THE PATHOGENESIS OF DISCIFORM DEGENERATION OF THE MACULA*

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In 1875 Pagenstecher described the macroscopic and microscopic appearances of a macular lesion found in an eye after its removal for adherent leukoma and secondary glaucoma. His descriptions and illustrations of this lesion leave little doubt but that the eye was affected with what is now known as disciform degeneration of the macula. Pagenstecher's is the first case of this disease that we can find recorded in the literature. He designated the condition *choroidioretinitis in regione maculae luteae.* The term *degeneratio maculae luteae disciformis* was first used by Oeller in 1905. In 1926 Junius and Kuhnt adopted this term, substituting, however, the word "Netzhautmitte" for "macula lutea," and definitely established the condition as a disease entity. A number of other designations for the disease employed prior to the publication of their monograph are found in the literature. The term favored by Junius and Kuhnt, although in several respects misleading, is the one now generally accepted. Following is an analysis of all the cases of senile disciform degeneration at the macula reported in the available literature. There were 84 cases of the disease, comprising 129 affected eyes. Thirteen of these eyes were examined microscopically. The three cases to be described in this paper are not included in the analysis.

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Analysis of Recorded Cases of Senile Disciform Degeneration of the Macula

Race.—No patient was stated to be other than white, but only a few reports specified the race of the individual.

Frequency.—There is no doubt but that the cases described in the literature represent only a fraction of the total number of those recognized as disciform degeneration at the macula. Kahler and O'Brien state that 12 cases were seen in one year in the ophthalmologic clinic of the State University of Iowa.

Age.—The majority of cases occurred in the fifth and sixth decades of life. The youngest patient was thirty-nine years of age (Neame), and the oldest was eighty-three (Kahler and O'Brien). The average age for the entire group was sixty-eight. Age, therefore, was a definite factor.

Sex.—Of the 84 patients, 47 were male and 34 female, and in 3 instances the sex was not stated.

Trauma and Inflammation.—There was no evidence that trauma and inflammation were factors in the disease.

General Condition.—Many of the reports contained little more than a description of the ocular lesion. Nineteen of the patients were recorded as having general hypertension. Fifteen had general arteriosclerosis. Eight cases were cardiac and four were nephritic. Four were diabetic. Only three were luetic. One patient was known to have lived eleven years after the ocular condition was first observed. Eight patients died from coronary disease.

Eye Affected.—In 39 cases the condition was unilateral, the right eye being affected in 18. In 21 of the bilateral cases it was determined that the right eye was the first affected in 12.

Symptoms and Mode of Onset.—In all cases central vision in the affected eye was greatly impaired or completely abolished when the patient first came under observation. Some patients noted a positive central scotoma. In no case was there any marked improvement in vision during the progress of the disease. It is impossible to determine whether the disease had the same mode of onset in all cases, and whether

the onset was gradual or sudden. The fact that only gradual loss of vision was noted by most patients may have been due to preceding development of senile macular changes which prevented any subjective recognition of the onset of disciform degeneration even if this onset was actually abrupt. In a few cases the patient complained of disturbances in vision, such as loss of acuity, metamorphopsia, and photopsia, before any definite lesion could be seen with the ophthalmoscope, but here again it is not clear that these were prodromal symptoms of disciform degeneration. On the other hand, when a patient stated that the loss of vision was sudden, it may actually have been gradual but only suddenly discovered. The only positive evidence regarding the mode of onset was that furnished by 12 eyes. In each of these the onset was undoubtedly sudden, since a subretinal hemorrhage was observed at the first ophthalmoscopic examination.

Except for Pagenstecher's case in which there was glaucoma secondary to adherent leukoma, glaucoma was not known to have developed in any case.

Ophthalmoscopic Signs.—In 12 eyes there was first observed a subretinal hemorrhage in the macular region, which elevated the retina in the form of a mound. Other hemorrhages adjacent to this were seen, and these, usually described also as subretinal, often outlined the mass. More remote hemorrhages were often described as occurring within the retina. These were observed to disappear, and new ones to occur at other points. In the majority of cases the lesions were first observed at a later stage, and in these adjacent hemorrhages were noted less frequently. However, in 75 of the 129 eyes hemorrhages were seen, and in 36 eyes hemorrhages adjacent to the mound were still in evidence.

The mound, as seen early, was described as grayish, greenish, or almost black. Later it became white, except for some pigment deposit. The retinal vessels in front of the mass were always visible. In several cases arteriovenous communications were noted. The mound varied in size from one-

half to several times that of the optic disc. In some cases it reached a considerable height—in one case that of six diopters. In some instances it showed central dimpling. It was usually more elevated early in the course of the disease and often appeared to "settle" as the disease progressed.

The margins of the mound were usually very distinct. Almost always at least a portion of the edge was sharply etched out against the adjacent retina. Its shape was often disciform, but sometimes it assumed another contour. The mass was situated in the macular region, between the superior and inferior temporal vessels. Only very rarely did the lesion exceed the limits of these vessels.

Associated Fundus Changes.—Sclerosis of the retinal vessels was recorded as existing in only 25 out of 129 affected eyes. In each of the five cases which later became bilateral the second eye exhibited senile macular changes before the disciform lesion developed. These senile changes included drusen, pigmentary deposits, and white spots in the papillomacular region and along the macular vessels. In 37 unilateral cases the other eye showed senile macular changes in 15, and was reported normal in only 16—four eyes had senile cataracts which prevented examination of the fundi and two had been enucleated for other causes.

In 61 eyes white or yellowish-white spots of degenerative or exudative nature were found near the lesion during some stage of its progress. These ranged from small pinpoint spots deep in the retina, to frank circinate retinitis in 22 eyes. In two of the latter circinate retinitis was observed first, and in one case fourteen months, and in the other a few months, later disciform degeneration was also found to be present. In the other cases circinate and disciform lesions were seen simultaneously, and it was impossible to determine which condition occurred first. In a case reported by Spicer in his discussion of Lawford's paper, and not included in this series, circinate retinitis existed in the other eye, and we have recently seen a similar case. In one case, briefly re-

ported by Neame, it is stated that angioid streaks were present in the other eye. In a unilateral case reported by Davis and Sheppard, and referred to again below, angioid streaks were present in both eyes. Feingold stated that "similar changes in the macula were observed in a patient showing all the characteristic fundus changes of angioid streaks," but gave no further details regarding the eye.

Microscopic Findings.—Thirteen eyes were examined microscopically. One eye was removed for glaucoma secondary to adherent leukoma, four were enucleated for suspected tumor, and eight were removed postmortem. The findings in these eyes can briefly be summarized as follows:

1. The retina over the mass was found to show degenerative and atrophic changes in all but two cases. These were believed by most observers to be secondary changes.

2. The pigment epithelium in all cases was seen to be markedly proliferated and formed a prominent part of the tumor mass.

3. In six of the eyes examined the lamina vitrea was found to be diseased. Michel, Verhoeff, and Behr found colloid excrescences upon it as well as variability in its staining properties and thickness. Six eyes showed ruptures in Bruch's membrane through which blood vessels passed. In four instances this membrane was reported intact and normal.

Except for signs of compression, the choroid of eight eyes was found to be completely normal. Elschnig discovered atheromatous changes. Verhoeff reported that the choroidal vessels were slightly sclerotic. Hanssen observed small collections of lymphocytes in the choriocapillaris in the region of the lesion, and Behr found proliferation of the intima of the middle-sized arteries.

The tumor mass was uniformly reported to consist chiefly of fibrous tissue with proliferated pigment cells. Behr reported that he found strands of elastic tissue which he believed had been lifted off from the outer one-fourth of the lamina vitrea. Small amounts of blood and albuminous

exudates in various stages of organization were occasionally found. Vessels, presumably chiefly from the choroid, were observed within the mound in all cases, and occasionally a capillary was seen to enter it from the retina. Choroidal vessels were seen by several observers to penetrate the lamina vitrea. Michel found cartilage within the pseudotumor, and Axenfeld reported an area of ossification within the mass.

Pathogenesis.—Elschnig placed the origin of this disturbance in the retina and its vessels; Junius and Kuhnt believed it arose in the inner layers of the retina; Ormond, Duynstee, and others were of the opinion that the disease originated in the capillaries of the outer retinal layers.

Michel contended that the origin of the growth was in the lamina vitrea. Behr evolved a theory of vital functions which he attributed to the lamina vitrea, and asserted that a pathologic disturbance of this membrane interferes with these functions and stimulates hyperplasia.

Hanssen, who noted lymphocytic infiltration of the choriocapillaris, concluded that the choroid was the chief offender.

Pagenstecher, Axenfeld, Hegner, Neame, Coppez and Danis attributed the condition to an inflammatory cause.

Oeller, Batten, Beatson, and Knapp believed that the mass originated from a subretinal exudate or hemorrhage or from both.

Possek assumed that the exudate was caused by arteriosclerotic changes in the tissues of the eye. Sclerotic changes in the choroidal vessels particularly were found and emphasized as a possible cause of nutritional disturbance, with resultant hyperplasia, by Cords, Pallarés, Verhoeff, and Paul.

Juvenile Disciform Degeneration of the Macula

In the literature cases have been described in which a macular condition resembling senile disciform degeneration has occurred in individuals less than forty years of age. For convenience we shall refer to this condition as juvenile disciform degeneration of the macula. It differs from the senile

type also in the fact that the lesion tends to heal, leaving few if any changes and slight or no impairment of vision. Just how frequently it occurs is problematic, since it may often have been mistaken for some other disorder. Special attention was called to this condition by Junius in 1929. He reported four cases under the classification, "Juvenil retinitis exudativa macularis," three of which seem to us to belong to the type under consideration. The patients were thirty-four, thirty-two, and twenty-seven years of age respectively, and in each case only one eye was affected. In the first case the condition reached its height in ten weeks, and vision was then reduced to counting of fingers at two meters. In six months the lesion had disappeared entirely and vision was normal. The patient was seen again twenty-four years later, at which time the fundus and vision were still normal. In the second case there were two small hemorrhages at the margin of the lesion. Vision was reduced to perception of hand movements. At the end of two months the lesion had almost disappeared, leaving a pale oval area partially demarcated by a fine pigmented line, and the vision was .3. In the other case the onset was sudden, and vision was reduced to counting of fingers at one meter. Whether or not vision improved later was not determined, as the patient was lost sight of. This patient was subject to attacks of ophthalmic migraine. The remaining case reported by Junius (his Case 3) seems to us to belong in an entirely different category. In this case there was within the retina in each eye an extensive white exudate around the optic disc and a massive white star figure around the fovea. The patient was fourteen years of age. The only important similarity this case bore to the others of this group lay in the fact that the exudate disappeared and that there was little permanent impairment of vision.

In 1935 Davis and Sheppard reported two cases which they believed belonged to the type described by Junius. In one case the patient was twenty-three years old. "In each mac-

ular region was found an oval golden yellow area over which the retinal vessels passed." The visual acuity was 20/20–2 in each eye. Whether or not the lesion was elevated was not stated. Two years later changes could still be seen in each macula, and the vision of the right eye was 20/100, and that of the left, 20/30. In their second case an elevated disciform lesion was observed in the right eye of a patient forty-one years old, who had angioid streaks in both eyes. The observation was made about two years after central vision was said to have been lost. No improvement in vision was noted. It seems to us that this case belongs to the senile type of disciform degeneration, and we have therefore included it in the list of cases previously analyzed. The assumption of Davis and Sheppard that the loss of central vision coincided with the onset of the disciform lesion is not necessarily correct, since sudden loss of central vision is a typical symptom in cases of angioid streaks.

Junius regarded the lesions in his cases as retinal in origin and due to a vascular disturbance, but concluded that their etiology was still obscure.

From the foregoing review of the literature it is obvious that the pathogenesis of senile disciform degeneration of the macula has not yet been determined. We have not yet fully examined the literature relating to the juvenile type, but thus far we have been unable to find any suggestive evidence as to the pathogenesis of the ocular lesions. We have studied the following cases and they seem definitely to reveal the pathogenesis of the senile, and strongly to indicate that of the juvenile, type of the affection.

Case Reports

Case 1.—Miss G. L., aged forty-nine years, white, first consulted Dr. Verhoeff April 6, 1931, complaining that four days previously she discovered that the sight of the right eye was blurred. The vision of the right eye with +2.50 sph. was 5/200; that of the left eye with +3.75 sph. ⊃ −1.00 cyl. ax. 125° was 20/15. On ophthalmoscopic examination of the right eye there was found occupy-

ing the macular region, and extending farther below than above, an almost black, mound-like elevation with a smooth surface. Extending beneath the retina from the margin of the mound there were several extravasates of blood. Otherwise the fundus appeared to be normal—there was no sclerosis of the retinal vessels. The fundus of the left eye was normal.

The patient stated that her general health was excellent. Her urine was free from sugar and showed only an insignificant trace of albumin.

A diagnosis of sarcoma of the choroid was made, and on April 9, 1931, the right eye was removed under local anesthesia and a glass ball implanted in the socket.

On May 8, 1936, the vision of the left eye with correction was 20/15 and the fundus was still normal. The general health of the patient remained excellent.

Pathologic Examination (10438).—Fixation in 10 per cent. formalin for forty-eight hours, followed by acid alcohol for twenty-four hours. Embedding in celloidin. Serial sections of lesion in fundus. Staining in hematoxylin and eosin and with Verhoeff's elastic tissue stain.

Microscopic Examination.—Except for the lesion in the macula and the presence of an unusual number of eosinophilic cells in the iris stroma the eye was normal. The eosinophilic cells were large, had small, round, solidly staining nuclei, and were packed with fine eosinophilic granules. Apparently they were eosinophilic myelocytes. As many as five of these cells were sometimes found in the high-power field. Aside from the eosinophiles, the iris contained no plasma cells or other inflammatory cells. The vessels of the retina and choroid and the posterior ciliary vessels were remarkably free from sclerosis. There was but slight peripheral cystoid degeneration of the retina. The suspected tumor of the choroid was found to be a large mass of fresh blood beneath the retina in the macular region (fig. 3). This elevated the retina in the form of a mound measuring 1.5 mm. in height and 6 mm. in diameter. The mass was somewhat excentric with reference to the fovea. It began at 2 mm. to the temporal side of the fovea, and extended to the margin of the disc. It reached its greatest height at a distance of 4 mm. from the disc, somewhat above the fovea. At least two-thirds of the total mass of blood lay beneath the pigment epithelium, which it had separated from Bruch's membrane in the form of a vesicle. The vesicle was solidly filled with blood, and was 4 mm. in diameter. Its inner margin was 2 mm. from the edge

of the optic disc, and its center was somewhat above the fovea. The vesicle was everywhere intact except on the nasal side, where in a few sections it showed a rupture about 0.25 mm. wide through which blood had exuded from the vesicle between the retina and pigment epithelium. In the region of the fovea the wall of the vesicle was still in contact with the neuro-epithelium of the retina in an area about 2 mm. in diameter, except immediately behind the fovea, where there was a slight amount of serum. In contrast to the blood within the vesicle, the blood outside of it contained lakes of serum free from blood cells, indicating that it had been subjected to less pressure than was originally the case with the blood within the vesicle. The choroid, including the membrane of Bruch, was normal and intact except in a small area at and just outside the lower outer margin of the vesicle. Here the source of the hemorrhage was apparent (fig. 4). In an area ⅔ mm. wide the choriocapillaris with the membrane of Bruch were torn up in a ragged manner by an extravasation of blood which raised up the pigment epithelium in the form of small vesicles and then extended into the large vesicle previously described. From this point for a short distance beneath the large vesicle the choroid showed slight infiltration with lymphocytes, and a little exudation of the latter cells into the mass of blood. At this point the blood mass contained a small amount of fibrin. From the margin of the vesicle outward the extravasate extended within the choroid just beneath the choriocapillaris for a distance of about 3 mm. Elsewhere the choroid was free from infiltration and hemorrhage. The retina proper was wrinkled in and around the fovea, probably as a result of the embedding process, but otherwise it appeared to be perfectly normal. It showed no exudation, hemorrhages, or edema.

CASE 2.—Daniel M., aged seventy-seven years, married, white, was admitted to the clinic of the Massachusetts Eye and Ear Infirmary January 15, 1936, complaining of blurred vision of his left eye.

In the summer of 1934 he observed a slight decrease of the visual acuity of his left eye. He was certain that in 1935 the vision of this eye was much less acute than that of his right eye. In November, 1935, he was told by an optometrist that his left eye was "stone blind."

Ocular Examination.—V.O.D. with +0.75 sph. = 20/30; V.O.S., less than 20/200. Both eyes were white and quiet. There was arcus senilis. The corneas and other media were clear. The pupils reacted normally to light and in accommodation.

Fundus Examination.—O.D.: The optic disc was normal. In the macular region there were many colloid excrescences (Tay's choroiditis). The fovea was sharply outlined. The retinal vessels showed no definite sclerosis. The fundus was otherwise normal. O.S.: The optic disc was normal in color. The retinal vessels showed slight if any sclerosis. Adjacent to the temporal margin of the disc there was a large elevated mound, almost black in color, about two to three disc-diameters in size, clearly demarcated and surrounded by a band of deep hemorrhage (Plate I). The retinal vessels coursed in front of the mass, and with the exception of one vessel and its two branches, they appeared to be normal. The vessel running from the edge of the optic disc became white as it crossed the mound, as did also its two branches. There were two diffuse whitish areas adjacent to the mass—one at its lower margin and the other at the upper border of the disc—each containing hemorrhagic spots.

At this time a definite diagnosis of hemorrhage behind the pigment epithelium was made.

Physical Examination.—Blood-pressure, 140/80. Heart negative. Radial and dorsalis pedis arteries not palpable. Urine: Negative for albumin, sugar, and casts. Rare blood cells and rare white cells. Wassermann reaction and Hinton test negative. Blood count: Hemoglobin, 75 per cent.; red blood cells, 4,640,000; white blood cells, 8,000; polymorphonuclears, 63 per cent.; lymphocytes, 30 per cent.; eosinophiles, 1 per cent.; mononuclears, 6 per cent.; platelets normal. Slight achromia and variation in size of red cells.

The patient was observed every two weeks during the next three months.

An area immediately adjacent to the temporal edge of the mound early became more shallow than the rest of the lesion, and ultimately flattened out to the retinal level. The reflex from this portion became red. At the end of six weeks this portion of the mound seemed to disappear, leaving the retina normal except for a few deep hemorrhages.

Within four weeks the lesion became white in its temporal portion, gradually shading into a gray and dark gray toward the nasal edge. The temporal edge was always sharply elevated. After ten weeks the lesion was entirely white except for a small gray edge at its upper border. There were a few heavy black pigment-granules near the outer margin.

Throughout its course the lesion remained completely surrounded

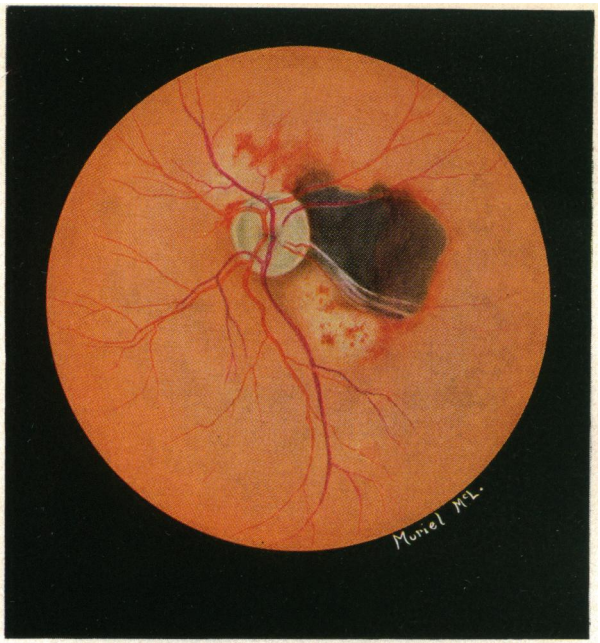

Fig. 1, Plate I, Case 2.—The ophthalmoscopic appearance of the macular lesion when first seen. The picture is practically identical with that seen in Case 1 except that in the latter case the retinal opacity below the mound and that above the optic disc were not present.

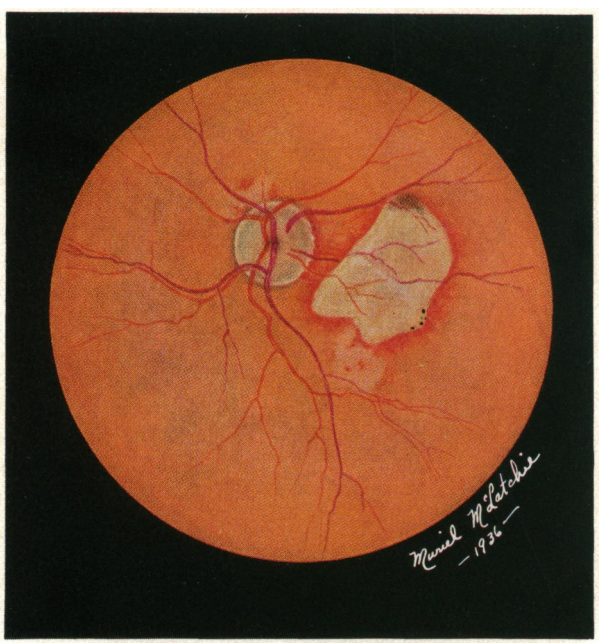

Fig. 2, Plate II, Case 2.—The ophthalmoscopic appearance of the lesion three months later. The mound has become almost completely white. The hemorrhagic extravasates around it still persist, as do also the two retinal opacities. The latter were found to be due to serum beneath the retina. The apparent minute retinal hemorrhages here were found to be collections of red corpuscles in this serum.

by a band of deep subretinal hemorrhage. The white areas at the upper border of the disc and the lower border of the lesion persisted. They were raised at first, but finally grew flatter, pinker, and less distinct. In the vessels that originally appeared white as they crossed the mound blood became visible in six weeks, and the vessels then assumed the same normal appearance as the other retinal vessels. The final appearance of the lesion at the end of three months is shown in Plate II.

Three months after his first visit the patient sought the advice of two other ophthalmologists. Both of these advised removal of the eye owing to the fact that it was practically blind and because of the possibility of malignancy being present. We told the patient that in our opinion the condition was not malignant, but this did not give him the positive assurance that he desired. At his request the eye was removed on April 15, 1936.

Pathologic Examination (10440).—Preparations were made as in the previous case.

Macroscopic Examination.—The vitreous humor was clear and was not separated from the fundus or lens. There were slight senile pigmentary changes at the ora serrata. In the macula there was an area 4.5 mm. in its greatest diameter, and elevated about 1.25 mm. It was roughly circular in outline, but showed some indentations. On the surface there was a slight grayish mottling; in the center the normal yellowish color of the macula was evident, but otherwise it appeared almost white. Around the area was a dark border, 0.25 to 0.75 mm. wide. Radiating from a point near the center were many fine white lines (artificial wrinkles?) which extended into the dark border. Otherwise the retina was *in situ* everywhere.

Microscopic Examination.—Aside from the lesion in the macula the eye showed no pathologic alterations and unusually slight senile changes. The ciliary processes exhibited only slight hyaline change. The two layers of epithelium of the pars plana showed fairly marked proliferative changes in some sections. There was almost no peripheral cystoid degeneration of the retina, and colloid excrescences were not found anywhere. An unusual finding was that the myelinization of the optic nerve fibers ended at about 1 mm. behind the lamina cribrosa. The optic disc was normal. The vessels of the iris, ciliary body, and retina and the posterior ciliary vessels were normal. The vessels of the choroid were also notably free from endovasculitis, although an occasional artery showed slight intimal proliferation—less than would be expected

considering the age of the patient. The lesion in the macula (fig. 5) was found to consist of a mound of finely fibrillated connective tissue permeated with blood and containing large masses of blood in process of organization. It was situated between the retina proper and Bruch's membrane, was thickest behind the fovea and gradually became thinner toward the entire periphery. It reached to about 0.5 mm. from the margin of the optic disc. The new tissue was everywhere closely applied to Bruch's membrane, which, except for a few small defects to be described later, was intact beneath it. In places the tissue was stained lightly by eosin, but more often, especially near the choroid, it was stained slightly bluish by hematoxylin. The largest masses of blood were situated in the upper part of the mound, and were nearer the retina than the choroid. In some sections they comprised about half the thickness of the mound (fig. 6). The tissue was fairly rich in fixed cells, but was free from lymphocytes, plasma cells, pus cells, and macrophages. It contained no hematogenous pigment, fatty acid crystals, or cholesterin. The original pigment epithelium could be identified only at the periphery of the mound. In the central portion of the mound no pigment epithelium, either new or old, remained adherent to Bruch's membrane or to the outer surface of the retina. At the periphery connective tissue continued from the mound as a thin layer between the original pigment epithelium and Bruch's membrane for a distance of about 0.5 mm. As the single layer of pigment epithelium extended toward the center of the mound, it was seen to have proliferated into two main layers which had diverged from each other and then further proliferated in an irregular fashion. Some sections showed a large central area of the mound entirely surrounded by a single layer of pigment epithelium. Posteriorly the latter had here undergone complete necrosis and appeared as an eosinophilic granular membrane free from nuclei but still containing pigment. In places, especially at the periphery, the pigment epithelium had proliferated in the form of irregular strands some of which suggested acini. The connective tissue about these strands tended to assume a more hyaline character than elsewhere. Here there were also spindle cells, some of which contained pigment, whereas others were free from pigment. The epithelial origin of many of the pigment-free cells was evidenced by their continuity or contiguity with the pigmented cells and their close resemblance to the latter. From this evidence it was clear that a large proportion of the cells in the mound were derived from pigment epithelium. Many of these cells were found within the masses of blood, and

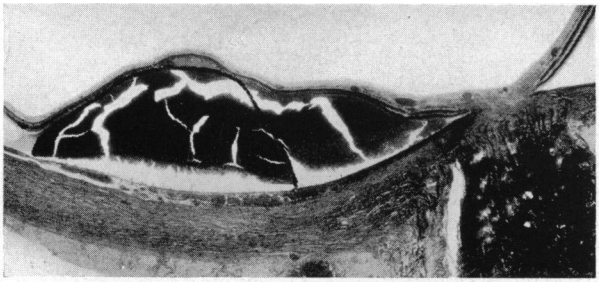

Fig. 3, Case 1.—Hemorrhagic extravasate in the macular region beneath the pigment epithelium. The latter has been outlined with ink to show its position more clearly. In this section the epithelium was intact except for obviously artificial breaks. The blood outside of the vesicle extending to the margin of the disc left the vesicle through a small break in its wall found in other sections. At the summit of the mound is a small amount of serum between the pigment epithelium and the retina proper (× 9).

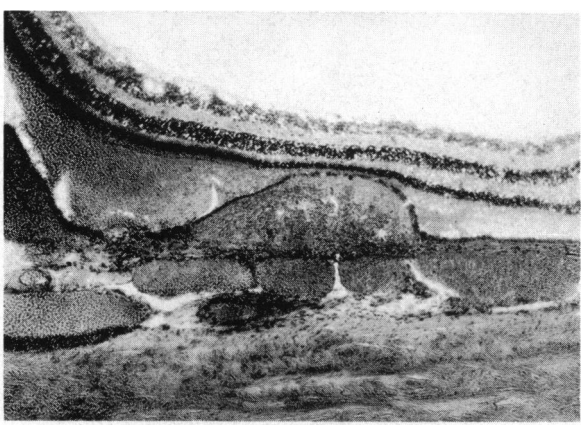

Fig. 4, Case 1.—Rupture of the choriocapillaris at the periphery of the mound, and the pigment epithelium elevated by hemorrhagic extravasate. Other sections showed this extravasate continuous with that forming the main mass on the left (× 48).

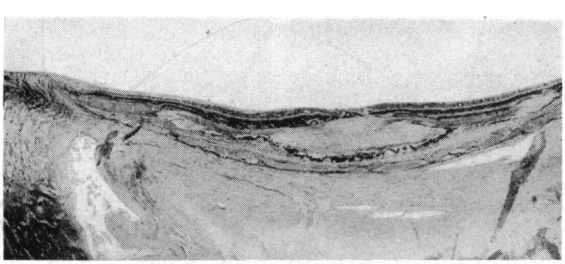

Fig. 5, Case 2.—The mound in the region of the fovea. The pigment epithelium in the posterior part of the mound is not the original pigment layer, but has been newly formed. It is widely separated from Bruch's membrane by connective tissue (× 13).

apparently played a large part in the process of organization. The mound contained a few thin-walled blood vessels, most of them slightly larger than capillaries, a few being about three times this size. These were found chiefly near the choroid and at the periphery. No vessels were seen to enter the mound from the retina, but after careful search two fairly large vessels were seen to extend into it from the choroid through sharp breaks in Bruch's membrane (figs. 7 and 8). One of these vessels was connected directly with a large choroidal vein. In addition a few microscopic breaks were found in the membrane through which fibroblasts extended into the mound from minute collections of newly formed fibroblasts in the choroid. In some places Bruch's membrane was slightly wrinkled, due evidently to contraction of the tissue forming the mound. Aside from these changes and slight compression, the choroid, including the choriocapillaris, appeared to be perfectly normal behind the mound as it was elsewhere. The source of the hemorrhage was no longer recognizable.

The retina over the mound was altered relatively little. The nuclear layers, the ganglion cells, and the nerve-fiber layer appeared to be normal. There were no hemorrhages, edema, or exudation, and the retinal vessels were normal. The outer surface was distorted and occasionally folded in the form of pseudo-rosettes. The rods and cones had been largely destroyed, but were often still recognizable. The external limiting membrane was almost completely intact. As has been stated, the pigment epithelium had completely disappeared from beneath the retina over the central portion of the mound, and the new connective tissue was directly applied to the neuro-epithelium. In the fovea there was a minute break into which the connective tissue extended.

Almost everywhere around the mound there was a layer of blood extending between the retina and the pigment epithelium for about 1 mm., and on the nasal side it reached the margin of the optic disc. Many pigment cells had migrated into this blood. Unlike the blood within the mound, it was not undergoing organization.

In sections passing through the retinal opacity below the mound, and in others passing through that above the disc, there was serum instead of blood between the retina and pigment epithelium.

CASE 3.—David W., aged sixty-three years, married, white, was admitted to the clinic November 19, 1935, complaining of blurred vision in the left eye. He had noticed a black spot (probably of no significance) before the left eye for about five months, and had double vision in this eye for about two weeks. The right eye was

normal, vision being 20/15 with +2.00 sph. ⊂ +0.75 cyl. ax. 90°. The optic disc showed an unusually deep and wide physiologic cup. The vision of the left eye with the glass he was wearing was 20/100, but with a +1.00 sph. added it was 20/30. The retina showed in the macula a grayish elevation about the size of the disc. The retinal vessels were normal. The disc was cupped, as in the right eye. There were no retinal hemorrhages. The vitreous was clear. November 22: V.O.S. with +1.50 sph. added = 20/30. December 13, 1935: V.O.S. with +1.50 sph. added to glass = 20/40. December 21, 1935: V.O.S. with +2.50 sph. ⊂ +1.25 cyl. ax. 90° = 20/40. January 21, 1936: A thorough general physical examination made at the Massachusetts General Hospital was negative except for numerous small telangiectases of the skin and slight hypochromic anemia. Blood-pressure, 160/80. Red blood cells, 4,390,000. Hinton test negative. *X*-ray examination of teeth and chest negative. Graham test of gallbladder negative. Tonsils negative. Urine negative. At one time a soft mass was felt in the abdomen, but this disappeared in a few days.

Personal History.—Except for measles in childhood and influenza in 1915 the patient had always been well.

Family History.—Unimportant.

April 3, 1936: V.O.S. with correction = 20/70. The retinal lesion was changed in appearance. Beneath the elevated retina a dark mass could be seen indistinctly. There were no retinal hemorrhages. The vitreous was clear. A diagnosis of probable sarcoma of the choroid was made. April 10, 1936: V.O.S. = 20/200. The left eye was enucleated.

Pathologic Examination (10439).—Fixation, embedding, and staining as in previous cases. Serial horizontal sections of lesion in fundus.

Macroscopic Examination.—On opening the eye, an elevated, irregular area was seen in the macular region, about twice the area of the disc. There were no hemorrhages around it. The surface was uneven, possibly due to the fixation. The yellow color of the macula was still well marked.

Microscopic Examination.—On microscopic examination the eye was found to be normal except for the lesion in the macula. Peripheral cystoid degeneration of the retina was slight below, extending backward from the ora serrata only about 1.5 mm., but it was excessive above, where it extended for a distance of more than 6 mm. behind the equator. At the equator it was most marked, and almost divided the retina into two thin layers. The optic disc

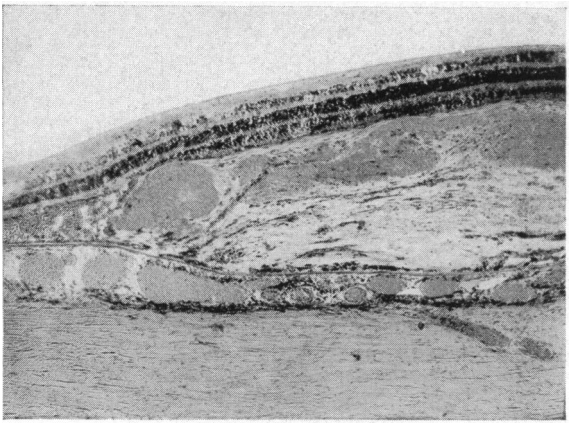

Fig. 6, Case 2.—The nasal two-thirds of the mound and large masses of old blood undergoing organization. The strands of pigment epithelium are taking part in the organization of the mass. Bruch's membrane is intact (× 44).

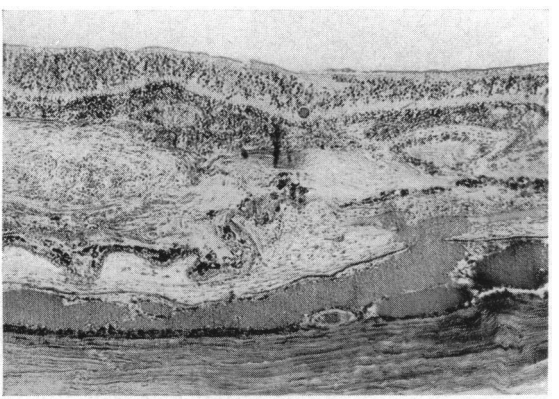

Fig. 7, Case 2.—A vein leaving the mound near its periphery and joining a large choroidal vein through a break in Bruch's membrane (× 54).

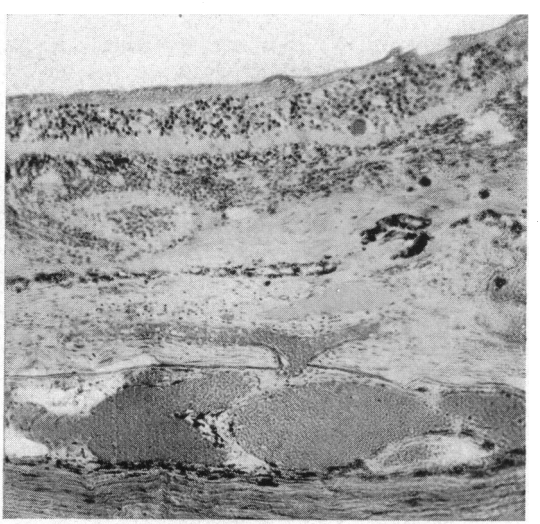

Fig. 8, Case 2.—An artery entering the mound from the choroid through a break in Bruch's membrane (× 87).

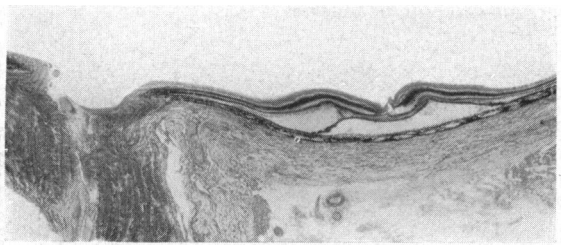

Fig. 9, Case 3.—The pigment epithelium is elevated in the form of a vesicle by serous exudate in the foveal region. Serum has exuded from the vesicle and collected beneath the retina proper (× 10)

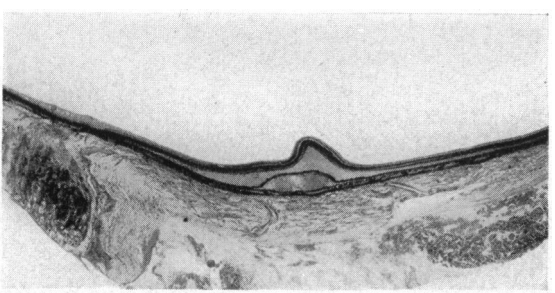

Fig. 10, Case 3.—Vesicle near its periphery containing two collections of red blood corpuscles. Here beneath the retina there is a considerable amount of serum which has been exuded through the epithelial walls of the vesicle (× 9).

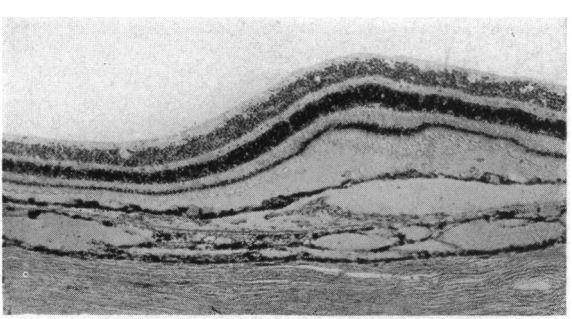

Fig. 11, Case 3.—Formation of connective tissue between the pigment epithelium and Bruch's membrane at the periphery of the vesicle. This tissue is entirely mesoblastic in origin and derived from fibroblasts that have penetrated Bruch's membrane (× 45).

showed an unusually deep physiologic cup. The retinal, choroidal, and posterior ciliary vessels were remarkably free from endovasculitis. The elevation of the retina in the macular region was found to be due to a subretinal exudate of serum. About half of this exudate was confined beneath the pigment epithelium, which was lifted up from Bruch's membrane in the form of a flattened, intact vesicle (fig. 9). The vesicle was somewhat excentric with reference to the fovea. Over its central portion the pigment epithelium was still adherent to the retinal neuro-epithelium, but elsewhere it was separated from it by serum. The vesicle was 2.2 mm. in greatest width, and 0.35 mm. in greatest height. Outside of the vesicle there was more serum below than above it. Just below the vesicle the retina was sharply elevated 0.8 mm. in an area 3 mm. wide, but the serum extended under the retina for a total distance of 7 mm. Outside the vesicle there were no blood corpuscles or fibrin. The upper half of the vesicle was also free from these elements, but in the lower half there were two globular masses of blood corpuscles which, in a few sections, occupied about one-half the area of the vesicle (fig. 10). There was at this point also a slight amount of delicate fibrin in the serum. The pigment epithelium forming the wall of the vesicle was generally only one cell in thickness, but here and there it had been increased to two cells. It showed no break anywhere. Many of the cells were greatly distended with serum and projected toward the retina, indicating that serum had been exuded from within the vesicle through the epithelium. At the nasal side of the vesicle there was a layer of newly formed connective tissue extending over Bruch's membrane for about 1 mm. (fig. 11). The serial sections showed that it extended vertically also about 1 mm. Beyond the margin of the vesicle it extended between the pigment layer and Bruch's membrane, gradually diminishing in thickness and disappearing at a distance of about 0.5 mm. from the margin of the vesicle. It reached its greatest thickness, about 0.4 mm., within the vesicle, where it was not in contact with the pigment epithelium. The stroma of the new tissue was hyaline and extremely delicate. It was fairly rich in fibroblasts, which were most abundant at and near its surface toward the cyst cavity. It contained a few vessels, some of them slightly larger than capillaries, but no more than two were seen in any one section. Except for two small microscopic breaks, Bruch's membrane was intact. Through these breaks actively proliferating fibroblasts could be seen extending from within the choroid, and a capillary was also found passing through one of the breaks. In a

few other places fibroblasts could be seen penetrating through Bruch's membrane into the new tissue without producing definite breaks in the membrane. Except that it showed a few lymphocytes along the walls of some of the veins, and possibly slight distention of the veins, the choroid beneath the new tissue was normal. The retina proper was slightly distorted over the vesicle, but otherwise it appeared to be perfectly normal.

REMARKS

The ophthalmoscopic picture seen in Case 1 and that seen early in Case 2 were essentially identical, and similar to those described in the literature as occurring early in cases of disciform degeneration of the macula. Except for the two areas of retinal opacity shown at the periphery of the mound, Plate I depicts the lesion in Case 1 almost as accurately as it does that in Case 2. In Case 2, in which the eye was not removed until three months later, the ophthalmoscopic picture was observed gradually to change into that typical of the later stage of this disease (Plate II).

On microscopic examination in Case 1 there was found a rupture of the choriocapillaris, and extending from this there was a large hemorrhagic extravasate which had separated the pigment epithelium from Bruch's membrane in the form of a large vesicle (fig. 3). That such a condition could occur has apparently never hitherto been demonstrated or even considered possible. It is interesting to note that the capillary rupture (fig. 4) took place not beneath the center of the vesicle, but at the periphery of the latter, and hence at the periphery of the macula.

In Case 2 the histologic picture was essentially the same as that found by many other observers, with the important exception that in this case masses of blood undergoing organization were still present, and thus furnished conclusive proof that the new tissue resulted from organization of blood. It was clearly evident that this blood was originally largely confined beneath the pigment epithelium, as in Case 1, but its exact source could not be discovered, owing, no doubt, to

the later stage at which the eye was removed. In this case, therefore, the possibility cannot be excluded that the blood was derived from the choriocapillaris by diapedesis. Since, as has just been pointed out, in Cases 1 and 2 the ophthalmoscopic appearances were essentially the same as those described in the literature as occurring at corresponding stages, and since, in Case 2, both the ophthalmoscopic and the microscopic findings were essentially the same as those described in later stages of the disease, it is reasonable to conclude that hemorrhage beneath the pigment epithelium is the usual cause of senile disciform degeneration of the macula.

In Case 3 a condition was found apparently not hitherto observed microscopically or ever recognized ophthalmoscopically, namely, a serous exudate occurring primarily beneath the pigment epithelium behind the macula, and elevating the retina at this point in the form of a mound (figs. 9 and 10). From the standpoint of pathogenesis, this case was evidently closely related to the two other cases, but it is unlikely that the process would finally have resulted in the clinical picture of senile disciform degeneration. It is true that at the time the eye was removed there was definite proliferation of connective tissue upon the surface of Bruch's membrane within the vesicle, but it is improbable that this would have gone on to the formation of a mass of connective tissue ophthalmoscopically conspicuous.

Clinically also Case 3 differed from the other two cases in two important respects, namely: in the ophthalmoscopic picture and in the visual impairment. At the outset there was present in the macula a mound-like elevation darker than the surrounding retina, but much lighter in color than those seen early in the two other cases. At this stage visual acuity was only slightly impaired in Case 3, whereas in Cases 1 and 2 central vision was almost, if not completely, abolished. The preservation of central vision for a time in Case 3 was, no doubt, due to the fact that the pigment epithelium remained in contact with the rods and cones. Later, as was revealed

by the microscopic examination, serum exuded through the epithelium and separated it from the rods and cones, thus causing loss of visual function at that point. At this stage the ophthalmoscope disclosed what appeared to be a darker mass beneath the retina. This, no doubt, was actually the pigment epithelium separated from the retina proper, but it was mistaken for a sarcoma and led to removal of the eye. The early loss of central vision in Cases 1 and 2 was probably due to the rapid and forcible elevation of the macula by hemorrhage and to the resulting distortion. It is noteworthy, however, that in each of these cases the pigment epithelium remained in contact with the fovea, although it was separated to some extent from the retina elsewhere beneath the macula by blood which had broken through at the periphery.

Owing to the age of the patient, sixty-three years, Case 3 would not ordinarily be regarded as belonging to the juvenile type of disciform degeneration of the macula. It is not unreasonable to suppose, however, that in any patient free from arteriosclerosis, a macular lesion identical with that in young individuals could occur. Certainly in this case the microscopic characteristics of the lesion seem to accord with the ophthalmoscopic appearances of the lesions in the juvenile type of disciform degeneration, and also explain the restoration of vision, with or without residual macular changes, that occurs in this affection, for it is obvious that if, in Case 3, the serous exudate had become absorbed and the slight formation of connective tissue had ceased, visual acuity would have been largely if not completely restored. Moreover, the prolonged preservation of central vision and the absence of hemorrhage in the early stage in Case 3 are characteristic of the juvenile, and not of the senile, type. Perhaps there will be found occurring at various ages cases in which the character of the lesion is intermediate between that of the senile and that of the juvenile type.

Another condition that must be considered in connection with Case 3 is so-called serous retinitis. This is often central

—in fact, it is only the central type that the present senior writer has ever observed. In such cases a large central area of the retina, including the macula, but often extending beyond it, becomes diffusely cloudy, and may present a wavy appearance resembling the ripples of sand at the seashore. Vision is markedly impaired at the outset, but the condition always subsides and terminates with recovery of useful vision. The cause of serous retinitis has never been determined, but Case 3 would suggest that it may be serous exudation from the choroid. In serous retinitis, perhaps, the serum is under less pressure, being slowly exuded through the pigment epithelium without lifting it up, and then permeating beneath or into the retina.

From a histologic standpoint the three cases here described showed several features of considerable additional interest. In Case 1 Bruch's membrane showed only one break—a small one at the site of the rupture of the choriocapillaris, from which the hemorrhage arose. In Case 2 only a few breaks in Bruch's membrane were found. These were very small, and through two of them new vessels passed from the choroid into the mound (figs. 7 and 8). The other breaks were filled with fibroblasts. Evidently, however, most of the connective-tissue cells in the mound were derived from cells that had penetrated Bruch's membrane without producing microscopically visible breaks.

In Case 3 only a very few small capillaries were found extending through Bruch's membrane. In this case the proliferation of connective-tissue cells through Bruch's membrane without causing breaks could be definitely recognized, for small spindle-shaped accumulations of such cells were found here and there on the inner surface of the membrane and occasionally a cell was seen extending through the membrane. In general there were no accumulations of cells beneath the membrane within the choroid, although in a few instances slight accumulations were found. The largest of these comprised about 30 cells in the section.

No evidence that the retinal vessels played any part in the process of organization in either Case 1 or Case 3 could be found. In Case 3 it was apparent that a transudate of serum passed from within the vesicle through the pigment epithelium. The latter showed no breaks, even microscopically, but many of its cells were distended with serum, which often could be seen to have broken from the cells into the space beneath the retina proper. A noteworthy feature in Case 2 was the absence of hematogenous pigment in spite of the large amount of blood still remaining in the tissue.

In Case 2 it was clearly evident that the pigment epithelium played an important part in the process of organization, for large strands of cells from the epithelium were found extending into masses of blood, and all stages in the formation from pigment cells of cells free from pigment and indistinguishable from fibroblasts were observed. In other places also the origin of the stroma cells from pigment epithelium was evident. In many places, however, it could not be determined whether the cells were of epithelial or of mesoblastic origin, although there is no doubt that those closely associated with the blood vessels were mesoblastic. In Case 3 the new tissue was almost if not entirely mesoblastic in origin. The cause of its formation in this case is not clear. There was no blood in its vicinity at the stage of the microscopic examination, but possibly blood had previously been present here. No condition in the choroid served to explain its formation.

A question that arises in connection with the histogenesis of these lesions is as to whether or not similar lesions occur elsewhere than beneath the macula. The senior writer has examined sections of a number of eyes in which there was extensive formation of connective tissue between the retina and Bruch's membrane elsewhere than in the macula—tissue similar to that seen in the advanced stage of disciform degeneration—but unfortunately has no evidence as to its histo-

genesis. Such cases would probably not be recognized clinically as analogous to disciform degeneration of the macula.

Another question that should be considered is as to whether or not the condition is related to Coats' disease. The senior writer has had an opportunity to examine sections of the lesions in the latter disease, both in the early and in the late stages, and has found that the new tissue is formed in the external part of the retina, but not primarily beneath the pigment epithelium. In the early stages a large amount of fibrin and hematogenous pigment is present. In the later stages cholesterin crystals surrounded by foreign giant cells may be numerous. It would seem, therefore, that Coats' disease is essentially different from disciform degeneration of the macula. The former disease seems to be primarily retinal, whereas the latter is choroidal, in origin.

In Cases 1 and 2 hemorrhagic extravasates extended beneath the retina from the periphery of the mass. The microscopic examination in Case 1 showed that such extravasates were the result of blood breaking through the pigment epithelium at one or more places at the periphery. In Case 2 small hemorrhagic extravasates were seen ophthalmoscopically that were apparently not connected with the main mass. These were found to be entirely subretinal, so that actually they must originally have been derived from the main mass of blood. No doubt many of the separate retinal hemorrhages described in recorded cases also had this origin. In Case 2 the gray retinal opacities below the mass and above the optic disc were found to be due to the presence of serum beneath the retina. This serum contained a few discrete collections of red blood cells. Since the retina showed no edema or hemorrhage, it is evident that this serum had separated from the main mass of blood, just as serum usually does from any accumulation of stagnant blood. Probably some of the peculiar appearances depicted in various recorded cases can be explained in this way.

The causes of the hemorrhages in Cases 1 and 2, and of the

serous exudate in Case 3, remain to be determined. Behr has advanced the view that disciform degeneration of the macula is due to some alteration in Bruch's membrane which permits an exudate to occur beneath the retina. To us this theory seems highly improbable. It is true that with advancing age certain changes occur in the elastic portion of Bruch's membrane, as was first pointed out by Verhoeff and Sisson, but these changes are not more marked in the macular region than elsewhere, and even when they are very marked, they are not necessarily associated with any alteration in the retina or impairment of vision. The inner portion of the membrane may also undergo senile change, such as is commonly associated with colloid excrescences, but neither does this lead to exudation from the choroid. Behr states that in his case Bruch's membrane was split into two layers at the margin of the lesion, but to us it seems more likely that a new cuticular membrane had been formed by the proliferating pigment epithelium here. In advanced cases such as Behr's, it seems remarkable not that Bruch's membrane is altered beneath the mass, but that it is so slightly altered.

Our cases clearly indicate that disciform degeneration is due to some disturbance, possibly only temporary, in the choriocapillaris of the macular region, since it is evident that the primary condition is hemorrhage or serous exudation beneath the pigment epithelium. Obviously, the cause of the vascular disturbance in the choroid could be the same or vary in different cases. The fact that the affection most commonly occurs in patients of advanced age suggests that general angiosclerosis is a predisposing factor, or that some condition associated with angiosclerosis is often an important factor in producing changes in the choriocapillaris. However, our cases, as well as those recorded in the literature, do not support the view that general angiosclerosis is always the cause of the affection, for in the published cases sclerosis of the retinal vessels is mentioned as occurring in only 25 out of 129 eyes, and in our cases there was no evidence of angiosclerosis,

either local or general, aside from an insignificant sclerosis of some of the choroidal vessels seen in Case 2. On the other hand, our cases do not exclude the possibility of a localized vascular lesion of infectious or other origin, since obstruction of a small vessel in the affected region could have escaped observation in spite of serial sections. In none of our cases did the choroid behind the lesion show recognizable edema, congestion, or hemorrhage, except for the blood coming from the site of the rupture in Case 1. Edema and congestion, however, could have disappeared before the eyes were removed if the vascular disturbance had been compensated or had subsided.

The fact that disciform degeneration of the macula has been observed in cases of angioid streaks accords with our own conclusions, for choroidal hemorrhages are frequent in these cases, and are indicative of vascular disturbances which might well lead to hemorrhage or serous exudation from the choriocapillaris behind the macula.

There are a considerable number of cases in which disciform degeneration of the macula and circinate retinitis coexist. These comprise a high percentage of the former, but a low percentage of the latter disease. It seems evident that the two conditions must have at least one important cause in common, or that one is responsible for the other in these cases. The lesions in circinate retinitis appear to be entirely retinal, and consist chiefly of deposits of lipoid substance within large spaces in the retina about the macula and the phagocytosis of this substance by macrophages. There are also often small retinal hemorrhages. Ophthalmoscopically recognizable sclerosis of the retinal vessels may be present, but it is often absent. There is no known systemic metabolic disturbance to explain the condition. Since lack of oxygen is a cause of deposition of fat in the tissues, it seems possible that disturbance in the capillary circulation of the macular region may be the chief factor in the production of circinate

retinitis, as it probably is of the retinal hemorrhages so often observed in these cases.

The macula is a specially differentiated vascular bed, as is also the choriocapillaris behind the macula. Hence it seems likely that when capillaries of the choriocapillaris are affected in some special way, those of the macular region of the retina are prone to be affected in the same way. For the same reason also it would be expected that both eyes would often be similarly affected, a conclusion that accords with the fact that disciform degeneration and circinate retinitis are frequently bilateral. The structure of the retina being entirely different from that of the choroid, similar vascular changes in them might well produce different effects—in the one, hemorrhages and deposits of fat; in the other, transudation of serum or hemorrhage by diapedesis or rupture. The fact that only rarely have disciform degeneration and circinate retinitis coexisted in opposite eyes can be explained by assuming that when alteration of the choroidal vessels is more marked in one eye, alteration of the retinal vessels is likely to be more evident in this eye than in the other.

On the other hand, the possibility cannot be dismissed that in at least some of the cases in which circinate retinitis and disciform degeneration coexist in the same eye the former has predisposed to or actually caused the latter, for in advanced cases of circinate retinitis the pigment epithelium shows marked changes, and it seems possible, therefore, that the same deleterious influence which produces these changes may cause hemorrhage or serous exudation from the choriocapillaris.

This reasoning suggests the possibility that senile pigmentary changes in the macula may predispose the eye to disciform degeneration, but this possibility seems remote, because such senile changes may be extremely marked without leading to hemorrhage from the choriocapillaris. It is, however, in accord with the facts that disciform degeneration in one eye is sometimes preceded by pigmentary macular

changes in the same eye, and that it is often associated with such changes in the other eye.

In arriving at a diagnosis of disciform degeneration of the macula the chief considerations are the size and situation of the elevated mass, the texture of its surface, the absence of inflammatory signs and of extensive separation of the retina, the coexistence of circinate retinitis, and the presence of subretinal hemorrhagic extravasates extending out from the periphery of the mass. Such extravasates existed in our Cases 1 and 2, and are described in many of the previously recorded cases; when present, they are, therefore, of great diagnostic importance. In Coats' disease the patient is almost always younger and the lesion larger than in any case of disciform degeneration. If, however, as might conceivably happen, the lesion in Coats' disease was small and confined to the macula, it could not be positively distinguished ophthalmoscopically from disciform degeneration. It is more important to differentiate the latter from malignant melanoma, and thus avoid needless removal of the eye. A small malignant melanoma situated in the macula and closely resembling disciform degeneration seldom occurs. In only one instance in the Massachusetts Eye and Ear Infirmary has such a tumor been mistaken for disciform degeneration. In this case the neoplasm showed several hemorrhagic extravasates, due, as was afterward determined by microscopic examination, to necrosis of the tumor. Although situated near the periphery, the extravasates did not extend from beneath the mass. The mistake in diagnosis was soon detected and did not delay removal of the eye more than two months. A much more frequent error is that of mistaking senile disciform degeneration for malignant melanoma. This mistake was made in Case 1. At that time it was unknown that a hemorrhage beneath the pigment epithelium could produce the appearance of a perfectly black mound in the macula. The experience afforded by this case enabled the senior writer immediately to make a correct diagnosis five years later when

early in Case 2 an almost identical ophthalmoscopic picture was seen. In Case 3 a diagnosis of disciform degeneration was later abandoned when the lesion presented a different appearance. This diagnostic error probably could have been rectified if enucleation had been delayed longer. We now believe that a malignant melanoma so seldom presents the appearance ophthalmoscopically of disciform degeneration that, in a case of suspected tumor, removal of the affected eye should be delayed until no suspicion remains that the lesion is that of disciform degeneration of the macula.

SUMMARY AND CONCLUSIONS

The literature relating to disciform degeneration of the macula is reviewed, and 84 cases of the senile type, comprising 129 eyes, are analyzed.

The clinical, ophthalmoscopic, and microscopic findings in three cases of macular disease are described.

In two of these cases the findings prove conclusively that a hemorrhagic extravasate can occur between the pigment epithelium and Bruch's membrane, undergo organization, and produce an ophthalmoscopic picture typical of senile disciform degeneration of the macula.

That this is the usual if not the only pathogenesis of this disease is strongly indicated by a comparison of these cases with those recorded in the literature.

In the third case the microscopic examination revealed that the pigment epithelium was lifted up in the form of a large vesicle by serous exudate. It is suggested that such a serous exudate may be the cause of the juvenile type of disciform degeneration of the macula, and that so-called serous retinitis may have a similar origin.

The extravasation of blood or serum beneath the pigment epithelium in disciform degeneration of the macula is due to some disturbance in the choriocapillaris. Since the affection is most commonly a senile disease, localized angiosclerosis is probably the usual cause of this vascular disturbance. In certain cases, especially in those of the juvenile type, the

vascular disturbance may have been dependent upon some cause or causes yet to be determined.

The frequent association of disciform degeneration of the macula with circinate retinitis may be due to the fact that both occur in specially differentiated vascular beds. The possibility cannot be excluded, however, that, in some cases at least, circinate retinitis actually causes disciform degeneration by producing hemorrhage or serous exudation from the choriocapillaris.

In a doubtful case of malignant melanoma of the choroid removal of the affected eye should be delayed until no suspicion remains that the lesion is that of disciform degeneration of the macula.

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DISCUSSION

DR. ALBERT N. LEMOINE, Kansas City, Mo.: The observations of Dr. Verhoeff and Dr. Grossman on the pathogenesis of disciform degeneration of the macula are exceedingly important to the ophthalmologist. These findings are not necessarily limited to lesions in the macula, but point to the possible pathogenesis of similar lesions elsewhere in the retina. About a year ago I had a patient, sixty-eight years of age, who had repeated multiple small hemorrhages of a year's duration throughout the retina of his only eye. He had had a physical examination in Chicago, with a diagnosis of cardiovascular-renal disease as the etiologic factor of his retinal hemorrhages, and all this time the treatment was directed toward this condition. Because of the appearance of the retinal vessels I was not satisfied with the diagnosis, and insisted on another examination. The physical and laboratory examinations were essentially negative, with the exception that microscopically blood was found in the urine. The tourniquet test for scurvy was made and proved positive. These being the only positive findings, the patient was given cevitamic acid, and in a month's time no hemorrhages were to be seen. Since that time I have had several similar cases, with similar pictures and findings, that also immediately responded to cevitamic acid. Recently I had a patient with a disciform macular degeneration. There was blood all around the lesion, and a few fine hemorrhages were present in the retina a short distance from the lesion. After eliminating other causes for the lesion, and because of the sudden onset in my previous experiences, I considered the possibility of the whole lesion being a hemorrhage. The tourniquet test was made and found to be positive. He was given cevitamic acid, and the small hemorrhages and the blood around the lesion rapidly disappeared. The lesion flattened out and the vision improved. It is too early to predict how much of the vision will return.

The tourniquet test is a very simple procedure. The instrument is applied above the elbow and tightened so that it will just permit the radial pulse to go through. The tourniquet is kept on for five minutes. Below the point of application many petechial hemorrhages in the skin will appear. In some of my cases there were hundreds of these. Such hemorrhages may occur in other conditions, but are rarely seen except in the various degrees of scurvy, hemophilia, and cardiovascular-renal disease. Hemophilia can readily be eliminated. Cardiovascular-renal disease still remains shrouded in much mystery.

Now that Dr. Verhoeff has demonstrated the pathogenesis of these lesions, with my observations as to the etiology of some of the intra-ocular capillary hemorrhages, it is highly possible that a number of these are due to vitamin C deficiency or a mild scurvy. With increased capillary permeability sufficient to cause hemorrhages in the retinal vessels or choriocapillaris, one must think of arteriosclerosis or cardiovascular-renal disease. However, we must not lose sight of the fact that some internists attribute some of those conditions to vitamin C deficiency. This deficiency might be due either to lack of assimilation or intake of the vitamin C.

There is enough evidence to point to the possibility of some capillary intra-ocular hemorrhages being due to vitamin C deficiency to justify making the tourniquet test in all cases of idiopathic hemorrhages, and if found to be positive, to administer cevitamic acid.

Dr. Arnold Knapp, New York: I am glad that Dr. Verhoeff has had the opportunity of examining some of these cases and elucidating the pathology. I have been interested in disciform degeneration of the macula since 1919, when I presented before this Society a case which I diagnosed as sarcoma. I would like particularly to speak of the clinical differentiation between a tumor and an extravasation of blood in the macular region. Disciform degeneration occurs, in my experience, in older persons; the elevation is never more than three or four diopters; the outline is fairly round or oval; the mass is amorphous, usually gray or grayish-white in color, and either in the affected eye or in the other eye there is definite evidence of arteriosclerosis (hemorrhages, etc.). In the abstract of the paper the authors mention the occurrence of discoid macular degeneration in circinate retinitis. While macular changes are frequent in retinitis circinata, they are not like those described in this paper.

Dr. Theodore L. Terry, Boston: A small macular lesion of the right eye in a woman, twenty-nine years of age, had the appearance of a malignant melanoma and produced a central scotoma. Dr. Beetham had the patient examined by several ophthalmologists before he removed the eye. The lesion proved to be typical disciform degeneration with associated hemorrhage and serum. In the choroid itself, subjacent to the disciform lesion, there was a nodule of chronic inflammatory cells. Another somewhat similar inflammatory lesion was situated near the nerve head.

Unfortunately, this case was brought to the attention of Dr.

Verhoeff and Dr. Grossman too late for them to be able to include it in their paper. Dr. Verhoeff has studied these slides, and I should like to hear his interpretation of the findings.

DR. HERMAN P. GROSSMAN, Providence, R. I.: Dr. Knapp has given us a few points in the diagnosis of senile disciform degeneration of the macula, particularly as to the differentiation of this condition from sarcoma of the choroid. This differentiation is based upon—(1) the shape and contour of the lesion; (2) the elevation of the mass, and (3) the associated presence of retinal arteriosclerosis in disciform degeneration.

In very many cases reported in the literature the contour of the lesion was not at all disciform. We are convinced that the configuration of the lesion is not helpful in the diagnosis. The height of the tumor is of little significance. The variation of elevation in the reported cases ranged from 0.5 diopter to 6 diopters. Sarcoma in its later stages no doubt reaches a much greater height, but at that late stage we no longer need this sign for confirmation of our diagnosis. In only 25 of the 129 eyes reported in the literature was any mention made of retinal arteriosclerosis. Retinal angiosclerotic vascular changes were found histologically in only a few of the eyes which came to microscopic examination. These figures are, of course, of no significance whatever in a group of patients whose average age is sixty-eight. We can, therefore, place little reliance upon this sign as an aid in differentiating disciform degeneration from sarcoma.

We believe that the important points in the differentiation of the conditions are these: The presence of typical subretinal hemorrhages adjacent to the lesion are seldom if ever seen in sarcoma. The location of the tumor is important, since sarcoma has no particular predilection for the macular region, and seldom occurs at that point, whereas disciform degeneration always includes the macula.

Finally, in sarcoma separation of the retina is very common and often appears to be entirely out of proportion to the size of the tumor. On the other hand, in disciform degeneration separation of the retina, when present, is very slight, and is often not sufficient to be recognizable by ordinary ophthalmoscopic investigation.

DR. E. V. L. BROWN, Chicago: I wish to refer to a recent case associated with Buerger's disease, in a woman, twenty-five years of age, in whom the vision improved five-tenths in the last three months. The ophthalmoscopic picture is almost identical with that

shown by Dr. Terry. The lesion is perhaps a little larger. She is under treatment for Buerger's disease by a general medical man, and he had reported great general improvement in the case.

DR. F. H. VERHOEFF, closing: I think Dr. Lemoine's observations are very interesting. There must, of course, be a great variety of causes of petechial hemorrhages, and vitamin deficiency may be one of them, but we have no evidence of that in our cases. We know that subconjunctival hemorrhages occur at times without our ever detecting the cause. No doubt, in the majority of the senile cases of disciform degeneration the hemorrhage results from an arteriosclerotic process. In some of these cases there are hemorrhages away from the lesion, but I think most of these are really blood that has extended under the retina from the main mass. In patients with arteriosclerosis there may be retinal hemorrhages independent and separate from it. In Dr. Lemoine's case there were a great many hemorrhages; the patient had a tendency to develop small hemorrhages, and I do not believe that the retinal hemorrhages had anything to do with the hemorrhage in the macula. The latter came from the choroid, and was under the pigment epithelium.

Dr. Knapp stated that he believed that there was no connection between this condition and circinate retinitis. In the literature a number of cases of circinate retinitis associated with this condition have been reported. I recently saw two cases in the clinic. In one there were circinate lesions in the retina over the mound. The relation of the two conditions is described in our paper.

In Dr. Beetham's case, referred to by Dr. Terry, it was evident the small lesion in the macula was of the same nature as those in the senile type of disciform degeneration. I found blood still present in the mound, and also blood around it. But the striking thing in this case was the marked lymphocytic infiltration of the choroid behind the mound. I saw Dr. Knapp's specimen,—he sent a section to me at the time,—and I have seen sections of the lesions in five other cases, and in none of them was there such marked lymphocytic infiltration. In Dr. Beetham's case there was also lymphocytic infiltration at the margin of the disc entirely independent of the other, so in this case it would seem that there must have been a very low-grade metastatic infection. Here is an instance in a young person of a disciform lesion similar to those occurring in old persons. The patient was only twenty-nine, and the lesion never could have subsided without leaving markedly impaired vision. In this way it was also like the senile type. In this case, however, the cause of the hemorrhage was different, no doubt.

This patient did not have arteriosclerosis. There are probably a great many conditions which lead to hemorrhage from the choriocapillaris. All we wish to point out is that a typical lesion is due to organization of a hemorrhagic extravasate which is primarily beneath the pigment epithelium. In some cases the hemorrhage may be due to urticaria. We can even bring our favorite factor, allergy, into the question. It is useless, however, to discuss all these points unless we really have definite evidence of them.

THE GENESIS OF THE CYCLITIC MEMBRANE

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The efficiency of the human eye is due in no minor degree to the integrity of the ciliary body. Because it is completely hidden from all ordinary clinical observation, this structure escapes the attention of the ophthalmologist. Unfortunately, it is only by the study of enucleated eyes that conditions in and on the ciliary body can be determined, although clinically we can frequently infer what is taking place from the nature of the precipitates in the aqueous or the inflammatory cells in the anterior vitreous.

The formation of cyclitic membranes from the inner free surface of the ciliary body occurs only in chronic inflammatory processes. Irritants causing acute inflammation with the production of polymorphonuclear leukocytes are intensive enough to lead to degeneration or necrosis of tissue. It is these chemical products of cellular disintegration that act upon the leukocytes in the adjacent capillaries of the blood and initiate their emigration through the vessel walls. The irritants of acute inflammation cause the infiltration of leukocytes within the ciliary body, particularly in its vascular layer, and the exudation of leukocytes and fibrin on the inner, free surface of the ciliary body or in the anterior portion of the vitreous. Such irritants are never productive nor pro-