CONGENITAL PIGMENTATION OF THE CORNEA (KRUKENBERG TYPE)*

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In 1899 Krukenberg[1] reported a case of pigmentation of the cornea under the title "Bilateral Congenital Melanosis of the Cornea"; later, the same writer[2] reported two similar cases. The arrangement of the pigment deposits was peculiar in that the granules were collected in a fusiform or spindle-shaped fashion in the deepest layers of the cornea. Later cases have often been alluded to as Krukenberg's spindles.

In 1910 Holloway[3] searched the literature and found that six cases had been reported. To these he added three that he had observed—the first recorded in American literature. Cardell[4] states, in his article, that about 21 cases have been reported since the original articles by Krukenberg, but mentions that Vogt was able to collect four cases for slit-lamp demonstration. While the literature, especially that of Germany, contains much discussion of pigmentation of the cornea, I have been able to find but seven cases published since Holloway's article that are undoubtedly of the type described by Krukenberg. Three of these were described by Kraupa,[5] one each by Mills,[6] Ezell,[7] Cardell,[4] and James.[8] Augstein[9] states that he has seen six cases in 12,000 examinations, but does not report his cases in detail. Dr. Emory Hill, of Richmond, Va., and Dr. Charles A. Young, of Roanoke, Va., have each described a typical case to me, neither of which has been published.

I have often observed isolated granules of pigment in the deepest layers of the cornea in healthy eyes—in fact, a care-

* Candidate's thesis for membership accepted by the Committee on Theses.

ful examination with the corneal microscope reveals them in a high percentage of individuals; not infrequently tiny unpigmented spots are also found. Moeschler,[10] in a slit-lamp examination of 395 eyes of 201 healthy persons, found some pigmentation in 47.1 per cent., the greatest number being in older people with defective pupillary margins; 6.3 per cent. of the eyes showed a rather heavy pigmentation, and the author remarks, "whether the cases with the heaviest pigment deposits form a transition to Krukenberg's spindles needs further investigation."

It is probable that this condition is not so rare as the scarcity of case reports indicates, although the one recorded here is the only one I have recognized. The spindle is not detected by a casual examination, but must be looked for searchingly with good illumination. Against the dark background of the pupil it is difficult to see with the naked eye, and many cases are no doubt overlooked. As ophthalmologists become accustomed to using the slit-lamp routinely, such anomalies will be found and reported more frequently.

As most of the literature on the subject was written before the advent of biomicroscopy, the following case seems worth while to record:

R. C., aged forty years, consulted me for correction of his error of refraction. He has one sister who is myopic. The irides were grayish-blue. Refraction: R.E. -0.75 sph. $\bigcirc$ -1.00 cyl. ax. $50° = 20/20$; L.E. -1.50 sph. $= 20/20$. During the preliminary examination no anomalies of the corneas were observed. Skiascopy with cycloplegia showed a slight interference with the shadow, similar to that occasionally noted when there are triangular pigmented plaques on the anterior lens-capsule. A more careful examination with oblique illumination revealed a fusiform pigmentation, apparently in the deepest layers of the corneas. The long axes of the spindles were in the vertical meridians of the corneæ, directly in front of the pupils, but slightly nasal to the center in each eye. Slit-lamp examination revealed that the spindles consisted of closely packed dots or granules of chocolate-brown color lying on Descemet's membrane or on the endothelial

cells of the corneæ. With a very thin beam and critical focusing no granules could be found in the plane anterior to Descemet's membrane, as in a case described by a previous observer; nor could I, by using the highest magnification available (×37), detect that the granules consisted of closely set rings with clear

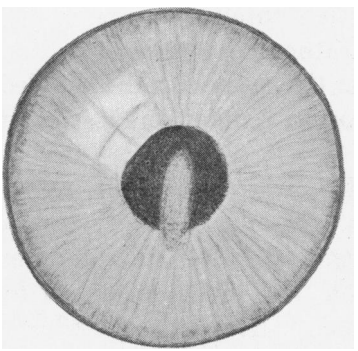

Fig. 1.—Right eye with oblique illumination and loupe.

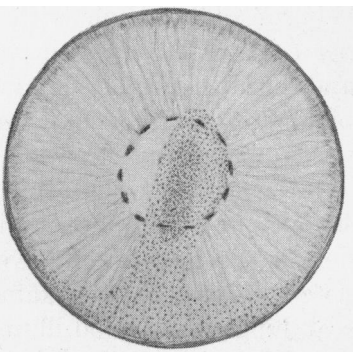

Fig. 2.—Right eye with slit-lamp and corneal microscope.

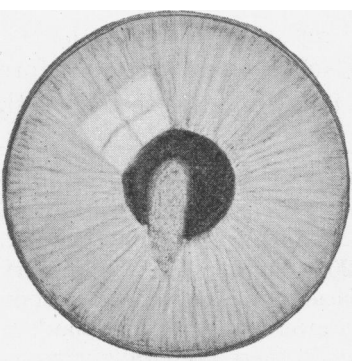

Fig. 3.—Left eye with oblique illumination and loupe.

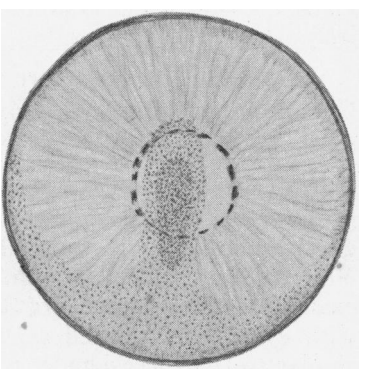

Fig. 4.—Left eye with slit-lamp and corneal microscope.

centers. Viewed in the axis of specular reflection, the pigmented dots seemed to lie in and between the endothelial cells. The corneal microscope revealed that the pigmentation was considerably more diffuse than one would suspect from the examination with the naked eye or loupe. Figures 1 and 3 illustrate the pigmentation

as seen in the right and left eyes respectively, when examined with oblique illumination and the binocular loupe. Figures 2 and 4 represent the deposits viewed through the corneal microscope (magnification ×25). Surrounding the spindles on all sides, rapidly diminishing in numbers toward the periphery of the corneas, were the same chocolate-brown dots. These reached the limbus below, flaring out laterally and mesially partially to encircle the corneæ close to the limbus. In the left eye the thin rim of sparsely packed dots extended as high as the lower border of the undilated pupil. The spindles then were more visible than the other pigmented areas only because, in that location, the granules were much more closely packed than elsewhere. There were no remnants of pupillary membranes and no other anomalies than the myopia and myopic astigmatism.

The puzzling features about this condition are the grouping of the pigment-granules into vertical spindles and the fact that it occurs usually in myopes. That neither of these is an essential part of the picture is shown by the fact that one case, that of Kraemer,[11] had the spindles in the horizontal meridians of the corneæ, and a few cases have been reported in hypermetropic eyes. Nevertheless, the grouping into vertical spindles and the occurrence in myopic eyes is too frequent to be regarded as accidental.

In Krukenberg's first article he offered the explanation that the cause of the pigmentation lay in the approximation of the pupillary membrane to the cornea in a certain stage of embryonic life. Wintersteiner[12] called attention to the fact that pigmentation could not occur at the time the iris and cornea are approximated, because at this time the iris contains no pigment. Stock[13] answered this objection by assuming that the cells remaining on the posterior surface of the cornea after the formation of the anterior chamber possess the power of developing pigment at the time of birth and later. Stock, in an addendum to his original article, reported a case from Professor Axenfeld's private practice which had the characteristics of cases previously reported

except that this one had gray dots instead of pigment-granules. He regarded this as evidence of the correctness of his contention, especially as the individual had gray irides. Stock suggested the name "Corneale Membrana pupillaris perseverans" as more suitable in this type, leaving the appellation "Congenital Melanosis of the Cornea" for the more highly pigmented groups.

Krukenberg was quite positive that fetal inflammation could be excluded as an etiologic factor in the pigmentation because of the bilateral character of the deposits, their site, configuration, and the absence of other evidence of inflammation. In all his cases the irides were brown, and Krukenberg suspected that the condition occurred only in dark eyes and that the pigment was the same as that in the iris stroma. Weinkauff[14] reported the case of a patient with acquired syphilis of two years' duration in which there were closely grouped pigment-granules on the posterior surface of the corneæ. This patient had also spots of choroidal pigment visible in the fundi and vitreous opacities. Weinkauff had not observed this patient prior to the syphilitic infection, and as in uveitis the pigment-spots usually disappear from the center of Descemet's membrane when the iris returns to normal, it is probable that this was a case of congenital pigmentation in a syphilitic. Kraupa[5] states that some cases of melanosis that have been described as congenital are possibly pathologic, and he believes that the pictures of congenital and acquired endothelial melanosis are similar.

The location of the pigment-granules is unquestionably in Descemet's membrane. Augstein[9] writes: "The melanosis corneæ which I saw in six cases exactly similar to that of Krukenberg and Stock always had spindle-shaped brown pigment lying expanded on Descemet's membrane, without entering the corneal lamellæ and without showing formation of threads on the iris." He remarks that melanosis corneæ has nothing to do with membrana pupillaris perseverans.

Cardell[4] states that "microscopic sections show the pigment to be in Descemet's membrane immediately under the cubical endothelium, beginning at a little distance from the angle of the anterior chamber, where the limitation of the pigmentation is sharply defined, and thence fades toward the center of the cornea."

So far as I know, no explanation for the morphology of the vertical spindles has been offered. It seems possible that, as the mesenchyme grows inward between the surface epithelium and lens saccule to form the primitive cornea and anlage of the iris stroma, it might fuse above and below, leaving at some stage a vertical slit (the future pupil) closed by a thin connective-tissue membrane, containing cells which, according to Stock's theory, possess the power of pigment formation. There is no agreement among authorities as to whether at any stage of development the pupil assumes the form of a vertical slit. Fehr (quoted by Greef)[15] thinks the slit-like pupils occasionally found in later life may be a retrogression to a form probably common in the early stages of the evolution of man. Other writers, notably Greef,[15] Tamanscheff,[16] Niederegger,[17] and Lindahl,[18] regard this condition as due to atypical colobomas of the iris. Keibel and Mall[19] show an illustration of the pupillary membrane of a human fetus of eight months in which the vascular loops enter from the periphery, leaving a diagonal slit where the arteries terminate. Textbooks on embryology are remarkably silent on the subject of the formation of the pupil, and further investigation may prove that, at some stage of development, the pupil is not round but vertical, as it is in many animals in post-embryonic life.

It is possible that Turck's theory of the currents in the aqueous humor might have some bearing upon the deposition of pigment. Minute particles in the aqueous may be seen with the corneal microscope in cases of early uveitis. The particles next to the iris ascend slowly, while those further

forward, adjacent to the posterior surface of the cornea, descend. This circulation of the aqueous is doubtless due to difference in temperature in the anterior chamber—that part of the aqueous lying next to the iris having a higher temperature than the portion next to the cooler cornea. Descemet's membrane develops in the human during the third month of life; according to Ranvier, it is deposited from the endothelial cells. If, for some reason which is obscure, pigment-granules should appear in the anterior chamber in early fetal life, they might well be deposited on that part of the anterior chamber where the temperature is lowest—the center of the posterior surface of the cornea. As the endothelial cells form the glass membrane, the pigment-granules may well take part in the process. Neither of these two theories may be the true explanation of the morphology of the spindles, but they furnish food for thought, and until further investigation furnishes more facts to base an opinion upon, we can only speculate as to the etiology.

Any attempt to explain the frequency of congenital pigmentation of the cornea in myopic eyes is purely conjectural. We know little of the pathology of myopia in the embryonic eye. Fuchs[20] states that about 5 per cent. of eyes are myopic at birth. That some inherent tissue weakness exists in the myopic and pre-myopic eye cannot be doubted. The fibrous tunic, which is the tissue primarily involved in myopia, is derived from the same germ layer as the cells deposited in the cornea in congenital pigmentation. Whether there is any significance in this fact awaits upon further knowledge of the pathogenesis of myopia and of congenital pigmentation of the cornea.

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A STUDY OF THE COMPARATIVE ANATOMY OF THE EXTRA-OCULAR MUSCLES*

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What changes take place in the extra-ocular muscles and what are their functions following the various surgical procedures commonly carried out on them? That is, what changes take place in the tendons following the various types of tenotomy and shortening operations, where do the tendons re-attach, how soon does union occur, what type of suture is most effective and for how long? The answers to these questions would be useful, but they are largely speculative at present. It would seem that they can be answered only by studying the after-effects of a series of operations on animals. It is necessary, then, that one become familiar first with the comparative anatomy of the extra-ocular muscles of the common laboratory animals. Such a study would enable one to select the animal best suited for the work and also give familiarity with the anatomic relations of the parts to be studied.

* Candidate's thesis for membership accepted by the Committee on Theses.