THE BRITISH JOURNAL OF OPHTHALMOLOGY

DECEMBER, 1919

COMMUNICATIONS

COLOBOMATOUS AND MICROPHTHALMIC EYES*

BY

DR. G. M. VAN DUYSE, JR.

True colobomata of the rudimentary optic nerves (glial plaques), aplasia of their retro-ocular segment, gliosis of colobomatous cyst, supernumerary nuclear arcs, entropion of the borders of the iris.

The specimens were derived from a rabbit one year old, fixed in Müller's fluid, and the sections stained in haematoxylin and eosin. The eye was placed in the ophthalmological collection of the University in the year 1901.

Left eye.—Dimensions: antero-posterior diameter, 13 mm. Equatorial diameter, 18 mm. The section plane was begun horizontally, as far as the lower segment of the lens; thence it was continued in the frontal plane, parallel to that of the iris.

Figure 1 takes the place of a long topographical description: the condition is one of a typical coloboma involving the iris, the ciliary region, the membranes of the ocular floor, viz., a choroido-retinal coloboma including the papilla.

Left Eye.—In this eye the interesting point is the arrangement of the mesodermic tissue surrounding the hyaloid artery and occupying

*From the Ophthalmological Laboratory of the University of Ghent: Director, Professor D. van Duyse. Translated by E. E. H.

the primary optic peduncle, which is under-developed and separated from the brain (total aplasia of the intra-orbital optic cord).

FIGURE I.

Description.—*Left eye*: horizontal section, magnified 2 diameters, *I.*, coloboma of the iris and ciliary body, *col. ci.*, joining on to a coloboma, *col. ch. r.*, choroido-retinal coloboma of the floor; *cr.* lens; *c.* cornea.

Let us examine a horizontal section (Fig. 2) passing under the optic peduncle: the section is through the fibrous mass in its most advanced position towards the lens, *c. hy.*, which starts from the thickened scleral tissue situated behind the posterior pole. Let us call this band *c. hy.*, the *hyaloid system*. It is the analogue of one of the thick fibrous bands sheathing the hyaloid artery, and described in the observation by us of *cyclopean microphthalmos*.*

That mesodermal fibrous mass, the anterior parts of which are made up of embryonic young cellular connective tissue, has a trapezoidal shape (Fig. 2). It attains its greatest size in the posterior part, or base; it gets smaller as it comes forward into the ocular cavity; it expands as it bends from the nasal side *N* (see figure above) and stretches out to embrace the back of the lens *cr.* The arterial trunks contained supply a vascular capsule *c.* to this area, which is directed towards the equator of the lens.

The hyaloid system reaches, as we have said, its greatest transverse size at the level of Figure 2 under the optic peduncle. It is covered on its nasal and temporal (inferior in the figure) sides by the inverted retina *R*¹. There is to be noted an interruption in the retinal folds at the level of that mesodermal mass and on its ventral part the *mesodermal cone* interposed in the peduncular gap at this level can be recognized, and is represented in a series of frontal sections, notably in Figures 6 C, D, E.

The first sections of the inferior segment of the eye (horizontal bisection of the globe) do not contain the dorsal sections of the bulbar peduncle. It was not possible to examine the superior bulbar

*Arch. Méd. belges, fig. 6, June, 1919.

segment. Since the inferior segment of the eye was somewhat larger than the superior, it may be admitted that Figure 3 corresponds to a raised segment of the optic peduncle, and it may be supposed that the separation into segments ceases as in the similar eye (Figure 12).

FIGURE 2.

Description: *Hyaloid system. Entropion of iris (at the level of the iris coloboma).* Horizontal bisection above the optic peduncle—magnified 6 diameters. *Col. col.*, nasal limits and temporal limits of the choroidal-retinal coloboma; *R¹*, colobomatous retina; *c. hy.*, atypical hyaloidean connective tissue; *R.*, retina outside the coloboma; *f.n.*, normal fibres, and *f.v.*, vesicular fibres of the lens, *c.r.*; *p.c.*, ciliary process; *i.*, iris; *c.*, cornea (the representation of the iris is borrowed from a section lower down). *N*, nasal side; *T*, temporal side.

The hyaloid system contains in its ventral part the main arterial trunk which ascends from below upwards, and in its windings gives off multiple and convoluted branches. The nasal part contains at the same level some bands of striated muscular fibres.

Optic Peduncle

Figure 3 represents the most extensive part of the hypoplastic optic nerve *n.o.*, *n.o.*,¹ *n.o.*². The hyaloid band *t. hy.*, reaches its minimum size and disappears ten sections higher; these optic segments become fused together. In reality the mesodermal cone stops before reaching the roof, at the dorsal part of the peduncle.

FIGURE 3:

Description: *Optic peduncle, partition of hyaloid tissue and vascular capsule* (Left eye: horizontal section; obj. 3, oc. 3; reduction 5:3). *N.o.*, *n.o.*¹, *n.o.*² optic peduncle divided by the partition, *t. hy* of interpeduncular hyaloid tissue; *R*, extra-colobomatous retina; *R.col*, colobomatous retina; *c.va*, vascular capsule; *c.cr*, lens capsule; *s*, sclera; *N* and *T*, nasal and temporal sides.

In Figure 3 the optic nerve occupies its greatest transverse area, at the level of the dorsal part of the peduncle. The segments *n.o.*, *n.o.*,¹ *n.o.*² are at this point separated only by some neuroglial fibres forming a sheath or slight partition. The segment

n.o. takes a more marked pouch-like shape; the segment *n.o.*¹ and the small subjacent segment coalesce; the segment *n.o.*² in its turn joins the other segments.

From the two swollen extremities of the pouch of the segment *n.o.* (Fig. 3) issue the retinas, of which one rejoins the intrabulbar retina *R*, the other *R*, *col* covering the posterior temporal scleral wall.

The character of the optic peduncle *n.o.*, *n.o.*¹ *n.o.*² is as follows: from the prolonged segment *n.o.*² with antero-posterior axis, arises a retina, a thin band of retina completely glial, one of whose extremities rejoins the ectatic posterior scleral wall, and the other, in front, the extra-colobomatous retina *R*. If the special histological arrangement of the temporal segment *n.o.*² was not completely similar to that of the nasal segment, we might consider we were dealing with a weak enlargement, with a retina in which the layers of nuclei more or less undifferentiated, as in some undifferentiated retinas, are situated on the adherent side and whose fibres of Müller come off from the free side, but these layers of nuclei are nuclear columns, similar to those of the neighbouring segment *n.o.*, the colouration and constitution of which are the same: the segments of the rudimentary nerve are sharply differentiated by their fundamental compact glial substance from the spongy and oedematous colobomatous and extracolobomatous retina. The fundamental texture of the optic peduncle consists in a web of glial fibres derived from the glial cells which occupy the centre or wall of a little alveolus (oedema). These cavities give a spongy appearance to the nerve. The glial fibres tend to stretch in the same direction: for the anterior segment of the nerve, *n.o.*, following the transverse axis *NT*; for the posterior segment, the direction is almost perpendicular to the preceding; in the segment *n.o.*, the fibres run in the grand axis, antero-posterior, and in the segment *n.o.*², the direction is perpendicular to the grand axis, consequently transverse. The directions of these fibres is the same as that given by the spindle-shaped fibres, fusiform connective tissue cells provided with isolated, double, elongated nuclei, flanked by stellate cells, whose most apparent processes also run in the same direction. These are bands of connective tissue cells which, placed at intervals, give a striation converging more or less toward the heel of the pouch of *n.o.*, and are the analogues of the partitions derived from the glial sheath of a normal nerve. A pial sheath here surrounds the peduncular segment. These partitions support the nutrient capillaries which run in a direction perpendicular to their own. These latter are, then, as in the normal eye, borne in longitudinal partitions rich in nuclei. The term hypoplasia given to the optic nerve postulates *the total absence of optic fibres*. The nerve would be complete without that, inasmuch as it

is provided with a vaginal sheath in which partitions carry capillaries. The nasal segment of the optic peduncle is enclosed by the scleral sheath, forming a dural sheath, and further forward by the hyaloid connective tissue, forming, in the shape of a transverse layer, a strong substratum for the vascular capsule *c.va.*

Retina: the absence of optic fibres and central vessels in the optic peduncle necessitates *a priori* absence of fibres and of vessels derived from the central artery in the extracolobomatous retina, and *a fortiori* in the colobomatous retina. The extracolobomatous retina (0.16 mm. thick), with the exception of these elements, contains the other parts that compose the normal retina; the degenerate ganglion cells of dimensions a little greater than the neighbouring glial cells, which are not numerous, are feebly stained. The retina measures from 0.05 to 0.2 mm. after taking into account the obliquity of the sections. As it covers the scleral ectasia in Fig. 3 there is to be seen: 1, the external limiting membrane with rods and cones turned towards the vitreous; 2, a nuclear layer; 3, a granular layer; 4, A layer with large meshes, of fibres and glial cells, meshes and alveoli of oedema; 5. Some ganglion cells transformed into angular hyalin blocks, with short, thick, hyalin processes and a nucleus very faintly stained with haematoxylin. It is characterized by its spongy state. The oedema is particularly marked, not in the peripheral parts of the extra-colobomatous retina, but in the part which decorates the perihyaloid territory, which is deprived of choroid and pigmentary epithelium and consequently is colobomatous. The retinal structure here consists of an irregular web of glial meshes where the nuclei are scattered in irregular groups. The alveoli occupy specially the middle layers of the retina. It is also at this level that the areas of oedema are most marked. The thickness of these layers varies greatly. The cones and rods are absent from the colobomatous segments; there is generally an irregular nuclear layer; rarified ganglion cells are present; optic fibres and vessels are absent; Müller's fibres are accentuated.

The extracolobomatous retina is provided with rods and cones and with two nuclear layers, but, as in the preceding case, neither optic fibres nor vessels. Moreover, it is not oedematous.

Vitreous body.—This makes its appearance in the form of fine, retracted, dichotomous tongues which run along the limiting membrane between the folds of the retina (Fig. 3).

Lens (Fig. 2).—The peripheral fibres, especially those of the posterior cortical layer, are vesicular. The capsule is ruptured at the posterior pole, and a plug of granular substance, derived from the disintegrated lens matter, issues from the solution of continuity and forms a hernia in the capsular wound. A relatively discrete degeneration of the vitreous is present about the peripheral fibres of the shell. Their course is still more

distinct at the level of the nuclear zones, four in number: two anterior and two posterior. The drawing (Fig. 2) slightly schematic of the lens (nuclear arcs drawn with a higher eyepiece) enables us to dispense with a detailed description.

The epithelium of the anterior capsule reaches to the nuclear zones or arcs, open in front and situated in front of the equator. The two nuclear arcs, open behind, join with the pseudo-epithelium of the posterior capsule. (The posterior temporal nuclear arc is taken from a section lower down in the series. That region was completely vesicular at the level of section of the other arcs.)

The coloboma of the iris is large and complete: the edges diverge slightly. In the first sections, at the level of the horizontal diameter of the iris, the pigmented epithelium does not reach the level of the stroma. The latter tends to constitute more and more the pupillary border and to reproduce the appearance shown by Figs. 4 and 5.

FIGURE 4.

FIGURE 5.

Description: Sections of the inferior segment of the iris coloboma. Folds of epithelium and radiating arrangement of the sphincter muscle, rarefied in the sections situated lower than 6 A.

This configuration becomes progressively more complex: the epithelium is frequently folded upon itself, it winds and is surrounded by segments of unstriated muscular fibres to which it gives origin. That arrangement of epithelium and of sphincter gives the key to the entropion of the pupillary border.

It is to be noted that in the upper half of the iris coloboma, the iris has a normal thickness, and that the two surfaces run parallel with each other. The thickness of the edge appropriate to the normal eye is shown in the lower half of the coloboma: the iris becomes clubbed as Bock has observed it. He states that the pigment epithelium is strongly developed, that the folds and warty thickenings appear on the posterior surface. In the colobomatous eyes studied by Bock (notably cases I, III, IV) the pigmented border bends forward and forms an *ectropion of the pupillary border*.

The *entropion* of the edge of the iris reappears in the frontal sections (see figure 6, A). The sphincter fibres are absent at present; they had become scanty in the later horizontal sections (Figure 5). Descemet's membrane and the endothelium which covers it are stretched over the scleral background to be lost in the angles of the anterior chamber, represented by a long gap. The scleral surface, where it reaches the iris coloboma, is raised by a muscular mass *m*, which has taken the place of a band and which has formed the concave impression represented in the figure B beneath the ciliary surface.

The two pillars of the iris in Figure A rapidly approach each other, become thin and coalesce at the level of the middle line, so causing the formation of a band of pigmented iris tissue which lies on the lens capsule at the sides, while the pigmented epithelium of the deep fold of the iris masses on the sides and rejoins the neighbouring ciliary processes shown in B.

The iris band further diminishes in thickness, the *ciliary coloboma* succeeds that of the iris, diverging slightly from the middle line, and the observer notes the constitution of a mesodermal cone *c. m*, coming from an atypical scleral tissue (compare Figure 6, C) where it is clearly defined.

Before the ciliary region is so sharply raised, the ciliary coloboma is marked out at the sides by processes, in reality reduplications of the pigment epithelium; a layer of retinal tissue, glial and very undifferentiated, appears: this is the beginning of the *choroido-retinal* coloboma. The drawn back retinal epithelium expresses the size of the coloboma of the ocular floor.

At the place where the mesodermal cone is strongly marked, a reduplication of the retina appears on its sides, better marked on the right: colobomatous retina *R Col* adherent to the sclerotic, retina *R¹* inverted beyond; normal retina *R* doubles itself with the pigmented epithelium and the choroid. The colobomatous retina is reduced to a glial layer with scattered nuclei and rises on the cone to be lost on the other slope towards which also advance an everted retina which is terminated by two or three layers of folded ciliary retina; the pigmented epithelium interrupted at the edge of

the coloboma, on the left, reappears in a fragmentary condition under the retinal reduplication of that side.

Figure 6, D represents the colobomatous retinal reduplications situated a little further back and the edges of the choroido-retinal coloboma.

FIGURE 6.

Frontal sections of the colobomatous ocular floor. A. Coloboma and entropion of the edge of the iris i; s, line of section of the last horizontal cut. B. Ciliary coloboma; cr, lens capsule; R, retina and ep, retinal epithelium; m muscular mass. C.D.E. Choroido-retinal coloboma at different levels. R, R extra colobomatous retina; R¹, R¹, colobomatous retina reduplicated; c.m., mesodermal cone reaching behind to the hyaloid system h (compare h in figure 7, horizontal section).

The same description applies to Figure E. The mesodermal cone is less voluminous, narrowed at the base, and has just left the atypical scleral surface.

On passing to the examination of the inferior horizontal sections we find a picture sensibly similar to that of figure E, frontal section as the last; the mesodermal cone reappears in the same form, detached from the scleral wall. We already know it under the name of the hyaloid connective tissue system.

FIGURE 7.

Inferior horizontal section of the *cone or hyaloid mesodermal vascular system*. To be compared with Figure 6 E, frontal and posterior.

Here we again find the terminal plateau of the vascular capsule *c.va*, that is left by certain vessels on their course to penetrate into the vitreous to be directed towards the lens capsule *c.cr*; reduplications of the pigment epithelium, *e.p.d.*, are found in front of the retina where it is in contact with the lens, *c.cr.* on the left; the edges of the coroido-retinal coloboma *R.R¹*; colobomatous retina *R.col.* covering on the left the bottom of the floor of the ectatic sclera; folds of the inverted retina *R¹* in contact with the hyaloid system, connective sheath of the hyaloid vessels, *which is only the continuation of the mesodermal cone* interrupting the continuity of the retina at its level.

Right eye. The essential teratological point is the method of formation of the hypoplastic optic nerve.

Other anomalies described in the associated eye are here found again, notably *the entropion of the edge of the colobomatous iris*, *the ciliary coloboma*, and *the choroido-retinal coloboma*, all typical. The latter is very extensive: it reaches very far forward to the *level of the coloboma* in the ciliary processes, and stretches to the equator on the nasal side, and to the upper limit of the peduncle of the optic nerve; it is complicated by a cystic ectasia at its entrance on the nasal and inferior nasal sides.

At the same time the mesodermal cone, the raised rib or crest springing from the ocular floor at the level of the ancient foetal

cleft, is missing, except behind, where the mesodermal tissue has caused an atypical disturbance at the level of the optic peduncle to be described.

FIGURES 8, 9, 10

Description: *Peduncular hyaloid system*, *hy*. (Obj. 3, oc. 2; reduced 3:2. The mesodermal cone carrying the hyaloid artery (peduncular *hy*), immediately of large size (Figure 8), is engaged in a spur between the retinal folds *R'* (Figure 9) and penetrates into the optic peduncle which it divides (Figure 10) into two segments *n.o.t.* and *n.o.n.*; *R. cy*, retina in the colobomatous cyst *K*; *va*, vascular capsule; *cr*, lens capsule; T and N, temporal and nasal sides.

The retroscleral orbital optic cord does not exist. The peduncle is disposed almost entirely *in front* and above the mesodermal hyaloid system.

An essential point of difference between the peduncle of the left and that of the right eye is the existence, at the point where the former reaches its greatest size (Figure 3) of the hyaloid plateau in front of the optic peduncle, while in the latter the reverse is the case (Figures 11 and 12). The peduncular mass of a quite unusual shape is placed in front and turns below to engage in the neck of the sub- and retro-peduncular cystic ectasia, to arrest us on a basis of anatomical relations, a real idea that pathological examination compels us to modify by employing the qualification of intra-peduncular.

The hyaloid peduncular system hy is at the point under consideration a fibrous tissue whose nasal part limits the neck of the colobomatous ectasia K (Figure 8) and whose temporal part opens out into the vascular plateau *va*, the base of the vascular lens capsule.

The sides of this protuberant mass are bordered on the temporal sides by retinal folds R^1 and on the nasal side by the retina as it penetrates the neck of the cyst *R.cy* (Figure 9) or by the rudimentary optic nerve's nasal segment *n.o.n.* (Figure 10).

The connective mass becomes smaller as it rises in the series of sections (Figure 9) and two peduncular glial nervous segments appear, at present separated by a conical mesodermal partition (Figure 10).

That partition after dividing into two parts of approximately the same size precedes the appearance of the optic nerve which is completely aplasic (Figure 11). This then appears, free in front, and giving out segments of retina at its temporal extremity, while its nasal extremity takes refuge in the cystic recess (Figure 12).

The nerve or optic peduncle occupies in its upper part a transverse position in front of the atypical scleral tissue where the hyaloid tissue which it had divided lower down is lost. This transverse position, naso-temporal, follows an angular form, a fibrous conical prolongation separating the glial plaque into two segments. The temporal segment looks forward; the nasal segment looks down until it is placed into the cystic neck. The former segment becomes slightly concave forwards in Figure 11 and 12; the other looks forwards to become concave backwards as it bends over the enlargement (Figure 11, *n.o.*) that we will call temporal cone of the cystic neck *c.t.* (Figure 12), and the other part nasal cone *c.n.* as the process which limits the neck on the nasal side (on the bottom of the figure, the two cones being marked by an asterisk).

The grand axis of the glial peduncle reaches here to 1.5 mm.;

its thickness is 0.3 mm. The characters of its fundamental structure are the same as in the associated eye:—1 *Glial fibres and cells* with a more or less spongy character; the fibres do not tend

FIGURE 11.

Optic peduncle of the right eye. (Obj. 3, oc. 3, Reduced 5 : 3).
Same lettering as in Figure 12.

in any definite direction. 2. *Connective partitioning fibres*, homologues of the partitions derived from the glial sheath of a normal nerve (rare in the specimen). 3. *Nuclear columns*, carrying scattered capillaries, more numerous on the anterior side. Some

supports, at considerable intervals, leave the posterior surface of the glial sheath of the glial peduncle, and act as partitions which follow the short axis of the peduncle. It is possible to speak of a vaginal space, the dural sheath being represented by a layer of more or less homogeneous connective fibres which surround the bulk of the temporal cone of the cystic neck (*c.t.* Figure 12) and are lost towards the extremity of the nerve where this latter is resolved into masses of glial plaques. A gap separates this layer or dural sheath from another layer of fibres, carrying vessels, and of an equally hyaline nature. It continues the pial sheath of the temporal segment of the rudimentary nerve, and finishes equally at the same level. It is not a question of an intervaginal space: we find no arachnoid supports cut obliquely or across, and furnished with endothelium, but only fibres stretched in the false intervaginal space, and belonging to a common solitary sheath of the nerve whose fibres are artificially separated.

On the opposite side the nerve is directly in contact with the glial tissue of a retina. If the nasal and posterior wall of the cyst, accidentally missing, correspond to the sheaths of the nerve, an idea which the topographic point of view justifies, it is not possible to give anatomical proof from the structure of that wall (? modifications due to age and distension of the cyst).

We do not find here the character of optic sheath described by Bergmeister (1913). On the internal side some irregular fibrous prolongations of the wall penetrate between the fibres of the glial investment. This latter re-enters the culs-de-sac or recesses of the wall, in a fairly intimate union therewith, for it is difficult to define the separation of the two tissues (meso-ectodermic penetration).

At the anterior side the peduncle is resolved into compact glial fibres, forming a network with elongated axial meshes, to constitute a border which separates the optic peduncle from a segment of retina. At its temporal extremity the glial fibres of the nerve mix with the glial fibres forming the internal layer of the fold R^1 inverted retina.

The hypoplastic nerve, bent over, forms with the temporal cone *c.t.* the temporal border of the neck, giving access to the cavity of the cyst *K*, the nasal edge being represented by a band, a process of the nasal cone *c.n.* The wall of the retrobulbar pouch *K* is formed from the external layers of the scleral envelope of the globe. It seems necessary to postulate here a contribution from the mesodermal layer surrounding the optic peduncle at its point of junction. That part of the cystic envelope, considering the interruption caused by the optic nerve, can only be furnished by the anterior wall of the cyst, that which is raised (Figure 10) behind the hyaloid vessels to double the atypical scleral wall at this level.

The communication between the pouch and the bulb is closed by

some retinal folds which penetrate partially into the cystic cavity. Some muscular bands which run along the cystic wall from the nasal side come almost in contact with the parietal intracystic glial tissue as a result of the reduction of the fibrous tissue of that envelope (*fm.*, Figure 12).

At its nasal extremity the intracystic rudimentary nerve, together with the glial meshwork of a segment of retina which follows the same direction, is lost in a neoplastic *glial tissue*, very different from that usually seen in the retro-palpebral cysts complicating colobomatous microphthalmos. Peduncular and retinal origin are both probable. It consists of glial elements united in a mass at the level indicated, but which are also found elsewhere at the edge of the cystic wall. The following appearances of the internal glial layer of the cyst along the *anterior* and *temporal wall* of the cyst (the posterior is missing) are to be noted.

(a) Cylindrical elevated cells, slightly regular, which stretch to the level of an eventual gap, from a re-entering angle of the wall, taking a fusiform shape as do their nuclei which are deeply stained (morphological tendency and result of settling).

(b) Irregular cubical cells, depressed, with tendency to a fusiform aspect.

(c) Stellar cells, astrocytes, voluminous with large oval nucleus (exceptional appearance). These are layers of quiescent glial cells.

Opposite the two first in a recess of the wall there is a border of elements reunited as at the entrance of the cystic neck; these are polymorphous epithelioid elements, resembling those of Ziegler in certain simple carcinomas, indifferent epithelial cells or slightly differentiated by their angular appearance. Their nucleus is irregularly rounded or oval, and karyokinesis may be observed in all stages. The protoplasmic contour of the cell is not always sharply defined. In places where the more deeply stained nuclei are crowded together, the appearance may be described as syncytial. This is a stratum of glial cells in formative activity, a glial hyperplasia, a gliosis. Blocks separated by connective trabeculae which have a marked tendency to become homogeneous and hyaline are also present, but not vessels showing sclerosis or hyaline degeneration. No retrogressive metamorphoses of the cellular protoplasm are noticeable; at the most some nuclei of masses of polymorphous elements show some destructive retrogressions to be explained by the absence of vessels. This glial hyperplasia extends to the glial elements of the internal layers of a segment of retina adjacent to the hyaline blocks at the entrance of the cystic neck.

The smaller breaks or gaps of the cystic wall are invaded by the epithelioid elements: in the gaps they are frayed out and become fusiform in the same way as carcinoma cells in the lymphatic spaces.

There is no connection between the cystic wall and the fibrous trabeculae of the mesoderm that act as partitions, or the glial elements that are in a state of hyperplasia.

FIGURE 12.

Optic peduncle n.o. and colobomatous cyst K. (Obj. 3, oc. 2, reduced 5:3). *s.* scleral wall rising from the pericocular and hyaloid mesoderm. On the temporal side (upper part of the figure), *R¹*, fold of the retina *R.*; *ep*, fold of pigmented epithelium.

The asterisks (**) mark the neck or isthmus of opening of the colobomatous cyst, between two fibrous processes. Near the inferior recurved segment of the *n.o.*, *gl.*, intracystic gliosis; *R.col.* colobomatous retina; *r.cy.* intracystic retina; *v.*, vitreous or coagulated intracystic fluid; *f.m.*, striated muscular fibres.

Beside the groups of polymorph elements, fusiform elements with long processes are present; with the astrocytes they are directly

reminiscent of the glial cells of certain gliomas or glioses. We shall return later to the epithelioid appearance.

Along the wall in the infero-nasal and nasal parts of the cyst there is found a highly undifferentiated and folded retina. The abnormal and confused arrangement make it impossible to say if it is inverted. No rosettes are to be found in the intracystic retina any more than in the colobomatous and extracolobomatous parts of that structure.

The intraocular fluids such as those of the anterior chamber, vitreous, subretinal and subchoroidal spaces and the cystic ectasia are for the most part coagulated.*

It is most frequently impossible, so much is the retina undifferentiated, to say whether the observed segments are inverted or not, seeing that they contain neither optic fibres nor vessels and that the nuclei are thinly sewn and disarranged by oedema throughout the structure. The determination of the localization of the layers is not at all easy for the extracolobomatous retina which itself is much folded; it is provided with a thick refractile limiting membrane which is also found in the intracystic portion. This, however, is of no use in orientation, for the external limiting membrane is equally thick in that region.

The cystic pouch reaches higher than the peduncle. Figure 12 shows it from behind, deprived of the posterior wall which has been lost in the enucleation. It descends from the infero-nasal side 1.5 mm. lower than the peduncle.

Lens. Alterations are more marked than in the associated eye. The cortical layers are greatly degenerated, both at the equator and poles. The lesions are so advanced that only one defined nuclear zone is left, namely, the superior and anterior temporal. It is also possible to recognize the posterior temporal: the zone of departure at the level of the capsule is but little defined, but its expansion and the fibres corresponding to it are sufficiently marked. The zone of departure of the anterior nasal nuclear arc can also be marked, but the cortical fibres are too much destroyed to allow of the localization of a nuclear arc. Study of the serial sections establishes the existence of an epithelium in front and a pseudo-epithelium behind; in the absence of epithelial cells in a portion of the equatorial region, these appearances allow of the admission of a condition similar to that of the left lens, namely, the existence of four nuclear arcs. The ante-equatorial situation of the anterior nuclear arcs should here again be noted; that of the posterior nuclear zone was carried sufficiently markedly back.

*While making the legitimate distinction between the colobomatous orbital cyst and the colobomatous ectasia, two very different arrangements of the colobomatous evolution of the eye, we mean here by cystic ectasia the real cyst.

Pathogenesis

Before giving a definite opinion on the teratological problem of the two eyes analysed above some brief considerations must be made.

If we must blame the volume of the persisting mesodermal cone at the time when it is interposed between the lips of the foetal cleft, for producing the malformations in relation with its extension, the left eye should show these to a greater extent. The reverse is the case. The mesodermal cone only makes evident a balance behind. It is an awkward situation at the level of the distal extremity of the optic peduncle: a malformation in both eyes and a more considerable echo on the formation of the vitreous of the right side. The development of the optic nerve may be conceived as follows.

The absence of the intraorbital optic cord may be explained, to cut short other hypotheses, by the schema of Spemann.

There remains the distal part of the optic peduncle into which should penetrate normally a hyaloid web and with it the ambient mesodermal cells. Succeeding sections show without doubt that the mesodermal cone, the hyaloid system whose axis is represented by the hyaloid artery, is engaged in that distal part without being absorbed; in the absence of optic fibres the epithelial cells of the peduncle have evolved a neuroglia in which the hyaloid system is engaged in the form of a corner.

In the left eye, it has separated the glial mass into two groups, a temporal group, the most voluminous, and a nasal group, at first transversely spaced, but coming nearer in proportion as the mesodermal cone, erected in a point, diminishes. We thus approach the roof of the dorsal part of the ocular peduncle and find ourselves before the *glial plaque*, best shown as such in the right eye. At this level the mesodermal spur has finished its course: the segments of the glial plaque are only separated on the left side by feeble glial partitions. The situation is analogous in the right eye. The glial plaque has been pushed forward in the form of an angle, the mesodermal cone equally in that direction in the form of a spur. When it is retracted and effaced, the two segments of the optic glial plaque rejoin in an angle pointing forward, the temporal looks in that direction, the nasal is bent over what we have termed the *scleral temporal cone* by analogy with the posterior scleral cone figured by Mannhardt (1897) and penetrates into the canal of the colobomatous cyst. The papilla is necessarily missing in an optic nerve so formed, as Professor van Duyse has observed in connection with the aplasia of the nerve described by him in a cyclops case (1899).

The hyaloid artery with its connective sheath complicates the

development of the vitreous and the nutrition of the lens (vesicular degeneration). On the other hand, as the artery does not develop in the optic cord and the optic fibres do not penetrate it, we find the presence of an undifferentiated retina of the value of a retina of the sixth or seventh week, and whose internal vascularization is missing. The absence of the choroid—it should always reach as far as the retinal epithelium—is a new condition of physiological poverty for the external retinal layers. We must, therefore, not be astonished to find the retina folded, colobomatous, and so to say unrecognizable, so great is the disarrangement of its layers. The absence of optic fibres implies the absence of a papilla as D. van Duyse has demonstrated in a cyclops (1898), an observation also made by Dötsch (1899).

In the left eye, which is slightly microphthalmic, the folding of the retina was less pronounced than in the right, where we had the impression of a space too small for the development of that membrane.

The causes producing the microphthalmia, the coloboma and its determining factor, the mesodermal cone, have produced more marked malformation on the right side. The space in which the retina develops has been all the more restricted since, other conditions being equal, the lens of the rabbit is very voluminous. The mesodermal obstacle to the development of the retina was carried back to the posterior extremity of the foetal cleft. The folds should then be more numerous and complex at this level, as is the case. Since the retinal folding gives rise to a certain degree of scleral ectasia, behind for the left eye and on the temporal side for the right, it produces here, on the nasal and infero-nasal side, the formation of a colobomatous cyst. The retina is pushed at an early stage to the outside of the situation proper for the ocular vesicle. A peri-peduncular and peri-ocular mesodermal envelope, in the guise of a relatively thin wall with winding passages is developed later.

A remarkable mass of mesoderm is found accumulated between the hyaloid artery and the posterior surface of the lens. The secretion of the vitreous fluid falls on the hyaloid vessels and their perivascular glial elements. The quantity formed could only be minimal; the primordial epithelial formative elements of the vitreous (probably retina) could only create a rudimentary vitreous. As a result, especially in the right eye, the folds and the conglomeration of retinal folds between which the vitreous tongues display their bordering of junction.

In all the area where these folds are prominent, the coloboma has been formed; hence the absence of the choroid and the pigmented epithelium and the defective development of the internal layers of the sclerotic. Apart from all increase of intraocular

pressure, an ectasia should tend to develop, a cyst to distend, at this level.

Intracystic gliosis. The origin of this gliosis must be placed in the nasal extremity of the optic plaque, and in the retina which takes refuge with it in the cyst. The three or four known observations, where it is a question of glial hyperplasia in cystic ectasias or in microphthalmic eyes, mention the hypoplasia or total aplasia of the optic nerve. This fact deserves attention, since it seems to establish a relation between the peduncular malformation and the gliosis, without any idea of contesting the retinal origin.

As a matter of fact, there is no essential difference between the peduncular and retinal origin, as both parts are derived from the primordial neural tube.

The hyperplastic glial tissue is most abundant in the neighbourhood of the optic plaque, but it has been directly observed on the internal layer of a stump of retina close to it. Let us recall with Krückman that the neuroglial spider cells only exist in the layer of ganglion cells and optic fibres. The absence of these isolates in some ways the glial cells. We have assumed that the retina under discussion, undifferentiated, was inverted because it had slipped forward into the cystic cavity.

The retinal layers are indistinct; if we could accurately orientate the retina, the folds found at the entrance to the cyst could only, in our opinion, proceed from the ectropion and folding of the retina.

Theoretically the glial hyperplasia should originate from that internal layer. Let us add that it must have originated soon after the invagination of the secondary optic vesicle, and that that vesicle is not closed in the infero-nasal segment by relation with the rudimentary peduncle. Some of the retinal folds form hernias outside as they lean on the mesodermal cone and being preserved, inverted, from the nasal side of the cyst; from the temporal side one of them, in concert with the optic plaque, has developed into a moderate gliosis in which the epithelioid aspect recalls its ancestry, but deviating from the type of primordial elements of the neural tube, peduncle and internal leaf of the secondary ocular vesicle. This fact noted in malignant tumours, especially gliomata (epithelial rosettes), is found here in a benign hyperplasia without any heteroplastic extension. It belongs to a simple gliosis and its characters are different from those observed by Bernheimer, Seefelder, and von Hippel. These three observers have studied in microphthalmic eyes glial hyperplasias of a much more marked gliomatous structure, going so far as to simulate a tumour. We will give an analytical account of them.

1. *Bernheimer* (1894). A neoplastic retinal tissue, in relation with some retinal folds, penetrates into the orbit at the level of the

rudimentary optic nerve, forming a mass of gliomatous tissue rich in nuclei.

2, *Seefelder* (1908). A microphthalmic eye, with orbito-palpebral cyst, colobomatous, is traversed by a vascular cord which traverses the sclera under the *rudimentary optic nerve*. A glial neoplastic tissue, issuing from the retina, accompanies the cord and passes into the orbit to develop there surrounded by a mesodermal shell.

3. *von Hippel* (1895) replies to the question, "Has it been shown that glioma of the retina can be met with in congenital microphthalmos?" in the negative. The case under discussion was that of a *quasi-tumour-like gliosis* observed in a non-colobomatous microphthalmic eye, with a congenital abnormality of the vitreous. There was noted in addition, *total absence of optic nerve*, plastic irido-choroiditis, with connective and bony formation on the internal surface of the choroid, absorption of the lens. The neoplastic gliomatous mass largely filled the globe.

That neoplastic mass was composed of two distinct parts: a sclerosed hyalinised vascular system (capillaries and arteries) and some cellular groups with haemorrhages and blood spaces filled with blood clot (recent traumatism).

The cellular part consists of nuclei very crowded or widely spaced, oval or fusiform or of long fibrillar cells without any relation to the vessels which do not pass into the cellular islets. They colour with the picric acid element of van Gieson's stain. Consequently they are glial elements.

von Hippel makes the observation that the case of *Helfreich* (1875), where the optic nerve was missing, is not at all a *glioma* but a *gliosis* (pseudo-glioma), and he gives the same opinion of the anomaly described by *Ginsberg* (1899).

We assign the cause of the glial hyperplasia to a modification of the relations between the supporting tissue of the retina so largely represented, and the nervous tissue proper, nervous fibres, and ganglion cells.

The physiological ties are thus broken as they are in certain exereses or destructions, which set the epithelial tissue in conflict with the dermal tissue (a typical proliferation of *Friedländer*).

It cannot be a question of a secondary gliosis consecutive to a chronic inflammatory process, or to a regeneration following a primary regression of the nervous substance of the retina, a natural result of nutritional or circulatory disturbances.

In fact, if we replace the word regression by *absence or non-formation of nervous tissue*, independently of disturbances of circulation and nutrition due to some malformations, we shall understand better the unobtrusive or moderate glial multiplication observed in these cases.

We have stated that the epithelioid glial plaques, which contain

the rudimentary nerve behind and spread along the cystic wall, have only indistinct limits. That peculiarity recalls the syncytial state that Terrien, in his Figure 3, attributed to the internal lining of the cyst that he made originate in the peduncular wall.

We will also recall that in Bergmeister's observation a gliomatous nodule (gliosis) developed in the cavity of one of the eyes, while in our specimen the glial neoplasm is intra-cystic.

Lens. Rindfleisch (1891) describes in a microphthalmic eye (sixth to seventh month foetus) in the horizontal sections made at a certain distance from the centre, a *second posterior nuclear arc*, situated towards the posterior pole, over an area of 2 mm., a peculiarity hitherto undescribed, and bringing the number of arcs up to four, (two anterior and two posterior). Rindfleisch estimates that this second arc corresponds to the marginal edge of the proximal fibrillar masses which cross in front in a mushroom shape, although it is evident that these nuclei, well developed, are still more proximal.

That impression is not derived from our Figure 2. We rather think of the annular ridges of von Hippel, but that study on sagittal and frontal sections in the embryonic eyes of colobomatous rabbits is not possible in adult eyes with lenses markedly cataractous.

Tear of capsule. The modifications of the vascular capsule and of the mesodermal hyaloid system are the cause of that cataract and of the capsular rupture at the posterior pole (see Note 1).

That *tear* is found in both eyes of the rabbit, at the posterior pole where the lens substance is liquefied. Some connection with the retraction of the vascular and retrolental mesodermal system is plausible, without losing sight of the possibility of a rupture due to the action of the preservative fluids.

The tear of the posterior lens capsule of the right eye takes place in an area comprised between Figures 8 and 9, opposite a prolongation of the connective vascular plateau—vascular capsule—and facing the ledge or cone that forms the temporal edge of the cystic neck. We have often alluded to the mesodermal cords going from the entrance of the neck of the colobomatous cyst to the posterior lens capsule, notably Hess (1900) and Natanson (1903).

Striated muscular fibres of the hyaloid mesoderm. Fibres of this sort (direction antero-posterior) found at the bottom of this part are borrowed from the rectus muscle and have been drawn in with the mesodermal peri-vascular tissue as it penetrates behind into the foetal cleft.

Entropion of the Iris. The only observation of entropion known in 1905 was that of Enslin. In an eye affected with complete cataract the iris is increased in height and diminished in breadth. The pigmented layer stops 0.4 mm. from the pupillary edge which is bent back, its stroma stretching to the extremity of the pigmental layer: *entropion of the iris*. The stroma gives an impression of

atrophy, crypts and folds of contraction are missing; no dilatator muscle. There is an excrescence in the shape of a mass of the pigmented layer, projecting behind and originating in a marked fold of this layer towards which the cells of the iris stroma, arranged in rows, converge. The circular and symmetrical arrangement of the feature discussed are against the inflammatory origin invoked by Enslin.

Although the observation is only known to us from an abstract in Michel's *Jahresbericht*, we find a strong analogy with our *entropion of the pupil*, at the level of the coloboma, consequently a partial entropion.

An entropion of the iris was shown by Klein at the Ophthalmological Society of Vienna (1910). The iris was largely adherent to the lens. In spite of the inflammatory evidences, it is permissible to think of an injury in the course of extra-uterine (? intra-uterine) life (congenital condition, patient, aged 23 years).

Seefelder (1910) has observed an entropion of the iris; the iris was slightly folded backwards, as also was the sphincter. At the edge of the pupil the stroma passed into a tissue of the same constitution, containing vessels cut transversely (remains of capsulo-pupillary membrane). This tissue was not adherent to the lens capsule.

Seefelder believes that the pupillary membrane is not separated from the sphincter at the pupillary edge, and, consequently, is incompletely absorbed. The consequence would be a slight inversion of the pupillary edge backwards, in the course of the later weeks of development.

The pathogenesis of the iris entropion seems to us to be expressed in our Figures 4 and 5.

It is due to duplications of the iris epithelium. Following the degree of folding, the number of folds of the retinal layers of the iris, the inversion is more or less pronounced. The inversion is less marked in Figure 4 than in Figure 5. The fact is that the epithelium forms a fold, a recess round which the iris parenchyma is disposed while bending and becoming entropionized. The segments of the epithelial muscle have taken a radial direction in conformity with that of the epithelial folds. At the other part, before descending to this level, the epithelial strata and the parenchyma were normally arranged on the frontal plane. In approaching the colobomatous level the position has altered with the method of epithelial arrangement. The anomaly is equally pronounced in the associated iris segment as regards those which have been drawn (see Figure 2).

Analytical Summary

In the microphthalmic colobomatous eyes of an adult rabbit we have established the existence of a true coloboma of the optic

nerves by means of horizontal sections; an anomaly recorded in a very small number of specimens. The mesodermal cone is connected with the optic peduncle by separating its lateral walls. The nerve may be represented as the arch of a dome resting on the mesodermal sector of the hyaloid artery. The nerve is rudimentary, deprived of optic fibres, in the state of a glial web (glial plaque), and bound to folded undifferentiated retinas with heterotopic nuclei.

The distal part of the nerve alone is developed; *the proximal part is aplasic*: the retro-ocular nerve is entirely absent.

The mesodermal hyaloid mass comes forward in the form of a trapezoidal band, encircling the hyaloid vessels and the vascular capsule, which brings about the usual disturbances: lental degeneration, ruptures of the posterior lens capsule.

In one of the eyes, on account of the minimal development of the vitreous, the small space devoted to the development of the retina has pushed that structure outside; it came in contact with the invaginated mesoderm; it is evaginated, herniated. Its external expansion, at the entrance of the rudimentary optic nerve on the infero-nasal side, has caused the formation of a peri-retinal, retro-ocular envelope, a *colobomatous orbital cyst*.

Taking into account the publications made in 1911 by Terrien and Bergmeister, the author, although unable to furnish certain anatomical proofs of the participation of the sheaths of the optic nerve in the formation of the adjacent orbital cyst in one of the eyes, believes that it is very probable from the topographical point of view. If, as he thinks, the retinal leaflets are due to an ectropion with folds of the retina at the level of the posterior intra-fissural mesodermal mass, there is no difficulty in admitting that the peduncular cavity and especially the optic sheaths have been laid under contribution for the formation of the cystic wall.

The development of the eye, in the absence of the proximal optic nerve, proves the considerable independence acquired by that organ after its separation from the brain in the course of its transformation into the optic cup according to the schema of Spemann.

An interesting point of the observation is the existence of four nuclear arcs in the lens, two posterior and two anterior. The author considers that there may be a direct relation between these arcs and the annular ridges described by von Hippel in the embryonic eyes of a colobomatous rabbit (interest phylogenetic). The direction of the sections and the marked lental degeneration do not permit of a definite opinion on this point.

Another particularity that merits attention is the intracystic production which follows on the glial plaque and retina which rejoins it at the entry of the cyst. While the opposite wall of the colobomatous cyst is covered by an undifferentiated retina, the wall

at the entry and the part following thereon present short and successive strata of elements where all varieties of glial cell are reproduced: astrocytes, fusiform cells with long processes and—primordial embryonic stages—elongated cylindrical, cubical, elliptical cells, all irregular. But there are some strata which assume a neoplastic appearance, and transform themselves into groups of polymorph cells, of an epithelioid aspect, to which the numerous karyokineses assign the character of undifferentiated embryonic cells suggesting a comparison with the cells so varied in form of a glandular carcinoma (in the sense of Ziegler). We are only concerned, however, with a gliosis, with a hyperplasia in no way heteroplastic, such as observed by von Hippel with less clearly defined characteristics. That multiplication has nothing in common with glioma. That gliosis will be secondary and due to the non-formation of the proper component nervous parts of the retina, nervous fibres and ganglionic cells (in part) and comparable to that which follows destruction of those elements. It is similar to the atypical proliferation of Friedländer.

The pathogenesis of the entropion of the edge of the iris, not hitherto noted, is brightly illuminated by inspection of the figures which show it; it is due to the excessive foldings of the retinal layers of the iris, to their multiple duplications which are marked towards the inferior part of the iris coloboma, foldings followed by the epithelial sphincter muscle as it radiates in the neighbourhood; this necessitates the reversal of the pupillary edge backwards.

To sum up: *Genuine coloboma of the rudimentary optic nerves (glial plaques), aplasia of their retro-ocular segment, gliosis of the colobomatous cyst,* supernumerary nuclear arcs of the lens, entropion of the edge of the iris.*

REFERENCES

1. **Bergmeister.**—"Ein Beitrag z. Genese der Orbitalcysten und der im Mikrophthalmus vorkommenden Netzhaut und Aderhautanomalien." *Arch. f. Ophthalm.*, Vol. LXXXV, p. 1, 1913.
2. **Bernheimer.**—"Ein Beitrag zur Kenntnis der Missbild. des Auges." *Arch. f. Augenheilk.*, Vol. XXVIII, 1894.
3. **Bock.**—"Die angeborenen Kolobome des Augapfels," 1893.
4. **Enslin.**—"Ueber eine bisher nicht beschriebene Missbildung der Iris-Entropion iridis." *Arch. f. Augenheilk.*, Vol. LI, p. 346, 1905.
5. **Doetsch.**—"Anatom. Untersuch. eines Falles von Mikrophthalmus congenitus bilateralis." *Arch. f. Ophthalm.*, Vol. XLVIII, 1899.
6. **Duyse, van D.**—"Aplasie du nerf optique et colobome maculaire." *Arch. d'Ophthalm.*, Vol. XIX., 1899.
7. **Idem.**—"Pathogénie de la cyclopie." *Arch. d'Ophthalm.*, 1898.
8. **Idem.**—"Encyclopédie d'Ophthalm." Vol. II, p. 490, Foetus, Vol. XII, 1905.
9. **Ginsberg.**—"Ueber embryonale Keimverlagerung in Retina und Centralnervensystem, ein Beitrag z. Kenntnis des Netzhautglioms." *Arch. f. Ophthalm.*, Vol. XLVIII, p. 92, 1899.
10. **Helfreich.**—"Beitrag zur Lehre von Glioma retinae." *Arch. f. Ophthalm.*, Vol. XXI, Part ii, p. 236, 1875.

* For the intrapeduncular part.

11. **Hippel, von.**—"Ist das Zusammenkommen von Mikrophthalmus congenitus und Glioma retinae im gleichem Auge sicher erwiesen?" *Arch. f. Ophthalm.*, Vol. LXI, p. 352, 1905.
12. **Klein.**—"Inversio iridis." *Wiener Ophth. Gesellsch.*, 16. November, 1910. *Zeitschr. f. Augenheilk.*, Vol. XXIII, p. 280, 1910.
13. **Mannhardt.**—"Das Colobom der Aderhaut und seine Folgen." *Arch. f. Ophthalm.*, Vol. XLIII, p. 127, 1897.
14. **Natanson.**—"Ueber Microphthalmus und Anophthalmus congenitus mit serösen Orbito-palpebralcysten." *Arch. f. Ophthalm.*, Vol. LXVII, p. 185, 1908.
15. **Rindfleisch.**—"Beit. z. Entwicklungsgesch. der angeb. Missbildungen des Auges." *Arch. f. Ophthalm.*, Vol. XXXVII, Part iii, p. 192, 1891.
16. **Seefelder.**—"Entropium des Pupillarrandes." *Ergebn. der allgem. Pathol.*, etc., p. 747, 1910.
17. **Spemann in Schwalbe.**—"Die Morpholog. und die Missbild. des Menschen und der Thiere," Vol. III, f. ii, 1913.
18. **Terrien.**—"Kyste rétro-oculaire et pseudo-microphthalmie." *Arch. d'Ophthalm.*, Vol. XXXI, p. 787, 1911.

INJURIES TO THE TROCHLEA

BY

A. S. PERCIVAL, M.A., M.B. Cantab.,

SENIOR SURGEON EYE INFIRMARY, NEWCASTLE-UPON-TYNE.

ON several occasions the trochlea of the superior oblique has, unfortunately, suffered during surgical operations in its neighbourhood; but, as far as I know, no case but one of my own has hitherto been reported of accidental damage to the trochlea. I have just seen a second case, and I think that if attention were directed towards its possibility, it would be found to be not so unusual as imagined.

My first case was reported in the *Northumberland and Durham Medical Journal*, 1898, in a paper on the Diagnosis of Ocular Paralyses.

The patient was a lady who, in 1895, had received an accidental injury to her right eye from the point of a walking stick. A small scar was seen over the site of the trochlea, and she had all the symptoms of right superior oblique paralysis except the tilting of the false image. Thus, she had homonymous diplopia on looking downwards, with considerable depression of the false image on looking downwards and to the left. I considered that the fibro-cartilaginous pulley had been torn from its situation and had reattached itself further back. In this way intorsion of the eye might only result when the muscle acted, so that there would be no tilting of the false image. I saw the lady only a year ago with her husband, who had caused the injury, and found that the curious prismatic combination I had ordered her twenty years ago was still quite satisfactory.

Last week (May 31, 1919) I saw a boy at the Eye Infirmary who