So long ago as 1896 Treacher Collins pointed out the resemblance between the general tumour cells of what is classically known as glioma retinae and foetal retinal cells of the third or fourth month of intra-uterine life.

One of the main points of this paper is an attempt to show, as Mawas has already done, that the columnar cells constituting the rosettes are essentially identical with those of the neuro-epithelium at about this period of gestation. The results here described were obtained with phosphotungstic acid haematoxylin after fixation with Zenker, and differ in important aspects from the classical descriptions of Flexner and Wintersteiner.

On section each rosette consists of a peripheral ring of nuclei situated at the bases of the cells. (Fig. 1.) The columnar cell bodies getting narrower as they pass inwards, point towards the centre of the ring, but usually stop a variable distance from it. Sometimes they do reach the centre and then no central cavity exists.

At or near their apices the cells are joined by dark staining junctional pieces which must surely if we compare them with Fig. 2, represent the external limiting membrane. Sometimes the junctional pieces are themselves joined by thinner lines probably present when the section does not cut the membrane absolutely perpendicularly.

A diplosome, so important in the development of the normal rods and cones and already described by Verhoeff in 1904, can often be made out near the apices of the cells (Figs. 1 and 3), and from this a thread running towards the nucleus of the cell may be present. As in the embryo, the cells may or may not project beyond the external limiting membrane. In the former case a thin process which one thinks represents the outer member of the visual cells may be seen arising from the apex of the cell.

From the general form of the cells (their narrowing towards, their apices being only due to their being placed in a circle), the presence of an external limiting membrane, diplosomes, and most probably an outer member, there can be little doubt that the rosettes represent developing rods and cones.

* From the pathological department of the Royal Westminster Ophthalmic Hospital. Received for publication, June 8, 1944.
Fig. 1.
Composite figure drawn from a number to show the structure of a rosette.

Fig. 2.
Developing cone cells from the paramacular region of a foetus of 345 mm. (From Bach and Seefelder.)
FIG. 3.
Photomicrograph of rosette (untouched). It shows columnar cells narrowing to their apices which project beyond the external limiting membrane and in which diplosomes can be clearly seen. Also pointed processes. X 1000.

FIG. 4.
The central area of a rosette. It is occupied by circular discs some of which contain a diplosome.

FIG. 5.
The central area here contains a net resembling a flat section of the external limiting membrane.
The contents of the central area of the rosette vary. Often it is partially or mainly filled with circular discs some of which contain a diplosome (Fig. 4). These represent the apices of those cells of the usually more or less spheric rosette at right angles to the plane of section. If we focus up and down on these circular discs we not infrequently see the external limiting membrane in the form of a net (Fig. 5): it is as if we were looking at a flat section of it which we remember has this appearance.

The contents of the central area may degenerate and may then take on many and curious shapes. Some of this degenerate material may be deposited on the external limiting membrane, and may quite easily (for one has done it oneself) be interpreted as representing rudimentary rods and cones. Sometimes the central area may be quite empty.

Now with regard to the nature of "glioma retinae." If we take it as established (and one does not think there can be a great deal of doubt about it) that the rosettes are derived from foetal rod and cone cells, Sattler cannot be right when he holds that even these structures are glial in origin. But that these tumours do contain glial fibres and cells can hardly be doubted. Otherwise we must regard the preparations of Greeff, of Urra and of Ascunce as artefacts, which is hardly likely. Moreover, as is well known the nuclei of the fibres of Müller can, in normal retinae, be quite easily distinguished in sections stained with phosphotungstic acid haematoxylin from the surrounding cells of the inner nuclear layer. They are angular, stain much darker and if cut along their length appear narrow and elongated. Now, angular, or elongated, darkly staining nuclei easily distinguished from the surrounding tumour cells, may be seen in sections of glioma retinae coloured by the above stain. One would suggest that these cells, also, are glial in origin.

Next, with regard to the origin of the general tumour cells. It has already been pointed out that these cells are very similar to foetal retinal cells of the third or fourth month of intra-uterine life. Moreover, the nuclei are identical with the nuclei of the rosettes (which probably rules out the possibility of their being glial). Further, it would seem that only rosettes will breed rosettes; for otherwise it would be very difficult to explain why one so often finds them in groups, with extensive areas or whole tumours without them.

Thus we see that, if our argument is correct, the general tumour cells do not arise from cells belonging to the future outer nuclear layer, nor are they glial cells; and it is generally agreed that ganglion cells and mesodermal cells belonging to the retinal blood vessels need not be considered. They must, then, arise from cells destined to form the inner nuclear layer.
We, therefore, come to the conclusion that glioma retinae arises from all the elements of the primitive nuclear zone* excepting probably the ganglion cells, i.e., from embryonic cells destined to form the inner and outer nuclear layers and glia.

To account for differences between one growth of this type and another, why, for instance some tumours consist almost entirely of rosettes while in others none can be found, one would suggest that the relative number of the original constituents may vary.

Finally as to nomenclature. Authors are now almost unanimous in condemning the name glioma retinae. Yet the term is exceedingly useful for, what is very important, everyone, the world over, understands exactly what is meant by it. Also it includes those tumours with, and those tumours without rosettes, so that emphasis can rightly be laid on the spread (common to both types) along dendritically dividing vessels producing the characteristic lobulated structure, and on the characteristic degeneration furthest from the feeding vessel, due to the relatively poor blood-supply, the absence of a capillary net, and the intra-ocular pressure.

Now, a new name must have the advantages of 'glioma retinae' without its drawbacks. One thinks that the best term to use is retinoblastoma suggested by Verhoeff in 1924 and adopted by the American Ophthalmological Society in 1926.

It indicates a growth from embryonic retinal cells and is already very widely used. But it must be made synonymous as Verhoeff intended with the classical 'glioma retinae.' To give a different name to those tumours which contain rosettes, as has been done latterly (Grinker, Duke-Elder), is unnecessary and has led to a great deal of confusion.

* It will be remembered that at an early stage of its development, the retina, before it has been divided by the two molecular layers into three cell layers, consists of a single nuclear zone and the marginal (almost non-nucleated) zone of His.

BIBLIOGRAPHY

ASCUNCE.—Soc. Franc. d’Ophtal., 1924.


MAWAS, J.—Traite d’Ophtal., 1939.

—— Soc. Franc. d’Ophtal., 1924.


—— Ibid., p. 351, 1904.