PERMEABILITY OF THE BLOOD-AQUEOUS BARRIER TO FLUORESCEIN DURING THE WATER-DRINKING TEST IN GLAUCOMATOUS EYES*†

BY

WOLFGANG LEYDHECKER

*From the Institute of Ophthalmology, University of London.
Director of Research, Sir Stewart Duke-Elder*

THE permeability of the blood-aqueous barrier to dyes has been studied by numerous observers, but it was not until Amsler and Huber (1946) developed the technique of the fluorescein test that such tests became of clinical value. Two ml. 10 per cent. sodium-fluorescein are injected intravenously and its appearance in the aqueous in a dark-room is observed by means of the slit-lamp, the beam of which then develops a greenish colour in the anterior chamber. The increasing concentration of fluorescein in the aqueous is measured by the decreasing intensity of light which is required to produce a perceptible colour.

This intensity is determined by the current through the lamp which is regulated by a resistance and measured by an ammeter. When the current is plotted against time, a curve is obtained which shows with sufficient exactness the permeability of the blood-aqueous barrier to fluorescein. The normal variations are represented on a chart by a broad band. The individual variations of the same normal subject are up to 0.8 amp. on different days, but always within this band (Haefeli, 1946). In glaucoma abnormally high curves have been described by Amsler and Huber.

In a previous paper (Leydhecker, 1950) I have reviewed the literature concerning the water-drinking test of Marx (1925-28) and Schmidt (1928-31), and have shown its mechanism to be a water flow into the eye as a result of the difference of osmotic pressure produced between blood and aqueous. In about 70 per cent. of all cases of primary glaucoma, a rise of the ocular tension results, which is significantly greater than in normal eyes. In the present paper the question whether the flow of water into the eye and the subsequent rise of tension are associated with an abnormally fast inflow of fluorescein is investigated.

Method

Patients with an established diagnosis of glaucoma, but no other general or ocular disease, drank 500 or 1,000 ml. water within 2 to 4 minutes in a state of fasting. Miotics were discontinued at least 24 hours previously. Two ml.

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sodium-fluorescein were injected into the cubital vein, in most cases 3 to 7 minutes after the patient had started the drinking, in some up to 15 minutes later. The apparatus used for the fluorescein test had been calibrated by Huber himself. The original method of Amsler and Huber was employed, with the exception that every few minutes the room was illuminated, during which time the investigator wore a pair of close-fitting dark goggles. Thus it was possible to record the effect of the water-drinking test alone, without possible interference from the mydriasis due to the darkness on the outflow of aqueous and the intra-ocular pressure.

The ocular tension was measured 30 minutes before, and immediately before, the ingestion of water, in some cases after 15 minutes, and in all cases after 25, 35, and 45 minutes. On another day a control fluorescein test and measurements of the tension were repeated by the same observer, without the drinking test being done.

Results

Altogether 39 tests were done on sixteen patients with bilateral primary glaucoma. There were 24 eyes which had not been operated on, thirteen of them suffering from chronic simple glaucoma, eleven of the chronic congestive type. Eight eyes had been operated on; three of these had chronic simple glaucoma, and five had chronic congestive glaucoma.

No significant difference between the fluorescein-curves obtained without drinking and those after the ingestion of water were found in any patient. The fluorescein-curves of the same eye were in some cases slightly higher during the first 10 minutes after drinking, in other cases, they were the same or slightly lower. The differences averaged 0.3 amp., and never exceeded 0.7 amp. They are therefore well within the range of the individual variations of normal eyes on different days.

There was also no significant difference between curves obtained after the ingestion of 500 ml. and those after 1,000 ml. water in the same patient, nor was there any obvious correlation between the rise of tension and the height of the fluorescein-curve. This is of special significance since in some drinking tests the rise of the ocular tension was as much as 23 mm. Hg while the fluorescein-curve was the same as that found in the same eye without the drinking test and with a normal tension.

The type of glaucoma was important only in so far as most eyes with the congestive type gave fluorescein-curves higher than those with simple glaucoma. These differences, however, were not sufficiently marked to permit of the differential diagnosis. All curves were abnormally high.

Discussion

The independence of the permeability of the blood-aqueous barrier to fluorescein from the movement of water across it,

suggests that conditions in the human eye are similar to those shown by Kinsey and his co-workers (1942) to exist in that of the rabbit, as far as the exchange of water is concerned. These authors found by the use of tracer substances that water moves into and out of the eye independently of ions of small size, such as Na, PO_4 , or Cl. It will therefore not be surprising to find in the present experiments that the relatively large ions of fluorescein diffuse separately from water.

The different experimental conditions, however, justified the investigation of this question for the human eye. Kinsey and others (1942) did not change the osmotic equilibrium between blood and aqueous, and their experiments were performed on the normal eye of the rabbit. In one instance only, when they injected D_2O into the vitreous, did an increased ocular tension result, and then much longer times for the exchange of water between eye and blood were obtained than when the intra-ocular pressure was undisturbed. In the present investigation the ocular tension was 32 to 54 mm. Hg before the ingestion of water in 33 cases, but its value had no influence on the positive or negative result of the water-drinking test, or on the height or shape of the fluorescein curve.

These results also support the view which has been put forward in a previous paper (Leydhecker, 1950) that alterations in the vascular condition of the eye are not a decisive factor in determining the outcome of the drinking test, since it is to be supposed that such alterations would be associated with changes in the permeability of the blood-aqueous barrier.

Summary

Sixteen patients with primary glaucoma have been subjected to a combination of the water-drinking test of Marx (1925-28) and Schmidt (1928-31) with the fluorescein test of Amsler and Huber (1946). It was found that the permeability of the blood-aqueous barrier of any one eye to fluorescein did not depend significantly on whether the tension rose after the ingestion of water or not, or whether the injection of fluorescein was made immediately after drinking, or up to 15 minutes later. The significance of these observations is discussed.

It is suggested that in fluorescein tests in glaucoma the room should be illuminated between each reading to prevent a possible interference of the mydriasis on the circulation of aqueous. A rise of the ocular tension due to this factor may otherwise be mistaken for a spontaneous phasic variation of the tension and

lead to erroneous conclusions. During these intervals the observer wears a pair of light-tight goggles.

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