IDIOPATHIC ATROPHY OF THE EPITHELIAL LAYERS OF THE IRIS AND CILIARY BODY

A CLINICAL STUDY

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INTRODUCTION

This paper reports 97 eyes (49 patients), all showing a group of intraocular pigment changes, due to an idiopathic atrophy of the retinal layers of the iris and probably the ciliary body, which the authors believe comprise a single clinical entity. The condition is often associated with glaucoma. Most of the pigment changes are well known, but usually they have been described with little or no attempt to correlate them into a disease complex. They consist of (1) punctate pigment deposition on the corneal endothelium, usually in the form of a Krukenberg spindle; (2) speckling of the anterior surface of the iris with pigment; (3) pigmentation of the trabecular area of the anterior chamber; (4) pigment on the posterior surface of the lens near the equator, occasionally in the form of a ring; and (5) atrophy of the epithelial layers of the iris. Glaucoma that follows a chronic simple (open-angle) course is frequently present.

Gonioscopic observations of the posterior chamber in this condition are described for the first time. The ciliary processes, anterior and posterior zonular fibers and membranes, and the periphery of the lens can be seen with the pupil widely dilated. The zonular fibers and membranes show rather characteristic pigmentation. The equator of the lens invariably shows punctate pigment deposition and at times a ring of pigment near the equator. The pigment of the epithelial layers of the iris is liberated and then deposited throughout the anterior portion of the eye.

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The pigment arises from the epithelium of the iris, and probably the ciliary body, as a result of an idiopathic atrophy. Pigment is released and deposited throughout the anterior portion of the eye. The atrophy can be demonstrated by transillumination, which reveals a rather typical pattern of transmission of light through the iris. Varying degrees may occur. When the atrophy is mild, small isolated triangular or elliptical dehiscences of pigment which transmit light can be seen at the periphery of the iris. When the atrophy is more severe, these areas are more numerous and may be continuous around the base of the entire circumference of the iris. When extreme, the entire iris up to and including portions of the pupillary space may transilluminate. However, even when the atrophic process is advanced, the periphery of the iris remains the most affected. The diagnostic importance of transillumination of the iris is emphasized. Most eyes with Krukenberg spindle formation and heavily pigmented trabecular regions transilluminate to some degree, but the atrophy is easily missed by other types of examination because the overlying stroma appears normal except when covered by pigment flecks.

HISTORICAL REVIEW

Krukenberg spindle formation was first described by Krukenberg (1) in 1899. An excellent review of the literature by Evans, Odom, and Wenaas (2) appeared in 1941; in it they published findings in 202 cases. Myopia was the most consistent finding, although Krukenberg spindle occurred in either hypermetropic or emmetropic eyes. It was found in only a slightly higher percentage in women and in eyes with dark irises. Most of the patients apparently had not been examined by gonioscopy, and no attempt was made to correlate spindle formation with pigmentation of the trabecular area. Forty-four of the patients showed some disturbance of iris pigment and pigment flecks on the iris. Pigmentation at the periphery of the lens in the form of an annular band was noted in 7 eyes. No common etiological factors were found. Zentmayer (3), in 1938, reported the first annular pigmentation of a lens associated with Krukenberg spindle in this country. He suggested that the pigment on the lens was of congenital origin and that the spindle might have originated from pigment which had migrated forward from the lenticular deposit. Cameron (4), reported a similar case in 1941. He found no free pigment in the retrolental space and concluded that the absence of free pigment behind the lens indicated that the spindles came from pigment derived entirely from the iris. Bellows (5), likewise reported a patient with Krukenberg spindle formation and a dense brown pigment ring

around the entire circumference of the lens, seen with the pupils dilated. Calhoun (6), in 1953, found two more lenticular pigment rings in 11 patients with Krukenberg spindles reported by him.

Although the origin of the pigmentation which comprises the spindle has been discussed at length in the literature, pathologic evidence implicating atrophy of the iris has been reported in eyes with Krukenberg spindle studied by Hanssen (7), Kayser (8), and Korobova (9). All reported degeneration of the retinal layers of the iris and to some extent of the ciliary body.

Evans, Odom, and Wenaas (2) found that 12 of 202 patients had glaucoma. Interest in glaucoma associated with pigmentary disturbances has increased in recent years because of the work of Barkan (10), Sugar (11), and Calhoun (6), and by growing interest in the outflow mechanism of the eye stimulated by the development and use of gonioscopy and tonography. Levinsohn (12) in 1908, Koeppe (13) in 1916, and many others since have suggested that pigment lodging in the trabecular area can cause glaucoma by producing an obstruction to outflow of aqueous. Van Beuningen (14) has been extremely interested in this phase of glaucoma and has attempted to measure pigmentation of the angle.

Interest in transillumination of the iris has been casual and usually only incidentally mentioned. Among these authors are Thiel (15), and Kayser (8). Kayser mentioned transillumination of the eyeball and described gaps in the retinal pigment layer of the iris which appeared as red lightning spots. Thiel stated that in extreme cases of pigment dispersal transillumination demonstrated considerable atrophy of the iris. Senile absorption of the pigment seam is mentioned throughout ophthalmic literature, but it is quite different in appearance from the pattern seen with Krukenberg spindle formation and the associated atrophy of the retinal layers of the iris. We have found no mention of gonioscopic study of the posterior chamber nor of the zonular fibers and membrane.

CLINICAL STUDY

The ocular findings of 49 patients (97 eyes) are outlined in Table 1. These observations were recorded by Dr. Scheie over a period of ten years on patients from his own private practice and those of Dr. Francis Heed Adler and Dr. William C. Frayer, as well as from the Glaucoma Clinic of the Hospital of the University of Pennsylvania. Interest was first aroused by the occasional patient with chronic simple glaucoma whose eyes showed massive pigmentation of the trabecular area. Special

TABLE 1

NO.	SEX	DATE	AGE	EYE	COLOR IRIS	GLAUCOMA (OPEN ANGLE)						PIGMENTARY PHENOMENA			
						Diagnosis established	*Tension*	*Water provocative test*	*Tonography*	*Optic nerve*	*Field loss*	*Transillumination*	*Krukenberg spindle*	*Angle*	*Posterior lens*
1	Female	6/43	35	O.D.	Blue	Yes	30–35	Positive	C = .13	None	Normal	Circumferential to pupillary border	+	Grade IV	Complete ring
				O.S.	Blue	Yes	30–35	Positive	C = .12	None	Normal	Circumferential to pupillary border	+	Grade IV	Complete ring
2	Female	8/47	48	O.D.	Brown	No	17	Negative	Not done	None	None	None	+	Grade III	Ring inferiorly
				O.S.	Brown	No	17	Negative	Not done	None	None	Localized	+	Grade IV	Ring inferiorly
3	Female	2/48	31	O.D.	Blue	No	17	Negative	Not done	None	None	Circumferential continuous	+	Grade IV	Incomplete ring
				O.S.	Blue	No	17	Negative	Not done	None	None	Circumferential continuous	+	Grade IV	Incomplete ring
4	Male	8/49	35	O.D.	Hazel	No	20	Negative	Not done	None	Normal	Circumferential continuous	+	Grade IV	Punctate
				O.S.	Hazel	No	20	Negative	Not done	None	Normal	Circumferential continuous	+	Grade IV	Punctate
5	Male	2/50	68	O.D.	Blue	Yes	43	Not done	Not done	Advanced	Advanced	Circumferential scattered	+	Grade IV	Not done
				O.S.	Blue	Yes	62	Not done	Not done	Advanced	Advanced	Circumferential scattered	+	Grade IV	Not done
6	Female	7/50	42	O.D.	Hazel	No	17	Negative	Not done	None	Normal	Circumferential continuous	+	Grade IV	Punctate
				O.S.	Hazel	No	20	Negative	Not done	None	Normal	Circumferential continuous	+	Grade IV	Punctate
7	Male	10/50	45	O.D.	Brown	Yes	24	Positive	Not done	No cupping	None	Localized	+	Grade IV	Punctate
				O S.	Brown	Yes	46	Positive	Not done	No cupping	Detached retina	Localized	+	Grade IV	Punctate
8	Male	1/51	52	O.D.	Brown	Yes	35	Positive	Not done	No cupping	None	Localized	+	Grade IV	Punctate
				O.S.	Brown	Yes	30	Positive	Not done	No cupping	None	Localized	+	Grade IV	Punctate

9 Male	4/51	39	O.D.	Blue	No	20	Negative	C = .18	No cupping	None	Circumferential continuous	+	Grade IV	Ring. Sheet-like on face of vitreous
			O.S.	Blue	No	20	Negative	C = .2	No cupping	None	Circumferential continuous	+	Grade IV	Ring. Sheet-like on face of vitreous
10 Male	8/51	30	O.D.	Brown	Yes	32	Positive	Not done	Early cupping		Circumferential continuous	+	Grade IV	Incomplete ring
			O.S.	Brown	Yes	37	Positive	Not done	Advanced cupping	Nasal loss	Circumferential continuous	+	Grade IV	Incomplete ring
11 Male	10/51	15	O.D.	Brown (Negro)	Yes	35	Not done	Not done	Marked cupping	Marked loss	None	+	Grade IV	Punctate
			O.S.	Brown (Negro)	Yes	46	Not done	Not done	Marked cupping	Marked loss	None	+	Grade IV	Punctate
12 Female	9/52	34	O.D.	Blue	No	17	Negative	Not done	None	Full	Circumferential scattered	+	Pigmented IV	Punctate
			O.S.	Blue	No	17	Negative	Not done	None	Full	Circumferential scattered	+	Pigmented IV	Punctate
13 Male	10/52	34	O.D.	Blue	No	20	Negative	C = .30	None	Normal	Localized	+	Grade IV	Punctate
			O.S.	Blue	No	20	Negative	C = .23	None	Normal	Localized	+	Grade IV	Punctate
14 Female	11/52	39	O.D.	Blue	No	17	Negative	Not done	None	None	Circumferential continuous	+	Grade IV	Punctate
			O.S.	Blue	No	20	Negative	Not done	None	None	Circumferential scattered	+	Grade III	Punctate
15 Male	1/53	39	O.D.	Blue	Yes	35	Not done	Not done	Marked cupping	Marked loss	Circumferential continuous	+	Grade IV	Ring. Sheet-like on face of vitreous. Ciliary processes pale
			O.S.	Blue	Yes	40	Not done	Not done	Marked cupping	Marked loss	Circumferential continuous	+	Grade IV	Ring. Sheet-like on face of vitreous. Ciliary processes pale
16 Male	4/53	63	O.D.	Blue	Yes	30	Positive	Not done	Early	None	Circumferential scattered	+	Grade III	Punctate
			O.S.	Blue	Yes	40	Positive	Not done	Early	Arcuate scotoma	Circumferential scattered	+	Grade III	Punctate
17 Male	4/53	42	O.D.	Brown	Yes	40	Not done	Not done	Marked cupping	Marked	Circumferential continuous	+	Pigmented IV, more dense than O.S.	Ring-sheet anterior vitreous
			O.S.	Brown	Yes	30	Not done	Not done	Early cupping	Early	Circumferential continuous	+	Pigment IV	Ring-sheet anterior vitreous

TABLE 1 *(Continued)*

NO.	SEX	DATE	AGE	EYE	COLOR IRIS	GLAUCOMA (OPEN ANGLE)						PIGMENTARY PHENOMENA			
						Diagnosis established	*Tension*	*Water provocative test*	*Tonography*	*Optic nerve*	*Field loss*	*Transillumination*	*Krukenberg spindle*	*Angle*	*Posterior lens*
18	Female	5/53	44	O.D.	Brown	Yes	24	Positive	C = .25	Normal	None	None	+	Pigment III	Punctate
				O.S.	Brown	Yes	24	Positive	C = .40	Normal	None	None	+	Pigment III	Punctate
19	Male	7/53	57	O.D.	Brown	No	20	Negative	Not done	None	None	Circumferential continuous	+	Grade IV	Punctate
				O.S.	Brown	No	20	Negative	Not done	None	None	Circumferential continuous	+	Grade IV	Punctate
20	Male	11/53	47	O.D.	Blue	No	17	Negative	Not done	Normal	None	Circumferential continuous	+	Open pigmented IV	Incomplete ring
				O.S.	Blue	No	17	Negative	Not done	Normal	None	Localized	+	Open pigmented IV	Incomplete ring
21	Male	3/54	65	O.D.	Blue	No	17	Not done	Not done	Normal	None	Circumferential continuous	+	Pigmented IV	Punctate
				O.S.	Blue	No	17	Not done	Not done	Normal	None	Circumferential continuous	+	Pigmented IV	Punctate
22	Male	5/54	29	O.D.	Blue	No	20	Negative	C = .20	Normal	None	Circumferential to pupillary border	+	Pigmented IV	Pigment dots
				O.S.	Blue	No	20	Negative	C = .30	Normal	None	Circumferential to pupillary border	+	Pigmented IV	Pigment dots
23	Male	7/54	30	O.D.	Blue	Yes	35	Positive	C = .12	Normal	None	Localized	+	Pigmented IV	Punctate
				O.S.	Blue	Yes	35	Positive	C = .12	Normal	None	Localized	+	Pigmented IV	Punctate
24	Male	3/55	30	O.D.	Blue	No	17	Negative	C = .17	Normal	None	Circumferential continuous	+	Pigmented IV	Incomplete ring
				O.S.	Blue	No	17	Negative	C = .15	Normal	None	Localized	+	Pigmented IV	Punctate
25	Female	5/55	69	O.D.	Brown	No	27	Negative	Not done	Normal	None	Circumferential scattered	+	Grade III	Punctate
				O.S.	Brown	No	20	Negative	Not done	Normal	None	Circumferential scattered	+	Grade III	Punctate
26	Female	6/55	67	O.D.	Brown	Yes	37	Not done	Not done	Advanced	Marked	Circumferential scattered	+	Grade III	Punctate
				O.S.	Brown	Yes	30	Not done	Not done	Moderate	Nasal step	Circumferential scattered	+	Grade III	Punctate
27	Male	8/55	46	O.D.	Blue	No	15	Negative	C = .14	Normal	None	Circumferential continuous	+	Grade IV	Incomplete ring
				O.S.	Blue	No	17	Negative	C = .14	Normal	None	Circumferential continuous O.D. > O.S.	+	Grade IV	Punctate

28 Female	10/55	32	O.D.	Brown	No	17	Not done	Not done	Normal	None	None	+	Pigmented III	Not done
			O.S.	Brown	No	17	Not done	Not done	Normal	None	Localized	+	Pigmented III	Not done
29 Male	10/55	51	O.D.	Blue	Yes	27	Positive	C = .17	Normal	None	Circumferential continuous	+	Pigmented III	Punctate
			O.S.	Blue	Yes	62	Positive	C = .06	Marked cupping	Marked	Circumferential continuous	+	Pigmented IV	Punctate
30 Female	12/55	58	O.D.	Brown	No	17	Negative	C = .25	None	None	Circumferential to pupillary border	+	Grade III	Incomplete ring
			O.S.	Brown	No	15	Negative	C = .28	None	None	Circumferential to pupillary border	+	Grade III	Incomplete ring
31 Male	1/56	46	O.D.	Blue	Yes	32	Positive	C = .13	Normal	None	Circumferential continuous	Punctate. No true spindle	Pigmented IV	Punctate
			O.S.	Blue	Yes	32	Positive	C = .20	Normal	None	Circumferential continuous	Punctate. No true spindle	Pigmented IV	Punctate
32 Male	1/56	51	O.D.	Hazel	No	20	Not done. Malignant hyper-tension	Not done	Normal	None	Circumferential continuous	+	Grade IV	Punctate
			O.S.	Hazel	No	20	Not done. Malignant hyper-tension	Not done	Normal	None	Localized	+	Grade III	Punctate
33 Female	1,56	48	O.D.	Hazel	No	20	Negative	C = .15	None	None	Circumferential scattered	+	Grade III pigmented	Punctate
			O.S.	Hazel	No	20	Negative	C = .18	None	None	Localized	+	Grade II pigmented	Punctate
34 Female	4/56	57	O.D.	Brown	Yes	35	Positive	C = .15	Normal	None	Localized	+	Open Grade III	Punctate
			O.S.	Brown	Yes	30	Positive	C = .15	Normal	None	Circumferential continuous	+	Grade IV	Incomplete ring inferiorly
35 Male	4/56	51	O.D	Hazel	No	27	Negative	C = .22	Normal	None	Circumferential continuous	+	Pigmented IV	Complete ring
			O.S.	Hazel	No	20	Negative	C = .17	Normal	None	Circumferential scattered	Punctate. No true spindle	Pigmented III	Punctate
36 Male	4/56	26	O.D.	Blue	Yes	40	Positive	C = .11	Early	Early	Circumferential to middle portion of iris	+	Pigmented IV	Punctate
			O.S.	Blue	Yes	40	Positive	C = .04	Marked	Advanced	Circumferential to middle portion of iris	+	Pigmented IV	Punctate
37 Male	6/56	31	O.D.	Brown	Yes	30	Positive	C = .10	Moderate	Arcuate scotoma	Circumferential continuous	+	Grade IV	Complete ring
			O.S.	Brown	Yes	30	Positive	C = .12	None	None	Circumferential continuous	+	Grade IV	Complete ring

TABLE 1 *(Continued)*

NO.	SEX	DATE	AGE	EYE	COLOR IRIS	GLAUCOMA (OPEN ANGLE)						PIGMENTARY PHENOMENA			
						Diagnosis established	*Tension*	*Water provocative test*	*Tonography*	*Optic nerve*	*Field loss*	*Transillumination*	*Krukenberg spindle*	*Angle*	*Posterior lens*
38	Female	8/56	44	O.D.	Brown	No	20	Negative	C = .25	Normal	None	Localized	+	Grade IV	Punctate
				O.S.	Brown	No	20	Negative	C = .30	Normal	None	Localized	+	Grade IV	Punctate
39	Male	8/56	26	O.D.	Brown (Negro)	Yes	35	Not done	Not done	Marked	Marked	None	+	Grade IV	Punctate
				O.S.	Brown (Negro)	Yes	50	Not done	Not done	Marked	Blind	None	+	Grade IV	Punctate
40	Female	9/56	60	O.D.	Blue	No	20	Negative	Not done	Normal	None	Localized	+	Grade IV	Punctate
				O.S.	Blue	No	20	Negative	Not done	Normal	None	None	+	Grade III	Punctate
41	Male	10/56	70	O.D.	Blue	Yes	35	Positive	C = .10	Normal	None	Circumferential continuous	+	Grade III	Punctate
				O.S.	Blue	Yes	35	Positive	C = .17	Normal	None	Circumferential continuous	+	Grade III	Punctate
42	Male	11/56	63	O.D.	Brown	Yes	35	Positive	Not done	Normal	None	Circumferential continuous	+	Grade IV	Not done
				O.S.	Brown	Yes	40	Positive	Not done	Normal	None	Circumferential continuous	+	Grade IV	Not done
43	Male	12/56	39	O.D.	Blue	No	17	Negative	Not done	Normal	None	Circumferential continuous	+	Grade IV	Punctate O.D. > O.S.
				O.S.	Blue	No	17	Negative	Not done	Normal	None	Localized	No spindle	Grade II	Punctate
44	Female	12/56	37	O.D.	Blue	No	20	Negative	C = .25	Normal	None	Circumferential continuous	+	Grade IV	Punctate
				O.S.	Blue	No	20	Negative	C = .25	Normal	None	Circumferential continuous	+	Grade IV	Punctate
45	Female	1/57	64	O.D.	Brown	No	20	Negative	C = .2	Normal	None	Circumferential continuous	+ O.D. > O.S.	Grade IV	Incomplete ring
				O.S.	Brown	No	20	Negative	C = .18	Normal	None	None	+	Grade I	Punctate
46	Female	3/57	53	O.D.	Brown	No	17	Negative	Not done	None	None	Circumferential continuous	+	Grade IV	Punctate
				O.S.	Brown	No	15	Negative	Not done	None	None	None	+	Grade III	Punctate

47 Male	3/57	62	O.D.			ENUCLEATED BECAUSE OF RETINAL DETACHMENT								
			O.S.	Blue	No	17	Negative	Not done	None	None	Circumferential continuous	+	Grade IV	Punctate. Sheet-like on face of vitreous
48 Female	3/57	38	O.D.	Brown	No	15	Negative	C = .10	None	None	Circumferential to midportion	+	Grade III	Punctate
			O.S.	Brown	No	17	Negative	C = .10	None	None	Circumferential to midportion	+	Grade III	Punctate
49 Male	3/57	48	O.D.	Blue	Yes	35	Positive	Not done	Advanced	Bierrum scotoma	Localized	+	Grade IV	Complete ring
			O.S.	Blue	Yes	27	Positive	Not done	Normal	None	None	Fine punctate	Grade II	Punctate

note was made of these patients, and as they accumulated it seemed that pigmentary glaucoma was probably only a complication of an extensive pigment disturbance within the eye.

All of the patients in this study had some pigmentation of the trabecular portion of the angles and nearly all were classified Grade IV or massively pigmented. A system of grading angle pigmentation was devised which employs categories based on increasing pigmentation ranging from angles with no pigment to those with very heavy pigmentation, or Grade IV (16). The amount of pigmentation in the trabecular portion of the angle of the anterior chamber varies greatly from individual to individual and tends to increase with age. When massively pigmented, the trabecular portion may be densely covered by pigment as if plastered by black mortar. In evaluating patients with chronic simple glaucoma it was presumed that when Grade IV pigmentation was present the pigment very probably contributed to the rise in tension by obstructing aqueous outflow.

Soon after becoming interested in eyes with heavily pigmented angles, we learned that the vast majority had Krukenberg spindles and that likewise most patients with Krukenberg spindles had marked pigmentation of the trabecula and many had glaucoma. We therefore grouped all patients whom we encountered with either so-called pigmentary glaucoma or Krukenberg spindles into the same category for purposes of this study. We also learned, at first accidentally by ophthalmoscopic examination, that light reflected from the retina of some of these eyes demonstrated dehiscences in the pigment layer at the periphery of the iris. This led to scleral transillumination with a transilluminator placed on the globe near the equator, a method which revealed dehiscences of pigment in most of the eyes with Krukenberg spindles or pigmentary glaucoma. The extensive changes found in the angle of the anterior chamber and in the iris led to gonioscopic examination with the pupils widely dilated to permit examination of the posterior chamber. Definite pigmentary changes were found on the lens and zonular fibers and membranes. A systematic study of this was therefore instituted. All eyes were subjected to detailed examination, including study of the anterior segments with a slit lamp and corneal microscope, ophthalmoscopic examination, gonioscopic examination with the pupils both normal size and widely dilated to reveal the posterior chamber, and transillumination.

PRESENTATION OF DATA

CORRELATION WITH AGE AND SEX

The group of patients in this study ranged in age from fifteen to seventy years (Table 1). Six of the patients were under thirty years, 14 were thirty-one to forty years, 12 were forty-one to fifty years, 8 were fifty-one to sixty and 9 were sixty-one to seventy years of age. The youngster of fifteen years, the 6 patients under thirty years, and 20 patients under forty years of age indicate a rather early onset of this pigmentary disturbance. Nineteen of the patients were female and 30 were male.

COLOR OF IRIS

No predilection for brown or blue eyes was revealed. There were 21 occurrences in brown eyes, 24 in blue, and 4 in hazel. Two patients were Negroes.

KRUKENBERG SPINDLE AND PIGMENTATION OF THE TRABECULA

Krukenberg spindle formation was present in 92 of 97 eyes. No attempt was made to grade the density of spindle formation, but occasionally it was more marked in one eye than in the other. In such instances, the pigment deposition elsewhere in the anterior segment was more marked in the eye with the more dense spindle and iris atrophy was also more apparent. Examination of these eyes with a slit lamp and corneal microscope almost invariably demonstrated considerable punctate pigment elsewhere on the corneal endothelium, especially near the periphery (Figures 1–4). Goar (17) has previously pointed this out.

The trabecular portion of the angle was usually heavily pigmented but in some eyes a lesser degree was found (Figures 1–4). This was true because the majority of eyes in this study were in patients where the suspicion of glaucoma or the presence of Krukenberg spindles had led to study of their angles. The evaluation, therefore, is largely one of studying the degree of pigmentation of the angle of the anterior chamber in eyes with Krukenberg spindle formation or glaucoma. Of the 92 eyes with Krukenberg spindles, 65 showed Grade IV, 25 showed Grade III, 1 showed Grade II, and 1 showed Grade I pigmentation of the angle. The pigmentation of the angle was more marked in eyes with the heaviest spindles and the most marked iris atrophy.

Krukenberg spindles were absent in only 5 eyes. In these some punctate pigment deposition was seen on the cornea, although not in spindle distribution. Two of these eyes were in one patient and showed in ad-

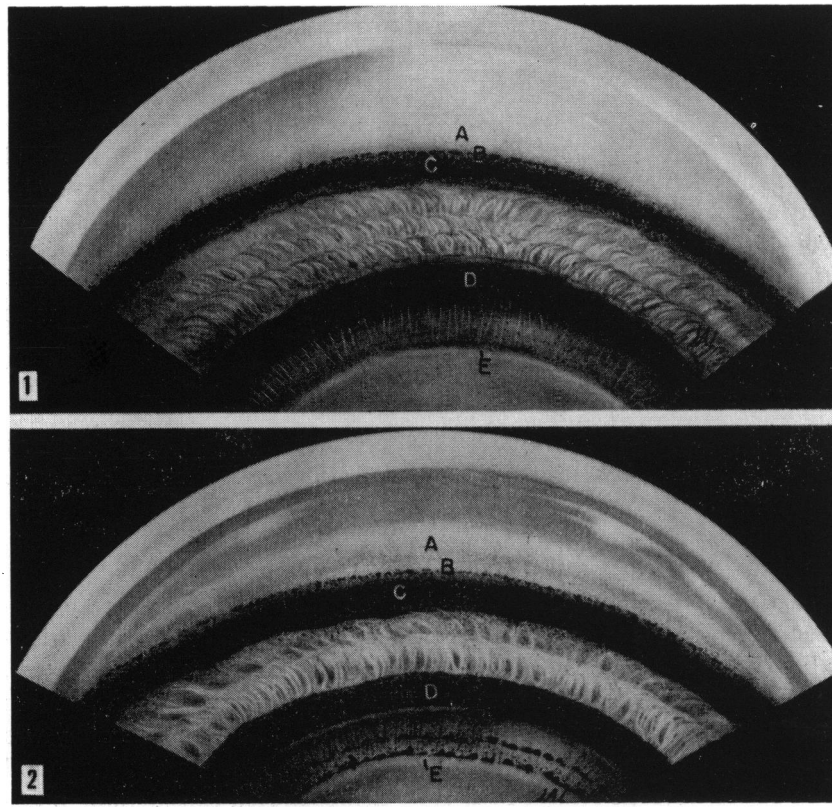

FIGURE 1. MASSIVE PIGMENTATION OF ANGLE OF ANTERIOR CHAMBER AND PUNCTATE PIGMENT DEPOSITION AT INSERTION OF POSTERIOR ZONULAR FIBERS

FIGURE 2. PUNCTATE PIGMENT DEPOSITION AT PERIPHERY OF CORNEA, MASSIVE PIGMENTATION OF ANGLE, PIGMENT ON SURFACE OF IRIS AND DISCRETE PIGMENT DEPOSITS ON POSTERIOR LENS CAPSULE OCCURRING AT TWO LEVELS, APPROACHING RING FORMATION

Key: A: Periphery of cornea. B: Schwalbe's line. C: Trabecula. D: Zonular fibers and membranes. E: Hyaloideocapsular ligament. F: Pigmentary deposit on anterior limiting membrane of vitreous.

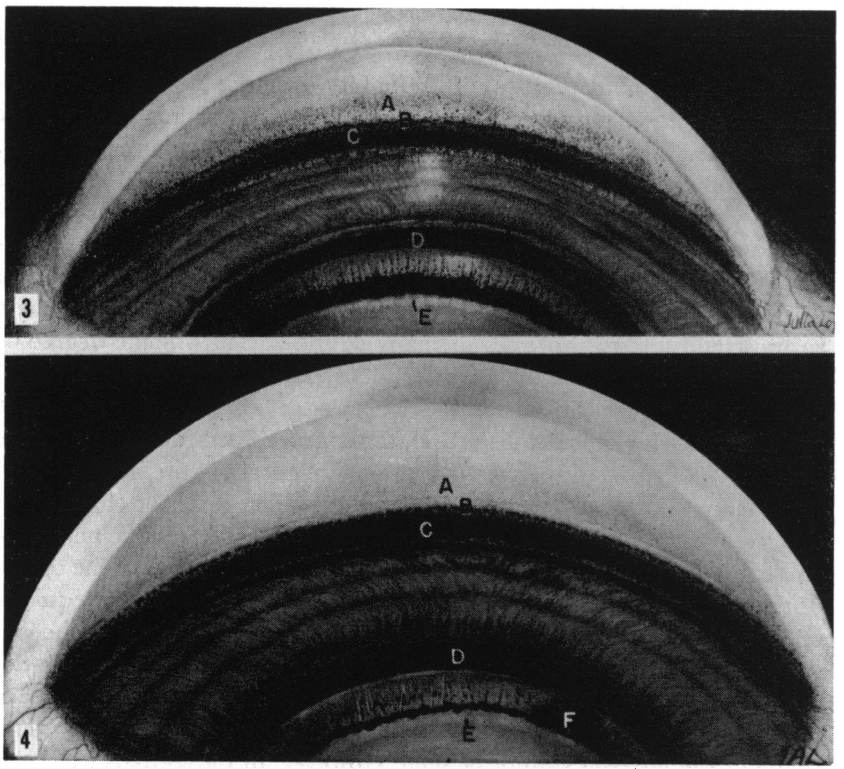

FIGURE 3. PUNCTATE PIGMENT DEPOSITION AT PERIPHERY OF CORNEA, MASSIVE PIGMENTATION OF ANGLE, AND COMPLETE RING OF PIGMENT ON POSTERIOR LENS CAPSULE

FIGURE 4. PUNCTATE PIGMENT DEPOSITION AT PERIPHERY OF CORNEA, MASSIVE PIGMENTATION OF ANGLE WITH PIGMENT ON POSTERIOR LENS CAPSULE EXTENDING ONTO ANTERIOR LIMITING MEMBRANE OF VITREOUS

dition Grade IV pigmented angles, iris atrophy by transillumination, and glaucoma. The other 3 were in patients where the fellow eye had a Krukenberg spindle. One eye showed Grade II pigmentation of the angle, and the other 2 showed Grade III pigmentation. Iris atrophy was noted by transillumination in 2 of the 3 eyes, but it was not as marked as in the fellow eye where spindle formation and pigmentation of the angle were more dense.

PIGMENTATION ON THE POSTERIOR ASPECT OF THE LENS AND ZONULAR FIBERS

Nearly all of the patients were studied for evidence of pigment deposition on the posterior aspect of the lens, the zonular fibers and zonular membranes. The ciliary processes were observed whenever possible. Gonioscopic examination of this area was accomplished by dilating the pupils widely by three instillations of homatropine, 4 percent or 2 percent, and Neo-Synephrine 10 percent at twenty-minute intervals. Examination was done thirty minutes after the last instillation. Visualization of the equatorial area of the lens was possible in all, the zonular fibers in most and ciliary processes in many of the patients. Some degree of pigment deposition on the posterior lens capsule over the peripheral 3 mm. was a constant occurrence (Figures 1–4). The deposit of pigment and the posterior capsule of the lens, the zonular fibers, and the anterior limiting membrane of the vitreous offered an excellent method of studying the anatomy of this portion of the angle of the anterior chamber in the living eye. Normally, little or no pigment is present. One sees a glistening, irregular, linear reflex with scalloped edges toward the center of the lens running in an area approximately 3 mm. within the equator on the posterior capsule which represents the attachment of the anterior vitreous to the lens, or the hyaloideocapsular ligament. With the Koeppe lens and Barkan hand light for focal illumination the space between the posterior zonular lamella and the anterior limiting membrane of the vitreous cannot be seen. However, in individuals with pigment dissemination, the pigment frequently lodges in the angle or crevice between the face or anterior limiting membrane of the vitreous and the periphery of the posterior surface of the lens and extends onto the surface of these structures away from the angle. In 12 eyes a complete ring of pigment formed around the entire periphery of the lens, the individual layers then became visible. In 14 others, a broken or incomplete ring involving varying degrees of the circumference could be seen. In a small number of eyes the pigment deposition was largely on the face of the vitreous, and in some formed a sheet-like deposit on the anterior limiting membrane which could be seen posterior to the zonular fibers and membranes (Figure 4). When pigmentation was less marked, a variable degree of pigment deposition in the form of discrete punctate dots on the posterior lens capsule could be seen, usually at the insertion of the zonular fibers. These frequently occurred at two levels. One was at the hyaloideocapsular ligament, and another was approximately half-way from there to the equator of the lens. The dots were most numerous and the pigment most dense at the site of the hyaloideo-

capsular ligament, which is the point where the continuous annular ring developed. Finer punctate dots of pigment could be seen elsewhere and extending over the zonular membranes, both anteriorly and posteriorly. The fibers themselves in many patients had a bronze appearance.

CILIARY PROCESSES

No consistent changes could be seen in the ciliary processes. In a few instances, the impression of a somewhat waxy or pale appearance was gathered, but we could never be certain of its significance.

TRANSILLUMINATION

Transcleral transillumination of all eyes was done with the pupil undilated. The eye was anesthetized, the transilluminator was placed on the sclera near the equator and the iris was observed through a binocular loupe in a dark room. Nearly all eyes showed characteristic wedge-shaped or elliptical areas at the periphery of the iris which transilluminated light (Figures 6A, B, C). When transillumination was minimal it was limited to one or two areas at the extreme periphery of the iris, most often in the 6:00 o'clock meridian. When more severe, multiple areas could be seen around the entire circumference of the iris, and when still more severe they were almost continuous. In extreme cases the atrophy extended to include the pupillary border at places, although always most marked at the periphery.

The pigmentary deposition in the anterior segment of the eye was always most marked in the eyes with marked iris atrophy: 20 eyes showed localized transillumination at the periphery of the iris limited to one quadrant of the iris; 13 showed scattered areas throughout the circumference of the iris; 46 showed continuous areas of basal transillumination, these being separated by fine lines, probably the skeletal meshwork of the iris stroma. In 6 the atrophy was so marked as to extend to the pupillary border, isolated blocks of intact pigment remaining here and there.

Only 12 eyes showed no evidence of transmission of light. Six of these occurred in patients where the fellow eye showed markedly pigmented angles, well developed Krukenberg spindles, pigmentary deposits posteriorly on the lens and iris atrophy, indicated by transillumination. The 6 eyes which did not transilluminate showed less evidence of pigment deposition and probably represented an earlier stage of the disease. The other 6 eyes were found in 3 patients with heavily pigmented irises. Two were in Negroes and one was in a Caucasian with dark

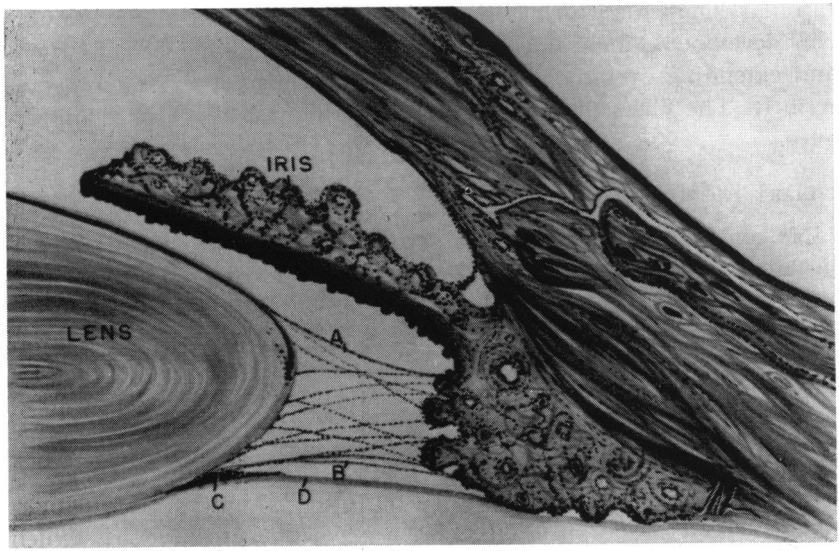

FIGURE 5. CROSS SECTION SHOWING DEPOSITION OF PIGMENT ON ANTERIOR LIMITING MEMBRANE OF VITREOUS

A: Anterior zonular fibers and membrane. B: Posterior zonular fibers and membrane. C: Pigmentary deposit. D: Anterior limiting membrane of vitreous.

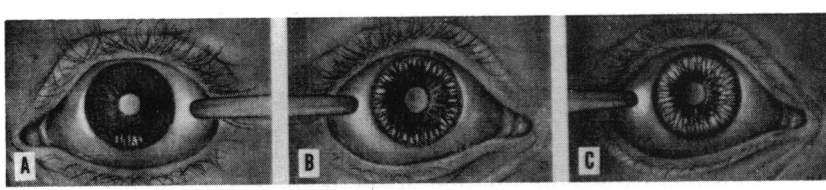

FIGURE 6. DRAWINGS SHOWING PERIPHERAL TRANSILLUMINATION OF IRIS

A: Localized. B: Circumferential continuous. C: To pupillary border.

brown eyes. Atrophy of the epithelial layers in such heavily pigmented individuals probably becomes apparent only at a later stage than in more lightly pigmented individuals.

PIGMENTARY GLAUCOMA

Each patient was studied carefully for evidence of glaucoma. The ocular tension was recorded repeatedly. The value listed in Table 1 is the average tension level untreated. Water provocative tests were done on all patients. The optic nerves were studied and visual fields were done, using small white test targets on the tangent screen at 1 mm. as well as 1/330 white on a perimeter. All patients were subjected to gonioscopy

and found to have open angles. In general the disease tended to be severe, particularly in younger individuals. The fifteen-year-old patient had residual fields when first seen.

A presumptive diagnosis of pigmentary glaucoma was made in 21 patients (42 eyes). This high incidence of glaucoma in patients with heavily pigmented angles is rather convincing. In studying these cases, although both angles were massively pigmented, the greater pigmentation usually was seen in the eye with more advanced glaucoma. This was also true of the degree of transillumination of the iris, for the pigmentation on the posterior lens capsule and zonule and the Krukenberg spindle. In two of the patients the trabecula was only Grade III pigmented, which raises the question as to the validity of the diagnosis of pigmentary glaucoma and certainly as to the mechanism of obstruction to outflow of aqueous. The fact that many patients with Grade IV pigmented angles did not have glaucoma also is disturbing. This might be explained by a varied response on the part of the drainage mechanism to pigment deposition in different individuals.

An attempt was made to control the glaucomatous process medically in all patients. This was successful in 27 eyes and unsuccessful in 15 eyes. Where medical treatment failed, surgery was advised. One patient declined surgery. Another patient will be operated in the near future. Pigmentary glaucoma seems to respond as well to fistulizing operations as ordinary chronic simple glaucoma. Six eyes were operated by goniopuncture. Of these the tension has been well controlled in both eyes of the fifteen-year-old patient for six years, in one of the patient who was twenty-nine years of age when operated for five years, and in one eye of the twenty-six-year-old patient for eight months, while the other has only recently been operated. Pigmentary phenomena tend to diminish following filtering operations, probably by escape from the eye. In three patients pigment deposit lodged in the filtering scar, where it had been carried as a result of aqueous flow.

DISCUSSION

Extensive pigment deposition throughout the anterior portion of the eye has been described in 97 eyes (49 patients). We believe this is an entity resulting from idiopathic atrophy of the epithelial layers of the iris and probably the ciliary body. The pigment was found (1) on the corneal endothelium, often in the form of a Krukenberg spindle, (2) the trabecular area of the anterior chamber, (3) the posterior surface of the lens near the equator and (4) the zonular fibers and membranes. Atrophy of the iris was demonstrated by transillumination of the eye

which demonstrates a characteristic pattern of dehiscences in the iris. Glaucoma frequently occurs as a complication.

Krukenberg spindle formation was first described in 1899 and at times has been reported occurring in association with heavily pigmented angles of the anterior chamber, glaucoma, and rarely annular pigmentation on the posterior surface of the lens near the equator. This paper has attempted to relate these findings more clearly into an entity and to emphasize the value of transillumination of the eye to demonstrate the rather typical changes in the iris. Gonioscopic observations of the posterior chamber, including the zonular fibers, periphery of the lens, and ciliary processes are described for the first time.

Krukenberg spindle formation, with little doubt, is only part of a generalized process of pigment dispersal and deposition. The pigment is distributed in the form of a spindle, probably as a result of convection currents. However, as other authors have speculated, it is difficult to understand why spindles should occur in some eyes and not in others, even when heavily pigmented elsewhere. This is true, for example, in essential atrophy of the iris, where a great deal of pigment is liberated, and was found in 5 of the 97 eyes studied in the present report. The degree of pigmentation of the various parts of the anterior portion of the eye was somewhat variable, but in general a very dense Krukenberg spindle usually indicated massive pigmentation of the trabecular area as well as heavy pigmentation on the posterior aspect of the lens and upon the zonular lamellae. Occasionally, however, spindle formation was absent when the angle was heavily pigmented, but punctate deposits of pigment always could be seen on the corneal endothelium. The consistent finding of pigment deposition at the periphery of the posterior lens and upon the posterior zonular membranes seemed to suggest clinically that the ciliary pigment epithelium participated in the same atrophic process that affected the iris. In view of the flow of aqueous forward from the ciliary processes, any other explanation for the pigment in these locations would be difficult. However, gonioscopic examination revealed no consistent changes in the ciliary processes although in occasional eyes they were thought to be more pale or waxy looking than normal but this was extremely difficult to evaluate.

Transillumination of the iris has been mentioned in the literature, but usually only in passing. This paper emphasizes the great value of this test in detecting atrophy of the epithelial layers of the iris because the diagnosis is readily overlooked by any other method of observation. The overlying stroma is normal in appearance and even the speckling of pigment, when present, is easily overlooked. Krukenberg spindle

usually suggests the diagnosis but occasionally is absent. The secondary nature of the pigment deposition is indicated by the very consistent relationship between the severity of the iris atrophy and the amount of pigmentary deposit on the cornea, angle, and lens. The type of transillumination seen in these eyes is not entirely specific because one rarely sees an isolated area or two of peripheral transillumination in eyes otherwise entirely normal. We are uncertain whether this represents a very early stage of the disease, before sufficient pigment dispersal has occurred to be noticeable, or whether it is a malformation of the iris. Transillumination of the iris can result from inflammation, trauma, and other causes, but the pattern is usually very different from the type of atrophy of the iris under discussion.

Chronic simple (open-angle) glaucoma was detected in 42 eyes (43.5 percent) of 21 patients, usually with heavily pigmented angles. This high incidence suggested that glaucoma might have resulted from the deposit of the pigment in the trabecular area. It is difficult to explain, however, why glaucoma did not occur in other eyes with equally pigmented angles. If pigment is presumed to be the cause of glaucoma, the assumption must be made that pigment on and within the trabecula has a different effect in different individuals. The fact that pigmentary glaucoma frequently occurs in young individuals and where it runs a severe course, is suggestive that the pigment is an important factor in development of the disease. In the authors' opinion, every patient with a heavily pigmented trabecula should be followed carefully for the future development of glaucoma.

SUMMARY

1. Ninety-seven eyes showing dissemination and deposition of pigment throughout the anterior segment of the eye have been described.

2. The pigment probably arose from the epithelial layers of the iris and ciliary processes from which it had been freed by an idiopathic type of atrophy.

3. Atrophy of the iris was demonstrated in a high percentage of eyes by transillumination which showed a characteristic pattern of dehiscences in the epithelial layer, most marked at the periphery of the iris.

4. Glaucoma occurred in 42 eyes, presumably on the basis of obstruction to outflow of aqueous by pigment deposited in the trabecula or by some tissue response to this pigment.

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DISCUSSION

DR. F. PHINIZY CALHOUN, JR. We are, indeed, greatly indebted to the author for his analysis of this large series of cases having a pigmentary disturbance, and for his further delineation of this as a definite clinical entity. I am entirely in agreement with him.

By gonioscopy he has demonstrated the distribution of free pigment in the anterior segment of the eye, and by transillumination of the iris he has demonstrated with this new test the atrophy of the epithelial layer of the iris, which is the probable site of the origin of the free pigment.

It is to be noted that there was considerable individual variation in the distribution of the pigment. In some cases the pigment was more dense on the back of the cornea and thin on the trabecular meshwork. In other cases the reverse was true.

Furthermore, although glaucoma was present in almost half the cases, there was no consistent relationship between the degree of pigmentation and the presence or severity of the glaucoma. It seems to me that we are unable to state with certainty that this is a secondary type of glaucoma, as suggested by Sugar, and it is still very difficult to prove that this glaucoma is due to pigment deposition in the trabecular meshwork.

I want to ask the author one or two questions which pertain to information not included in his paper.

One of the questions is: Did any of the cases with glaucoma in this series show the paradoxical elevation in pressure following mydriasis which was a characteristic described by Sugar in his original article?

In the paper on the subject of pigmentary glaucoma which I gave before this Society in 1952, on the basis of the findings in a small series of only six cases, I found that the condition occurred predominantly in young, myopic males of large stature, and a few additional cases which I have seen since that time have confirmed this observation.

I also found in my own series of patients that the male with Krukenberg's spindles was much more likely to have an associated glaucoma than was the female.

It would be most interesting to know the sex distribution and the physical characteristics of the patients in Dr. Scheie's large series, especially in the 42 patients with glaucoma.

I stated in 1952 that it was my belief that the corneal pigmentation of the Krukenberg type was an expression of a concomitant degenerative condition of the eye in which glaucoma was likely to supervene, but that there was no definite proof that the pigment was causing the glaucoma.

It would be most interesting to know if Dr. Scheie could confirm my findings about the physical changes and other characteristics. In other words, could he prove or disprove that this distinct clinical entity with its vast pigmentary disturbance went farther than just the eye but included other parts of the body or was a manifestation of some other general disease.

I believe that investigations in the field of endocrinology and pathologic physiology will probably add to our knowledge of this distinct clinical entity.

DR. FREDERICK W. STOCKER. I should like to show two slides which confirm histologically the accumulation of pigment in the meshwork of the chamber angle which the essayists have so ably demonstrated to be found gonioscopically in certain cases of glaucoma.

In the first slide, even at low magnification, we can see that the trabecular meshwork is packed with pigment cells.

The second slide makes the condition more obvious at high magnification. Some of the pigment is in process of being phagocytosed. Both cases in which I was able to demonstrate histologically this marked accumulation of pigment in the chamber angle were high myopes in which the glaucoma had developed very insidiously. The degenerative process which accompanies high myopia is

generally characterized by pigment degeneration throughout the globe. If this is noted, it might be well to look out for glaucoma, which often seems to be overlooked in myopes. Neither of the two cases had a Krukenberg's spindle.

DR. HERMANN M. BURIAN. This has been an extremely interesting and valuable paper, particularly because of the fact that Doctors Scheie and Fleischhauer had such an unusually large series of cases to present to us.

I want to ask Dr. Scheie two questions. One has already been touched upon by Dr. Calhoun. Dr. Scheie divides the pigmentation of the trabecular zone into four groups. Has he found any relationship between the severity of the pigmentation and the occurrence of glaucoma?

The second question I want to ask him is whether he has noted, either in external or gonioscopic examination, in addition to iris atrophy and pigmentation other abnormalities such as prominent rings of Schwalbe and pectinate ligament features. I should suspect that they must have been present at least in some of his numerous patients.

DR. MICHAEL J. HOGAN. I should like to ask Dr. Scheie if he recognizes a precursor to this condition. I have two young patients, both females, nonmyopes, who do not have the Krukenberg spindles but who have dispersed pigment on the back of the cornea and constantly show a large amount of pigment floating in the aqueous humor. Both have normal tensions.

DR. HAROLD G. SCHEIE. I should like to answer Dr. Hogan's question with the description of a case that I saw only this week, that of a young man twenty-four years old. There were no spindles, heavily pigmented angle, pigment cells in his aqueous, densely pigmented trabeculas, complete pigment ring behind the lens in one eye, partial in the other, and normal tension. I suspect that he may have a Krukenberg spindle some day. Why a spindle forms in some persons and not in others I do not know, but it seems to me fairly certain that this patient will develop one, and I would fear glaucoma.

The point that I should like to make is that all of these patients should be considered as having incipient glaucoma; in my opinion, with an incidence of 50 percent. They should be studied carefully and followed repeatedly for the rest of their lives.

As to Dr. Burian's question of the relationship between the amount of pigmentation and glaucoma, there was such a relationship, although glaucoma did occur in those with Grade III pigmentation. The only way you could explain it, as I said before, is the variability of individual response of tissues to the pigment if it is pigmentary glaucoma.

Another bit of evidence in favor of the glaucoma occurring on the basis of pigment is that almost invariably, in eyes where the glaucoma is more advanced on one side than the other, the pigmentary phenomena and the iris atrophy are more marked in the eye with the more advanced disease. I have found it associated with no other anomalies of the angle.

Dr. Calhoun mentioned the variability of these findings, and he is quite right. You can find a dense spindle with a more lightly pigmented trabecula and dense pigmentation behind the lens, or almost any combination.

The paradoxical rise in pressure is something we did not study carefully,

and we did mydriasis on not more than three or four of the patients with this type of glaucoma. I cannot answer the question.

Males did predominate, but I do not have the proportional figures at the moment. It occurs in both sexes.

As Dr. Stocker suggested, the condition can occur in the absence of spindles, but then you see punctate pigment elsewhere on the cornea.