SNOWBALL VITREOUS OPACITIES—ADDITIONAL CASES.*

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This paper adds reports of four cases to those previously published. It discusses the character of the opacities and their probable etiology.

Three years ago I placed on record four case histories of the condition described by Benson as Asteroid Hyalitis or Snowball Opacities of the Vitreous; and when doing so pointed out that while I was confident that these differed from the cholesterol crystals sometimes seen in this structure, they developed in the presence of the same general and local clinical conditions.

My personal experience seems to indicate that at least two types of opacities that may be differentiated clinically have been grouped under the term of synchysis scintillans; first, those that are typical cholesterol crystals, and secondly, those opacities that to my mind are not cholesterol crystals but typical or atypical types of snowball opacities. Why should they not be differentiated?

Judging from the literature, one would imagine that the condition under discussion was a rare one, since but fourteen cases have been recorded. This I believe to be far from the truth, since ten cases have been personally observed in the past twelve years, while during the same time I have not seen more than two cases of cholesterol crystals in the vitreous. As a consequence, I have almost come to the conclusion that deposition of cholesterol crystals in the vitreous is an unusual manifestation, whereas these snowball opacities, either in the early stage or when well formed, are by no means as infrequently encountered.

While a clinical differentiation, in the light of our present knowledge, is of no significance, the difference between these two types of opacities, as they appear to me, is just as striking as the difference between a piece of tinsel and a tiny cotton ball, or cholesterol in the retina and a white punctate exudate.

Since my last report, six cases have been observed by me; one patient's report is not available for review and another record has been mislaid, the remaining four are as follows:

CASE I.—J. H. S., aged 56, was referred to me in October, 1904, by Dr. Wharton Sinkler. He was seen at more or less regular intervals up to 1916. From the time of his early examination, his pupils were of the mitotic type, unequal, of somewhat irregular contour, with sluggish reactions. In the left eye in the peripheral nasal field, several well defined choroidal erosions could be seen. The discs were healthy. Full visual acuteness could be obtained by a compound hyperopic correction. The case was specific. In later years he developed incipient lens changes and well defined evidences of sclerosis of his retinal vessels, but no hemorrhages or exudates.

In 1915, he was in a hospital for two weeks owing to bladder trouble, and while there a serum and spinal Wassermann were found to be weakly positive. He was given two injections of salvarsan by the Swift-Ellis method.

In 1919 at the age of 70 years, he again returned with a frequent complaint of smarting and burning of the lids and eyeache. At this time, the pupils were as above noted; incipient opacities were present in each lens. The discs were healthy, but scattered about the posterior pole of each eye were a few yellowish pinhead sized lesions, with a large split pea sized choroidal erosion in the right eye and the previously noted erosions in the left. While a few translucent opacities were present in the vitreous of the right eye, the left vitreous contained numerous characteristic snowball opacities.

The vision of the right eye = 6/9?; the left eye = 6/6?.

CASE II.—C. R. E., aged 60, came to me in April, 1920, complaining of pres-

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byopic symptoms. His vision without a correction was 6/6 and 6/6+. He read .50 type at 48 cm. with a +.75 sphere which he was then wearing. The only glass he would accept for distance was a +.25 cyl. ax. 90° and a + 2.00 sphere added gave him a near point of 24 cm., with a range of 46 cm. There were no pupillary or extraocular muscle lesions.

In each lens there could be noted a delicate annular ring in the cortical layers, made up of fine punctate dots, the diameter of the ring being 7 mm. In the right eye, the whole vitreous body was studded with these suspended snowball opacities, usually round, a few oval, but no strands. While searching the extreme periphery of the eyeground, a curious effect was produced by a large cluster of these opacities. They were situated at the extreme limits of perception; and when seen momentarily, and obliquely, they presented the appearance of a whitish expanse or whitish streaks that I first thought was an exudate, but after more minute study the true character of the manifestation could be determined. The disc was of rather mellow type with soft margins, the superior nasal quadrant being a trifle pale; and here and there on its surface could be noted tiny dots, evidencing the earliest visible stages of hyalin deposits. No lesions of the choroid or retina could be detected, and the retinal vessels did not show distinct evidence of sclerosis and might well be called normal for his age, as far as ophthalmoscopic appearances were concerned.

In the left eye the general appearance of the disc was the same as that described for the right eye, but no hyalin points were as yet visible. In the examination of the vitreous, I had about concluded no snowball vitreous opacities were present, when a passing glimpse of the same manifestation noted in the periphery of the right eye, was detected in the extreme lower and outer periphery. A little further study soon revealed a cluster of some half dozen snowball opacities at this site.

No changes were seen in the choroid or retina and no distinct evidence of angiosclerosis.

CASE III.—J. G., aged 50, was admitted to Dr. Stengel's service at the University Hospital on January 20th. He gave a history of swelling of the legs as early as 1904. In January, 1919, he began to have headaches, palpitation of the heart, and dyspnea had set in about a month before. On January 17, he went to bed feeling as well as usual, but was awakened with a severe pain in the head, and then discovered he could not see with the right eye.

I shall not enumerate the results of the thoro examination except to say that his blood pressure was 205-140. The phenolphthalein test showed but 10 per cent in two hours. The Wassermann test was negative. Blood cholesterol 219 mgm. per 100 cc. He was found to have a chronic diffuse nephritis; arteriosclerosis of the senile type; myocardial hypertrophy and weakness; relative mitral and aortic regurgitation; hepatic enlargement from congestion. For this report and for certain studies, I am indebted to Dr. O. H. P. Pepper.

As to his eyes: The vision of the right eye was reduced to counting fingers at about five inches, while the vision of the left eye was 6/60. When examining this patient, it was noted that, suspended in the vitreous in the right eye, there were numerous white snowball opacities, characteristic in appearance but smaller than usually seen; varying in size from almost pinpoint to approximately 1 mm., a few tending to the elongated or spindle form. The disc has a pale yellowish tint in the temporal portion, better capillarity on the nasal side. There is an excessive angiosclerosis, characterized by silver wire arteries, with irregular caliber in both sets of vessels, and distinct pressure signs of the veins. There is a well marked perivasculitis, especially along the superior temporal veins. Between the macula and the disc there is a large cluster of pinhead sized whitish exudates. A few

of these, less pronounced, can be noted about other portions of the posterior pole. The whole posterior pole on both sides of the disc appears faintly yellowish, and scattered about this area are a number of linear and flame shaped hemorrhages of varying degrees of intensity. I think there is but little doubt that a thrombosis occurred in this eye.

In the left eye a few delicate fine opacities can be noted in the vitreous, but these are not of the snowball type. The disc margins are almost completely blurred by a well marked exudation and striation, which extend well towards the midzones on all sides. Just beyond the disc, superimposed on this exudation, there is a corona of streak and flame shaped hemorrhages. The macular region shows punctate and mass like yellowish white exudates, such as are usually seen in cases of vasculorenal type. A few punctate hemorrhages are scattered among these. The vessels for some distance beyond the disc are partially or completely covered by the uniform yellowish exudate. The vessels show the same excessive angiosclerosis as in the right eye. Some of the major venous branches appear overfilled.

CASE IV.—Mrs. E. R., aged 64 years, first consulted Dr. G. E. de Schweinitz, 1.25.12, for a change in her correction. At that time there were no intraocular changes. She was first seen by me in January, 1918, when her eyes showed incipient lens changes and decided angiosclerosis of the retinal vessels, but no hemorrhages or exudates. The central part of the vitreous of the right eye contained a few snowball opacities, not of advanced type. Opportunities for complete medical studies were not available.

REMARKS.

Recently, Verhoeff¹ has placed on record the clinical notes of a similar case, and owing to the development of an acute glaucoma, he was enabled to examine the vitreous pathologically and microchemically with his usual thoroness. His findings are of partic-

ular interest, because it was the first case so diagnosed to come to pathologic examination.

The patient was a male, aged 75, who had a hemorrhagic retinitis when first seen. Snowball opacities were observed in the affected eye only. Verhoeff's studies permitted him to conclude that the opacities, "consist chiefly of calcium soaps, calcium carbonates, and certain amounts of fatty or lipid substances in combinations of various grades of stability. Their formation is usually, if not always, dependent upon intraocular angiosclerosis in association with an altered condition of the blood." When speaking somewhat more specifically, he refers to "calcium soap, probably calcium margarate, possibly admixed with insoluble compounds of cholesterol and lecithin." Likewise he very aptly points out that "fats, fatty acids, lipoids and lime salts are apt to be deposited where there is deficient oxygen as in necrotic infarcts and scar tissue.

Elsewhere² in speaking of synchysis scintillans, the statement was made that some factor must be required to produce it other than the local condition. This I believe to be equally true of snowball opacities, and it prompted my comments upon hypercholesterolemia and diabetic lipemia. Naturally, I am in accord with Verhoeff's belief that it is a degenerative process, but I hesitate to accept the view that intraocular angiosclerosis is the most important factor, altho it is doubtless a conspicuous one.

I venture to say that clinically the condition is not encountered in one percent of the cases of excessive angiosclerosis; neither has it been present in a definite percentage of the cases of thrombotic obstruction of the central artery or vein that I have seen. Still further, it has been observed in cases where there were but slight if any clinical evidences of angiosclerosis, as in the woman aged 35, as reported by Starck, and in Case II of the present report.

Should not more stress be put on the altered condition of the blood, to which both Verhoeff and myself have

referred? Just what this is, or where, why and how certain elements gain access to the blood stream, is still undetermined. Given a case of bilateral excessive angiosclerosis of the retinal vessels, or if you please, of the intra-ocular vessels, it is just as difficult to explain why the opacities are usually unilateral, as it is to explain it in the presence of a probably much altered blood picture. Considering the ages of the patients usually affected, the relationship of a general arteriosclerosis, as this may affect the functional activity of some distant organ or structure as well as the eye, is not to be overlooked; but here again the important link is missing.

Comment has already been made (previous report) upon the fact that these opacities are not cholesterol as we are accustomed to seeing it. In the light of our present knowledge of the chemistry of the group of substances probably concerned in snowball vitreous opacities, I made the vague, but possibly not far afield, suggestion that these opacities were formed during the same or similar process that has to do with the deposition of cholesterol in the vitreous. What conditions must pertain to the eye, the blood, possibly in the fats or lipoids themselves, if these are the offending agents, and probably in some distant structures or organs, still remains to be solved. If the leads in this branch of chemistry are short and abrupt in their terminations, our clinical interpretations must necessarily be vague and conjectural.

In my previous article I referred to the work of Chauffard and Laroche, and in a recent report on deposits of cholesterol these same two investigators in association with Grigaut³ point out some interesting observations. They believe that we may have an active hypercholesterolemia which is chiefly of suprarenal origin, that it may be passive owing to hepatic insufficiency, while food hypercholesterolemia may be regarded as a third type. It may exist as a blood manifestation alone, or this may be as-

sociated with a tendency to local deposits, as in xanthelasma. As ocular manifestations, they refer particularly to the white patches seen in the retina in cases of nephritis, diabetes and in certain cases of pregnancy. They also comment upon the infiltration of atheromatous arteries with lipoids and among them, cholesterol.

Mention is also made of the experimental work of Anitchkow Wacker and Hueck, who produced arteriosclerosis in rabbits by the injection of large doses of cholesterol. I might add that Mueller⁴ of California has shown that the cholesterol fed to dogs was absorbed from the alimentary tract thru the lymphatic system.

As far as I am aware, the cholesterol content of the blood has not been determined in any case of snowball vitreous opacities, prior to this report; and while it was found to be increased in Case III, other clinical findings present tend to oppose its being regarded as having direct relationship.

Altho not particularly pertinent, it is interesting to refer to the recent contribution of Wagener and Wilder in their study of 300 cases of diabetics observed at the Mayo Clinic, 44 of whom showed evidence of retinitis. After referring to the observations of Onfray, Garrod and Moore, they conclude that this manifestation is almost always accompanied by vasculorenal disease and that the pathologic vascular changes are the primary cause.

It is now the vogue to refer various unexplained questions to the realm of the endocrines, and since thinking aloud as well as presenting well conceived ideas is permissible at a meeting of this character, why might not some of the other ductless glands have the same relation to lipoids, as yet unknown, that the suprarenals, according to Chauffard, Laroche and Grigaut, may have to cholesterol?

What conditions might possibly be confused with these opacities?

First, synchysis scintillans, but here the *glittering* shower ought to be distinguished from the almost *dead white* or *lardaceous appearance* of those snow-

ball opacities that are in focus, and the vague corpuscle appearance of those which are not in focus, which gives an appearance somewhat analagous to that of phosphates in the urine. Still further, the snowball opacities when well developed, have a greater tendency to be globular and not flat. The movement in the vitreous is also distinctly different. Hill Griffith has referred to opacities that were white, glistening, round discs. In some of the cases I have observed that certain of the opacities, for they are not all of uniform size, have been small and white and hardly well enough developed to appreciate readily a third dimension, but they have never been glistening and they do not scintillate or sparkle. One cannot study these cases without wondering to what extent, these white opacities may have figured in the controversy as to whether a silver or golden appearance was more frequent in cases of synchysis scintillans.

Second, those rounded and whitish opacities sometimes seen on the surface of detached portions of the retina. In my first report reference was made to a history recorded by D'Oench; and while it was clearly stated that the white dots were scattered over the detached portion of the retina, Valk, who cited the case, assumed they were in the vitreous. These rounded opacities are seen in certain cases of detached retina and are doubtless familiar to all of us. A patient that I now have under observation affords a beautiful illustration of them. These may be the dots to which Elliot refers as observed on the retina in so many of the eyes examined pathologically after couching.

Third, they are not to be confused with the large round corpuscle like vitreous opacity seen in certain of the severer types of uveitis, in my experience chiefly in those of a tuberculous character.

Fourth, when clusters of these opacities occur in the extreme periphery, they might be mistaken in a hurried examination for the margin of an ex-

udate. Case 2 illustrates such a possibility.

Fifth, mention might be made of the small white nodes seen in the vitreous in certain cases of glioma of the retina, such as have been described by a number of observers.

In conclusion, I may say that judging solely from my personal experience, I believe that the type of opacity under discussion has contributed more to the diagnosis of synchysis scintillans than has the actual cholesterol crystal. Verhoeff's observations have done much towards providing more definite knowledge in regard to this condition and it is to be hoped that those who may chance to secure material of this character will afford him further opportunities for the study of these opacities.

Since the above paper was read, I have found an interesting study by Valentin (Hoppe-Seyler Zeitschr. f. physiol. Chemie, 1919, cv. 33) "On the Fat-like Substances Found in the Vitreous Body of the Eye of the Horse." His work was based on a study of more than 200 eyes. In addition to the usual constituents, grape sugar and lactic acid were demonstrated in the vitreous.

In speaking of tyrosin, he concluded that the amount even of combined tyrosin in the vitreous is so slight that its excretion must necessarily be doubtful. The opaque particles were examined in polarized light, with various chemical reagents and with Sudan II, neutral red and Nile blue sulphat. In nearly all the tests, the presence of cholesterol, phosphoric acid, cholesterol crystals, phosphatids, soaps, neutral fats and occasionally glycerinester and nitrogen could be demonstrated. The tests also showed that the fatty and fat like substances in the vitreous play an important part in the turbidity referred to.

As a result of his studies of the normal vitreous, he found that it contained soaps which hold various lipoid substances in solution, such as: glycerinester, cholesterolinester, free cholesterolin and phosphatid containing cholin.

Under abnormal circumstances these substances, normally held in solution, occur in the form of droplets, and in addition there is an excretion of soaps. The study also shows that the opacities as a rule are not caused by a single substance, but by a combination of several substances, of which sometimes one, sometimes another predominates. All of the substances show lipid characteristics, sometimes neutral fat,

sometimes free cholesterol or cholesterol ester or phosphatid. In addition to the flakes (exudate residue) no substances except those of a lipid nature were found as constituents of the opaque particles, in spite of the large number of eyes examined. Tyrosin was never excreted. The opacities therefore seem to be based on a process analogous to that which causes formation of gall stones from the bile.

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THE VISUAL PATHWAY AND THE PARANASAL SINUSES.

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This address by the Professor of Anatomy of Jefferson Medical College brings into convenient form the leading facts regarding the anatomic relations of the optic tracts, chiasm and nerves to the accessory sinuses and the nose. It was given before the Section on Ophthalmology of the American Medical Association, June 8, 1921, and is published here by courtesy of the *Journal of the A. M. A.*

Before entering into a discussion of the anatomic relationships which exist between portions of the visual pathway and the paranasal sinuses, it is essential that reference be made to a few cardinal points in the intrinsic anatomy of the visual pathway: The retina from the point of view of ontogenesis or embryology is a part of the brain, and the so-called optic nerve is a brain fiber tract supported by neuroglia and other elements. Moreover, the nerve is surrounded by tubular prolongations of the three meningeal membranes—pia, arachnoid and dura.

The meningeal extensions also prolong the subdural and the subarachnoid spaces along and around the optic nerve as far as the sclera, where they become continuous with the posterior group of tissue spaces of the eyeball (Figs. 1-3).

Strictly speaking, there is nothing in the visual apparatus which morphologically corresponds to a peripheral nerve. The percipient elements—the rods and the cones of the retina—are directly stimulated by the light waves.

There is, of course, an analogy between the rods and cones and a peripheral nerve, but they are not morphologic equivalents. Indeed, the retina is not unlike the brain proper, since, it is made up of supporting elements and neurons; the important neurons being (a) the rods and cones, (b) the bipolar cells, (c) the horizontally placed correlation neurons and (d) the so-called ganglion cells. The axons of the latter converge toward the optic disc, pierce the vascular and fibrous tunics of the eyeball, and then course centrally as the conventional optic nerve, the optic commissure and the optic tract, to terminate variously in the thalamus, the metathalamus and the midbrain. Since identically the same fibers or axons form without interruption and in order from before backward the optic nerve, the optic commissure and the optic tract, it would be more appropriate to designate the entire pathway the optic tract.

The principal fibers of the optic tract above referred to, together with their cell bodies or nutritional centers in