paralytic variety. Almost all observers agree that the abducens nerve is the one most often involved, and that its paralysis causes an esotropia.

For example, Uhthoff cited 15 cases out of 110 as showing abnormalities of the ocular muscles. These were divided as follows: eight paralyses of the sixth nerve, five conjugate deviations, one ptosis, and one total ophthalmoplegia. This preponderance of involvement of the abducens was observed in the author's small number of cases; in the entire number—seven—the eyes were convergent—the left eye four times and the right three. Randolph's findings were markedly dissimilar. In his series of 40 cases of meningitis he observed paralytic strabismus eight times, all being of the divergent type. Other cranial nerves may be involved and the paralysis may be complete or partial. Total third nerve paralysis is rare, as is also paralysis of the fourth nerve. Davis claims that paralysis of the fifth nerve may occur, with anesthesia of the cornea and a neuroparalytic keratitis, but Romer asserts that the latter is no more frequent in epidemic than in tuberculous meningitis.

According to most observers nystagmus rarely occurs although Lichtenstern commented on its frequency. It was present in only one of the author's cases. In 25 of 50 cases convalescent from meningitis Doesschate found a spontaneous nystagmus. This was certainly a most unusual observation.

The prognosis in these cases of strabismus, as pointed out by Wohlmann, is good. Improvement usually begins with the subsidence of the meningeal symptoms. However, at times the paralysis is permanent. The number of cases in this series was too small to permit one to draw conclusions. All seven cases occurred in children, and all were of the convergent type. Two patients died of meningitis. Of the remaining five, two recovered completely from the strabismus, one showed marked improvement when last seen (about ten weeks after illness), and in two the final result was unknown as they did not return after leaving the hospital.

6. THE PUPILS.—Parsons makes the following statement: "The pupils vary much, showing usually miosis in the early

stages, mydriasis when coma sets in. Loss of reaction to light is relatively rare." The frequency with which pupillary changes occur evidently varies greatly. Of 73 cases, Ballentyne found only six with normal pupils. He mentioned finding inequality, mydriasis, hippus, and deficient reflexes. Borovsky, on the other hand, observed only three cases of pupillary disturbances in 190 patients. Uhthoff found pupillary abnormalities in only eight out of 110 cases, whereas Terrien and Boudier recorded anomalies in 30 out of 42 cases. Romer asserted that pupillary disturbances are rarely encountered, and quoted Lichtenstern as saying that extreme dilatation with loss of reactivity is far more frequent in tuberculous than in epidemic meningitis. The author saw only 12 cases, or 6 per cent., with pupillary disturbances. However, over half of the patients in the entire series had their pupils dilated with atropin or homatropin before they came under observation. Therefore, conclusions regarding the frequency of pupillary disturbances cannot be drawn from this group of cases. Many patients were admitted after having received large doses of morphin and had pinpoint pupils. For that reason, and also because in these cases fundus examinations are often very difficult, it was made a routine measure to instil mydriatics in all cases as soon as possible after admission. If this had not been done, rapid death would have prevented ophthalmoscopic study in a great many of the cases.

The author's 12 cases were divided as follows: miosis three and mydriasis nine. In three of the latter cases the patients were blind without any other ocular pathologic change. No case showed appreciable anisocoria. In most instances the dilated pupils reacted only slightly or not at all to light. The seven patients that survived regained their normal pupillary reflexes.

7. The Lens.—Involvement of the lens in meningococcic meningitis is rare. In the literature on meningitis only one reference to the lens by Lindstrom was found. He mentioned

cataract as occurring in the meningitis epidemic in Sweden in 1855–1857. Foster described a case of iritis with pus in the anterior chamber, and also a clouding of the lens, which cleared up so that vision returned to normal. The only lens disturbance which occurred in the author's series was a temporary cloudiness of the lens in two patients who developed endophthalmitis. In one case (O. F., Case 6 under Endophthalmitis) the latter condition was bilateral and progressed to complete blindness in both eyes. The cloudiness of the lens, which appeared on the third day of the illness, and was associated with a marked iritis and hypopyon, involved the right eye only. After about three weeks the lens began to clear, and in about ten days more it was apparently transparent.

The second case (E. H., Case 2 under Endophthalmitis) developed a swollen, cloudy lens on the third day of the illness. The cornea was hazy, and there were moderate iritis and hypopyon. Five days later the entire anterior segment had cleared so that it appeared to be normal. At this time yellow exudates could be seen in the vitreous. Thus in both cases the lens involvement was part of a metastatic endophthalmitis. The lens involvement was transient and not important as compared with the posterior segment infection, which caused complete blindness.

One patient (B. D., Case 7 under Endophthalmitis) with a bilateral endophthalmitis was seen again four years after her illness. The lens of each eye had become entirely opaque. In another case (J. P., Case 1 under Endophthalmitis) the lens was extruded completely when the cornea ruptured.

8. THE UVEAL TRACT AND VITREOUS BODY.—Involvement of these structures is best considered under the heading of Endophthalmitis.

ENDOPHTHALMITIS

This condition, when it occurs as a complication of epidemic meningitis, is a most interesting and important de-

velopment. It has long been known and has been variously designated. Thus many authors termed it panophthalmitis, whereas others called it suppurative iridochoroiditis; still others designate it pseudoglioma, abscess of the vitreous, or metastatic ophthalmia. The most descriptive term for this condition is endophthalmitis metastatica.

The earliest mention of this complication found in the literature was by Toudes in 1842, and again by Daga in 1851. Both observers described a cloudiness throughout the media of the eye which they designated simply as ophthalmia. Toudes saw one case of iritis, six with a mild ophthalmia, and a severe ophthalmia in several fatal cases. This investigator commented on the abundant formation of pus. Lindstrom, in writing of the Swedish epidemic of 1855–1857, mentioned purulent inflammation of the entire eye as a complication. Endophthalmitis was described clinically by several observers practically simultaneously in 1865 and 1866. Herman Knapp saw 10 of these cases and considered the condition a hyperplastic choroiditis, with consecutive retinal detachment and iritis. Kreitmair noted the same condition in 12 and Salomon in six cases. Both observers considered the disease a simple iridochoroiditis. Jacobi regarded it as a purulent inflammation of the iris, choroid, and ciliary body. Uhthoff saw four cases in 110, and Heine five in 100. Romer also estimated about 5 per cent. as the usual incidence of this complication. This agreed fairly closely with the findings in most other epidemics of meningococcic meningitis except those in which the eyes were not examined routinely by an ophthalmologist. However, there are numerous exceptions to Romer's finding. Randolph in 40 cases, and Terrien and Boudier in 42, saw none at all. Mantuljak reported five cases among 46 children from one and one-half to seven years of age.

Among the 200 cases reported in this paper, endophthalmitis occurred in 15, or 7.5 per cent., of the patients. In four of these the condition was bilateral. Thus 19 eyes were involved, and this appears to be the highest percentage for any

large epidemic of meningitis and also the greatest number of cases of this complication ever reported. It is generally agreed that the condition occurs most frequently in children. Only three of our patients were adults. The youngest patient was sixteen months old, and the oldest was forty-five years. The average age was twelve years. Most of these patients recovered from the meningitis. Only three, or 20 per cent., died, which was much lower than the mortality rate for the whole epidemic. Two of the fatal cases were adults, aged thirty-eight and forty-five years respectively. Both patients died soon after admission—one on the second and one on the third day. The child who died had a recurrence of the meningitis twice after apparent recovery. There is probably no relation between the severity of the meningitis and the occurrence of endophthalmitis. The prognosis as regards life seems to be better than in cases that show no ocular involvement.

TABLE 3.—ENDOPHTHALMITIS

Initials	*Age*	*Sex*	*Race*	*Day of Disease*	*Eye Involved*	*Blood Culture*	*End-Result*
J. P.....	14	M.	Negro	8	Both	—	Total blindness; enucleated
W. T.....	10	F.	Negro	4	Left	—	Left eye blind. Died (recurrence)
S. M.....	38	F.	Negro	2	Left	+	Died: two days
D. K.....	6	F.	Negro	5	Both	+	Total blindness
H. N.....	3	M.	Negro	7	Right	—	Right eye blind
J. H.....	6	M.	Negro	4	Right	—	Right eye blind
R. G.....	4	M.	Negro	12	Right	+	Right eye blind
R. P.....	8	F.	Negro	10	Right	—	Right eye blind
B. D.....	16 mos.	F.	White	7	Both	—	Total blindness
L. W.....	9	F.	Negro	5	Right	—	Right eye blind; enucleated
E. H.....	4	F.	Negro	3	Right	+	Right eye blind; enucleated
I. M.....	5	F.	Negro	8	Right	—	Right eye blind; enucleated
O. F.....	21	F.	Negro	3	Both	+	Total blindness
W. D.....	10	M.	Negro	5	Left	—	Recovered vision
P. S.....	45	M	Negro	Unknown	Left	+	Died in three days

As may be seen in Table 3, the sexes were divided about equally. Only one white patient developed endophthalmitis.

As a rule, the condition manifested itself early in the course of the meningitis, the earliest time being the second day, and the latest being the twelfth day. The average was the sixth day. In four patients both eyes were involved. All four recovered but with total permanent blindness. Of the remaining 11 patients, the left eye was affected in four, and the right eye in seven. Blood cultures taken on admission were positive in six patients only. Spinal-fluid cultures were positive in all cases.

Symptoms and Signs.—Patients with endophthalmitis seldom complained about their eyes. Only in one case was pain a prominent symptom, and often it was absent. Photophobia and lacrimation were rare, and were present in only one patient in this series. Patients who were rational and of appropriate age complained of the loss of vision. Usually there was a slight or moderate ciliary injection—this being the only external sign evident. Often the condition was discovered only during the routine examination of the eyes. In several cases the eyes were normal when first examined, or showed merely an engorgement of the retinal veins. On a second examination a few days later the condition was found to be well developed in certain cases, or iritis or other anterior segment changes were present; later the vitreous also would become involved. As was previously stated, the condition usually develops early in the course of the disease—generally within the first week. Mantuljak found that it appeared most frequently on the third day of the illness.

The following were the typical findings in these cases: Ciliary injection of moderate degree; cornea clear and only occasionally pus in the anterior chamber; iris swollen and muddy in appearance, with posterior synechiae and often a grayish exudate behind the pupillary border; lens usually clear, but at times swollen and cloudy; vitreous filled with an exudate or cyclitic membrane; fundus not visible; eye totally blind.

There was nothing characteristic about the iritis in these

cases, but the author was frequently amazed at the strength of the adhesions to the lens capsule and the difficulty experienced in dilating the pupil. Often epinephrin was necessary to secure dilatation, and at times even that failed to break up the adhesions. In view of the mildness or absence of symptoms in these cases one would naturally expect that dilatation would be easy after the early use of atropin. The general tendency was for the involvement of the anterior segment to subside or to clear up entirely, whereas changes in the posterior segment were permanent. Several observers (Bovaird, Tooke, Daulroy, Zweig, Pillat) have reported cases of iritis or iridocyclitis without involvement of the posterior segment. Iritis and cyclitis alone as a complication of meningococcic meningitis must be very infrequent. Observers of large epidemics rarely report a case. In the present series there was no iritis except when it occurred simultaneously with or was followed by infection in the posterior segment.

The vitreous exudate varied considerably in different cases. It usually appeared first as a grayish-white membrane which in most cases rapidly became yellow. It was always fixed in position, and was situated in the anterior portion of the vitreous, close to the posterior lens capsule. The appearance was typical of a cyclitic membrane. In several cases this exudate was distinctly funnel shaped. The ciliary injection gradually faded in these cases, but marked shrinking of the eyeballs did not occur. As a rule only a moderate degree of softening developed. Romer states that so benign a form of metastatic ophthalmia is excited only by the pneumococcus and the meningococcus, and that in cerebrospinal meningitis the phenomenon is explained by the fact that meningococci die very soon in the vitreous. Usually only one eye is affected, but in the present series the condition was bilateral four times. Other observers, such as Kreitmair and Knapp, have reported cases of bilateral infection. When the condition is bilateral, it may occur simultaneously in the two eyes, or the

involvement of the second eye may be deferred for several days.

Transmission of Infection to the Eye.—Almost all authors agree that the mode of transmission is through the blood stream. However, a few observers (Foster and Councilman, Mallory, and Wright) have claimed that the infection is due to direct extension of the inflammation around the optic nerve and the central retinal artery. Romer made the following statement: "The metastatic ophthalmia may start either in the vessels of the retina or in those of the choroid, but it must not be thought that the inflammation is transmitted along the optic nerve from the meninges; it is of hematogenous origin." Foster recorded two cases of direct transmission from the optic nerve, but his reasoning is open to grave question. His conclusion that infection of the globe was due to direct extension was based on the finding of pus in the sheaths of the optic nerve at autopsy of two cases. This, of course, is not sufficient evidence. Axenfeld asserted that there was no known case of infection of the interior of the eye from the optic sheath. According to this observer, organisms may fill the vaginal spaces of the optic nerve as far as the sclera without passing from this point into the eye. He believes that no case of transmission by this method has ever been proved.

In only six of the author's cases of endophthalmitis was a culture from the blood stream found to be positive. However, only one specimen of blood was taken in each case, due to the limitations of the laboratory facilities. In these cases one negative blood culture is no more conclusive proof that the blood is free of meningococci than is one negative report in a patient with sinus thrombosis or a negative report in a patient with an obvious malarial infection. Repeated cultures, especially if taken early in the course of the disease, and before the administration of antimeningococcic serum, would undoubtedly have shown a high percentage of positive findings.

The demonstration of meningococci within the globe is

difficult. Clinically, each one of these 15 patients had a definite meningitis. Smears and cultures from the spinal fluid taken on several different days were in every case repeatedly positive for meningococci. Blood cultures were positive in six cases. There is, therefore, no reason to doubt that the endophthalmitis was due to meningococci. However, this is not easily proved. Axenfeld stated: "Meningococci in the infected eye rapidly die out, and when the eye is available for examination, they can no longer be demonstrated." This was also the author's experience. Cultures of the organisms could not be grown from any of the eyes enucleated for endophthalmitis. Berens suggested that incubation of the eyeball for twenty-four hours be made immediately after enucleation, and that cultures from within the globe then be taken, but since receiving this suggestion no case has been encountered on which to try it. As a rule, in these cases enucleation is delayed and, as pointed out by Axenfeld and Romer, the micro-organisms die and disappear rapidly from within the eye.

Cultures from the conjunctiva, taken from a patient with epidemic meningitis, are frequently positive for meningococci, as many observers have pointed out. Cultures from the interior of the eye made during the early days of infection are difficult to obtain, due to objections on the part of the patient or his family, and when they are taken are likely to be negative. This was the case in the author's experience, and it agrees with that of many other investigators (de Schweinitz and Hosmer).*

* Since writing this thesis and submitting it to the Committee in the autumn of 1935 the author has studied 98 additional cases of meningococcic meningitis. Only three of them developed endophthalmitis, which reduces the percentage for the entire group to about 6 per cent. In two of these cases the writer succeeded in growing a pure culture of meningococci from the aqueous. Brain-broth media were used. In the case which was negative, consent to take the culture could not be obtained until more than two weeks after the endophthalmitis developed. It is possible that former failures to obtain positive intra-ocular cultures were due to this factor, and also to the carelessness of attendants in not taking the culture tubes promptly to the laboratory for immediate incubation. Certain technical difficulties arise in withdrawing the material from these eyes for culturing: (1) As a rule, the eyes are quite

However, the organisms from within the globe have been demonstrated. Thus, in one fatal case, Tooke reported finding micro-organisms, probably meningococci, in the iris and about Descemet's membrane. He found them also between the arachnoid and the dural sheaths of the optic nerve. McKee reported an abundant growth of meningococci from pus in the anterior chamber in a case of meningitis. Weakley also reported one case of metastatic endophthalmitis in which he obtained a pure growth of meningococci from pus taken from the anterior chamber. Verhoeff succeeded in demonstrating meningococci in the sections of an eye enucleated because of endophthalmitis complicating a meningococcic septicemia.

Pathology.—The findings in these cases are not characteristic of meningococcic infection, but are essentially those seen in endophthalmitis due to other causes. However, the condition is seen more frequently as a complication of meningococcic meningitis than of any other disease. The endophthalmitis encountered by the author, in contrast to panophthalmitis, did not end in phthisis bulbi. In some cases in the present series no shrinkage of the globe could be made out, and usually there was only slight atrophy of the eyeball. Apparently not many eyes with meningococcic endophthalmitis have been enucleated and examined. Cornell, in a personal communication, stated that in the large collection in the Army Medical Museum there were only three cases of metastatic uveitis due to epidemic cerebrospinal meningitis. Verhoeff has had only one case and Holloway none. In 1933, after searching the records and pathologic material in the

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tender and the patient is likely to be unruly. For these reasons it is always advisable to give a subconjunctival and a retrobulbar injection of procain hydrochlorid. If the patient is very unmanageable, nitrous oxid gas anesthesia should be administered, or the lens may easily be injured. (2) Penetration of the eyeball may be difficult if the needle is too large or not very sharp. (3) If the needle is too small, it will be impossible to withdraw the purulent material. A needle ¾ inch in length and of 22 gage has been found to be the most satisfactory in the author's hands. The syringe must have a very tightly fitting piston, or the thick fluid cannot be withdrawn. For this purpose the writer has found the small insulin syringe to be most satisfactory.

collection at the New York Eye and Ear Infirmary, the author succeeded in finding only one specimen. In this case sections yielded findings similar to those in the present series, except that the lens was more involved.

The material for this pathologic study consisted of four globes enucleated for endophthalmitis out of the 19 eyes with endophthalmitis in this series. These four eyes were sent to Lt. Col. George R. Callendar, of the Army Medical Museum, Washington, D. C. An elaboration of his description of each eye follows the individual case reports. Certain changes are common to all four cases. Thus abscess formation in the vitreous, with a tendency to organization and the forming of a cyclitic membrane, was present in every case. Detachment, with great infiltration of the retina, was also always present. Involvement of the ciliary body, iris, and choroid occurred in every case. It consisted of edema, thickening, and an infiltration with mononuclear wandering cells and some polymorphonuclear leukocytes.

CASE REPORTS

The course of events in these 19 cases of endophthalmitis was sufficiently similar to make it unnecessary to report them all. The four cases in which the eye was enucleated, and four others with certain interesting or unusual features, are reported here:

CASE 1.—ENDOPHTHALMITIS, ORBITAL CELLULITIS, CORNEAL ULCERATION AND PERFORATION. EXTRUSION OF LENS.

J. P., a colored male, aged fourteen years, was ill for thirty-six hours before he was admitted to the hospital on March 23, 1930. The typical physical and laboratory findings of acute cerebrospinal meningitis were present. Blood cultures, however, were negative, and the blood Wassermann reaction for syphilis was also negative. The pupils were slightly dilated and reacted very sluggishly to light. The patient was immediately given 30 c.c. of antimeningococcic serum intravenously, and this dose was repeated the next day. Every twelve hours from 30 to 65 c.c. of very cloudy spinal

fluid were removed. The fluid was replaced by smaller amounts—10 to 30 c.c.—of serum.

On the fifth day of the disease a slight conjunctivitis was observed. Three days later this had cleared up, but a mild ciliary injection and a slight haziness of the media were seen. Atropin sulphate, 1 per cent., three times daily, was ordered for both eyes. A few days later the following signs were present in both eyes: ciliary injection; swollen and discolored irides; pupils only partially dilated, due to posterior synechiae; a grayish-white exudate in the vitreous just behind the lens; no fundus reflex; vision totally lost. There was no pain present at that time.

On the twenty-third day of his illness the patient for the first time complained of pain in the left eye; this became intense on the following day. The clinical picture presented was that of severe orbital cellulitis. The eyelids were greatly swollen, there was marked exophthalmos, and the edematous conjunctiva protruded through the palpebral fissure. The patient was unable to move the eye in any direction. As the condition continued to grow worse, two days later incisions were made deep into the orbit, under nitrous oxid gas anesthesia. Profuse bleeding occurred, but no pus was encountered. The proptosis became even more marked, and in spite of a constant cover the cornea ulcerated and perforated. Enucleation was performed, after which the edema slowly subsided and a good socket was obtained.

On the forty-second day of the patient's illness severe pain occurred in the remaining eye. There was moderate proptosis, and an orbital cellulitis was anticipated. Ice compresses were applied constantly, and the proptosis subsided in three or four days. On his discharge on May 10, 1930, fifty days after the illness began, the patient's general condition was good, and no other complications except the ocular one had occurred. The eye still showed some ciliary injection, the anterior chamber was very shallow, and the pupil was irregular due to the presence of several adhesions of the iris to the anterior lens capsule. The vitreous appeared as a solid fixed mass of cream-colored exudate. The eye was quite soft, but there was no apparent shrinkage of the globe. Shortly after this the patient was sent to the State Blind School.

Pathologic Examination.—Macroscopic.—There was a large perforation of the cornea, with a firm mass of whitish exudate protruding through the opening. Prolapsed iris tissue was bound in with the exudate. There was no shrinkage of the globe. The lens was absent. The retina was completely detached and drawn for-

ward into a mass just posterior to the former site of the lens. The choroid appeared to be very thick and was partly separated from the sclera. The sclera was greatly thickened.

Microscopic.—There was a large dehiscence of the central portion of the cornea. The whitish mass protruding through the opening in the cornea was made up of inflammatory granulation tissue with the prolapsed iris and the ciliary body partly covering it. The iris, with a large part of the ciliary body from the median side of the globe, was torn loose and lay upon an organizing mass of exudate entirely outside the perforated cornea. The iris, ciliary body, and choroid were thickened by edema and the infiltration of numerous wandering cells. These cells consisted of polymorphonuclear leukocytes, small and large lymphocytes, numerous plasma cells, and several epithelioid cells. The vessels were engorged with blood. The lens was absent. The retina was completely detached, degenerated, and profusely infiltrated with an inflammatory exudate which was undergoing organization and was continuous with a cyclitic membrane. This membrane, by contraction, had partially separated the ciliary body and the anterior layers of the choroid from the sclera. A bloody albuminous fluid filled the posterior segment of the eye behind the detached retina. The sclera was greatly thickened and infiltrated with various types of wandering cells. This was especially marked around the blood vessels.

CASE 2.—TYPICAL METASTATIC ENDOPHTHALMITIS.

E. H., a colored female child, aged four years, was ill only eight hours before her admission to the hospital on April 3, 1931. At that time the spinal fluid was clear and colorless, and the cell count was only eight. The white blood cells numbered 37,000, of which 80 per cent. were polymorphonuclear leukocytes. The blood culture for meningococci was positive. The pupils were moderately dilated, but reacted normally. On the following day the spinal-fluid cell count had increased to over 14,000, with 95 per cent. polymorphonuclear leukocytes. Both smear and culture were positive for meningococci. On that day the eyes were normal. Two days later the right eye had become involved. There was ciliary injection, the cornea was hazy, and pus appeared in the anterior chamber. The lens appeared to be swollen and cloudy, and the fundus reflex was absent. Atropin was instilled to dilate the pupil. The anterior segment cleared rapidly, so that in a few days the pus had disappeared from the anterior chamber and the cornea and lens were clear. A yellow exudate could now be seen in the vitreous,

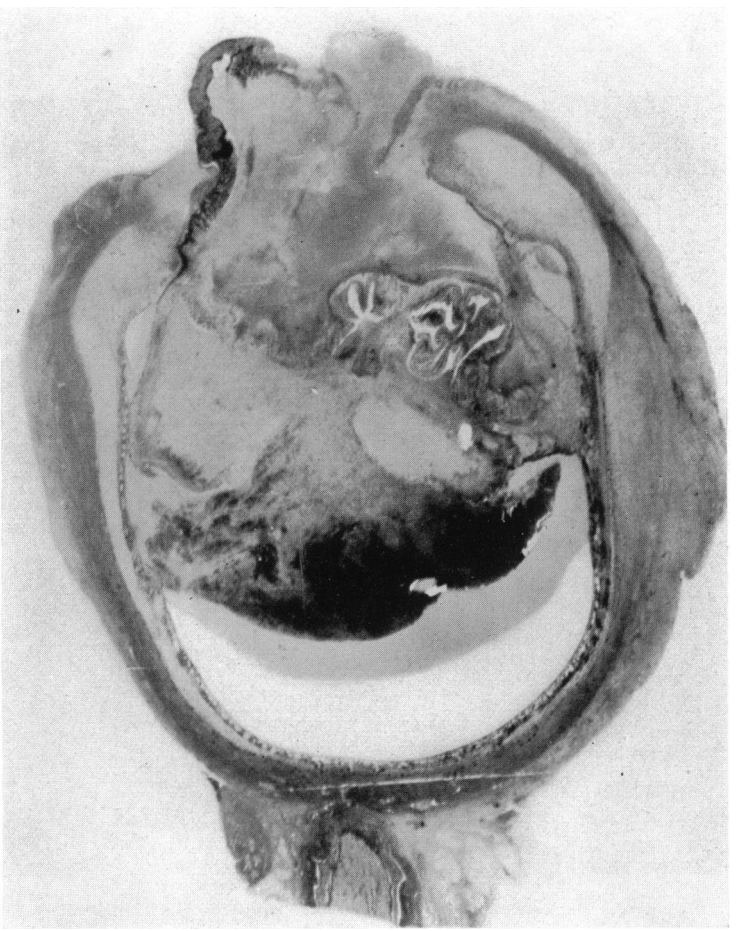

Fig. 1.—J. P., Case 1. Endophthalmitis. Rupture of cornea with protrusion of whitish mass of granulation tissue, partly covered by prolapsed iris and ciliary body. Lens absent. Retina detached and degenerated. Choroid and sclera greatly thickened (× 7).

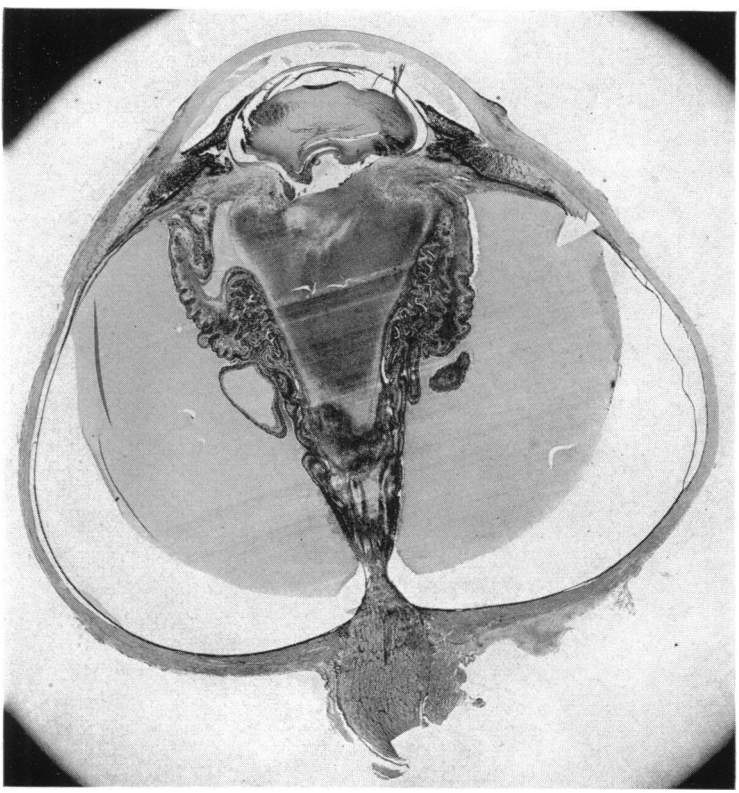

Fig. 2.—E. H., Case 2. Endophthalmitis. Typical case. Note cyclitic membrane behind lens, vitreous abscess, and completely detached retina (× 7).

and contrary to the usual findings, appeared to be freely movable. The anterior chamber remained clear for nineteen days, and then pus again appeared, and the anterior lens capsule became covered with a thick exudate. The anterior chamber cleared up again, suddenly, so that in four days the entire anterior segment was free of all exudate. A fixed, yellow, cyclitic membrane was then seen just behind the lens. After this convalescence was uninterrupted. Enucleation with glass-ball implantation was performed on May 17, 1931, ten days after the patient was free of all symptoms. She remained in the hospital for fifty-two days, and was discharged May 26, 1931, in good condition except for the loss of one eye.

Pathologic Examination.—Macroscopic.—The eyeball was somewhat flattened anteroposteriorly. The pupil was irregular. Just behind the lens there was a cyclitic membrane and immediately behind this there was a large vitreous abscess in the folds of the completely detached retina. The abscess was triangular in shape, the base of the triangle being against the lens and the apex toward the optic nerve. It measured 7 mm. across and 7 mm. anteroposteriorly. The subretinal space was filled with albuminous fluid. The choroid was in normal position and apparently not thickened.

Microscopic.—There was some exudate of mononuclear cells in the limbus tissues. The cornea was normal. Serum and a few leukocytes were present in the anterior chamber. The iris and ciliary body were edematous, thickened, and infiltrated with an exudate of mononuclear and polymorphonuclear cells. Some large, pale-staining epithelioid cells were present in the ciliary body. The iris was adherent to the periphery of the anterior lens capsule. The lens was somewhat flattened and shrunken. The posterior capsule, having been ruptured in sectioning, was adherent to the cyclitic membrane behind it. Behind the cyclitic membrane, in the folds of the separated retina, there was a vitreous abscess. It was made up of an exudate consisting mostly of polymorphonuclear cells, many of which were disintegrating. Near the borders of the abscess mononuclear cells were more numerous. Early organization of the exudate into fibrous tissue was taking place all around the margin.

The retina was completely detached, drawn forward around the abscess and cyclitic membrane, and its normal structure was greatly distorted. Edema and infiltration with wandering cells were marked. Some epithelioid and plasma cells were present, but polymorphonuclear leukocytes and lymphocytes, both small and large, were most numerous. Behind the retina was a large serous

exudate containing numerous mononuclear cells and a considerable number of polymorphonuclear leukocytes, especially along the choroidal surface of the retina. The choroid was in position, with very little infiltration. Neither the choroid nor the sclera was thickened in this case. The central vessels were dilated and did not appear to be thrombosed.

CASE 3.—TYPICAL METASTATIC ENDOPHTHALMITIS.

L. W., a colored female child, aged nine years, was admitted to the hospital March 21, 1931, on the fourth day of her illness. The usual physical and serologic findings of meningococcic meningitis were present. The blood culture was negative, but spinal-fluid cultures were positive for meningococci several times during the first ten days. The left pupil was moderately dilated, but reacted normally to light. The right eye showed a mild acute conjunctivitis, slight haziness of the cornea, and hypopyon. There was inflammation of the iris, with posterior synechiae already formed. A thin film of exudate over the anterior lens capsule veiled the normal fundus reflex. As atropin would not dilate the pupil, epinephrin was used; it was applied on a pledget under the upper eyelid and also injected subconjunctivally. Five days later the iritis had subsided greatly and the pupil was dilated. The lens was clear, but a grayish-white membrane in the anterior portion of the vitreous was seen. A week later the eye still showed considerable ciliary injection, it was tender to palpation, somewhat soft, and was totally blind. Except for dilatation of the retinal veins the left eye remained normal. During the patient's sixth week in the hospital enucleation of the right eye with glass-ball implantation was performed. After forty-five days in the hospital she was discharged on May 6, 1931. Serum sickness was the only other complication.

Pathologic Examination.—Macroscopic.—At the time of removal the eyeball was of normal size and shape. The cornea, sclera, and lens appeared to be normal. The pupil was dilated slightly irregularly. Just behind the lens was a yellowish-white mass, conical in shape, with the apex posterior, 4 mm. in front of the papilla. The base of the conical-shaped mass, which was in contact with the posterior surface of the lens, measured 8.5 mm. across. The anteroposterior measurement was 9 mm. The retina was completely detached. Seven millimeters of the optic nerve remained attached to the eyeball.

Microscopic.—The sclera was somewhat thickened. The cornea

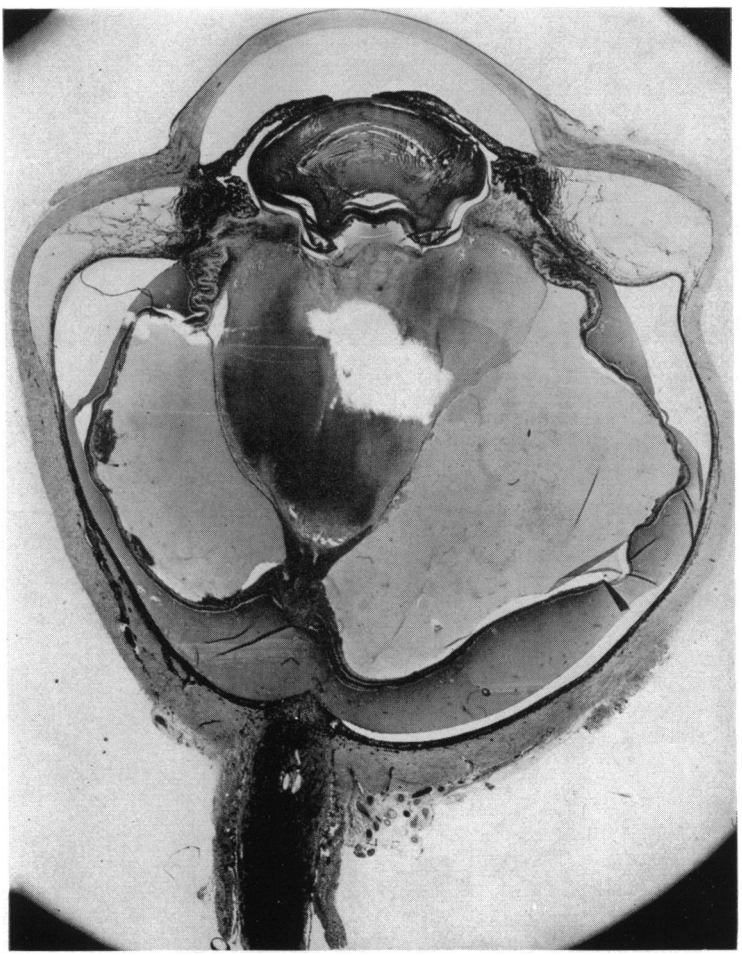

Fig. 3.—L. W., Case 3. Endophthalmitis. Note the choroidal detachment anteriorly and the partial separation of the ciliary body. Vitreous abscess and retinal detachment (× 7).

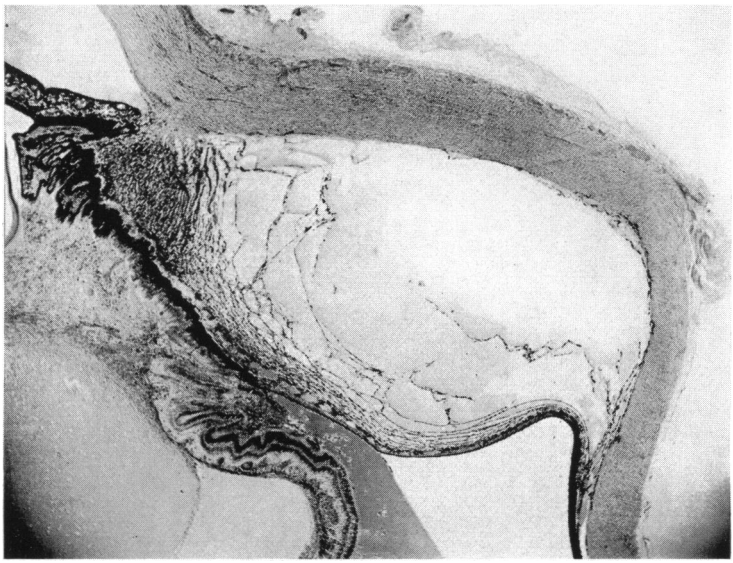

Fig. 4.—L. W., Case 3. Endophthalmitis. Showing detachment of choroid anteriorly and the ciliary body rotated on the scleral spur toward the lens. Organization of the exudate into fibrous tissue may be noted just posterior to the ciliary body (× 22).

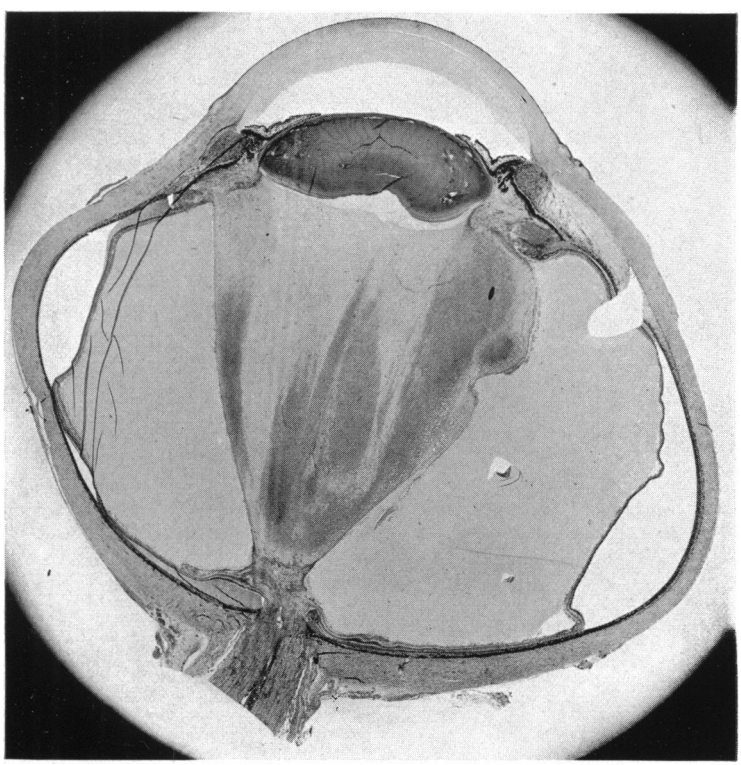

Fig. 5.—I. M., Case 4. Endophthalmitis. Cyclitic membrane and vitreous abscess. Peripapillary detachment of the retina (× 7).

was normal. There was some perivascular exudate, containing mononuclear cells, at the limbus, and the anterior chamber contained a little serum. The iris was slightly thickened, and near the pupillary border it was adherent to the anterior lens capsule. Except for the posterior lens capsule, which was ruptured on sectioning, the lens was normal. Just behind the lens was a large vitreous abscess, composed mainly of polymorphonuclear leukocytes, some of which were disintegrating. Numerous lymphocytes and large mononuclear cells were also present. The cyclitis in this case was less marked than in the previous two cases. Organization of the vitreous exudate was in progress just behind the ciliary body. The retina was completely detached, being separated from the choroid by an albuminous fluid containing a few wandering cells, mostly polymorphonuclear leukocytes. At several points on the inner surface of the retina, along the border of the abscess, in clumps of wandering cells, organization was taking place. New blood vessels and young connective tissue were present. The choroid was separated from the sclera anteriorly by edema. The ciliary body was also partly separated, being rotated on the scleral spur toward the center of the eye. The choroid was only slightly thickened, and the stroma but little infiltrated. The central vessels were dilated but not thrombosed.

CASE 4.—METASTATIC ENDOPHTHALMITIS. EMBOLISM AND THROMBOSIS OF CENTRAL VESSELS.

I. M., a colored female child, aged five years, was admitted to the hospital on May 16, 1931, on the second day of her illness. She had the usual physical signs and laboratory findings of meningococcic meningitis. The eyes on admission were reported as normal. Two days later the eyes were found to be still normal, except for dilatation and tortuosity of the retinal veins. The blood culture was negative, but the spinal-fluid culture was positive. On the eighth day of the illness a plastic iritis of the right eye was noticed. This may have been present even a few days earlier, as the eye had not been examined for five days. Ciliary injection, swelling of the iris, and an exudate in the pupillary area were present, so that no fundus reflex could be obtained. Atropin was instilled frequently, but as it had not dilated the pupil by the following day, epinephrin 1:1,000 was injected subconjunctivally. This served to dilate the pupil and revealed the presence of a whitish exudate in the anterior portion of the vitreous. This exudate was fixed in position and resembled in appearance a cyclitic membrane. The exudate gradually became a deeper yellow and

somewhat funnel shaped. On June 12, 1931, four weeks after the onset of the disease, enucleation with glass-ball implantation was performed. After thirty-seven days in the hospital the patient was discharged in good condition.

Pathologic Examination.—Macroscopic.—At the time of enucleation the size and shape of the eyeball were normal. The cornea and sclera also appeared to be normal. The pupil was irregularly dilated. The anterior chamber was deep (2.7 mm.) and partly filled with serum. The lens appeared to be normal. There was a large vitreous abscess, 9 mm. across at its base, and 11 mm. anteroposteriorly. The retina was in normal position except just around the disc and far forward near the ora serrata. The choroid was not detached.

Microscopic.—The cornea was normal. The anterior chamber was deep and about half filled with serum. A few leukocytes and some iris pigment were adherent to the anterior capsule of the lens. The iris was thickened, slightly infiltrated, and adherent to the anterior lens capsule near the periphery. Several plasma cells were present in the stroma of the iris and the ciliary body. The posterior capsule of the lens was shrunken and thrown into folds. The vitreous fibers were prominent, and the vitreous was infiltrated with pus, and funnel-like in shape. The cells consisted mostly of polymorphonuclear leukocytes, many of which were in various stages of disintegration. Just behind the ciliary body organization into a cyclitic membrane was taking place. Posteriorly, vessels from the disc were projecting into the abscess in an attempt at organization. There was a peripapillary detachment of the retina by albuminous fluid containing a few leukocytes, and a similar condition was present at the anterior extremity of the retina. Elsewhere the retina was in position, but was thickened and infiltrated with leukocytes, many of which were mononuclear cells. The choroid was in normal position, and showed only slight thickening and moderate wandering-cell infiltration. In the central vein there was a thrombus of quite recent origin. A cross-section of the nerve showed a recent extension of a thrombus in both artery and vein.

Four other cases presented unusual or especially interesting features and are therefore reported here in detail, although the eyes were not secured for pathologic study.

CASE 5.—RECURRENT MENINGITIS, ENDOPHTHALMITIS, ORBITAL CELLULITIS, DEATH.

W. T., a colored female child, aged ten years, was admitted to the hospital on April 11, 1930, on the second day of her illness. The

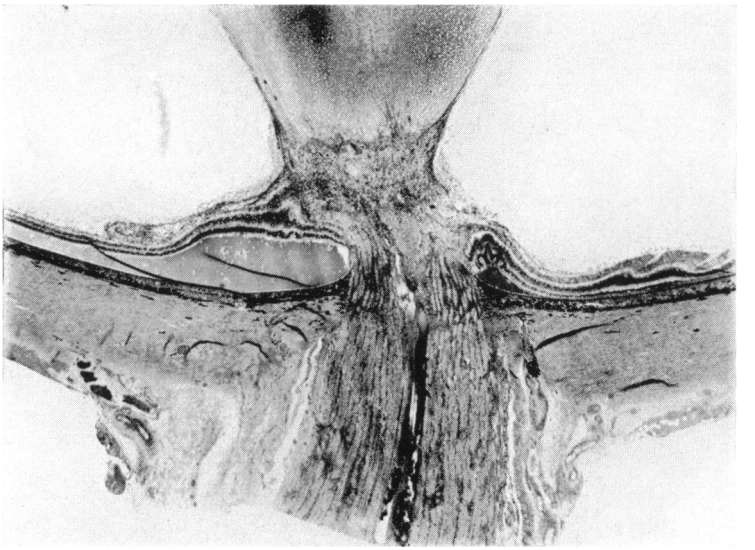

Fig. 6.—I. M., Case 4. Endophthalmitis. Showing posterior tip of the vitreous abscess, with new vessels from disc growing into it. Peripapillary detachment of the retina. Longitudinal section of nerve, showing edema and thrombosis of the central vessels (× 20).

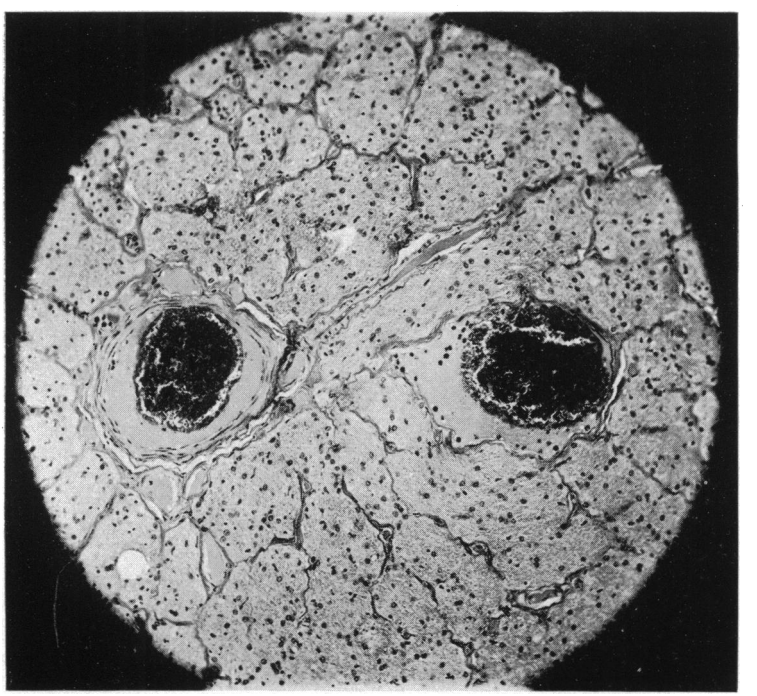

Fig. 7.—I. M., Case 4. Endophthalmitis. Cross-section of nerve, showing recent thrombus in both central vessels (× 142).

typical findings of cerebrospinal meningitis were present, and the usual treatment was instituted. The blood culture was negative. On admission the eyes were normal. On the fourth day the left eye showed moderate ciliary injection, iris congestion, and posterior synechiae. The pupil was dilated with difficulty. The following day a purulent exudate was seen in the vitreous. The exudate was fixed in position, and occupied the entire anterior portion of the vitreous so that no fundus reflex could be obtained. The eye was totally blind. The right eye was normal.

On April 28 an enormous edema of the orbital tissues developed, so that the globe was greatly proptosed and immobile. The eyelids were tensely swollen, and the conjunctiva was so edematous that it protruded through the palpebral fissure. Apparently an orbital cellulitis was present. Ice compresses, with mercury bichlorid ointment to protect the cornea, were applied constantly. In about ten days the cellulitis subsided but left the conjunctiva protruding over the lower eyelid and hanging down on the cheek. This protruding mass showed no tendency to recede, so it was replaced by means of Gaillard sutures, which were left in position for nine days, and gave an excellent result.

On May 27, about a month after the spinal fluid had returned to normal and all signs of meningitis had disappeared, the patient developed a second attack, with typical symptoms and positive spinal-fluid findings. The serum was again administered, both intravenously and intraspinally. The spinal fluid rapidly became clear and negative for meningococci. The child improved quickly, so that on June 14, after sixty-four days in the hospital, she was discharged, apparently well except for blindness of the left eye. Enucleation was refused. At that time the eye showed only slight ciliary and conjunctival injection, no proptosis, and normal motility. The pupil was irregularly dilated, with posterior synechiae and several pigment deposits on the anterior lens capsule. The anterior chamber and lens were normal. A yellow cyclitic membrane was seen immediately behind the lens. There was no apparent shrinkage of the globe.

On June 16, two days after returning to her home, she was readmitted in a delirious state, with another recurrence of meningitis. The culture of the spinal fluid was again positive for meningococci. On June 18 the spinal fluid was so thick that it would not run through the needle. Puncture of the cistern was performed on the following day, and the same condition of the fluid

was found. She died the next day. Permission for necropsy could not be obtained.

CASE 6.—BILATERAL ENDOPHTHALMITIS WITH SEVERE PAIN.

O. F., a colored female, aged twenty-one years, was admitted to the hospital on November 21, 1930, on the first day of her illness. She showed the typical signs of meningitis, and the blood culture was positive. Her eyelids were somewhat edematous, and the pupils were slightly dilated and inactive. On the third day of the illness the right eye showed numerous petechial hemorrhages of the conjunctiva, and conjunctival and ciliary injection; the iris was swollen, with some posterior synechiae; there was a slight hypopyon, and the lens, which was hazy throughout, was swollen. The left eye was normal except for great dilatation of the retinal veins, which also appeared to be very dark. Two days later the left eye also became involved. The lens was not swollen, and a grayish exudate could be seen in the vitreous. Both eyes showed marked ciliary injection, which is unusual, and there was quite severe pain, which is rare in these cases.

On December 5, 1930, both eyes exhibited a severe iritis, with posterior synechiae and a grayish-yellow exudate in the vitreous. The lens of the right eye was more cloudy than that of the left eye. The cloudiness of the right lens gradually lessened, so that on January 2, 1931, it was practically clear. The patient still complained of pain and there was considerable lacrimation. The exudate in the vitreous of the right eye was yellow, and that in the left eye was gray. On January 15 a reddish color could be seen on and just beneath the surface of the exudate in the right eye. Close examination showed that the redness was due to newly formed blood vessels. The patient was discharged on the following day, after having spent fifty-six days in the hospital. She was seen only once after dismissal from the hospital. At that time—about three months later—there was still some ciliary injection. Her eyes were beginning to show some atrophy. She was totally blind.

The unusual features of this case were the severe pain, the marked and prolonged ciliary injection, and the long-existing cloudiness of one lens, with subsequent clearing. The visible vascularization of the cyclitic membrane was not seen in any other case.

CASE 7.—BILATERAL ENDOPHTHALMITIS, TOTAL DEAFNESS, AND LATE CATARACTS.

B. D., a white female infant, aged sixteen months, was admitted to the hospital on May 9, 1930, two days after her illness began.

The usual physical and laboratory findings of meningococcic meningitis were present. The blood culture was negative. Her illness followed the usual course, requiring a total of 11 lumbar punctures and eight intraspinal and three intravenous administrations of antimeningococcic serum. The complications that arose, however, were very serious, causing complete blindness and deafness, both of which remained permanently. On the seventh day of the illness a ciliary injection was first noticed. Examination on the following day showed the irides to be swollen and the pupils irregular and inactive. In each eye a whitish-gray exudate bound the iris to the anterior capsule of the lens. Otherwise the lenses were normal. A pale yellow, fixed exudate could be seen in the vitreous of each eye. Attempts to dilate the pupils with atropin and epinephrin were only partly successful. The vitreous exudates became a deeper yellow as time went on. The patient was discharged after twenty-two days in the hospital. Shortly before this it was noticed that she did not seem to hear. Tests and observation proved that there was a total nerve deafness in both ears.

This patient was seen frequently during the next few months. Contrary to the course run by other similar cases in the present series, her eyes never became quiet or free from inflammation. The ciliary injection persisted, and her eyes seemed to be painful. Her family would not consent to enucleation. She was not seen from the latter part of 1930 until April, 1934, almost four years after her illness. Both lenses had become completely opaque and seemed to be swollen. The anterior chambers were almost entirely obliterated, the lenses and irides being thrust forward against the corneas. The eyes were not inflamed, and apparently were not painful. Tension by palpation was reduced. There was some atrophy of the irides, and a slight shrinkage of the globes was noticed. She was also totally deaf.

CASE 8.—UNILATERAL HYALITIS, RECOVERY OF VISION.

W. D., a colored male, aged ten years, was admitted to the hospital on the first day of his illness, June 12, 1931. The customary findings in meningococcic meningitis were present. Examination of the eyes on the fifth day showed that the vitreous of the left eye was so filled with large opacities that it presented a grayish appearance. It was not a fixed exudate or membrane, as was seen in the other cases. The iris was not involved, and there was no ciliary injection. After a week the opacities absorbed rapidly, and before discharge, on July 3, they had completely disappeared. The fundus was found to be normal.

This case was entirely different from the others in the series, and probably should not be classed as an endophthalmitis. Apparently only the vitreous was involved, and this was the only eye to recover completely. The fact that antimeningococcic serum was given intravenously and intraspinally the day the symptoms first appeared should be taken into consideration. It may have prevented the usual course of events.

9. THE OPTIC NERVES AND PATHWAYS.—(*a*) *Papillitis.*—Optic neuritis, or papillitis, is an extremely important complication of epidemic meningitis. The frequency of its occurrence has been variously stated by different authors. According to Romer, optic neuritis assumes first place among ocular complications, whereas choked disc is very rare, a statement with which most observers agree. The highest percentage of papillitis reported is that by Fairley and Stewart. These observers claim to have found 116 cases out of a total of 184, or 63 per cent. This percentage is so much greater than the incidence reported by other observers that it raises a doubt as to its accuracy. The next highest figure is that of Terrien and Boudier—16 out of 42 cases, or 38 per cent. So great a frequency is certainly most unusual. Randolph found optic neuritis in 15 per cent. of his cases. Uhthoff reported 16 per cent., and Heine, 10 per cent. In the author's series of 200 cases papillitis occurred 12 times, or in only 6 per cent. However, 22 patients showed a definite hyperemia of the discs. The papillae in these cases were not elevated, but were abnormally red, and some observers might have classified the condition as a true neuritis. As pointed out by the author in a paper read before the Southern Medical Association in 1932, the line to be drawn between a well-developed hyperemia and a mild neuritis is undoubtedly very fine.

There is nothing distinctive about the optic neuritis that complicates meningococcic meningitis. This opinion disagrees with that expressed by Davis, who considers the condition of the optic disc rather characteristic, presenting as it does a certain "smoky" or "misty" appearance. Most

observers do not mention a particular characteristic. The elevation is usually slight—¼ to ¾ diopter. Only very occasionally is it higher. In one patient in this series who died there was a bilateral elevation of from three to four diopters. Necropsy disclosed a massive fibrinopurulent exudate covering the entire base of the brain, being most pronounced in the region of the chiasm and around the cerebellum. The ventricles were all distended, and the canal of the spinal cord was filled with purulent exudate. Increased intracranial pressure was evidently responsible for the marked swelling of the papillae in this case.

The color and appearance of the discs are not different from those of optic neuritis resulting from other causes. The condition is almost always bilateral, although it is usually more pronounced on one side than on the other. As a rule, the papillitis develops during the first week or ten days of the disease, and reaches its height in the second or third week. Gradual subsidence, with the late appearance of a partial, secondary optic atrophy, is the usual sequence of events.

Optic neuritis may develop indirectly from the pressure of distended ventricles or from the pressure of exudate within the vaginal sheaths. In the patient with marked elevation who was examined postmortem, the former was the case. No micro-organisms within the nerve could be demonstrated. Parsons, in his Pathology of the Eye, stated: "Whether perineuritis is due to the presence of organisms or to toxins alone is uncertain; the cocci may be absent in such cases of pneumococcic meningitis (Axenfeld). On the other hand, micro-organisms may be plentiful in the sheaths in purulent meningitis without causing papillitis; even abscess formation may occur in the nerve without setting up intra-ocular inflammation (V. Hoffman). Very early optic neuritis is attributed by Westenhoeffer to hematogenous propagation. Direct continuity of inflammation from the meninges to the nerve sheaths is shown by the observations of Cheatham and Radman." Two of the patients in the present series with neu-

ritis died. Of the 10 who lived, all recovered fairly useful vision. A partial secondary optic atrophy developed in four cases, these being the only ones whose course could be followed. Sector-like defects in the fields of one or both eyes were not unusual. The prognosis regarding useful vision, however, is good.

A report of a typical severe case of papillitis follows:

H. R., a white male, aged twenty-nine years, was admitted to the hospital on February 1, 1931. He presented the usual clinical and laboratory findings of acute epidemic cerebrospinal meningitis, and the customary treatment for this condition was administered. Two days later ophthalmoscopic examination showed a hyperemia of the discs and retinas. On February 8 the condition had passed beyond the stage of hyperemia. Both discs were slightly elevated. The neuritis increased until, on February 13, the elevation of the right disc was ¾ diopter and of the left about 1½ diopters. The margins were greatly blurred, and a few small hemorrhages were observed on the papillae. The neuritis persisted for another week and then began to subside. By the end of February the elevation of the discs had almost disappeared, but the vision was still only hand movements. By the time the patient left the hospital on March 14, the vision had improved so that he could read large print and the fundi appeared to be almost normal.

On April 4, 1931, the vision had improved to 20/60 in the right eye and 20/30 in the left. The margins of the discs were indistinct, but otherwise the eyes appeared to be completely normal. Almost the entire lower field of the right eye was lost, and there was a moderate contraction of the temporal and other fields (fig. 8). The field of the left eye was normal; there were no scotomas and the blind-spot was normal.

On April 27, over ten weeks after the neuritis had reached its height, the first sign of optic atrophy appeared and then only in the right eye. The fields and vision were about the same. The accommodation was weak, being only five diopters. One month later the vision had improved to 20/50 in the right and 20/20–3 in the left eye. The field of the right eye improved, but a large defect in the lower half of the field was still present (fig. 9).

When last seen, ten months after his illness, both discs appeared to be rather white, although the vision and other subjective findings were unchanged. He was able to work regularly at his occupation of "starter" for a bus company.

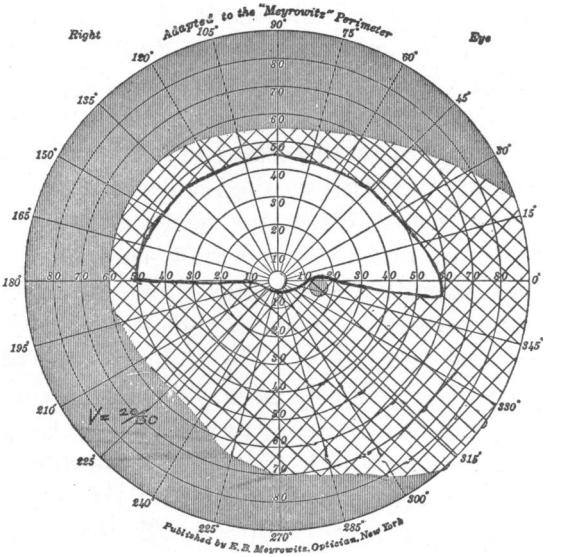

Fig. 8.—Visual field of Case H. R. on April 4, 1931; 5 mm. test object. Entire inferior field lost.

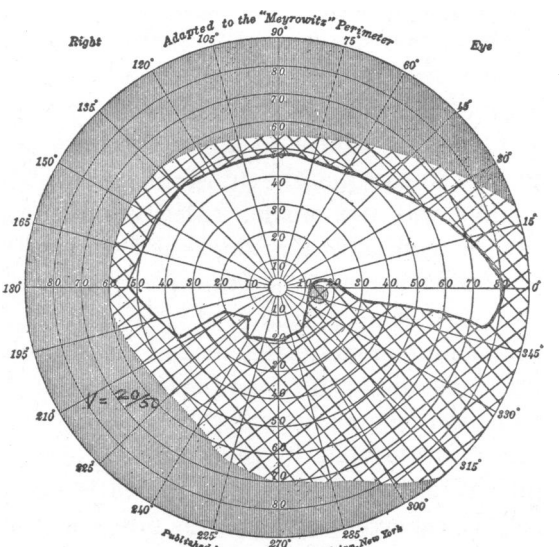

Fig. 9.—Visual field of Case H. R. on May 25, 1931. Considerable improvement, but most of inferior field permanently blind.

(*b*) *Amaurosis.*—Total blindness in meningococcic meningitis with normal ophthalmoscopic findings has long been known to those who have studied the disease. Parsons states: "A peculiarity of this disease which I have frequently seen is complete amaurosis with normal pupillary reactions, pointing to the action of toxins on the higher visual centers. The blindness may persist for many weeks after subsidence of other symptoms, and sight may be completely restored. Chronic basal meningitis sometimes shows the same features, but in these cases optic neuritis and post-neuritic atrophy may occur from secondary hydrocephalus and pressure of the distended third ventricle upon the chiasma and tracts."

The largest number of cases was reported by Kotlarevskaia in 1933. He has observed 13 instances of blindness with negative fundus findings in a series of 75 children. Many observers report no cases of amaurosis. In the author's series of 200 cases there were four definitely blind and one doubtful case, all having normal fundi. Three were infants, all of whom died—the first after forty-three days in the hospital; the second after twenty-five days, and the last after eighteen days. Autopsy was refused in two cases, and in the third it did not reveal the cause of the blindness. Distended ventricles and numerous adhesions along the base of the brain were found, but unfortunately sufficient investigation of the optic pathways was not made. Microscopic examination showed that the meninges were thickened, and the blood vessels dilated and packed with polymorphonuclear leukocytes. There was an extensive exudation of serum, fibrin, and polymorphonuclear and mononuclear cells. It is probable that pressure of the distended third ventricle upon the optic tracts and chiasm caused the amaurosis.

Most writers state that in their cases of amaurosis the pupils react to light normally, thus indicating involvement of the higher visual centers. This was not true in any of the cases in the present series. In three cases, both pupils were found dilated although a mydriatic had not been used. In

one case the right pupil was widely dilated whereas the left was at mid-dilatation. In none of these cases did the pupils react at all to light. Reaction to accommodation and convergence could not be determined in any but the adult case, and in this the pupils failed to respond. This patient, who recovered, has afforded an interesting study, and the case is, therefore, briefly reported.

W. N., a colored male, aged twenty-one years, was admitted to the hospital on April 17, 1930, with meningococcic meningitis. The usual physical and bacteriologic findings of the disease were present and the customary treatment was administered. On the morning of the sixteenth day of his illness the patient awoke to find that he could not see. Prior to this he had not noticed any visual disturbance. Examination showed that he could not perceive even a bright light. Beyond the fact that the pupils were dilated and did not react the eyes were objectively normal. Total blindness, with normal fundi, remained for almost three weeks and then light perception returned. He was discharged from the hospital on May 23 with a vision of light perception only, and in the right eye only in the superior field. The fundi were still normal. Gradual improvement continued until, on July 11, the right eye had a vision of 3/200 and the left, 20/30. The patient appeared to have difficulty in getting about, and on testing the fields they were found to be practically telescopic. Colors were recognized only centrally. The vision in the right eye was so poor that recording of the field was found to be impractical. By confrontation, however, there was no vision except in a small central area (fig. 10).

When the patient was next seen, on August 1, there was a pallor of the right disc. This was the first sign of any pathologic condition present in the fundi. The vision and fields were practically unchanged. On September 11 there was definite atrophy of the right disc, and the left disc showed a beginning pallor. On January 9, 1931, the vision in the right eye was 20/50 and in the left eye, 20/30+. Both discs were now white, moderately cupped, and the lamina cribrosa was plainly visible. The patient was not seen again until May 5, 1931, one year after his illness. The vision with proper lenses, + 0.50 cyl. ax. 180°, both eyes, was: right eye, 20/40, and left eye, 20/20–2. The fields had improved, but the right was still very defective and the left had an absolute scotoma of the entire lower nasal quadrant. No color except red

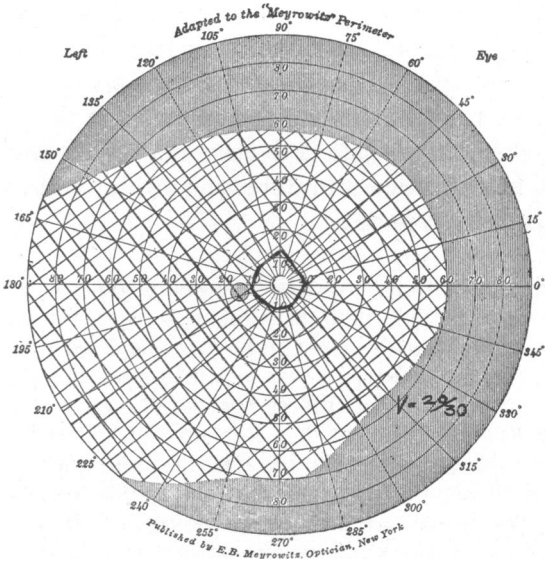

Fig. 10.—Visual field of Case W. N. on July 11, 1930; 10 mm. test object. Blind except for about 10 degrees centrally.

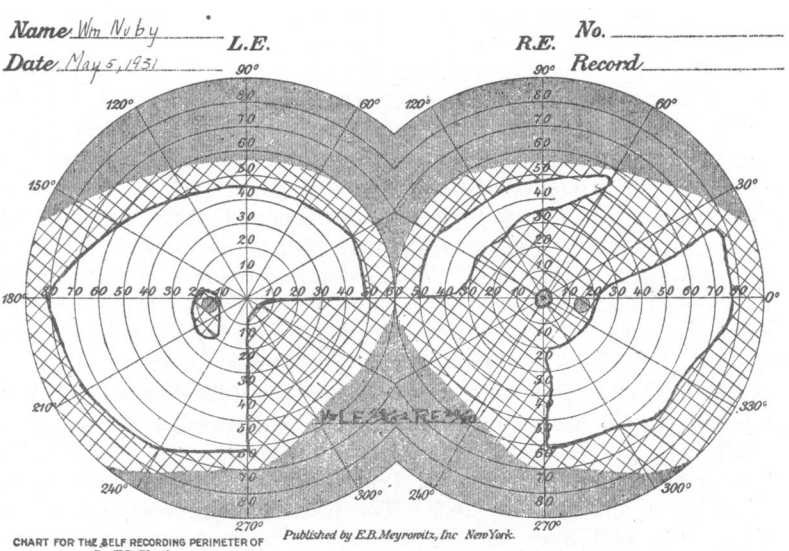

Fig. 11.—Visual fields of Case W. N. on May 5, 1931; 5 mm. test object. Binasal inferior quadrant anopsia.

was perceived with the right eye, and that only centrally. With the left eye color vision was good centrally, but was lost beyond eight degrees. The blind-spot was moderately enlarged (fig. 11).

The patient has been seen two or three times each year since 1931, but no appreciable change in the vision, fields, or in the appearance of the discs has occurred. The papillae are so atrophic that it is surprising to find the central vision so satisfactory.

Comment

Sudden blindness affecting both eyes simultaneously is unusual. When it occurs, it is due most frequently to some disturbance or lesion affecting the visual areas of both occipital lobes. Such a condition is seen in the amaurosis which occurs occasionally as a complication of uremia. In those cases of meningitis in which an amaurosis develops but which have normally reacting pupils, the lesion must be posterior to the primary optic centers. In these cases the blindness is due probably to the infiltration of toxins or to actual pressure affecting both visual areas simultaneously. In the four cases which occurred in our series the pupils were inactive, indicating that the lesion was anterior to the primary optic centers. Furthermore, in the case just reported, optic atrophy developed later, a complication that could not occur from a cortical blindness. Another point against the lesion being in the cortex is found in the fields of W. N. (fig. 11). An examination here discloses lower binasal quadrant defects, which do not represent corresponding parts of the retina, such as would result from a posterior lesion, but indicate rather that the lesion was in the chiasm itself.

An interesting question raised by the case reported here is: why is central vision recovered before and more completely than peripheral vision? This is undoubtedly due to the anatomic arrangement of the nerve fibers in the optic nerve and chiasm. In the posterior portion of the optic nerve and in the chiasm the papillomacular bundle is centrally located, and is not, therefore, subjected to the same degree and intensity of damage as the fibers from the peripheral portions of the retina.

While the amaurosis which complicates meningitis undoubtedly is due in some cases to posterior lesions, in the patients seen by the author the lesions were anterior to the primary optic centers. In the one patient who lived, and whose fields were accurately followed, the lesion involved the optic chiasm. Probably the pathologic condition is an intense neuritis. This may be due to one or more of several things: (1) It may be due to the mechanical pres-

sure of exudate or adhesions, or of both; (2) the infiltration of toxins into the nerve may be responsible, and (3) the neuritis may result from the actual invasion of the nerve by meningococci, coming either through the blood stream or by direct extension from the surrounding meninges.

10. THE RETINA AND RETINAL VESSELS.—Involvement of the retina alone was not observed in any of the cases here reported. A surrounding area of retinitis was present in every severe papillitis. Heine observed a preretinal hemorrhage, but evidently these are very rare. Retinal detachment with great edema, wandering-cell infiltration, and degeneration probably occurs in all severe cases of metastatic endophthalmitis, but this condition cannot be diagnosed clinically because of the purulent exudate in the anterior portion of the vitreous. Separation of the retina, with varying degrees of retinitis, was present in the four cases examined pathologically in this series.

Hyperemia of the discs and retinas was quite frequent, being present in 22 cases, or 11 per cent. In these cases the condition could hardly be classified as true neuroretinitis because there was no elevation of the discs and no edema of the retina or hemorrhages or exudates were apparent. The only changes from the normal were an increased redness of the retinas and discs and a dilatation of the retinal vessels. Several cases showing this hyperemia, when seen a few days later, exhibited a definite neuroretinitis. The majority of them, however, did not progress beyond the stage of hyperemia, and with the improvement of the patient the fundi returned to normal. Thus, hyperemia of the discs and retinas probably represents simply an early stage of what may become a neuroretinitis. Early and effective treatment, such as is now given, undoubtedly frequently prevents the neuritis from developing. If this is correct, it would explain the greater frequency of neuritis described by the older writers on the subject. Provided these observers did not make fundus examinations early in meningitis, it would also explain

why very few of them even mention hyperemia of the disc and retina. The exceptions are Randolph, who reported hyperemia of the disc and retina in 19 cases, or about 50 per cent., and Terrien and Boudier, who found it in seven, or 17 per cent.

Another type of change seen in the retinal vessels apparently concerned only the veins. These were dilated or engorged with blood, thus making them appear not only larger but also darker than normal. The impression received from the ophthalmoscopic examination was that there was an interference with the return circulation through the central vein in these cases. If this had been true, it would undoubtedly have manifested itself by some other signs. For example, if the accumulation of exudate had exerted sufficient pressure around the cavernous sinus, or on the superior ophthalmic vein, it would have affected not only the central retinal vein, but also the entire venous return from the orbit. Therefore, edema of the eyelids, proptosis, and an engorgement of all the vessels should have been present. The exact cause of this venous change was not clear. It is possible that some congestion in the nerve around the central vein was responsible.

Randolph called attention to this venous engorgement in a number of his cases. Thirty-two patients in the present series, or 16 per cent., showed this type of vascular change but no other abnormality. Nine, or 28 per cent., of these patients died. The remainder showed a gradual return to a normal appearance along with the improvement in their general condition.

Thrombosis of the central vein has been observed only rarely as a complication of meningococcic meningitis. Randolph reported one case in a twenty-months-old infant who died on the first day Randolph saw the case. Michel reported seven cases, all in adults, ranging in age from fifty-one to eighty-one years, and all showing arteriosclerosis. This observer stated that the thrombosis may be complete, incomplete, or only a slight closure, causing more or less stasis

in the veins. Retinal hemorrhages and great engorgement of the veins were present in every case.

In this series of 200 cases one patient with endophthalmitis was found, on microscopic examination of the enucleated eye, to have a recent thrombosis of both central vessels. (See Case 4, fig. 7.)

SUMMARY AND CONCLUSIONS

The eyes of 200 patients with meningococcic meningitis were examined routinely, and repeated examinations were made when indicated. Forty-nine per cent. of the cases showed some ocular involvement. Each structure of the eye is dealt with separately in this paper and positive findings are described. Any or all of the structures of the eye may be affected in this disease, and about 50 per cent. of the cases show some ocular abnormality. The lens is probably the structure least often involved. Metastatic endophthalmitis was the most outstanding and the most disastrous complication encountered in this series. Photomicrographs of the four eyes enucleated for endophthalmitis, together with a description of the pathologic changes, have been included here. Among the larger collections of pathologic eye specimens in this country, similar cases were found to be rare.

Ocular examinations of all cases of epidemic cerebrospinal meningitis should be made at frequent intervals. They are especially valuable in cases of papillitis, in which an increasing elevation of the disc may serve as an additional guide to the attending physician as to the frequency of repeating lumbar or cistern punctures, and in certain cases severe or complete optic atrophy may thereby be prevented. Likewise involvement of the conjunctiva, cornea, uveal tract, and other structures may be treated appropriately at an early and more hopeful stage.

The author wishes to acknowledge with thanks his indebtedness to Dr. Conrad Berens and Dr. E. C. Ellett for their many helpful suggestions in the preparation of this paper;

also to Dr. Gilbert Levy, Director of the Isolation Hospital, and the staffs of the Departments of Pathology and Bacteriology of the University of Tennessee, for their assistance in making this study.

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EXPERIMENTAL IRITIS: THE OCULAR REACTIONS IN RABBITS SENSITIZED TO STREPTOCOCCUS VIRIDANS*

ANGUS L. MACLEAN, M.D.
Baltimore

The recent experiments of Swift, Derick, Andrews, and Hitchcock[1a, 1b, 2, 3, 4] have indicated that an isolated streptococcic infection, and the absorption of living streptococci, will, under certain conditions, produce a hypersensitivity of the organism as a whole. Furthermore, these authors have demonstrated that the cornea participated in the general reaction, and that the sensitized cornea, when brought into contact with the specific sensitizing antigen, reacts with def-

* From the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital. Candidate's thesis for membership accepted by the Committee on Theses.