De SCHWEINITZ (G. E.)

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PHILADELPHIA, PA.

(PHOTO-MICROGRAPHS BY WILLIAM M. GRAY, M.D.)

[*Reprinted from American Ophthalmological Society Transactions*, 1892.]

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Since Heinrich Mueller * found in preparations from eyes of elderly people, globular masses, 0.0008 to 0.003 mm. in diameter, close to the inner margin of the optic nerve ring, and also that the circular tissue around the optic nerve trunk very often contains a peculiar formation of globular masses, which he suggested might be discovered with the ophthalmoscope,† to the most recent communication upon this subject by Terson,‡ more than a score of communications have appeared concerning an affection of the nerve-head characterized by the formation of small excrescences in its tissue, which have been called globular masses, hyaline bodies, hyaline verrucosities, and "drusen" of the optic papilla.

It is evident from an examination of the cases which have been reported that they may be variously classified. For example, Nieden, § writing from the ophthalmoscopic standpoint, shows that the globular formations may arise: (1) As a non-senile occurrence in young persons; (2) As wholly confined to

* *Archiv. f. Ophth.*, Bd. II, 2, p. 25, and Ibid., Bd. IV, 2, 13.

† Compare Nieden's paper, *Archives of Ophthalmology*, Vol. XVIII, p. 198.

‡ *Archiv d'Ophthalmologie*, June, 1892, p. 367. This paper contains a complete bibliography.

§ Loc. cit.

the optic nerve; and (3) As confined to the optic nerve, with good vision, and in an otherwise normal fundus. That is, they may occur in association with retinitis pigmentosa, choroido-retinitis, optic neuritis, and with alterations incident to Bright's disease (Nieden, Stood, Ancke, Remak, Oeller, and Gurwitsch); or they may appear in an eye free from other pathological changes (Nieden, Jany, Iwanoff). So far as our knowledge of the nature and origin of these bodies is concerned, the reported cases naturally divide themselves into those in which the bodies have been found incidentally in the examination of sections of eyes, and those in which they have been submitted first to ophthalmoscopic and afterwards to microscopic examination. To the latter class the case which I present for your consideration belongs, although the bodies occurred in a nerve-head that was notably diseased independently of their presence.

Daniel Fix, aged 45, married, a native of France, and a cabinet-maker, was admitted to the Insane Wards of the Philadelphia Hospital June 21, 1890. Physical condition negative, with the exception of "a linear scar one-half inch long, beginning two inches above the external angular process of the frontal bone, and running backward." His mental condition was apathetic and forgetful, but no evidences of insanity were present. "His eyesight was poor."

He was discharged to the Nervous Wards, May 8, 1891, a short time before which I examined his eyes thoroughly and on many occasions. The V. equaled counting fingers at three and six feet, respectively. The pupils were round and acted equally, though slowly, to the reactions of shade and light. The form field was concentrically contracted; the color field was not measured.

In each eye the ophthalmoscopic appearances were closely similar: An oval, slightly prominent papilla, grayish white in color, and largely devoid of capillarity. In a circle, slightly within the apparent margin of the nerve-head, were a number of globular masses. These were most prominent above, where they seemed to overlap the border, and, particularly in the right eye, were capped with shining particles which glistened like cholesterin crystals. The center of the disc was filled in, the lamina cribrosa was obscured, the vessels were not much changed in size, and the veins exhibited about their usual degree of tortuosity. Some white tissue was apparent at the emergence spot of the arteries. There was no change in the surrounding eye-ground; and no evidence of former inflammatory or hemorrhagic condition.

I am indebted to Dr. Francis X. Dercum for the following additional notes:

The man had been an immoderate drinker. About two years ago he had severe head-pains which confined him to bed for five months, during which time he had one convulsion. Neither fever, delirium, nor loss of consciousness was present. There is a history that he was shot in the head twenty years ago.* He had a pecu-

* Iwanoff found globules (3 out of 5) in eyes which had lost their vision from injury. In several of Nieden's patients there had been severe injury to the skull. The same condition has been noted by Gessner.

FIGURE 1. Hyaline bodies or drusen on each side of the central vessels, showing their position anterior to the lamina cribrosa and their relation to the choroid, from which, however, they are distinctly separated. (× 75).

FIGURE 2. Drusen more highly magnified; also change in the vessel wall most marked upon the right side. (× 200.)

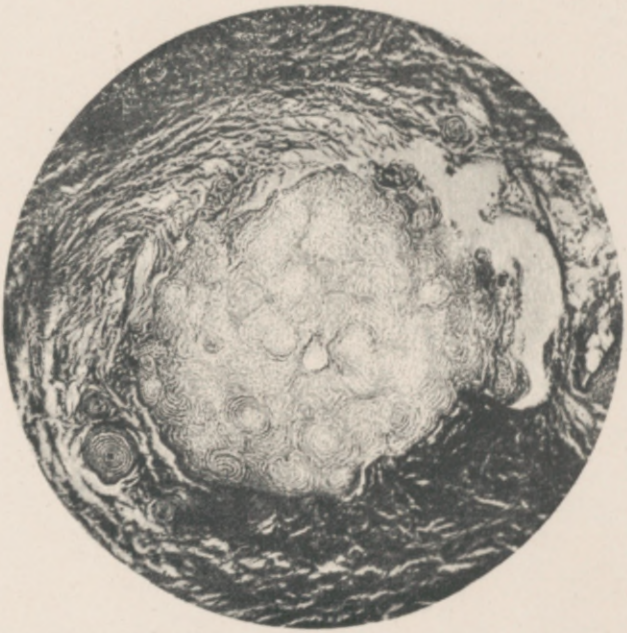

FIGURE 3. Single, large hyaline body showing concentric markings, and several smaller bodies detached from the main one. (× 500.)

liar, shuffling gate, while his shoulders were stooped and his head bent forward. Apparently all functions were normal except the eye sight, although, as before stated, there was some mental apathy, and occasionally he complained of pain in the head. During the latter part of the winter of the present year, he died quite suddenly. The autopsy was performed by Dr. Dercum and myself, and the brain and posterior halves of the eves reserved for microscopical examinationby preservation in Müller's fluid. Longitudinal sections of the nerve entrance were prepared by Dr. William M. Gray, and the following lesions were found:

Microscopic Examinations: Anterior to the lamina cribrosa, and on either side of the central vessels, are two oval masses, of whitish color, and composed of a series of smaller bodies in which the markings with concentric lines is very distinct. The mass to the right side is the larger, measuring in its long diameter $\frac{4}{10}$ of a mm.. and in its short diameter $\frac{3}{10}$ of a mm. The measurements of the other mass are respectively $\frac{3}{10}$ of a mm. and $\frac{2}{10}$ of a mm. (Figure I). In other words, these sections are compound hyaline bodies. In immediate proximity to these masses are several smaller bodies of like structure, but of somewhat pinkish tint, owing to the absorption of the staining fluid (Figs. I and II). From an examination of a series of sections, it seems likely that these masses represent cross cuts of a ring of hyaline tissue which, of varying circumference, occupied the tissue of the nerve-head in advance of the lamina and surrounded the central vessels, but did not pass beyond the outer margin of the papilla. Even in those sections which have not included the vessels, small hyaline bodies can be seen in the upper central part of the cuts. This arrangement represents what Hirschberg and Cirincione have called a "drusen ring." The tissue surrounding the cavity in which the "drusen" lie is somewhat matted and condensed, probably by pressure. The hyaline body for the most part is separated from immediate contact with the adjoining structures by a clear space, no doubt the result of contraction of the hardening process Most of the sections show the well marked concentric lines, and exhibit the appearance which has led to a comparison between these bodies and the corpora amylacea (Fig. III), but in some slides the concentric lines and glass-like structure are replaced by a yellowish and more granular composition interspersed with dark granules, indicating a calcareous change.

The optic nerve, in general, exhibits the lesions of well

marked atrophy: Increase in connective tissue, thickening of the bloodvessel walls, and wasting of the nerve fibers. There is marked alteration in the vessel walls, consisting chiefly of thickening of the adventitious coat, and in some of the smaller arterioles in the body of the nerve below the lamina this thickening and condensation of the fibrous coat presents a well-nigh homogeneous appearance. Above the lamina, near the right branch of the central artery, the wall is greatly increased in size, nearly homogeneous, of whitish color, except on the margins, which have imbibed some of the carmine stain, and contains here and there, particularly near the lumen of the vessels, some small semi-transparent drops. This condition seems to be analogous to the hyaline change which has been found and often described in the adventitious coats of arteries.* (Fig. II.)

In the retina gross lesions are absent, and with the exception of some oedema of the various strata, particularly of the nuclear layers, there is no very evident pathological change. The layer of the rods and cones is entirely absent, or so deficient that it cannot be effectively studied. Wherever vessels are manifest their coats are thickened, but a hyaline change cannot be seen.

The layers of the choroid are well preserved. The lamina vitrea is everywhere intact, and with the exception of somewhat undue filling of the larger bloodvessels, many of which are plugged with blood-clots, there is no special pathological change. The hyaline excrescences which have so often been seen and described in this membrane are nowhere present.

Dr. Dercum has made a most thorough examination of the brain. I append the notes which he has kindly furnished: "Examination of a large number of sections of the angular gyrus and cuneus of either hemisphere yielded a negative result. The nerve cells, their contents and their processes, are well preserved. Here and there the peri-ganglionic lymph spaces seem a little dilated, but even this appearance is infre-

* In the sections stained by Weigert's method, the "drusen" have been colored a deep black, but the coat of the vessel has not been affected by the coloring material, indicating that the "drusen" and the altered tissue in the adventitious coat are not composed of the same material.

quent. The neuroglia has undergone no change. The vessels also are normal, although a few of the larger ones appear to have slightly thickened walls. No distinct degenerative change is anywhere present."

I also removed portions of the other cranial nerves and examined them microscopically without finding the slightest lesion.

The notes of the general post-mortem examination follow: Calvarium normal. Dura much thickened; pia and arachnoid thickened, especially at the base. Brain tissues soft and oedematous. Extensive dilatation of all ventricles due to ependymitis. Walls of the ventricles velvety. Infundibulum and floor of the third ventricle cystic and oedematous. In the position of the optic tracts nothing but a slight increase in density in the surrounding oedematous tissue is observed. The optic nerves are apparently shrunken. In the other organs of the body, thoracic and abdominal, no gross lesion is present save very general venous congestion, most marked in the lungs, together with oedema of the bases. Some spots of atheromatous change are present in the aorta and coronary arteries. The spinal cord was not examined.

From these examinations it is evident that the following lesions are present:

(1) Compound hyaline bodies, or "drusen," in the nerve-head, situated in their seat of predilection, within the tissue of the papilla, anterior to the lamina cribrosa.

(2) Atrophy of the optic nerve, which may or may not have antedated the formation of the "drusen," but which evidently was not caused by them.

(3) Thickening of the coats of the arterioles in the optic nerve below the lamina, and above, in the central artery, in the neighborhood of the "drusen," a change in the adventitious coat of the vessel, suggesting the appearance of hyaline degeneration, but shown by a differential stain to be of different composition from the "drusen."

As negative results it may be stated that:

(1) The retina and choroid exhibit no distinct pathological lesion, save some thickening of the vessel walls. Hyaline bodies springing from the lamina vitrea are absent.

(2) The other cranial nerves, so far as examined, were normal.

(3) The investigation of the structure of the brain yielded a negative result, and hyaline changes in the bloodvessels were not present (Dercum).

Nature of the Pathological Material. In the series of sections which I present for your consideration, the ordinary staining fluids have been employed, without special endeavor to utilize reagents that would give some information in regard to the exact pathological nature of the material which has been designated "hyaline." About a year ago Hirschberg and Cirincione * published a communication in regard to "drusen" in the nerve-head. These investigators carefully employed differential reagents, and as their case in many respects is singularly like the one which I report to-day, I may quote some of their results in this respect:

"Concentrated hydrochloric acid affects the yellowish fragments slowly, developing large gas bubbles which form in a wreath around each single piece, but the pieces are not dissolved. This acid does not have any effect upon the more peripheral, round, reddish, rough flakes. On the addition of concentrated acetic acid, exactly the opposite results seems to take place, the acid leaving the central fragments intact and attacking the peripheral flakes. But this is only apparent. The influence of the acid extends only to the tissue between the deposits, which becomes transparent and invisible in the greater part of the microscopical visual field, and not to the concrements, which, on the contrary, become more distinct, due to their power of absorbing light. The concentrically striped pieces do not give any amyloid reactions with saffranin and methylviolet; tincture of iodine imparts a yellowish color to them."

From these experiments Hirschberg and Cirincione conclude that the deposits should be regarded as hyaline masses whose more exact composition is unknown, and which are partly calcified secondarily in the interior of the papilla. With the assistance of Dr. Perles, still other reactions were utilized in this in-

* Centralbl. f. prakt. Augenheilk., June and July, 1891.

vestigation. The transparent, faintly yellowish bodies in the head of the optic nerve were proved with the polarization microscope to be, very probably, not crystalized. Viewed simply with the direct and transmitted light, they appeared as broken fragments, with sharp corners, generally provided with acute angles, frequently resembling rhomboidal tables, with a fine substance lying in lamellae. On single, small pieces, a very fine concentric drawing, with faintly colored rings, could be observed, which were evidently due to interference, and pointed to a stratiform arrangement of thin lamellae. To still further investigate their nature, Hirschberg and Cirincione had recourse to micro-chemical reactions, for the details of which I must refer to their original paper. Suffice it to say, that these investigations seem to prove that the bodies were amorphous and organic, but that they did not partake of the nature of cells, neither did they yield albumin, fat, nor glue reactions, and on account of their indifferent behavior toward the most usual solvents, their composition appeared most to resemble that of elastin.

Assuming that the bodies in the case which I describe today are exactly analogous to those which were so thoroughly investigated by these two observers, it is reasonable to believe that their composition is identical, and these results have been quoted as the most authoritative opinion in regard to the nature of the tissue in question. However, the observation with Weigert's stain (see foot note, page 352) should be taken into consideration.

Origin of the "Drusen" and Nature of the Process which Caused them. Two views have been prominently maintained in regard to the origin of the "drusen."

1. They are hyaline excrescences of the vitreous lamina of the choroid, imbedded in the head of the optic nerve and have there become partly calcified, in this respect presenting a senile change. (Müller, Iwanoff, Wedl and Bock, Nieden.*)

2 They have nothing in common with the choroidal excrescences, but are the expression of a pathological process con-

* This observer, basing his belief on Kuhnt's observation of the relation of the lamina vitrea to the optic nerve and choroid ring, considers the hyaline bodies as a degeneration product of the lamina elastica of the choroid. His own investigations of this disease, however, depend alone upon ophthalmoscopic examination.

fined to a small portion of the optic nerve, possibly on account of local anatomical reasons, and finding their counterpart in the calcification of other tissues, particularly the cheesy nodules in the lung. (Hirschberg, Cirincione, Gurwitsch.)

The first view depends largely upon the support which was given to it by previous observers, especially Müller and Iwanoff, and also upon topographical relations, inasmuch as the lamina vitrea approaches very near to the optic nerve tissue, the fibres of which curve around this structure on their way to form the retina. In my own specimens it is easy to see the very close relation of the hyaline bodies to the vitreous lamina, and yet, in spite of their immediate proximity, the boundary between the two is unbroken and distinct. Terson,* although admitting the intimate connection which has just been stated, thinks that it is not safe to base an argument upon these topographical relations, but that a decision must be reached by the aid of convincing histological preparations.

Supporters of the second view place no faith in an argument based upon topographical relations. Indeed, according to them this, as has just been intimated, is not correct. The choroid does not exist in the place where the change developed, and consequently there is no vitreous lamina. Moreover, it would seem reasonable, if this view were accurate, that the hyaline bodies should not be located alone in one small confined portion of the optic nerve, and that certain transition stages should be found. Again, a similar process in the choroid as a point of origin ought to be present. Independently of these considerations, the histological aspect of the disease is the one upon which a differential consideration should be based. The choroidal excrescences are more or less extensive masses in concentric layers, attached with a broad base to the vitreous lamella of the choroid, and always project toward the interior of the bulbus. Their surface is covered with epithelial cells more or less developed, and they frequently contain within their interior one or more cells. Their consistency is that of fibrous tissue, but they are not so firm as to prevent an appearance of connective tissue cells and even secondary ossification. The

* Loc. cit.

most satisfactory investigation in regard to their nature seems to indicate that they are a colloid transformation of the protoplasm of the pigment epithelium. The argument just recited is the one employed by Hirschberg and Cirincione in the paper several times quoted, and seems to be convincing, especially when taken into consideration with the differential stains and micro-chemical reactions which these observers employed. The hyaline bodies in question, as they occur in the optic nerve, lack every trace of epithelial covering, and contain neither cells, nuclei, nor pigment. They are not attached with a broad base, but are practically free in the tissue. So far as my own examinations are concerned, they point very distinctly to a confirmation of the results which have just been quoted and of the arguments which are so forcibly used by the observers from whose research they have been abstracted. It may be interesting at this point to refer to the paper of Gurwitsch, who has described these bodies in eyes which were removed from cases of Bright's disease. He is quite in accord with the view that the bodies have nothing to do with the choroidal excrescences. He suggests that possibly the hyaline degeneration precedes an amyloid transformation.

My own case tends to confirm the views of those who believe that the "drusen" in the nerve-head represent a disease entirely distinct from excrescences springing from the lamina vitrea of the choroid. It adds somewhat more to our knowledge of this disease than we have previously been able to obtain, because the examinations include not only the nerve-head, but in addition, the entire optic nerves, the other cranial nerves and the brain, with the practically negative results that have already been recorded — results which seem to emphasize the local nature of the process.

The apparent hyaline transformation of the adventitious coat of a part of the central artery of the retina does not, it seems to me, count for very much when we consider the inflammatory process which must have been present in the optic nerve at some earlier date. According to Hirschberg, in those cases in which the "drusen" occur in the head of the optic nerve in connection with pigmentary degeneration of the retina, their

deposition is favored by the stenosis of the vessels in the retina, and they do not contribute anything to the disturbed vision. Perhaps in this case a similar argument might apply, but I hardly think so, and am constrained to believe that the optic atrophy and the "drusen" are two entirely distinct processes, the atrophy being a condition which probably came on after the compound hyaline bodies had been formed. Moreover, the differential stain to which I have referred before, gives evidence that the "drusen" and the change in the vessel wall are not analogous tissues.

Cirincione, in concluding his report on the microscopic lesions of this disease, says, "the first cause of this hyaline transformation and subsequent calcareous deposit in the papilla, however, remains to be determined, and likewise the reason why it remained confined to this small territory alone, instead of expanding or appearing scattered in other parts of the bulbus. We have not found sufficient proofs to solve this question and therefore, instead of indulging in more or less probable hypotheses, leave the solution of this question to future examinations." Unfortunately, the present case does not give any information which helps to solve the question which this observer, as well as others before him, have found it impossible to answer.