

CLINICAL CONTRIBUTION TO THE ETIOLOGY OF DYSTROPHIA EPITHELIALIS CORNEÆ

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In a rather careful survey of the literature upon the subject of corneal dystrophies the writer has been unable to find a single case with diabetes as either the exciting or the indirect cause, barring the instance reported by himself in the Johns Hopkins Hospital Bulletin of May, 1914. In fact, those who have described the condition, Fuchs, Paul Knapp, Troncoso, Reese, Guist, and Uhthoff, have consistently failed to detect any definite etiologic factor whatever. They agree, however, in almost all the following points: that it occurs most frequently in middle life, usually affects the female sex, with a predisposition for the right eye, is usually associated with slight and transitory rises in the intra-ocular tension, and, finally, that the course of the degeneration, as well as the visual diminution, is gradually progressive despite any known form of treatment.

The condition, as such, was unknown until 1910, when Fuchs' interesting monograph appeared, describing the 13 cases he had seen since 1900. As he says, many cases prior to that time had undoubtedly been diagnosed and treated as glaucoma, owing to the elevation of intra-ocular tension and the almost characteristic appearance of the corneal epithelium. Since his splendid description of the course and character of the condition, however, several observers have diagnosed similar cases, and added their reports to the literature upon the subject, a total of nineteen cases.

The slow and progressive course of this condition distinguishes it clinically from any of the inflammations, for the

latter are marked by a period of progression, followed later by one of regression, while anatomically the dystrophies are characterized by degenerative changes as opposed to the cellular invasion of inflammatory lesions.

The majority of dystrophies are the expression either of a local disturbance of nutrition or, as Reese has pointed out, some general malnutrition; for example, the deposits of mucin in myxedematous subjects after thyroidectomy, the grayish-green discoloration of the cornea occurring in disseminated sclerosis, and, according to Weeks, disease of the Gasserian ganglion and traumatism. But to dystrophy of the corneal epithelium no definite etiologic factor has been ascribed. Hence the writer feels some hesitation in advancing his opinion that diabetes was the direct or remote cause in the cases to be reported, even though the diet, insulin, and presence or absence of sugar did so markedly influence the ocular condition.

If the metabolic disease in question did bear some definite relation to the trophic disturbances which took place in the cornea, some interesting conjectures as to the *modus operandi* might be made. Was the process caused by a direct toxic action on the trophic apparatus, for instance, by a temporary flooding of the blood or lymph with diacetic acid or beta-oxybutyric acid? Or was the degeneration purely a nutritive one, caused by a perversion of the pabulum normally carried to the corneal epithelium, and due to a degeneration in the walls of the small blood-vessels? Again, might the bullous condition of the epithelium be analogous to the desquamative dermatitis so constantly observed in diabetes?

Epithelial dystrophy is easily differentiated from family nodular keratitis, from affections due to noxious vapors, from keratitis vasculosa with herpes, from post-operative sclerosis, and from hyaline or fatty degeneration of the cornea.

The pathology of *dystrophia epithelialis corneæ* is rather vague: Paul Knapp contends that it is due to a chronic

edema of the epithelium. Fuchs has had the opportunity of making a microscopic examination of one case. There was grayish opacity and roughening of the surface of the cornea from small vacuoles in the epithelial cells, and *newly formed tissue between Bowman's membrane and the epithelium*. This tissue was homogeneous, and without signs of hyaline or mucoid degeneration. The epithelium covering it was thinner than normal, but the cells were not flattened or hornified. He thinks that in the earlier stages the epithelium is probably thickened and vacuolated.

Uhthoff, writing of degenerative changes of the cornea in 1916, concludes that, in dystrophia epithelialis corneæ, Bowman's membrane is affected very little, if at all, and admonishes against confounding this disease with the so-called dystrophia calcarea of Axenfeld. Four years later he had the opportunity of studying a case most minutely, his results being abstracted as follows:

The patient had had the disease for over ten years, affecting first the right eye, later the left, and presenting the clinical picture accurately described by Fuchs a decade before. In the right eye the dystrophy finally resulted in an intense grayish-white opacity of the entire cornea, barring a narrow strip at the margin with some vascularization. The surface was smooth, but the diseased area was slightly swollen. The superficial layers of a portion of the diseased cornea were removed for examination and the epithelial layer was found thickened, the superficial portion swollen in places. The upper epithelial cells were in places drawn out longitudinally, so that occasionally they seemed to be parallel fibers. The lowest layer of the basal cells alone could be called practically normal, but even here some of them showed pathologic changes. Bowman's membrane was entirely absent. The superficial layers of the cornea were, in places, completely degenerated and transformed into a matted tissue of fine fibers with a sparse amount of degenerated cornea. In other places the corneal tissue was broken down into broad, wavy lines, and edematous. The changes affected the superficial layers of the cornea particularly, while the deeper ones seemed to be still transparent.

CASE 1.—The patient, a negro, aged fifty-three years, married, and a whitewasher by occupation, came to the clinic on June 9, 1913, complaining that, for several weeks prior to that date, there had been gradual diminution in the vision of his right eye, unaccompanied by pain. There seemed to be a "shadow" before his eye, and for the past week the eye had been slightly sore.

Previous medical history negative; no malaria, trauma, or syphilis. Gross inspection revealed a well-nourished, vigorous man with a rather dry, coarse skin, and a coated tongue, but, on the whole, presenting no abnormal appearance.

Minute inspection of the cornea of the right eye with the binocular loupe showed a small, central, superficial, herpetic, epithelial loss, which was clear, uninfiltated, and stained faintly with fluorescein. Midway between the center of the cornea and the limbus a very faint, whitish crescent was seen, evidently lying between the epithelium and Bowman's membrane, or in the anterior lamellæ of the substantia propria. The corneal epithelium itself surrounding this area, and extending to within about 3 mm. of the limbus, was diffusely clouded and hazy, as though edematous; minute distinct vesicles were present. There was only slight congestion of the ciliary vessels, and the iris was normal in appearance, although the pupillary reactions were sluggish. The tension of the globe was not elevated, and the anterior chamber was not shallowed. No view of the fundus could be obtained with the ophthalmoscope. Vision was limited to counting fingers at 40 cm.

The observer's first thought was of a rare, ring-shaped keratitis, which was somewhat borne out by the fact that the crescent later completely encircled the center of the cornea. However, the inflammatory evidences, excluding the vague pericorneal congestion, were so slight, and so out of proportion to the corneal disturbances, that one felt inclined to abandon the diagnosis of an actual keratitis and look upon the condition as a trophic or nutritional affection, an epithelial dystrophy, due, perhaps, to some general dyscrasia, a view which was partially substantiated by finding diminished sensibility of that cornea as compared with its fellow, both being hypo-normal in that respect.

The patient was advised to enter the hospital, and the following examinations were made:

Neurologic and physical: negative. Blood: Pale, slowly coagulable, little fibrin, Hb 68 per cent. R.B.C., 3,650,000; W.B.C., 6200. Differential count: Small mononuclears, 24 per cent.,

large mononuclears, 4 per cent., polymorphonuclears, 70 per cent., eosinophiles, 2 per cent. Blood-pressure, 148 mm. Tuberculin test (von Pirquet), negative. Wassermann blood test, negative.

The patient was placed under an appropriate local and general regimen, with no appreciable change in the corneal condition until June 24, when urinalysis showed a specific gravity of 1030 and 0.5 per cent. sugar. A strict "sugar-free" diet was at once ordered; in six days there was a complete restoration of the corneal epithelium, and on June 30th the patient was discharged and told to report at regular intervals for treatment in the dispensary.

He failed to do so, however, and did not come back until August 18th, when he returned to the clinic with the haziness of the cornea much deeper, more diffusely located, and amounting to a positive stippling, giving the epithelium a roughened appearance, as of glass which had been breathed upon.

It is interesting to note, in this connection, that on an intervening and unrecorded occasion the man returned to the dispensary with a foreign body impacted upon the diseased cornea. My colleague, who was in charge at the time, upon brushing off the particle with a cotton-wound spud, noticed that the hazy epithelium at that situation was wiped away also, leaving clear *substantia propria* beneath. This demonstrates how superficial was the edema.

Upon his return, in addition to an increase in the edema, there was a large, central, bullous loss of epithelium, deeper than the first, and staining markedly with fluorescein. The whitish ring was more pronounced. He was promptly readmitted, and again placed upon a rigid sugar-free diet, close questioning having revealed the fact that he had been partaking freely and indiscriminately of starch-containing foods. The same local and general treatment was ordered as on the previous visit. On this occasion a slight transitory hypertony was several times noticed, although ophthalmometry was not resorted to, because of the epithelial disturbances. In fact, the epithelium did not respond to therapeutic and dietetic measures as rapidly as before, and complete restoration did not occur for eighteen days. This time the patient complained, once or twice, of slight local pain, which was promptly relieved by instillations of a 1 per cent. holocain hydrochlorid solution.

On September 8th he was again discharged from the hospital with the corneal haziness much less marked, while a very dim, undetailed view of the fundus could, for the first time, be obtained with the ophthalmoscope. His vision, 4/100, also showed great

improvement. Urinalysis gave a high specific gravity, 1031, but no sugar, acetone, or diacetic acid. In this connection let it be noted that while the diet caused a loss of weight and less healthy general appearance, the corneal disturbance was steadily ameliorated thereby.

He was next seen on October 10th, when his vision had improved to 20/120, and the edematous haze of the cornea had cleared markedly. The iris was clearly visible, but the white ring was still present, while the corneal apex was marked by a small, almost circular, opaque spot, the site of the previous tissue loss. Four days later, however, 2 per cent. sugar was found, in conjunction with a specific gravity of 1032, although there were no decomposition products, such as acetone or diacetic acid.

Strict dietary instructions were again given him, and he was told to instil 5 per cent. dionin collyrium locally each day.

The man was last observed on October 31st, when the cloudiness had diminished greatly, but below the corneal center, and above the white ring, a small cyst had formed, evidently containing a clear liquid. This was directly beneath the epithelium, and moved in any direction when pressure was made against it through the lower lid. Vision had fallen slightly, being 20/160++ , although a 2.25 diopter convex sphere, tried for the first time, brought it to 20/50.

CASE 2.—W. M. H., white, aged fifty-three years, single, a theatrical manager, experienced the first intimation of ocular trouble on January 25, 1923, while in Wheeling, W. Va., when, because of a little vague annoyance, he consulted a local oculist, who prescribed some simple remedy with the immediate alleviation of the discomfort.

On March 6th, while in New York, the irritation recurred, and within two days became so annoying that he consulted Dr. G. H. Bell, who treated his eyes on four consecutive occasions. As the soreness returned severely in a few weeks, he consulted Dr. C. E. Williams, also of New York, on April 4th, the latter diagnosing "fibrous ulcer of the cornea" and advocating the removal of a molar which proved undiseased and bore out the previous Roentgen diagnosis of normality. On April 18th he left with his company for Trenton, being turned over, by Dr. Williams, to Dr. Howard Ivins, under whose care he remained from April 20th to July 4th. During this period the use of ultraviolet rays seemed to strengthen and relieve the eye.

On July 9th he transferred to Long Branch, N. J., and was treated, up to August 11th, by Dr. W. K. Campbell, who told him that nothing could be done for the eye and that absolute rest alone could avail to relieve him. This he was unable to realize.

On September 13, 1923, he consulted Dr. Dolan, of Worcester, Mass., under whose care he remained until October 19, 1923, when he transferred to Dr. Chapman, of Springfield, Mass., whom he deserted after one consultation, enucleation having been advised. It is interesting to note that the patient had noticed a decided lessening in pain or ache as the months wore on, but an increase in sensitiveness to light and feeling of *ocular weakness*.

The writer first saw him on December 20, 1923, when the above history was given, the patient complaining that the eye had been excessively photophobic and weak for the previous week, the vision unusually blurred, and lacrimation extraordinarily copious.

He was questioned as to his later treatments and it was discovered that constitutional therapy had never been resorted to and that he had been under a local atropin regimen for months. Family ocular and previous ocular history negative, but patient *had had diabetes* for past six or seven years.

Present Condition.—O.D. negative. Lids of left eye swollen, palpebral and bulbar conjunctiva congested, the veins of the latter greatly distended, tremendous circumcorneal engorgement of ciliary vessels. Cornea steamy, grayish, and lack-luster, sensitiveness impaired, epithelium desquamated centrally, surrounding cells edematous, and underlying layers infiltrated. Tension of globe “stony hard” to palpating finger-tips (tonometry not resorted to owing to denudation of corneal epithelium centrally). V.R.E. = 6/6; L.E. = hand movements.

Treatment.—Discontinued atropin and ordered holocain and hot compresses, pilocarpin 0.5 per cent. solution and 5 per cent. solution dionin, advising immediate consultation with Dr. Walter Baetjer, who has epitomized his findings as follows:

“The general data in the case of Mr. H. is about as follows:

“Complaints: (1) Diabetes; (2) eye trouble. The only important points in his history are as follows: General health in the past entirely normal.

“Present Illness: He has had diabetes for six to eight years, but without any effect on his general health unless in relation to his present eye trouble. The trouble with his eye began six to eight months ago, with obscured vision. The condition has been vari-

able, but, in general, has been progressive since that time. The history is otherwise quite normal, except that he has lost from 165 pounds to his present weight of 135.

"General physical examination entirely normal except for the condition of the eyes, which you know about.

"Laboratory Examinations: Negative, except the urine shows sugar in amount of 3.3 per cent. without evidences of any acidosis. Blood sugar, 266 mg. Blood Wassermann, normal.

"On simple diet regulation and insulin the urine became and remained sugar free and the blood sugar dropped to normal. I heard from him the last time on April 14th, at which time his urine was still sugar free and he was apparently feeling very much better. I have, of course, more detailed notes that I will gladly send if you want them."

Under insulin injections and local regimen, eserine being substituted for pilocarpin, tension was reduced from +3 to +2 on December 28th, and normal on December 31st. Later aspirin was exhibited for the persistent symptoms of iritis, and dionin increased to 10 per cent. solution. By January 10, 1924, he was greatly improved, the cornea clearer, the epithelium regenerated, and the circumcorneal congestion diminished, while the sense of weakness was less noticeable.

As he had to leave for Cleveland with his company he was referred to Dr. Clark of that city, who continued the same local treatment with the result that, on January 24th, he wrote: "The eye feels pretty good, stronger, and I think the sight a tiny, winy bit better."

Next he went to New York, writing, on February 14th, that the "eye has been pretty good ever since I left your care." He was instructed, by return mail, to place himself in Dr. John Wheeler's care immediately, whom he consulted on February 21, 1924, and who wrote, under date of February 25, 1924, as follows:

"I found the left eye doing well and Mr. H. was almost free from symptoms. I advised him to continue the treatment you ordered. I should consider your diagnosis the proper one, namely, dystrophia epithelialis corneæ. The slit-lamp corneal microscope examination reveals cysts of the epithelium and facets where the cysts have ruptured. The cornea is nearly anesthetic now and there is very little discomfort."

On February 29th, after his second visit to Dr. Wheeler, the patient wrote that he had been discharged and told to continue

with the same treatment. He added that his eye felt much stronger but that his vision was unimproved.

On March 6th the patient told of the continued ocular relief and stated that Dr. Tenney, of the Fifth Avenue Hospital, had just reported both blood and urine "sugar free," and that the insulin injections had been reduced to once daily.

The last report, April 14th, was just as favorable, urine sugar free, blood sugar normal, and patient feeling constitutionally and ocularly "very much better."

DISCUSSION

DR. T. B. HOLLOWAY, Philadelphia: I have seen two of these cases of epithelial dystrophy, the first was at the Polyclinic Hospital about 1916, in which but one eye was affected. Unfortunately, the woman was examined too freely the first day at the clinic and never returned.

In 1919 another case came under observation, in this instance with bilateral manifestations. This man gave a history of first noting trouble ten years prior to the time of examination. The failure of vision was slow but progressive. The manifestations were absolutely typical, inasmuch as he had the diffuse central haze of the cornea with disseminated clear or black spaces which Dr. Whitham has described. Certain of the lesions in the left eye, if situated deeper in the cornea, could readily be mistaken for a rupture of Descemet's membrane. These were not the ordinary round vesicular lesions, such as we are accustomed to see, but linear, and extended a quarter of the distance across the cornea.

Dr. Whitham has referred to the pigmentation that occurs in patients with symptoms simulating multiple sclerosis. How any one could possibly confuse the pigmentation that occurs in such cases with epithelial dystrophy is beyond my conception. The pigmentation in the former is a distinctly peripheral manifestation encircling the cornea and extending but 3 or 4 mm. toward the central part of this membrane. These cases were first described by Salus and Fleischer. As far as I know, the only case on record in this country is the one recorded by me about ten years ago. Still further, in this type the pigmentation is deep. If I mistake not, these cases are now grouped with those first described by Wilson as instances of bilateral degeneration of the lenticular ganglion and to which I referred in my paper on this subject.

The lesions of epithelial dystrophy are more apt to be central and are superficial.

I might add that the lesions in my second case had a slightly rusty color. This man is in a profession allied to our own, but I have never been able to persuade him to come into the hospital for a complete medical examination. I do know he did not have sugar in the urine at the time he was under observation. What his sugar tolerance would be I have not the slightest idea.

DR. LLOYD B. WHITHAM, closing: From my experience with these two cases I believe it would be advisable in investigating any case to have an examination for blood sugar. I believe that bears more relationship to the condition than the urine.

TWO CASES OF TRAUMATIC KERATITIS IN THE NEW-BORN

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The two following cases of traumatic keratitis in the new-born are of special interest because of the findings in the corneæ with the slit-lamp. The pathologic changes underlying this disorder have been well understood since the classic article of Thompson and Buchanan,¹ to whom we are also indebted for our first general description of the clinical picture; but up to the present time apparently no one has had the opportunity of studying these changes with the Gullstrand apparatus.

CASE I.—Mrs. —, aged thirty years, a patient in the University Maternity Hospital under Dr. J. W. Duncan, was seized with labor pains at 6 P. M. on June 2, 1918. The following day, because of inefficient uterine contractions and irregularity of the fetal heart-beats, forceps were applied (mid-forceps case), and the child was delivered at 4.10 P. M. Great difficulty was encountered in this case owing to the fact that the head presented face to pubes. The pelvic measurements were normal.

The child was of normal size, and weighed eight pounds. It was