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OBSERVATIONS ON THE HUMAN RETINA

BY

D. J. WOOD

CAPE TOWN

DURING the last year I have had the opportunity of examining two eyes which so far as one could find were quite normal as regards the posterior segments. One was removed for an epithelioma of the limbus and had 6/18 vision, the other for a sarcoma of the orbit with 6/12 vision. Both corneae were distorted by the growth, sufficiently to account for the imperfect vision.

After hardening in Bouin's fluid the eyes were embedded in celloidin and cut, one in antero-posterior sections, the other in coronal sections. Staining was mostly by phospho-tungstic acid haematoxylin, but also by Heidenhain's haematoxylin. The former is a beautiful polychromic stain which shows up neuroglial elements well, and to a less extent nerve fibres.

Antero-posterior sections show how large a part is taken by the neuroglia in the retina. Not only does it support the different structures, but it separates them into groups, possibly units which function together.

Fig. 1, a section through the entire retina, shows the neuroglial elements well, from their beginning in the membrana limitans interna, to their other apparent termination in the membrana limitans externa. Such sections will show how the nerve fibre layer is divided into radial sheets by neuroglial elements which can be seen passing now in front, and elsewhere behind the nerve

FIG. 1.

Antero-posterior section of retina under low power. The alternating layers of nerve fibres and Müller fibres are seen.

FIG. 2.

Section near edge of optic disc. The nerve fibres, shown in longitudinal bundles, are separated by neuroglial fibres cut across. The ganglion cell layer and inner molecular layer are cut on the slant.

fibres. If we examine a section cut in the opposite direction as in Fig. 2, we can see how the nerve fibres as they arise from ganglion cells are separated into bundles of very uniform size by neuroglial fibres, shown here cut across. The appearance suggests not merely an intermixture to impart strength, but also a division into, or an isolation of bundles. Antero-posterior sections at the edge of the disc (Figs. 3 and 4) show how these

FIG. 3.

Antero-posterior section at disc margin to show the nerve fibres collected up into bundles by stout Müller fibres.

bundles are collected up into still larger units by stout Müller fibres lying between them.

One does not need to be imaginative to see that these bundles at the margin of the disc are the units which are involved in chronic glaucoma, and are implicated in the scotomata which are so characteristic of that disease. Each bundle probably does, in fact, represent a retinal area.

I have lately seen an interesting case of juvenile glaucoma where the choroidal part of the lamina cribrosa has stood up to somewhat increased tension while the scleral part has given way. The result was a ring of intact tissue with a hole in the centre through which one saw, at the bottom of a deep cup, the nerve and blood vessels. As there was no stretching of nerve fibres over the sharp edge of the membrane of Bruch, though central vision was bad, there was a full field. In the fellow eye the choroidal part of the lamina had given way also and there was a very deep ordinary cup with a field contracted almost to the fixation area.

FIG. 4.

The same under a higher magnification.

The enlarged photograph gives a somewhat different appearance of the Müller fibres from that shown in some even modern text-books. Had that very careful observer, Marcus Gunn, seen it he would at once have recognized that the trumpet-shaped ends were the agents responsible for the appearance which he modestly called after the family in which he first saw it. What he called "Crick" dots, and what we now know as Gunn's dots, are almost certainly due to reflections from these trumpet-shaped ends. Gunn noticed their association with retinal sensitiveness to light. I have also seen evidence that early oedema of the retina may produce an exaggerated show of these brilliant specks of light. Some time ago I saw a patient with no visible fundus abnormality at all, who was complaining of headache and occasional sickness. Two weeks later he returned with a brilliant display of Gunn's dots, and a month

later I found him in hospital for symptoms of brain tumour with well marked papilloedema. Gunn's dots tend to become much less visible in age, possibly due to absorption of light by the lens. In young persons they can almost always be made visible by red-free light.

The nuclei of Müller's fibres usually lie in the bipolar cell layer, but often they are numerous in the external layer of dendrites, where their pyramidal shape, and dark staining make them conspicuous.

External to the layer of bipolar cells one finds a layer of closely-packed dendrites usually 7μ thick, and immediately external to this an interrupted layer which Krause called the *membrana fenestrata*. This, one knows, is made up of the arborisations of amacrine cells, horizontal cells, and horizontal processes of neuroglial fibres. It is not a membrane, but it has a definite structure, with segments about 10μ in length which lie in alternating rows and very regularly. Under a high power the segments show dotted markings or knobs which are probably the ends of horizontal

FIG. 5.

FIG. 6.

Antero-posterior sections of retina showing (a) the layer of dendrites external to the bipolar cells, (b) the segments of "Krause's membrane," (c) the spaces external to (b) bounded by neuroglial and nerve fibres. They are probably exaggerated in this specimen.

fibrils cut across. Figs. 5 and 6 show this line as it appears in ordinary retinal sections. Fig. 7 cut in a plane more or less at right angles to this indicates the arrangement of the segments, but, being nerve tissue and thin, they stain poorly. Just external to these segments we find in all retinae, spaces bounded by neuroglial and nerve fibrils. In size they vary considerably. The appearance is shown in Figs. 5 and 6. They are produced by the bowing out of fibres before they end in the segments described. I have not seen the photographs of the condition described by M. Fortin in 1925, but I think they refer to the same structures.

Passing now to the external part of the retina we come to the structure which was described by Professor Verhoef of Harvard (Fig. 8) as a new membrane in the retina.

In sagittal sections it is inconspicuous, but in coronal sections which have been bleached and stained by phospho-tungstic haematoxylin the appearance is striking.

It is not a membrane but a series of hexagonal cell walls containing the pigment cells, and though it is described as an "intercellular cement substance," that is a poor name for so beautiful a structure.

FIG. 7.

Section through (b) of last figure to show the segments on the flat. The section is somewhat oblique and the bipolar cells are seen below.

FIG. 8.

Section through hexagonal pigment cells, more or less parallel with the layer. Bleached and stained to show the "cell walls." Below is choroidal tissue, above are the terminals of the rods and cones, and higher their bodies and nuclei.

The planes which make up this honeycomb are mathematically straight, and one feels that if it were possible to get a section not on the slant the hexagons would be truly such. As it is the cell spaces are usually elongated and most are about 15μ in length. They contain a single bold round nucleus with two nucleoli, or, if the section is through the front part of the cell, the terminations of the rods and cones also. Some cell spaces contain two nuclei, and occasionally three, in which case they reach 30 or 35μ in length.

The "cell walls"—I do not know what else to call them, as there are no other structures in the body like them—stain a clear blue of the same tint as the "walls" of haemocytes which are visible in numbers cut across in the subjacent choroid. The appearance is shown in Fig. 8, but it does poor justice to the beauty of the stained specimen.

What strikes one at once is that one is looking, not at a cementing substance, but at a contrivance for isolating or insulating groups of rods and cones which function together. The terminals of the rods and cones which are embedded in the protoplasm with its acicular pigment of any one of the hexagonal cells would be subjected to similar changes in the pigment particles and in the visual purple.

Professor Verhoef believed that he could trace his membrane into the *membrana limitans externa*. It is difficult to corroborate this, though one must admit that the *limitans externa* does curl round at its end, as if to fuse with the retinal part of the membrane of Bruch. If the attractive hypothesis of Sir J. H. Parsons is correct, that the two represent the basement membrane of the primitive ependyma, the two layers have developed very differently. The openings in the *membrana limitans externa* are 1.5 to 2μ for the rods and about 6μ for the cones, while the honeycomb containing the pigment epithelium is from 15 to 30μ across. It may be that it would be correct to consider the prolongations of the *limitans externa* on to the cones and rods as analogous to the honeycomb formation to enclose the pigment epithelium.

Several ideas gather round these points. Since the rods and cones radiate out from a sphere, and become thinner at their terminal segments, they must be separated by fluid in what was once the cavity of the secondary optic vesicle. This is the reason why it is so difficult to avoid damage to the bacillary layer in cutting sections.

From the point of good vision it may be of importance that this fluid shall be unvarying in composition and tension. Hence the reason for the two layers of the membrane of Bruch, and of the associated honeycomb cells which arise probably from the

retinal layer of that membrane. They filter and damp down irregularities in the supply of fluid from the choroidal capillaries. This would seem to postulate a second membrane beyond the rods and cones to retain the fluid in the bacillary layer.

The *membrana limitans externa* may, therefore, serve a double purpose, to keep the rods and cones regular in their emplacement, and, by retaining fluid, to subserve regular nutrition and a normal tension.

It occurs to one as a possibility that the nutrition and in consequence the rate of metabolic change, and therefore the efficiency of response, may be to some extent related to the diameter of the cones. The long thin macular cones will get their nutritive supplies quicker and better from the surrounding fluid, than the short thick cones of the periphery. The bowing forward of the *membrana limitans externa* at the macula allows for this increased length.

In cases of inflammatory disease it is difficult to see traces of the hexagonal honeycomb. This would perhaps render more understandable the occurrence of metamorphopsia in central choroiditis. Insulation has broken down, and displacement has followed. A severe oedema whether on account of a retinal thrombosis, or of a choroiditis will break down all barriers. The bacillary layer of the retina can be damaged by oedema whether it comes from retinal or choroidal vessels.

Ordinary histological methods seem, therefore, to suggest that we can observe in the retina three positions where retinal elements functioning together are collected into groups. We have first the grouping of rods and cones in the cells of the hexagonal epithelium, with an arrangement to ensure equal metabolic changes in the groups.

Secondly, before the nerve fibrils enter the next neuron chain there is a grouping, possibly to form larger units of impressions, and thirdly we have nerve fibres from retinal areas collected up into bundles before they enter the optic nerve.

I have failed to find any grouping arrangement between the bipolar cells and the next neurone, unless this is subserved by the laminated arrangement of the dendrites in the inner molecular layer.

We can, however, trace the Müller fibres at the disc margin back into the neuroglia which divides the nerve into small bundles in the anterior part of the lamina cribrosa, thence to merge into the larger bundles divided by fibrous tissue in the posterior part of the lamina and in the nerve.

We can also see how in the nerve, in longitudinal sections, the bundles divide and rearrange themselves into different bundles doubtless with reference to retinal areas, such as is well-known in the case of the macular bundle.