IX. STUDIES ON THE VITREOUS BODY. I.

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(Received November 2nd, 1934.)

THE aim of the studies detailed below was to elucidate the phenomenon of the rise of intra-ocular pressure associated with chronic glaucoma (*glaucoma simplex*).

The facts of the shallow anterior chamber, the pushing forward of the lens and iris, the thinning of the choroid and the compression of the retina, combined with the freedom of the iris in numerous cases of the disease, lead to the conclusion that a swelling of the vitreous body is most probably the determining factor. The view of Heesch [1926, 1] that the increase in pressure might be due to negative osmosis across the scleral membrane is contradicted by the fact of the compression of the sclera to less than its normal thickness. Furthermore any theory postulating that the increased pressure is due to the failure of elimination of fluid from the anterior chamber is unable to account for one of the most obvious symptoms of the disease, *viz.* the shallow anterior chamber.

The vitreous body is a true gel showing an ultra-microscopic fibrillar structure [Baurmann, 1923; 1926; 1932; Heesch, 1926, 2; Duke-Elder, 1929; Goedbloed, 1934] with the characteristic vapour pressure isotherm of a gel formed from a lyophilic colloid [Duke-Elder, 1930], and typical elastic properties [Robertson and Duke-Elder, 1933]. It contains a protein called "residual protein" [Duke-Elder, 1930] in a concentration of 0.025 % which is responsible for its gel nature.

The combined isolated proteins of the vitreous body show degrees of swelling depending on the p_H of the swelling medium rising from a minimum at about p_H 4.5 to a maximum at about p_H 8.0 [Duke-Elder, 1930]. Large variations in the volume of the vitreous body are achieved by placing it in solutions of different p_H [Baurmann, 1924; Duke-Elder, 1930], but owing to the crudeness of the technique employed any deductions drawn from these experiments must be treated with caution. It is true that Redslob and Reiss [1928] found considerable variations in the total volume of an intact eye in a modified dilatometer on varying the p_H . Two maxima at p_H 8.1 and 8.7 were obtained. Since however the sclera is known to increase in volume with varying p_H these results do not allow of any conclusions as to the behaviour of the vitreous body to be made. On the other hand, Löbeck [1929], using the isolated vitreous body, failed to record any increase in volume on the alkaline side of normal p_H .

So far there is no conclusive evidence that the vitreous body, *in vivo*, is capable of increasing its volume on altering the p_H of its surrounding medium. Glaucoma however is not associated with any detectable abnormality in the p_H of the blood [see *e.g.* Schmerl, 1928], so that experiments on the variation of this factor are only of interest to the extent that they show that the vitreous body is capable of modification of its volume in response to a changed environment.

A factor in the swelling of proteins often more potent than the p_H is the presence of specific ions, *e.g.* I^- or CNS^- , or the so-called hydrotropic substances of Neuberg [1916]. The recent work of Katz [1933] on the swelling of starch and gelatin has shown that substances such as the sodium and potassium salts of long-chain fatty acids, and in general dipolar substances with both hydrophilic and hydrophobic groups in their molecules, will increase the rate of swelling to an enormous extent. Since the increased swelling so produced is due to adsorption on to the micelles of the colloid, it is obvious that these substances may be effective in low concentrations, and hence it is not impossible that they are effective in the causation of glaucoma. The occurrence of abnormal quantities of substances of a soapy nature in the eye in advanced glaucoma and similar degenerative conditions of the eye lends support to this view. It may be remarked here that Baurmann and Thiessen [1922] noted that KCNS delayed the occurrence of "age-changes" in the vitreous body, and Goedbloed [1934] observed ultra-microscopic changes in it after treatment with KCNS solutions for 24 hours which he interpreted as due to increased hydration of the micelles.

In this paper the results of experiments are described which are designed to show whether substances such as sodium oleate and sodium laurate in aqueous solution may affect the volume of the vitreous body. A full discussion of the possibilities that a gel, in such a state of dilution as is the vitreous body, may exhibit an increase in volume or hydration even under the most favourable conditions, will be left to a succeeding communication when it is hoped that the results of experiments on other swollen gels, at present under way, will have given us sufficient information to allow of a more than tentative decision to be made.

EXPERIMENTAL.

The apparatus of Schmidt [1931], used for the determination of the water-uptake of powders, was modified to suit the peculiarities of the vitreous body (see Fig. 1). The tap, T_1 , allows connections to be made between the reservoir, R , and the capillary, C ; between R and the chamber, P ; between P and C , and between R , P and C . The vitreous body is placed in the chamber, P , which is separated from the fluid in the rest of the apparatus by a sintered glass disc, S , and which has a mark on it showing the level of the tap, T_1 . Any uptake of water is measured by the movement of the meniscus in the capillary. The procedure is to fill the reservoir with the given solution and make connection, with T_2 open, to P and C until fluid flows through T_2 when the latter is closed and connection is made between R and C alone until the latter is half filled. T_1 is then half-turned so that no connections are made, and the vitreous body of an ox is placed in P to just above the mark. When the tap T_1 is turned to make connection between P and C the meniscus will move along the capillary to the right due to the slight excess of hydrostatic pressure in P . To counteract this the whole apparatus is tilted slightly as the tap is turned so that the meniscus stops after it has moved a few inches. The tilting must not be so steep that the meniscus starts to move backwards, otherwise water will enter P and the experiment must be started again. Solutions of 0.9 % NaCl buffered with phosphate to p_H 7.8 and 8.0, and solutions of 1 % sodium oleate and laurate were used.

Results.

In all cases no water-uptake was observed in 24 hours.

As will be appreciated, the apparatus described determines whether the gel takes up water, but not whether a volume increase occurs, although the one

process is always associated with the other. Küntzel [1929] has divided the swelling process into two parts, one due to water-uptake and the other due to the mutual repulsion of charged micelles. Neville and Theis [1930] have shown that a maximum of swelling need not necessarily correspond with a maximum of water-uptake. In view of the possible independence of the two processes at

Fig. 1.

Fig. 2.

certain stages of swelling it was thought that there was just a chance that the vitreous body might alter its volume by a re-orientation of the charged micelles, produced by the adsorption of a polar compound, without necessarily taking up water. To put this to the test, the apparatus shown in Fig. 2 was devised.

The hollow hemisphere, *A*, fits into the dome, *B*, by a ground joint. *B* is connected to a capillary, *C*, and a reservoir, *R*. *A* is filled with vitreous and fitted into *B*. *R* is filled with a saturated solution of sodium laurate in amyl alcohol dried with sodium sulphate. The whole is allowed to equilibrate in a thermostat at 25° (constant to 0.002°). When thermal equilibrium has been established the tap *T* is turned and the solution is allowed to fill up *B* and run along the capillary tube. The tap is turned off and the position of the meniscus fixed on the cross-wires of a telescope. Any increase in the volume of the vitreous would be registered by a movement of the meniscus to the right. A control was run using pure dry amyl alcohol.

Repeated experiments failed to show an increase of volume; in general a slight contraction in both control and test experiments was observed.

DISCUSSION.

The absence of any water-uptake near p_H 8 in the first experiment is in agreement with the findings of Löbeck; the experiments with soaps show that under more extreme conditions than that of changed p_H the vitreous body does not increase in volume within 24 hours.

These results however can hardly be treated as absolutely demonstrating that the vitreous body is incapable of increasing in volume in *glaucoma simplex*,

as the increase in intra-ocular pressure associated with this disease is slow, frequently taking years to reach its maximum value. Furthermore, there seems to be a definite difference in the behaviour of the vitreous body according as it is *in vitro* or *in vivo*. For example, in the latter state it is capable of withstanding unbalanced stresses of quite a high order, whereas *in vitro* the slightest unbalanced stress tends towards liquefaction. Considerations such as these make it difficult, in the present state of our knowledge, to reason from the behaviour of the vitreous body *in vitro* as to its probable behaviour *in vivo*.

We have pleasure in recording our indebtedness to Profs. J. C. Drummond and H. Freundlich for their sustained interest and criticism, and to the Medical Research Council for defraying the expenses of this research and for personal grants to two of us (E. B. R. and H. D.).

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