droplets infiltrating the substantia propria in the posterior layers. There are many pits in the endothelium arranged in arc-like manner on the nasal side. In the second stage there is a coalescence of the droplets and the cornea loses its transparency accordingly. A vascular ingrowth continues, with straight entering arteries and wider, irregularly coursing venules. The eye with the disc-like infiltration and posterior bulging has apparently become quiet, so far as uveitis is concerned. There is astonishingly little evidence of inflammatory change outside of the cornea.

DYSTROPHY OF THE CORNEAL ENDOTHELIUM (CORNEA GUTTATA), WITH REPORT OF A HISTOLOGIC EXAMINATION

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Few articles have been written on this subject and the condition is not very generally recognized. I have been interested in this disease for several years, and have made some observations that seem worth recording. So far as I know, there has been but one previous effort made to tabulate the incidence of the disease, and this covered only a small series of cases; and only one other case has been studied clinically and the eyeballs subjected to histologic examination.

Vogt[1] first called attention to the condition in 1921. He described it as consisting of "drop-like endothelial prominences"; in 1930, in the second edition of his Atlas,[2] he defines it under the name of "cornea guttata." In 1924 Basil Graves,[3] in his report to the Lang Clinical Research Committee, described the condition under the title, "A Bilateral Chronic Affection of the Endothelial Face of the Cornea of Elderly Persons, with an Account of the Technical and Clinical Principles of Its Slit-Lamp Observations." Dr. Daniel B. Kirby,[4] in 1925, published a short article entitled, "Excrescences of the Central Area of Descemet's Mem-

brane," and in the same year Drs. Harry and Jonas S. Friedenwald[5] referred to five cases they had studied, with three others that showed epithelial dystrophy, together with advanced endothelial changes. In 1931 Dr. Luther C. Peter[6] described the condition under the title "Dystrophy of the Corneal Endothelium." This name seems to be the simplest and most suitable designation yet offered.

Several years ago, while examining a woman aged forty years, I discovered a condition on the back of the cornea that interested me greatly. Her vision was a trifle below normal, and in seeking the cause I could find nothing until the examination with the corneal microscope was made. It was then noticed that, on sweeping the beam across the cornea, innumerable bright lines appeared on the deep face of the cornea. When viewed in the axis of specular reflection, dark areas several times the size of the endothelial cells were seen, surrounded by a mosaic of normal cells. I puzzled over the condition for months, until Dr. Kirby referred me to Graves' article. Since then I have made routine slit-lamp examinations on hundreds of patients and have seen the condition many times. I cite this experience because many well-informed ophthalmologists who use biomicroscopy somewhat cursorily have told me that they have never observed the affection.

Previous writers have given excellent descriptions of the disease and of the technique employed for its recognition. The condition is always bilateral, although it is often more advanced in one eye than in the other. The early stages can be recognized only by means of the slit-lamp, but more advanced cases may readily be seen with the ophthalmoscope. Beginning in the central area of the cornea, the first sign that can be observed is a few bright silvery lines or flecks, irregular in contour. Graves has well designated these as "glints." They are seen best just outside the posterior reflecting zone. These peculiar silvery reflexes are no doubt due to the fact

that the posterior surfaces of the excrescences act as concave mirrors. Those who are conversant with slit-lamp technique are familiar with the mosaic of hexagonal cells that is seen when the corneal endothelium is in the axis of specular reflection. To obtain this view the arm of the slit-lamp must be at right angles to the tube of the microscope, and the latter must be in critical focus. The observer looks through one eye-piece and observes the condition of the cells; then he shifts the light laterally a short distance, and through the other ocular views a different area. By having the patient shift the gaze, any spot on the corneal endothelium may be examined in the axis of specular reflection. In early cases of dystrophy, when the central area of the cornea is thrown into the axis of specular reflection, a few dark areas several times the size of an endothelial cell and surrounded by normal endothelium will be seen.

As the disease progresses it spreads from the center toward the periphery, and the normal endothelial cells become fewer. The glints may be observed over a larger area, and the dark areas in the posterior reflecting zone become numerous. Vision is impaired but little, if at all, at this stage. In the third stage no normal endothelial cells are found in the central area, and by direct inspection with the corneal microscope Descemet's membrane is seen as a distinct white line, irregularly thickened. At this advanced stage, fine, dust-like pigment-granules are often seen between the excrescences; when they are numerous, this pigment probably reduces the visual acuity. It will be remembered that the normal Descemet's membrane cannot be distinguished optically from corneal stroma. At this stage, with the +20 lens of the ophthalmoscope, the appearance is that of glazing of the deep part of the cornea, but details are lacking. This is best seen against the dark background of the dilated pupil. Two other methods of examination by the corneal microscope give characteristic pictures. Retro-illumination

from the iris presents much the same appearance as raindrops against a window-pane when viewed from within. With a dilated pupil and the microscope focused on the endothelial face of the cornea in the axis of specular reflection from the posterior lens capsule, the excrescences appear as discrete, well-defined, rounded areas which Graves has called "punctate elements." At this stage vision is usually reduced one or two lines. In the most advanced stages of endothelial dystrophy the corneal epithelium is sometimes unhealthy. In one of my patients in this stage, placing a tonometer on his cornea caused such severe destruction of the epithelium that it was necessary to place him in the hospital, where he reremained for several days before healing took place. I have studied several cases in which the vision was lowered to 6/21 in which no cause for the reduction could be found except the clouding of the deep face of the cornea. It is true that often in such patients a clear view of the macular region cannot be obtained.

The pathogenesis of this condition is obscure, but it is probably degenerative in character, and is merely an amplification of the process that produces Hassall-Henle warts, which are commonly found near the limbus and have been regarded as a senile change. The fact that dystrophy never occurs in young persons suggests that it is a senile or presenile condition. However, many aged persons show no evidence of this change, although careful search with the corneal microscope will reveal an occasional "glint" in a large percentage of persons over forty. It is a singular fact that drusen are not found oftener with the ophthalmoscope in cases of dystrophy than in those without it. We know that Descemet's membrane is a glass membrane, and that it is laid down by the endothelial cells, which are mesoblastic in origin. Unlike Bowman's membrane, Descemet's membrane has a marked tendency to regenerate and to respond to insult by over-regeneration. Graves adduces the theory

that the endothelium, threatened in places with loss (senile?) of its very necessary impervious qualities, may, in an attempt at forming a protective barrier against the incursion of the aqueous, resort to the formation of hyaline material. If one regards Descemet's membrane as a hyaline substance, this is a fair assumption. My sections show that the excrescences are similar in every staining characteristic with that membrane, which is apparently mostly elastic tissue. Vogt believes that a close relationship exists between cornea guttata and Fuchs' epithelial dystrophy. This observer is of the opinion that in certain cases, due to the thinning of or absence of endothelium over the excrescences, aqueous may enter the cornea and produce permanent injury to the stroma and the epithelium. This may account for the epithelial changes in certain advanced cases, although in such eyes, when dystrophy is uncomplicated by inflammatory lesions, I have seen no evidence of injury to the parenchyma of the cornea. Drs. Harry and Jonas S. Friedenwald express the opinion that the endothelial changes described are to be considered as the beginning of the epithelial dystrophy of Fuchs, although many cases do not reach the terminal stage in which the epithelium is involved. They quote Kraupa as sharing this belief.

Recognition of this affection by the corneal microscope presents little difficulty, although a few conditions simulate it very closely. Occasionally, in acute iridocyclitis, there is seen a bedewing of the posterior surface of the cornea which gives rise to a glistening appearance resembling that of dystrophy. However, when viewed in the axis of specular reflection, the cell outlines are obscured, and the deposits are smaller and more irregular in size than are those of dystrophy. This appearance subsides as the signs of inflammation disappear. A similar appearance follows perforating injuries of the cornea, but this lasts only two or three days. I have observed these pictures in low-grade uveitis, also following an

iris inclusion operation for glaucoma simplex, and in vascularized corneas years after an attack of interstitial keratitis. I have always regarded the type of bedewing of the endothelium found in inflammatory conditions as due to edema of the cells, but Vogt asserts—and Harrison Butler agrees with him—that it is caused by the deposit of lymphocytes on the endothelium and that there is no posterior edema.

The cases I have studied in an effort to establish the approximate incidence of the disease have brought out some interesting facts. The data of the 800 patients here tabulated were taken from the records of private patients examined in my office. Four in this series had well-marked Krukenberg's spindles, which indicates that this condition is less rare than is commonly supposed.

Males....359
Females..441
800

Age	*21–30 yrs.*	*31–40 yrs.*	*41–50 yrs.*	*51–60 yrs.*	*61–70 yrs.*	*71–80 yrs.*	*81–90 yrs.*
Number of patients.....	172	194	229	91	74	34	6
Dystrophy:							
Male.....	0	2	5	4	1	1	0
Female.....	0	9	15	6	7	3	0

13 males.....3.62 per cent. males examined
40 females.....9.07 per cent. females examined
6.62 per cent. all patients examined

Dystrophy is found in some degree in over 6 per cent. of adults. Moeschler[7] found it in 4.5 per cent. of 176 eyes in persons over fifty. It begins in the fourth decade of life. In the series the youngest patient to show the condition was thirty-two years of age. It is about three times as frequent in women as in men. The advanced cases always occur in elderly persons, the youngest of this series being a man of fifty-nine. These cases have not been watched for a sufficient length of time to warrant a statement that they represent

different stages in the same process, although I have observed in one patient, within four years, a decrease in vision from 6/12 to 6/21, and an apparent concomitant increase in the clouding of the deep layers of the cornea. Vogt states that he followed a case for fifteen years and watched a definite increase in prominences with a reduction of vision to 6/12. Although it is true that in advanced cases other evidence of degenerative disease is often present, I do not believe that it is found more commonly with dystrophy than without it in persons of like ages. Many well-advanced cases in my series showed no other evidence of disease.

The sections are from the eyes of a man, aged seventy-two years, whom I first examined June 9, 1932. His corrected vision was O.D. 6/21; O.S. 6/30−. In the right fundus there was a flat hemorrhage just below the macula. In the left fundus there were several areas of degeneration in the macular region and a few tiny hemorrhages. In the left eye the visual fields showed an absolute scotoma reaching from the periphery of the nasal field temporally almost to the blind-spot, just sparing the fixation point. In the right visual field there was a small absolute scotoma below and nasal to fixation. The peripheral fields were moderately and irregularly contracted. At the last examination, September 3, 1932, the vision was unimproved, and the appearance of the fundi had changed but little, except for the absorption of some hemorrhagic areas and the appearance of a few new ones. There were a few spicules in the left lens; the right lens was clear. By oblique illumination a clouding of the corneas could readily be seen, and with the ophthalmoscope it was observed that the deepest layers were involved. Examination by direct inspection with the corneal microscope showed that Descemet's membrane was a heavy white line, irregularly thickened toward the periphery. Outside the posterior reflecting zone the back of the cornea gave a reflex resembling beaten silver. I could find no endothelial cells in the central area, but in a rim about 3 mm. wide inside the limbus endothelial cells could be seen between the excrescences, which were numerous and large. The corneal epithelium was smooth and showed no irregularities or areas that stained.

A few weeks after the last examination the patient died of pneu-

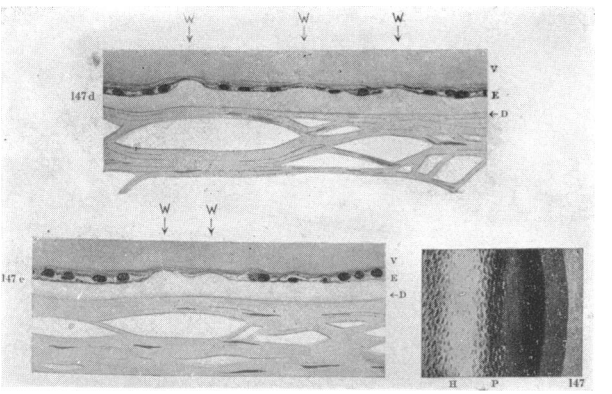

Plate 1.—(From Vogt's Atlas.) W, Excrescences. V, Aqueous. E, Endothelium. D, Descemet's membrane. 147, Beaten-silver appearance of deep face of cornea. (Photomicrograph × 460.) 147 d and 147 e.

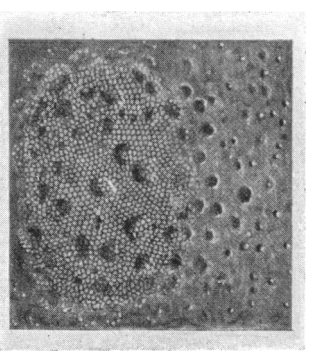

Plate 2.—(From Vogt's Atlas.) Endothelium and excrescences in axis of specular reflection.

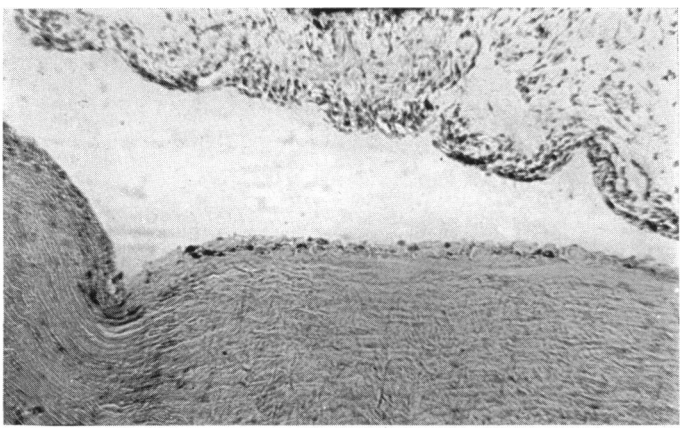

Plate 3.—Peripheral area of Descemet's membrane. (Goar's case.) (Photomicrograph × 120.)

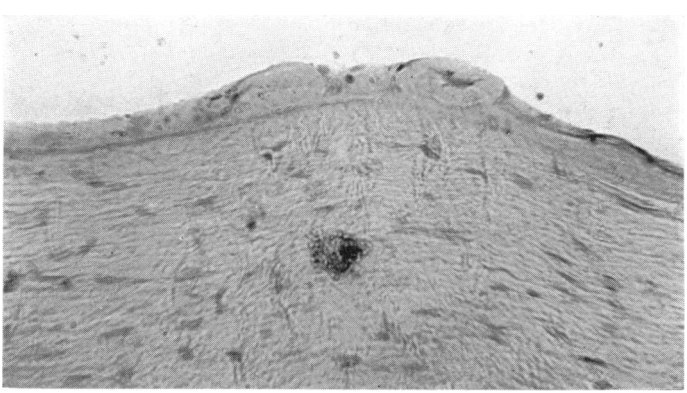

Plate 4.—Excrescences in central area. (Goar's case.) (Photomicrograph × 350.)

monia. I was unable to obtain the eyeballs before embalming was done, but the corneas were well preserved. In certain areas the sections showed the excrescences very prominently. Descemet's membrane was two or three times its normal thickness, and the thickening was somewhat irregular. The central third of the membrane contained some excrescences; the outer thirds contained a great many—in places they were so numerous that they appeared to be piled one upon another. Some of the warts were flattened, with broad bases; others were semi-spherical or ovoid. Descemet's membrane was thickest in the areas where the excrescences were most numerous. Differential tissue stains showed that the excrescences and the membrane had identical staining properties. The endothelium consisted for the most part of a single layer of cells, but in certain areas there appeared to be more than one layer. In these areas the cell bodies appeared to be edematous, but this may have been a postmortem change. Mitotic figures were not found. The cytoplasm of the endothelial cells contained many pigment-granules. Over the excrescences the endothelial cells were evident only by their nuclei, and these, together with the pigment-granules, were frequently crowded in between the closely packed excrescences. The corneal stroma and the epithelium appeared to be normal. There were few excrescences of the lamina vitrea of the choroid.

Vogt gave the first anatomic description of the condition, as well as the first report of its clinical characteristics in the living eye. The eye was that of a woman, aged fifty-five years, removed because of intumescent cataract and glaucoma associated with a myopia of 10 D., in which Vogt had previously found cornea guttata of a mild degree. His sections show excrescences that are somewhat flat and differ only from Hassall-Henle warts in that they are in the center of the cornea. Most of the prominences are directed toward the anterior chamber, but occasionally one is reversed. The endothelium over the warts is thin, and the nuclei usually are lacking. This case of Vogt's was much less advanced both clinically and histologically than the one I have described.

SUMMARY

1. Dystrophy of the corneal endothelium, or cornea guttata (Vogt), is a clinical entity occurring in some degree in about 6 per cent. of persons over twenty years of age.

2. It usually begins in the fourth or fifth decade, and is three times as common in women as in men.

3. It is a chronic, slowly progressive disease of the corneal endothelium, resulting in irregular thickenings and excrescences of Descemet's membrane. These excrescences are usually directed posteriorly, and the staining properties are identical to those of the membrane from which they are derived.

4. Advanced cases of this disease reduce the vision very materially, and these may be recognized by oblique illumination and with the ophthalmoscope. Early cases may be diagnosed only by biomicroscopy.

5. Epithelial dystrophy is often found in advanced cases, and it may be the late stage of the process which is represented by endothelial dystrophy as an earlier stage.

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DISCUSSION

DR. ROBERT VON DER HEYDT, Chicago: The condition reported is that first described by Hassall in 1846. It is not an endothelial dystrophy, because the changes in the endothelium are secondary. In the type called cornea guttata by Vogt, the changes begin in the middle of the cornea. In that first described by Hassall-Henle, Mueller, and Leber they begin in the periphery. In both instances the original change is a wart-like posterior excrescence on Descemet's membrane. In the type beginning in the middle of

the cornea, which may be called cornea guttata centralis, the secondary changes, such as the denuding of the endothelium on the apices of the excrescences, may be due to a trauma of the convection current. This secondary change may cause an imbibition of the corneal tissues by aqueous fluid, and thus bring about the epithelial dystrophy of Fuchs. This has been suggested by the findings of Vogt, Graves, and Friedenwald.

In my office practice I examined 22 cases of cornea guttata centralis during 1932. Eighteen of them were in women and four were in men. In four cases the process was so far advanced that it caused the epithelial dystrophy of Fuchs. Cornea guttata centralis, as well as cornea guttata marginalis, should be classified among the senile changes of the cornea.

DR. LUTHER C. PETER, Philadelphia: In 1931 I reported 22 cases of endothelial dystrophy before the Pacific Coast Oto-Ophthalmological Society, and my experience coincides practically with that of Dr. Goar. I am impressed with his statistics regarding the frequency of this condition, but probably he found more cases than I did, because my slit-lamp studies are only routine after the age of forty. Under this age the slit-lamp is used as indicated. The youngest of my series was forty-two; the average age was sixty years. In all the cases reported the incidence of either incipient senile cataract in some stage or nuclear cataract was significant.

The type of patient in whom I found the condition was interesting. In every instance there was evidence of lowered general health. As Dr. Goar states, it is associated undoubtedly with senile or presenile changes.

From a clinical standpoint, lowered vision is important, because this occurred in a number of instances in which cataract did not contribute. Another phase of importance is the significance of this condition in relation to surgery. In my experience these patients are not good surgical risks. I have operated on several patients for cataract complicated by advanced stages of this form of dystrophy, and in each instance there was delayed healing of the wound. I do not think that it is of itself a contraindication to intra-ocular surgery. It is, however, the accompanying general condition that, in the presence of advanced dystrophy, renders the patient a poor surgical risk.

DR. SANFORD R. GIFFORD, Chicago: Since the relation of this condition to epithelial dystrophy has been discussed, I am much interested and would like to mention two points.

The first is the question of the clinical distinction between the two conditions without the use of the slit-lamp, because I believe we should be able to distinguish at least advanced cases on ophthalmoscopic examination. We cannot expect that every case will be examined with a slit-lamp. In cornea guttata the changes can be seen easily with the ophthalmoscope. These excrescences are fairly large, and they are regularly spaced. In epithelial dystrophy, on the other hand, with the slit-lamp we can see very fine droplets that can barely be seen with the ophthalmoscope with a +20 lens. They are much more numerous in epithelial dystrophy, and are irregularly spaced. Of course, when we examine these droplets with the slit-lamp, we find that the epithelial changes stain with fluorescein, whereas the excrescences do not stain.

There has been some discussion by various other investigators as to the relation of epithelial dystrophy to this condition, and a number of observers believe that in most instances, when they see epithelial dystrophy, they will find guttata also. I must insist that I have seen some far advanced cases of epithelial dystrophy without this change, and that there are mild cases of epithelial dystrophy with fine epithelial changes and almost no change in the deeper layers of the cornea which have nothing to do with this condition at all, but which may simply coexist in the same subject. I believe the advanced cases are likely to have both conditions, but not necessarily so.

DR. EVERETT L. GOAR, closing: I agree with Dr. von der Heydt that cornea guttata is probably an amplification of a process similar to that resulting in the so-called Hassall-Henle warts. The difference is that the excrescences of cornea guttata appear first in the central area of the cornea and spread toward the periphery whereas the Hassall-Henle excrescences do just the opposite. The excrescences in the central area become much more numerous than those that originate near the limbus.

Dr. Peter states that in practically all his cases he finds some evidence of cataract. This has not been my experience. Advanced cases of dystrophy are usually found in patients over sixty years of age, and naturally such patients show a fairly high percentage of lens changes. I have seen many eyes that showed no other evidence of disease than dystrophy. I do not believe that endothelial dystrophy is an early stage of epithelial dystrophy. The former condition is fairly common; the latter is rare. Many

advanced cases of endothelial dystrophy have smooth, normal epithelium. In the one case of true epithelial dystrophy of the Fuchs type that I have seen since beginning this study there are only a few excrescences on Descemet's membrane. The sections I have shown are from advanced endothelial dystrophy, yet the epithelium and corneal stroma appear to be normal. In certain persons there may be some relationship between the two diseases, but I am inclined to believe that it is a mere coincidence if they do occur in the same eye.

TUBERCLE-LIKE NODULES OF EPISCLERA AND EYELIDS, BILATERAL*

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The following case is reported for the reason that it is unique in my experience, and because it presents a picture interesting from clinical, pathologic, and differential diagnostic viewpoints.

Mrs. W. F. D., aged fifty-six years, whose general health had always been good, was first seen on November 25, 1932. She complained of extreme fatigue, puffiness of the eyelids, and inflammation of the eyes.

Family History.—The patient's father died at the age of eighty-two. During his later years he suffered from glaucoma. A brother had had one eye enucleated on account of a malignant growth.

Past History.—Aside from the diseases of childhood, and later a slight arthritis, the patient's health had been excellent. Eighteen months before examination she noticed puffiness of the eyelids and painless swelling over the external eye muscles. Fifteen months later a diagnosis of chronic glaucoma in the right eye was made.

Present Illness.—Six weeks ago she consulted the late Dr. Hilliard Wood, who examined the tumors of the eyelids, and wrote: "Their nature I do not understand." He diagnosed the bulbar lesions as "episcleritis." Recently the swellings in the eyelids and over the muscles of the eyes have increased.

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