

PATHOLOGICAL EXAMINATION OF THE FRESHLY FIXED EYES FROM A CASE OF AMAUROTIC FAMILY IDIOCY.

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IN a case of amaurotic family idiocy recently reported in BRAIN (J. F. Poynton, J. H. Parsons, and G. Holmes [6]) the pathological examination of the eyes was admittedly incomplete, as they were only obtained thirty hours after death, and had suffered much from *post-mortem* change. The following case, in which the eyes were excised immediately after death and in which fixation left nothing to be desired, may serve to supply some missing details. For the notes of the patient's condition during her residence in hospital, and for the trouble taken to obtain the eyes, we are deeply indebted to Mr. Hildred Carlyll, Resident Medical Officer to the East London Hospital for Children.

CLINICAL NOTES.

The patient, Jenny M., was the child of Russian Jews who were not related. She was the youngest of five children, of whom the first and third died in infancy, not of this disease; the second is now 8 years old and well; the fourth was an amaurotic idiot, and died at the East London Hospital for Children. This case was reported by Dr. F. W. Mott [8].

The present patient was brought to the hospital first when one month old, and again two months later, because the mother thought she was not observant. At the second visit the fundi were found to show the typical picture of amaurotic family idiocy, with partial optic atrophy. The patient was a full-time child; she was breast-fed for eleven months, and when $1\frac{1}{2}$ years of age was admitted as an in-patient.

On admission her weight was 1 st. 6 lb. She was fairly well nourished, ate

and slept well, and cried less than other children. Heart and lungs normal. No convulsions. Limbs spastic. The eyes were kept open, but she took no notice of external objects; the pupils were dilated, but reacted sluggishly to a strong light. No nystagmus or strabismus.

For four or five months nasal feeding was employed, but the child gradually went downhill and became more stuporose. The limbs were more spastic, the head retracted, and she lay as she was placed without offering to move. The forearms were pronated, the wrists flexed, the thumbs much adducted, and claw hand was present. Knee-joints flexed; very great drop foot. Sores gradually developed at the site of contractures; and at death were present to an extreme degree, as was also the muscular wasting. Extensor plantar reflex on each side. The optic atrophy became complete. Latterly several attacks of bronchitis occurred, with pyrexia, but for the greater part tempera-

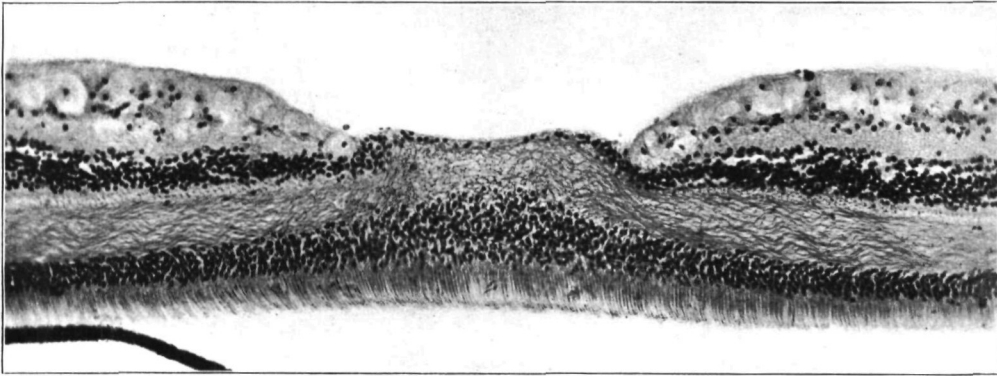


FIG. 1.

General view of the macula. The foveal pit is shallower than normal owing to thinning of the ganglion cell and nerve-fibre layers on each side. All the other layers are strictly normal. In the ganglion cell layer large, round, swollen-looking cells occur; they sometimes lie in spaces which they do not completely fill. Many of the small dark nuclei also belong to ganglion cells; some are neuroglial.

ture was normal. Death occurred when the child was a little over 2 years of age. Permission having been previously obtained, the eyes were immediately enucleated and fixed, one in Zenker's fluid, one in Müller. Further than this, no *post-mortem* examination was allowed.

PATHOLOGICAL EXAMINATION.

Both eyes were divided horizontally immediately above the level of the macula. The halves containing the macula were embedded in celloidin, and a complete series was cut through that region, every section containing the foveal pit being mounted. Paraffin sections were made from the retina of the other half.

The stains used were hæmatoxylin and eosin, v. Lenhössek's modification of the Nissl method, and Mayou's modification of Pappenheim's stain [13],

which proved excellent for the study of the nucleolus and of the finer changes in the nucleus and protoplasm. Giemsa's stain was also used, but, beyond defining the cell bodies, rendered no special service. The Müller-fixed eye was stained by the Weigert-Pal process.

Probably owing to the methods of fixation, Bielschowsky's method did not yield satisfactory staining. By far the best results were obtained from the Zenker-fixed eye, in which the histological preservation, as judged by the state of the rods and cones, was practically perfect.

MICROSCOPICAL EXAMINATION.

The changes are absolutely confined to the ganglion cells and their corresponding nerve-fibres. Owing to a certain diminution of these elements the foveal depression is shallower than normal; otherwise the general architecture of the macula is quite unchanged; there is no folding, œdema, or detachment, and the nuclear, reticular, and rod and cone layers are strictly normal (fig. 1).

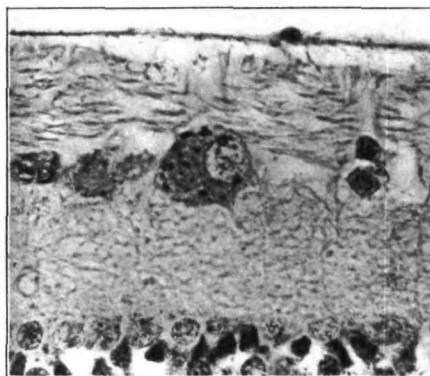


FIG. 2.

× 600. A normal ganglion cell, stained with Mayou's modification of Pappenheim's stain.

In reality, the loss of ganglion cells is not nearly so great as it seems, the appearance being due partly to the poor staining and inconspicuousness of the cell body, chiefly to the shrinkage of the nucleus; in the vicinity of the fovea, three to four layers of ganglion cells can usually be counted, the average in this situation being about five. Ganglion cells are found right out to the periphery of the retina, and in that situation seem to be, on the whole, less affected than in the macula. The ganglion cells which normally occur in the inner nuclear layer are also degenerate. The nerve-fibre layer is atrophied, but less completely so on the nasal than on the temporal side. The choroid beneath the macula and elsewhere is normal. The central vessels are normal, both in the nerve and in the retina.

The most striking change in the cell protoplasm is the total absence of Nissl granules. Not a single cell is to be found in which they are normal;

only exceptionally are they indicated at all by the presence of a rather coarsely granular material which takes on a purplish or violet tinge with thionin (fig. 4); for the most part all trace of them has disappeared.

In the cells which have undergone least change the normal cyto-reticulum is fairly well preserved, and the protoplasm is finely granular. Advancing

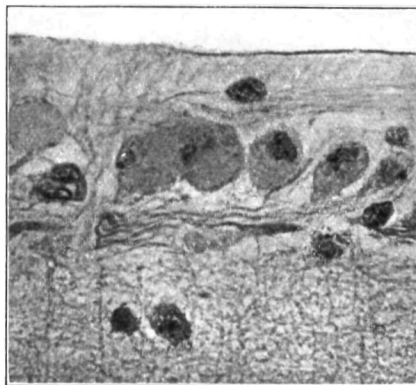


FIG. 3.

× 600. Ganglion cells from the present case, stained by the same method. The cells are round in shape, but not enlarged; the Nissl granules are lost. The protoplasm is finely granular, but one of the cells shows a large area in which it is homogeneous (and stained greenish). The nuclei are shrunken and crenated. The nucleolus is visible in the right hand cells.

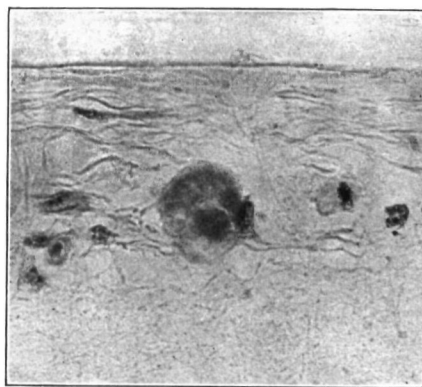


FIG. 4.

× 600. A ganglion cell, stained by v. Lenhössek's modification of the Nissl method. It is enlarged and filled with a granular material which stains purplish. This type of cell is very exceptional. All trace of the granules is usually lost.

degeneration is indicated by the appearance within the cell, usually near the nucleus, of a vacuole-like area filled with a perfectly homogeneous substance, the remains of the granular protoplasm being displaced to the periphery (figs. 3 and 4). With Mayou's modification of Pappenheim's stain this new

substance takes on a light greenish tinge which is quite foreign to the normal cell ; in hæmatoxylin-eosin specimens it is slightly bluish. These homogeneous areas increase at the expense of the normal cytoplasm, and finally may replace it entirely ; it is rare to find more than one area in a single cell, but sometimes there are several separated by a network of granular protoplasm. True vacuoles, without contents, are not found.

Only exceptionally is a cell found with any indication of the normal cell processes ; for the most part they have completely disappeared. In consequence the cells have a more or less rounded shape, and this, together with the homogeneous nature of their contents, and the shrinkage of the nucleus, gives them a swollen, bloated appearance. Comparison with normal ganglion cells shows, however, that though there is considerable variation, the average size of the cells is, if anything, below rather than above the normal. True swelling is almost confined to the vicinity of the fovea, where some of the cells are greatly enlarged, have a perfectly homogeneous protoplasm, and lie within spaces which they do not completely fill (fig. 1).

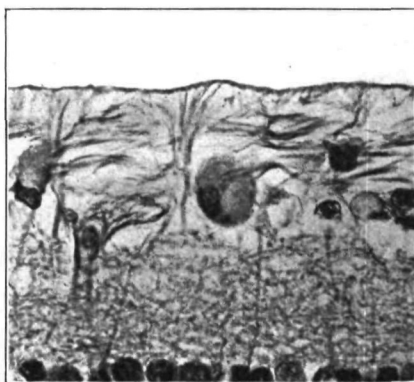


FIG. 5.

× 600. A ganglion cell stained with hæmatoxylin and eosin. It shows the rounded form, the eccentric nucleus, and the formation of a vacuole-like homogeneous area in the protoplasm.

Normal nuclei are scarcely to be found. The characteristic change is a shrinkage whereby the outline becomes crenated and the chromatin reticulum condensed. In the more degenerate cells the reticulum becomes indistinct, the nucleus being filled with irregularly disposed granules of varying degrees of coarseness. The ordinary nuclear stains are consequently taken on very darkly and diffusely. The nucleus is always eccentric, but this is its normal position in the retinal ganglion cells : it frequently projects on the surface, and sometimes a crescentic shrunken nucleus seems to form a sort of cap outside the contour of a balloon-shaped cell. The nucleolus is preserved up to an advanced stage of degeneration. Cells without a nucleus are found, but the appearance is probably due to peripheral cutting. The occurrence of nuclei not surrounded by protoplasm is probably due to the breaking up of the cell ; such nuclei are

not always easily distinguished from those of the neuroglia, which are perhaps increased in number, but whereas the neuroglial nuclei are plump and show the normal reticulum, the others show the characteristic changes already described.

In the nasal half of the optic nerve a few broken-up and varicose nerve-sheaths are still stainable by the Weigert-Pal process. In hæmatoxylin-eosin specimens the nerve appears to be unduly cellular, perhaps from increase of neuroglia; the increase of cells is confined to the nervous substance, and does not affect the trabeculæ.

The above description sufficiently establishes the identity of the changes in the ganglion cells of the retina and of the central nervous system. This identity was first proved by Holden. The only notable point in which we differ from the excellent account of the changes in

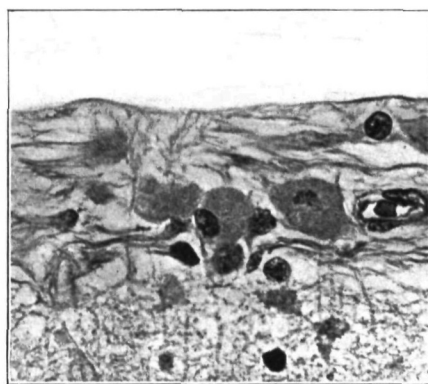


FIG. 6.

× 600. Ganglion cells stained with hæmatoxylin and eosin. In the cell on the right the nucleus is much shrunken, in that on the left it projects beyond the cell body.

the central nervous system recently published in this periodical [6] is this, that whereas in that paper the nucleus is described as being usually "about normal" in size, in the present case it was almost invariably shrunken. We regret that the failure of Bielschowsky's method prevented us from studying the neuro-fibrils.

Our results are also essentially the same as those of other recent authors who have obtained the eyes sufficiently soon after death to be of much value.¹ From a study of these cases it may now be stated with certainty that folds and detachments at the macula, oedema of the retina,

¹ M. Cohen and G. S. Dixon. Eyes obtained two and a half hours *post-mortem*. F. H. Verhoeff: Eyes obtained fifteen minutes after death. In Mott's second case the eyes were exsised immediately after death, but no pathological examination of them seems to have been recorded. According to Birch-Hirschfeld [7] the retinal ganglion cells begin to show *post-mortem* changes in two hours and their characteristic structure is lost in about seven hours.

holes in the fovea, and thickenings of the reticular and nuclear layers are artefacts, and due to imperfect fixation or *post-mortem* change. A hole in the fovea has been observed by one of us as a *post-mortem* change quite apart from amaurotic family idiocy.

The proof that a change in the protoplasm of the ganglion cells is capable of causing the ophthalmoscopic appearance of retinal opacity with a foveal cherry-red spot is of interest in connexion with the subject of obstruction of the central artery of the retina, and lends support to Elschnig's contention that the similar ophthalmoscopic changes in that condition are due not to œdema, but to a coagulation necrosis of the ganglion cell from the cutting off of their blood supply. The subject has been more fully discussed by us elsewhere (G. Coats [11], W. I. Hancock [12]).

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