PSEUDOEXFOLIATION OF THE LENS CAPSULE: RELATION TO TRUE EXFOLIATION OF THE LENS CAPSULE AS REPORTED IN THE LITERATURE, AND ROLE IN THE PRODUCTION OF GLAUCOMA CAPSULOCUTICULARE

BY *Georgiana Dvorak-Theobald,* M.D.*

ALTHOUGH exfoliation of the lens capsule has been recognized as a pathologic condition for many years, it is apparent from the studies herein reported that there is another form of capsular change which, in its superficial pathologic characteristics, is so similar to true exfoliation of the lens capsule that it has repeatedly been mistaken for it, even by so great an authority as Vogt.

This second form of capsular change—which I propose to call pseudo-, or false, exfoliation of the lens capsule—is characterized by deposits or accretions of an unknown material on the lens capsule, ciliary body, and zonules. As yet the nature of this material is unknown but, since it is moderately positive with periodic acid and to the Schiff and Millon tests (made by Dr. George Gomori of the University of Chicago), it may be assumed that mucopolysaccharides and tyrosine are present.

Busacca has stated that exfoliation consists in the deposition of a granular substance which he assumes to be normally present in solution in the aqueous humor. Hoorgina (18) thought it was due to the action of a chemically changed aqueous on the lens.

PRESENT STUDY

It is the purpose of this paper to:

1. Report the histopathologic study of three eyes, removed in the Glaucoma Clinic of the Illinois Eye and Ear Infirmary, with

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the clinical diagnosis of "wide-angle glaucoma with exfoliation of the lens capsule," which revealed findings incompatible with the classic description of lens exfoliation.

2. Review briefly the literature on true exfoliation of the lens capsule.

3. Point out the similarities and differences in true and false exfoliation of the lens capsule.

4. Suggest that pseudoexfoliation is related to glaucoma capsulocuticulare and that true exfoliation is related to certain forms (glassblower's cataract) of cataract.

CASE REPORTS

During routine histopathologic study of three eyes which were removed in the Glaucoma Clinic with the clinical diagnosis of "wide-angle glaucoma, with exfoliation of the lens capsule," I found that, although my findings coincided in part with those in earlier reports, these eyes revealed some pathologic findings which had not been recognized nor fully appreciated by previous authors.

CASE 1. A man, aged sixty years, first noted halos around lights with his right eye about three years ago. There had been no light perception in this eye for the last year and a half. It had been severely painful for the past eight months.

The tension was absolute. Examination showed exfoliation of the anterior lens capsule, but the cortex and nucleus remained clear. Flocculent debris was seen in the anterior chamber.

The chamber angle was wide, although blocked with deposits of fluffy white material. There was a wide, heavily pigmented trabecular ring. Tufts of flaky material were seen on the iris, both at the pupillary margin and over the surface. The iris appeared slightly atrophic. There was a deep glaucomatous excavation of the disc.

CASE 2. A man, aged seventy-two years, had had failing vision in the right eye for a number of years and had been blind for the past three years.

The tension was absolute. Bullous keratopathy and corneal edema prevented detailed examination of the anterior chamber. It was observed, however, that the angles of the anterior chamber were deep and that there was iridodonesis.

The left eye showed early exfoliation of the lens capsule in the pupillary area and flakes on the iris surface. The trabeculum and Schwalbe's line were heavily pigmented.

CASE 3. A man, aged seventy-four years, had been treated for glaucoma for the past two and a half years. The left eye had had no light perception for the past two years.

One month before he had developed pain in the left eye which could not be controlled by medication. The tension was absolute. Exfoliation of the lens capsule was noted, and fine white deposits were seen on the iris and in the angle. The lens was cataractous. The tension of the right eye was being controlled with miotics and fluctuated between 23 mm. Hg and 30 mm. Hg (Schiötz).

DISCUSSION

Since the essential clinical findings in these three eyes are similar, they can be discussed together.

Clinically, each of these three patients had typical "capsular exfoliation" with accumulations in the anterior chamber, on the surface of the cornea and iris, and in the chamber angles. All three were known to have had glaucoma for two to three years, which did not respond to treatment. Enucleation was done because the eyes were blind and painful.

PATHOLOGIC STUDY

The pathologic picture of the tissues was similar in the three eyes and differed only in degree. It was a degenerative process which gave no evidence of previous inflammation.

In evaluating the findings, the pathology of the aging process, as well as the pathology of the abnormal material and resulting glaucoma, had to be considered. The angles of the anterior chambers were wide, the discs cupped, and the retinas atrophic.

The eyes were sectioned serially and stained with hematoxylin-eosin and with the trichrome stain. With the latter stain, the accretions of precipitous deposits were more readily demonstrated than with the former. The trichrome stain showed the lens capsule to be thick, many layered, sclerosed, and hyalinized. Especially hyalinized was the pericapsular membrane.

The serial sections revealed that the accretions had formed on the anterior surface of the capsule as far back as the equator. They were, however, *separated* from the lens capsule by a clear, unstaining line (Figure 1) which has not, as yet, been identified.

The appearance of the accretions differed with the site of oc-

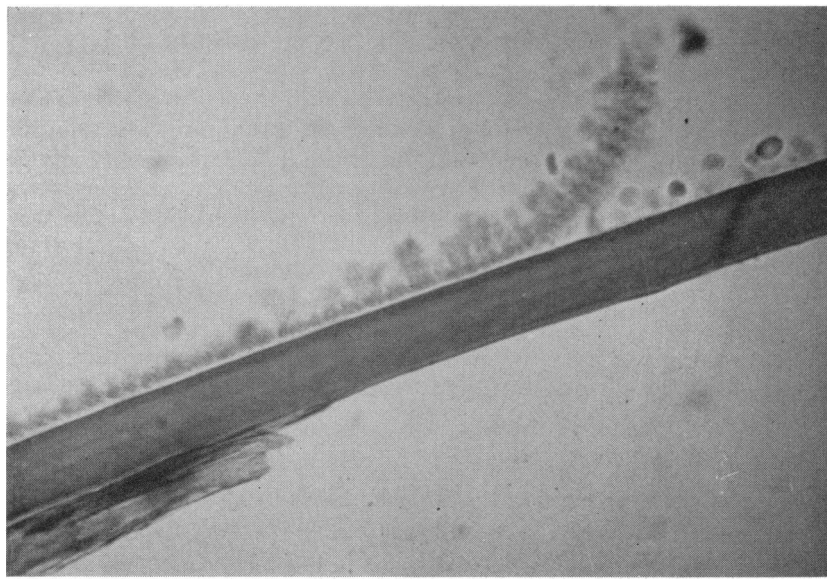


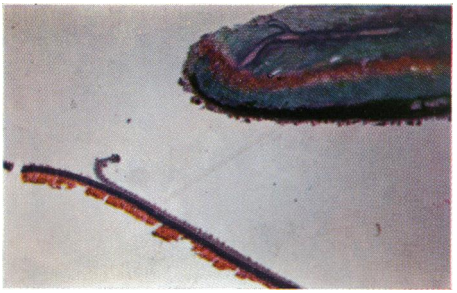
FIGURE 1. ACCRETIONS ON THE ANTERIOR LENS CAPSULE, SEPARATED FROM THE CAPSULE BY A CLEAR UNSTAINING LINE. (X 430)

currence. In some sections the distribution was spotty, as noted clinically by Vogt and others, but in many other sections the entire anterior capsular surface seemed to be involved.

In the pupillary area and just peripheral to it, the accretions were short and stubby (color plate, *a* and *b*), and were arranged in tufts or irregular bundles standing side by side on the lens surface like shrubs in a hedge.

Evidently, they were composed of some sticky material, for where they were especially numerous they clung together (color plate, *a* and *b*) and crowded into the anterior chamber in the form of curls. Here and there the end of a curl doubled on itself to form a knob. Although the curls have been described clinically, I can find no histologic description of them. The curls appeared not only in the pupillary area but also some distance from it beneath the iris.

Midway between the pupillary border and the equator, the accretions were feathery and branched (color plate, *c*) in appearance. Busacca and Sohby Bey descriptively used the term "myceliumlike" to designate the branching formations.



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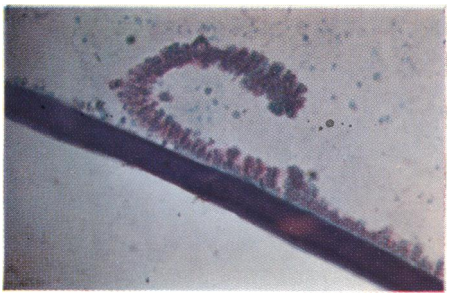

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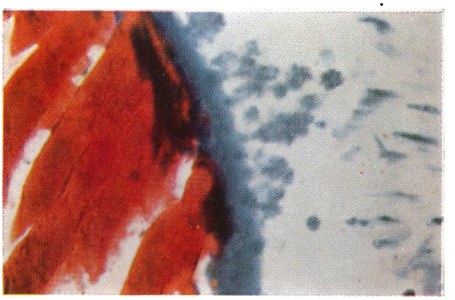

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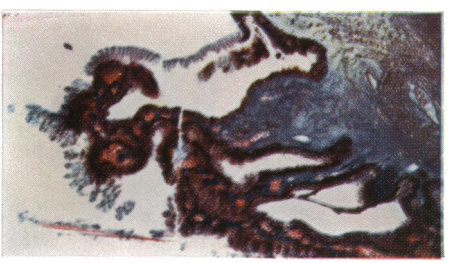

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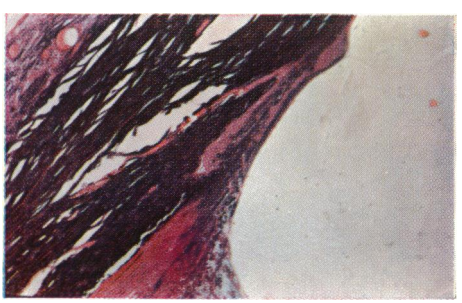

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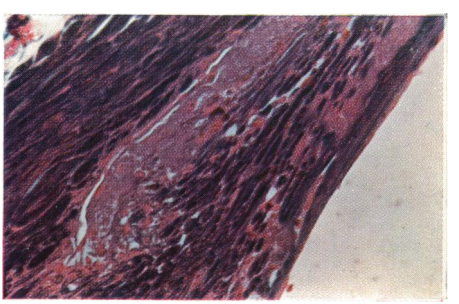


h

a. Accretions on anterior lens surface, peeling off in form of a curl; also deposits on posterior surface and pupillary margin of the iris. Trichrome stain (× 25). *b*. High-power view of accretions on lens surface. Trichrome stain (× 430). *c*. Midway between pupil and equator, deposits are feathery and branching. Hematoxylin and eosin stain (× 430). *d*. Soft, fluffy-appearing accretions near equator of lens. Trichrome stain (× 430). *e*. Accretions deposited on posterior iris surface, ciliary processes, and zonular fibers. Trichrome stain (× 25). *f*. Accretions deposited on ciliary body, zonular fibers, and anterior surface of vitreous. Trichrome stain (× 100). *g*. Accretions filling intratrabecular spaces, canal of Schlemm, and external collector channel. Trichrome stain (× 100). *h*. High power of *g*. Trichrome stain (× 430).

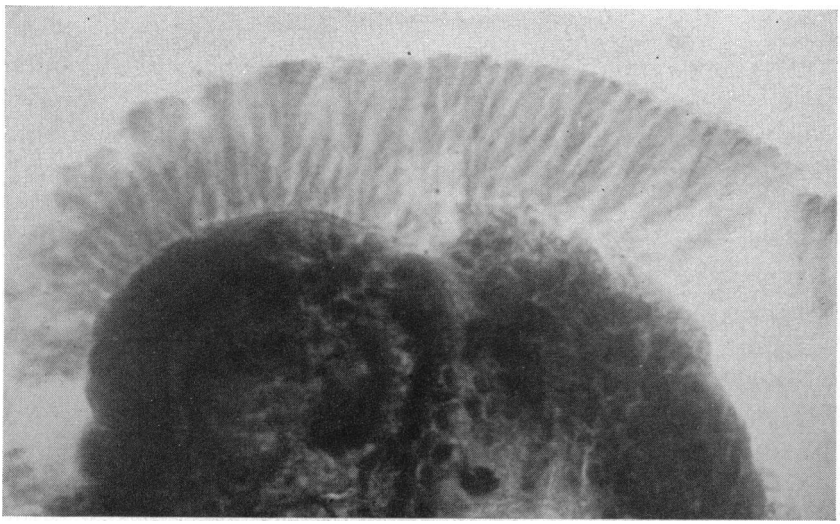


FIGURE 2. DEPOSITS OR ACCRETIONS CLING TO CILIARY PROCESSES. (HIGH POWER OF *f* ON COLOR PLATE). (X 430)

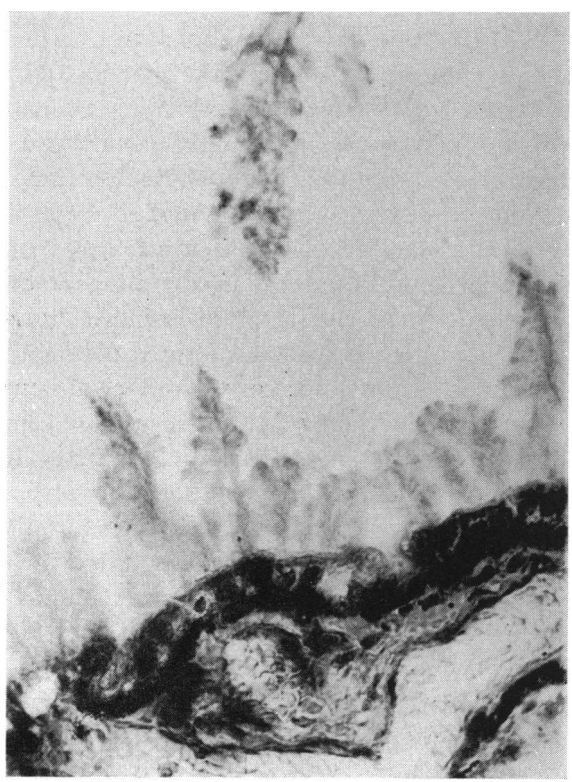


FIGURE 3. DEPOSITS (ACCRETIONS) CLING TO CILIARY PROCESSES. (X 430)

The pericapsular membrane beneath these branchlike accumulations stained less densely than in the pupillary area, thereby denoting a lesser degree of sclerosis and hyalinization. In the region of the zonular attachments near the equator, the pericapsular membrane stained faintly (color plate, *d*) and the accretions appeared soft and fluffy. Both Vogt and Sohby Bey observed vacuoles in the lens capsule in some of their cases; however, none were found in these sections.

In the anterior segment of the eyeball, the accretions arranged themselves about the tissues in various ways. In the posterior chamber, they clung to the limiting membrane of the vitreous, the zonular (color plate, *e*) fibers of the lens, the ciliary processes (Figures 2 and 3), and the posterior iris surface. They appeared as a homogeneous cover or layer, but mostly in the shape of feathery (color plate, *f*), triangular wedges, stacked side by side and attached to the tissues in much the same way iron filings cling to a magnet (Figures 2 and 3).

The question has been raised as to whether the zonules exfoliate. The trichrome stain shows the zonules and the accretions to have different staining properties, which probably indicates that the red-staining zonules are simply providing a roosting place for the blue accretions and are not producing them (color plate, *e* and *f*).

The anterior chamber contained large amounts of fluffy material, the deposition of which was very interesting. Not only did the accretions lie loosely in the anterior chamber but they were absorbed by the endothelium lining it. Large globules and masses of the material, as well as migrated pigment, were phagocytized by the endothelium of the cornea and iris (Figure 4).

Busacca and Sohby Bey found massed formations of "exfoliated capsule" in the angle from the pectinate ligament to the iris. In the three eyes herein reported, the amorphous accretions not only covered the surface of the trabeculum but filled the intratrabecular spaces (Figure 5). In one eye they filled the canal of Schlemm, apparently entering it by way of the inner canals of Sondermann (color plate, *g* and *h*). This also was best seen with the trichrome stain.

The deposits had entered the iris stroma through Fuchs's crypts, as was demonstrated by differential staining. The iris appeared

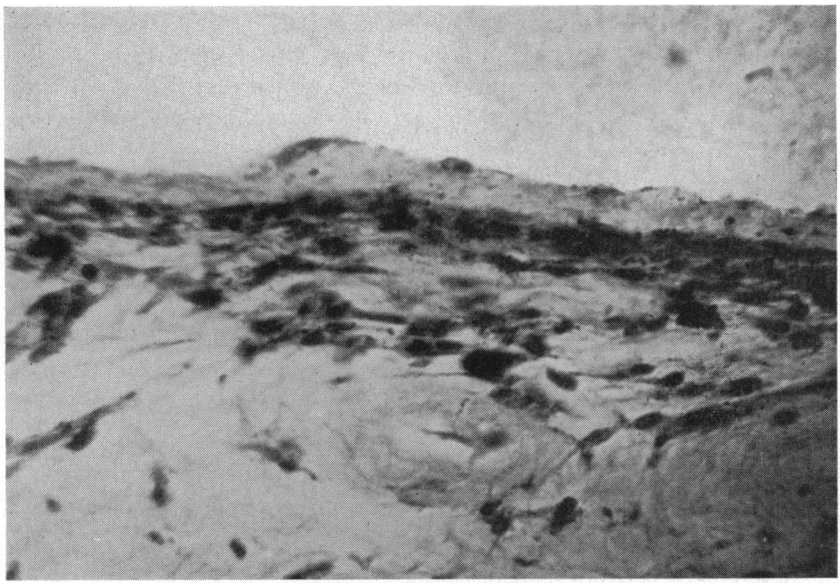


FIGURE 4. AMORPHOUS MATERIAL IN ANTERIOR CHAMBER; PHAGOCYTIZED BY IRIS ENDOTHELIUM. (X 430)

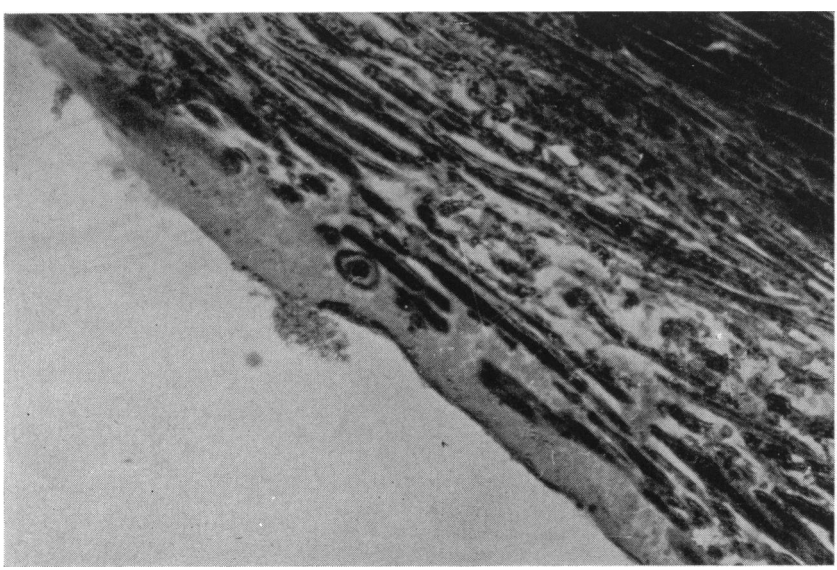


FIGURE 5. DEPOSITS LINE TRABECULAR SURFACE AND FILL INTRATRABECULAR SPACES. (X 430)

rather solid and the vessel lumens were narrowed and, in some instances, obliterated. In none of these three eyes was the iris found to be in apposition with the lens surface, although it may have been so in vivo. There also was no evidence of posterior synechias.

The pigment epithelium in all three eyes had disintegrated and migrated in varying degrees. Pigment granules were found in and on the iris, on the posterior corneal surface, and especially in the intratrabecular spaces. The disintegration and migration of the pigment was probably due to local malnutrition caused by clogging of the iris with the accretions. Apparently, it was not incidental to the rubbing action of the iris on the anterior lens surface, as has been considered by a number of authors. This type of pigment disturbance is not uncommon in aged individuals with degenerative diseases, and is usually attributable to arteriosclerosis and related angiopathy.

Indeed, the presence of pigment granules in the trabeculae of patients over thirty-five years of age is quite frequently seen clinically on gonioscopic examination and also in microscopic sections. It is, moreover, a recognized clinical fact that glaucoma is produced by the clogging of the trabeculae with migrated pigment particles—a condition for which the name pigmentary glaucoma has been coined.

Since, in these three eyes, the accretions were found to be as numerous beneath the iris as they were in the pupillary areas, it does not seem likely that friction of the iris on the lens capsule is necessary in their formation or migration. Rather, it seems more likely that the accretions played a part in producing a secondary iris atrophy, thus promoting the degeneration and migration of the iris epithelium.

The source and nature of these accretions are, however, obscure. The material does not have the histologic characteristics of lens capsule. Under high power, a thin, shiny membrane is seen between the lens capsule and the accretions on its surface (Figure 1), and the pericapsular membrane is intact.

Although these three cases exhibited the clinical picture which has been called "exfoliation of the lens capsule," it seems quite clear that in these three eyes there was no true exfoliation of the

lens capsule and that these pseudoexfoliations are merely capable of mimicking that condition.

RE-EVALUATION OF THE LITERATURE

With the histopathologic findings presented by these three eyes in mind, it was decided to review the literature on exfoliation of the lens capsule in order to determine which of the previous reports described true exfoliation and which described the condition characterized by accretions of an unknown substance and herein termed pseudoexfoliation.

TABLE 1. COMPARISON OF FINDINGS IN PSEUDOEXFOLIATION AND TRUE EXFOLIATION OF THE LENS CAPSULE

	Pseudoexfoliation	*True Exfoliation*
Age	Beyond 4th decade	Beyond 4th decade
Occupational	No	Yes (glassblowers, stokers, puddlers, heaters)
Clinical appearance	Frostlike, roughened appearance of lens capsule	Thin, homogeneous, water clear, transparent membrane that glistens
	Roughened membrane detaches and curls forward away from lens surface	Membrane curls like scroll, or lamellae are loose and lie on lens surface as strands
	Blue-gray, feltlike flakes, tufts, or fuzz float in anterior chamber, fill angles and are attached to iris and zonular fibers	
Pathology	Accretions on anterior lens surface, on zonular fibers and anterior vitreous membrane	Pathologic material not available
	Phagocytized by endothelial cells of iris, cornea and canal of Schlemm	
	Block trabecular spaces	
	Separated from lens by clear membrane	
Associated conditions	Eventually glaucoma	Eventually cataract
	May, but do not always, get cataract	May, but do not always, get glaucoma

This re-evaluation of the literature has shown that many of the cases clinically diagnosed as exfoliation of the lens capsule are, in reality, pseudoexfoliation, and that the findings described herein as accretions have been repeatedly mistaken for true exfoliation.

DIAGNOSTIC DIFFERENTIATION

In order to classify the criteria by which we are attempting to establish the two conditions as separate entities, a comparative outline is shown in Table 1.

The true exfoliation occurs in persons exposed to extreme heat over a long period of time. In them there is a rupture of the superficial layer of the capsule which either becomes shredded in appearance or curls up in a scroll-like manner. From the viewpoint of this study, it is unfortunate that no eye with true exfoliation of the lens capsule was available for histopathologic study.

Pseudo- or false exfoliation is caused by accretions of an unknown material which deposits itself upon the anterior lens surface and other structures in the anterior one half of the eyeball.

Although differential staining shows the presence of mucopolysaccharides and tyrosine, chemical analysis of the aqueous of these patients may lead to discovery of the real composition of these accretions.

As may be seen from Table 1, the clinical and pathologic criteria for differentiating pseudoexfoliation of the lens capsule from true exfoliation can be clearly established, and Table 1 may be used as a basis for the classification of cases in the literature.

PSEUDOEXFOLIATION

Exfoliation of the lens capsule has been recognized as a pathologic condition for many years but it was not until 1925 that its causal relationship to wide-angle glaucoma was first clearly pointed out.

In that year, the Swiss author, Alfred Vogt, published (16) in the *Klinische Monatsblätter für Augenheilkunde* the first complete and precise description of twelve cases, nine of them with glaucoma, the condition to which he later gave the name *Exfoliata superficiale capsulae anterioris.*

Some years before Vogt, Lindberg (9; 1917) in Sweden, reported

the presence of flakes at the pupillary border of the iris in about one half of 60 patients with chronic glaucoma, and believed these flakes to be mostly the result of earlier inflammatory exudate.

Another Swedish author, Malling, published (10; 1923) his finding of "exfoliation" in 33 out of 88 cases of primary chronic glaucoma and called attention to the possibility of a relationship existing between the flakes and the increased intraocular pressure.

As early as 1918, Vogt (14) described the presence of a film with crinkled edges on the anterior lens capsule of a seventy-two-year-old man who later developed glaucoma, and thought that the film might consist of pupillary membrane remnants.

In 1923, Vogt examined the condition anew with a slit lamp and concluded that the film on the lens and the flakes on the iris were the result of exfoliation of the superficial layers of the lens capsule. Two years later, he published what has been generally accepted as the first complete and satisfactory description of exfoliation of the lens capsule (16).

Vogt noted that the manifestation of this condition is independent of the pigmented iris epithelium and that the exfoliations consist of new masses which simply stick to the surface of that layer. He had observed them on the surface of the lens capsule, on the iris, or on the back of the cornea, and had found them to change from time to time in number and position. Simultaneously with the blue, fluffy masses on the iris, he had noted a special condition on the anterior surface of the lens which had not previously been described.

On the pupillary border of the iris, he found light blue or white flocculi of a scaly, feltlike consistency and, in the center of the capsule, he observed a grayish disk about the size of the pupillary opening, which was surrounded by a clear black area, corresponding in size to the sphincter area of the iris. He also noted that the motion of the iris had abraded the grayish capsular lamella in this area, thus accounting for the debris on the pupillary edge of the iris.

Peripherally to this area he found further evidence of the grayish membrane. The central edge was often curled forward and away from the capsule.

In brief, the capsule displayed, in most instances, superficial

changes which were either central or peripheral, or both. The peripheral changes took the shape of a festooned ring or crown of fine, granular opacity, quite distinct from the disk just mentioned, or took the shape of a wheel, the radial zones of which were attached to this disk. The distal boundary of the crown stopped one or two mm. within the zone of attachment of the anterior fibers of the zonula. At this portion of the capsule, the distal edge of the crown curled on itself.

In the illustrations which supplement the article published by Vogt in 1925, some of the exfoliations (accretions) have the shape of tufts which are broadly attached to the capsule, while others are perched on thin pedicles and seem ready to drop off.

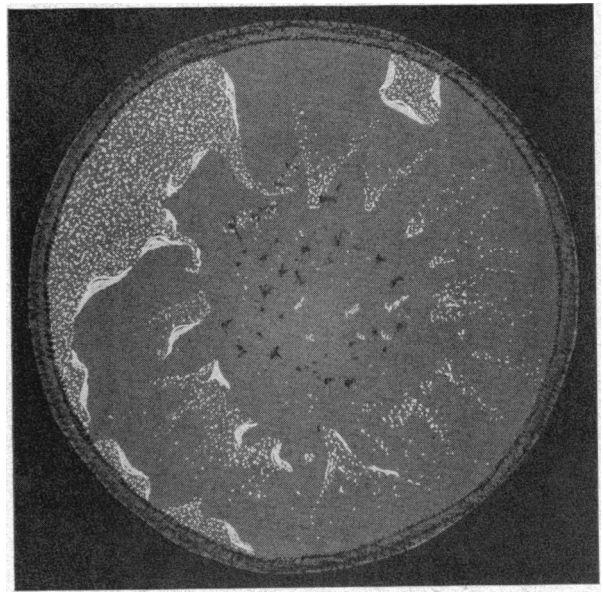
It has been observed by various workers that the flakes occur in relatively large numbers and are difficult to dissolve or absorb. They float in the anterior chamber and become attached to the iris and posterior corneal surface, choking the drainage angle in some instances, thus giving rise to glaucoma.

Busacca (2; 1927), Garrow (5; 1938), and others are in agreement with Vogt about the correctness of these findings. Garrow, for example, has described a milky film which was nonhomogeneous and had a dotted or grained appearance. The graining was of a fine texture in the center of a tear and coarser near its edge.

Sohby Bey (11; 1932) found laminated masses on the pupillary margins and the posterior surface of the iris which were thicker in the furrows and thinner along the edges. He also noted that this material had the same refractile structure and characteristics as the lens capsule.

Depigmentation of the iris, Sohby Bey observed, went hand in hand with exfoliation. Furthermore, the massed formations which crossed the angle from the pectinate ligament to the iris, he assumed to be accumulations of exfoliated capsular lamellae.

Another early observer, Hörven (1937), found zonular changes a constant characteristic and an integral part of the clinical picture whenever "exfoliation" was present and the suspensory ligament was at all visible. The fibers were, in all instances, seen to be densely covered with white scurflike particles which were also present on the pupillary border. This condition has since been



FIGURES 6 AND 7. DEPOSITS ON ANTERIOR LENS SURFACE, DIAGNOSED CLINICALLY AS CAPSULAR EXFOLIATION

After Holloway and Cowan, "Concerning Lamellar Membranes of the Anterior Surface of the Lens," *American Journal of Ophthalmology,* March, 1931.

reported independently by many authors, especially when an iridectomy allowed them to view the posterior chamber. It is questionable, however, that the zonules undergo degenerative changes similar to those of the lens capsule.

Holloway and Cowan (7; 1931) report two distinctly different conditions (Figures 6, 7, 8, and 9).

Their first case (Figures 6 and 7) is similar to the ones reported by Vogt and his followers (which I do not consider to be true exfoliation) in which the deposits on the anterior lens capsule are described as frostlike and wholly or partly covered with "blue-gray fuzz or scalelike opacities," many of them with ruptured edges.

The illustrations in this case of Holloway and Cowan (Figures 6 and 7) correspond with those of Vogt and others and are excellent examples of pseudoexfoliation.

In discussing their Case 1, Holloway and Cowan say:

> Since Vogt's observation, similar cases have been reported. . . . All of these cases are strikingly similar: many of the gray flakes, scales or plaques have free, curled margins, while at times similar membranous tags are adherent to the pupillary margin and to the posterior surface of the cornea.
>
> The majority of observers now regard this type of case as due to degeneration of the zonular lamella. Wollenberg, Alling, and Vogt are practically in accord in their belief that the distribution of the flakes, and doubtless their adherence to the pupillary margin, depend upon the normal movements of the iris.
>
> In this type of case, the pupillary area is generally practically free and most of the manifestations are behind the iris. Kraupa prefers to regard these as dependent upon senile changes, in contradistinction to the type of case presently to be described [Holloway and Cowan's Cases 2 and 3; see our Figures 8 and 9], where the manifestations are chiefly in the pupillary area and which are frequently observed in glass workers, puddlers, and blacksmiths (doubtless chainmakers and tinplate workers would also show these changes). Kraupa is also of the opinion that the central area, which is generally clear, may ultimately show similar changes.
>
> Schieck . . . regarded these manifestations as deposits upon the lens surface. He believed the posterior iris cells to be the origin of the disturbance. Still later, Busacca and Hoorgina looked upon it as a deposition; the latter expressing the opinion that it was due to the action of a chemically changed aqueous upon the lenticular surface.

Concerning the cause and implications of this capsular change

(pseudoexfoliation), reference should be made to the clarifying views contributed notably by Vogt, Trantas, and Hörven.

Vogt said that the capsular changes might be in the nature of sclerosis. Trantas (1932) suggested that the capsular lesions might be the result of senile degenerative changes which attacked not only the anterior capsule but also most of the other ocular tissues as well, and especially the glass membranes and the transparent media, including the vitreous body. Consequently, the capsular surface would take on the appearance of having been sprinkled with powder. Corresponding changes occurring in the excretory channels for the intraocular fluids would then explain the tendency toward glaucoma. The exfoliations which become free in the aqueous would be deposited in the angle of the anterior chamber, thereby adding to the obstruction of the degenerated pectinate ligament and also of Schlemm's canal.

Trantas also observed that the size of the disk was not the same as that of the pupil in old age, and that therefore the edge of the disk was not fashioned by the pupillary action on the lens.

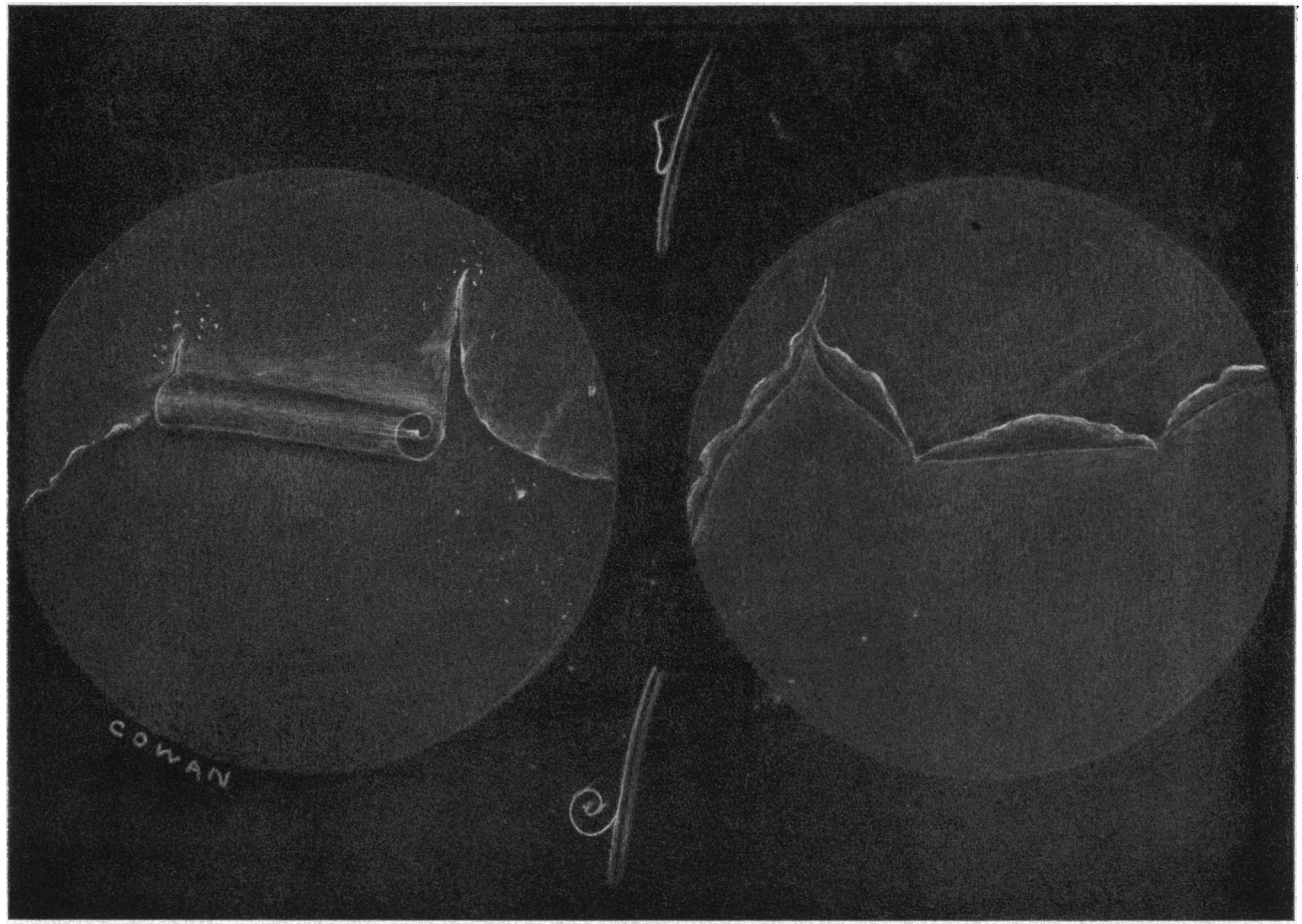
Furthermore, both Trantas and Vogt agree that a second exfoliation may superimpose itself on a preexisting one, thus indicating that all the superficial capsular lamellae take part in the degenerative process progressively.

TRUE EXFOLIATION

Although the use of ordinary stains gives the impression that the lens capsule is structureless, maceration and the application of special staining methods reveal it to be a composite structure, that is, to consist of several layers.

Busacca (1930), Berger, and Elschnig are agreed as to the presence of a pericapsular membrane. Some authors believe that the pericapsular membrane and zonular lamella are one and the same structure, while others are of the opinion that the zonular lamella is confined to the equatorial region. However, true exfoliation of the lens capsule affects first the pericapsular membrane and then the capsule itself.

True exfoliation of the lens capsule has been described clinically by a number of authors but, of the cases recorded in the literature, Cases 2 and 3 of Holloway and Cowan are of particular interest



FIGURES 8 AND 9. TRUE EXFOLIATION OF LENS CAPSULE
After Holloway and Cowan, "Concerning Lamellar Membranes of the Anterior Surface of the Lens," *American Journal of Ophthalmology*, March, 1931.

and value in pointing out the differences between this condition and the pseudoexfoliation so frequently mistaken for it. The illustrations taken from Holloway and Cowan (Figures 8 and 9) show with dramatic clarity how the slightly serrated, glistening, curled-up or scroll-like margins of true exfoliation depict a condition entirely different from pseudoexfoliation.

The second case described by Holloway and Cowan was that of a man, aged seventy years, who had been a puddler and heater in a rolling mill for 40 years. The illustration of this patient's condition (Figure 8) shows entirely different findings from those in their first case (Figures 6 and 7), as well as from those found in the cases herein described—"the curled margins of a homogeneous transparent membrane which were slightly serrated and glistening, and projected into the anterior chamber."

The third case reported in the paper by Holloway and Cowan showed a similar "thin homogeneous transparent membrane that curled upward and rolled up much like a scroll." (See Figure 9).

In 1922, Elschnig reported three cases of lamellar exfoliation occurring in glass blowers and described the exfoliation as "water-clear membranes." In 1930, Vogt reported capsular exfoliations in an eighty-year-old man who had been observed over a period of a year before his death. The lamella became loose and lay on the anterior lens surface. In this case, the histologic sections showed a true exfoliation of the lens surface in horizontal strands. This would well illustrate the findings in Holloway and Cowan's second and third cases, but is entirely different from the picture seen in my three cases.

In discussing their second and third cases, Holloway and Cowan remark "The vast majority of patients exhibiting changes of this character have been exposed to undue and prolonged heat; in a few instances, such as Case 3, this has not been the case."

Elschnig differed from Kraupa as to the origin of the rupture in the lens capsule. He believes that the rupture and detachment are the result of the heat changing the elasticity of the zonula rather than a diminution in the size of the lens.

Kraupa later stated that the genesis of this type of capsular detachment was not known. He was not, however, prepared to accept the opinion of Elschnig, but he stated that a change in

volume did occur in glassworker's cataract and that this might lead to protrusion of the lamella. He had also noted a rupture of the lens capsule lamella following a severe contusion of the globe. He further stated that the entire anterior layer of the capsule may detach in the form of a flat vesicle and subsequently rupture. Following this, there may be some adherence to the capsule.

Verhoeff, in conjunction with Bell and Walker, noted that glassblower's cataract was produced by heat.

Holloway and Cowan, in continuing this discussion, make what seems to me a particularly revealing statement indicating that confusion existed in Vogt's mind concerning the cases which he had reported:

> Vogt (1929) excluded heat and attributed it [true exfoliation] to the infrared rays, and stated that, in addition to the axial lens opacities, a partial or complete detachment of the anterior lamella of the anterior lens capsule may occur. These changes were only found in those over 40 years of age; therefore, age must be a factor. He believed the same process was involved in those cases that developed capsulocuticular glaucoma, except that in these individuals the cuticle was fragile and crumbled, while in the other instance the membrane retained its elasticity.

COMMENT

Needless to say, the literature on exfoliation of the lens capsule has increased considerably since the notable publications of Vogt, Busacca, Trantas, and Hörven, as may readily be seen by consulting the bibliography which Berliner has included in Volume II of his *Biomicroscopy of the Eye* (1949).

Four years after Vogt described glaucoma capsulocuticulare, Dr. Robert von der Heydt saw his first case at the Illinois Eye and Ear Infirmary. His enthusiasm and teaching led to the search for and study of many such cases, 77 of which were reported by Gradle and Sugar (6) in 1947. Many other cases of capsular exfoliation are presently under observation at the Glaucoma Clinic of the Infirmary, and data are constantly being collected on the relation of this condition to glaucoma.

SUMMARY AND CONCLUSIONS

1. Three cases are reported which clinically were diagnosed as "glaucoma with exfoliated lens capsule." Pathologically these cases

did not show exfoliation of the lens capsule, but rather precipitates or accretions of an unknown substance in the anterior segment. I propose to call this condition "pseudoexfoliation of the lens capsule."

2. Many of the cases previously described in the literature as capsular exfoliation are in reality "pseudo capsular exfoliation." An attempt has been made to separate these into two distinct clinically and pathologically recognizable entities.

3. In the posterior chamber, the accretions clung to the posterior surface of the iris, ciliary body, and zonular fibers, and to the anterior limiting membrane of the vitreous.

4. In the anterior chamber, the accretions were not only loosely attached to the iris, cornea, and trabeculum, but were phagocytized by the endothelium lining these structures.

5. The debris invaded the iris and filled the intratrabecular spaces and even the canal of Schlemm, thus blocking all avenues of egress for the aqueous, thereby producing a condition directly favoring an increase in intraocular pressure.

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DISCUSSION

DR. HAROLD GIFFORD. This to me is a very interesting and exciting thing, that we became interested in first about three years ago. I did not know what Dr. Theobald was going to show, and I went over our pathological collection to see what we had. As you know, the percentage of exfoliation of the lens capsule varies from around 3 to 75 percent, depending on what part of the world you come from; in Sweden the incidence is 75 percent, in Switzerland about 50 percent, and in Los Angeles 3 percent. It depends on whether you work in a glaucoma clinic or as an average eye doctor. We found 30 clinical cases, and I am reporting on these later.

There is one eye I want to show which is entirely different from the clinical picture. How we are going to reconcile the clinical and pathologic pictures we do not know.

Here is a similar kind of eye. This woman had glaucoma for four or five years, with two unsuccessful alcohol injections. The other eye showed chronic glaucoma, not well controlled by drops. We did not have a good description of the other eye, so we do not know whether it had exfoliation. That is the one eye in 39 cases of chronic simple glaucoma we looked over in the pathological laboratory. Then we went over 125 other eyes with secondary glaucoma and we only found one other eye which vaguely resembled this. The scarcity of pathologic material is surprising. Clinically we see it more often than in the pathologic material, which seems strange. This is growing on both sides of the zonular fibers, it seems to grow, or it may be deposited as a layer and be eroded out. This is the same material along the posterior iris as Busacca described as *baumartig,* and it is not pathologic exfoliation of the capsule, but has been reported years after as such.

Here is a highly magnified one in the posterior iris; this is a little creamy and granular, and this is the same thing in the trichrome stain; the other was a Van Gieson's stain. The next is a higher power of this *baumartig* material.

This was my interpretation: All these eyes showed hemorrhage. They had glaucoma for many years, and there has been a posterior detachment and hemorrhage. My impression is that blood was laid

down at an earlier date and as the blood was absorbed an erosion rather than a deposition occurred. The missing links between these have not been found completely, but in these hemorrhagic glaucomatous eyes we can almost see this occur step by step. First there is a sheet, then a little erosion, and finally something like this *baumartig* figure produced in the anterior chamber.

DR. ARTHUR J. BEDELL. It is a pleasure to express my appreciation of Dr. Theobald's beautiful exposition. You will recall that Rodman Irvine presented excellent colored pictures several years ago.

Clinically you are familiar with the granular nature of the exfoliation in cases, either with or without glaucoma. An expert ophthalmoscopist can often recognize the condition even if the pupil is only 3 mm., but details of structure can only be completely studied when the pupil is dilated to 4.5 mm. or more, at which time the clear zone between the furled, white inner and outer circles is easily seen.

Three black and white photographs are presented to show the ophthalmoscopic appearances and correlate them with the wonderful pathologic demonstration that we have just viewed.

DR. S. RODMAN IRVINE. We are indebted to Dr. Theobald for reviving our interest in a subject which has been neglected in the American literature for the past decade. After writing two papers on Exfoliation of the Lens Capsule in 1940 I stopped thinking about it until hearing Dr. Theobald's paper and seeing her splendid slides which show the scurflike fluff on the capsule arranged in such a way as to suggest a deposition rather than exfoliation. I have always thought that the zonule lamellar layer of the capsule, formed by the zonule and extending an unknown distance around the lens, was the exfoliating tissue. The reasons for this belief were:

1. Clinically, one can see the material coming off the capsule in sheets as well as in the form of fine dandruff. The sheetlike layer that is separating is stippled and the impression is the same as one has when looking at sunburned skin, namely, exfoliation of the layer in sheets as well as in smaller amorphous particles, depending upon the amount of rubbing of the surface that has occurred. The iris moving on the lens alters the picture of the exfoliating material.

2. Through an operative coloboma the zonule membrane shows a stippled appearance and exfoliation, the same as the most anterior surface of the lens except that there is less scurfing.

3. The zonulae are notoriously weak in such cases, the affected lens dislocating easily. This is additional evidence that the zonular lamellar layer is primarily diseased.

4. The pigment of the iris is also altered in these cases as showers of pigment, giving a smoke-cloud effect, can often be seen when the

pupil is dilated. Conceivably, the pigmented material could be deposited on the lens and later scurfed by the action of the iris, but I believe it is more reasonable to assume that the pigment layer of the iris is exfoliating as well as the zonular lamellar membrane.

5. The different staining characteristics of the exfoliating substance and the capsule can be explained as readily on the basis of the staining qualities of the zonular lamellar membrane being different from those of the capsule proper as on the basis of the superficial substance being a deposition.

6. Finally, when the lens is removed in these cases, apparently no further exfoliation or deposition occurs. I have never seen exfoliating material on the vitreous face or on a vitreous membrane. I have seen it on the capsule remnants following extracapsular extraction.

Dr. Theobald has brought up an interesting point, and because of her work it behooves us all to observe our cases carefully before operation and again during the postoperative follow-up period to see whether or not the exfoliation material seems to lessen on the iris after operation. If so, one would be inclined to think that the material is exfoliating zonular lamellar capsule, and not a precipitate or deposition of unknown origin. On the other hand, if it is a deposition, then "dandruff" on the iris should continue to appear.

DR. DANIEL B. KIRBY. I wish to add my compliments to Dr. Theobald for a beautiful demonstration and new information on this subject. Dr. Irvine has said a number of things I would have said, and I may reiterate them. I believe that the pericapsular membrane which is on the anterior surface of the lens and the viscous material which invests these zonular fibers are of similar origin and similar nature. I believe that Dr. Theobald has added further information which will lend credence to my postulate that the zonule is of two origins, first the zonular fibers that developed as extensions of the protoplasmic processes, which develop when the optical vesicle touches the surface ectoderm. When the optical vesicle invaginates and the lens recedes into the optic cup, the fibrillar connections are stretched out. At the time of the formation of the tertiary vitreous the viscous material may be added. Thus we may say there is a dual origin for the zonule. In the adult position the fibers measure about 7 mm. I believe in some cases there is degeneration of the viscous material of the pericapsular membrane and of the material which invests the zonular fibers. I thank Dr. Theobald.

DR. ALGERNON B. REESE. The changes described by Dr. Theobald are probably more frequent than we realize, because in order to see them it is usually necessary to have the pupils dilated. We are naturally reluctant to dilate pupils in cases of glaucoma.

Dr. Theobald, I think you have given us a most important contribution, and I congratulate you.

DR. GEORGIANA DVORAK-THEOBALD. I thank each discusser for his kind words. Dr. Gifford's findings agree with mine—that the accretions on the various membranes are a precipitate and not an exfoliation of the lens capsule. In regard to Dr. Gifford's last slide: I cannot agree with him that the hemorrhage has anything to do with the accretions. In none of our cases was there a history of hemorrhage or inflammation. This condition is a degenerative process. The treelike conformations found on the lens surface also occur on the ciliary epithelium, suspensory ligament, and anterior vitreous membrane. Busacca said the material might be a condensation of something normally found in the aqueous humor. I have not done any histologic research work on the capsule of the lens, but some think the zonular membrane is separate from the pericapsular membrane. However, most of the authors whom I consulted believe they are one and the same membrane.

The accretions and the zonular fibers stain entirely differently; the former perch on the zonulas like birds on telegraph wires or like iron filings clinging to a magnet.

We do not really know what this material is, or definitely where it originates. Perhaps other differential stains or chemical analysis of the aqueous from such patients will help solve the problem.