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M.D.

Congenital Clouding of the Cornea Affecting Two Sisters.

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CONGENITAL CLOUDING OF THE CORNEA AFFECTING TWO SISTERS.

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This condition is of such rare occurrence that both cases seem to be worthy of record.

Case I.—K. M., four years old. Blue irides. A bluish haze of both corneæ. Some nystagmus. Slight conjunctival injection. The clouding appears to involve the epithelial layers of the cornea, together with the upper layers of the *substantia propria*. Pupils react perfectly. Can discern large objects at a short distance. Both eyes of normal size. The child prefers shady places and avoids the bright light of the sun. Bad teeth, but not the typical Hutchinson's teeth. Very profuse secretion of saliva. Excoriation on upper lip from a long existing running at the nose.

Head well developed, and intellect in keeping with her age. The skin smooth and white. The limbs straight and well formed. Has a good appetite, rosy cheeks, and runs all about. The family physician tells me that at birth the corneæ were almost perfectly blue, and since her birth he has noticed that the clouding has grown less and less, and it is only within the past year that the irides could be seen. The epithelial layers of the corneæ have a granular appearance and lack the usual lustre. The fundus is not to be seen.

Case II.—Jeannette M., ten years old; sister of the former. Well developed and bright. Blue irides. Her mother says that at birth her eyes were exactly like those of her sister. Dr. Cromwell, the family physician, has observed since he knew the family—now six years—that the corneæ have been gradually clearing up. There is present the same distinct bluish haze as in the case of the younger sister, but to a much less degree. The corneæ have not the lustre peculiar to the healthy eye, but still they lack the granular appearance seen in Case I. There is no nystagmus. The child has suffered off and on during her entire life with coryza, the excoriated upper lip giving evidence to this fact. Teeth very unsound, but not as much affected as in Case I. Like her sister, she dislikes bright, sunny days. It is possible to see the fundus, but not distinctly. It appears as though seen through a cloud. She uses her eyes for near work, and reads with considerable ease. The clouding, as is the case with her sister, pervades the superficial layers of the corneæ, and is homogeneous throughout, except in the case of the left eye, in which the returning transparency seems to be more marked at the upper border of the corneæ.

The slight photophobia present in both cases was the only annoying subjective symptom. Whether this latter—as is usually the case in corneal affections—is a reflex disturbance, having its origin in ciliary irritation, I am unable to say. It could have been due to rays of light playing upon a retina not yet accustomed to bright light, a retina which has always been shaded by what the Germans call a darkening—Verdunkelung—of the cornea. And this photophobia was less marked in the older case, seeming to indicate that with the fading away of the corneal cloud the retina was gradually accustoming itself to the increased supply of light as well as to the brighter quality of the rays.

I questioned the mother clearly, but could draw out no specific history. The father had become bald quite early in life. The mother had had eight children. At the birth of the younger of these two sisters she had experienced a great nervous shock, which I do not regard as signifying anything pertinent. After Case I. the mother was delivered of one more child, which died in convulsions six weeks after birth.

I should call the affection then a *diffuse interstitial keratitis*, sluggish in character as it frequently is, indeed almost passive, beginning in the latter part of pregnancy, and gradually disappearing with the further growth and constitutional development of the child.

As I have said, I was unable to gather any information from the mother which would indicate a specific origin, but the whole aspect of the disease, its rarity, and its occurrence in sisters, seem to point to some single and definite cause, and that was most probably an hereditary taint.

The subject of interstitial keratitis, particularly from the point of view of its relations to inherited syphilis, has been the theme of many discussions, and notable among these latter stands out the work of Mr. Jonathan Hutchinson. In his *Clinical Memoir*,[1] Mr. Hutchinson takes the ground that this form of keratitis is the effect of inherited syphilis.

He draws his conclusions from the observation of one hundred and two cases of interstitial keratitis. The point in the diagnosis upon which he lays most particular stress, as indicating inherited syphilis, is the condition of the teeth. "The subjects of this form of corneal inflammation," he says, "almost invariably have their upper central incisor-teeth of the permanent set dwarfed and notched in a peculiar and characteristic manner," the condition commonly known as the "Hutchinson teeth." He has never seen a typical form of interstitial keratitis in which the teeth were of normal size and shape.

Parinaud[2] regards the miscarriages of the mother, the number of deaths among the brothers and sisters as the important factors which

[1] Syphilitic Diseases of the Eye and Ear. A clinical memoir by Jonathan Hutchinson, F.R.C.S. London, 1863.

[2] Arch. gén. de Méd., Nov. 1883.

should lead us to attribute a case of interstitial keratitis to inherited syphilis. In twenty-three out of thirty-two cases he finds these two points well marked. He thinks that diffuse interstitial keratitis is a manifestation of *syphilis atténuée* in the parents. In conjunction with the disease he has frequently found changes in the teeth. These changes, however, may accompany other affections.

The majority of ophthalmic surgeons of the present day, I think, attribute the disease to hereditary syphilis,[1] though this theory has been strongly opposed by Panas, Buffé, Mooren, and others. Panas doubts very seriously the syphilitic origin of the keratitis. "The abnormal configuration of the teeth," he says, "is not always constant, and when it does exist it recalls exactly what we see in rachitis." Another point which, he thinks, strengthens the idea that it has a common cause with rachitis, is that mercurials avail but little in its treatment, and that iodide of potash gives the best results. He suggests the name kératite cachectique diffuse instead of kératite hérédito-syphilitique. Neither Hutchinson nor Panas alludes in his discussion to a congenital form of interstitial keratitis; in short, to cases similar to the ones now reported by myself. Hutchinson[2] asserts that he has never witnessed the occurrence of interstitial keratitis earlier than at the age of two years. The youngest case reported by Panas[3] in his remarks was of a boy twelve years old.

It is undoubtedly true that in a large proportion of cases the disease is developed between the ages of eight and fifteen.

Although the cases reported by me were congenital, I do not regard the disease in itself as differing in one whit from that form of keratitis which has been fruitful of so much discussion, and to which I have just alluded. The outbreak, however, of the inflammation *in utero*, and the exceeding rarity of such an occurrence would appear to justify me in assigning these two cases, and like ones, to a separate and distinct branch of the subject. It behooves me, then, to touch more particularly upon the congenital forms of interstitial keratitis.

The following description of the affection was given eighty years ago by a French writer:[4]

"The child comes into the world with a peculiar form of blindness, due to the darkening of the transparent cornea. This latter is of a dull blue color, and thicker than in the normal state. This trouble appears to be produced by a relaxation of the tissue of the transparent cornea by the presence of a lymphatic humor which is absorbed after birth, most often without medical attention, the cornea becoming transparent at the end of a few months. In such a case the transparency appears first on the outer edge of the cornea, then in a circular direction around its border, and so, from place to place, until the entire cornea has assumed its natural color."

[1] Gaz. des Hôp., 1871, Nos. 139, 140, 142.

[2] Clinical Memoir, etc., p. 116.

[3] Gaz. des Hôp., No. 142.

[4] Mayor: Essai sur quelque maladies congénitales des yeux. Une thèse inaugurale. Montpellier, 1808.

The first cases reported were by Wardrop, in 1739, and by Klinkosh, in 1766. In 1790 there appeared a very interesting report of three cases by Mr. Farar.[1] The children were sisters, and they were born with corneæ so opaque that the irides could not be seen. The opacities gradually disappeared without treatment. In the first and second cases the recovery was complete in ten months after birth. In the third case the clouding had markedly diminished at the end of the first year. At this point he lost sight of the case.

In 1841 Mr. S. Crompton,[2] of Manchester, reported two cases. The children were brothers. One of the cases seems to have been of doubtful origin, purulent ophthalmia might have been the cause. There was no doubt about the younger one. For a history of the older boy the author says he relied very largely upon the testimony of the mother. In the same year I find two cases reported by Mr. R. Middlemore,[3] of Birmingham. When first seen the corneæ were so opaque that the irides were not visible. The cloudings finally disappeared, leaving the corneæ wholly transparent.

In 1855 a most interesting history of this subject was given by Dr. Fronmüller,[4] in his monograph on "Congenital Cloudings of the Cornea." According to Fronmüller, the highest grade of the affection is sclerophthalmus, which is an arrest in the development of the eye, taking place in the first or second months of pregnancy, at the time when there is no difference between the cornea and the sclera, when the former is thick, flat, leucomatous. There is, at this stage, no trace of the anterior chamber, and the iris lies immediately under the cornea. With this malformation we necessarily have microphthalmus. The peripheral cloudings generally have their existence in the third and fourth months of pregnancy, at the time when the watery elements and the anterior chamber form, and when the cornea begins to elevate itself and the lamellar formation is in process of growth. The other congenital corneal cloudings date from the later months of pregnancy. He divides the whole subject into two classes: First, *congenital leucomatous opacities*, in which the lamellar structure of the cornea is absent and there is an arrest in development, the eye being always reduced in size; the prognosis is absolutely bad. Second, *congenital cloudy opacities*, having their seat immediately under the external epithelium of the cornea, the latter preserving its normal texture; the prognosis here is favorable.

The only case that I can find reported in the American medical journals is that by Dr. Bethune,[5] in 1870. The patient was twenty-five

[1] An Account of a Very Uncommon Blindness in the Eyes of Newly Born Children. Medical Communications, vol. ii, London, 1790.

[2] Medical Gazette, vol. xxvii., London, 1841.

[3] Medical Gazette, vol. xxviii., London, 1841.

[4] Ueber die angeborenen Hornhautverdunklungen. Vierteljahrschrift für die prak. Heilkunde, B. xlv. S. 57–70.

[5] Boston Medical and Surgical Journal, vol. v., 1870.

years old. The mother had noticed at birth an opacity the size of a pin's head, and instead of disappearing it had progressively increased in size. This cannot, though, be regarded as a perfectly fair and typical case, for too many important points in the history depended for their existence simply upon the mother's recollection of what the condition was twenty-five years before. It was quite possible that this opacity had its origin in purulent ophthalmia.

The most complete history of the subject I find is that by Hubert.[1] "It may be due," he says, "to an arrest in development, or possibly the clearing up of the cornea goes on unusually slowly, and when delivery comes it is not yet transparent, or it may be the cornea underwent during intra-uterine life an inflammation the traces of which at birth had not entirely disappeared." He refers to the fact, however, that there is only one case on record in which the condition of the eye was due to a clearly defined intra-uterine disease. This case, he says, occurred in the practice of M. Panas, and is that of a woman twenty-five years old. The right eye was perfect in every respect. The left eye was less than half the normal size, and had all the muscular movements except abduction, which was rather imperfect. Of course, there was no light-perception. The patient affirmed that she was born with the eye just as small as it was then, and, to confirm her statement, the conformation of the orbit showed an arrest in development in proportion to the duration of the condition. The mother had gone through with smallpox during pregnancy, and the patient was born with marks of the disease on her body. There were still clearly defined scars on her breasts. Syphilis was absolutely excluded. Here, then, we have the eye disease due to the variola The essay comprises a treatise on the embryology of the cornea, its normal histology, and the pathological changes seen in congenital opacities. He inclines to Hutchinson's view as to its origin.

In 1880 M. Lèclere,[2] in an article on congenital opacities of the cornea, reported seven cases in addition to the ones just quoted in this article. He concludes that such affections are the results of intra-uterine inflammation. In 1883 Couzon[3] reports a case occurring in the practice of Prof. Parinaud. The infant was ten days old when first seen, and was born with opaque corneæ. The latter were the seat of an interstitial keratitis, characterized by a diffuse infiltration which occupied the cornea in its whole extent. The cornea had a pale bluish tint. The opacity hid the iris completely from view. Totally blind. No pericorneal injection. History of congenital syphilis. The child was put

[1] Étude sur le dévelopment de la cornée et sur les opacités congénitales de cette membrane. Thèse, Paris, 1876.

[2] Des opacités congénitales de la cornée. Paris, Thèse, 1880.

[3] Contribution à l'étude de la kératite interstitielle dans la syphilis héréditaire et dans la syphilis acquise. Ibid., 1883.

on iod. potash, and in three months the clouding on the right cornea had nearly disappeared, that on the left cornea had diminished in intensity.

From the preceding it will be seen that the weight of evidence seems to be in favor of the syphilitic theory. If, then, hereditary syphilis be the cause of that form of keratitis most often met with in children between the ages of eight and fifteen, there would be nothing in conflict with such an idea to suppose that this cause can and does sometimes exert its activity at a much earlier stage in the life of the child.

There is, however, another point of view, from which many scientific observers have regarded such cases. Hubert, in his essay, though inclining to the Hutchinson theory, suggests the possibility of such corneal cloudings being due to retarded development. Fronmüller also touches upon this point. One of the strongest advocates of this theory is Steffan.[1] The latter bases his conclusions upon the anatomical examination of an eye in which the cornea was leucomatous everywhere, except at the periphery. He thinks that all such conditions are due to a retarded development on the part of the lens, the sac of the latter being at birth adherent to the posterior wall of the cornea, and thus the cornea was practically wrapped in darkness. Normally the cornea and lens have parted at birth.

The following three cases, occurring in the practice of M. Jules Gérard,[2] a veterinary surgeon, would seem to speak in favor of this theory; certainly the syphilitic theory can be excluded. The colts had a common mother and father. The corneæ in each case were completely opaque, and the affection had evidently commenced *in utero*. They were treated with the ointment of the red oxide of mercury, and they cleared up completely.

Another case is reported by Rückert,[3] and is that of congenital clouding of the cornea in a hog. Rückert admits the possibility of intrauterine inflammations as the cause of such anomalies, but in his case he says that inflammation could be excluded. "Against its inflammatory origin speaks the nature of the tissue in the opaque portion of the cornea. It was impossible to distinguish it from scleral tissue. It was rather a high process of organization which had taken place, for which the peculiar vascular conditions of the area concerned might offer a solution."

It is evident from the brief review of the literature of the subject which I have given, that under the designation of congenital clouding of the cornea conditions etiologically and pathologically different have been described. It seems plain that cases in which the cornea presents

[1] Steffan: Beitrag zur Erklärung angeborener Anomalien der Hornhaut. Monatsblätter für Augenheilkunde, July and August, 1867, S. 209–217.

[2] Kératite du fœtus de l'éspèce chevaline. Archives Médicales Belges, xii., 1870.

[3] Rückert: Ein Beitrag zur Lehre von den angeborenen Hornhauttrübungen. Diss. München, 1885.

a fibrous structure like that of the sclera, in which the lens has not separated from the cornea, in which there is microphthalmus, and in which there is no tendency to improvement of these abnormal conditions, should be separated from the cases in which the only pathological change in the eye is a superficial bluish cloudiness, which has a marked tendency to clear up after birth. The cases belonging to the first category we need not hesitate to refer to arrest or abnormalities of development.

Furthermore, it is urged that, as we have undoubted evidence of arrested development in the first set of cases, cases such as I report may be regarded simply as the slighter grades of this abnormal development. In opposition to this view it is to be said that there are little analogy and not sufficient evidence of transitional forms between the cases of undoubted arrest of development, and the cases of simple diffuse clouding of the corneæ, without other ocular changes. These latter cases of diffuse clouding of the corneæ are indistinguishable in their general aspect from the well-known instances of diffuse interstitial keratitis occurring in childhood, and it is reasonable to suppose that they depend upon similar pathological changes. Again, it will be remembered that physical defects, which clearly owe their existence to a want of completeness in the developmental process of the fœtus, rarely, if ever, adjust themselves in the infant to the proper order of things. Consider the coloboma of the iris, of the choroid, of the lids, the persisting pupillary membrane, and hyaloid artery, all these indicate imperfect and unusual terminations to the process of development in particular regions of the eye. Such imperfections are permanent, they are not remedied under the changed conditions surrounding the subject after birth. And this is quite as true of other parts of the body as well as of the eye.

I am inclined, therefore, to refer my cases of congenital corneal clouding, and similar ones, to intra-uterine inflammation and not to arrest of development.

It will be observed that in nearly every instance more than one member of the same family is afflicted, that relationship plays an important rôle, relationship the result of a common father and mother. In other words, that the offspring were exposed to some specific condition or cause. Such troubles occur in all classes of a population, among the well-fed and under-fed, among the residents in the most healthy situations as well as those of the most crowded cities. These last facts would suggest other than a strumous origin; they would, on the contrary, together with the other well-established symptoms which I have mentioned, speak in favor of the syphilitic origin of such affections.

While this is the position which I am inclined to assume regarding the pathology and etiology of this affection, it must be admitted that

considerable caution should be exercised before reaching any positive conclusion on these disputed points. The fact that an apparently similar affection has been observed in the domestic animals is not easily reconcilable with the theory of its syphilitic origin. Undoubtedly, a conservative view would admit different causes as capable of producing this disease. I am, however, so much impressed with the resemblance between the congenital and the post-natal forms of diffuse interstitial keratitis and the syphilitic origin seems so well established for the latter, and has been demonstrated for a certain number of cases of the former, that for the present, at least, I prefer to regard the congenital and the post-natal forms as etiologically as well as pathologically the same.