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SYNDROME OF UNILATERAL RECURRENT ATTACKS OF GLAUCOMA WITH CYCLITIC SYMPTOMS

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In order to form a complete picture of a case of glaucoma, it is essential to observe the patient at frequent intervals and over a relatively long period. A case, ideal in this sense, presented itself in a physician who lived in the immediate vicinity and thus was able to visit our office at the earliest indication of an oncoming attack. This patient had recurrent unilateral attacks of ocular hypertension associated with cells in the aqueous and a few keratic precipitates, which disappeared shortly after the tension returned to normal. The time relation of the appearance of the hypertension and the cyclitic phenomena could be accurately studied. Also, an attempt was made to evaluate the response of the symptoms to various drugs.

This case aroused our interest in the relation between glaucoma and cyclitis. A survey of our glaucoma files disclosed 7 more such cases, and a new case occurred in our practice during the preparation of this paper. All these 9 cases, which were followed for periods varying from one month to nineteen years, were characterized by a striking uniformity in symptoms, course of the disease and response to treatment.

The chief features of this syndrome may be briefly described as follows:

1. The disease is unilateral. In 3 cases there was some degree of heterochromia, and in each instance the lighter-colored eye was involved. In 3 cases anisocoria was present, the affected eye having the wider pupil.

2. The presenting symptom is usually slight discomfort, colored halos or blurring of vision. However, no symptoms may be present. There is no pain. Vision is usually good, even at the height of the attack.

Read at a meeting of the New York Society for Clinical Ophthalmology, May 5, 1947.

3. The eye is white, or a few dilated conjunctival vessels may be visible. Ciliary injection is never present. If the tension is very high, mild congestion of the sclera or edema of the corneal epithelium may be noted.

4. Ocular hypertension may appear a day or so before, or simultaneously with, cells in the aqueous. It is followed within the next twenty-four hours by from one to twenty small, well defined, unpigmented precipitates on the posterior surface of the cornea. These soon begin to disappear, and, if the hypertension persists, fresh ones may appear. After subsidence of the hypertension, the precipitates fade away within a few days to a month. Although precipitates are present as a rule, they may be absent during some of the attacks (case 3). At no time is there more than a trace of aqueous flare. Posterior synechias are never formed.

5. The angles were open in all 4 cases in which gonioscopic studies were made. In 2 cases they were wide and in 2 moderately narrow.

6. The individual attacks of ocular hypertension have lasted from a few hours to one month, but rarely over two weeks. Attacks which have been observed without treatment have cleared within two weeks. It is possible that overtreatment, whether with miotics or with mydriatics, may prolong the attack.

7. Episodes may occur with varying frequency and without any apparent cause. One patient has had five attacks in a period of eight months; another has been having two or three attacks a year for the past thirteen years, and still another had four attacks up to thirteen years ago and has been free from symptoms since. The visual fields may show enlargement of the angioscotomas during the acute phase. In 1 case, in which there were deep cupping and pallor of the nerve head, the field became progressively contracted. In all other cases the field remained normal during the course of the disease. During the intervals of freedom from glaucoma, provocative tests, such as the liability and the water-drinking test, give negative results, and there are no signs or symptoms either of iridocyclitis or of glaucoma.

8. Treatment does not seem to shorten the course of the attack. One-half to 2 per cent pilocarpine hydrochloride N. F. may lower the tension temporarily. Physostigmine and stronger concentrations of pilocarpine usually give rise to extreme discomfort and pain and may even cause a rise in tension. Homatropine and atropine usually have no pronounced effect on the tension, but, apparently, they are not detrimental to the eye. Epinephrine bitartrate, 2 per cent, and phenylephrine ("neo-synephrine") hydrochloride, 10 per cent, may produce an evanescent reduction of the tension. Since the attack is self limited, it

is safe to procrastinate and use no treatment (or placebo therapy) until the diagnosis has been established and the course has been followed through at least one attack. Surgical intervention did not have to be resorted to in any of our cases. Kraupa[1] found that in 2 of his 4 cases surgical treatment did not affect the subsequent course of the disease, since the patients continued to have acute attacks.

REPORT OF CASES

CASE 1.—E. W., a white physician aged 43, consulted an ophthalmologist because, for the first time, he had experienced blurring of vision for three hours. The tension in the right eye was 70 mm. (McLean), while that in the left eye was normal. A diagnosis of primary glaucoma was made. With use of pilocarpine, the tension dropped to normal but soon rose to 50 mm. (McLean). After several days of therapy with miotics, keratic precipitates were observed in the right eye, and the diagnosis was changed to that of secondary glaucoma. Use of pilocarpine was stopped after one week of treatment. Three days after the discontinuation of the miotic (or ten days after the onset), the tension was 25 mm. (McLean). The patient was free from symptoms except that the left pupil was dilated and accommodation was temporarily suspended, owing to the inadvertent use of atropine sulfate. During this attack his temperature, which was normally below 98 F., rose to 99 F. on three occasions. The white blood cell count rose from 7,000 to 11,100 per cubic millimeter.

When the patient was first seen by us, on Aug. 19, 1946, two weeks after the onset, the tension was 18 mm. (Schiotz) in the right eye and 22 mm. in the left eye. The right pupil was 3.5 mm. and the left 5 mm. in diameter (atropine mydriasis). Both irises were brown, but the right was of slightly lighter color than the left. In the right eye, a few nonpigmented, small, well defined keratic precipitates were present on the posterior surface of the cornea. There were no cells in the aqueous and no posterior synechias. The media were clear, and the fundus was normal. The left eye was normal. Vision was 20/15 in each eye with a —1.75 D. sphere for the right eye and a —2.25 D. sphere for the left eye. Gonioscopic examination of both eyes showed wide angles throughout. The lower part of Schlemm's canal contained blood.

The patch test gave a 3 plus reaction to tuberculin. A roentgenogram of the chest showed no evidence of tuberculosis. Brucellosis was excluded by serologic study. The Wassermann reaction of the blood was negative.

The patient gave a history of old nongonococcic prostatitis and of mild and variable hypertensive vascular disease, as well as of hay fever, of fifteen years' duration, associated with asthma during the first two years.

He remained free from symptoms until October 7, when he presented himself two hours after he had begun to see rainbows with his right eye. At this time tension was 49 mm. in the right eye and 20 mm. in the left eye. The eye was white. There were a few deposits on the posterior surface of the cornea and numerous cells in the aqueous, but no flare was noted. With 1 drop of 10 per cent phenylephrine hydrochloride N.N.R., the right pupil was almost maximal. The tension fell to 41 mm. in forty-five minutes and then dropped to 22 mm. within four hours. The following morning, tension in the right eye was 24 mm., the cells were less numerous but the deposits had increased in number.

1. Kraupa, E.: Ocular Hypertension in Acute Angioneurosis of the Ciliary Body ("Glaucoma Allergicum"): Its Relationship to Cyclitic and Heterochromic Glaucoma, Arch. f. Augenh. **109**:416, 1935.

Another ophthalmologist saw the patient that evening and, finding the tension normal, instilled a drop of homatropine hydrobromide into the right eye. That night the patient had an uncomfortable sensation in his right eye. The following morning, October 9, the right pupil measured 5 mm. and the tension was 53 mm. (Schiotz), while the left pupil was normal. The eye was white except for a few dilated conjunctival vessels. Cells were seen in the aqueous, and a few fresh deposits were visible on the posterior surface of the cornea. This time 10 per cent phenylephrine hydrochloride failed to lower the tension, but 2 per cent pilocarpine hydrochloride brought it down to 20 mm. within two hours. A 3 D. increase in myopia was noted, which lasted two hours. Pilocarpine hydrochloride, 2 per cent, given every four hours, controlled the tension. No cells were observed after October 10 (three days after onset of the second attack). The keratic precipitates, however, persisted until October 24. Miotics were discontinued on October 16, and the tension remained even lower than that in the left eye.

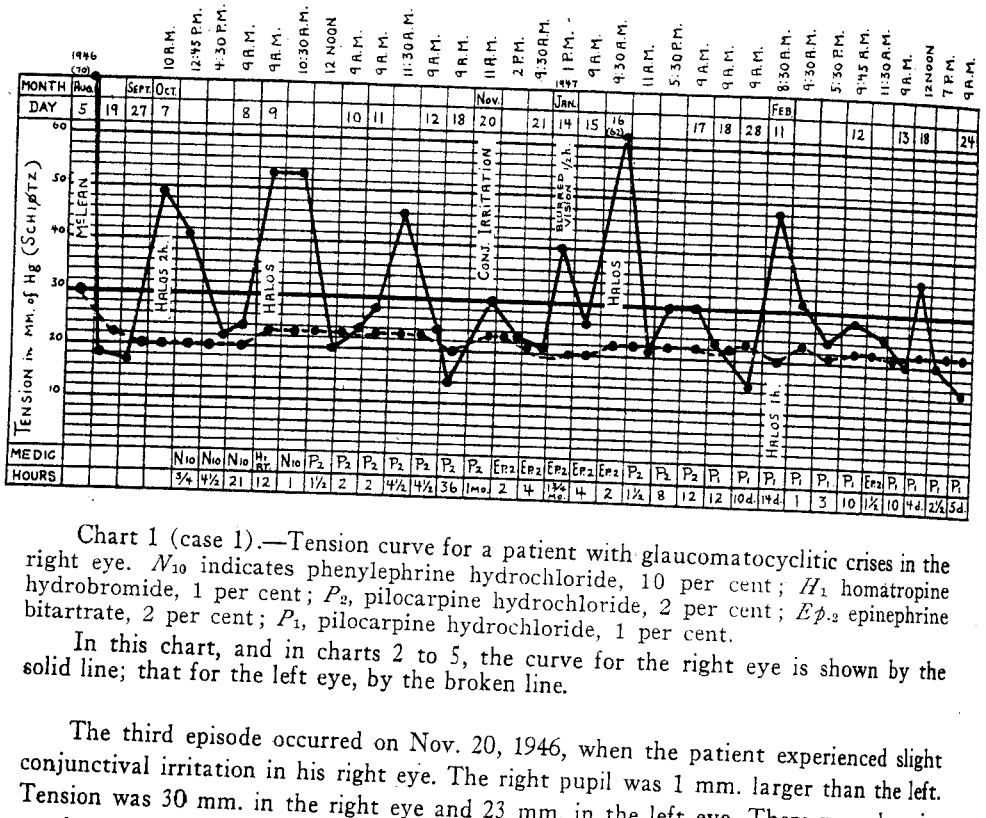

Chart 1 (case 1).—Tension curve for a patient with glaucomatocyclitic crises in the right eye. N_{10} indicates phenylephrine hydrochloride, 10 per cent; H_1 homatropine hydrobromide, 1 per cent; P_2, pilocarpine hydrochloride, 2 per cent; $E\phi_{.2}$ epinephrine bitartrate, 2 per cent; P_1, pilocarpine hydrochloride, 1 per cent.

In this chart, and in charts 2 to 5, the curve for the right eye is shown by the solid line; that for the left eye, by the broken line.

The third episode occurred on Nov. 20, 1946, when the patient experienced slight conjunctival irritation in his right eye. The right pupil was 1 mm. larger than the left. Tension was 30 mm. in the right eye and 23 mm. in the left eye. There were deposits on the posterior surface of the cornea and numerous cells in the aqueous. The patient suggested the use of 2 per cent epinephrine bitartrate. Within three hours the tension dropped to 23 mm. He had no visual disturbance, and the irritation promptly disappeared. The tension remained normal. On Jan. 8, 1947 only two minute keratic precipitates remained.

On Jan. 14, 1947, one-half hour after the onset of blurring of vision and irritation in the right eye, the tension measured 40 mm. in the right eye and 20 mm. in the left eye. There were no cells in the aqueous, and the eye was white. The two precipitates which had been noted previously were still present. Epinephrine bitartrate, 2 per cent, was used every four hours, and the following morning the tension was 26 mm. in the

right eye and 20 mm. in the left eye, but this time a few cells were present in the aqueous and about a dozen new keratic precipitates were noted. In spite of the continued use of epinephrine bitartrate, the tension rose to 62 mm. on the following day (third day after onset of attack). Pilocarpine hydrochloride, 2 per cent, brought the tension down to 21 mm. within an hour and a half and increased the myopia by 4 D. The tension fluctuated around 30 mm. until January 18 (unaffected by use of pilocarpine, epinephrine or phenylephrine). It then dropped sharply to between 15 and 18 mm. On February 4, only one keratic precipitate was visible.

The fifth attack occurred on February 11. It had a similar course. Again, cells were seen and fresh precipitates noted. They disappeared within ten days.

Pupillographic studies, made on two occasions by Dr. Otto Lowenstein, showed a curve which indicated sympathetic phenomena, such as are noted in cases of hypertensive vascular disease. A diurnal tension curve was normal. The water-drinking test, used as a provocative, gave negative results. The tension curve is shown in figure 1.

CASE 2.—M. S., a dentist aged 41, had the first attack of hazy vision and colored halos in the left eye in September 1934, when he was 28 years of age. An ophthalmologist made a diagnosis of low grade cyclitis with secondary glaucoma and treated him with atropine and salicylates. The attack subsided within a few days.

A similar episode occurred in September 1938. A different ophthalmologist treated him at first with pilocarpine for three weeks, then, when keratic precipitates were noted, atropine was substituted. This attack subsided after six weeks. Third and fourth attacks, each lasting three weeks, occurred in August 1939 and February 1940, respectively. In these attacks treatment was with homatropine.

The patient was first seen in this office on May 11, 1940, on the third day following the onset of hazy vision and colored halos in the left eye. The day prior to his visit, he had used 1 per cent pilocarpine hydrochloride, and the symptoms subsided after one hour. Examination showed vision to be 20/20 in the right eye with a correction of —0.75 cyl., axis 170, and 20/15 in the left eye with a correction of +0.50 sph. —1.00 cyl., axis 180. Both eyes were white. The irises were brown and of the same color. The pupils were regular and reacted to light. The right pupil measured 3.5 mm. and the left 4 mm. The fundi were normal. Examination with the slit lamp revealed twelve minute keratic precipitates in the left eye. Both anterior chambers were of normal depth. Tension was 15 mm. in the right eye and 31 mm. in the left eye. The fields and blindspots were normal.

A patch test gave a negative reaction to tuberculin. Medical examination revealed nongonococcic urethritis. The electrocardiogram and the basal metabolic rate were normal. Roentgenograms of the sinuses, teeth and chest revealed a normal condition. The patient gave a history of hay fever due to ragweed.

He was given a 1 per cent solution of pilocarpine hydrochloride to use three times a day in his left eye. On May 15, 1940 the tension in this eye was 22 mm. The precipitates were gone by June 10 (one month after the onset).

The patient returned a few times for examination. The tension was always normal, and no signs of cyclitis were present. On October 15, he was seen three hours after he began to see rainbows and twelve hours after onset of hazy vision in the left eye. The eye was white, but the tension was 38 mm. Tension in the right eye was 17 mm. Vision was normal in both eyes. Examination with the slit lamp revealed eight fresh, discrete, small keratic precipitates. Two hours after use of 10 per cent pilocarpine hydrochloride, tension in the left eye was 31 mm. He used 2 per cent pilocarpine hydrochloride every two hours, and the following day the tension was normal. By November 10 all signs of

cyclitis had disappeared. He continued to use 1 per cent pilocarpine hydrochloride three times a week for one year.

On Feb. 5, 1942 he had another attack of seeing rainbows and hazy vision in the left eye, with recurrence the following day despite the use of 1 per cent pilocarpine nitrate. He was seen on the third day after onset, when tension was 36 mm. in the left eye. Three precipitates were found. Tension in the left eye was normalized in nine days, and the keratic precipitates were gone in three weeks.

He joined the Army and was well until April 1944, when he had another attack and was treated with epinephrine packs in an Army hospital. The tension returned to normal in three days. After his discharge, he had another mild episode on Oct. 17, 1944 and has been well ever since. On his last visit, in February 1947, the right pupil was slightly smaller than the left, but the eyes were otherwise normal.

Pupillographic studies in April 1947 showed a curve similar to that associated with primary glaucoma.

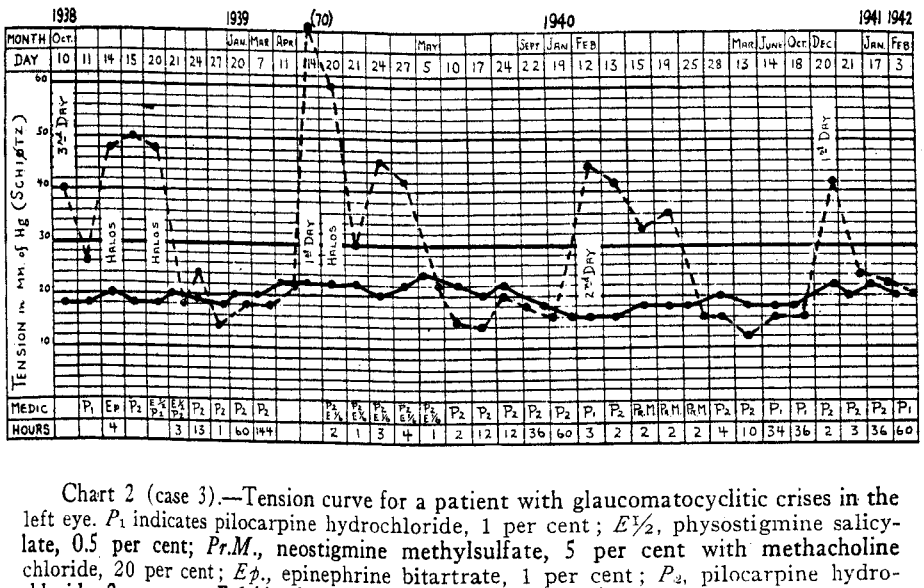

Chart 2 (case 3).—Tension curve for a patient with glaucomatocyclitic crises in the left eye. P_1 indicates pilocarpine hydrochloride, 1 per cent; $E\frac{1}{2}$, physostigmine salicylate, 0.5 per cent; *Pr.M.*, neostigmine methylsulfate, 5 per cent with methacholine chloride, 20 per cent; *Ep.*, epinephrine bitartrate, 1 per cent; P_2, pilocarpine hydrochloride, 2 per cent; *E* 1/6, physostigmine salicylate, 0.16+ per cent.

CASE 3.—A. S., a physician aged 49, was seen on Oct. 24, 1938, seventeen days after the onset of foggy vision in his left eye. He gave no history of similar episodes. He received treatment from another ophthalmologist, who had found the tension in the left eye to be 40 mm. After use of 1 per cent pilocarpine hydrochloride and 1 per cent epinephrine bitartrate, the tension quickly dropped to 24 mm., but rose again progressively to 48 mm. on October 14 (seventh day of the attack). At this time he saw colored halos around lights. The tension became normal fourteen days after the onset.

Examination revealed vision of 20/20 in each eye with a correction of —5.00 sph. —0.50 cyl., axis 180. The left eye was white. The fundi were normal. Tension was 19 mm. in the right eye and 24 mm. in the left eye (thirteen hours after the last use of a miotic). The fields and blindspots were normal. Examination with the slit lamp showed an atypical Krukenberg spindle in each eye, atrophy of the pupillary border of the left iris and deposits of pigment on the lens capsule. Two white precipitates were present on the posterior surface of the left cornea. These were gone by November 3 (four weeks after onset).

The family history revealed that one other member of the family, an aunt on the paternal side, had glaucoma. The patient had been subject to severe right-sided migraine headaches for the past two years. He has a highstrung, neurotic nature.

On April 14, 1939, he awoke with foggy vision in the left eye, followed by his seeing colored halos. The tension was 22 mm. in the right eye and 70 mm. in the left eye (three days previously the tension had been 22 mm. in each eye). The eye was white. Vision was 20/30 in the left eye. There were cells in the aqueous and a few white precipitates on the posterior surface of the cornea. He used pilocarpine and physostigmine at frequent intervals. Tension fluctuated between 30 and 60 mm. but was normalized by May 5, 1939. The deposits had disappeared by May 24, 1939.

The next episode occurred on Feb. 11, 1940, when the patient began to see rainbows with his left eye. After a few instillations of 1 per cent pilocarpine hydrochloride, the halos disappeared. The next day tension in the left eye was 45 mm. Examination with the slit lamp at this time did not reveal any cells in the aqueous or keratic precipitates. When the hypertension failed to recede after two days, he began to use 20 per cent methacholine chloride with 5 per cent neostigmine methylsulfate. The tension returned to normal on February 25. No precipitates or cells appeared during the entire course of this attack.

On Dec. 20, 1940, the tension rose to 42 mm. and was quickly controlled with pilocarpine. No cells or deposits were noted with this attack. The tension curve is shown in chart 2.

The patient has been free from symptoms and tension has remained normal up to the time of writing. Pupillographic studies showed a bilateral curve similar to that associated with primary glaucoma. He was carefully studied for foci of infection. One abscessed tooth was extracted in May 1939, and he received a course of injections of autogenous vaccine. This treatment failed to influence the course of the attacks. He never saw halos when the tension was below 40 mm., although occasionally he had no visual disturbance with a tension as high as 60 or 70 mm. Miotics increased his myopia by as much as 4 D.

CASE 4.—M. C., a white man aged 45, was first seen on April 21, 1944. He gave a history of having had attacks of blurred vision and seeing colored halos in the right eye every four to six months for the past ten years. These attacks would last three to ten days and wear off without any treatment, leaving no sequelae.

The present attack began on April 18, and had been preceded by a similar episode ten days previously. The patient decided to consult a physician because, for the first time, he had experienced two attacks within so short a period. He had never had any symptoms in the left eye. Examination showed 20/20 vision in the right eye with a correction of +3.50 sph. +0.25 cyl., axis 90, and 20/200 in the left eye with a correction of +3.75 sph. +1.75 cyl., axis 115. The left eye had been amblyopic since childhood. The right pupil was larger than the left and reacted sluggishly to light and in accommodation. Tension was 65 mm. (Schiotz) in the right eye and 28 mm. in the left eye. The fundi were normal. The anterior chambers were of normal depth. Examination with the slit lamp showed a few deposits on the posterior surface of the right cornea. The left cornea was normal. He was given 2 per cent pilocarpine hydrochloride, to be used four times a day. The drops caused pain and blurring of vision, which lasted two hours. The tension continued to be elevated all this time, despite the drops. On May 1 the deposits were much fewer. He was not seen until June 15, when no precipitates were found.

The patient returned again on April 26, 1946, two days after he began to have blurred vision and see rainbows in his right eye. He used pilocarpine of his own accord, but the eye felt worse and he became alarmed. He had had three attacks since he was

last seen (June 15, 1944). The first one, in September 1944, lasted three days and subsided with the use of pilocarpine. The other two, which occurred on Jan. 1 and Nov. 7, 1945, lasted one week each.

There was slight scleral congestion. The cornea was somewhat steamy. The right pupil was larger than the left but reacted normally. The fundus was clearly visible and was normal. The slit lamp showed three deposits on the posterior surface of the right cornea. The tension was 70 mm. in the right eye and 28 mm. in the left eye. Phenylephrine hydrochloride, 10 per cent, and pilocarpine hydrochloride, 5 per cent, failed to affect the tension. In view of this fact, and because of the self-limited nature of the crises, the patient was instructed to use nothing but acetylsalicylic acid and ice applications. On May 3 the symptoms subsided, and the tension remained normal until Dec. 25, 1946. At this time he consulted another ophthalmologist, who found that the tension was 50 mm. in the right eye and that precipitates were present on the posterior surface of the cornea. This attack subsided in ten days.

The patient was last seen on March 9, 1947, when the right eye appeared perfectly normal. The fields and blindspots were normal. Gonioscopic examination showed the angles to be moderately narrow. The right pupil was 0.5 mm. larger than the left. No heterochromia was noted. Pupillographic studies showed central sympathetic phenomena. The patient has no systemic disease and is not subject to any allergic manifestations.

CASE 5.—E. T., a white woman aged 32, came to our office on Oct. 30, 1939. She gave a history of an attack of blurred vision in the right eye on Aug. 15, 1939. Another ophthalmologist had prescribed pilocarpine, and the attack wore off in one day. She continued to use pilocarpine and physostigmine, but she had another attack in the right eye on October 23. The tension did not respond to miotics at this time, and surgical intervention was advised but was not carried out because the eye began to improve soon thereafter.

The patient was slender and somewhat underweight and appeared tense and excitable. She had no family history of glaucoma. No history of allergy was given. Examination showed vision of 20/20 in each eye with a —0.75 D. sphere. The pupils were pinpoint, owing to the use of miotics. Tension was 31 mm. in the right eye and 20 mm. in the left eye. Examination with the slit lamp showed that the anterior chambers were of normal depth. There were about six small, discrete, white deposits on the posterior surface of the right cornea. The fields and blindspots were normal. Thorough medical examination disclosed no pathologic condition. Roentgenograms of the sinuses revealed nothing abnormal, but two impacted teeth were discovered and removed. Use of pilocarpine hydrochloride, 1 per cent, twice a day, was continued. The symptoms did not recur, and the tension remained normal. The keratic precipitates disappeared by November 24 (four weeks after onset).

The patient remained well until Jan. 1, 1940, when she noticed haziness of vision and rainbows in the right eye. This attack coincided with the end of the menstrual period. She was seen on January 3, when the tension was 42 mm. in the right eye and 22 mm. in the left eye. Vision was normal, and the eye was white. There were eight minute deposits on the posterior surface of the right cornea. Tension subsided by January 5 with the use of pilocarpine, and the deposits disappeared by January 23. She has remained well since this time.

CASE 6.—E. D., a white man aged 59, a pharmacist, had been subject to recurrent attacks of slight pain and blurring of vision every few months for ten to fifteen years prior to his first visit to our office, on March 9, 1936. The present attack occurred on March 2 and was the severest he had yet had. When he was first seen by another

ophthalmologist, on the fourth day of his attack, a diagnosis of acute glaucoma was made and operation was advised. A second ophthalmologist, however, treated him with 2 per cent pilocarpine hydrochloride and 0.25 per cent physostigmine salicylate. The attack subsided and vision improved. Thus, the attack lasted one week. The patient had a mild hypertensive vascular disease. There was no family history of glaucoma.

Examination showed vision of 20/20 in the right eye with a correction of +0.25 sph. +0.50 cyl., axis 180 and 20/15 in the left eye with a correction of +1.00 D. sph. +1.00 cyl., axis 75. The right eye was normal in appearance except that the right iris was gray and the left one brown. The right pupil was smaller than the left because of the use of pilocarpine. The right disk was pale and showed moderate glaucomatous excavation. The left eye was normal. Examination with the slit lamp showed two unpigmented deposits on the posterior surface of the right cornea. The tension was 22 mm. in each eye. There was absence of the upper half of the right field, with a pronounced contraction of the lower half. The left field was normal.

During the two years following this attack, the patient used pilocarpine irregularly once or twice a week; the tension remained normal, and no keratic precipitates were seen. On June 7, 1938, the tension was found to be 36 mm. The patient had had symptoms of blurred vision for the past few days and, although the eye (right) was white, examination with the slit lamp showed several fresh, well circumscribed deposits on the posterior surface of the cornea. Tension responded to 1 per cent pilocarpine hydrochloride, and the symptoms subsided.

On June 14, 1940 another routine check-up revealed that tension in the right eye was increased. In July the tension was back to normal; but it rose again on Oct. 25, 1940, and fresh deposits were noted. The hypertensive phases became more frequent after November 1940. Although the patient did not have any symptoms, the visual field in his right eye rapidly diminished, and vision was reduced to light perception by June 1941. He instilled pilocarpine irregularly, and only when he thought he had increased tension. This drug, although it usually lowered the tension, did not prevent attacks.

CASE 7.—R. M., a white housewife aged 51, began to have attacks of edematous swellings in various parts of the right side of the face and neck, associated with headache and misty vision of the right eye, in the summer of 1927. (She was 31 years of age at this time.) An ophthalmologist found the tension in the right eye to be 70 mm. and prescribed pilocarpine. The following day the tension was normal. She continued to use low concentrations of pilocarpine. Her tension remained normal, but in June 1933 she complained of blurred vision in the right eye, of two days' duration. The eye was white. The tension was 43 mm., and a few fresh keratic precipitates were present in the right eye. This time she was given homatropine, and the tension subsided within three days. Medical examination showed no foci of infection. The precipitates disappeared within three weeks. In February 1934 she had a similar episode. Tension was 31 mm., and a few fresh deposits were noted. This attack improved in a few days with the use of homatropine. The drug was continued prophylactically for nine months. During the next year she had another attack and was treated with pilocarpine.

When she came to this office, on May 23, 1942, she had been using miotics in the right eye for the past few years. Tension was 17 mm. in the right eye and 19 mm. in the left eye. Vision was 20/25 in each eye with a correction of —2.50 cyl., axis 45 for the right eye and —1.75 sph. —2.00 cyl., axis 135 for the left eye. The irises were brown and of the same color. The fundi were normal. The media were clear. The anterior chambers were of normal depth, and gonioscopic examination showed that both angles were open and wide. Examination with the slit lamp revealed nothing abnormal.

The patient has been followed at monthly intervals up to the present. At no time during this period, from 1942 to 1947, were any deposits noted on the cornea or were cells present in the aqueous, and the tension remained consistently normal in each eye. The patient has used 0.5 per cent pilocarpine hydrochloride twice a day in the right eye, mainly for psychologic reasons. During this time, her health has been good, but a mild hypertensive vascular disease developed.

Pupillographic examination on March 13, 1947, after the patient had discontinued use of pilocarpine for one week, showed a bilateral curve similar to that found in cases of primary glaucoma. The lability test produced no increase in tension. The fields were normal.

CASE 8.—L. E., a housewife aged 43, first seen on March 12, 1947, one week after the onset of blurred vision and "itching" in her right eye, had had a similar attack one year before but did not consult a physician. This time she visited an ophthalmologist, who found a tension of over 70 mm. in her right eye. The eye was white, and no keratic precipitates were noted at this time. He instilled a drop of 0.5 per cent physostigmine salicylate into her right eye, whereupon the eye became inflamed and tender to touch. The tension remained high. Examination by us the following day revealed that her right eye was white and that tension was 77 mm. in the right eye and 24 mm. in the left eye. The iris of the right eye was a light gray, whereas that of the left eye was brown. Examination with the slit lamp revealed approximately seven translucent, small, round precipitates on the posterior surface of the cornea of the right eye. The left eye was normal. The fundi and fields were normal. Vision was 20/20 in each eye without correction. Gonioscopic examination showed that both angles were moderately narrow, the corneoscleral trabeculum was somewhat pigmented and Schwalbe's line was indistinct. Phenylephrine hydrochloride, 10 per cent, lowered the tension in the right eye to 56 mm. She was instructed to do nothing to the eye except to apply cold compresses. She was comfortable thereafter, and the tension gradually fell, becoming normal by March 19 (fifteen days after onset). On March 26 the keratic precipitates were disappearing. The pupils were equal in size.

Her medical history was interesting. For many years she had been subject to attacks of migraine and crying spells. Her blood pressure was 160 systolic and 100 diastolic. In 1937 she had a cholecystectomy for typical recurring attacks of cholecystitis. The attacks continued to recur for several years after the operation. Each episode was followed by urticaria on the right side of the face and neck, extending to the right half of the forehead and the back of the right hand. The urticaria was associated with tearing of the right eye. No cause was found for these urticarial attacks. The patient did not have hay fever. Pupillographic examination showed central sympathetic phenomena similar to those found in patients with hypertensive vascular disease.

CASE 9.—B. T., a woman aged 60, a bookkeeper, had been subject to recurring attacks of blurring of vision in the left eye since 1937. These attacks lasted a few days to one week and recurred every eight to twelve months. Several years ago, she was given 2 per cent pilocarpine hydrochloride by an ophthalmologist, but she did not use this drug regularly because it engendered blurring of vision. Her sister has been under our care for chronic simple glaucoma for a number of years.

The patient came to this office on March 10, 1945, two weeks after the intermittent appearance of rainbows and blurring of vision, which began about one hour after arising in the morning and disappeared toward evening.

Examination revealed vision of 20/20 in each eye with a correction of —0.25 D. sphere for the right eye and —0.25 sph. —0.25 cyl., axis 150 for the left eye. The ten-

sion was 25 mm. in the right eye and 84 mm. in the left eye. The ciliary body was not injected, but the sclera showed slight generalized congestion. Ophthalmoscopic examination showed a large, irregular-shaped opacity in the vitreous of the left eye in front of the disk. The nerve head was of normal color, but slightly cupped. The right fundus was normal. Examination with the slit lamp revealed four unpigmented deposits on the posterior surface of the left cornea and bedewing of the corneal epithelium. The patient was given 2 per cent pilocarpine hydrochloride, and the tension dropped to 33 mm. within two hours. The tension returned to normal in two days, and the deposits disappeared within two weeks.

COMMENT

The importance of the recognition of this syndrome lies in its forming a link between the primary and the secondary glaucomas, since it cannot be classified in either category. For this reason, this group of cases assumes a significance far greater than is warranted by the low incidence of the syndrome.

A review of the literature reveals two papers dealing with this syndrome. Terrien and Veil[2] described a heterogenous group of cases to illustrate the importance of careful examination with the slit lamp in every case of glaucoma. Among them were 3 cases, perhaps 4, which belonged to this type, and only 1 of these was followed sufficiently long to permit observation of more than one attack. The authors did not attempt to classify these cases except to place them in the general category of secondary glaucomas. Kraupa described 4 similar cases and recognized that they represented a distinct clinical entity (1935).[1] He noted the relation between heterochromia and this type of glaucoma. He reasoned that the underlying pathologic mechanism of both types (with and without heterochromia) is in some way related to the sympathetic nervous system and called it "glaucoma allergicum" for want of a better name. Since it is generally accepted that the autonomic nervous system plays a role in all glaucomas, we felt that this name would not circumscribe this special group of cases. Moreover, Kraupa's title carries etiologic implications which we are not yet prepared to corroborate or to disprove. There is no article in the English literature dealing with this syndrome. Kronfeld, in one of his papers,[3] mentioned a group of "cases of acute elevation of intraocular pressure occurring simultaneously with mild recurrent cyclitis." He mentioned them only to exclude them from a general discussion of secondary glaucomas because, in his opinion, this condition represents "a clinical entity." Since he did not define them further, it is difficult for us to know whether he

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2. Terrien, F., and Veil, P.: Certain So-Called Primary Glaucomas, Bull. et mem. Soc. Franc. d'opht. **42**:349, 1929.

3. Kronfeld, P. C.: Gonioscopic Correlates of Responsiveness to Miotics, Arch. Ophth. **32**:447 (Dec.) 1944.

referred to the syndrome discussed here. Textbooks on ophthalomolgy, including Duke-Elder's,[4] do not separate this type, and the more recent papers[5] dealing with the over-all relation of glaucoma to cyclitis take no cognizance of the specific symptomatology and clinical behavior of this entity.

According to the generally accepted teaching, the findings of keratic precipitates or cells in the aqueous stamps a case of glaucoma as secondary to uveitis. Some authors even regard the presence of pigment dust on the posterior surface of the cornea[5] or the anterior surface of the lens[6] as evidence of associated uveal involvement. Since a large proportion of normal persons, especially in the older age group, show such precipitates, this criterion has been discarded by more recent observers.

We wish to emphasize that the presence of keratic precipitates is only one of several factors which have a bearing on the pathogenesis and clinical course of a specific case of ocular hypertension. The classification of a case as one of secondary glaucoma does not of itself help one in the management or the prognosis. It has been stated by a number of writers that glaucomas secondary to uveitis are extremely variable and that their course is unpredictable. We feel, therefore, that if a homogeneous group of cases can be segregated from the general class of secondary glaucomas, it represents a definite advance in knowledge of this poorly understood subject.

This leaves the over-all relation of glaucoma to iridocyclitis still unsolved. A few clues, however, presented themselves in the course of this study.

Two patients, who have been followed for fourteen and nineteen years, respectively, showed a combination of true primary glaucoma and iridocyclitis.

CASE 10.—A. M., a housewife aged 67, was first seen in 1933 with acute iridocyclitis of the left eye, which was followed the next day by a similar inflammation of the right eye. She improved under treatment with atropine and scopolamine, but the ocular tension remained elevated. The eyes became quiet, and the patient did not return to the office until two years later. At this time she had tension of 65 mm. in each eye and deep cupping of both disks. The right field was normal, but the left field showed pronounced nasal contraction.

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4. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 3288.

5. *(a)* Malling, B.: Relationship Between Iridocyclitis and Glaucoma, Acta ophth. **1**:97, 1923. *(b)* Larson, H.: Relationship Between Iridocyclitis and Glaucoma, ibid. **1**:345, 1923. *(c)* Fralick, F. B.; Cooper, J. H., and Armstrong, R. C.: Uveitis with Secondary Glaucoma, Tr. Am. Acad. Ophth. **47**:92, 1942-1943. *(d)* Weekers, L.: Treatment of Ocular Hypertension Complicating Iridocyclitis, Arch. d'opht. **53**:166, 1936.

6. Risley, S. S.: Simple Glaucoma, Ann. Ophth. **23**:437, 1914.

The picture was that of chronic simple glaucoma without symptoms. An Elliot trephine operation on both eyes normalized the tension, and her status has remained unchanged to the present. The tension curve is shown in chart 3.

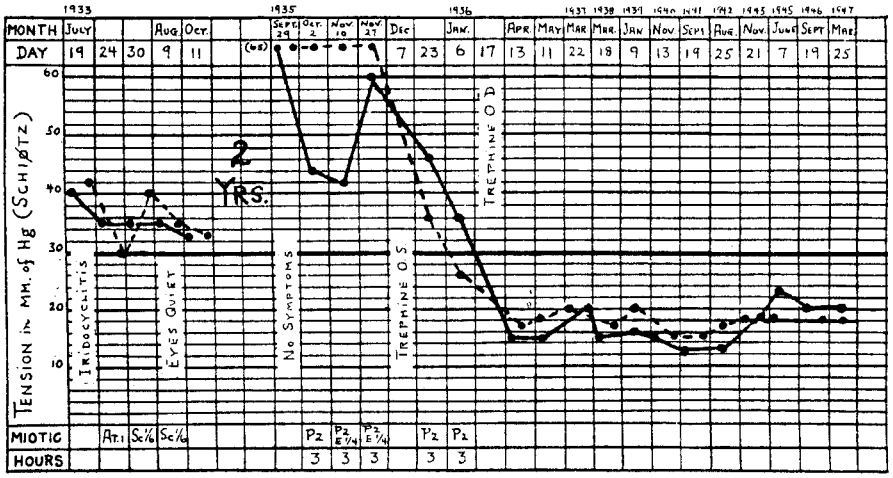

Chart 3 (case 10).—Tension curve for a patient with glaucoma simplex complicated by iridocyclitis in both eyes. At_1 indicates atropine sulfate, 1 per cent; $Sc.$ 1/6, scopolamine hydrobromide, 0.16+ per cent; p_2, pilocarpine hydrochloride, 2 per cent; $E1/4$, physostigmine salicylate, 0.25 per cent.

CASE 11.—M. N., a business man aged 64, was first seen in 1929 with an acute attack of iridocyclitis and hypertension in his left eye. The eye was intensely injected. A 2 plus aqueous flare and keratic precipitates were present. He gave a history of having seen colored halos intermittently for two years.

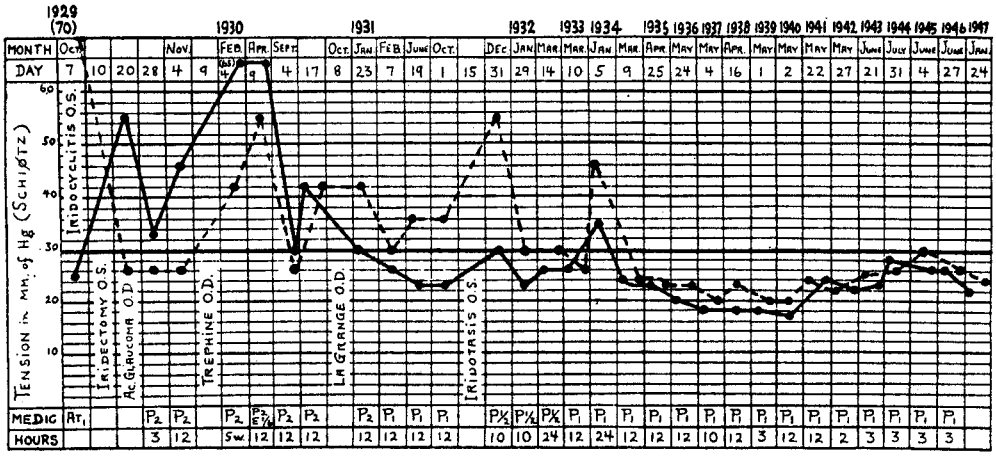

Chart 4 (case 11).—Tension curve for a patient with chronic congestive glaucoma complicated by iridocyclitis in the left eye. At_1 indicates atropine sulfate, 1 per cent; P_2, pilocarpine hydrochloride, 2 per cent; E 1/6, physostigmine salicylate, 0.16+ per cent; P_1, pilocarpine hydrochloride, 1 per cent; $P1/2$, pilocarpine hydrochloride, 0.5 per cent.

Since atropine did not control the attack, an iridectomy was performed one week later. Ten days after the operation, an attack of acute congestive glaucoma occurred in the other eye, without any manifestations of iridocyclitis. The tension at first responded to miotics but later rose again, and an Elliot trephination was performed. After a Lagrange sclerectomy on the right eye in 1930 and iridotasis on the left eye in 1931, tension, with the use of miotics, became relatively normal and has remained so up to the present time. The tension curve is shown in chart 4.

In these two cases a diagnosis of secondary glaucoma was originally made, but the subsequent course has given conclusive proof that the iridocyclitis was incidental to a primary glaucoma. The iridocyclitis may have acted as a precipitating factor, or the atropine used in treating the uveitis may have made the primary glaucoma manifest. It is important to guard against a hasty diagnosis of secondary glaucoma, on the basis of a brief period of observation.

These 2 cases (cases 10 and 11), which were uncovered only in retrospect after careful analysis of their course, illustrate the pitfalls in the present day approach to the problem of the relation of glaucoma to iridocyclitis and of iridocyclitis to glaucoma.

The following classification of glaucoma associated with iridocyclitis may prove helpful.

(1) Iridocyclitis occurring in a patient with primary glaucoma.
(2) Relatively mild cyclitis in which ocular hypertension occurs at the onset, or early in the course, of the disease.
  (a) Syndrome of recurrent glaucomatocyclitic crises.
  (b) Iridocyclitis without posterior synechias (or with old synechias) associated with the early appearance of ocular hypertension.
(3) True secondary glaucoma resulting from iridocyclitis.
  (a) Early stage, associated with plasmoid aqueous, active iridocyclitis and fresh posterior synechias.
  (b) Later stage, associated with structural changes in the filtration channels or with long-standing uveitis.

Other clues which have a bearing on the over-all relation of glaucoma to iridocyclitis may be derived from a careful interpretation of the features presented by the syndrome of glaucomatocyclitic crises, since this represents a true intermediate group between the primary and the secondary glaucomas. The following features relate this syndrome to secondary glaucoma:

1. Strict unilaterality of the ocular hypertension over many years of observation
2. The presence of cells in the aqueous and keratic precipitates during, and for a short time after, most attacks
3. The occurrence of glaucoma in the lighter-colored eye in 3 cases with heterochromia
4. Lack of uniformity in response to miotics and mydriatics

The following features relate it to the primary glaucomas:

1. In 3 out of 6 cases, pupillographic studies showed the type of curve usually found with primary glaucoma.

2. In all 6 cases the pupillographic responses were the same in the two eyes. This has been shown to be characteristic of unilateral primary glaucoma (Lowenstein and Schoenberg).

3. The attacks of ocular hypertension sometimes preceded the appearance of cyclitic signs by a day or two.

4. The severity of the glaucomatous attack was out of proportion to the cyclitic manifestations.

5. In 2 cases in this series primary glaucoma was present in another member of the family. This ratio is in line with the percentage of cases of hereditary glaucoma found by us in a study of 400 cases of primary glaucoma.[8]

6. Individual attacks might occur without any keratic precipitates or cells in the aqueous, although previous episodes were accompanied with these changes. In this connection, we wish to report a case which puzzled not only us but other ophthalmologists as well, and which may be understood better in the light of the present concept.

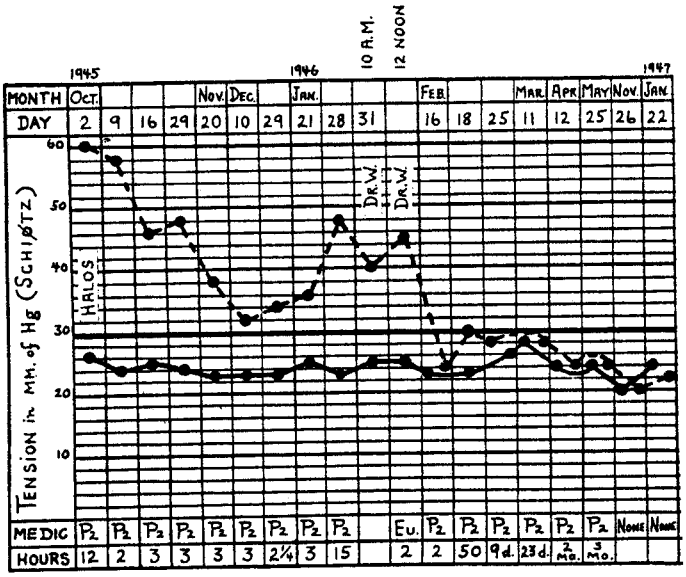

Chart 5 (case 12).—Tension curve for a patient with glaucoma (self limited) in the left eye. *P*₂ indicates pilocarpine hydrochloride, 2 per cent; *Eu*, eucatropine hydrochloride, 5 per cent.

CASE 12.—M. G., a housewife aged 49, was first seen by us on Oct. 2, 1945. She had had recurrent blurred vision and noted rainbows in her left eye, especially at night, for two weeks. Tonometric readings were 26 mm. in the right eye and 60 mm. in the left eye. Corrected vision was 20/30 in the right eye and 20/25 in the left eye. The pupils were equal. The irises were of the same color. Examination with the slit lamp failed to show any cells or deposits. Both anterior chambers were of normal depth, but the angles were moderately narrow. In spite of the use of 2 per cent pilocarpine hydrochloride, the tension remained between 45 and 60 mm. for nearly two months, after

7. Lowenstein, O., and Schoenberg, M. J.: Pupillary Reactions of the Seemingly Unaffected Eye in Clinically Unilateral Simple Glaucoma: Pupillographic Contributions to Diagnosis of Glaucoma in Preclinical Stage, Arch. Ophth. **31**:392 (May) 1944.

8. Posner, A., and Schlossman, A.: Development of Changes in Visual Fields Associated with Glaucoma, Arch. Ophth., to be published.

which it dropped to 30 mm. Vision in the right eye improved to 20/15. The fields showed no change. On November 9 the patient had, for the first time, an attack of bronchial asthma and a temperature of 99.8 F. She had a family history of allergy.

On Jan. 29, 1946, the tension rose again to 49 mm. in the left eye, and she complained of seeing a black circle and dots in the central field of that eye. Another ophthalmologist dilated her left pupil with eucatropine hydrochloride U.S.P., which raised the tension only by 5 mm. With mydriasis, a curved line surrounded by dusty opacities was seen in the vitreous adjacent to the retina in the macular zone. No focus of choroiditis was present. Surgical intervention was suggested by this, and still another, prominent ophthalmologist, the latter making the diagnosis of primary glaucoma. Operation was temporarily deferred. On Feb. 16, 1946, the tension was down to 24 mm., and the patient complained of severe, sharp pain in her eye after use of the miotic. All medication was discontinued. The pain subsided, and the tension has remained normal and equal in the eyes up to the time of this report. The opacities in the vitreous have since disappeared. Pupillographic studies on March 24, 1946, six weeks after discontinuation of miotics, revealed a bilateral curve similar to that found in cases of primary glaucoma (chart 5).

This case of self-limited unilateral glaucoma of the congestive type, which was regarded as primary at first, shows several obvious points of similarity to the syndrome of glaucomatocyclitic crises. It differs from the latter in the absence of signs of cyclitis. However, several opacities in the vitreous, which may well have been cells or clumps of cells, were observed adjacent to the retina without any visible choroiditis. These appeared during the course of the glaucoma and disappeared after subsidence of the hypertension.

Like the pathogenesis of glaucoma in general, the mechanism involved in the production of glaucomatocyclitic crises is obscure. However, we shall venture to advance a hypothesis based, to a certain extent, on established physiologic principles. It is our impression that this syndrome is engendered by a central disturbance in the hypothalamus, superimposed on a labile peripheral autonomic nervous system. The central factor is expressed by the bilaterality of the pupillographic findings (even when the curve is not the same as that found in cases of primary glaucoma) and by the association with hypertensive vascular disease, migraine and allergies, and with fever in 1 case. The peripheral factor was evidenced by the unilaterality of the disease, anisocoria, heterochromia and homolateral urticarial manifestations in 2 cases. It is possible, however, that a unilateral disease picture, such as this is, may be explained entirely on the basis of a central disturbance in the hypothalamus.

The fact that the disease in this group of cases was unilateral does not exclude the possibility, on the one hand, that certain cases of bilateral uveitis with glaucoma in which the latter is out of proportion to the former, and, on the other, some cases of glaucoma which pass as

primary only because of the absence of keratic precipitates, may also be related to this entity.

Treatment should be administered cautiously. Pilocarpine hydrochloride may be used in low concentrations of 0.5 to 2 per cent. Phenylephrine hydrochloride, 10 per cent, or epinephrine bitartrate, 2 per cent, may be tried; but the patient should be under observation for a few hours. Physostigmine, neostigmine and occasionally even pilocarpine may cause acute discomfort and redness of the eye. We were loath to use di-isopropyl fluorophosphate in this group of cases. Although the drug proved extremely beneficial in some of our cases of refractory glaucoma, it gave rise to severe discomfort in a few patients of the younger group.[9] In a case of acute glaucoma with minimal subjective and objective signs, it is advisable to use medication cautiously until the nature of the disease becomes evident. Surgical intervention is contraindicated, since the course is not influenced by it. Paracentesis has been reported to be of value in relieving an acute attack.[2]

SUMMARY

Nine cases, forming a homogeneous group which represents a type of glaucoma intermediate between primary and secondary glaucoma, are described.

It is proposed to call this condition a syndrome of glaucomatocyclitic crises, to distinguish it from primary glaucoma, on the one hand, and secondary glaucoma, on the other.

A tentative hypothesis is advanced which relates this syndrome to a disturbance of the central and the peripheral autonomic nervous system.

Treatment should be confined to the use of low concentrations of pilocarpine hydrochloride.

A classification of glaucoma associated with iridocyclitis is presented.

667 Madison Avenue.

A few of these cases were originally those of the late Dr. Mark J. Schoenberg. His carefully kept records and detailed notes helped us greatly in the preparation of this paper.

The pupillographic studies were made by Dr. Otto Lowenstein. All tension readings refer to the 1924 Schiotz graph unless otherwise stated.

9. A patient, aged 57, who is subject to recurring attacks of unilateral glaucoma without congestive or cyclitic signs, received 1 drop of di-isopropyl fluorophosphate ("DFP"). This was followed by marked reduction of tension. However, extreme discomfort, injection of the bulbar conjunctiva and pain when he attempted to read lasted for two weeks and was only temporarily relieved by homatropine.

DISCUSSION

DR. L. VON SALLMANN, New York: It was of great benefit to us to have Dr. Posner and Dr. Schlossman direct our attention to a type of unilateral glaucoma so far scarcely considered or recognized as a definite syndrome. Such recurrent attacks of increased intraocular tension with transient cellular and larger deposits on the cornea are usually considered of borderline type, and treatment is rather arbitrary, depending on the ophthalmologist's intuition. From the authors' description, it is evident that this syndrome can be fairly well distinguished from typical primary glaucoma with a few deposits on the cornea, from primary glaucoma with superimposed cyclitis unrelated to the glaucoma, from secondary cyclitic glaucoma and from the so-called sympathetic glaucoma of Streiff, with and without heterochromia.

It may not be easy to make this distinction in an isolated case, since similar signs and symptoms are common to other groups, and since, as we have learned from Posner and Schlossman's paper, close study of the course of the disease over long periods is necessary to obtain conclusive diagnostic data. However, the observations presented here, together with those in Kraupa's and a few other cases reported in the literature, round out the picture and strengthen the impression that the disease represents an entity.

Posner added to the general symptomatology of the disease the results of the pupillographic examinations and concluded from them, on the basis of Otto Lowenstein's work, that the sympathetic center in the diencephalon was involved. I must leave it to the experts in this field to evaluate and to interpret the pupillographic curves. There is no reason to doubt the correctness of this interpretation. Nevertheless, the question may be raised whether, in view of the unilaterality of the lesion, a disorder in the subordinate ciliospinal center of Budge can be completely disregarded. In 3 of Posner's cases, in 1 of Passow's cases and in several of Kraupa's series there were varying degrees of heterochromia. Heterochromia, especially complicated heterochromia, was pathogenetically related by Passow, and recently by Appel and Leo Hess, to Bremer's status dysraphicus, which is said to be due to a congenital anomaly in the cervical area of the spinal cord. I believe that the authors' cases were not examined from this neurologic standpoint.

In addition to the hypothalamic disturbance, Posner assumes the coexistence of a peripherally operating mechanism, such as a labile peripheral autonomic system; this factor must be present unilaterally. There seems to be a considerable range of alternative explanations and speculations. One could assume that the functions of the terminal nerves or the capillary motor response of other intraocular mechanisms of regulation are at fault in the one eye. In view of the presence of infective foci and the strong allergic reactions of some of the patients, the question arises whether an antigen-antibody reaction or a toxic factor could not be responsible for the onset of the periodic attacks in a disposed eye. That is, the cells in the aqueous and the precipitates on the cornea could be the expression of a transient, low grade inflammation rather than of a primarily nervous disturbance.

What further studies may reveal on the relation between disorders of the sympathetic centers and between the centers and a peripheral mechanism remains to be seen. At present, it seems likely that a transient increase in the permeability of the ciliary capillaries is the most important single peripheral factor which has a bearing on the development of the recurrent attacks. In the last year studies were conducted in the Knapp Laboratory on an experimental glaucoma induced by increased permeability of the ciliary capillaries. Various therapeutic approaches were studied on experimental animals. The effects of adrenergic drugs, of posterior pituitary injection U. S. P,. of substances acting on the intracellular cement, such as calcium ions and adrenal cortex hormone, and of a series of histamine antagonists were tested, and promising results were obtained in respect both to the reduction of increased permeability of intraocular capillaries and the lowering of intraocular tension. There is some hope that one or another of these therapeutic measures will be of help in the glaucomatocyclitic crises described by Posner and Schlossman.