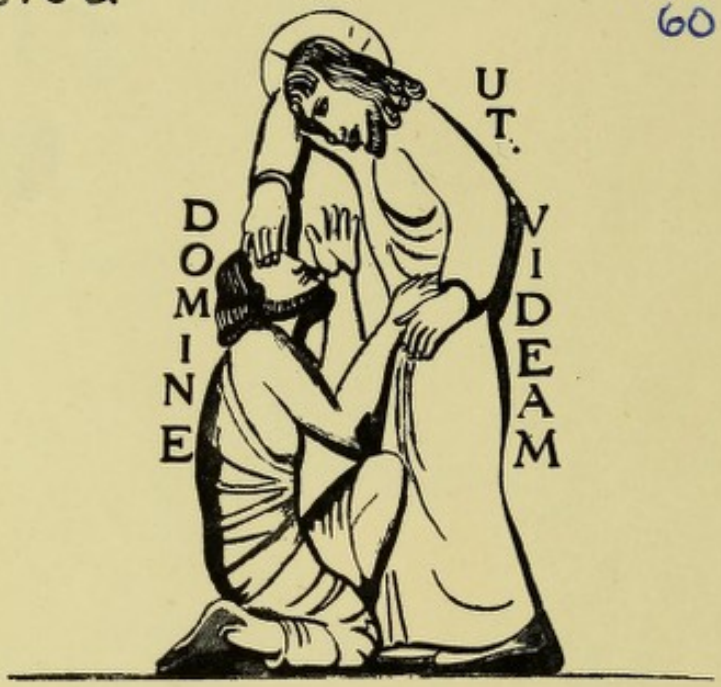
The ocular circulation / by J. Herbert Parsons.



① The Ocular Circulation

② The Neurology of Vision.

THE OCULAR CIRCULATION

THE
OCULAR CIRCULATION

BY

J. HERBERT PARSONS, B.S., B.Sc., F.R.C.S.

Arris and Gale Lecturer, R.C.S. (1903)

Curator, Royal London (Moorfields) Ophthalmic Hospital

London

JOHN BALE, SONS & DANIELSSON, LTD.

OXFORD HOUSE

83-89, GREAT TITCHFIELD STREET, OXFORD STREET, W.

1903

PREFACE.

I HAVE printed these Lectures on the Ocular Circulation in the hope that a fuller account than is found in the ordinary text-books may prove useful.

I should like to take this opportunity of expressing my indebtedness to Messrs. Erskine Henderson and Thomas Snowball for their invaluable help, to Mr. Nettleship for some very beautiful specimens, to Prof. Starling for allowing me to work in his laboratory and for his ever-ready advice, and to the Royal Society for the assistance of a Government grant.

J. HERBERT PARSONS.

CONTENTS.

THE OCULAR CIRCULATION.

I.—ANATOMY.

THE ocular blood supply in man is derived almost entirely from the internal carotid artery, whilst it is within the skull. This is not the case in lower mammals; and as all experimental investigation must be made upon these, it is essential to determine accurately the differences which obtain.

The general tendency as we ascend the animal scale is for the principal ophthalmic artery, which in the lower members is derived from the external carotid, to be derived from the internal carotid. On the border line, there are usually two or more ophthalmic arteries—generally one derived from each source, and there is commonly an anastomotic branch linking the two systems. It is only to be expected that individual variations should be of frequent occurrence, and such is the case.

Rabbit.—The common carotid in the rabbit gives off the thyroid artery and the ascending pharyngeal (fig. 1). At the level of the hypoglossal nerve the artery divides into the internal and external carotids. The former is much the smaller, runs without branching to the bulla tympani, and enters the skull by the carotid foramen. It then winds round the lateral side of the body of the sphenoid bone, and after crossing the oculo-motor nerve, gives off the anterior communicating and superior ophthalmic arteries. It ends by dividing into the anterior and middle cerebral. In four out of six dissections one was able to trace a fine

branch of communication between the internal carotid, as it lies on the side of the body of the sphenoid, and the internal maxillary close to the origin of the inferior ophthalmic artery. The external carotid gives from its inner side the laryngeal, lingual, and external maxillary in that order from below upwards. The last-named artery gives off the facial. From the posterior wall is given off the

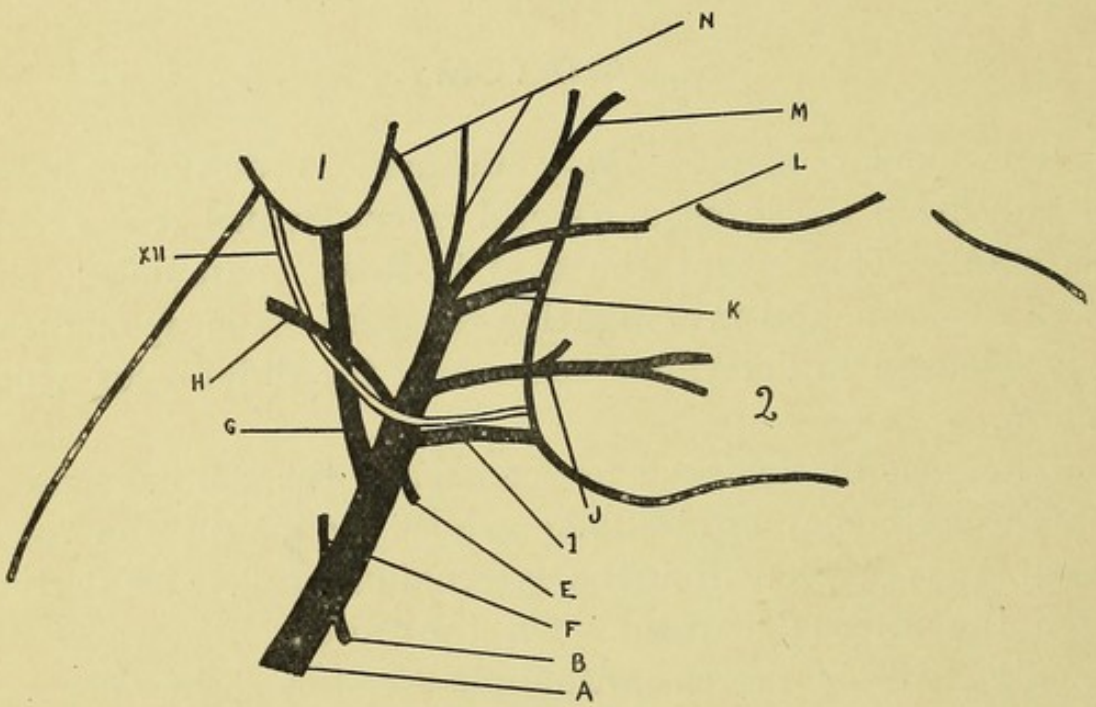


FIG. 1.—Scheme of the carotid arteries in the rabbit:—A, common carotid artery; B, thyroid artery; E, laryngeal artery; F, ascending pharyngeal artery; G, internal carotid artery; H, occipital artery; I, lingual artery; J, external maxillary artery; K, internal maxillary artery; L, transverse facial artery; M, superficial temporal artery; N, auricular artery. Hypoglossal nerve. 1, placed on the bulla tympani 2, on the lower jaw. (Henderson.)

occipital. A little below the neck of the jaw the artery divides into the superficial temporal and the internal maxillary. The former gives off the transverse facial and the auricular. The internal maxillary runs deep to the internal pterygoid behind the lower jaw. It gives off the tympanic, the inferior alveolar, some muscular branches, and the middle meningeal. It then passes through the pterygoid canal, and gives off the inferior ophthalmic. It

ends by supplying a superior alveolar branch and divides into the infra-orbital and pterygo-palatine arteries.

So far in these dissections the arrangement of the branches of the carotid arteries is in entire agreement with the description given in Krause.[1] I have therefore followed his nomenclature. I now quote in full his description of the ophthalmic arteries (fig. 2).

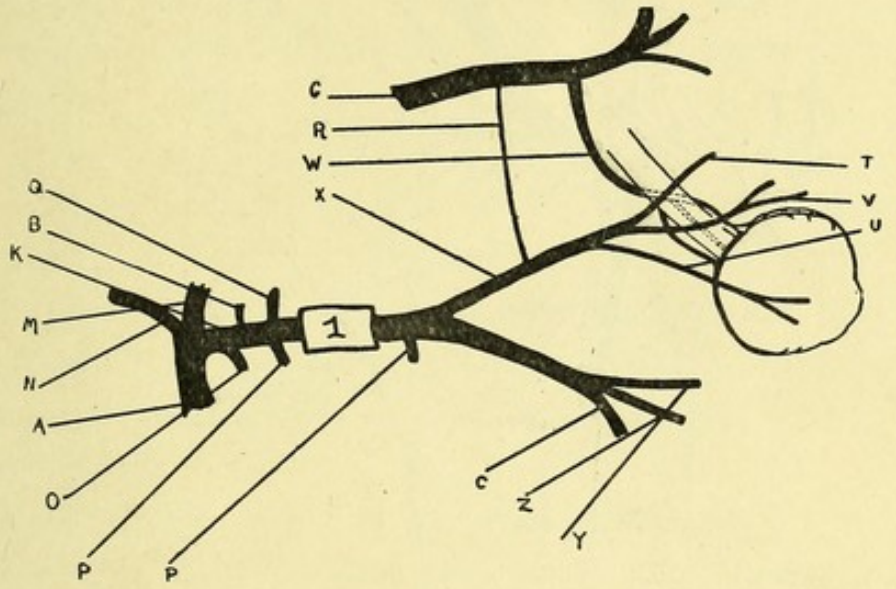


FIG. 2.—Scheme of the internal maxillary and ophthalmic arteries of the rabbit: A, external carotid artery; B, tympanic artery; C, superior alveolar artery; G, internal carotid artery; K, internal maxillary artery; M, superficial temporal artery; N, auricular artery; O, inferior alveolar artery; P, muscular arteries; Q, middle meningeal artery; R, ramus anastomoticus; T, ethmoidal artery; U, lacrymal artery; V, frontal artery; W, superior ophthalmic artery; X, inferior ophthalmic artery; Y, infraorbital artery; Z, pterygopalatine artery. 1, placed on the pterygoid canal. (Henderson.)

"The inferior ophthalmic artery runs on the anterior surface of the upper part of the great wing of the sphenoid, bends forward over the optic nerve, and reaches its anterior side. It there anastomoses with the superior ophthalmic artery. Its branches are as follows:—(1) Lacrymal, which appears through the posterior supra-orbital foramen as the supra-orbital artery. (2) Frontal, which in the same way goes through the anterior supra-orbital foramen.

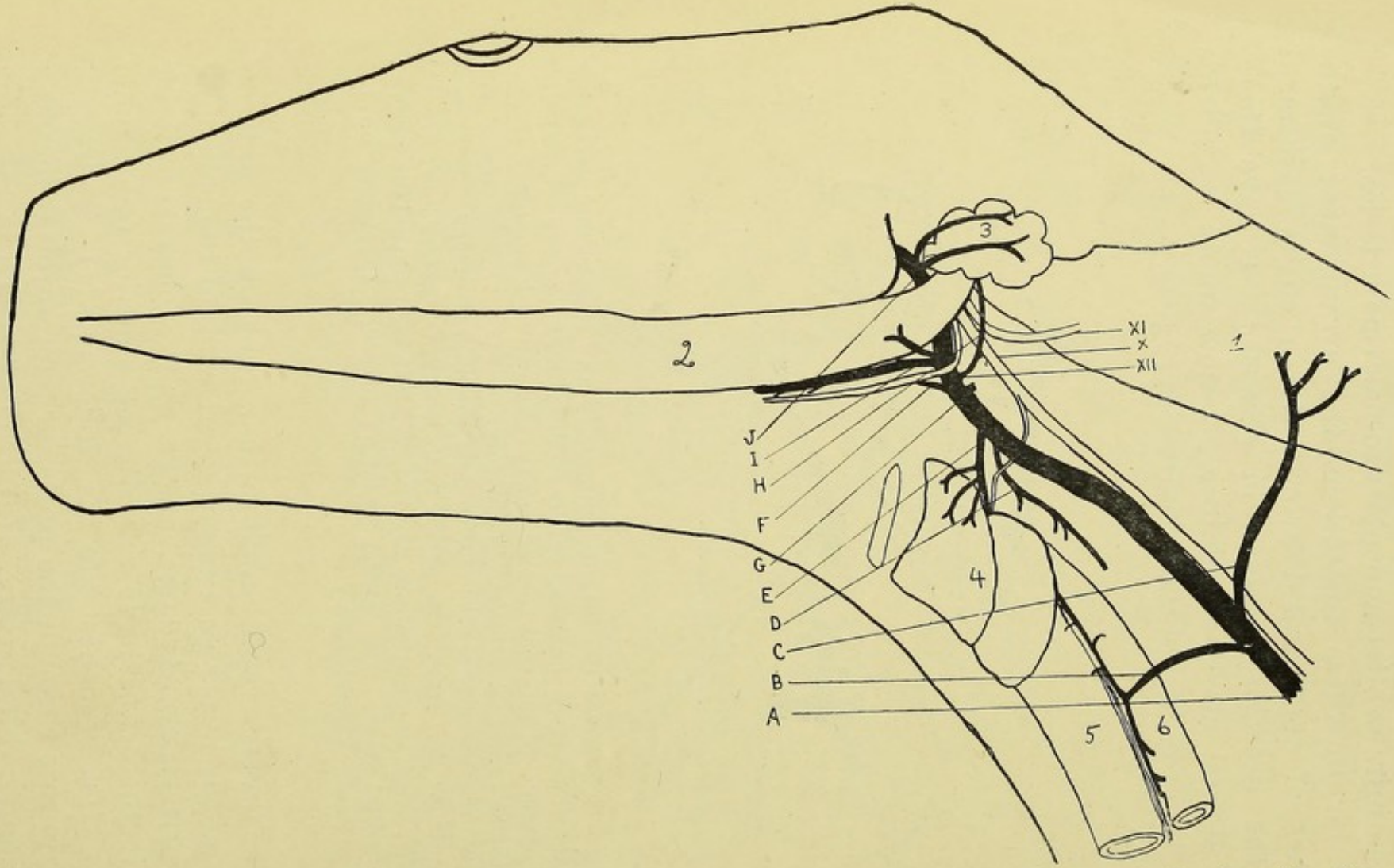


FIG. 3.—Scheme of the carotid arteries in the dog: A, common carotid artery; B, thyroid artery; C, muscular branch to sternomastoid; D, muscular branch to deep neck muscles; E, laryngeal artery; F, ascending pharyngeal artery; G, internal carotid artery; H, occipital artery; I, lingual artery; J, external maxillary artery; X., XI., XII., vagus, spinal accessory, and hypoglossal nerves. 1, placed on the sternomastoid; 2, on the digastric; 3, on the salivary gland; 4, on the larynx; 5, on the trachea; 6 on the œsophagus. (Henderson.)

Immediately after its origin it usually gives off the well-developed anterior ethmoidal artery which goes through the ethmoidal foramen into the nasal cavity. (3) Muscular branches to the eye muscles.

"The superior ophthalmic artery is but little developed. It runs forward to the optic foramen, and goes through this on the under and lateral side of the optic nerve into the orbit, winds under the nerve to its anterior side, and anastomoses with the inferior ophthalmic artery. It gives off the ciliary arteries and the central artery of the retina." (Krause).[1]

In two of the dissections there was no anastomosis between the two ophthalmic arteries in the situation here described. In both these cases the anastomotic branch between the internal carotid and the inferior ophthalmic was present. In two others this anastomotic branch was also present, and in these the superior ophthalmic artery was very small.

Dog.—In the dog the carotid artery gives off as its first branch a thyroid artery (fig. 3). A muscular branch to the sternomastoid usually arises at about the same level as the thyroid. A little higher the ascending pharyngeal and the laryngeal arise. The artery now divides into the internal and external carotids. The internal carotid is always the first postero-external branch (fig. 4). It takes origin just at the level of the hypoglossal nerve. It is most easily reached in the living animal by retracting the common carotid outwards and tracing up its inner side. There is always present an enlargement close to its origin.

The artery runs straight up with the vagus to the bulla, and enters the skull through the carotid foramen. It gives no branches in the neck. The external carotid gives as its first branch on the outer side the occipital. This artery arises close to the internal carotid, and is of about the same size. In the living animal it may readily be mistaken for it. It is somewhat more superficial in origin, and will usually be found to give an anterior branch

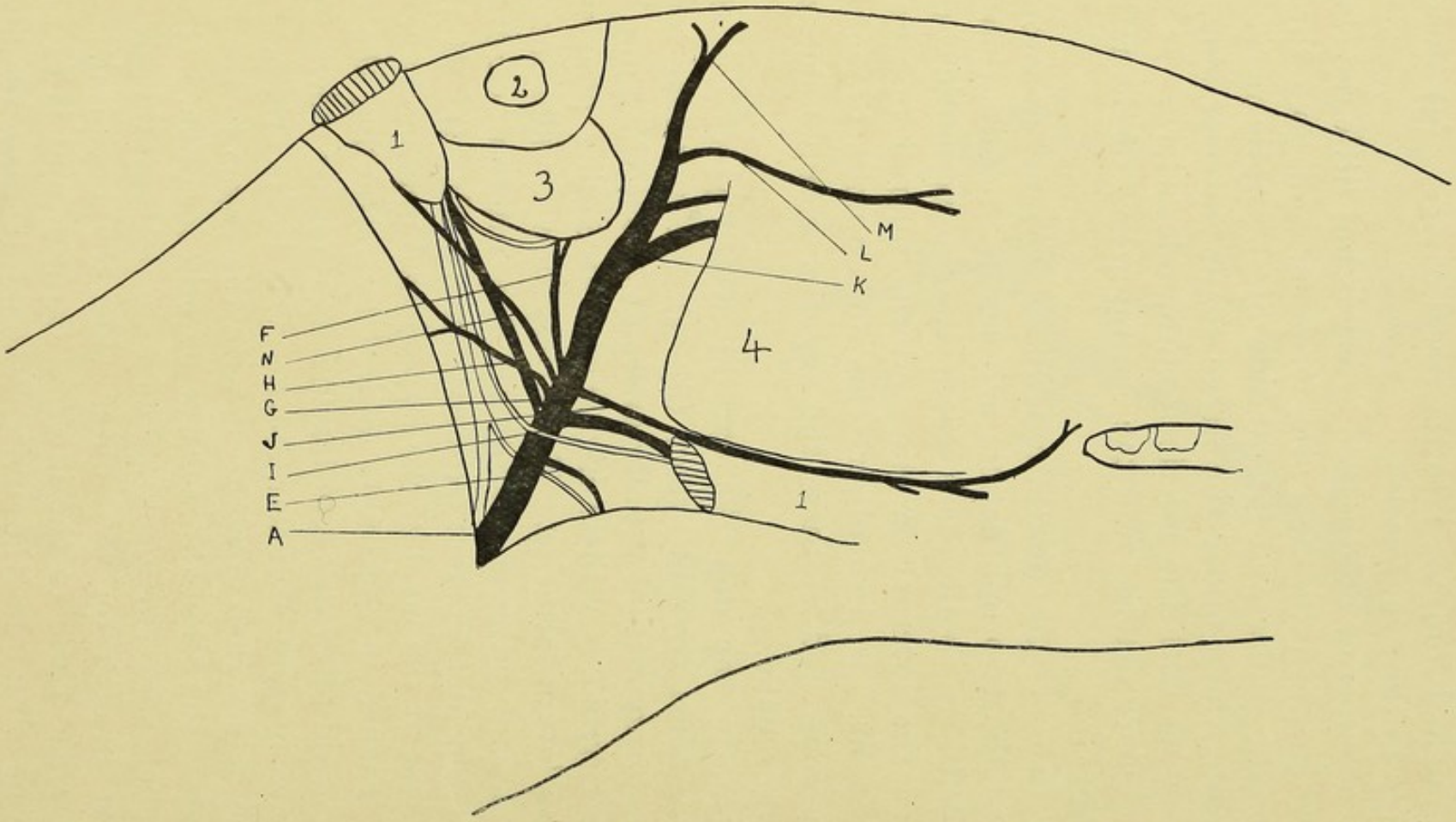


FIG. 4.—Scheme of carotid arteries in the dog, traced higher after division of the digastric: A to N as in fig. 3. 1, placed on the digastric; 2, on the ear; 3, on the bulla tympani; 4, on the lower jaw. (Henderson.)

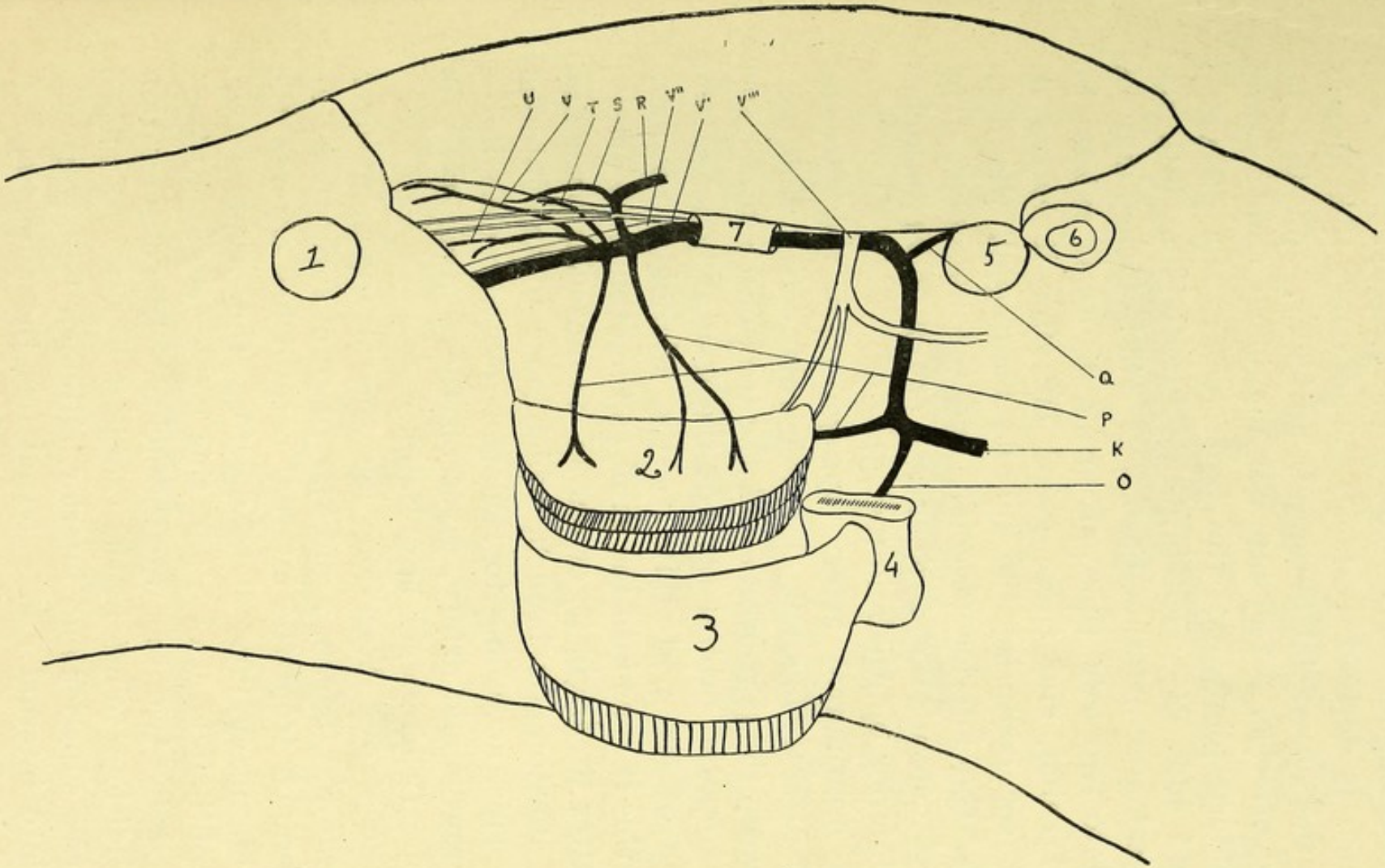
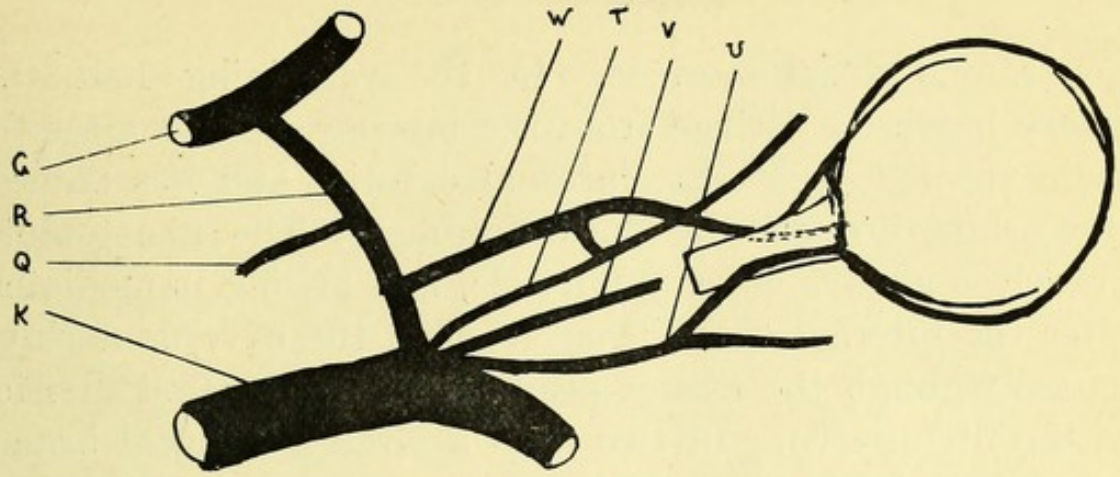


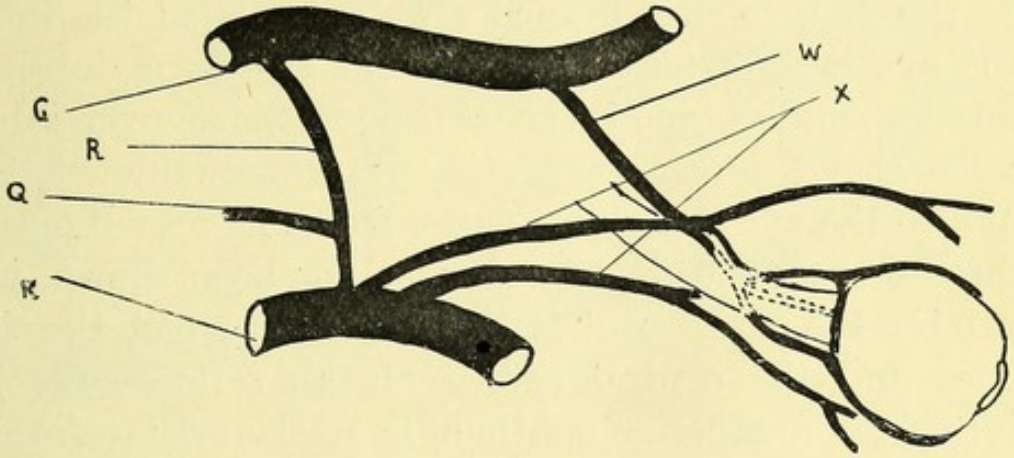
FIG 5.—Scheme of internal maxillary and ophthalmic arteries in the dog: K, internal maxillary artery; O, inferior alveolar artery; P, deep temporal artery; Q, middle meningeal artery; R, ramus anastomoticus; S, superior ophthalmic artery (inferior of Bellarminow); T, ethmoidal artery; U, lacrymal artery; V, frontal artery. V′ V″ V‴, the three parts of the fifth nerve. 1, placed on the eye; 2, on the temporal and pterygoid muscles, cut and turned down; 3, on the masseter, also turned down; 4, on the lower jaw; 5, on the bulla tympani; 6, on the ear; 7, on the pterygoid canal. (Henderson.)

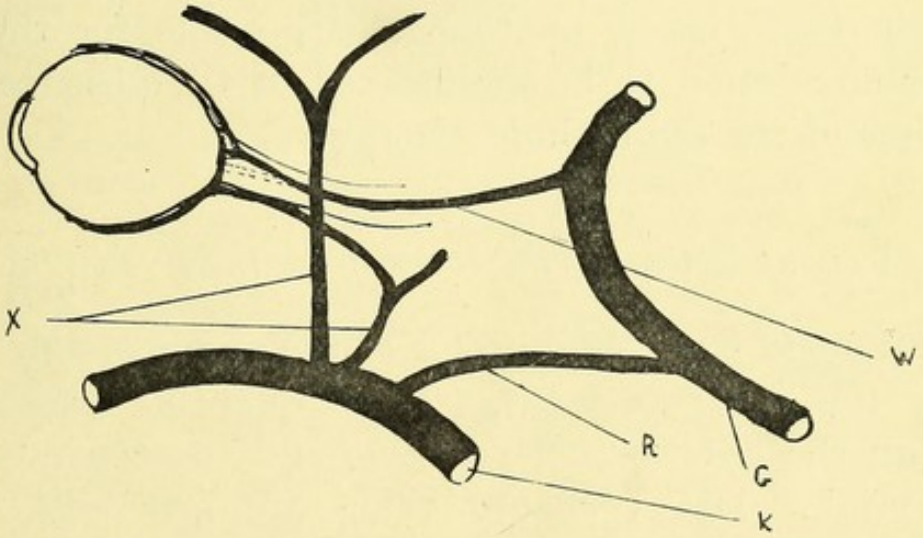
soon after its origin. The next branch and one of the largest is the lingual. Then comes the external maxillary, from which is derived the facial. The artery then breaks up into the superficial temporal, auricular, and internal maxillary arteries. The internal maxillary winds round the maxillary joint over the bulla, enters the pterygoid canal, and ends after leaving this by dividing into the infra-orbital and palatine branches. Its branches may be divided into two sets, those given off before it enters the pterygoid canal, and those given off after it leaves it. The first set comprise the middle meningeal, the deep temporals, the inferior alveolar, and the muscular. The second set comprise a further set of muscular branches and the inferior ophthalmic (fig. 5).

"The ophthalmic artery springs from the internal maxillary after it has left the pterygoid canal, and next runs between the peri-orbita and the temporal muscle, and further in on the orbital part of the frontal bone on the outer side of the peri-orbita to the ethmoidal foramen. Through this it runs into the skull as the ethmoidal artery. Shortly after its origin it, or one of its muscular branches, gives an anastomotic branch, which goes to the internal carotid. This, according to Bellarminow, who calls it the internal ophthalmic artery, gives off the central artery of the retina. (Ellenberger and Baum.)[2]

In none of our dissections has this arrangement been exactly followed (figs. 6, 7 and 8). In all of them the anastomotic branch from the internal carotid has entered the internal maxillary immediately before the origin of the inferior ophthalmic artery, and this latter has in all been represented by two separate branches. In consideration of the conditions found in the rabbit it is wiser to adhere to the terms superior and inferior, although Bellarminow's division into internal and external has the advantage of indicating their source from the internal and external carotids respectively. In only half the dissections has there been present a superior ophthalmic artery arising from







FIGS. 6, 7 and 8.—These represent variations in the orbital arteries in the dog:—G, internal carotid; K, internal maxillary artery; Q, middle meningeal artery; R, ramus anastomoticus; W, superior ophthalmic artery; X, inferior ophthalmic artery; T, ethmoidal artery; U, lacrymal artery; V, frontal artery. (Henderson.)

the ramus anastomoticus. In the remaining half this artery has been derived from the internal carotid after the main trunk has left the internal carotid, and has entered the orbit through the optic foramen. The anastomotic branch is always of very fair size, and arising immediately after the internal carotid has reached the cavernous sinus, passes through the fissura orbitalis below the first division of the fifth nerve. In two dogs a large meningeal branch has arisen from the ramus anastomoticus on both sides. This branch has apparently taken in these cases the place of the middle meningeal.

If the anastomotic branch always supplied the interior of the eye it is certainly of sufficient size to maintain the circulation, and as blood reaches it equally from the internal maxillary and internal carotid, it is probable that the supply to the eye would not suffer from the loss of only one of these sources. This, however, as has been shown, is not invariably the case. But in those cases in which the ciliary arteries and the central artery of the retina have been derived from a superior ophthalmic artery arising from the internal carotid, a free anastomoses has always been present between this superior ophthalmic artery and one of the branches of the inferior ophthalmic artery. It is then, even in these cases, anatomically possible for the intra-ocular circulation to be maintained in the absence of one or other of the ophthalmic arteries.

The Venous Return of the Blood from the Eye in the Dog.

The blood from the interior of the eye is mainly carried off by the vorticose veins, a small quantity also escaping through the anterior ciliary veins and the central vein of the retina. The vorticose veins are generally four in number, which ultimately unite to form two main trunks. The inferior and external one joins the ophthalmo-cerebral or inferior ophthalmic vein. The superior and mesial trunk runs into the cerebro-facial or superior ophthalmic vein.

The two ophthalmic veins communicate with each other in the back part of the orbit and run into the cavernous sinus. The inferior one usually also communicates with the tributaries of the internal maxillary vein. Both veins receive

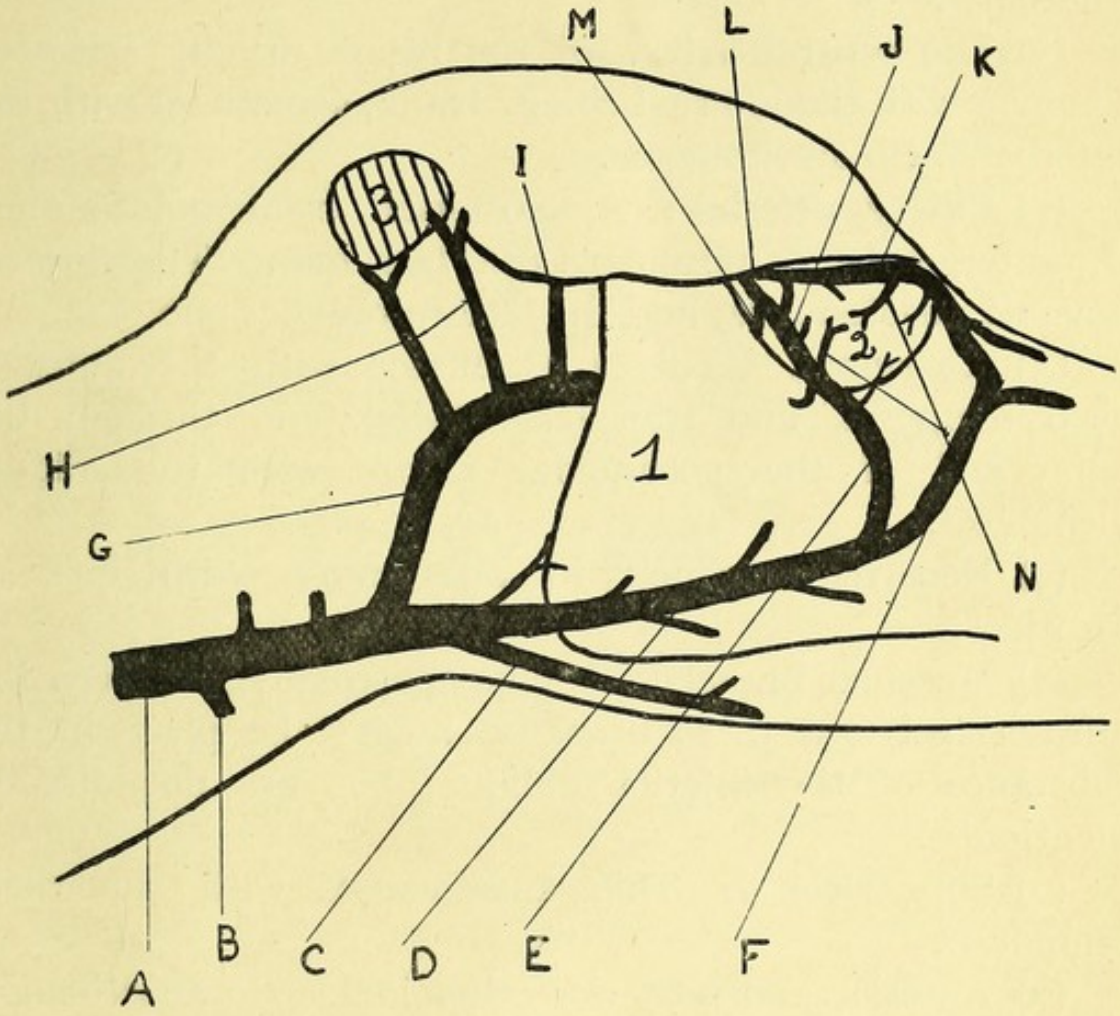


FIG. 9.—Scheme of the external jugular and ophthalmic veins in the dog; the eyeball, margin of the orbit, and masseter have been removed:—A, external jugular vein; B, commuincation to external jugular of the opposite side; C, lingual; D, common facial; E, deep facial; F, superficial facial; G, internal maxillary; H, auricular; I, to lateral sinus; J, *inferior ophthalmic or ophthalmo-cerebral vein;* K, *superior ophthalmic or cerebro-facial vein;* L, to cavernous sinus; M, to infraorbital vein; N, vorticose veins. 1 is placed on the inferior maxilla; 2, on the floor of the orbit; 3, on the ear. (Henderson.)

numerous tributaries from all the structures in the orbit. The superior vein at the inner canthus joins the nasal veins and becomes the superficial facial. The inferior vein runs under the external wall of the orbit, and at the anterior

border of the masseter joins the superficial facial to form the common facial trunk.

Man.—In man, the anastomoses between branches of the ophthalmic artery and those of the external carotid are very few and very small. On the authority of Quain's Anatomy :—

(1) The central artery of the retina usually arises in common with the internal ciliary trunk, sometimes with the external. No anastomoses.

(2) Ciliary arteries : A, posterior from ophthalmic ; B, anterior from muscular and lacrymal. The former have no anastomoses, and the latter no direct one.

(3) Lacrymal. This anastomoses with the anterior deep temporal, and transverse facial, and through the outer end of the sphenoidal fissure with the middle meningeal.

(4) Recurrent branch to anastomose with internal carotid.

(5) Muscular branches. Some anastomoses between the infra-orbital and these branches must take place in the substance of the inferior oblique, but are not directly mentioned.

(6) Supra-orbital. This anastomoses with superficial temporal.

(7) Anterior and posterior ethmoidal. No anastomoses given.

(8) Palpebrals. No anastomoses given.

(9) Nasals. Anastomose with facial.

(10) Frontals. No anastomoses given.

The following variations are also enumerated. The ophthalmic artery may enter the orbit through the sphenoidal fissure. The lacrymal artery not unfrequently, and in rare cases, a large part, or even the whole of the ophthalmic artery itself, arises from the middle meningeal. The lacrymal artery may also be reinforced by the anterior deep temporal artery. The ophthalmic artery has been seen to give off the middle meningeal.

Fr. Meyer,[3] in discussing a case in which an abnormal course of the branches of the ophthalmic artery led to free arterial bleeding, and in which a subsequent *post-mortem* examination showed that the lacrymal and frontal arteries were derived by a common stem from the middle meningeal, sums up the literature of the subject and enumerates the possible varieties. There is, however, no mention made of the morphology. In view of the conditions found in the animals now under discussion, the occasional origin of the ophthalmic artery, or of some of its branches, from the middle meningeal may be of morphological importance.

REFERENCES.

[1] KRAUSE, *Die Anatomie des Kaninchens*. Leipzig, 1868.

[2] ELLENBERGER AND BAUM, *Anatomie des Hundes*. Berlin, 1891.

[3] FR. MEYER, *Morphologisches Jahrbuch*, 1887, Th. 12.

See especially HENDERSON, *R.L.O.H. Reports*, XV., pt. 3, 1903.

THE INTRAOCULAR VESSELS.

The Optic Nerve.—The intracranial portion of the optic nerve is supplied by perforating blood-vessels from the pia mater, like other parts of the brain. The same occurs in the intra-orbital portion, but the supply is here reinforced by small inconstant twigs from the dural sheath, derived from the ophthalmic artery and vein and their branches. The vessels here form networks in each sheath, the meshes of which are elongated in the direction of the course of the nerve. Before the entry of the central vessels of the retina into the nerve, 15-20 mm. from the globe in man, but usually close to the sclerotic in lower mammals, with the exception of monkeys, the nerve is supplied entirely by perforating branches from these networks, which intercommunicate. After the central vessels have entered, they also contribute branches which anastomose freely with the others. All the vessels run in the supporting connective-tissue framework of the nerve, and hence the reticulum

conforms to the distribution of these partitions. This is clearly exemplified by the change which occurs when the lamina cribrosa is reached, the vessels here being smaller and more numerous, and the meshes closer and transversely elongated, whereas they were formerly more open, consisting of larger vessels running longitudinally with transverse and oblique anastomoses. At the lamina cribrosa, the vessels

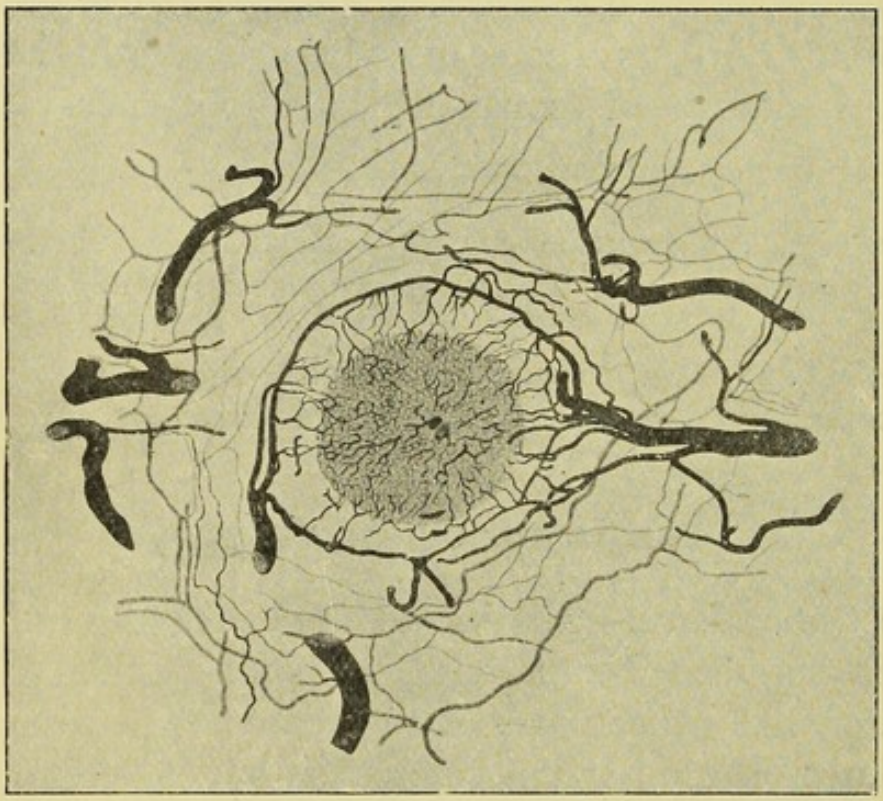


FIG. 10.—*Circulus arteriosus nervi optici* or *Circle of Zinn.* Optic nerve and sclerotic injected, retina and choroid removed; arteries black, veins paler. The central artery and vein of the retina are seen in section in the centre of the nerve; at the periphery are several large short posterior ciliary vessels; surrounding the nerve is the circle of Zinn. Note the relative size of the short posterior ciliary arteries and veins. (After Leber.)

are not only derived from the sclera, representing the dural supply, but also from the choroidal vessels. Anterior to the lamina cribrosa, in the intra-ocular end of the nerve, the network again becomes more open, with rounder meshes.

The pial sheath ends at the level of the lamina cribrosa. Its contribution to the blood supply of the nerve is repre-

sented farther forwards by the *circulus arteriosus nervi optici*, or *circle of Zinn*. Two or three of the short (posterior) ciliary arteries are given off at the sides of the optic nerve, and form a ring by the anastomosis of their branches in the sclerotic, just external to the nerve (fig. 10). Small twigs are given off from this ring to the nerve, and others run back to anastomose with the network of the pial sheath. These vessels apparently have no corresponding veins and they are further of interest in that they afford an indirect anastomosis between the choroidal and the retinal vascular systems.

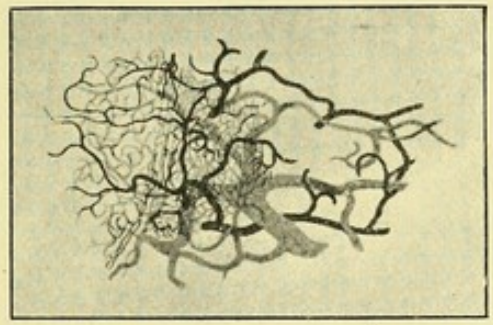


FIG. 11.—*Direct anastomosis between the vessels of the choroid and the optic nerve.* The choroid is to the right, the optic nerve to the left ; the capillary network is only partially filled in. (After Leber.)

There is also a direct anastomosis constantly present between these sets of vessels in this neighbourhood, for both arteries and veins are given off from the choroidal vessels to the nerve head, and communicate with those derived from the central vessels of the retina (fig. 11). This anastomosis is limited normally to the nerve-head, and as is well known, it is only exceptionally that any visible cilio-retinal artery can be seen ophthalmoscopically.

This duplex, direct and indirect, anastomosis between the ciliary and retinal vascular systems in the vicinity of the optic disc is the only communication which occurs normally between them. Elsewhere, as at the ora serrata, they are completely separate. Even these posterior anastomoses are vessels of little more than capillary dimen-

sions, and must be regarded as of relatively small importance under physiological conditions.

The Vitreous.—In most adult mammals the vitreous is normally free from blood-vessels. In the embryo the central artery of the retina is continued forwards through the vitreous as the *hyaloid artery*, to supply the posterior vascular sheath of the lens. This vessel occasionally persists as a congenital anomaly, either as a functional blood-carrying vessel (fig. 12), as a short pulsating cæcal vessel

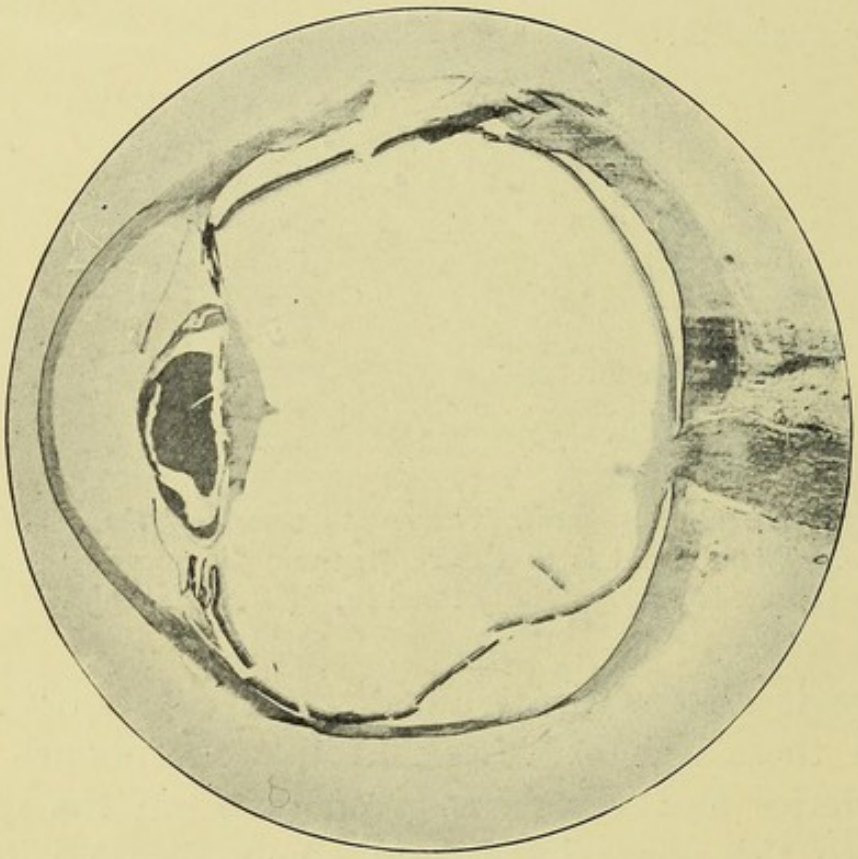


FIG. 12.—*Persistent hyaloid artery.* Section of a microphthalmic eye: the anterior and posterior ends of the persistent hyaloid artery are seen, attached to the persistent posterior vascular lens-sheath and to the optic nerve respectively. × 4. (From *Trans. Ophth. Soc.*, vol. xxii., pl. xvi., fig. 2.)

filled with blood, as a bloodless trumpet-shaped process with its base attached to the disc, or as a fibrous cord stretching for a varying distance into the vitreous. It is found normally in a very rudimentary condition in all ruminants (*e.g.*, ox), and in many rodents (*e.g.*, guinea-pig).

In all birds, many reptiles and some mammals, a special vascular organ, the *pecten*, is found projecting from the disc into the vitreous. Structurally, it is homologous with the ciliary processes, consisting of a vascular plexus covered by pigmented cells, and it is probably analogous to them in function as a secreting organ. It occurs in its most complicated form in birds (fig. 13), but it varies enormously

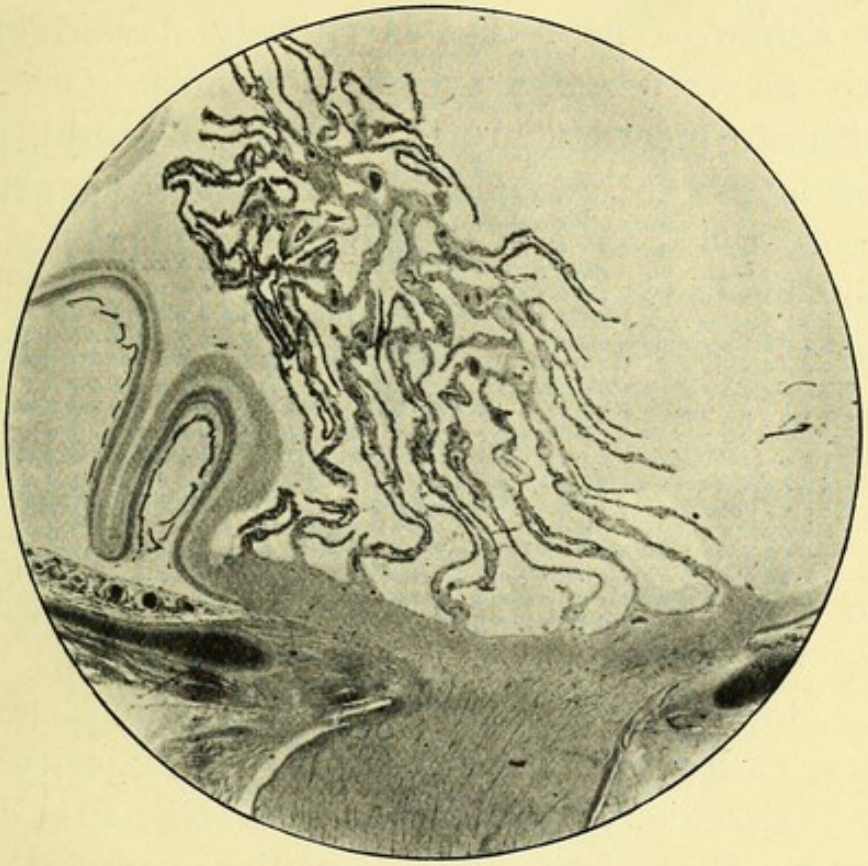


FIG. 13.—*Pecten of Rhea.* Section of head of optic nerve, with the pecten attached to it and stretching forward into the vitreous. Note that the retina, seen folded to the left, is devoid of blood-vessels. (I am indebted to the Zoological Society of London for this eye.)

in shape in various animals, being most rudimentary in rodents (*e.g.*, agoutis) and marsupials. Amongst the latter, the form found in the rat kangaroo (*Hypsiprymnus rufescens*), the rabbit-eared perameles (*Perameles lagotis*) &c., is approximated in rare cases in man. These cases, however, are probably not vestigial, but pathological new-formed vessels.

In elasmobranchs, the vitreous itself is vascularised from

a *processus falciformis*. In all holostean fishes and those teleosteans which have no processus falciformis, and in most reptiles which have no pecten, there is a network of vessels upon the hyaloid membrane. In the frog, for example, the circulation of the blood can be observed ophthalmoscopically. The main vessels do not enter by the optic nerve, but behind the insertion of the superior rectus, passing downwards over the disc.

The Retina.—The retina is entirely devoid of vessels in nearly all vertebrates except mammals. Other exceptions hitherto recorded are the eel (W. Krause), in which the inner layers are vascularised as far as the inner nuclear layer, and the boa and python (examined ophthalmoscopically by Lindsay Johnson).

Many of the lower mammals, *e.g.*, Echidna, Perameles lagotis, Dasypus, Hystrix, Castor, Chinchilla, Myopotamus, Pteropus, Rhinoceros, belonging to the Monotremes, Marsupials, Edentata and Rodentia, are also anangiotic.

The vessels are extremely small, extending only over the disc or a short distance from it, in Hyrax, Elephas, Tapirus, Equus, Myrmecophaga, Phalangista, Belideus, Petaurus, Perameles obesula, Hypsiprymnus, Dendrolagus, Capybara, Cælogenys, Cavia, *i.e.*, in the majority of Marsupials, Perissodactyls, Edentata, and Rodentia (Lindsay Johnson).* The guinea-pig is a familiar example.

Next come those mammals in which only a portion of the retina has a direct supply, comprising most of the carnivora (especially Felidæ, Viverridæ, Mephitis, Meles, Ursidæ) and some rodents (Sciuridæ, Leporidæ, Myoxidæ). The typical example in this group is the rabbit, in which the vessels are limited to the horizontal expansion of medullated fibres which is found in this animal (fig. 22).

In those mammals in which the whole retina has a direct blood-supply, the lower members of the group have several arteriæ and venæ centrales scattered over the disc,

[1] Lindsay Johnson, *Phil. Trans.*, B., vol. cxciv., 1902.

as in the dog (fig. 14). Others have very elongated discs, with parallel vessels bending over the edges (Sciuromorpha); and even multiple discs, each with a central vessel, are found (Cervidæ). The vessels are most centralised in primates.

These variations apparently occur irrespective of phylogenetic position, thus tending to show that specific vas-

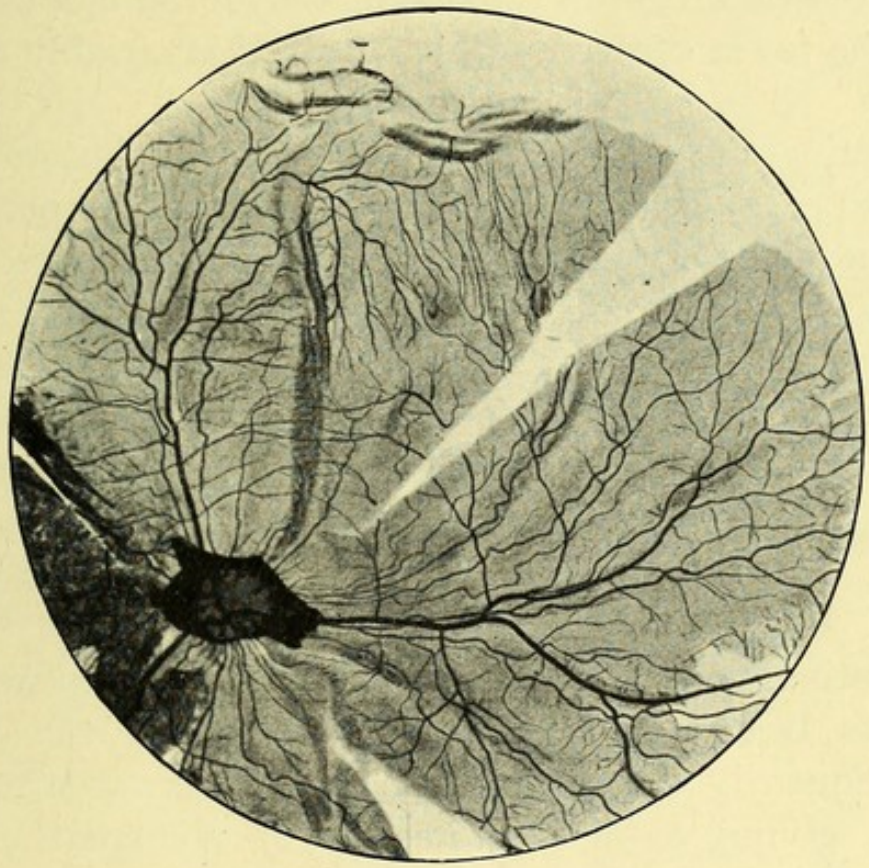


FIG. 14.—Dog's retina, injected. (From a preparation by Henderson.)

cularisation of the retina is not an inherited feature of mammals as a class, but an independent development.

In man, the central artery of the retina divides in the middle of the disc, or shortly before it reaches the surface, into a superior and inferior papillary artery, running upwards and downwards respectively. Each of these quickly bifurcates, usually upon the disc, into the superior and inferior temporal and nasal branches. One of the main branches generally gives off a small median artery, running

horizontally towards the nasal side. The nasal arteries are rather smaller than the temporal, and run radially towards the ora serrata ; whilst the temporal arteries, on the other hand, curve in such a manner as to avoid the macula lutea, sending, however, minute branches towards it. There are also two fine macular arteries, which pass horizontally outwards from the disc, usually arising from the central artery before it has reached the surface. The macular vessels break up into capillaries, forming a network around the fovea centralis, which is itself invariably devoid of vessels.

The retinal veins correspond to the arteries, but are more subject to variation, and do not closely accompany the corresponding arteries in their more peripheral course.

The arteries do not anastomose, even as far as their finest divisions, only communicating through the capillary reticulum. There are a few small anastomoses of the minute veins near the ora serrata, which, however, are quite unlike the large ring of venous anastomoses which occurs in this situation in the ox (circulus venosus retinæ anterior).

The retinal venules bend in a circular direction near the ora serrata, but not so the arteries. In the dog, the arteries not unfrequently bend round and run backwards towards the disc, giving a false impression of recurrent arteries from the ciliary region. As mentioned before, there is no communication with the ciliary vessels at the ora serrata, nor are there any recurrent ciliary vessels to the retina (fig. 14).

The larger vessels lie immediately external to the internal limiting membrane, which is raised up by them. In a few mammals, *e.g.*, the rabbit, and indeed all the Leporidæ, the vessels are internal to this membrane, and cast a distinct shadow ophthalmoscopically.

The capillaries do not extend farther outwards than the external reticular layer, so that the outer nuclear layer, the rods and cones, and the pigment epithelium are depen-

dent for their nourishment upon osmosis from the choroidal or retinal vessels. The capillaries are extremely fine, forming fairly wide meshes (0·02—0·75 mm., Leber). There is an area on each side of the larger vessels which is free from capillaries (fig. 15); this is occupied in part by the perivascular lymph-sheaths. Since at the fovea centralis the layers of the retina are reduced to such, as are elsewhere

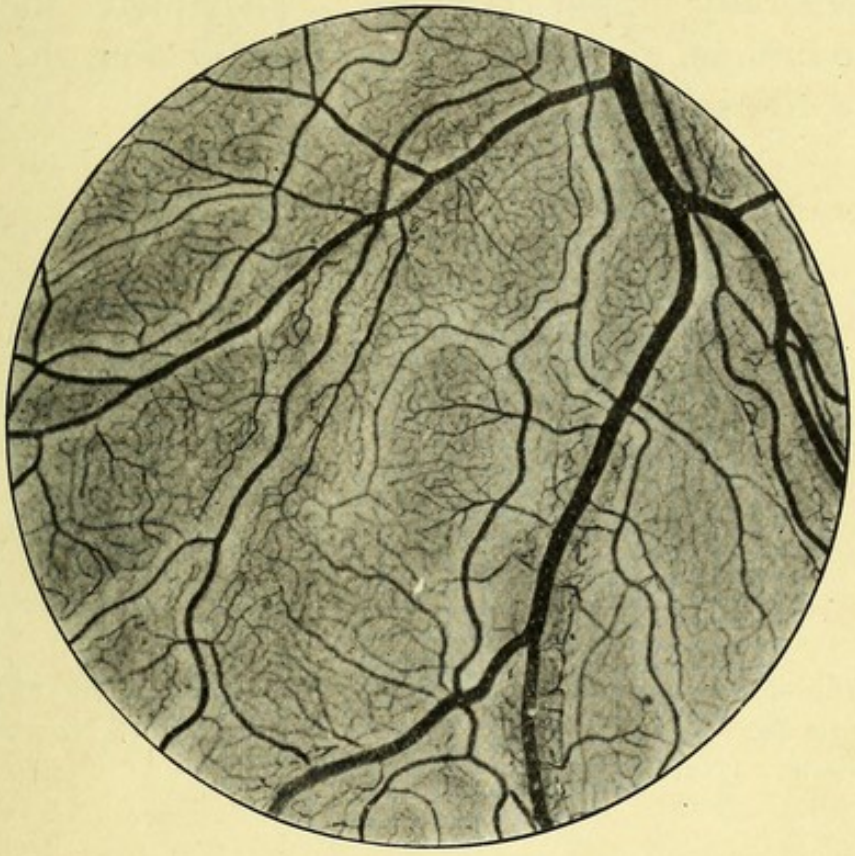


FIG. 15.—Dog's retina, injected. Higher power, showing perivascular spaces devoid of capillaries.

evascular, so here too there are no vessels, as previously mentioned (fig. 16).

The Uveal Tract.—The uveal tract is supplied by the ciliary arteries, which are divided into three groups—the short posterior, the long posterior, and the anterior (fig. 17). The *short posterior ciliary arteries*, about twenty in number, pierce the sclerotic in a ring around the optic nerve, running almost perpendicularly through the sclera, to which fine branches are given off, as well as to the optic nerve.

The long posterior ciliary arteries, two in number, pierce the sclerotic slightly farther away from the nerve, in the horizontal meridian, one on the medial, the other on the temporal side. They traverse the sclerotic very obliquely, running in it for a distance of 4 mm. The *anterior ciliary arteries* are derived from the muscular branches of the ophthalmic artery to the four recti. There are usually two from each rectus, with the exception of the rectus externus which generally supplies only one. They pierce the sclerotic near the limbus, giving off twigs to this region, the conjunctiva and the sclerotic.

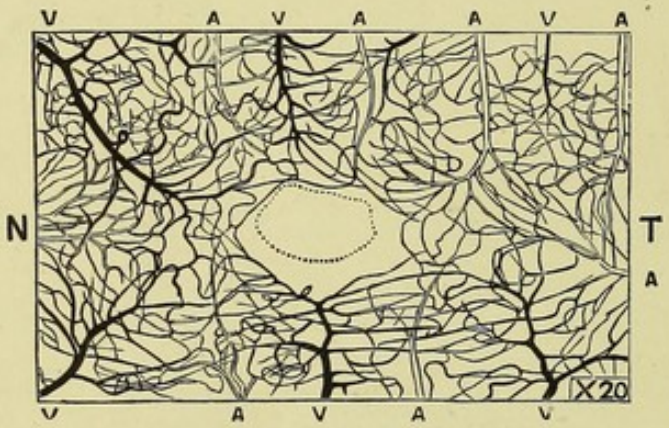


FIG. 16.—Human macular region, injected. The central gap corresponds with the fovea centralis. A, arteries; V, veins; N, nasal side; T, temporal side. (Nettleship.)

The ciliary veins also form three groups—the short posterior ciliary, the venæ vorticosæ, and the anterior ciliary. The *short posterior ciliary veins* are unimportant; they do not receive any blood from the choroid, but only accompany the minute scleral twigs from the posterior ciliary arteries, and are even smaller than the corresponding arteries. The *vorticose veins* are the most important, consisting usually of four large trunks which open into the ophthalmic vein, or some of the muscular branches. They enter the sclerotic rather behind the equator of the globe, two above and two below. One or more often divides before entry, but there are seldom more than six. They pass very

obliquely through the sclera, and often give off smaller branches to the choroid. They also receive blood from the sclera and episclera. The *anterior ciliary veins* are smaller

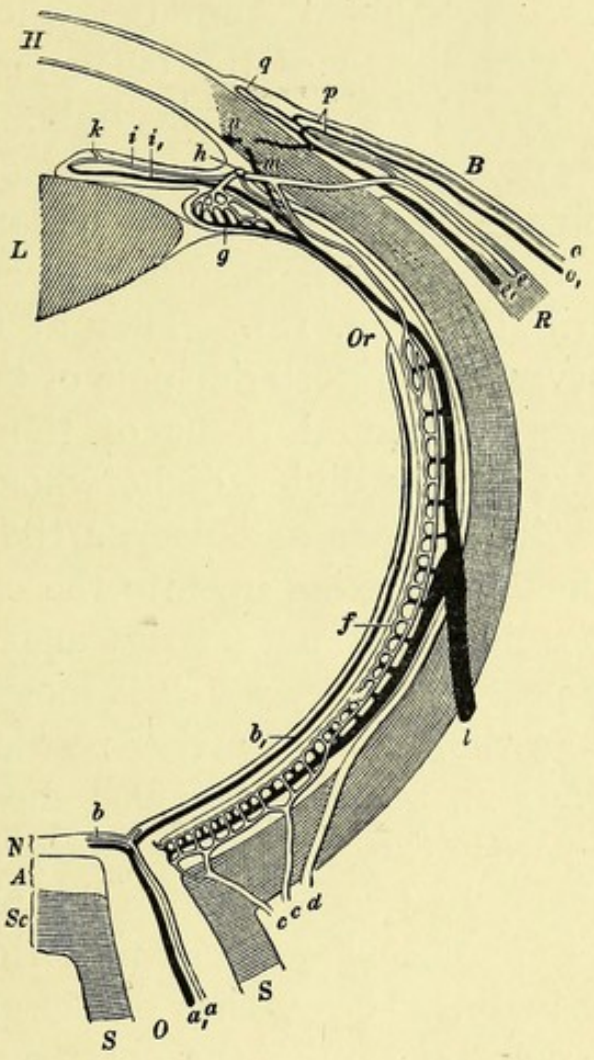


FIG. 17.—Scheme of ocular blood-vessels. *a*, arteria centralis retinæ, a_1, vena centralis retinæ; *b*, retinal arteries, b_1, retinal veins; *c*, *c*, posterior short ciliary arteries; *d*, posterior long ciliary arteries; *e*, anterior ciliary arteries; *f*, choroidal capillaries; *g*, capillaries of ciliary body; *h*, circulus arteriosus iridis major; *i*, arteries of iris; *k*, circulus arteriosus iridis minor; i_1, veins of iris; *l*, venæ vorticosæ; *m*, veins from ciliary muscle; e_1, anterior ciliary veins; *o*, o_1, posterior conjunctival vessels; *p*, anterior conjunctival vessels; *q*, marginal loops of cornea. *O*, optic nerve; *S*, its sheath; *Sc*, sclera; *A*, choroid; *N*, retina; *L*, lens; *H*, cornea; *R*, internal rectus; *B*, conjunctiva. (Fuchs, after Leber.)

than the corresponding arteries, since they receive blood only from the outer part of the ciliary muscle. There are usually two or three to each rectus muscle.

Of these ciliary vessels, the short posterior ciliary arteries supply the whole of the choroid, being reinforced by recurrent branches from the ciliary body, which, with the iris, is supplied by the long posterior and anterior ciliary arteries. The blood from the whole of the uveal tract, with the exception of the ciliary muscle, normally leaves the eye by the vorticose veins only.

The short posterior ciliary arteries, on reaching the choroid, run in the outer layers for a distance which varies directly with the situation, posterior or anterior, of their ultimate distribution (fig. 18). They at first make sharp twists and curves at the posterior pole of the globe, as they lie in the loose pigmented tissue of the suprachoroidea. Passing forwards, they divide dichotomously, the smaller branches invading deeper and deeper the inner layers of the choroid, finally breaking up into the capillary network of the choriocapillaris. The arteries anastomose to some extent at the posterior pole, which is most richly supplied, but less so than the veins. Farther forwards, they do not anastomose *inter se*, but a fresh anastomosis occurs in the anterior parts with the *recurrent ciliary arteries* (fig. 19). These are generally ten or twelve in number, and are derived from the anterior and long posterior ciliary arteries in the ciliary body. The meshes of the capillary network are fine and polygonal near the optic nerve, but become more and more elongated farther forwards, whilst the capillaries also increase in diameter. There is no relationship between the size of the capillaries and the width of the meshes, and the size of the eye in various animals (Sömmering).

The two long posterior ciliary arteries pass forwards between the choroid and the sclerotic, without dividing, as far as the posterior part of the ciliary body. Here each divides into two branches the bifurcation having an angle of about 45°. They run forwards in the substance of the ciliary muscle, and at its anterior part bend round in a circular direction, anastomosing with each other, and

FIG. 19.

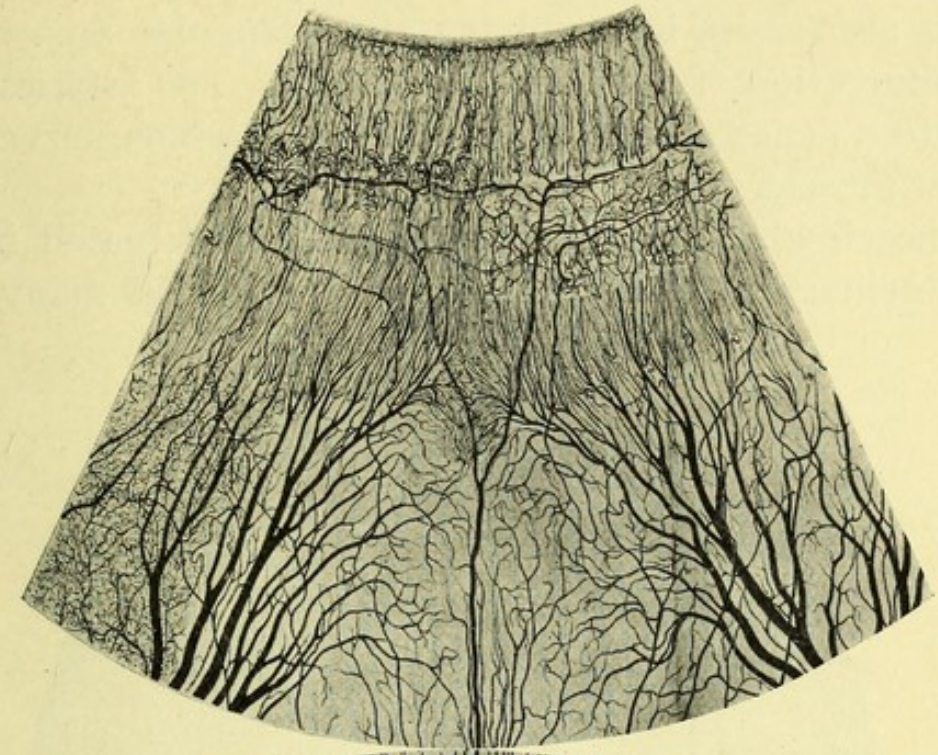


FIG. 18.

FIGS. 18 AND 19.—Vessels of the human uveal tract, injected, from the optic disc to the edge of the iris. Two vorticose veins and their branches are seen. Running up the centre is a long posterior ciliary artery. The capillaries are only partially filled in. Arteries, black; veins paler (After Leber.)

thus forming the *circulus arteriosus iridis major*. This is reinforced by branches from the anterior ciliary arteries, which also assist in supplying the triangular area left by the bifurcation of the posterior vessels. The arteries break up into a dense meshwork of capillaries, which pervade the ciliary muscle.

The circulus arteriosus iridis major is situated in man in the ciliary body at the base of the iris, in many lower

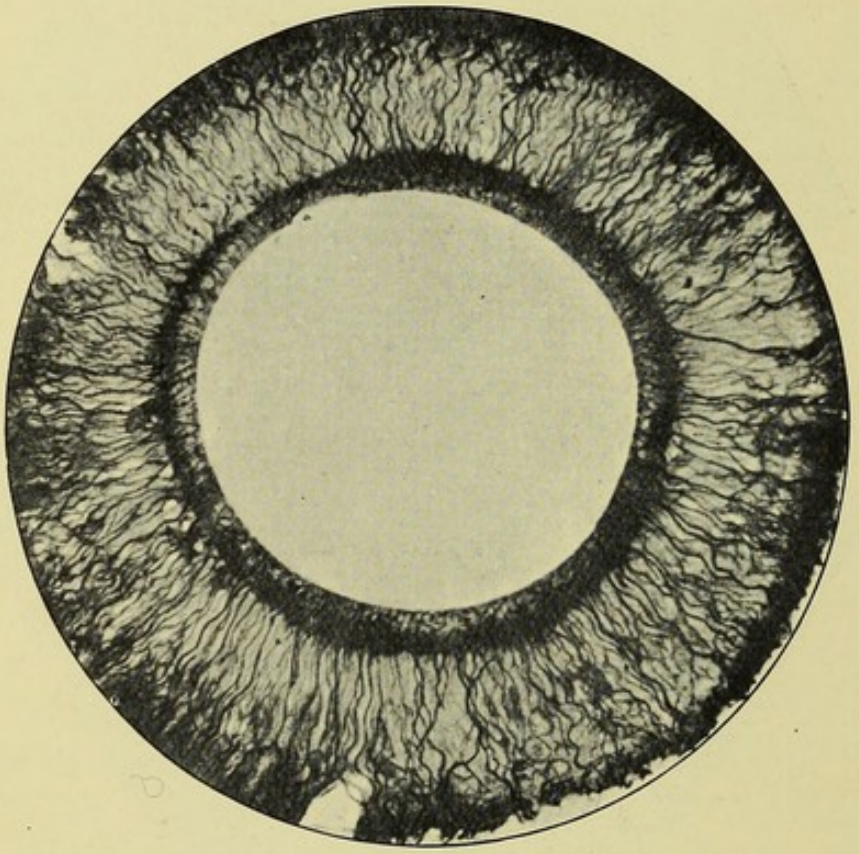


FIG. 20.—Human iris, injected. (From a preparation by Nettleship.)

animals, *e.g.*, the rabbit, in which the ciliary processes invade the back of the iris, it lies in the iris itself. From it are supplied the ciliary processes and the iris. A branch from the circle may supply only one ciliary process, or break up into two or three, for an equal number of processes. It is to be noted that these vessels must run through the ciliary muscle in order to reach the processes, which are therefore supplied from in front. The artery of each process breaks up into many anastomosing arterioles, which then

form a very rich capillary network, the ciliary processes in fact consisting of little more than a dense bunch of vessels.

Other branches from the major arterial circle run radially through the iris, dividing dendritically, and ending in loops at the pupillary edge (figs. 20 and 21). These iridic arteries are unusually thick-walled in the adult, and difficult to inject. A circular anastomosis takes place a little outside the pupillary margin, the *circulus arteriosus iridis*

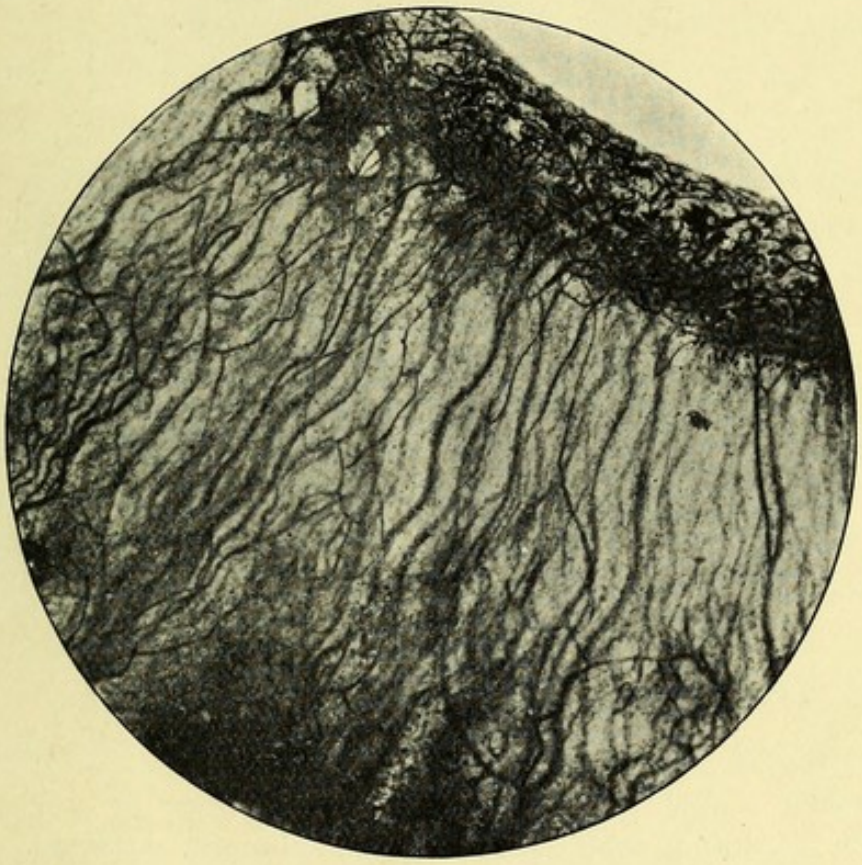


FIG. 21.—Human iris, injected. Higher power.

minor. This marks the place of origin of the fœtal pupillary membrane, and is only developed after the latter has disappeared. The capillaries of the iris have a very open network, except those of the sphincter iridis.

The whole of the venous blood from the choroid leaves the eye by the vorticose veins. No veins pass from the choroid with either the short or long posterior ciliary vessels. The tributaries of the vorticose veins are arranged radially, the radii being bent, so as to give a whorled appearance

(fig. 22). The capillaries joining to form the venules in the choriocapillaris also form whorls, called the *stars of Winslow*, though this arrangement is not so marked as in the case of animals which possess a tapetum. The veins from the front and back are naturally the longest, and the posterior branches of neighbouring vortices anastomose, forming U-shaped curves over half the distance from the

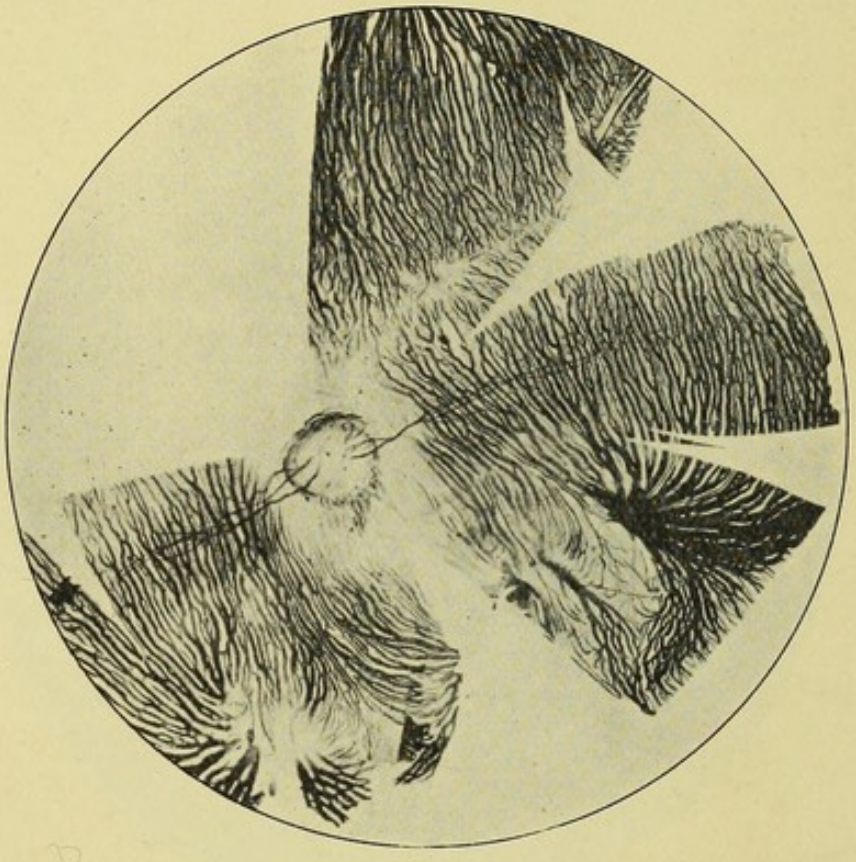


FIG. 22.—Albino rabbit's retina and choroid, injected. Note the retinal vessels, limited to the horizontal expansion of medullated fibres. (From a preparation by Henderson.)

disc to the equator. The veins from the anterior half of this distance, in the area between two vortices, pass back into these anastomoses and not directly into the vortices (fig. 18).

The veins of the iris are gathered together into radial bundles which correspond more or less to the ciliary processes. They pass backwards through the ciliary body, lying towards the inner surface. Here they are joined by the large branches coming from the ciliary processes, and by smaller ones from the ciliary muscle. The whole are

gathered together into an immense number of veins running backwards, parallel to each other, through the smooth posterior part of the ciliary body. After reaching the choroid they gradually converge, and unite to form the larger anterior tributaries of the vorticose veins.

In most mammals which have been examined (ox, sheep, horse, pig, dog, rabbit, &c.) there is a large anterior choroidal venous anastomosis, the *circulus venosus Hovii*, into which the veins from the iris and ciliary body open.

The veins from the outer part of the ciliary muscle do not pass backwards with the others, but forwards to become connected with the *circulus venosus ciliaris* or *canal of Schlemm*. This is in reality a plexus of veins forming a ring in the anterior part of the sclreotic, just outside the ligamentum pectinatum iridis. The plexiform nature is most marked where it is joined by anastomoses from the veins of the ciliary muscle. Efferent veins pass from this plexus through the sclerotic to anastomose with the veins from the sclera and episclera, finally joining the anterior ciliary veins, which run with the corresponding arteries. Upon the plexus of the canal of Schlemm and its efferent anastomoses devolves the important function of carrying away the major part of the lymph from the eye, draining particularly that large lymph space, the anterior chamber.

Branches of the anterior ciliary arteries, after giving off the anterior conjunctival arteries, break up dichotomously into excessively fine vessels, which anastomose freely with each other, and end in minute loops at the edge of the cornea. These invade the cornea for a very short distance only—1-1½ mm. above and below, ½-1 mm. at the sides—the remainder being free from vessels (figs. 23 and 24).

The anterior conjunctival vessels are also given off from the anterior ciliaries, not far from the corneal margin. They form a superficial group of vessels, and run backwards in a radial direction immediately after their origin, and finally contribute to the loose capillary network of the conjunctiva. The anastomosis which occurs between the

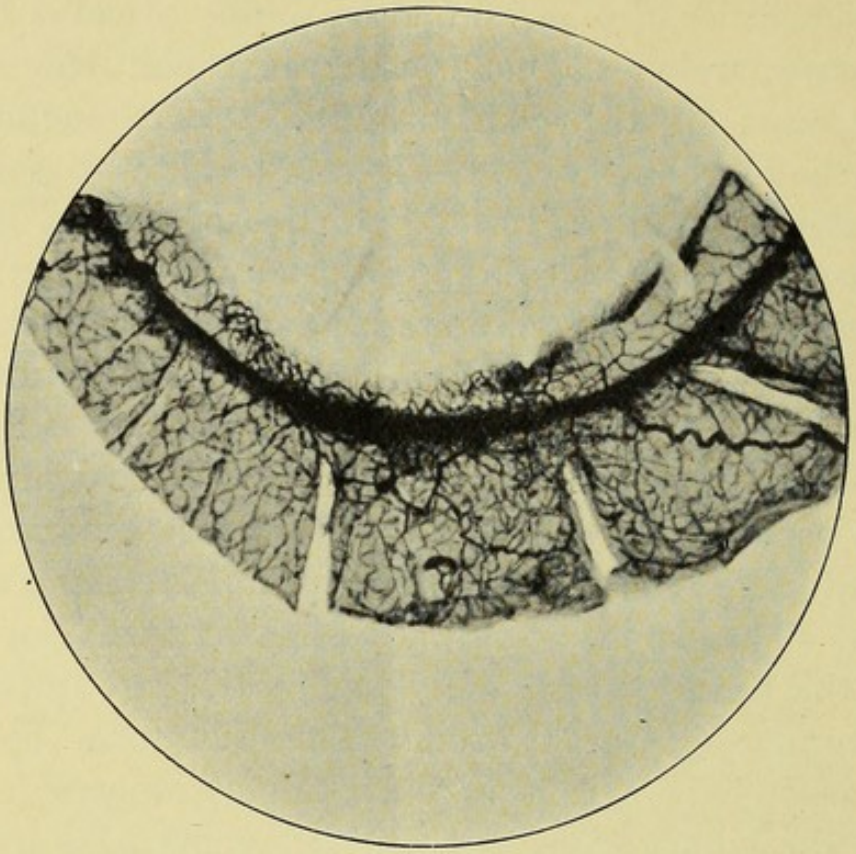


FIG. 23.—Human conjunctiva, injected. (From a preparation by Nettleship.)

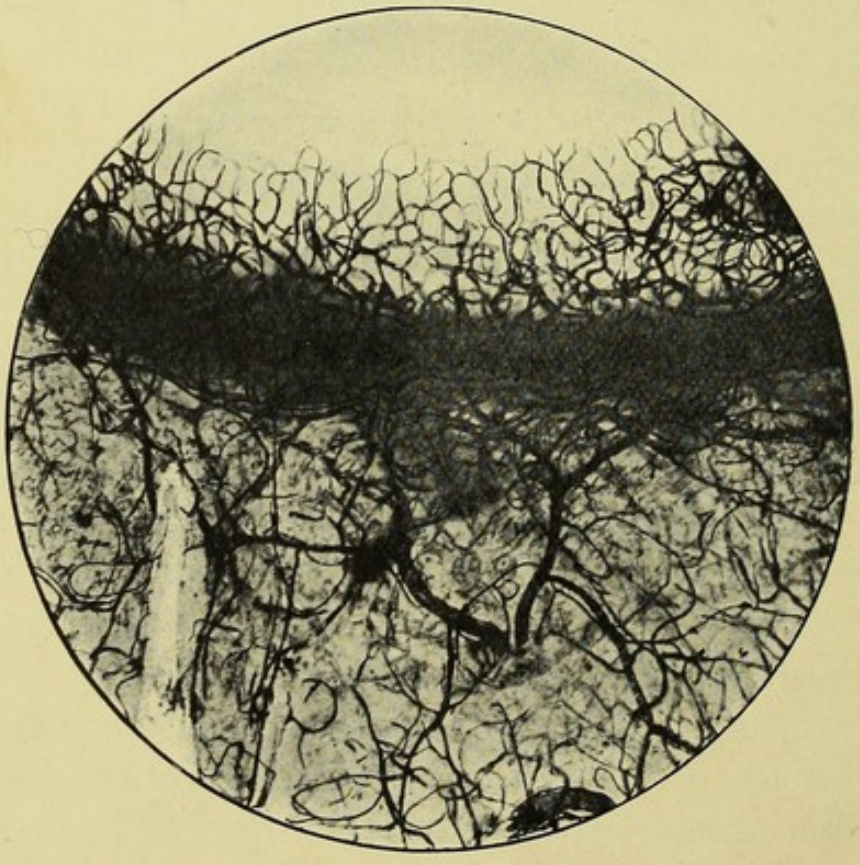


FIG. 24.—Human conjunctiva, injected; showing corneal marginal loops. Higher power.

more superficial, conjunctival, and the deeper, episcleral vessels increases from behind forwards, being richest at the limbus, a fact which is demonstrated so often clinically.

REFERENCE.

[1] LEBER. *Graefe-Saemisch, Handbuch der gesammten Augenheilkunde,* 1st edition, vol. ii., Leipzig, 1876; also, *Denkschrift d. k. Akad. der Wiss. zu Wien : Math.-naturwiss. Cl.*, xxiv., pp. 297-330.

Anomalies of the Intra-ocular Vessels.

As might be expected, most of the anomalies of the intra-ocular circulation have been observed ophthalmoscopically, and are limited for the most part to the retinal vessels. The commonest abnormalities are *cilio-retinal vessels*. These were discovered by H. Müller, and were first demonstrated anatomically by Nettleship.[1] They are usually small cilio-retinal arteries or retino-ciliary veins, these names describing the direction of the blood-flow. They are always situated on the temporal side of the disc and pass to or from the yellow-spot region of the retina. Typically, they appear at the edge of the disc, and the possibility of their origin from the central retinal vessels before these have reached the surface cannot always be eliminated. They do not anastomose with the other retinal vessels, and they seem to be most commonly derived from the scleral ciliary vessels, and not from the choroidal ones. These vessels are so familiar that it is unnecessary to illustrate them. Much rarer are vessels of the same group, but derived from the retinal vessels. These are the retino-ciliary arteries (Benson[2]), and cilio-retinal veins (Lawford[3]).

Extreme *tortuosity* of the retinal vessels has been observed in a considerable number of cases. It is sometimes confined to the veins, but often occurs in both arteries and veins. It is particularly associated with hypermetropia (Benson,[4] Nettleship,[5] Stephen Mackenzie[6]) and with nævoid conditions of the skin (Horrocks,[7] Work Dodd,[8] Hartridge[9]). The association with hypermetropia may be ascribed to a normal growth of the vessels, with insufficient

expansion of the globe, but as mentioned, the veins alone may be tortuous, and the retina is not folded. When associated with nævi there is no anastomosis of the vessels.

Arterio-venous anastomosis has been observed (Marcus Gunn[10]), but is excessively rare. In such cases no varicose condition of the vein occurs, probably owing to the support afforded by the intra-ocular tension.

Bifurcation of the veins has been seen (Adams Frost,[11] Werner,[12] Stephenson[13]), and they then not unfrequently communicate.

Abnormal retinal vessels are rarely congenital (Story[14]), but generally of pathological new formation (Frost,[15] Nettleship[16]). The occasional resemblance to a low type of pecten must be regarded as fallacious.

Pathological communications of inflammatory origin between the retinal and choroidal vessels often occur in patches of choroidal atrophy.

Aberrant insertions of the remains of the hyaloid artery into the macula (Silcock[17]), and other parts of the retina, are varieties of which the explanations adduced are purely speculative.

References.

[1] Nettleship, *R.L.O.H. Reports*, ix., p. 161, 1877. See also Lang and Barrett, *Ibid.*, xii., p. 59; Elschnig, *Archiv f. Ophth.*, xliii., p. 144, 1897.

[2] Benson, *Tr. Oph. Soc. U.K.*, iii., pl. iv.

[3] Lawford, *Ibid.*, xv., pl. viii.

[4] Benson, *Ibid.*, ii., pl. iii.

[5] Nettleship, *Ibid.*, ii., pl. iii.

[6] Stephen Mackenzie, *Ibid.*, iv., pls. v. and vi.

[7] Horrocks, *Ibid.*, iii., pl. v.

[8] Work Dodd, *Ibid.*, xxi., pl. iii.

[9] Hartridge, *Ibid.*, xxi., pl. iii.

[10] Marcus Gunn, *Ibid.*, iv., pl. vi.

[11] Adams Frost, *Ibid.*, ix., pl. vi.

[12] Werner, *Ibid.*, x., p. 152.

[13] Stephenson, *Ibid.*, xi., p. 222.

[14] Story, *Ibid.*, iii., pl. iv.

[15] Frost, *Ibid.*, vii., pl. ii.

[16] Nettleship, *Ibid.*, iv., pl. iv.

[17] Silcock, *Ibid.*, xx., pl. viii.

II.—PHYSIOLOGY.

The ophthalmic artery, from which the whole of the blood supply of the eye is derived in man, is a branch of the internal carotid within the cranium. It is therefore a direct offshoot from the intracranial circulation, and much stress has been laid upon this fact clinically, so that the condition of the retinal arteries has been assumed to be a criterion of the circulation within the skull. More minute investigation of this question, however, educes many facts which so seriously modify such an assumption, that it can only be accepted with severe limitations.

After traversing the orbit without, as far as is known, having any large or important communication with extra-cranial blood vessels, the branches of the ophthalmic artery which are distributed to the eye enter the globe, and are then placed under special physical conditions. Like the arteries which enter the cranium, they, too, enter a closed box. Unlike the cranium, however, the eyeball is not a rigid case, but is capable of variations in form according to the forces which are brought to bear upon it, either from without or from within. Under normal conditions, the fluid contents of the globe exert a pressure of 20 to 30 mm. Hg. above the atmospheric pressure, which may be regarded as the measure of the external pressure when the eye is at rest. The blood-vessels which enter the eye, therefore, are now subjected to an increased pressure of 20 to 30 mm. Hg. The blood pressure in the ophthalmic artery has been measured by v. Schultén in the rabbit by inserting a cannula into the vitreous and driving in saline solution under known pressure until the blood-flow in the retinal arteries was just stopped, as observed ophthalmoscopically. It was

found to be only a few (2 to 15) mm. Hg. below that in the large arteries (carotid or femoral). The capillary pressure in most parts of the body is normally about 15 to 20 mm. Hg. (Starling). No means has yet been devised for measuring the intraocular capillary pressure, since the veins are so small and anastomose so quickly and profusely after leaving the eye, that it is impossible to measure the venous pressure. It is just possible that this may be found feasible in the dog or some larger animal by utilising the communication with the angular vein and tying off the posterior communication with the cavernous sinus. In any case, it is clear that, with an external pressure—the normal intraocular pressure of 20 to 30 mm. Hg.—the capillary pressure must be considerably above this level, and we shall probably not be far wrong in considering it equal to 40 or 50 mm. Hg. It is most likely that this is the highest capillary pressure of any organ of the body whilst at rest, though many organs are doubtless subject to wide variations in this respect during activity.

We know that the outflow of blood from the eye by the veins is usually a steady stream. It therefore follows that the venous pressure must also be considerably above the average in other parts of the body,[1] since, if it were below the intraocular pressure, the veins would collapse, and would only be reopened when the internal pressure rose above that level. It has been thought that increase of intraocular pressure would tend to close the venæ vorticosæ, but experimental investigation does not bear out this view. The very oblique course of these vessels through the sclerotic is further a protective mechanism against kinking, such as might be produced by the action of the ciliary muscle in dragging forward the equatorial region

[1] Small veins of the arm .. .. .. + 9 mm. Hg.
Portal vein .. .. + 10 „ „
Inferior vena cava .. .. .. + 3 „ „
Large veins of the neck .. 0 to — 8 „ „
(Starling).

of the choroid. As long as the intraocular tension is constant, the fluid contents of the globe must be constant, any outflow of fluid, either blood or lymph, being equalised by a corresponding in-flow or secretion. Under these circumstances, the eye is temporarily a rigid box, and as shown to be the case in the brain by Leonard Hill, the venous pressure is equal to the intracranial pressure, so here too the venous pressure will also be equal to the intraocular pressure. This will not hold for variations of intraocular pressure, as it does in the case of the brain, because under these circumstances the eyeball is no longer a rigid case.

The fundamental problem which requires solution is the mechanism which brings about the normal intraocular tension, and which constantly sustains it at so high a level. Unfortunately, the problem yet awaits complete solution. It is obvious that it is allied to the problem of secretion in other parts of the body, and more particularly to the production of lymph, for there can be no doubt now that the aqueous fluid, which is the essential factor, must be considered rather as lymph, modified by the peculiar conditions of its production, rather than as a secretion allied to saliva, &c. It may be argued that this does not simplify the question much ; in one sense, however, it does. Like lymph, the secretions of the body are ultimately derived from the blood, but there is an increasing volume of evidence to show that they are more remotely dependent upon the physical conditions of the circulation than is the case with lymph. Thus, saliva can be secreted at a pressure far above the blood pressure of the carotid artery ; whereas, even if lymph is produced by a " vital " secretory process, no such inconsistency with the physical laws of filtration is observed. Indeed, the repetition of Heidenhain's work upon the subject by Starling has led to a reversal of the former's conclusions, so that the evidence is now rather in favour of a purely physical process in the production of lymph. Starling and Pflüger have carried

these researches into the domain of ocular physiology in recent experiments, which have not yet been published. Under normal conditions the aqueous contains a very small proportion of proteids—only about 0·12 per cent. These consist of serum albumin, serum globulin, and fibrinogen, the proteids of the blood. If, however, the anterior chamber is tapped, so that the intraocular tension falls to zero, the aqueous secreted now contains much larger percentages of the same proteids. This tends to show that the process of production is one of physical filtration, the reduction of pressure on the negative side of the membrane allowing the transfusion of greater quantities of the large-moleculed proteids. Extended researches have confirmed these results. Anatomical researches, such as the demonstration of "glands" in the ciliary body, by Treacher Collins, cannot be held to controvert these results; and the absence of these "glands" in many animals, *e.g.*, albino rabbits, proves that they are not essential. At the same time it is probable that here, and indeed in the whole domain of lymph production, the question is not quite so simple as the physical theory supposes. What principally interests us now is the fact that everything tends to show that the secretion of aqueous is directly dependent upon the intracapillary pressure, and that it varies *pari passu* with that pressure.

I have already stated that there is no means at present of directly, or even indirectly, measuring the intracapillary pressure accurately. We can, however, measure the intraocular tension, and if the deductions which we have already drawn are reliable, this will afford an index to the capillary pressure. So far with accuracy; beyond this, with regard more especially to the condition of the arteries, in the absence of any knowledge of the concomitant venous pressures, our deductions must remain somewhat conjectural. Since the venous pressures, with a few exceptions to which attention will be drawn, are not likely to vary within wide limits, we shall not go far wrong in regarding

a rise of intraocular pressure as equivalent to a dilatation of arterioles, a fall being equivalent to a constriction, for a rise of tension means increased fluid content. The increased fluid may be intra- or extra-vascular ; in the former case it means dilatation of vessels, in the latter either increased production or diminished excretion of lymph. In general the changes during the comparatively rapid observations which we shall consider will be due to vascular dilatation or constriction, for the variations of secretion and excretion are relatively slow. Even if they occur, they will generally be in the same sense as the vascular changes, and will not vitiate the results. Thus, increased production of fluid means increased intracapillary pressure, which may be due either to increased arterial or increased venous pressure. The latter probably only occurs in specific cases, being caused either by increased general venous pressure, or by mechanical constriction of the local veins : we have no evidence of physiological venous constriction, though it is by no means improbable that it may occur. Increased arterial pressure may be due to increased general arterial pressure, the ocular arterioles remaining unchanged, or more frequently dilating passively, or by local dilatation. Thus the dilatation may be either a passive one, brought about by the constriction of other larger areas, notably the splanchnic area, or an active vaso-dilatation. In general, then, rise of intraocular tension under the given experimental conditions will be due to arterial vaso-dilatation, with certain definite exceptions.

These are the main considerations by which the results must be judged. There is yet, however, an important possibility which must be eliminated. If the walls of the eyeball were rigid, no change in the volume of its contents could occur—vaso-dilatation could only happen at the expense of vaso-constriction of an equivalent intraocular area, or by the expulsion of an equal volume of lymph from the eye : in fact the conditions would be identical with those found by Leonard Hill to obtain in the intra-

cranial circulation, anticipated in theory by the Monro-Kellie doctrine. We must therefore consider the effect of changes of pressure upon the wall of the globe.

This has been carefully investigated, both on animals' eyes and on the human eye, by Koster Gzn. The presence of a large amount of elastic tissue in the sclerotic, which is the most resistant coat of the eye, would lead one, *à priori*, to infer its elasticity. If the globe were a perfect sphere, any increase in internal pressure would bring this elasticity into play. It is not, however, a perfect sphere, and the first expenditure of energy, even up to a pressure of 100 mm. Hg., is chiefly devoted to approximating it to that form. It is not to be concluded that the elasticity is entirely in abeyance under these conditions, but it is of such relatively small influence as to be negligible. As the pressures we shall be dealing with will be below the level indicated, we may leave the elasticity out of account, and regard the eye as somewhat plastic, so that variations in the volume of its contents are possible within narrow limits.

Experience derived from the examination of human eyes with the ophthalmoscope afford an immense amount of evidence that very considerable changes occur in the volume of the arteries and veins of the retina, and that too in the absence of any pathological variations of tension. Changes may also occur physiologically, but the investigation of the human eye affords no proof that they are directly under the control of specific vasomotor nerves.

Method.—The animals used in my experiments were dogs and a few cats. They were anæsthetised with morphia, followed by A.C.E. mixture; in most cases they were also curarised. The blood pressure was usually taken from the femoral artery, occasionally from the carotid on the opposite side to the eye which was being observed.

The apparatus used for the measurement of the intra-ocular tension consisted of a cannula, A, a fine bored glass tube, B, a manometer, and a pressure-bottle (fig. 25). The

cannula, A, is a modified form of Leber's intraocular pressure cannula, and is the same as that used by Starling and Pflüger for determining the rate of flow of the aqueous secretion. It consists of a gilt hollow needle, having two small lateral openings at *a* and *b*, upon opposite sides near the pointed end, which is also open. This ensures free communication with the interior of the eye. The distal end, *c*, is closed by a plug, which can be replaced by a stylet for cleaning out any clot or other obstruction. A side tube, *d*, near the distal end, leads off to the manometer by means of two fine-bored glass tubes, *e* and *B*, connected by india-rubber joints. The tube *e* is not essential, but is inserted for convenience. The flexible joints allow a

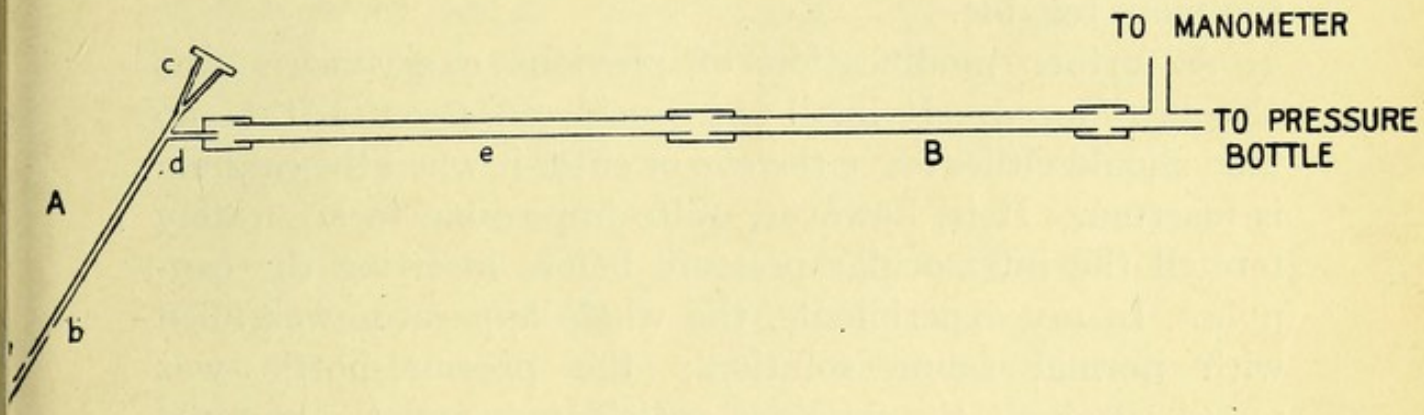


FIG. 25.—Intraocular pressure cannula.

limited amount of mobility for the necessary manipulations, they are made as little elastic as possible by bringing the glass tubes nearly into apposition, and using thick-walled pressure-tubing for the junctions. A glass T-tube connects *B* with the manometer and the pressure-bottle.

The manometer used for obtaining graphic records was either a Hürthle manometer, provided with a thin rubber membrane, or an ordinary Marey tambour, about twice the diameter of the Hürthle, with a rather thicker membrane. In most of the experiments only qualitative changes were observed, so that it was unnecessary to calibrate the manometer. In a few cases in which absolute measure-

ments were taken, it was simpler and more accurate to use a fine-bored mercury manometer.

In many of the earlier experiments, the cannula was inserted into the vitreous chamber of the eye. When this method worked well, it gave as conclusive results as in the later experiments, in which the cannula was inserted into the anterior chamber. There can be no doubt that the pressures in the two chambers are equal. The former, however, is not so reliable as the latter, owing to the consistency of the vitreous, which often prevents a free to and fro movement in the cannula, and may give rise to a valvular effect. It is of interest as demonstrating the identity of the results obtained from the two chambers, but those obtained from the anterior chamber are generally the more reliable.

A further modification of previous experiments was also introduced. It has been considered essential that no fluid should either leave the eye or enter it when the cannula is inserted. It is, however, quite impossible to accurately foretell the intra-ocular pressure before inserting the cannula. In my experiments, the whole apparatus was filled with normal saline solution; the pressure-bottle was raised to about the pressure anticipated, and the cannula was introduced whilst the fluid was flowing from it. It is very important that the cannula be perfectly sharp and smooth, so that it may be pushed across the anterior chamber very quickly; otherwise the aqueous escapes, and the iris and lens are wounded and block the apertures in the cannula. Immediately after insertion, an air-bubble is let into the tube *B*. The pressure-bottle is then raised or lowered according to the movements of this bubble. In a few minutes it assumes a mean position, varying only in accordance to the transmitted cardiac and respiratory waves.

In determining the effects of changes in the general blood pressure, &c., upon the intraocular tension, it is first necessary to eliminate other possible sources of variation. Of these the most important are the effects of con-

traction of the extrinsic and intrinsic muscles of the eye. The former consist of two groups, the striated and the unstriated. Contraction of the extrinsic striped muscles, closure of the lids, &c., produce marked changes in the intraocular tension. It is therefore necessary to fully curarise the animal. The extrinsic unstriped muscles have been found to be without effect in the dog, though they are a source of error, as will be seen later, in the cat. Movements of the intrinsic muscles of the eye produce no effect upon the intraocular pressure; or if any, it is too slight to be manifested by the methods used. Thus, the effects obtained in various ways, with and without complete paralysis of the iris and ciliary muscle by atropin are identical.

Vasomotor Nerves.—The presence of vasomotor nerves to the intraocular blood-vessels is rendered probable by the ophthalmoscopic observations upon men and animals. This method, as applied to animals, is open to grave doubt, as it is almost impossible to be certain of such minute changes, especially when the optical conditions and the bias of preconceived ideas are taken into consideration.

In the case of the iris, however, there is no doubt whatever that vasomotor changes occur, and that the vasoconstrictor fibres run in the cervical sympathetic nerve.

The Cervical Sympathetic Nerve.—Stimulation of the peripheral (*i.e.* oral) end of the cervical sympathetic was first investigated in the cat. It was invariably followed by a considerable rise in intraocular tension, irrespective of any change in the general blood pressure (fig. 26). This confirms the result obtained by Adamük, v. Hippel and Grünhagen, &c. It is not due, however, to vascular changes occurring in the eye. It is not due to movements of the iris, since it occurs after prolonged instillation of atropin previous to the operation, and also after large intravenous injections of atropin, sufficient to abolish inhibition of the heart on strong stimulation of the vagi. It was finally proved not to be due to vascular changes, since it occurred

for a considerable period after the death of a curarised cat, and is therefore undoubtedly due to pressure exerted upon the globe by the contraction of unstriped muscle

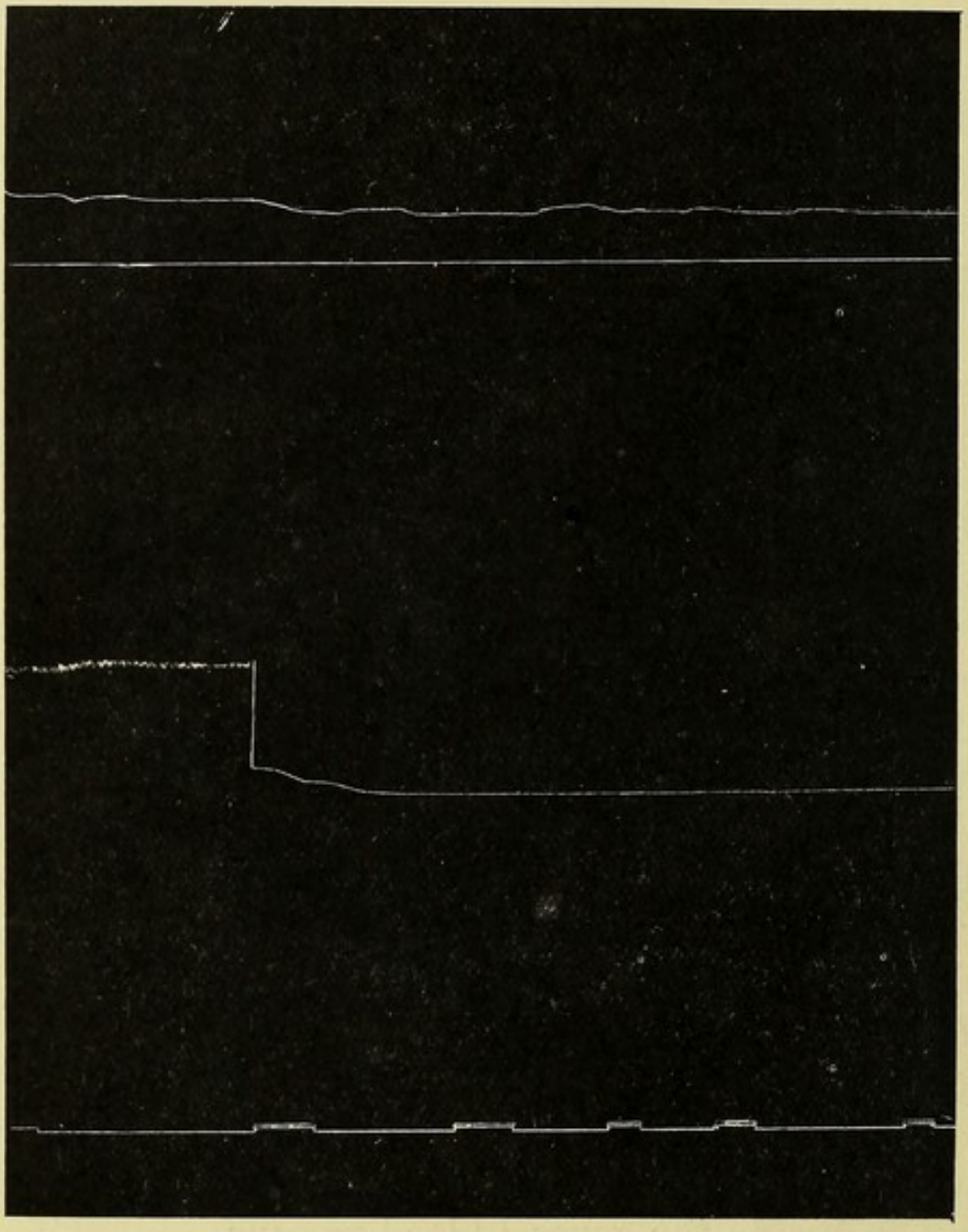


FIG. 26.—Cat. Morphia, A.C.E., and curare. Carotid blood pressure; cannula in vitreous. Stimulation of cervical sympathetic after atropin. Note that the effect is obtained repeatedly after the death of the animal. Top line, intraocular pressure; third line, blood pressure; bottom line, signal.

contained in the orbit and innervated by the cervical sympathetic (fig. 26). It seemed therefore impossible to demonstrate by this method any changes in the intraocular vessels by stimulation of the cervical sympathetic.

The dog is less suitable than the cat for experiments upon this nerve, since it runs in the same sheath with the vagus, and they can only be separated with difficulty. It

FIG. 27.—Dog. Morphia, A.C.E., and curare. Femoral blood pressure; cannula in anterior chamber. Stimulation of superior cervical ganglion. From above down: signal, time in 10-second intervals, blood-pressure, intraocular pressure.

is possible, however, to stimulate the nerve high up in the neck, where it leaves the vagus to join the superior cervical ganglion, or to stimulate the ganglion itself. In this manner

I have succeeded in obtaining positive results (figs. 27, 28, and 29).

In fig. 27 the vagi were intact, and no atropin had been given. The effect of the stimulus was to cause rapid wide

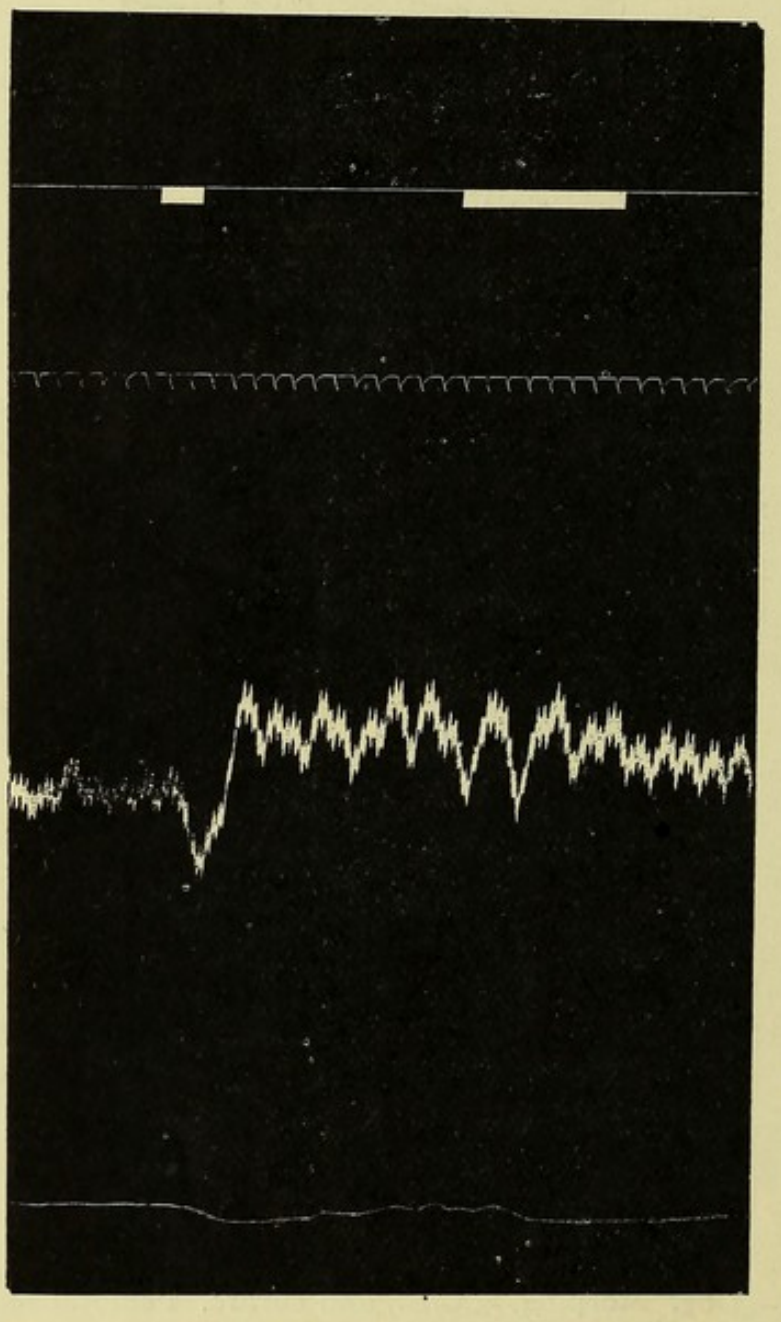


FIG. 28.—The same, with vagi cut.

dilatation of the pupil. This was followed, after a distinct latent period, by a well marked fall of intraocular tension, due to constriction of the intraocular arterioles. The blood pressure in the meantime rose very slightly, due

doubtless to slight spread of the current to the vagus or other sensory nerves. This, in itself, might have produced a slight rise of intraocular pressure, due to passive dilatation, so that it makes the observation still more conclusive.

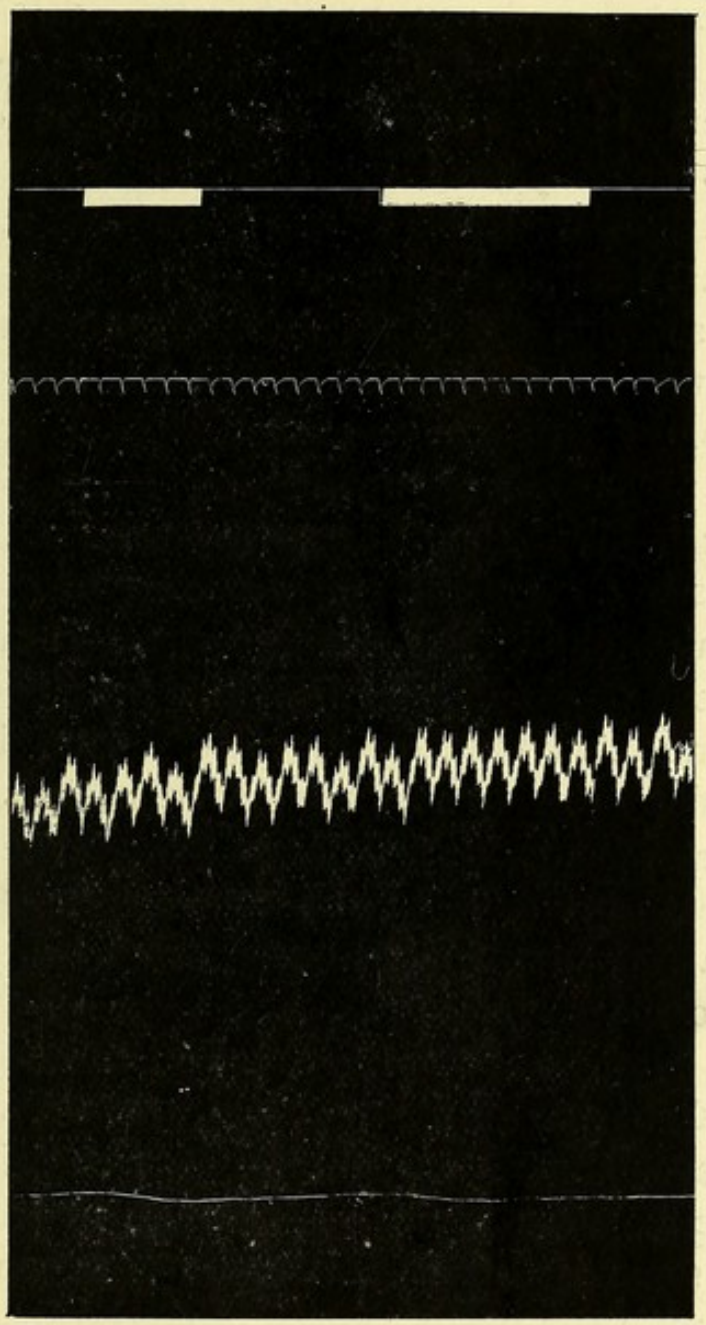


FIG. 29.—The same, after atropin.

Moreover, the latent interval which occurs between the dilatation of the iris and the fall of tension strongly confirms the opinion that the fall is due to vaso-constriction, since in the case of the iris it has been shown by Langley

and Anderson and others that the slow constriction of the arterioles follows the dilatation of the pupil after a distinct interval.

In fig. 28 the vagi were cut. They show very well that the vaso constriction, as well as being slow in onset is also prolonged and can persist even against a strong tendency to passive dilatation produced by a considerable rise in general blood pressure. In fact, the constriction is doubtless accompanied by a diminished secretion of fluid, which persists until after the normal condition of the vessels has been re-established.

Fig. 29, showing the effect after the administration of atropin, so that all movement of the iris was completely abolished, prove that the constrictor effect still remains, though it is perhaps somewhat less marked.

Trigeminal.—We should expect to find the vaso-dilator fibres in the fifth nerve, if such exist. I have not succeeded in obtaining an unequivocal result in this case. The conditions of experiment are difficult, since the nerve must be stimulated immediately after its origin from the brain, in order to avoid the sympathetic fibres which join it at the Gasserian ganglion. It is difficult here to avoid stimulating sensory fires in the dura mater, &c., and so producing a rise of blood pressure which would cause a passive vaso-dilatation.

Fig. 30 shows one result obtained from this nerve. There is a slight rise of blood pressure and a well-marked rise of intraocular tension, but how much of the latter is due to active vaso-dilatation it would be impossible to say. That some is due to this cause is probable from a comparison with the passive effect produced by stimulating the peripheral cut end of the medulla oblongata which is shown in the same figure.

Changes in the Blood Supply of the Eye.—We have seen that in lower mammals the intraocular blood supply is derived almost entirely from the internal maxillary artery, which forms the termination of the external carotid. In

the dog, there is a large anastomotic branch from the internal carotid within the skull, which usually joins the internal maxillary just before the ophthalmic artery or arteries are given off. Tying the external carotid, therefore, cuts off the main blood supply to the eye. In spite

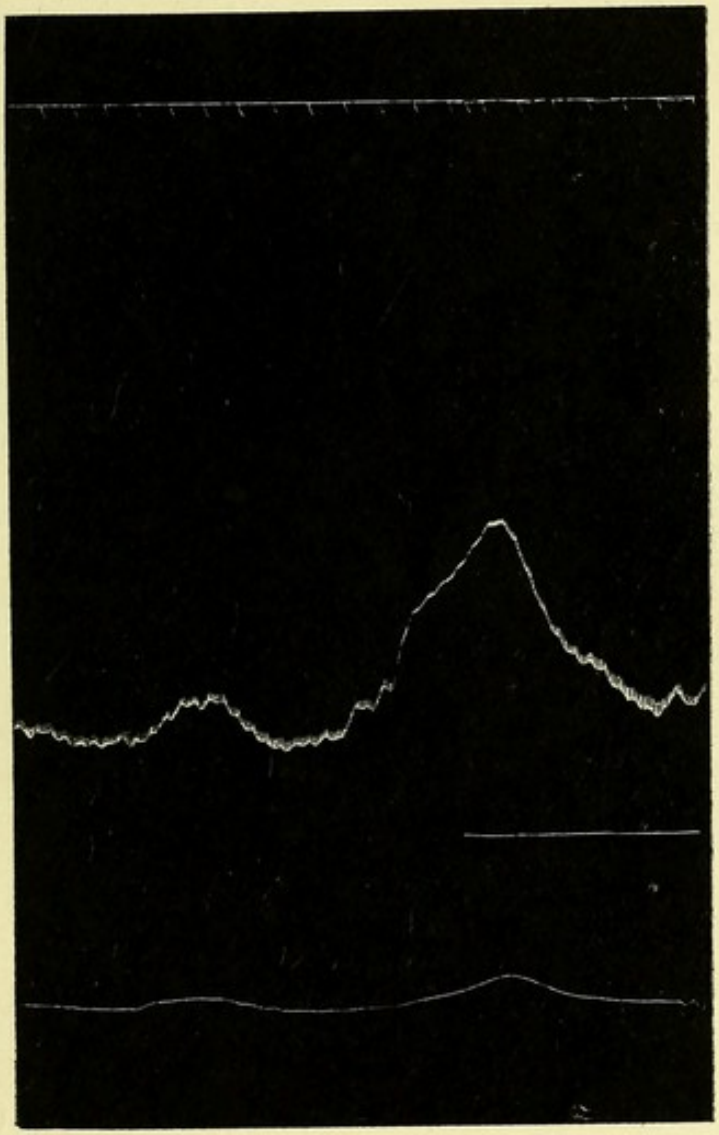


FIG. 30.—Dog. Morphia, A.C.E., and curare. Femoral blood pressure; cannula in a.c. Stimulation of fifth nerve intracranially, followed by stimulation of medulla oblongata. Time in 10-second intervals.

of the slight rise in general blood pressure which this operation causes, there is invariably a well-marked fall of intraocular tension. Ligature of the internal carotid, which is much smaller than the external, causes no change in intraocular tension if the external is still patent. If

the external is tied, although the intraocular tension falls and remains subnormal for a considerable period, the eye is still efficiently supplied with blood through the internal and through the circle of Willis by the anastomotic branch ; so that changes in the general blood pressure still affect the eye.

Ligature of the common carotid on the opposite side causes no effect.

Changes in the General Blood Pressure.—It may be stated that in general, the intraocular tension responds passively to all large variations in the general blood pressure and that, whether the external carotid is tied, or the skull freely laid open. This passive response is due, as in other areas of the body, to the overwhelming effect of the rise or fall of blood pressure produced by wide-spread vaso-constriction or dilatation in other areas, particularly in that great vascular reservoir, the splanchnic area. Vaso-constriction in the splanchnic area, for example, leads to so large a rise of blood pressure, that any attempt at vaso-constriction in the ocular area is overcome, the arterioles are burst open, and passive dilatation occurs.

The delicacy of the response of the ocular tension to changes in the general blood pressure is shown by the method used in the representation of the cardiac and respiratory oscillations upon the air-bubble in the capillary tube (fig. 25, B). These are only rarely recorded by the manometer. The passive effect of larger changes is, however, clearly shown by the reproduction of the general curve of the blood pressure. The intraocular curve is slightly delayed and is flatter, owing to the inertia of the eye, which acts as a natural plethysmograph.

The blood pressure has been influenced by various means.

(*a*) *Mechanical.*—Rise of blood pressure in the anterior part of the body has been brought about by ligature of the subclavian arteries, or compression of the abdominal or thoracic aorta (fig. 31). It is accompanied by a passive dilatation of the intraocular vessels.

(*b*) *Stimulation of Nerves.*—Stimulation of the central end of sensory and mixed (*e.g.*, sciatic) nerves causes rise in both pressures. The central end of the vagus has

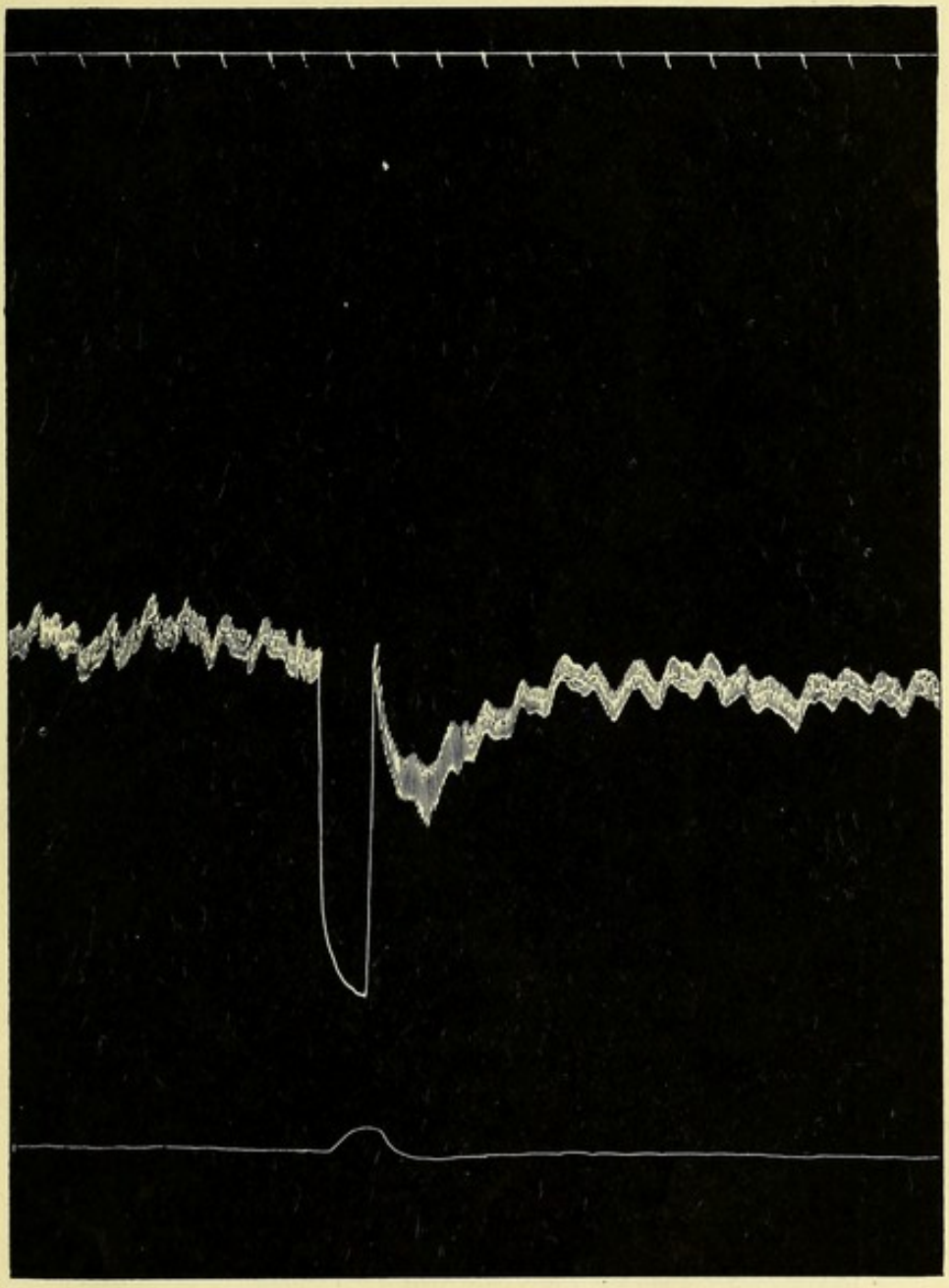


FIG. 31.—Dog. Morphia, A.C.E., and curare. Femoral blood pressure; cannula in a.c. Compression of thoracic aorta. Time in 10-second intervals.

generally given a pressor effect, but the opposite response has been obtained with a depressor effect. Cardiac inhibition through the peripheral end of the vagus causes a sharp fall in the intraocular pressure. The usual passive

rise is given by stimulation of the vasomotor centre (fig. 32) peripheral cut end of the cervical cord, and the peripheral ends of the splanchnic nerves. Traube-Hering curves are accurately reproduced (fig. 32).

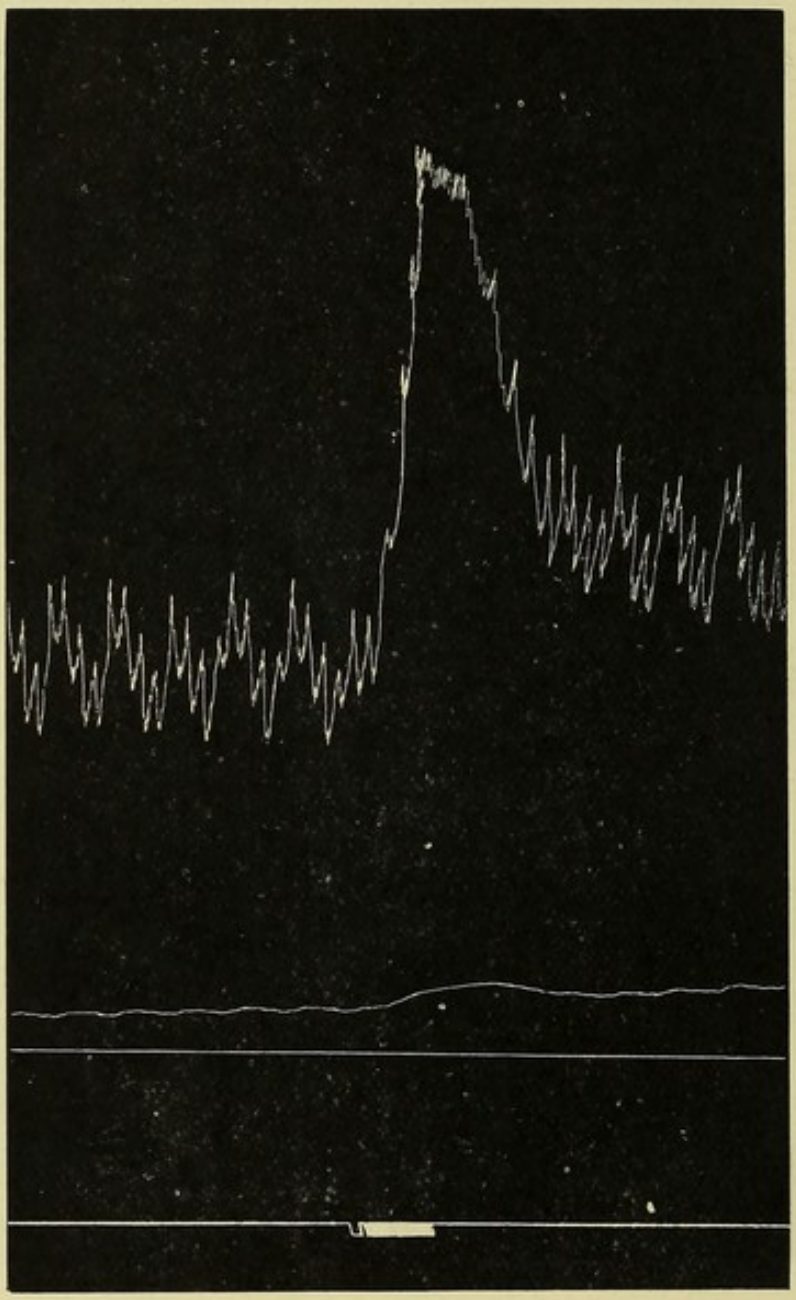


FIG. 32.—Dog. Morphia, A.C.E., and curare. R. carotid blood pressure; L. intraocular pressure from a.c. Traube-Hering curves; stimulation of vaso-motor centre.

(*c*) *Drugs*.—Adrenalin, nicotin (fig. 33), strychnine, pilocarpine, quinine, amyl nitrite, and large doses of chloroform, give results in accordance with their effects upon

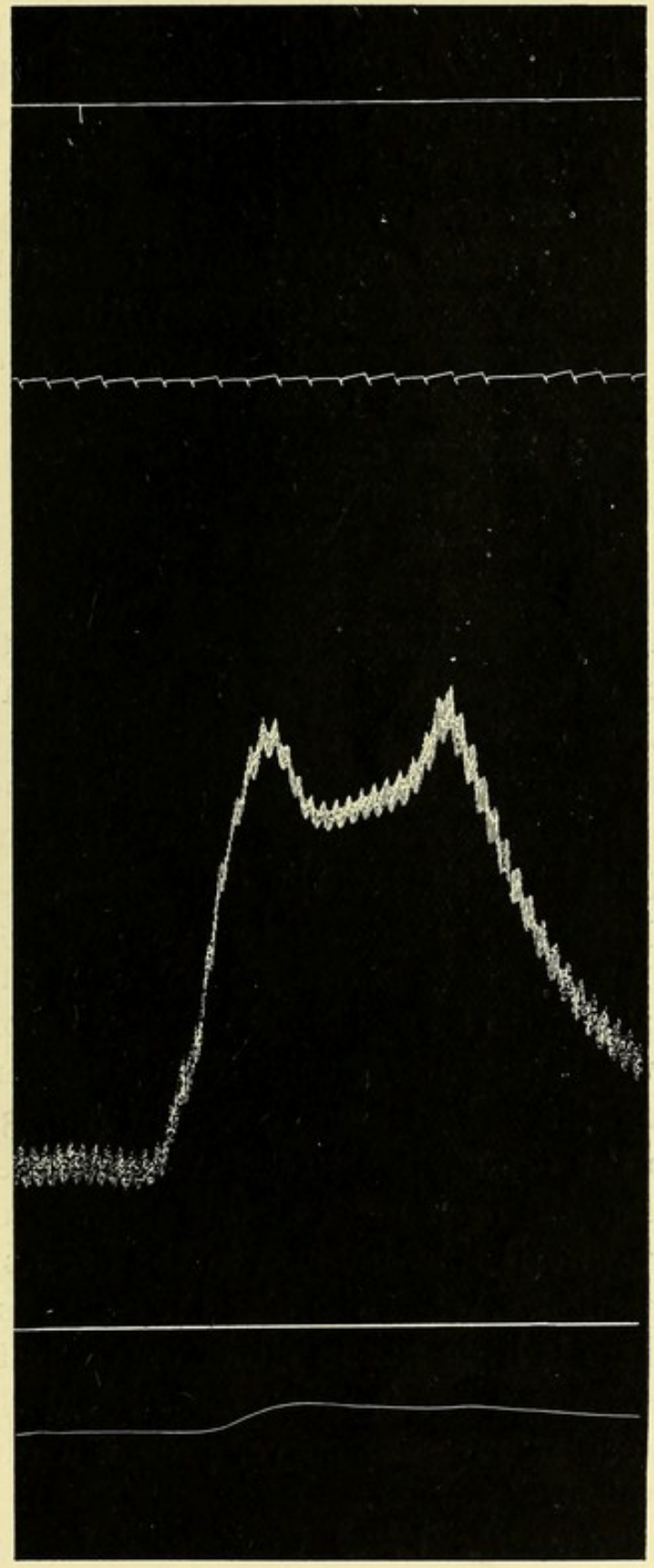


FIG. 33.—Dog. Morphia, A.C.E., and curare. Femoral blood pressure ; external carotid tied. One minim of 5 per cent. solution of nicotin injected into femoral vein. Time in 10-second intervals.

the blood pressure. It may be noted that pilocarpine apparently has no specific secretory effect. Drugs were occasionally injected directly into the carotid artery, so that they reached the eye before they entered the body circulation. This was with a view to obtaining an active vaso-constrictor effect. With nicotin, no result was obtained until the cardiac effect manifested itself, and was therefore secondary and passive. With adrenalin, an analysis of the curves shows that there is a distinct fall in the intraocular tension before the passive rise due to the rise in blood pressure caused by the action of the drug upon the body vessels. These results are in accordance with expectation, nicotin having a relatively poor effect upon the blood-vessels as compared with its enormous effect upon the sympathetic ganglia, whilst the preponderant effect of adrenalin is upon the vessel walls.

(*d*) *Asphyxia.*—The rise of blood pressure during the first stage of asphyxia is accompanied by a corresponding rise in the intraocular tension. If air is admitted into the lungs again at this stage, the intraocular curve follows the blood pressure curve. If, however, the asphyxia is continued, the results apparently vary with the condition of the animal. With a good blood pressure before asphyxia the rise in the intraocular tension continues, and may increase during the fall of blood pressure (fig. 34). This I attribute to the obstruction to the return of venous blood to the overcharged right heart at this stage. An increased capillary pressure is thus induced in the eye as a result of venous congestion. When the blood pressure is low before asphyxia, there is little rise in either curve, but the fall in the blood pressure curve is much more rapid than the fall in the intraocular pressure curve, probably owing to the same mechanism.

(*e*) *Ligature of the Venæ Vorticosæ.*—Ligature of the four venæ vorticosæ in rabbits leads to an enormous rise in the intraocular tension (= about 70 mm. Hg.)[1] It is

[1] Koster, Gzn. *Archiv f. Ophth.* xli., 2, 30, 1895 (with literature).

followed by inflammatory changes, and by degenerative changes (cataract) in the lens. The rise in tension is much less marked if only three or two veins are tied. In albinos a local hyperæmia of the iris and ciliary body is seen. The

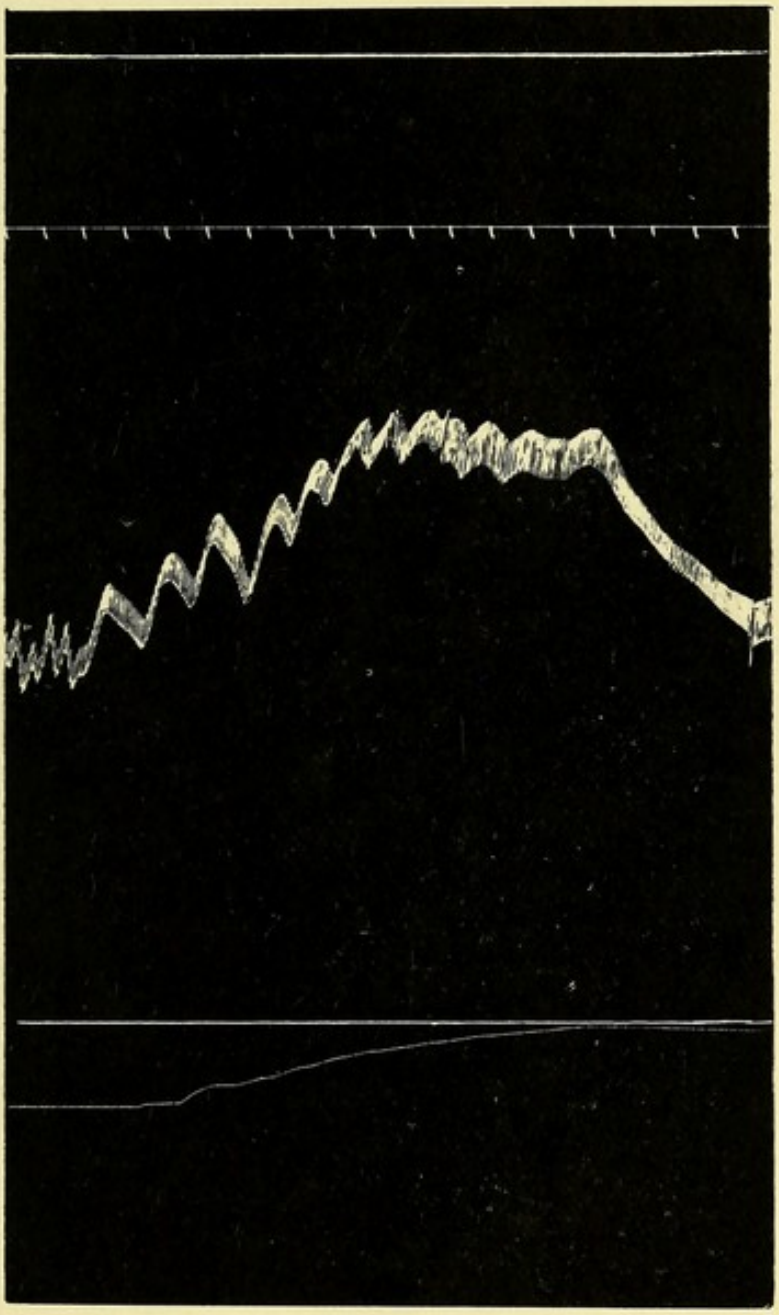


FIG. 34.—Dog. Conditions as before ; asphyxia.

rise in tension is of course due, primarily to the dilatation of the vessels, especially the veins, and secondarily to the high capillary pressure leading to increased transudation of fluid. The anterior chamber becomes shallow, and the

filtration of fluid from the eye is thereby at first diminished, so that increased production is accompanied by diminished excretion.

(*f*) *Death.*—The normal intraocular pressure of the dog varies from 20 to 30 mm. Hg. After death it gradually and very slowly falls to zero.

References.

Parsons and Snowball, *R.L.O.H. Reports*, xv., pt. 3, 1903.

The most important earlier work on Ophthalmometry will be found in the following papers :—

C. Weber, "Dissertation." Marburg., 1850.

Wegner, *Arch. f. Ophth.*, xii., 2, p. 1, 1866.

Grünhagen and v. Hippel, *Arch. f. Ophth.*, xiv., 3, p. 219, 1868 ; xv., 1, p. 265, 1869 ; xvi., 1, p. 27, 1870.

Adamük, *Med. Centralbl.*, 1866, p. 561 ; *Sitzungsb. d. Wiener Akad. d. Wiss., math.-naturw. Cl.*, lix., 2.

Schöler, "Dissertation." Dorpat, 1869.

Leber, *Arch. f. Ophth.*, xix., 2, p. 112, 1873.

Schöler, *Arch, f. Ophth.*, xxv., 4, p. 63, 1879.

Holtzke, *Arch. f. Ophth.*, xxix, 2, p. 5, 1883.

v. Schültén, *Arch. f. Ophth.*, xxx., 3, p. 1, 1884.

Bellarminow, *Pflüger's Archiv*, xxxix., 1886 ; translated in *Annales d'oculistique*, xcvii., p. 181.

III.—THE RELATIONS OF THE INTRAOCULAR TO THE INTRACRANIAL CIRCULATION.

Mention has already been made of the fact that possibly an undue amount of importance has been attached to the conditions of the retinal circulation as an index to those of the intracranial vessels. As we have already seen, the major vascular supply of the eye in lower mammals is derived from the external carotid artery, *i.e.*, from a purely extracranial source, though the intimacy of relationship with the internal carotid in its intracranial course, which obtains in the higher primates, reaching its acme in man, is foreshadowed by minor anastomoses even in the inferior species. Morphology therefore affords a strong argument which we have already seen put to the crucial test of experimental proof, against the overwhelming importance of intracranial conditions as affecting the ocular circulation. Whilst the still more searching experiments which I am about to describe on the whole confirm this position, it is yet impossible, on anatomical grounds alone, to suppose that it can be completely maintained for man and the higher primates. There are obvious reasons which militate against as full an investigation of the question in these animals as one would desire, but I hope shortly to carry the research farther in this direction. In the meantime we must be content with the indications which are obtained from dogs in which the external carotid has been previously ligatured, so that the circulation of the eye which is being observed is derived solely from the internal carotid and the circle of Willis by means of the ramus anastomoticus, *i.e.*, from a pure intracranial source.

Previous experiments upon this subject have been

extremely few in number, and have led to no definite conclusion. Only those of v. Schultén require passing mention. Indeed, it is only since the exhaustive researches of Leonard Hill upon the cerebral circulation, which have demonstrated the accuracy of the Monro-Kellie doctrine, that the time has become ripe for the investigation. We now know the very small part which is played in the cerebral circulation by the cerebro-spinal fluid—that this fluid normally exists inside the skull in such small quantities that its ebb and flow are totally inadequate to counteract the larger changes of volume induced by experimental procedures in the intracranial vessels. At the same time, if a minor criticism is permissible, it is quite possible that extremely small vasomotor changes over a very limited area, *e.g.*, over one or more of the nerve nuclei in the medulla oblongata, might be so counteracted, and yet be accompanied by physiological results of profound importance, although the actual changes in volume might be so minute as to entirely elude the comparatively gross methods of observation. The demonstration of nerve fibrils upon the cerebral vessels—fibrils whose destination can hardly be other than the muscle walls of the vessels—must be regarded as strong evidence in favour of this view. As regards the larger variations, the correctness of the Monro-Kellie doctrine is placed beyond cavil, and so far we may consider the quantity of blood inside the cranium to be constant.

It follows from this law that, with the possible exceptions indicated above, all changes in the general blood pressure produce only passive changes in the cerebral circulation. Unlike what happens in other parts of the body, these changes are not manifested as changes in the volume—dilatation or constriction—of the vessels, but as variations in the rate of flow of the blood. Thus, if the aortic pressure rises, as, *e.g.*, by constriction of the vessels of the splanchnic area, the vena cava pressure remaining constant, there will be an increased velocity of flow through

the brain. The increased pressure in the arterioles cannot be relieved by dilatation, but the blood is hurried on.

Let us suppose for a moment that the ocular circulation is a direct offshoot from the intracranial circulation, the ophthalmic artery forming the connecting link between the two systems. When the blood reaches the orbit, one of two things may occur—the ophthalmic artery may dilate passively, the flow being again retarded to the normal rate, or it may remain constant, the increased velocity continuing. There is no evidence that the larger arteries can accommodate themselves—at any rate to the required extent—in the manner suggested by the first alternative, their function being to transmit the blood with as little loss of pressure and velocity as is consistent with friction and other physical conditions. On reaching the eye, the vessels again become shut up in a closed box. If this were rigid, like the skull, the same conditions would obtain, and increased velocity of flow would be the only result of a rise in general blood-pressure, unless indeed dilatation of the vessels occurred at the expense of the intraocular fluid. There is no evidence that filtration from the eye varies thus with the rapid changes in blood pressure, but there is evidence that the globe is not rigid, and that the vessels do dilate. Consequently, the results which we have already obtained are not inconsistent with the view that the ocular circulation is a direct offshoot from the intracranial, but on the other hand they are equally consistent with the view that the ocular circulation is a mere offshoot from the general extracranial circulation; for as is well known, when vaso-constriction occurs in a large area of the body, notably in the splanchnic area, the large increase in general blood pressure thereby induced leads to the passive dilatation of other—for the time being—less important areas, so that accommodation is thus afforded to the displaced blood.

A rise in general venous pressure, with coincident constant or diminished arterial pressure, will produce diametri-

cally opposite results, viz., retardation of the cerebral blood flow, with passive constriction of the intraocular arterioles, and that irrespective of the rich anastomosis of the extra-ocular veins with the facial, pterygoid, and other veins of the extracranial system, which obtains in all mammals, whether their arterial ocular supply is mainly extra- or intracranial.

Under normal intracranial conditions, therefore, it would seem to be immaterial, physiologically, whether the ocular circulation is derived from intra- or extracranial sources, or both. If, however, the arterial supply is wholly or mainly of intracranial origin, as in man, or in the dog with ligatured external carotid, whilst the ocular veins communicate freely with both the intra- and extracranial systems, it is clear that intracranial complications may be expected to profoundly affect the ocular circulation, both from the arterial side and also to a less extent from the venous. Any intracranial condition which impedes the flow of blood in the internal carotid may be expected to lead to passive constriction of the intraocular arterioles ; but such intracranial conditions usually affect the venous sinuses even more profoundly, leading to partial blockage, with coincident slowing of the circulation. This latter effect, however, will not necessarily lead to increased ocular venous pressure, owing to the free communication with the general system of veins, which themselves anastomose so freely as to tend rapidly to the equalisation of pressures. There are besides physiological complications to which it will be necessary to draw attention now.

I refer to conditions which have been observed at various times by many experimenters, but which had never been accurately correllated, and therefore cannot be said to have been understood, until Hill reinvestigated the whole subject. Two physical conditions—that the skull is an hermetically sealed box, and that the quantity of cerebro-spinal fluid is unimportant, except as a lubricant—have already been mentioned. To these a third must be added

—the fact that the brain substance is incompressible, though the brain as a whole, with its contained vascular channels, is as compressible as a sponge. It follows from these conditions, that under normal circumstances, with the skull intact, the intracranial pressure is already raised, and that its amount is equal to the coincident cerebral capillary pressure. When the skull is freely opened, the intracranial pressure falls to the level of the atmospheric pressure. When the intracranial pressure is artificially raised by the introduction into the skull of a foreign body of known volume, two results follow : (1) by virtue of its compressibility as a vascular network, blood is squeezed out of a certain portion of the brain ; (2) by virtue of its incompressibility *quâ* brain-substance, it is bodily dislocated slightly, and the pressure is transmitted to other parts. Now the pressure is not transmitted equally in all directions, a fact which is due chiefly to the resistance, partly of the falx cerebri, but principally of the tentorium cerebelli, which seems to be architecturally designed to protect the cerebellum, and through it the pons and medulla, from pressure.

The intracranial tension can be raised by other means such as the injection of an innocuous fluid. In order to keep it raised and constant the injection must be continuous, as the fluid is rapidly absorbed into the venous sinuses. The actual amount absorbed during an ordinary experiment is small, and is not sufficient to embarrass the right heart, as has been suggested. By this method, when applied with fair rapidity in the parietal region, the brain is first forced down towards the isthmus tentorii and foramen magnum, which are effectually plugged. The pressure is then nearly equally distributed over the surface of the brain, which does not happen by the method of local compression.

A combination of the two methods is obtained by bleeding the animal from one carotid into its skull. In this experiment, the pressure is at first one of fluid pressure

though probably never so equally distributed as with saline solution ; later the blood coagulates, and acts as a foreign body, taking up a definite space, the serum alone being capable of rapid absorption. The clot then produces a condition of local compression.

Since an accurate knowledge of the effects of increased intracranial pressure upon the cerebral circulation form the basis of a correct interpretation of the results obtained in the ocular circulation, it is necessary to describe them somewhat fully. The first effect of a rise of tension by the application of fluid pressure is venous stasis. This can be observed by watching the small vessels of the pia mater —magnified if necessary—through a glass window let into the skull. The skull must of course be completely closed, so as to avoid the errors of the old observers. If the window includes the longitudinal sinus, it will be seen that this gradually becomes narrower as the pressure rises, and may even be completely obliterated (Cushing).[1] The venous stasis leads to irritation of the bulbar centres, but only when the pressure is high, and is approaching the arterial tension, for the metabolism of the brain is very slow, so that the vital centres are protected. They are specially protected from local pressure applied to other parts of the brain by the notable pressure discontinuity, the blocking of the isthmus tentorii by the translocation downwards of the cerebrum, and by the partial escape of the medulla in some animals below the level of the foramen magnum. When, however, the fluid pressure is high, the cardio-inhibitory and respiratory centres are stimulated—the heart is slowed and may be stopped, even fatally, through the vagi. Mechanical compression of the vagi against the bone may be a factor in producing this result ; in any case it is avoided by section of these nerves. The vasomotor centre is also stimulated. If the cortex is inspected through a window in the skull, the circulation is seen to stop when

[1] Cushing, *Amer. Jour. of Med. Sciences.* September, 1902.

the pressure rises to the arterial tension. The brain becomes pale; the veins in the sulci remain filled with stagnant blood, and the larger arterioles pulsate, but the capillary circulation has ceased. The animal, however, does not die. What is seen to occur in the cortex also occurs in the medulla. The vasomotor centre is asphyxiated, and thereby stimulated. The vessels of the splanchnic area contract, the blood pressure rises, the blood is forced on, and the circulation is re-established. This process can be repeated over and over again, until the pressure—intracranial and arterial—may be raised as high as 250 mm. Hg. Eventually the vasomotor apparatus is paralysed, and the animal dies. If the spinal cord is cut high up, or the medulla cocainised, no rise of blood-tension accompanies the increase of intracranial pressure; the response too is feeble if the animal is in a bad condition.

The experiments which I will now describe were all performed upon dogs in which the external carotid was previously tied upon the side of the eye which was being observed. The intraocular tension was recorded as before. The intracranial pressure was raised by each of the methods which have been mentioned. The skull was trephined, usually in the parietal region; one of Hill's brain pressure gauges was then screwed in tightly, so that there was no leakage. Local compression was produced by means of an india-rubber bag tied on to the inner tube of the pressure gauge, and mercury was then run in from a burette. The height of the mercury column gives no reliable indication of the pressure exerted, owing to the resistance of the bag. Fluid pressure was exerted by connecting the inner tube of the gauge with a pressure bottle filled with water, or more commonly, normal saline solution; the height of the bottle indicated the pressure. In other cases the fluid was pumped in, a side tube leading to a mercury manometer, which showed the pressure. This method was more convenient for high pressures. In a few experiments, air was pumped in in this manner. When the dog was

bled into its own cranium, the carotid on the side opposite to the eye under observation was connected with the inner tube of the gauge, a clip being interposed. The clip was opened for a few seconds and the results observed.

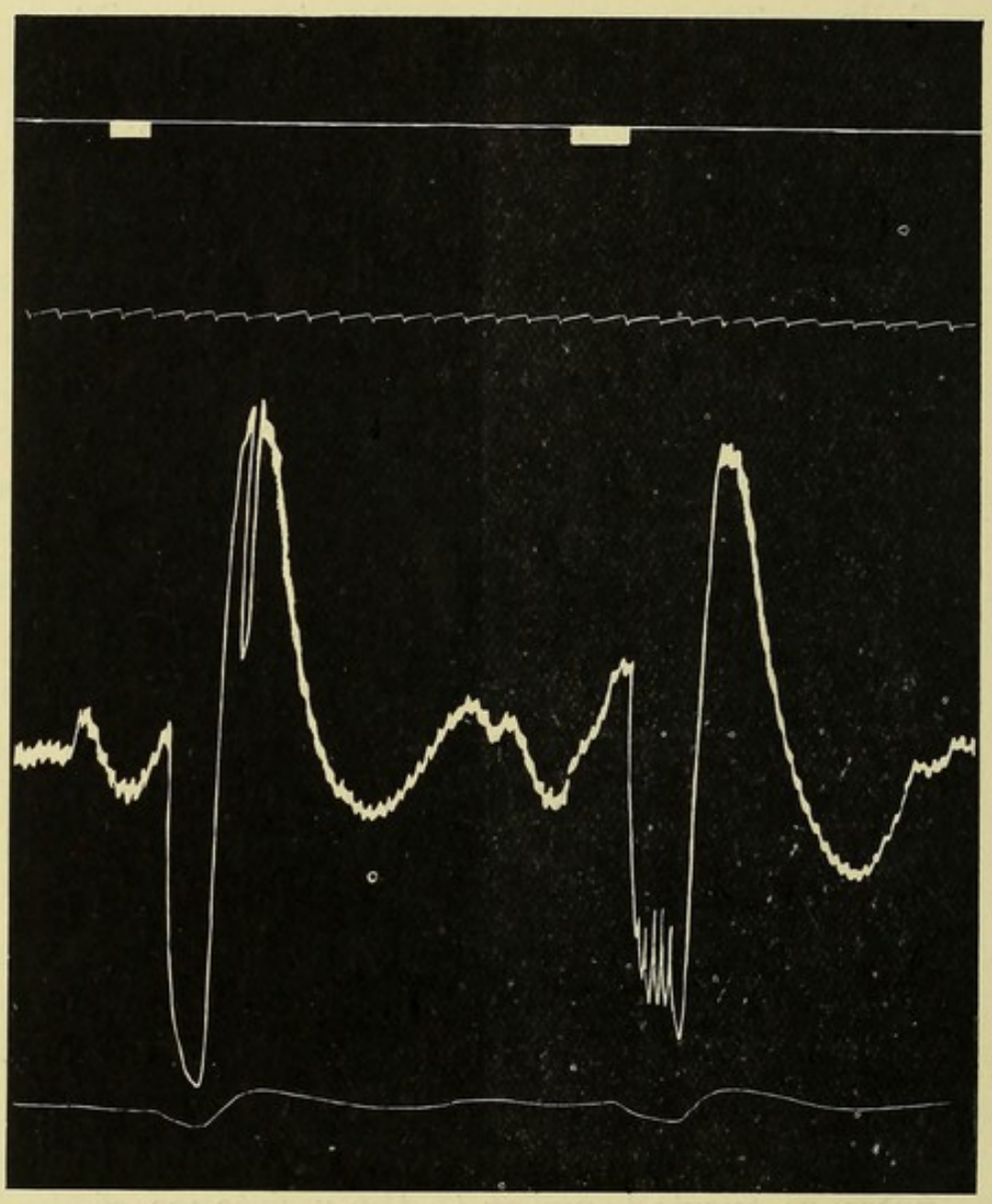


FIG. 35.—Dog. Conditions as before. Intracranial pressure raised to 135 mm. Hg., by injection of normal saline into the skull through a pressure-gauge inserted in the parietal region. Both vagi cut. Stimulation of peripheral end of R. vagus.

Local compression applied in the parietal region alters the effects of variations in the general blood pressure very little, even with the application of considerable pressure, and in other cases not at all. Thus the curves of the intra-

ocular tension produced by equal stimulation of the peripheral end of the vagus, or by equal doses of nicotin, adrenalin, &c., before and during local cerebral compression are practically identical, or at most there is slight flattening

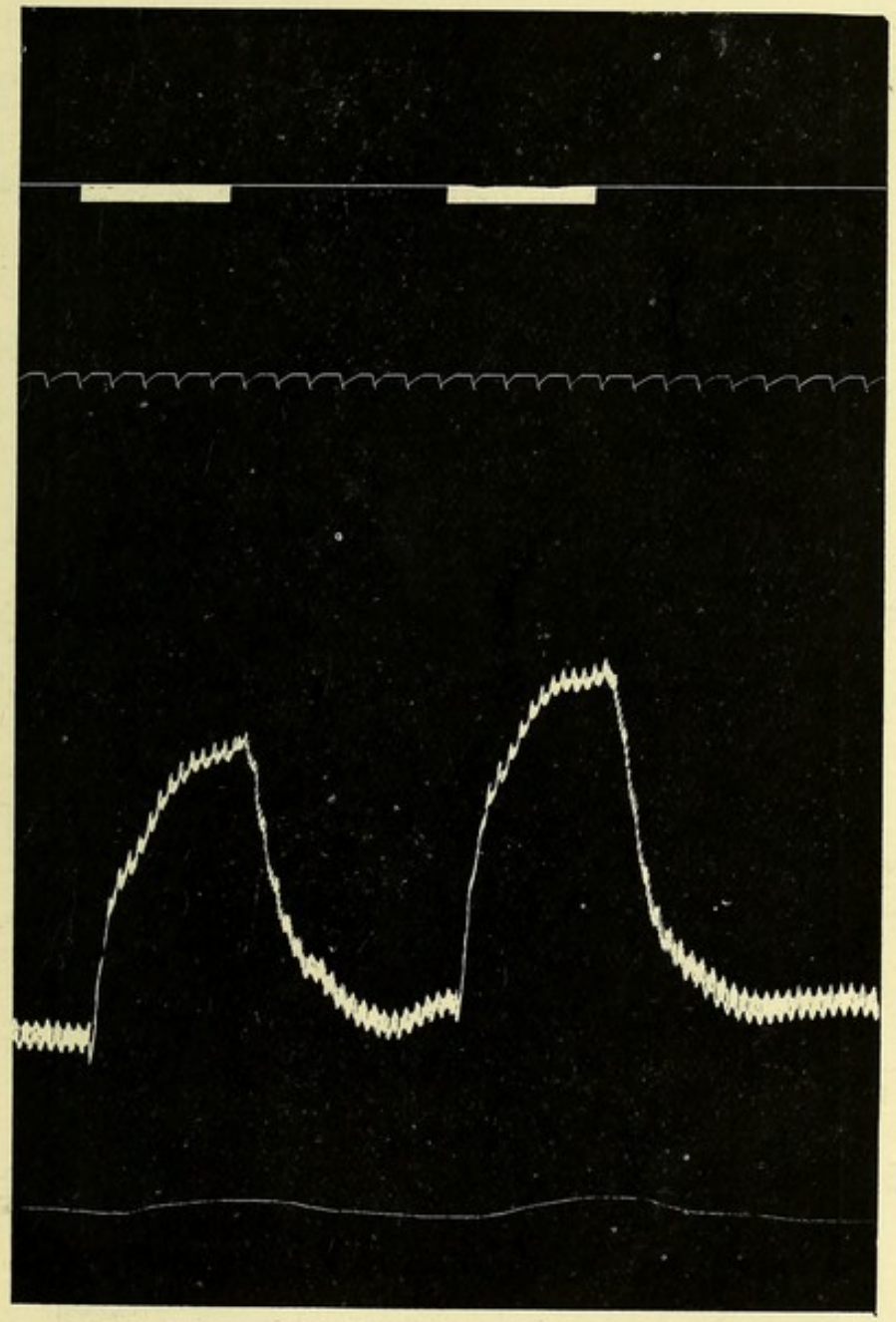


FIG. 36.—Dog, Conditions as before. Cord cut in upper cervical region. (See text.)

of the curve. Any effect produced is doubtless masked by the coincident alteration in the general venous pressure, but the vessels at the base of the skull are certainly well protected from pressure. Any vasomotor effect produced

by the compression is reproduced upon the ocular curve. The rise in blood pressure following the cardiac inhibition through the vagus is more marked during cerebral compression (fig. 35).

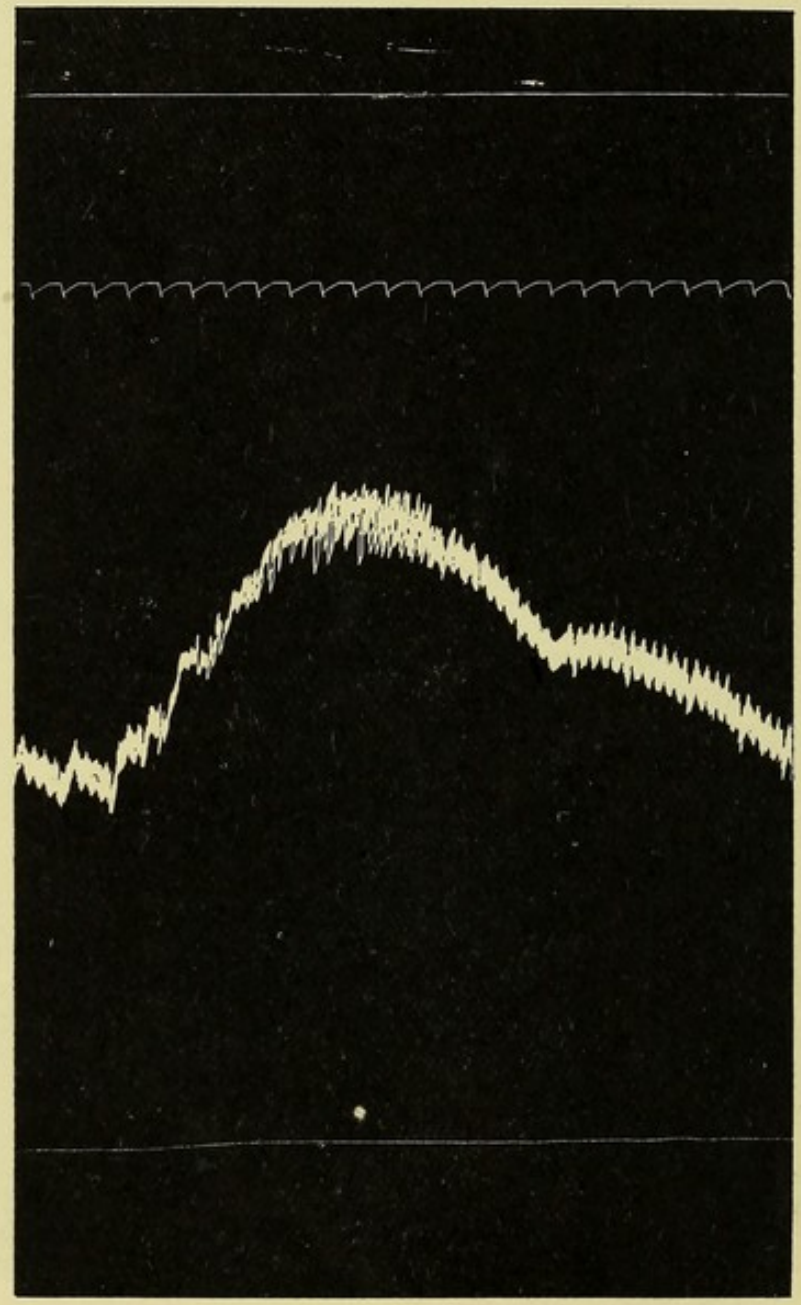


FIG. 37.—Dog. Conditions as before. (See text.)

The effects of fluid pressure are often more marked, as might be expected; but the results are difficult to estimate owing to the vasomotor effects produced by the mere compression. In fig. 36, the cord was cut in the upper

cervical region. The first curve represents the effect of stimulation of the peripheral cut end. The intracranial pressure was then rapidly raised to 200 mm. Hg., by injecting normal saline solution, and the experiment was then repeated.

In fig. 37 one minim of nicotin was injected into the femoral vein, the intracranial pressure being 140 mm. Hg. There is only a very slight effect upon the intraocular tension, although the same dose applied shortly before the application of increased intracranial pressure gave the normal curve.

The main results which I deduce from my experiments is that local pressure applied for a short time to the parietal region is without effect upon the intraocular circulation, but that fluid pressure is more equally distributed and may have a very definite influence. It seems clear that, at any rate in the dog, the arteries at the base of the skull are very well protected from pressure, especially the transmission of pressure applied at a distance; and that any effect upon the venous sinuses is counteracted by the free anastomosis of the ocular veins with those of the general circulation. It is practically impossible to tie off the anastomoses, but valuable results, both with regard to the normal ocular circulation and to its relationship with the intracranial circulation would result from any method whereby the ocular venous pressure could be measured. It is in this direction, and in experiments upon monkeys, that further investigation is required.

REFERENCE.

LEONARD HILL, "The Cerebral Circulation." London, 1896.

Optic Neuritis.—It would be a mistake to conclude that local compression is without effect upon the ocular circulation when it is prolonged, as in the case of cerebral tumours, &c. The cardinal ocular symptom of these pathological conditions is optic neuritis, and an overwhelming

amount of clinical evidence has accumulated in recent years confirming the association of this symptom with raised intracranial pressure. Our ignorance of a subject may often be roughly estimated by the number of theories which are said to explain it. If this be so, our ignorance of optic neuritis is colossal. It is not my intention to discuss these theories, but merely to hint at the possibility of a new one.

It has often been noticed that the portion of brain surrounding a tumour, blood clot, or other foreign body, is œdematous. Dean[1] found that the brain substance compressed by a glass disc introduced into the skull contained 3 per cent. more water than normal. What is the explanation of this? A reasonable one has recently been given by Cannon.[2] Loeb[3] has shown that if one leg of a frog is ligatured, so that it is deprived of its blood supply, the muscles take up water, so that the gastrocnemius in eighteen hours contains 1 to 3 per cent., in forty-eight hours 15 per cent., and in seven days 25 to 40 per cent. more water than the other. This assumption of water by a muscle deprived of its blood supply is due to chemical changes in the muscle increasing the internal osmotic pressure, and these chemical changes are probaly due to lack of oxygen. The normal osmotic pressure of frog's gastrocnemius is equal to that of isotonic saline solution, *i.e.*, about five atmospheres. If the muscle is placed in 4·9 per cent. Na Cl solution, which has an osmotic pressure of over thirty atmospheres, it first loses water—as one would expect—but later it absorbs water against this enormous pressure. Cannon has shown that brain substance acts in the same manner. He concludes that "under circumstances of non-nutrition the brain will take up water from a solution isotonic with blood, and will thereby exert a

---

[1] Dean, *Jour. of Path.*, i., p. 39, 1893.
[2] Cannon, *Amer. Jour. of Phys.*, vi., No. 2, 1901.
[3] Loeb, *Pflüger's Archiv.*, lxxi, p. 470 1898.

pressure sufficient to exclude the blood from the cerebral vessels." The pressure of a foreign body, as Hill has emphasised, squeezes the blood out of a given volume of brain substance, whilst the neighbouring areas are also badly supplied. These areas will absorb water, owing to the retention of chemical products which alter their osmotic pressures. They will therefore swell and thus press on other areas, reducing them to the same condition, so that a circulus vitiosus is set up. Diminution of the intracranial space by one-twelfth eventuates in death, but doubtless before this occurs, protective mechanisms are brought into play. Asphyxiation of the vasomotor centre is probably one, whereby the blood pressure is raised, the vascular channels are re-opened, and the deleterious products are swept away. Nevertheless, it is clear that under pathological conditions, a purely local compression may be transformed into a wider spread one. In this way it is by no means improbable that the blood flow in the basal arteries and sinuses is impeded.

In those animals, then, in which the ocular blood supply is mainly of cerebral origin, we may expect high intracranial pressure to be accompanied by slowing of the orbital and intraocular blood flow, with resultant malnutrition. Why the œdema of the optic nerve should manifest itself almost entirely at the intraocular end must be due to local causes, and these are not far to seek. A very slight œdema of the nerve at the lamina cribrosa will compress the capillaries, lead to greater anæmia and greater œdema; until finally the larger vessels are also compressed.

In favour of this view, is the fact that the typical "choked disc," as distinguished from true optic neuritis, is at first a pure œdema; and it is only later, when the products of disintegration have accumulated and acted as a chemical stimulus that infiltration with leucocytes occurs. However, it would be foolish to press the hypothesis too far, but I think it may be of value in guiding future researches.

IV.—SOME PHYSIOLOGICAL AND PATHOLOGICAL ANOMALIES OF THE OCULAR CIRCULATION.

Arterial Pulsation.—v. Schultén has shown that the blood pressure in the ophthalmic artery is only a few mm. Hg. below that of the carotid. Considering the very different blood supply of the eye, it would be unwise to apply this result to man. Nevertheless, we may be sure that the arterial pressure is far above the normal intra-ocular pressure. It would not be surprising, therefore, if the pulse wave was transmitted to the central artery of the retina, and could be observed ophthalmoscopically. This, however, is seldom if ever the case under normal circumstances. This is doubtless due to two causes: (1) The intraocular pressure damps the pulsation, and the increase of pressure which accompanies each pulsation is spread over the whole volume of the contents of the globe, and is transmitted to the plastic sclerotic; (2) such pulsations as survive this damping effect are too small to be observed in these small vessels by ordinary ophthalmoscopic magnification.

Two types of arterial pulsation occur pathologically: (1) A true pulse wave, accompanied by locomotion of the vessels; (2) an intermittent flow of blood, or pressure pulse. In the latter, the arteries fill with blood only with the heart beats, being empty between them; it is only visible upon the disc. This type of pulsation is a pure pressure phenomenon, and is caused by any considerable increase of intra-ocular tension with normal or lowered blood pressure, as in glaucoma, or by any considerable diminution of blood pressure with normal intraocular tension, as in syncope, orbital tumours, &c. The true arterial pulse occurs in

cases of aortic regurgitation or aneurysm, in Graves' disease, &c.; it is not confined to the optic disc. It is equally a pressure phenomenon, but the differences of pressure are smaller.

Capillary Pulsation is seen only in aortic regurgitation as a systolic reddening and diastolic paling of the disc.

Venous Pulsation occurs in three forms: (1) The normal negative venous pulse; (2) the positive venous pulse; (3) the transmitted centripetal venous pulse.

The normal venous pulse occurs in 70 to 80 per cent. of people (Lang and Barrett[1]); it is negative or diastolic, *i.e.*, the veins are narrowed when the arteries are dilated. It is generally absent in lower animals. It can only be seen upon and near the disc. It is probably caused in exactly the same manner that the venous pulse is caused in the intracranial sinuses. There "the brain, as is shown by the cerebral pressure gauge, is lifted up by the stroke of the arteries at its base, and is thrown against the cerebral veins" (Hill). In the eye, the incompressible vitreous corresponds to the brain, but the sclerotic will also yield slightly to the shock, and so the pulsation in the veins will be less marked. In this manner, each systole of the heart produces a dilatation of the central artery, which is transmitted through the vitreous to the central veins, leading to a constriction, with diminished outflow of blood. This is the classical explanation of Donders.[2] The constriction manifests itself first at the disc, and hence first affects the termination of the veins there, damming back the blood in the smaller veins. Moreover this is the spot where the venous pressure is lowest, and it therefore responds most readily and most completely. The increased intraocular tension induced by the cardiac systole does not act equally and simultaneously upon the whole of the veins, leading to constriction and more rapid outflow of blood, as was suggested by Coccius.[3] But there are other important factors which must be taken into account. One of these is direct pressure of the artery upon the vein during their

course in the optic nerve, before entering the eye (Jäger[4]). Moreover, the response of the wall of the eye to the increased pressure will be most marked at the disc (Jacobi[5]) where, although the nerve substance is incompressible, the lamina cribrosa contains much elastic tissue, and where there is a normal exit of lymph. Further, there is a tendency to a transmitted wave, caused by the high extravascular tension inside the globe, so that there may normally be some transmission of the pulse through the capillaries into the veins (Türk[6]). More important in man is the relationship to the intracranial circulation, though this factor can be of little importance in most animals. Helfreich[7] thinks that the venous constriction occurs before the cardiac systole, and may continue awhile during it. He attributes this to the blocking of the cavernous sinus during the systole, and its expansion during the diastole. If, however, this were the sole cause, we should expect to find actual dilatation of the veins during the systole, and not constriction. Probably Haab[8] is right in attempting to reconcile Helfreich's theory with that of Donders. It seems most likely that what happens is this. The intraocular effect of the cardiac systole is constriction of the veins; at the same moment the blood is dammed back from the cavernous sinus. It cannot flow back into the eye, but the communication with the facial and other veins tends to relieve the pressure. Soon after the diastole has commenced, the pressure in the orbital veins is still high, and the blood is streaming through the intraocular capillaries and the veins dilate.

The positive venous pulse is presystolic—systolic. It commences with the auricular and continues through the ventricular systole. It is due to tricuspid regurgitation, and is permitted by the normal insufficiency or absence of the valves of the jugular veins.

The transmitted centripetal venous pulse is an accentuation of the normal tendency of the pulse wave to progress through the capillaries into the veins, owing to the

intraocular tension. It is due to venous congestion, with or without increased *vis a tergo* (Holz[9]).

REFERENCES.

[1] LANG and BARRETT, *R. L. O. H. Reports*, xii., p. 60.
[2] DONDERS, *Arch. f. Ophth.*, i., 2, p. 75, 1855.
[3] COCCIUS, *U. die Anwendung des Augenspiegels*. Leipzig, 1853.
[4] JÄGER, *Wiener med. Wochenschrift*, 1854.
[5] JACOBI, *Arch. f. Ophth.*, xxii., 1, p. 111, 1876.
[6] TÜRK, *Arch, f. Ophth.*, xlviii., p. 513, 1899.
[7] HELFREICH, *Arch. f. Ophth.*, xxviii., 3, p. 1, 1882.
[8] HAAB, *Atlas u. Grundriss der Ophthalmoscopie*, 2nd edition, p. 77, 1897 ; also in Norris and Oliver's System, iv., p. 493.
[9] HOLZ, *Berliner klin. Wochenschrift*, 1889, p. 1086.

Embolism of the Retinal Arteries.—In this interesting condition the arteries are extremely small, but they still contain blood. The veins are narrow at the disc, and full or abnormally distended towards the periphery. The intraocular tension is not appreciably altered, owing to the intact ciliary circulation, and this accounts for the absence of the formation of infarcts, such as occur when "end arteries" are blocked in other parts of the body. They have been described, however, when only a small arterial branch has been blocked (Knapp,[1] Landesberg[2]).

It is not easy to understand why the intraocular tension does not actually force the blood out of the veins, especially when we consider that the pressure in the orbital veins must be considerably less. This is shown by the fact that in dogs the cerebral venous pressure is normally about 100 to 130 mm. H_2O (Hill), *i.e.*, about 10 mm. Hg., whilst the intraocular tension is from 20 to 30 mm. Hg. Probably in most cases of embolism due to mitral stenosis, &c., the general venous pressure, and with it the cerebral venous pressure, is raised ; but the ocular venous pressure and with it the capillary and intraocular tension, will also be raised, so that this fact affords no explanation. The elasticity of the arteries tending to keep them open, and so produce a negative pressure, must be extremely small,

and well below the intraocular tension. The fall in tension at each cardiac diastole will also tend to draw the blood back into the eye, but this effect must also be negligible. On the other hand, it is surprising that no pulsation of the veins is noticeable, due to this cause. The anastomosis with the ciliary system at the disc would tend to fill the veins from the centre towards the periphery, so this cannot be the full explanation. The most potent factor is probably the fact that the ocular venous tension is lowest at the disc, so that the veins are stopped here first by the extravascular pressure, and the blood is dammed back.

Both the constriction of the veins here in embolism, and the normal venous pulsation, tend to point to some definite obstruction at this spot, impeding the exit of blood, and this is most likely to be found in the elasticity of the lamina cribrosa, which acts under such advantageous conditions in the narrow scleral canal.

The question is nearly allied to the condition in which the central vessels are cut across, as in optico-ciliary neurotomy, orbital wounds, &c.

References.

[1] Knapp, *Arch. f. Augenheilkunde*, i., 1, p. 29, 1869.
[2] Landesberg, *Ibid.*, iv., 1, p. 109, 1874.

Section of the Central Retinal Vessels.—When the optico-ciliary bundle is cut across, as in excision of the eye, the arteries are probably emptied at once in a centripetal direction by the intraocular tension. As this only falls to zero very gradually, the veins will be constricted at the disc, and the blood kept in, as in embolism. This accounts for the fact that in excised eyes the veins often contain blood. In experiments on rabbits and rats, the veins become very small and the arteries scarcely visible (Berlin and Leber[1]); but such experiments cannot be directly applied to man, owing to the entrance of the central vessels into the nerve close to the sclerotic, and the different con-

figuration of the disc, &c. As far as I am aware, the disc in man has not been observed at the moment of section.

As the intraocular tension slowly falls, the veins will become empty or nearly so; at any rate they become invisible ophthalmoscopically owing to the œdematous swelling of the retinal elements. This is proved by a case in which the eye was examined three days after excision of an extra-dural tumour of the optic nerve, with retention of the eyeball (Knapp[2]). The retina was white all over; the disc was indistinguishable, and no vessels were visible. On the fourth day, there were two short dark red stripes, which gradually became thicker, and extended peripherally. These were the main branches of the central vein. Arteries only reappeared after several veins had become visible, and they also filled from the centre and extended peripherally. They were of the same colour as the veins. The veins continued most swollen at the disc, but their distension continued to increase until a condition of extreme venous congestion, with hæmorrhages, was set up. Meanwhile the œdema cleared gradually from the periphery towards the centre but the retina subsequently atrophied, with the formation of fibrous tissue, pigmentation marking the sites of the hæmorrhages; the choroid also partially atrophied.

These observations are borne out by a case which I have had the opportunity of watching lately, in which the optic nerve, most of the short ciliary nerves, and the sixth nerve, were all severed.

The probable explanation of the changes is as follows: The veins first fill up in a centrifugal direction owing to the capillary and venous anastomoses with the choroidal vessels at the disc. The blood is supplied by the intact recurrent ciliary arteries, 10—12 in number, derived from the anterior ciliary arteries. These also serve to restore very rapidly the normal intraocular tension. Revascularisation can only commence when the cut ends of the central vessels are efficiently sealed, which doubtless occurs very quickly by retraction into the nerve, clotting, &c.

This closure of the central vein is one of the chief factors added to the picture of embolism. Next, the more imperfect anastomoses with the arteries is gradually rendered efficient, and the veins are now further reinforced by blood through the retinal capillaries. The whole of the blood can only leave the eye by the venæ vorticosæ, a circuitous course, offering considerable resistance, thus leading to intense venous congestion, with its usual results.

References.

[1] Berlin and Leber, *Zehender's Monatsbl.*, ix., p. 278, 1871.
[2] Knapp, *Arch. f. Augenheilkunde*, iv., p. 209, 1874.

Glaucoma.—The intraocular pressure is conditioned by the blood pressure. It is therefore not surprising that the cause of primary glaucoma has long been sought for in the conditions of the ocular circulation. It must be admitted that manometric experiments afford little or no support to this theory. It is indeed probable that ciliary congestion may be the final exciting cause in many of these cases (Priestley Smith[1]), but beyond this there is no reliable evidence. Extirpations of the ciliary and superior cervical ganglia have been performed upon wholly insufficient grounds, and the results are not of a nature to encourage repetition of the experiments.

Reference.

[1] Priestley Smith, "On the Pathology and Treatment of Glaucoma." London, 1891. p. 124.

Toxic Amblyopias.—I have elsewhere[1] advanced the view that tobacco amblyopia is the result of two chief factors, viz.: (1) A toxic effect upon the nerve cells, leading to paralysis of some of the retinal elements; (2) a vascular effect, causing vaso-constriction of the retinal arterioles. The effect of nicotin upon nerve-cells is firstly excitatory, and secondly paralytic. There are at first no histological changes in the cells,[2] but later, degenerative changes manifest themselves.[3] The poison acts first upon the synapses,

and has a particularly potent effect upon sympathetic ganglion cells. We have seen that in large doses, applied rapidly, it causes an enormous rise of blood pressure, due to stimulation of all the sympathetic ganglia in the body, and that this leads to a passive dilatation of the intraocular vessels. It does not follow that this passive dilatation will occur with minute doses spread over a long period. It is further probable that the sympathetic ganglia are much more resistant to toxic effects than such highly differentiated cells as those of the retina, and above all those of the macula. It is therefore probable, and there is now good histological evidence in favour of the view,[4] that the retinal cells will show the paralytic and degenerative effect of the drug earlier than the sympathetic ganglia. In fact, the retinal cells and especially the macular cells, will be in the paralytic stage, whilst the sympathetic cells are still in the excitable stage.

My experimental results show that it is not possible to be as certain of the vascular effect as I had anticipated. It is impossible to foretell whether, in the condition of chronic poisoning with small doses, the vascular effect will still be one of passive dilatation in the eye or of active constriction. If it is the latter, it will still be an additional reason why the macular area is so peculiarly susceptible in these cases.

In quinine amblyopia there can be little doubt that the vascular condition is the essential factor. Ophthalmoscopically, the arteries are intensely constricted. The condition is a much more acute one, and therefore may be expected to agree more accurately with my experimental results. They, as we have seen, show that quinine leads to vaso-dilatation of the splanchnic area, with passive constriction of the intraocular vessels, and are therefore in agreement with the clinical picture. An intense uniform constriction of all the retinal arteries may naturally be expected to cause general amaurosis ; in slightly less degree it will act most upon the periphery, where the vessels are

almost or quite obliterated, and possibly upon the macula, where the retinal supply is deficient. This agrees with the complete amaurosis or the contracted fields found clinically.

It seems probable, then, that tobacco amblyopia is essentially a neuro-paralytic condition, with slight active vaso-constriction as a subsidiary factor; whilst quinine amblyopia is essentially a vascular condition, with marked passive vaso-constriction.

References.

[1] Parsons, *Brit. Med. Journ.*, June 8, 1901; *Ophth. Rev.*, July, 1901.

[2] Parsons, *Journ. of Physiology*, xxvi., p. xxxviii.

[3] Pándi, *Ungar. Arch. f. Med.*, ii., p. 257, 1893.

[4] Birch-Hirschfeld, *Arch. f. Ophth.*, liii., 1, p. 79; see also, *Ibid.*, l., 1, p. 166; lii., 2, p. 835.

By the Same Author.

ELEMENTARY OPHTHALMIC OPTICS,

INCLUDING

OPHTHALMOSCOPY AND RETINOSCOPY.

N.B.—This is the original work published under this title, which has recently been adopted by another Author.

London: J. & A. CHURCHILL, 7, Gt. Marlborough Street.

In Preparation.

THE

PATHOLOGY OF THE EYE:

Part I.—HISTOLOGY.

Part II.—GENERAL PATHOLOGY.

The Arris and Gale Lectures

ON

THE NEUROLOGY OF VISION.

BY

J. HERBERT PARSONS, B.S., D.Sc., F.R.C.S.,

Assistant Ophthalmic Surgeon, University College Hospital; Curator, Royal London Ophthalmic Hospital; Lecturer on Physiological Optics, University College, London; Arris and Gale Lecturer, R.C.S. (1904).

LONDON:
HODDER AND STOUGHTON,
27, PATERNOSTER ROW.

1904.

LONDON:
PRINTED BY HARRISON AND SONS,
PRINTERS IN ORDINARY TO HIS MAJESTY, ST. MARTIN'S LANE.

The Arris and Gale Lectures

ON

THE NEUROLOGY OF VISION.

LECTURE I.

THE AFFERENT VISUAL PATHS.

The nerves which deal with the special senses are specially differentiated sensory nerves. In the process of differentiation, however, the analogies which they present to the ordinary spinal sensory nerves are greatly obscured, and may be easily overlooked. Just as the segmental arrangement of the central nervous system is most manifest in the cord, becomes obscured in the medulla oblongata, and is scarcely appreciable in the higher parts of the brain, so the cranial nerves assume that increased complexity which is characteristic of the evolutionary process wherever it occurs.

Considering first the mechanism of transmission and transmutation of an ordinary sensory impulse, we find that the physical stimulus is received by an end-organ, and is there transformed into a nervous impulse. This is carried by a nerve fibre along the sensory nerve and the dorsal spinal root to the cord. It travels up in the posterior columns of the cord to the nucleus gracilis or the nucleus cuneatus as the case may be. The whole of this course is along the processes of a single cell or neurone, which has been called the neurone of the first order. The impulse is taken up in the nucleus gracilis or nucleus cuneatus by a second cell, and is carried along the nucleo-thalamic tract or

mesial fillet to the opposite optic thalamus; other fibres, especially those derived from the nucleus cuneatus, pass to the superior colliculus or corpus quadrigeminum. These cells in the nuclei gracilis and cuneatus are the neurones of the second order. A third cell, the neurone of the third order, situated in the thalamus or colliculus, carries on the impulse to the cortex cerebri. Here the nervous impulse is transformed into a psychic impulse, a change which is not, and probably never can be understood. This is the simplest path of an afferent impulse, though by no means the only one; it best serves our present purpose, since it is the most typical.

Returning to the genesis of the impulse in some physical stimulus, there is, as far as we are aware, no preparation of the physical forces before they fall upon the sentient surface. This applies to all sensory nerves, with the exception of the nerve of vision, and to a less extent, the auditory nerve. In the former case, with which we are immediately concerned, the whole eye, with the exception of the retina, is a complicated mechanism for preparing the physical force, light, so that it may produce specific and complex sensations. It is well, therefore, to emphasise the fact that in dealing with visual sensations the stimuli themselves are composite, and for all we know, each component may be provided with its own transmitting apparatus.

At the outset of our comparison of the anatomical structures for the transmission of visual and common sensations, we are met with difficulty. The so-called optic nerve is in no sense comparable with an ordinary sensory nerve. Morphologically and physiologically it is part of the brain. Careful investigation shows that the true optic nerve, corresponding with the sensory neurone of the first order, must be sought in the retina itself. Even so, the analogy is not absolutely complete, for the dorsal root ganglion cell, which forms the first neurone, emigrates at an early stage of development from the neural crest and loses its connection with the cord, only to regain it at a later stage. The retina,

on the other hand, develops entirely in the invaginated primary optic vesicle.

THE MORPHOLOGY OF THE RODS AND CONES.—If we seek the analogues of the successive sensory neurones in the optic system, we are met with further difficulties. Histological investigations of the retina have shown that the conducting elements may be divided into three orders: (1) The rods and cones, with their nuclei, which form the main mass of the outer nuclear layer and their processes, which contribute to the outer reticular layer; (2) The rod and cone bipolars, which form the main mass of the inner nuclear layer, with their axones, which contribute to the inner reticular layer; (3) The ganglion cells, the axones of which form the nerve fibre layer, and the main mass of the so-called optic nerve. We shall see later that the ganglion cells and their processes behave exactly like the second order of sensory neurones, a fact which affords further evidence that the optic nerve belongs essentially to the central nervous system. The neurones of the first order, therefore, must be either the rods and cones, or the bipolars. In the former case an extra neurone is intercalated in the visual afferent path; in the latter no such assumption is necessary, but it remains to explain the nature of the rods and cones.

There can be no doubt that the second view is the simpler and more probable. If we adopt it, the rods and cones will be epithelial ependymal cells, corresponding with Merkel's *Tastzellen* or touch cells and the epithelial cells of end-organs, with the neuro-epithelial cells of taste buds, the epithelium of the organ of Corti, &c. The olfactory nerve will prove the sole exception to such a scheme, the sensory neurones of the first order being here situated actually upon the surface, like the sensory cells of some invertebrata.

If we consider the position of the retinal pigment epithelium and the rods and cones from an embryological standpoint, it will be seen that they correspond with the lining of the primary optic vesicle, *i.e.*, with a part of the central neural canal. This is itself an invagination from the

surface epiblast, and its lining epithelium, therefore, will correspond with the superficial epithelium of the body. In the neural canal these cells become ciliated ependymal cells, so that their condition in the retina is merely a specific differentiation.

Evidence in favour of the ependymal nature of the rods and cones has been brought forward by Krause. This tends to show that the outer limbs are really coiled up cilia.

Verhoeff, working in the laboratory at Moorfields, supports and extends this theory by further observations. If the rods and cones are ependymal cells we might reasonably expect to find the pigment epithelium also showing traces of the same origin. By bleaching and special staining methods, *e.g.*, Mallory's phosphotungstic acid hæmatoxylin, a membrane, resembling the external limiting membrane, can be made out surrounding the internal ends of the pigmented epithelial cells. The appearance in transverse sections is that of a delicate line running along near the inner margins of the cells. The latter project beyond it in the form of processes of variable length, showing that the line does not represent the inner contour of the cells. Black dots occur at regular intervals along the line, each occurring at the line of junction of two cells. On careful focussing it can be seen that the line is not always at the same level, evidently passing sometimes behind and sometimes in front of the cells. Hence it is difficult to photograph the membrane. In oblique sections the true structure is made more apparent, the membrane appearing not as a straight line, but as a series of hexagonal loops, which are fused together at the lines of contact so as to form a screen into the openings of which the pigment cells project. The little dots are the points of junction of the loops, *i.e.*, the sections of the lines of contact.

It would take too long to discuss the bearing of these observations upon the generally received idea that the membrana limitans externa is formed by Muller's fibres, *i.e.*, by neuroglia. Reference must be made to the original paper in the Royal London Ophthalmic Hospital Reports. Suffice

it to say here that there is reason to think that neuroglia is absent in this situation in glioma retinæ.

There are other staining reactions which tend to show that the rod and cone cells differ essentially from the bipolar cells of the retina. In some specimens, more particularly in cases in which the nutrition of the retina has suffered from some cause, the rod and cone nuclei stain differently from the nuclei of the bipolars. This may be seen with the ordinary hæmatoxylin and eosin staining, but as shown by Verhoeff, it is brought out much more clearly by Mallory's acid hæmatoxylin after hardening in 4 per cent. formaldehyde for 4 days or longer. The inner nuclear layers then remain unstained. The contrast between the two layers may be further intensified by staining for 24 hours in lithium carmin after differentiating in ferric chloride solution. The inner nuclei then take on the carmin stain. In some specimens only portions of the retina show this differentiation. It occurs most frequently in cases of detachment of the retina or choroiditis, but it also occurs in apparently normal retinæ. The condition is present also in the retina of the guinea-pig and in that of the frog.

The other theory—that the rods and cones are true peripheral neurones—is supported chiefly by observations on lower types. This has been shown particularly by van Lenhossék in cephalopods. Thus, in eledone, the retina consists entirely of complicated rod cells. From these the retinal fibres pass through the cartilaginous sclerotic to the visual lobe, which contains a peripheral or external nuclear layer, followed by a reticular layer, then an inner nuclear layer, and finally a layer of white fibres. These layers are themselves complex, and until the morphology of the individual cells is more accurately determined the evidence in favour of the purely nervous nature of the rod apparatus is not overwhelming.

Phylogeny, indeed gives better support to the theory in the analogy of the ordinary sensory neurones of the first order, though here, too, the other interpretation is not

disproved. In man the spinal ganglion cells are bipolar when first developed; only in the cochlear and vestibular ganglia is this condition retained through life. In the fish it is retained in all the posterior root ganglia. In invertebrates transition stages are found in which the cell body lies farther and farther from the central nervous system, until finally, as in the earthworm, it is actually situated in the surface epithelium (Retzius). One vertebrate, amphioxus, has its bipolar sensory cells within the spinal cord, and some animals, in a comparatively limited space, show a number of transitional stages between the peripheral and the central position (Edinger). In only one undoubted instance in man the peripheral situation is maintained, viz., the peripheral olfactory neurones.

THE NEURONES OF THE FIRST ORDER.—We pass on now to consider very briefly the neurones of the first order, viz., the rod and cone bipolars. Ramon y Cayal's work by a modified Golgi method has shown most clearly the relationship between the various cells of the retina. The bipolar cells come into relation peripherally by vertical dendrones with several rods. The dendrones of the bipolar cells for the cones lie in a deeper plane and are horizontal, but similarly come into relation with several cones. The axones of the rod bipolars run centrally to the inner part of the inner reticular layer, whilst the axones of the cone bipolars may form their arborisations at any of the five layers of the inner reticular layer. Over the greater part of the retina there are about a hundred rods and cones to one ganglion cell. The fovea centralis has been investigated only in the bird and chamæleon. In both, cones alone are present; their axones end in knobs without fibrils, or with only a pair of very short rudimentary fibrils. The dendrones of each ganglion cell in this region seem to come into relation with only a single bipolar, and possibly several amacrine cells; so that here each cone has its own bipolar and ganglion cell—it remains, so to speak, "individualisirt" (Cayal).

THE NEURONES OF THE SECOND ORDER.—The neurones

of the second order, or the ganglion cells and their processes, will be considered at greater length. Their axones pass into the nerve fibre layer of the retina, thence into the optic nerve; most cross in the chiasma to the opposite optic tract, some only passing along the tract of the same side; from both optic tracts most are distributed to the external geniculate bodies, whilst others pass to the superior colliculi, and yet others to the pulvinar of each optic thalamus. In man probably 80 per cent. pass to the external geniculate body (von Monakow). In lower animals the optic lobes, *i.e.*, the region of the corpora quadrigemina, are the main visual organs. In fish, almost the whole of the optic nerve ends in the mid-brain; in birds, there is a differentiation of a mesencephalic nucleus, the superior colliculus, from a diencephalic nucleus, the lateral geniculate body, and in them for the first time one meets with a genuine occipital cortex (Edinger). This anatomical differentiation is accompanied by a parallel redistribution of function, and is, therefore, of prime importance in analysing the results derived from experiments upon animals.

Most of our knowledge of the arrangement of the fibres of the optic nerves, apart from the broad question of the relative amount of decussation in the chiasma, is derived from clinico-pathological investigation. I propose here to limit myself to a description of my own researches by the experimental method upon monkeys.

Following the ordinary Wallerian law of degeneration, the afferent fibres of the visual paths degenerate on the central side of a lesion which separates them from their cells of origin, the ganglion cells. The method adopted was to introduce a Graefe cataract knife into the eye 4 or 5 mm. behind the corneo-scleral margin, at either the nasal or temporal side, thus avoiding dangerous injury to the ciliary body and minimising injury to the retina. (The monkeys were of course completely anæsthetised.) The knife was passed across the eye through the vitreous to the opposite side, and the retina wounded there to the required extent,

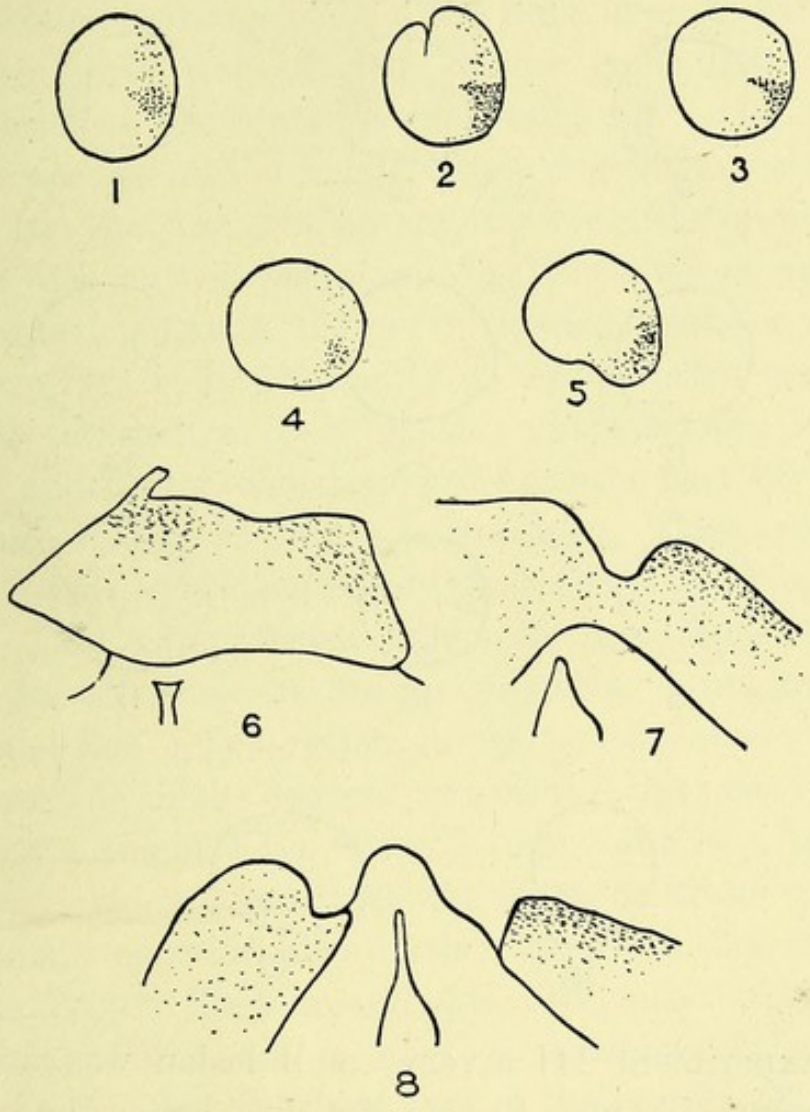
the position of the point of the knife being in some cases observed by the ophthalmoscope (direct method). The opthalmoscope was especially used in lesions near the disc or macula. In other cases the slight resistance encountered was sufficient to show that the retina had been reached. The exact position and nature of the wound were subsequently determined by ophthalmoscopic examination, which was repeated after an interval of a few days, and also shortly before killing the animal. The lesions were all investigated macroscopically by a suitable section of the eye *post-mortem*, and were then prepared for microscopic examination. The monkeys were chloroformed to death from a fortnight to three weeks after the operation. Great care was taken to preserve the accurate orientation of the nerves. The degenerations were examined by the Busch-Marchi method.

In Experiment I, a lesion about 2 mm. long, in a direction tangential to the disc, was made near the equator in the lower nasal quadrant of the right eye. The main area of degeneration is wedge-shaped near the eye, the apex of the wedge being towards the centre of the nerve, and the base at the periphery, the whole lying in the upper part of the inferior nasal quadrant (Figs. 1–5). There are scattered degenerated fibres over the whole nasal side, and a few isolated ones upon the temporal side. In sections taken more posteriorly, behind the entrance of the central retinal vessels, the shape of the area occupied by the degenerated fibres becomes more crescentic, but is still nasal. In the chiasma the fibres cross principally in the inferior or ventral part (Fig. 6). Fig. 7 is a slightly more oblique section farther back, being in a direction downwards and forwards; the degeneration is therefore ventral and anterior. Fig. 8 is still more oblique, approaching the horizontal, and the tracts are cut more or less longitudinally. Very few dots of degeneration are seen in the chiasma and tract of the same side, the main area of degeneration being in the outer part of the contra-lateral tract. Farther back the fibres spread

out over a larger area of the section of the tract, becoming diffuse as they approach their termination.

In Experiment II, a lesion about 3 mm. long was made in a direction tangential to the disc a little in front of the equator in the lower temporal quadrant of the retina of the left eye. The main area of degeneration is on the temporal

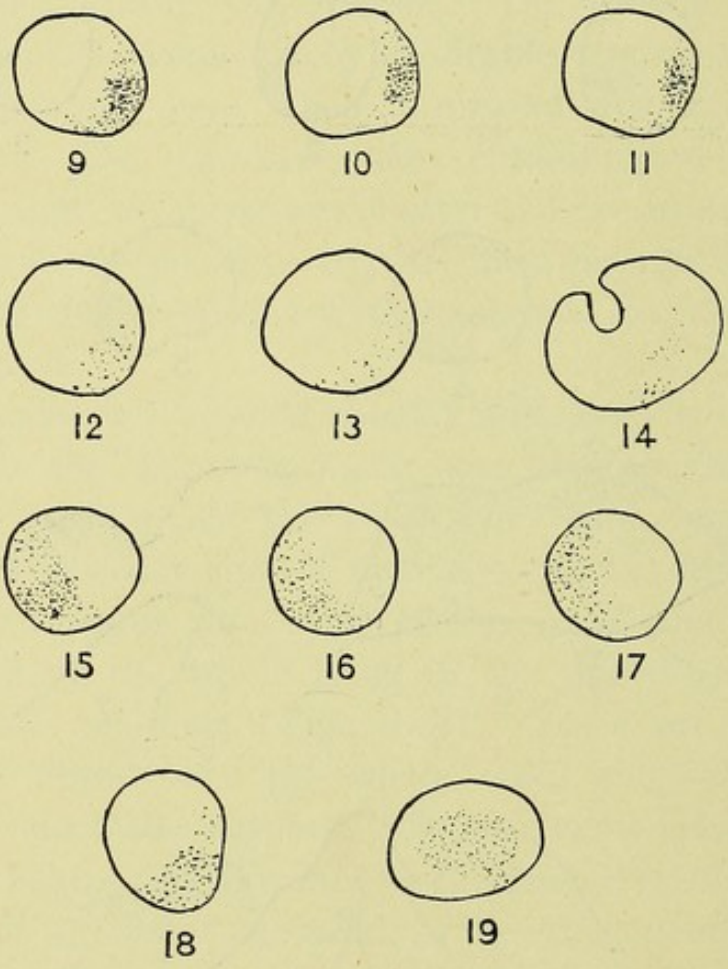
FIGS. 1–8.



side along the whole course of the nerve (Figs. 9–11). It is most marked and is very dense in the lower temporal quadrant, being more or less wedge-shaped near the eye, and becoming rounder farther back. It tends to become more dorsal near the chiasma, but it is possible that this may be due to slight error in orientation. There is some diffuse degeneration, most marked on the temporal side. The fibres lie princi-

pally in the dorsal part of the chiasma. Many degenerated fibres are seen crossing to the opposite tract. Farther back the fibres lie principally in the central part of the tract of the same side. Posteriorly they spread out and become more diffuse. In a similar area of the tract of the opposite side, *i.e.*, dorsally and centrally in front, becoming broader behind, there are many finer black spots of degeneration.

FIGS. 9-19.



In Experiment III a very small lesion was made upon the temporal side near the equator, just below the horizontal meridian of the left eye. The degeneration is almost limited to the inferior temporal quadrant, and is very slight (Figs. 12–14). In the chiasma it is at first ventral and anterior in position, gradually tending towards the dorsal surface. In the tract of the same side it is central and dorsal at first, becoming more diffuse posteriorly. There are only a few scattered fibres degenerated in the contra-lateral tract.

In Experiment IV the lesion was larger, about 3 mm. long. It was on the temporal side of the right eye, a little behind the equator, and extended above and below the horizontal meridian. The degeneration is diffused over the whole temporal side of the nerve, without any special area of concentration (Figs. 15–17). In the chiasma it occupies the central and dorsal parts. There are no fibres degenerated in the ventral part. In the tract of the same side the degeneration is arranged much the same as in Experiment II, but more fibres are affected. There is a finer, scattered degeneration in the contra-lateral tract.

In Experiment V a small lesion was made between the macula and the disc, but at slightly lower level in the left eye. It was rather deep, injuring the choroid and sclera. In the anterior part of the nerve the degeneration was down and out (Fig. 18); posteriorly it became more central. It occupied the central part of the chiasma, and continued central, and rather dorsal in the anterior part of the same tract, becoming more diffuse posteriorly. There was a large amount of degeneration considering the small extent of the lesion. This was probably due to its proximity to the disc, and to its situation in the neighbourhood of the macula. There was fine degeneration in the contra-lateral tract, the fibres crossing in the central part of the chiasma.

In Experiment VI a lesion, 2 mm. long, was made in a direction down and out from the fovea centralis of the left eye. In the anterior part of the nerve the degeneration is most marked on the temporal side, especially just below the horizontal; but there is also a considerable amount of degeneration over the whole area of the section (Fig. 19). It is chiefly central in the anterior part of the chiasma; in the posterior part where the sections are more oblique, *i.e.*, about half way between vertical and horizontal, it occupies a crescentic area at the periphery of each side with a connecting band in front. In this situation, therefore, the degeneration tends to become dorsal and external. Farther back, at the commencement of the tracts, there is degeneration in the

central and slightly dorsal parts of each side; and this becomes diffused over the whole tract more posteriorly.

These experiments agree, upon the whole, with some observations made upon rabbits by Pick and by Dean and Usher. They also confirm the results arrived at by pathological investigation of cases of toxic amblyopia, in which the papillo-macular bundle is particularly involved (Samelsohn, Nettleship, Uhthoff, Birch-Hirschfeld, and others). This disease, or rather group of diseases, has long been regarded as a form of retrobulbar neuritis. Recent investigations by the extremely delicate Nissl method, carried out principally by Birch-Hirschfeld, strongly support the view, which I had already advanced from theoretical considerations, that there is no true neuritis, but that there is degeneration, chiefly confined to the papillo-macular bundle, and in every respect comparable with those under discussion. They are due to the action of the toxic substances upon the retina. The degeneration in the nerve is actually caused by the destruction of some of the ganglion cells. Most of the toxic agents, whilst acting to some extent upon these cells themselves, act principally upon the terminal arborisations or synapses around them. It has been shown by Warrington that section of a spinal posterior root leads to degeneration of certain groups of cells in the anterior horns, probably by the removal of afferent impulses which are necessary for the nutrition of the cells. The same probably occurs in toxic amblyopias, the arborisations of bipolars suffering most, and causing degeneration of the ganglion cells. These diseases, therefore, afford good evidence of the course of the fibres from the macular region. Indeed, so far as their very limited application admits, they are better than the experimental lesions, for in the latter there is invariably some diffuse degeneration. This is not surprising, owing to the impossibility of absolutely controlling the amount of injury. The lesion made by the point of a Graefe knife is minimal, probably much less than by the galvano-cautery, which was used by the other observers. It is, however, rarely possible to

effect one's purpose without injury of the choroid or even the sclerotic, and it is impossible to avoid entirely the retinal vessels. A slight amount of hæmorrhage into the vitreous usually occurs, and the mere passage of the narrow knife across the eye must lead to reactive changes, probably accompanied by transient shrinking of the vitreous, which may well interfere with the nutrition of the ganglion cells in other parts of the retina.

As might be expected, the nearer the lesion to the optic disc the greater is the resultant degeneration, for not only are ganglion cells destroyed, but the axones of ganglion cells over a large peripheral area are alsc cut through. As these cells lie within the central nervous system, no regeneration takes place ; moreover the time allowed is too short.

We see that, speaking generally, the fibres derived from various parts of the retina retain their relative position in the optic nerve, *i.e.*, temporal fibres remain external, nasal internal, &c. The temporal fibres, however, tend towards the dorsal side as they approach the chiasma, and the nasal towards the ventral side. A further dislocation, affecting the temporal fibres most, occurs as the result of the intercalation of the papillo-macular bundle.

It is probable that there is really some degree of variation in different individuals. Thus in the famous case reported by Ganser, the uncrossed temporal fibres of the right side formed a separate and isolated bundle, which passed to the ventral side of the tract of the same side, and fused with it near the external geniculate body ; and in the unique case figured by Vesalius, there was no chiasma, the whole optic nerve running directly into the tract of the same side. The number of uncrossed fibres bears some relationship to the development of binocular vision, and as this occurs late in the evolution of mammals, slight variation is less to be wondered at than the extreme constancy which apparently obtains.

I invariably found some degeneration in the optic nerve of the opposite side, an unexpected result which, however,

confirms the work of previous observers. In all the specimens it was a diffuse degeneration, usually without very definite areas of concentration, and always much less than on the injured side. The degeneration could be traced throughout the length of the nerve, and such concentration of fibres as occurred retained its relative position in all the sections. As a rule it was on the homonymous side of the nerve, as compared with the side of the lesion. I have eliminated, as far as is possible, any error of technique, which is further unlikely because all the degenerations were confined to visual paths, although much of the rest of the brain was examined.

There is one pathological examination which affords some support to the experimental result. Kellermann, in a case of old-standing atrophy of the left optic nerve, found a small tract of degeneration in the right nerve, ventro-lateral near the eye, becoming central near the chiasma, and therefore running in the course of the macular bundle. No abnormality of vision was noticed during life, and the central vessels entered the nerve at the inner and lower part, which is not invariably the case; hence the bundle ran independently of them. Kellermann attributes the degeneration to compression of the fibres in the chiasma, due to skrinking from atrophy of the fibres of the left nerve. Hebold, in a similar case, found the nerve sound, as shown by Pal's method, but this is not sufficiently sensitive for the purpose. Dean and Usher suggest that fat may be removed from the degenerated nerve and carried by lymphatics and deposited in the opposite nerve. This is disproved by its absence in other parts of the nervous system, in spite of the innumerable researches carried out by the Marchi method.

We are forced to conclude that the degeneration is a genuine one, and if so, what is the nature of the fibres involved? It is not probable, as Dean and Usher point out, that they are concerned in the pupillary reflexes, as these remain absolutely unimpaired. They must belong to some form of inter-retinal fibres—a reversion, in a sense, to

the much disputed inter-retinal tract (commissura arcuata anterior of Hannover, vordere Bogencommissur of Stilling). Ramon y Cayal has demonstrated, by the methylene blue method in rabbits, a division of the optic fibres, and Kölliker discovered an isolated example in a human fœtus. Bernheimer was struck by the variety in size of the fibres in the chiasma, so that it appears in many places as if the larger fibres divided. It is not improbable that the degenerated fibres in the nerve of the uninjured side are collaterals, and that they may be distributed to physiologically corresponding parts of the opposite retina, possibly inducing chemical changes in the visual substances or movements in the cells, and so afferent impulses which subserve a modified type of binocular vision.

These fibres would, therefore, be centrifugal fibres. That fibres which are undoubtedly centrifugal occur in the optic tracts and nerves was first proved by the Golgi method by Ramon y Cayal, and has been confirmed since by other methods (van Gehuchten, Held, Kölliker, v. Monakow). They arise in the external geniculate body, the superior colliculus, and probably in the pulvinar of the optic thalamus. They end by arborisation in the inner reticular layer. Their functions can only be conjectured, and are possibly those already suggested for the inter-retinal collaterals.

In all of my experiments there was some degeneration in both tracts. This may be explained partly by the diffuse injury which probably always results from the lesion, and which is manifested by diffuse degeneration in the nerve. I do not think that this accounts for it entirely. There are apparently more fibres degenerated in the tracts than in the nerve, and we are here more powerfully forced to the conclusion that division of the fibres occurs. Most of the experiments were temporal lesions, with a view of obtaining, if possible, a pure degeneration in the homolateral tract. In these cases the degeneration in the contralateral tract usually showed smaller black globules, as if

less myelin was present. Probably these were finer fibres, in fact, collaterals.

THE BASAL VISUAL CENTRES, AND THE NEURONES OF THE THIRD ORDER.—The optic tract runs round the cerebral peduncle, and divides posteriorly into two branches, a lateral and a mesial. The lateral root contains the visual fibres, and ends in the lateral geniculate body ; the mesial joins the mesial geniculate body, and consists of fibres which are not connected with vision.

The lateral geniculate body, in which the great majority of the visual fibres end in man, consists of alternating layers of white and grey matter. The grey matter contains the cell bodies and dendrones of the optic neurones of the third order. The white matter consists of the axones of the neurones of the second and third orders, *i.e.*, the ends of the fibres from the optic tract and the beginnings of the fibres from the geniculate body to the cortex cerebri. The latter pass out laterally into an area situated on the outer side of the external geniculate body known as Wernicke's field. Here they are joined by similar fibres from the superior colliculus and pulvinar, the latter being ventral to those derived from the geniculate body. They all turn round the caudate nucleus and enter the optic radiation of Gratiolet. This forms a large sagittal bundle which passes backwards and upwards, outside the posterior horn of the lateral ventricle, to the occipital lobe. The fibres from the lateral geniculate body tend towards the neighbourhood of the calcarine fissure. They are well seen in Weigert sections of the brain of the new-born child, the other fibres being unstained, owing to their medullary sheaths not having yet developed (Flechsig). Flechsig thinks that the fibres from the geniculate body end exclusively in the calcarine fissure, and represent the fibres from the macula.

Other fibres from the optic tract pass into the pulvinar of the optic thalamus, which very much resembles the external geniculate body in histological appearance. The cells here, around which the fibres arborise, are also optic

neurones of the third order. We have already referred to the relation of their axones, dorsal to those derived from the geniculate body. Their ultimate distribution is probably less localised, extending over a large area of the occipital lobe.

The last group of fibres from the optic tract pass to the superior colliculus or corpus quadrigeminum. Although this has a complicated structure in man, it is a mere rudiment as compared with its condition in the lower animals. Without going into the details of its structure in man, it may be said that it consists of alternate layers of white and grey matter, the actual surface being covered by a thin layer of white fibres. The function of these is unknown; they do not degenerate after removal of the eye. The principal optic fibres enter the middle white zone, which is separated from the superficial white layer by the superficial grey layer or cappa cinerea (Tartuferi). Their terminal arborisations are around the cells in the superficial and also in the deeper grey matter. It is noteworthy that the deeper fibres pass to the region in which the fibres from the lateral fillet end. These ganglion cells of the superior colliculus are also optic neurones of the third order. A few of their axones pass to join the optic radiation, though this is doubted by some. Most of them pass down and bend round the grey matter surrounding the aqueduct of Silvius, decussate with those from the opposite side beneath the III nuclei and the posterior longitudinal bundle, forming Meynert's "fontänenartige Haubenkreuzung," and finally entering the posterior longitudinal bundle as they pass downwards towards the medulla. In their course they give off collaterals which pass to the opposite superior colliculus, to the III, IV and VI, and probably to other nuclei. It is certain at any rate that they enter into intimate relation with the nuclei which govern the eye muscles, a fact which accounts for the mechanism of the eye-muscle reflexes.

The effects of experimental destruction of the corpora quadrigemina are important. Most of the earlier observers,

Flourens, Longet, McKendrick, Bechterew, Ferrier, and others, found a constant relation between the anterior lobes and the visual sense. The loss of vision following destruction depended upon the amount of decussation at the chiasma. In animals with total decussation—any below the rabbit, including the guinea-pig, birds, and fish—removal of one optic lobe caused blindness of the opposite eye. In animals with binocular vision, heteronymous hemianopsia occurred, as Bechterew showed upon dogs; bilateral destruction produced complete blindness. More recent experiments on Testudo palustris (Fano), and birds (Stefani), show that the blindness is not complete. Nothnagel and Eisenlohr, from pathological data in man, found no interference with vision which could be ascribed to the corpora quadrigemina, and the later experiments of Ferrier and Turner contradict the earlier observation of Ferrier that complete blindness follows destruction of both superior colliculi in the monkey.

Confining our attention to primates, histological evidence all points to the dorsal and superficial layers as being most intimately connected with the visual afferent system, whilst the deeper layers are concerned with the ocular motor nuclei. Stimulation of the superior colliculus in monkeys, causes, amongst other phenomena, widening of the palpebral fissures, elevation of the eyebrows, and conjugate deviation of the eyes to the opposite side, accompanied by a similar movement of the head and neck. These results may be attributed to spread of the current to the subjacent motor nuclei, but this is contra-indicated by the different effects obtained from the superior as compared with the inferior colliculi.

Ablation causes temporary deviation of the eyes to the same side, lasting only a few hours. No ptosis or ophthalmoplegia follows as long as the lesion is not sufficiently deep to interfere with the third nuclei. The anatomical relations involve the removal of one occipital lobe, with consequent hemianopia. Apart from this, there are no visual effects which can be ascribed to the corpora quadrigemina.

We are forced to conclude that the superior colliculi are

relatively unimportant as regards visual functions in primates, though they still probably retain some importance in the co-ordination of the ocular movements, acting principally as a reflex centre, receiving afferent impulses from the retinæ, the cortex, the acoustic-vestibular system, and the spinal sensory system through the fillet and cerebellum. These functions are too complex and too easily replaced vicariously to be elucidated by the coarse methods of experiment.

As the size and importance of the mesencephalic visual nuclei diminish in ascending the animal scale, so the size and importance of the diencephalic nuclei—the lateral geniculate body and the pulvinar of the optic thalamus, both of which must be regarded as nuclei of the diencephalon—increases. The pulvinar is large only in primates. Excitation of the thalamus produces very little result; ablation results in visual defects. A very important pathological observation was made by Hughlings Jackson in 1875. There was localised softening of the posterior part of the right optic thalamus; the visual defect consisted in left hemianopia. Ferrier, and Turner, and Lo Monaco, from experimental lesions found contra-lateral hemianopia plus amblyopia of the whole field.

We are now in a position to realise the parallelism which exists between the nuclei under consideration and those belonging to the afferent tracts of common sensibility. The ganglion cell layer is found to correspond with the nuclei gracilis and cuneatus, whilst the termination of the optic tract in the superior colliculus and thalamus (lateral geniculate body and pulvinar) corresponds with the terminations of the nucleo-thalamic (mesial fillet) tract in the mesencephalon and diencephalon respectively.

Ramon y Cayal divides the optic path from these lower centres to the occipital cortex into two parts, a superficial and a deep. The superficial path, which is the less important, arises in the superficial layers of the lateral geniculate body and possibly from the stratum zonale of the thalamus. It curves towards the middle line, passing into the "central

optic path" (Ramon y Cayal) of the cerebral peduncle. The deep path arises from the deep cells of the lateral geniculate body, as well as from the stratum zonale, and enters the central optic path on its mesial border. Some of the axones entering the central optic path undergo bifurcation, one branch ascending with the main bundle into the corpus striatum, the other descending towards the tegmentum. Ramon y Cayal suggests that the descending branches may represent a reflex path between the visual centres and the motor nuclei for the eyes, head, and neck. (See Lecture II.)

Ramon y Cayal succeeded in following the axones of the central optic path throughout their entire course from their entrance into the corpus striatum to their termination in the occipital lobe in the new-born mouse. He found that they were distributed to those areas of the cortex in which the white stripe of Gennari is best developed. This agrees with the embryological results obtained by Flechsig.

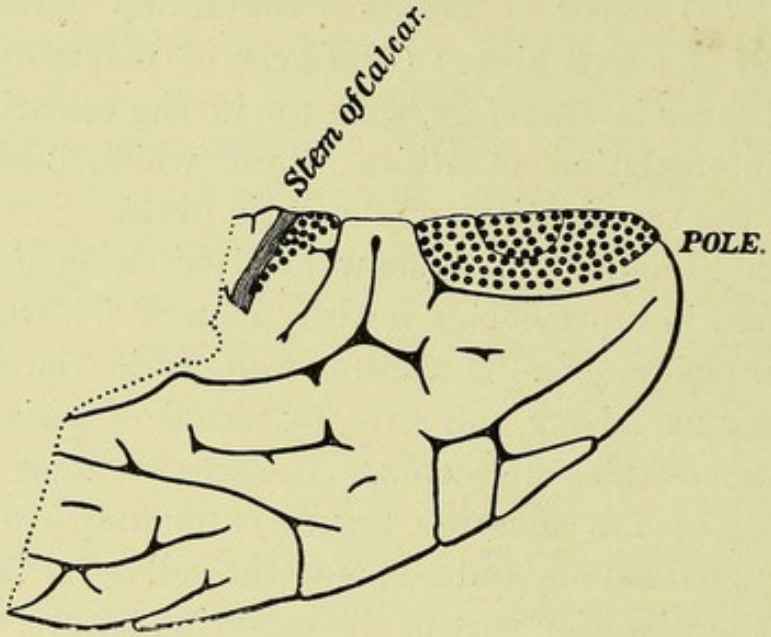
The Cerebral Visual Centres.—Since the early part of the last century, it has been known that the cortex cerebri in the neighbourhood of the calcarine fissure possesses a characteristic structure owing to the existence in the centre of the grey matter of a white line, which is easily visible to the naked eye. This has been variously termed the line of Gennari, of Vicq d'Azyr, or of Baillarger, after the original investigators. Since the earlier descriptions of Meynert, Krause and Betz, this region of the cortex has received special attention from Leonova, Hammarberg, Schlapp, Cayal and most recently and most exhaustively from Bolton. According to the last-named author, the calcarine or visuo-sensory cortex may be divided into the following layers:—(1) Outer layer of nerve fibres; (2) Layer of small pyramidal cells; (3) Outer layer of granules containing pyramids; (3*a*) Middle layer of nerve fibres or line of Gennari, containing the solitary cells of Meynert; (3*b*) Inner layer of granules; (4) Inner layer of nerve fibres, containing the solitary cells of Meynert; (5) Layer of polymorphic cells. In the neighbouring visuo-psychic cortex the layers are:—(1)

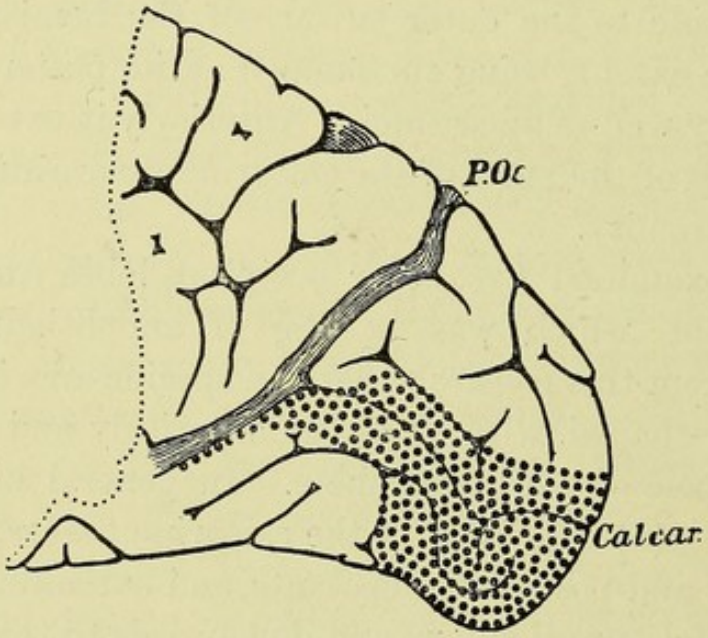
Outer layer of nerve fibres; (2) Layer of small and large pyramids; (3) Layer of granules containing pyramids; (4) Inner layer of nerve fibres; (5) Layer of polymorphic cells. The third layer is, therefore, split up in the calcarine region by the intercalation of white fibres which undoubtedly represent the terminations of the optic fibres.

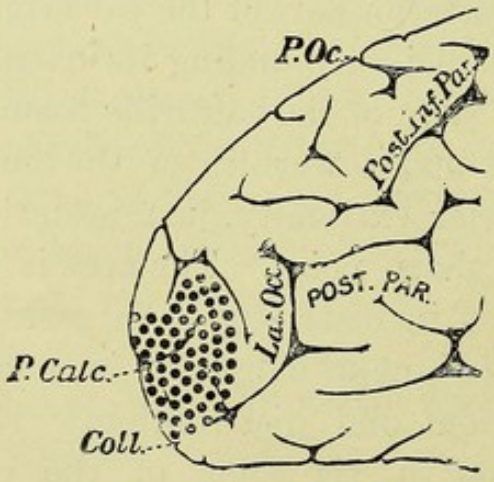
Figs. 20, 21 and 22 (p. 24) show the distribution of the visuo-sensory area in a previously healthy man of 55, who died of right lobar pneumonia. The results were worked out by Bolton with enormous labour and care, by means of serial sections and micrometer measurements. The area occupies the whole of the body of the calcarine fissure extending above to the parallel cuneal sulcus, and below to the collateral fissure. It occupies the posterior part of the calcarine fissure, extending round the pole to the outer surface of the hemisphere to a considerable extent, being surrounded at its postero-external extremity by well-defined sulci. Anteriorly it extends along the lower lip of the stem of the calcarine fissure almost to its anterior extremity.

Bolton examined five other occipital lobes from various cases, one of which was a case of anophthalmia. He concludes from this research that the specific area is approximately pear-shaped, with the apex anteriorly and the thick end at the pole of the hemisphere. In general distribution it occupies:—(*a*) The body of the calcarine fissure, including the anterior and posterior annectants, and extending upwards to the parallel cuneal sulcus and downwards to the collateral fissure; (*b*) The posterior part of the calcarine fissure extending to the polar sulci surrounding its extremities; (*c*) The inferior lip of the stem of the calcarine fissure (including the superficial surface and lower lip of the cuneal annectant) nearly to its interior extremity, just posterior to which the area tails off to a sharp point. The area is much decreased in extent, but not in distribution, in cases of old standing optic atrophy. In anophthalmia it is much contracted as regards both extent and distribution. It then occupies the usual position in the stem of the calcarine fissure,

FIGS. 20–22.


Stem of Calcar.
POLE.


P.Oc
Calcar.


P.Oc.
Post. Inf. Par.
Lu. Occ.
POST. PAR.
P. Calc.
Coll.

but only extends backwards as far as the posterior cuneo-lingual annectant, and it is confined to a portion of the inferior lip of the fissure and to the cortex between this and the collateral sulcus.

At the junction of the area of special lamination with the surrounding cortex the line of Gennari suddenly ceases. In the area itself the line is decreased nearly 50 per cent. in thickness in old standing optic atrophy, and the outer granule layer more than 10 per cent. On the other hand, in the cortex surrounding the area referred to, old standing optic atrophy causes no modification of the lamination. In anophthalmia, the combined outer granule layer and line of Gennari are narrowed down to two-thirds of the normal thickness, the other layers of the cortex being approximately unchanged. This amount of narrowing is the same as that found in cases of old standing optic atrophy.

Hence it may be reasonably concluded that the area thus localised is the primary visual region of the cortex cerebri, and that the part of this area to which afferent visual impulses primarily pass is the region of the line of Gennari. Bolton thinks that the area can probably be described as the cortical projection of the corresponding halves of both retinæ. In this projection the part above the caltarine fissure represents the upper corresponding quadrants, and the part below the lower corresponding quadrants of both retinæ.

Ferrier first described the occipital lobes in various animals as being excitable and giving rise to movements of the eyes to the opposite side. In experiments with Yeo, he found that destruction of the angular gyri in monkeys produced loss of vision of the opposite eye. This result has since been quite disproved by Schäfer and Sanger Brown and others, the explanation of Ferrier's results being probably the injury of the underlying fibres in the corona radiata passing from the occipital lobes. H. Munk first showed that removal of the occipital lobe alone in the monkey caused heteronymous hemianopia, *i.e.*, blindness of

the corresponding halves of both retinæ with loss of the opposite halves of both fields of vision. All optical reflexes, with the exception of the pupillary reflex, were abolished. Munk tried to discover localisation within this visual area in dogs and monkeys by partial extirpations. He came to the conclusion that in the dog the upper part of the retina corresponds with the anterior part of the visual area, the lower with the posterior, the mesial or internal with the mesial or internal, and the lateral with the lateral. Central vision was most represented at the posterior pole. Schäfer and Sanger Brown came to the conclusion that in the monkey central vision is represented in the neighbourhood of the anterior part of the calcarine fissure. Schäfer considers that in the monkey and in man the whole of the visual area of one hemisphere is connected with the corresponding halves of both retinæ; that the upper zone of the visual area of one hemisphere is connected with the upper zone of the corresponding lateral halves of both retinæ; similarly for the lower zones; and that the focal point of the visual area, which is placed on the anterior part of the mesial surface of the occipital lobe, is connected with rather more than the corresponding halves of both maculæ. Pathological observations confirm these statements for the most part. Lesions of the occipital lobe produce hemianopia, without affecting the pupil reflexes. The fovea almost invariably escapes. Lesions of the mesial surface, near the calcarine fissure, produce the most serious disturbance for their size.

von Monakow limits the visual area to the cuneus, the lingual lobule, and the occipital gyri; all parts of the macula are represented in both hemispheres, and over the whole visual cortex.

According to Henschen, the visual centre is confined to the neighbourhood of the calcarine fissure, the upper lip being connected with the upper quadrant of the retina, the lower with the lower quadrant, and the macula with the anterior part of the area, each macula being represented on both sides.

As far as anatomical evidence goes it seems certain that most of the fibres from the lateral geniculate body end in the region of the calcarine fissure. According to Henschen all the visual fibres of the optic tract end in the external geniculate body, whence new fibres are carried to the calcarine fissure. Flechsig, too, finds the termination of the fibres of Gratiolet's radiation in the mesial surface of the occipital lobe and a small area close to the longitudinal fissure. On the other hand von Monakow and others trace the thalamo-occipital fibres to the whole of the occipital cortex, and possibly to the posterior part of the parietal lobe; those from the external geniculate body pass principally to the cuneus and lingual lobule.

The idea that the macular region is represented only in the anterior part of the calcarine fissure is opposed by some pathological observations, so that Forster and Sachs consider the posterior part of the fissure the more probable. This view is similarly negatived by other cases, so that it seems probable that the whole length of the calcarine fissure is concerned in representation of the macula (Barker).

von Monakow assumes a wide distribution of the macular fibres in the external geniculate body, so that almost any portion of the occipital cortex is capable of receiving macular impulses. This view is opposed by cases of localised bilateral lesions of the occipital lobes, causing complete blindness, though in some of these there has been double hemianopia with partial escape of central vision.

Bibliography.

Krause. Schmidt's Jahrb., ccxlix, 1896.
Verhoeff. R. L. O. H. Rep., xv, 4, 1903.
Retzius. Biol Untersuch., iv, 1899.
Ramon y Cayal. Die Retina der Wirbelthiere. Wiesbaden, 1894.
Edinger. Vorlesungen über den Bau der nervösen Centralorgane. Leipzig, 1895.
Parsons. Brain, 1902.
Pick. Nova Acta derk. Leop. Carol. deutschen Acad. der Naturforscher, lxvi.

Dean and Usher. Trans. Ophth. Soc., xvi, 1896.
Samelsohn. In Graefe-Saemisch, v, 1877.
Nettleship. Trans. Ophth. Soc., i, 1881.
Uhthoff. Arch. f. Ophth., xxxii, 3, 1886.
Birch-Hirschfeld. Arch. f. Ophth., liii, 1901.
Kellermann. Klin. Monatsbl f. Augenheilkunde, xvii, 1879, Beilageheft.
Hebold. Arch. f. Ophth., xxxviii, 1, 1892.
Bernheimer. In Graefe-Saemisch, Lfg. 15, 1900.
Flourens. Récherches experimentales, 1824.
Longet. Anat. et Phys. du Sys. nerv., 1869.
McKendrick. Trans Roy. Soc., Edin., 1873.
Bechterew. Arch. f. Phys., 1884.
Ferrier. Functions of the Brain, 1886.
Fano. Quoted by Sherrington in Schäfer's Physiology, ii, p. 913.
Stefani. First Internat. Congr. Phys. Basle, 1889.
Nothnagel. Brain, 1889.
Eisenlohr. Neurol. Centralbl., 1890.
Ferrier and Turner. Brain, 1901.
Hughlings Jackson. Lond. Hosp. Rep., viii, 1875.
Ferrier and Turner. Phil Trans., 1894.
Lo Monaco. Arch. ital. de Biol., xxx, 101.
Ramon y Cayal. Structur des Thalamus Opticus. Leipzig, 1896.
Meynert. Der Bau der Grosshirnrinde, 1872.
Krause. Allgemeine und microscopische Anatomie. Hanover, 1876.
Betz. Centralbl. f. d. med. Wiss., 1881.
Leonova. Arch. f. Anat. u. Entwick, 1893.
Hammarberg. Studien über Klinik und Pathologie der Idiotie. Upsala, 1895.
Schlapp. Arch. f. Psychiat., xxx.
Ramon y Cayal. Hirnrinde des Menschen, Heft. I, Die Sehrinde. Leipzig, 1900.
Bolton. Phil. Trans., 1900.
Sanger Brown and Schäfer. Phil. Trans., 1888.
H. Munk. Die Functionen der Grosshirnrinde, 1890.
Schäfer. See Schäfer's Physiology, II, p. 757.
v. Monakow. Arch. f. Psychiatrie, xxiii, 1891; xxiv, 1892.
Henschen. Klin. u. anat. Beitr. z. Path. des Gehirns. Upsala, 1890–94.
Forster. Arch. f. Ophth., xxxvi.
Sachs. Arbeiten aus d. psychiat. Klinik im Breslau, 1895.

LECTURE II.*

THE INNERVATION OF THE PUPIL.

THE iris consists of a highly vascular membrane, the blood vessels of which are arranged radially. It also contains two muscles, composed of unstriped fibres—the sphincter and the dilatator. Of these, the former is a compact ring of muscle, situated near the pupillary margin; the latter is a thin layer of muscle, situated near the posterior surface, the constituent fibres being arranged radially. Each muscle has a separate and independent motor nerve supply.

The sphincter is innervated by the third cranial nerve, the pupil-constrictor fibres originating in the third nucleus in the floor of the aqueduct of Sylvius, passing out of the mesencephalon in the third nerve, and running in the main trunk of the nerve as far as the orbit. The fibres here pass into the branch which supplies the inferior oblique, leaving it by the short root of the ciliary ganglion. From the ciliary ganglion, they pass by the short ciliary nerves to the eye, piercing the sclerotic around the optic nerve, and forwards in the choroid and ciliary body to the iris.

The dilatator pupillæ is supplied by the cervical sympathetic nerve. The dilatator tract probably commences in the neighbourhood of the third nucleus in the mesencephalon, passing through the medulla oblongata, where its exact path is still unknown, into the lateral columns of the cord. The fibres leave the cord by the ventral roots of the first three thoracic nerves (cat, dog, ape), enter the rami communicantes, and run to the first thoracic or stellate ganglion. From here they mostly pass into the anterior limb of the annulus of

* This is an extended version of Lecture II, with an historical *résumé*, the literature upon the subject being somewhat scattered and difficult of access.

Vieussens, though some run in the posterior limb. They pass up the neck in the cervical sympathetic to the superior cervical ganglion. From here the dilator tract enters the skull by the cervico-Gasserian strand, running independently of the carotid plexus. It joins the Gasserian ganglion, and passes thence into the first or ophthalmic division of the fifth nerve, following the nasal branch, which it leaves finally to enter the long ciliary nerves, thus avoiding the ciliary ganglion. The long ciliary nerves enter the eye on each side of the optic nerve, and running forwards between the choroid and the sclerotic, pass through the ciliary body to be distributed to the iris. (See Plate I.)

These bald statements are the conclusions arrived at as the result of a vast amount of research during the latter part of last century. In many cases the results have been contradictory or apparently so, but recent work tends to establish the given statements as incontrovertible facts. There are still, however, many unsolved problems, and these are intimately bound up with the apparently contradictory results of the early experiments. No one attacking the subject afresh can afford to ignore these investigations. It will be well, therefore, to give a brief *résumé* of the evidence upon which the principal statements are founded.

The Mechanism of Constriction and Dilatation of the Pupil.—Given constrictor and dilator muscles, each with its own independent nerve supply, together with radially disposed blood vessels, it is clear that constriction of the iris may be due to any of three causes:—(1) contraction of the constrictor muscle; (2) relaxation of the dilator muscle; (3) dilatation of the blood vessels. Similarly dilatation may be due to:—(1) contraction of the dilator muscle; (2) relaxation of the constrictor muscle; (3) constriction of the blood vessels. There is ample evidence to support the view that each of these methods is actually brought into use, and that the three causes are effectual in diminishing degree in the order named.

The Dilatator Pupillæ.—Histological evidence alone has

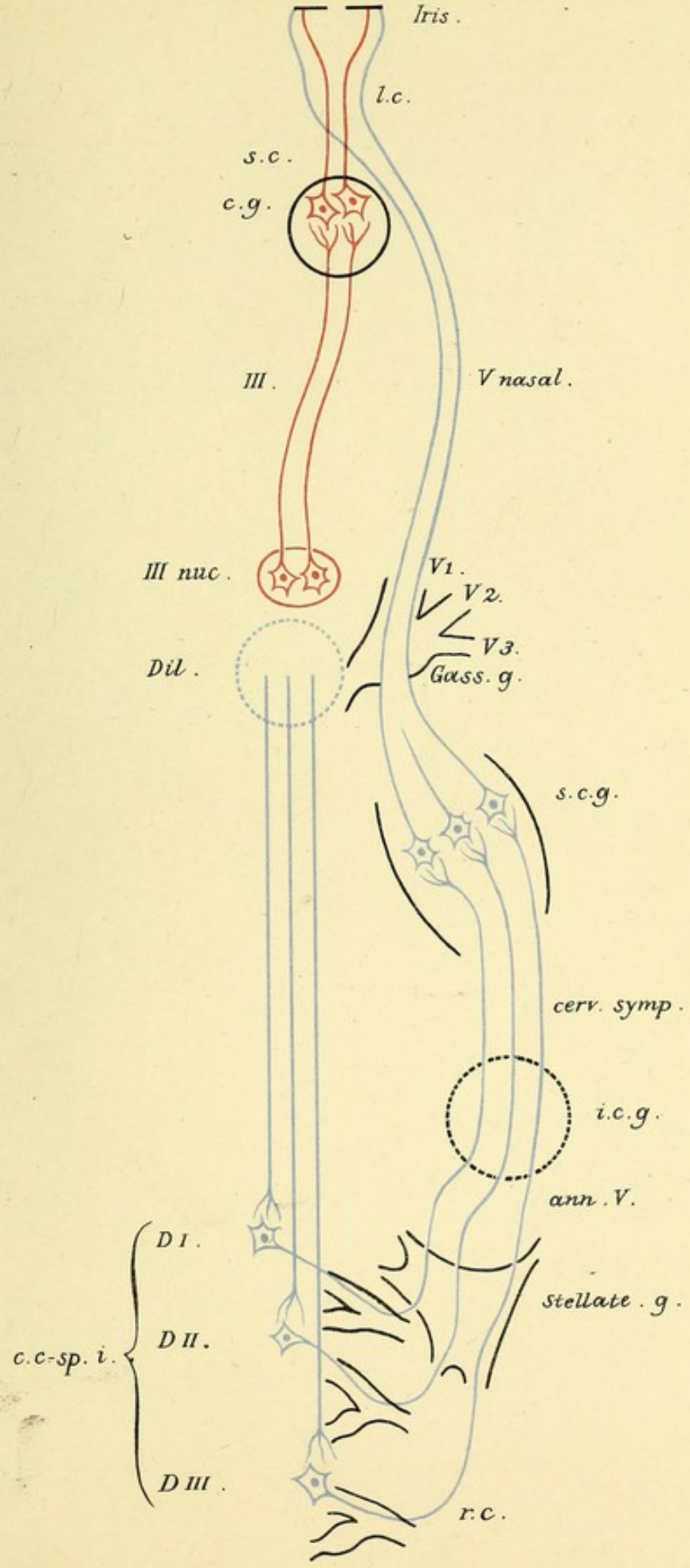
PLATE I.

The Efferent Pupillo-constrictor (red) and Pupillo-dilator (blue) Paths.

III. nuc., nucleus of third nerve; *III.* third nerve; *c.g.*, ciliary ganglion; *s.c.*, short ciliary nerves.

Dil., hypothetical dilator centre in medulla; *c.c.sp.i.*, centrum ciliospinale inferius; D I, D II, D III, first, second, and third dorsal nerves; *r.c.*, ramus communicans; *stellate g.*, stellate ganglion; *ann. V.*, annulus of Vieussens; *i.c.g.*, inferior cervical ganglion; *cerv. symp.*, cervical sympathetic; *s.c.g.* superior cervical ganglion; *Gass. g.*, Gasserian ganglion; V1, V2, V3, first second, and third divisions of the fifth nerve; *V nasal*, nasal branch of the ophthalmic (first) division of the fifth nerve; *l.c.*, long ciliary nerves.

Plate I.



Bale & Danielsson Ltd, lith.

not succeeded in demonstrating beyond cavil the existence of a dilator muscle in the iris, but taken in conjunction with the physiological evidence it must now be considered proved. The histological difficulties are to be found in (1) the proof of the presence of radial muscle fibres, other than those in the walls of the vessels ; and in (2) the interpretation of the nature of the cells forming the posterior layers of the iris.

Maunoir first stated the existence of a circular sphincter and a radial dilator. This view was supported by Valentin (1837), Krohn (1837), Bruch, Brücke, Kölliker, Henle, Luschka, Merkel, v. Hüttenbrenner, Faber, Dogiel, Hulke, Iwanoff, Jeropheeff, and others. It was controverted on the anatomical side by Arnold, Hall, Hampeln, v. Michel, Schwalbe, Koganei, Fuchs, Eversbusch, Retzius, and others. The present state of the question is that the anterior layer of retinal pigment epithelium acts as a dilator muscle (Juler, L. Müller, Gabriélidès, Grunert). On bleaching, the cells of this layer resemble in all respects unstriped muscle fibres. They stain in the same manner, and may be well demonstrated, for example, with Mallory's phosphotungstic acid hæmatoxylin after hardening in Zenker's fluid (Verhoeff). Further, Szili has brought forward evidence to show that the sphincter pupillæ is also derived from the retinal epiblast. These muscles would therefore resemble the arectores pilorum of the skin in being formed from epiblast.

The physiological evidence in favour of a distinct dilator contractile tissue in the iris is stronger than the histological, the researches of Langley and Anderson being quite conclusive. Historically it is inextricably mixed up with the vaso-motor theory, so the two are best considered together.

In 1840, Crimelli showed that injection of coloured oil into young eyes (children) caused constriction of the pupil ; and Rouget (1866) proved the same fact by injecting fluid into the ophthalmic artery. The early literature will be found in the papers of Zeglinski and Heese.

Grünhagen, in a series of papers from 1864 to 1893,

warmly supported the vaso-motor theory, whereby a diminished quantity of blood in the vessels leads to shrinkage of the iris. It is clear also that constriction of the arteries, accompanied by contraction of the longitudinal muscle fibres in their walls, may lead to dilatation of the iris by dragging the sphincter outwards (Langley and Anderson). Budge and Waller (1851) and Budge (1855) proved that dilatation through the sympathetic can occur in the absence of variations of blood supply, *e.g.*, after death. Waller (1856) showed that making the iris of a white rat bloodless by pressing upon the eye had no effect upon the pupil. Brown-Séquard (1859) found barely appreciable constriction of the pupil on injecting blood into the ophthalmic artery, though the effect is greater a day or two after death (Mosso, 1874). François-Franck (1880) obtained dilatation through the sympathetic after bleeding the animal to death.

Claude Bernard (1852), and Waller (1853) demonstrated vaso-motor nerves to the ears, etc., and Kuyper (1859) to the iris, in the cervical sympathetic. Salkowski (1867) also proved that constriction of the vessels accompanied dilatation of the pupil, Donders noting the same fact in albino rabbits, and Becker in human albinoes. Sinitzin showed that excision of the superior cervical ganglion was followed by dilatation of the vessels. Arlt. Jr. (1869) and François-Franck (1880) proved that dilatation of the iris and constriction of the vessels of the ear do not occur synchronously. Langley and Anderson (1892) proved the same fact for the iris vessels, showing at the same time that no deductions can be made as to time relations from the vessels of the ear.

There is evidence that the vaso-motor and pupillo-dilator fibres run independent paths. Bernard (1862) found in the dog that section of the first and second thoracic nerves caused dilatation of the pupil, but no vascular change in the skin of the head, whereas section of the thoracic sympathetic between the second and third ribs caused the reverse effects. Langley and Anderson (1892) showed that dilatation of the

pupils and distinct constriction of the vessels of the iris were caused by the first three thoracic nerves and by these only, but the readiness and extent of the pupillary dilatation was not proportional with the several nerves, to the readiness and extent of the arterial constriction. Schiff (1872) showed that the two sets of fibres could occasionally be isolated as separate bundles in the cervical sympathetic, and one or other effect obtained alone. Budge and Waller (1851) found that the pupillo-dilator fibres, after leaving the superior cervical ganglion, accompanied the internal carotid artery in its canal, running to the Gasserian ganglion ; whilst François-Franck (1880) showed that the superior cervical ganglion gives off two strands to the carotid canal, and the external causes dilatation of the pupil, but no increase in pressure in the peripheral end of the carotid, the other strand causes the reverse effects. François-Franck also found separation of the two tracts in the annulus of Vieussens, but these experiments are inconclusive (Langley and Anderson). Some of the short ciliary nerves cause constriction, others dilatation of the pupil, according to François-Franck, whilst neither cause variation of the retinal vessels or change in intra-ocular pressure. These experiments are also inconclusive. Jegorow (1886) found that after section of the long ciliary nerves, stimulation of the central end of the vago-sympathetic causes strong contraction of the retinal vessels, but no pupillo-dilatation, whilst stimulation of the peripheral end of a long ciliary nerve causes the reverse effect.

Waller (1856) and Vulpian (1873) noticed in the white rat that no constriction of the iridic vessels accompanies dilatation of the pupil by atropin. Langley and Dickinson (1890) showed that intravenous injection of brucin may eliminate pupillo-dilatation from the sympathetic, the vaso-constriction of the vessels of the ear still remaining, and Langley and Anderson (1892), by the same method, were able to obtain complete constriction of the vessels of the iris without any change in the size of the pupil.

Even if the relative unimportance of the vaso-motor changes be conceded, the dilatation of the pupil may be due to inhibition of the sphincter pupillæ. This possibility was announced by Grünhagen and Samkowy (1875), without further investigation, except that they showed that the tone of the sphincter can be diminished by direct stimulation, the muscle becoming elongated. François-Franck (1880) expressed the same view with some reserve, whilst Gaskell (1886), influenced largely by dubious analogies, definitely advanced the inhibitory theory. Kölliker (1855) had already obtained dilatation after removal of the sphincter, but the conditions of the experiment prevent its being accepted as positive evidence. The inhibition of antagonists on stimulation of muscles is definitely proved in many cases, and inhibition of the sphincter tone is also proved, but whether the cervical sympathetic has this property must still be considered *sub judice*, though with distinct bias to the negative. In any case it would afford no disproof of the existence of a dilator muscle.

The possibility of pupillo-dilatation as the result of relaxation of the ciliary muscle was advanced and controverted by Langley and Anderson (1892).

Most important are the experiments which definitely prove the existence of a contractile dilator mechanism. Weber first showed that stimulation of the sclerotic near the limbus caused dilatation of the pupil, whilst stimulation of the cornea was followed by constriction of the pupil. Bernstein and Dogiel (1865–67) found that the result might be varied by other arrangements of the electrodes (see Langley and Anderson (1892)); their experiments were confirmed by Engelhardt (1869).

Local dilatation can be obtained by other means. Hensen and Völkers (1868) found it on stimulating a single ciliary nerve, but this may be followed by general dilatation or general constriction (François-Franck). Jegorow (1886) obtained local dilatation in the dog from stimulation of a single long ciliary nerve; on section of all but one ciliary

nerve, subsequent excitation of the cervical sympathetic or of a sensory nerve causes well-marked local dilatation.

The effects of stimulation of the sclerotic near the cornea have been exhaustively investigated by Langley and Anderson (1892). They obtained: (1) Movement of the iris on the side opposite to local dilatation, which was of such a nature that it could not be explained by inhibition of the sphincter in the presence of radial elastic fibres; (2) local dilatation of the pupil with simultaneous local contraction of the sphincter; (3) contraction of a radial strip of the iris. They also proved the absence of any great elasticity in the iris, such as might account for some of the results on the theory of sphincter inhibition.

THE EFFERENT PUPILLO-CONSTRICTOR PATH. *The Third Nerve.*—Romberg (1851), in his text-book on "Nervous Diseases," refers to dilatation of the pupil as a symptom of paralysis of the third nerve. Budge (1851) states that constriction of the pupil follows stimulation of the third nerve in recently killed animals and man; this observation was confirmed by v. Trautvetter (1866). Schiff (1868) thought that the iris fibres were on the inner side of the trunk of the nerve, since section of the inner fibres caused paralysis of the iris movements without abrogating the movements of the globe. Hensen and Völkers (1868) found pupil constriction from stimulation of the ciliary ganglion and the short ciliary nerves; excitation of single short ciliary nerves caused local constriction, whilst section caused local dilatation. Adamük (1870) confirmed the importance of the ciliary ganglion; he further stimulated the origin of the third nerve in the floor of the aqueduct of Sylvius, and adduced evidence to the effect that the pupillary fibres passed backwards from the nucleus on their way to the trunk of the nerve. Hensen and Völkers (1878) proved that the fibres pass forwards rather than backwards, Adamük's results being due probably to stimulation of afferent fibres running forwards in the medulla to join the centre.

This course for the pupillo-constrictor fibres has been confirmed by all subsequent observers, the only discovery of importance being that there is a cell station in the ciliary ganglion. This was proved by Langley and Anderson (1892), both by the nicotin method and by the degeneration method. If the third nerve is cut within the skull, many degenerated fibres are found running to the ganglion, but none peripherally of it (Apolant, 1896). The preganglionic fibres running from the third nerve to the ciliary ganglion are mostly small medullated fibres. The postganglionic fibres running in the short ciliary nerves are three or four times as numerous as the preganglionic ones, and also consist chiefly of small medullated fibres. These facts were stated by Bidder and Volkmann (1842). These autonomic (Langley) postganglionic fibres differ, therefore, from the rule which applies, though with many exceptions, to the postganglionic fibres of the sympathetic system in being medullated.

Further proof of the origin of the postganglionic pupillo-constrictor fibres in the cells of the ciliary ganglion is afforded by the Nissl method. This method is extremely delicate, but demands the greatest care in the interpretation of the results. In this case it gives valuable confirmatory evidence; in others the conclusions deduced from it must be accepted with reserve. There is even considerable divergence of opinion in the results of experiments upon the ciliary ganglion. Thus Bach (1899) found that nearly all the cells were degenerated after excision of the iris and ciliary body; none when the cornea was removed. Marina (1899–1901) found degeneration from destruction of the cornea, but much more after iridectomy. Bumm (1902) counted the cells, and found the normal average to be 6432. After cutting the ciliary nerves, 3854 remained unaffected; after excising the superior cervical ganglion, the cells were reduced to 2587. The latter result may be due to the removal of afferent impulses (*cf.* Warrington).

Paradoxical Pupillo-Constriction.—Under ordinary con-

ditions the pupillo-constrictor centre emits tonic impulses, so that when these are cut off by section of the constrictor path in any position the pupil becomes slightly larger than normal. It has occasionally been observed that the pupil is smaller than normal; this is called paradoxical pupillo-constriction. It has been less frequently seen than paradoxical pupillo-dilatation, to which reference will be made later.

Paradoxical pupillo-constriction has been investigated by Anderson (1902), only an abstract of his results having been as yet published. He found that after excision of the left ciliary ganglion and section of the right third nerve proximally of the ganglion in a kitten, the two pupils were equally dilated until regeneration occurred on the right side 8 days later. In a cat the right pupil continued to be widely dilated 38 days after division of the right short ciliary nerves. Under certain circumstances, however, the pupil on the side of the excision was smaller, *e.g.*, in the cat the right pupil was smaller in dim light than the left after local application of eserin to both eyes in equal quantity; and 18 days later the right pupil was smaller after the death of the cat.

In another cat the left pupil immediately after excision of the left ciliary ganglion was very widely dilated, but next day the left pupil had become slightly smaller, and was smaller than the right in dim light if the cat became restless under observation. On the same day after administration of ether and section of both cervical sympathetic nerves the left pupil became a slit, though the right was almost maximally dilated, and for 48 hours after death the left pupil remained much smaller than the right.

In other observations made 2 and 318 days after denervation of the sphincter on one side, the pupil on the side of the lesion was smaller after the death of the animal, though previously it had been the larger since the denervation.

Anderson concludes that the paradoxical pupillo-con-

striction is due to increased excitability of the denervated sphincter, the exciting stimuli in the observations mentioned being alterations in the blood supply, eserin, and probably ether (see, however, the observations on paradoxical pupillo-dilatation).

THE EFFERENT PUPILLO-DILATOR PATH.—Investigations on the pupillo-dilator path have been attended with more ambiguous results than those on the constrictor path.

The Cervical Sympathetic Nerve.—Parfour du Petit (1727) first showed that section of the cervical sympathetic was followed by constriction of the pupil upon the same side, as well as by other symptoms which do not concern us here. The observation was confirmed by Molinelli (1755), Arnold, Stilling and others. Valentin pointed out that section caused a short and transitory dilatation of the pupil, followed by constriction which remained permanent. Serafino Biffi (1846), repeated Petit's experiments and confirmed them, and further supplemented them by showing that stimulation of the sympathetic causes dilatation. Reid (1848) isolated the sympathetic from the vagus fibres in the cat and showed that only the sympathetic caused dilatation of the pupil on stimulating the peripheral end.

Budge (1851–55) first seriously attacked the problem of the innervation of the pupil, and it is only within the last few years that anything of importance has been added to his results, though they have been corrected in details. He found that if the spinal cord between the sixth cervical and the fourth thoracic vertebræ is isolated by transverse section above and below, then stimulation of this area causes dilatation of both pupils, which is abrogated on one side if the corresponding sympathetic is cut. Stimulation of the cord above or below this region caused no effect. Hence Budge concluded that there was a centre for the dilatation of the pupil here; he called it the *centrum cilio-spinale inferius.* He also traced the dilator fibres from this centre to the cervical sympathetic, showing that they leave the cord by the anterior roots of the seventh and eighth cervical

and first and second thoracic nerves; Budge also described a *centrum cilio-spinale superius*, which he thought was in the region of the nucleus of the hypoglossal nerve. He thought that the superior cervical ganglion received pupillo-dilator fibres directly from this centre as well as from the inferior one through the sympathetic. The experiments upon which the idea was founded are open to another interpretation, and afford no evidence of a superior centre. Schiff (1855) confirmed Budge's results, but opposed his idea that the centrum cilio-spinale inferius was an automatic and independent centre. He gave good evidence to show that it was under the control of impulses descending from above, so that hemisection of the cord above the fourth cervical vertebræ caused constriction of the pupil on the same side and the other effects of cutting the sympathetic. He therefore considered that the superior centre alone was automatic.

The complete demonstration of the dilator path was intimately bound up with the discovery and investigation of the sensory pupillary reflex, which must, therefore, be referred to in this connection. Chauveau (1861) discovered that dilatation of the pupil followed excitation of the posterior columns of the cord; this only occurred with the intact cord in his experiments. (It had long been known that pupil dilatation often occurred in trigeminal neuralgia (Notta, 1854)). Claude Bernard (1862) first showed that excitation of the central end of any sensory nerve caused dilatation of the pupil; he found that the effect was abolished by section of the anterior roots which are known to carry the pupillo-dilator fibres.

Balogh (1861) noticed dilatation during asphyxia, even if the superior cervical ganglion had been removed. Stimulation of the trunk of the fifth nerve, or of the Gasserian ganglion, or of the ophthalmic division of the fifth, caused dilatation. If the trunk of the fifth nerve was cut, stimulation of the medulla caused no change in the pupil. He therefore arrived at the deduction that the fifth, nucleus is the upper centre for the dilator fibres, and that the dilator

fibres all pass through the Gasserian ganglion and thence into the ophthalmic division of the fifth.

Oehl (1862) obtained dilatation of the pupil from the first division of the fifth after excision of the superior cervical ganglion; there were no dilator fibres in the trunk of the fifth nerve. Hence he concluded that the dilators arise in the Gasserian ganglion—an erroneous deduction. Guttman (1864) supported this view; he opposed the medullary centre and found slight pupillo-constriction after dividing the fifth just proximal to the Gasserian ganglion.

Salkowski (1867) confirmed Budge's experiments and supported the view of the medullary centre, which he found to be the reflex centre for the sensory stimuli. He asseverated the existence of a single pupillo-dilator path from the medulla through the centrum cilio-spinale inferius to the cervical sympathetic.

Nawalichin (1869) confirmed Balogh's results and fell into several errors:—he found that the sensory reflex was eliminated by section of the cord above the spinal centre of Budge; and also that the sympathetic is not the only dilator tract. The latter view was founded upon two chief observations: (1) if the cord is cut at the level of the third cervical vertebra, stimulation of the upper cut end causes dilatation; (2) if the cord is cut below the medulla, asphyxia still causes pupillo-dilatation. Both of these observations are correct, but they are open to other interpretation. Vulpian (1874) also thought that the trunk of the fifth nerve contained dilator fibres, both from his experiments in which it was cut, and also because the sensory reflex from the sciatic nerve persisted after extirpation of the superior cervical and stellate ganglia.

Hurwitz (1878) repeated Vulpian's experiments and performed two new ones which are of some importance. If the superior cervical ganglion was removed, then after at least 120 hours' interval it is found that direct stimulation of the iris of the atropinised eye of a curarised animal causes not the slightest trace of dilatation. If the sympathetic is cut

a few days before stimulation of a sensory nerve, pupillo-dilatation is not abolished but is slower in onset and more prolonged.

Schiff and Foa (1874) devoted special attention to the sensory reflex, and found that the pupil may be regarded as an æsthesiometer. They confirmed Chauveau's result that the afferent path runs in the posterior columns of the cord, adding also the grey matter; they obtained no sensory reflex after section above or below the medulla.

François-Franck (1878–80) made an exhaustive investigation of the whole subject. The results which concern us here are as follow. From the fact that section of the trunk of the fifth nerve is followed by constriction of the pupil, he concluded that that nerve contains dilator fibres. He also found dilator fibres in the vertebral nerve. He showed that the dilators pass by the rami communicantes of the fourth cervical to the sixth or seventh thoracic in cuts to the thoracic sympathetic. Thence they pass into the stellate ganglion, and from there, by the anterior limb of the annulus of Vieussens, to the cervical sympathetic. He found no pupillo-dilators in the posterior limb of the annulus, but this is untrue (Langley and Anderson). The sympathetic receives no other dilator fibres in the neck. All the ciliary nerves are pupillo-constrictors with the exception of two or three. The short ciliaries cause rapid constriction, whilst the long ciliaries cause slow dilatation. Extirpation of the stellate, or of the superior cervical ganglion, causes greater dilatation of the pupil than simple section of the sympathetic nerve; hence he concludes that these ganglia exert a tonic influence over the irido-dilator mechanism. Guillebeau and Luchsinger (1880) ascribed the dilatation from the vertebral nerve to sensory fibres contained in it.

Luchsinger (1880) supported the view that the inferior cilio-spinal centre is automatic. He obtained the sensory reflex after section of the cord, if the excitability is increased by picrotoxin or strychnin. Tuwim (1881) failed to obtain dilatation from sensory stimuli after cutting the cord. He

confirmed the discovery of François-Franck that the superior cervical ganglion exerts a tonic influence; he found the pupil smaller on the side in which the ganglion was extirpated than on the side in which the sympathetic was cut. Guillebeau and Luchsinger (1882) obtained the sensory reflex in young cats after section of the cord without artificially increasing the excitability of the cord, and this result was also found in cats by Ott (1882).

Sheglinski (1885) showed that the pupillo-dilators in birds run in the first division of the fifth. They do not run in the cervical sympathetic. This statement was controverted by Grünhagen, but has been substantiated by Langley (1903). It was also confirmed by Jegorow (1886), who found vaso-motor fibres in the sympathetic, but no pupillo-dilators. This observer also confirmed the course of the dilators in mammals in the ophthalmic division of the fifth, and in the long ciliary nerves.

Bellarminow (1886) first used the photographic method for recording the pupillary movements. He distinguishes between (1) direct (sympathetic) dilation and (2) reflex dilation. The latter occurs whether the sympathetic is intact or not. He found that the pupil varies independently of the blood pressure or the intraocular pressure.

Katharina Schipilow (1886) traced the dilators in the frog. She found no difference between cutting the sympathetic and excising the sympathetic ganglia.

Nawrocki and Przybylski (1891) found that in cats the dilators leave the cord by the ventral roots of the eighth cervical and first and second thoracic nerves. The fibres do not pass through the ciliary ganglion, but enter the long ciliary nerves. These authors also admit a cranial dilator path, though they deny the presence of dilators in the vertebral nerve. There is a centre in the brain, but there are no sufficient grounds for supposing that there is an inferior cilio-spinal centre.

Braunstein (1894) re-investigated the whole subject in an extremely careful research, using Bellarminow's photo-

graphic method. He found the dilator fibres in the rami communicantes of the seventh and eighth cervical and first and second thoracic nerves of the cat. He found no dilators in the posterior limb of the annulus of Vieussens. Above the superior cervical ganglion the dilators run in a special branch, separate from the carotid branches, to the Gasserian ganglion. Stimulation of a long ciliary nerve caused partial dilatation (as opposed to general dilatation found by François-Franck and Bellarminow).

The pupillo-dilator fibres in the cervical sympathetic end around the cells in the superior cervical ganglion. This has been proved by the degeneration method by Waller and Budge (1851-53), and by the nicotin method by Langley and Dickinson (1899–1900).

Langley (1892, sqq.) found the dilator fibres in the first three thoracic nerves. In the cat and dog the third has much less effect than the other two; in the rabbit, and apparently in the ape, the third may have a greater effect than the first, but never so great an effect as the second. It has already been mentioned that Langley and Anderson (1892) found dilator fibres in the posterior limb of the annulus of Vieussens, as well as in the anterior limb, though they were not so numerous.

The preganglionic fibres of the cervical sympathetic, including, therefore, the pupillo-dilator fibres, consist of fine medullated fibres. The postganglionic fibres in the branches from the superior cervical ganglion consist for the most part of non-medullated fibres. Degeneration of these fibres has been specially investigated by Tuckett (1896).

By the Nissl method, according to Marina, some of the cells of the superior cervical ganglion degenerate when the ciliary nerves are cut.

The Fifth Nerve.—We have already seen that several observers considered that there were pupillo-dilator fibres in the fifth nerve. Magendie (1824) first proved that section of the fifth within the skull in the rabbit caused constriction of the pupil. This was denied by Longet

(1842). Valentin and Claude Bernard showed that the effect was transitory, whilst the effect of section of the ophthalmic division of the fifth was lasting. Balogh, Nawalichin, Vulpian, and François-Franck all confirmed the presence of dilators in the trunk of the fifth. Schiff (1867) thought they were sympathetic fibres from the cavum tympani. Rembold (1880) agreed with Schiff that the tone of the dilator was kept up by afferent sensory stimuli, explaining thereby the miosis which follows section of the fifth. In order to explain the constriction caused, according to several authors, by excitation of the trunk of the fifth, he considered it probable that there were actually pupillo-constrictor fibres in the fifth nerve. Eckhard (1892) also thinks that there are constrictors in the fifth.

It is unnecessary to enumerate all the authors who consider that there are dilators or constrictors in the trigeminal. Braunstein and Hurwitz may be held to have proved their absence. Further, Langley could not obtain local dilatation of the pupil from stimulation of the sclerotic after excision of the superior cervical ganglion some time before, and Anderson failed to obtain it even on stimulating the iris under the same conditions. Other observers, amongst them myself, have failed to obtain any movement of the pupil after section of the third nerve and the cervical sympathetic. It may, therefore, be considered definitely proved that all the dilator fibres run in the cervical sympathetic.

Paradoxical Pupillo-Dilatation.—Paradoxical pupillo-dilatation is the antithesis of paradoxical pupillo-constriction. "Section of the cervical sympathetic causes constriction of the pupil, and simultaneous removal of the superior cervical ganglion on the other side causes slightly greater constriction, as first shown by Budge, but in certain circumstances the pupil on the side without the ganglion becomes larger than the pupil on the side with the nerve alone cut. This greater dilatation on the more paralysed side has been called parodoxical pupil-dilatation by Langendorff. Moreover, if only a superior cervical ganglion be excised, the pupil on the

paralysed side may nevertheless become larger in certain circumstances than the normal pupil. This is also spoken of as paradoxical dilatation." (Anderson.)

Budge (1855) first called attention to the occurrence of paradoxical pupillo-dilatation. After section of the left sympathetic and of the branches above the right superior cervical ganglion in a young rabbit he found the right pupil smaller than the left ½ hour later, equal after 24 hours, and the right larger than the left after 48 hours. Schiff (1868) observed the effect after section of the sympathetic, and after excision of the ganglion; he connected the phenomenon with oxygenation of the blood after previous asphyxiation. Surminski (1869) and Tuwim (1881) observed it after atropin. Kowalewski (1886) saw it in a kitten after the administration of chloroform. Braunstein (1894) observed it after curare; and Tuckett (1896) incidentally in the course of another research. Langendorff (1900) investigated the subject specially, and noticed the phenomenon after anæsthetics and after death. Lewandowski (1900) also called attention to these paradoxical effects, and showed that they could be produced by dyspnœa. It was also observed incidentally by Langley (1901) and Levinsohn (1902).

The subject has been exhaustively investigated recently by Anderson (1903). He proved that the effect might be observed as soon as 1 day after the lesion, and as long as more than a year. Excitement, dyspnœa, anæsthesia, death, are conditions which evoke the effect. It is produced much more readily by slight dyspnœa in kittens than in cats. The paradoxical effect persists even when the postganglionic branches of the ganglion have been allowed to regenerate. Immediately after removal of the ganglion on one side, and section of the sympathetic on the other, there is always greater paralysis on the side without the ganglion. Later there is frequently greater paralysis on the side with the nerve cut, but if sufficient care is taken to insure a quiet condition of the cat, the signs of greater paralysis are often transferred to the side without the ganglion.

In the quiet condition of the cat the evidence is therefore often against the views (1) that the sphincter is weakened on the side without the ganglion (Budge, Tuwim, Levinsohn), or (2) that there is permanent contracture of the vessels of the iris, or dilatation on this side (Surminski, Langendorff), or (3) that on the side with the ganglion the dilator is inhibited (Kowalewski).

After the local application of eserin to the eyes of a kitten the pupil is smaller on the side from which the superior cervical ganglion has been removed so long as the kitten is quiet, but slight dyspnœa will cause the pupil to become almost maximal though the normal control pupil is very small. A similar result may be obtained when the sphincters are contracting strongly in bright light instead of under the influence of eserin.

This paradoxical pupillo-dilatation must therefore result from an actual increase of tone in the dilator on the side without the ganglion. This increase of tone may be directly demonstrated in the nictitating membrane and lids. The paradoxical effect is therefore due to an increased excitability of the contractile tissues on the side without the ganglion (Lewandowski, Anderson).

The great accentuation of the paradoxical effect seen under anæsthesia does not occur until dyspnœa arises. If only the sympathetic has been cut, the paradoxical effects occur much later, and are much less pronounced.

The paradoxical effects show that the ganglion cannot inhibit the automatic excitability of the contractile tissues with which it is still in connection.

Bright light cannot inhibit the paradoxical dilatation through the third nerve, since the effect will still persist in bright sunlight for more than a minute.

Inhibition of Antagonists.—It is known that in the case of the skeletal muscles contraction of a given group is accompanied by simultaneous active relaxation of the antagonistic group (Sherrington). By analogy, therefore, it is not improbable that constriction of the pupil through the

third nerve should be accompanied by simultaneous active inhibition of the dilator, also carried out through the third nerve by means of inhibitory dilator fibres. And, indeed, Waymouth Reid (1895), from consideration of the electrical phenomena occurring during contraction of the sphincter, concluded that this actually happened. Anderson (1903), however, has brought forward strong arguments against this view. Thus, using bright light as a stimulus to contraction of the sphincter, it is found that the paradoxical dilatation may arise and continue for more than a minute in bright sunlight; and further, under the same conditions, a difference between the two pupils caused by paralysis of one dilator is not diminished, but increased by brighter illumination of the eyes. Neither of these observations is consistent with inhibition of the sphincter through the third nerve.

The iris is not under the control of the will, hence these motor nerves are invariably set in action indirectly, either by reflex stimuli, or by what I shall call *synkinesis, i.e.*, association with other voluntary or involuntary movements.* There are two chief reflexes, and two chief synkineses or associated movements. (1) The Light Reflex; (2) The Accommodation Synkinesis; (3) The Sensory Reflex; (4) The Cerebral Synkinesis.

THE LIGHT REFLEX is carried out entirely through the mechanism of the constrictor centre. Of the afferent paths we know very little for certain. The fibres are contained in the optic nerve, and they arise from all parts of the retina. The optic nerve contains large and small fibres; it is possible that the large fibres are concerned with visual sensations, and that some of the fine ones are afferent pupillo-constrictor fibres. The opposite view has also been advanced. It is certain that the pupillary fibres undergo partial decussation

* The corresponding term for the association of ideas, or an associated idea, would obviously be *synpsychosis*.

in the chiasma, and enter the optic tracts. It is also certain that they do not enter the lateral geniculate body, but leave the tract to pass by a path which is as yet conjectural to the third nucleus. The tone of the constrictor centre is kept up by constant afferent impulses along this tract; it is possible that it also possesses inherent tone. The tone is probably continually depressed by less effectual impulses along the fifth and other sensory nerves.

There are two types of light reflex, viz., that through the retina of the same side, or the direct reflex, and that through the retina of the opposite side, or the consensual reflex; *i.e.*, light falling upon the retina causes constriction of the pupil —a direct reflex, but it also causes constriction of the opposite pupil—a consensual reflex.

Lambert (1760) found that the constriction increased with the area of the retina which was stimulated. E. H. Weber (1851) found that it was stronger the nearer the affected part lay to the macula, and was strongest of all when the luminous body was the object of fixation.

Herbert Mayo first obtained constriction of the pupil from experimental stimulation of the optic nerve. Flourens (1824) placed the reflex centre in the corpora quadrigemina, a view concurred with by Longet, Budge, and others. Knoll (1869) showed that the whole anterior colliculus might be destroyed without preventing the light reflex. This was confirmed by v. Bechterew (1884) and others—recently by Ferrier and Turner (1901).

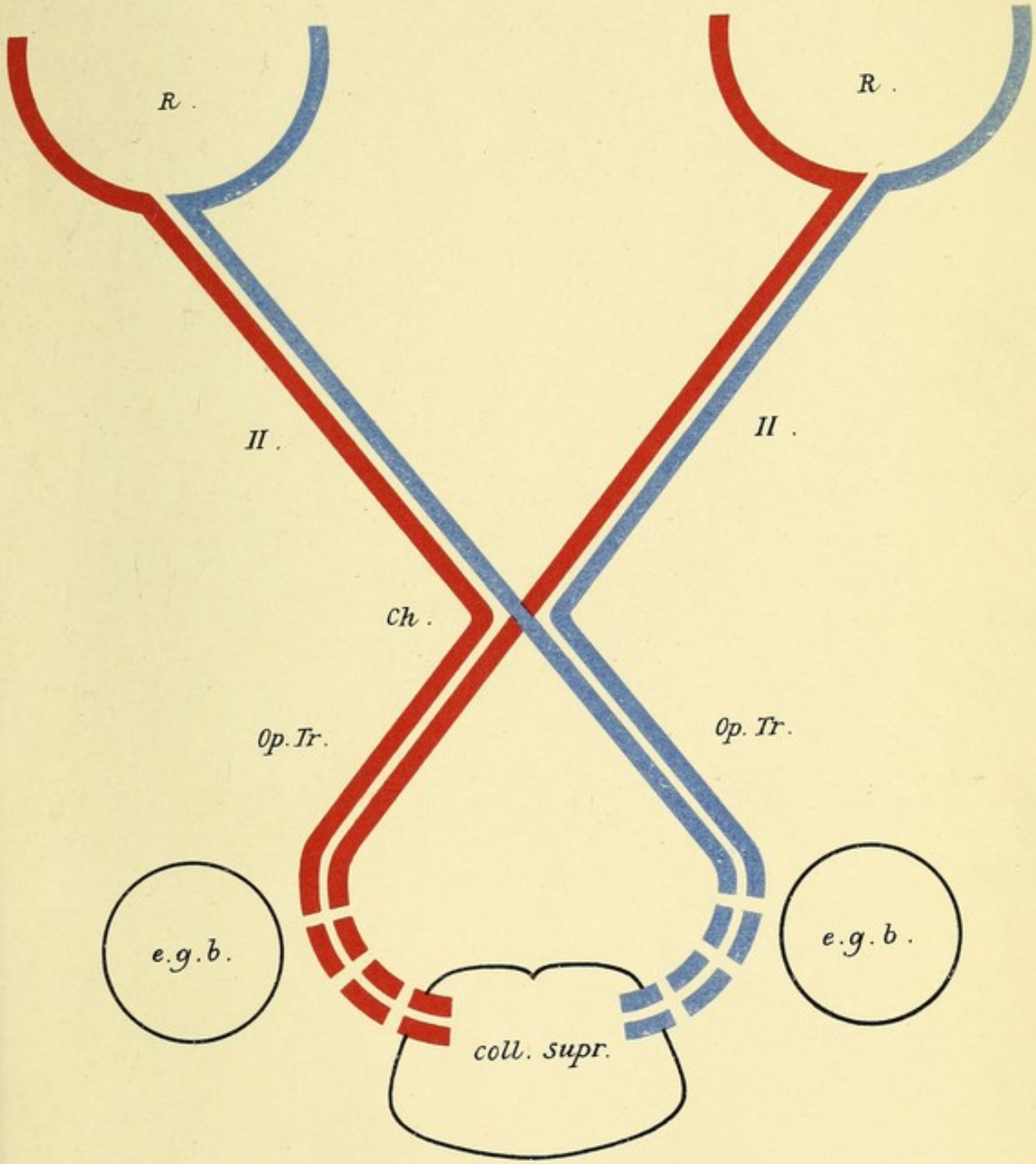
The Afferent Pupillo-Constrictor Path (Plate II).—The fact that, like the afferent visual fibres, the afferent pupillo-constrictor fibres undergo partial decussation in the chiasma is proved by the hemiopic pupil reaction of Wernicke. This observer found that any lesion which destroyed one optic tract caused loss of the light reflex on stimulation of the corresponding halves of both retinæ, whilst stimulation of the opposite halves gave the normal reaction. Attention was called to the fact that the pupillary and visual paths are not identical by the effects of destruction of the superior

PLATE II.

The Afferent Pupillo-constrictor Path.

R., retinæ; *II*, optic nerves; *Ch.*, chiasma; *Op. Tr.*, optic tracts; *e.g.b.*, external geniculate bodies; *coll. supr.*, superior colliculus or anterior quadrigeminal body.

Plate II.



Bale & Danielsson Ltd lith.

colliculi, and this was confirmed by the effects of destruction of the lateral geniculate body. I have in the first lecture given additional evidence that the visual fibres divide, probably more frequently than has hitherto been supposed. It is not improbable that the pupillary reflex is carried out by means of collaterals.

In any case, destruction of the lateral geniculate body does not abolish the light reflex (v. Bechterew, Henschen and others). Hence the pupillary fibres leave the tract before it reaches the geniculate body. Bogroff and Flechsig (1886) describe a tract passing directly into the stratum griseum centrale of the third ventricle. According to an earlier view of v. Bechterew (1883), the fibres do not enter the optic tract, but pass into the grey matter of the third ventricle close behind the chiasma. Such a view is negatived by the Wernicke reaction, and has apparently been abandoned by v. Bechterew (1900); he now thinks they leave the optic tract at the level between the corpus cinereum and the root fibres of the third nerve, *i.e.*, near the entrance of the optic tract into the geniculate body, running thence to the posterior part of the third ventricle, where they make connections with cells which send axones to the third nucleus of the same side.

Darkschewitsch (1886) thinks that the pupillary fibres leave the optic tract near the geniculate body and pass through the thalamus to the ganglion habenulæ. Thence fresh fibres pass through the posterior commissure to his obere Oculomotoriuskern. This, however, has been shown by v. Bechterew and others to have nothing to do with the third nerve. His results have been supported on comparative anatomical grounds by Bellonci, and also by Mendel.

The evidence is in favour of the afferent pupillo-constrictor fibres making new connections before reaching the third nucleus. Bernheimer (1899), however, thinks that they pass direct to the third nucleus, but Bach (1900) was unable to confirm his results. It must be admitted that the question is by no means settled. It seems most likely that

the fibres pass through the superior brachium into the superior colliculus, there making new connections with cells which convey the impulses to the third nucleus of the same and also of the opposite side. This view is held by Barker, and is probable from the histological researches of Held. It would account satisfactorily for all the facts, including both the consensual reaction and the hemiopic pupil reaction. The effects of extirpation of the superior colliculus are not necessarily fatal to this theory. It is most probable that the afferent pupillary fibres end in the lateral part of the colliculus, and this may quite easily have escaped destruction in experiments in which it is so important that the lesion should be strictly localised.

The Pupillo-Constrictor Centre.—I do not intend to attempt in this lecture to unravel the tangle of speculations as to the reflex pupillary centres. The number of these centres which have been described and localised by various writers, each with the utmost assurance, is bewildering in the extreme. To name only a few, we have several constrictor centres, several dilator centres, not to mention various cortical and sub-cortical centres of each kind, and finally Bach has added to the confusion by hypothecating an inhibitory constrictor, and even in his last paper an inhibitory dilator centre. The explanation is to be found in wild theorising upon quite inadequate data, and much of this is due to the use of the unfortunate term "centre." One is inclined to wish that this term might be abolished from neurology, so great is the ambiguity and confusion to which it has given rise. The intercommunications between the cells of the central nervous system are so complex that there are almost innumerable alternative paths whereby any given group of efferent cells may receive excitatory impulses. Our aim should be, first to determine the efferent cells governing any given movement, second to determine as far as is possible which are the afferent tracts which can lead directly or indirectly to those cells, and third to find out *how* each of those afferent tracts leads to the efferent cells. The last

problem is the most difficult, and we shall find that many of the afferent tracts are very devious, and have many cell-stations on their way. Each of these may be dignified with the title "centre," or better, none of them.

There are one or two points, however, which must be mentioned in spite of the obscurity of the subject. We have seen that the third nerve contains all the constrictor fibres for the iris. We have reason to believe that the light reflex is an active constrictor effect and not an inhibitory dilator effect; for, seeing that probably both centres exert a tonic influence, it is obvious that the result might arise from either of these causes. If this reasoning is sound, the only true centre for the light reflex is the part of the nucleus of the third nerve which gives rise to the pupillo-constrictor fibres. Most authors are inclined to agree that this is the Edinger-Westphal nucleus, which consists of small cells occupying the median part of the third nucleus. It may be subdivided into two parts, an anterior paired nucleus and a posterior unpaired nucleus. The former, according to Bernheimer, contains the pupillo-constrictor cells.

This view is not universally adopted, and there are still some—chiefly neuro-pathologists (*e.g.*, Sacki and Schmaus, Schaffer), who adhere to the inhibitory dilator theory, or a modified form of it. Argyll Robertson (1869) must be considered principally responsible for this view, which he held best explained the pupil phenomenon which bears his name. Pathological evidence in favour of it has been collected by Wolff (1899), and it has received some support from the (inconclusive) experiments of Bach, Ruge and others.

Marina (1901–3) thinks that the ciliary ganglion is the centre for the light reflex, and he brings forward some ingenious experiments to prove his point. They cannot, however, be considered conclusive.

Very conclusive evidence in favour of the supreme importance of the third nucleus in the light reflex is afforded by the fact that variations in illumination have no effect on the pupil after section of the third nerve (Braunstein and others).

Anderson (1903) points out the necessity for care in eliminating all tactile and other sensory reflexes in these experiments. They prove that the light reflex is entirely through the pupillo-constrictor mechanism, and that inhibition of the dilator tone plays no part. This is additional evidence that the sphincter and dilator do not follow the law of contraction and relaxation of antagonists (see p. 46).

THE ACCOMMODATION SYNKINESIS is a constrictor effect commonly associated with accommodation. It is more nearly related, however, to the convergence which normally synchronises with accommodation, since it is possible to accommodate without inducing constriction of the pupil, whereas this invariably occurs during convergence. Very little is known about this phenomenon; even the views stated are open to doubt, but there can be no doubt that it is not a true reflex, but a case of associated movement. The same remark applies to the well-known lid-closing phenomenon.

The accommodation synkinesis has been known since Scheiner (1619). The efferent fibres for accommodation were investigated by v. Trautvetter (1866), Hensen and Völkers (1868, 1878), Kaiser (1868), Adamük and Woinow (1871), and others. Adamük and Woinow found that the pupillo-constriction was not proportional to the distance of the point of fixation. Olbers (1780), on the other hand, had already shown that it was proportional to the angle of convergence, and E. H. Weber (1851) proved that constriction of the pupil occurred on convergence without accommodation, but not on accommodation without convergence; this can be shown by the use of prisms. Hering (1868) devised an experiment for showing that constriction of the pupil also occurs on accommodation without convergence, but Verwoort (1899) thinks that this was due to imperfect exclusion of convergence.

Adamük (1870) obtained depression of the eyes, strong convergence, and pupillo-constriction on stimulating the posterior part of the anterior colliculus in dogs and cats,

similarly convergence and pupillo-constriction from the floor of the aqueduct. These results were confirmed by Hensen and Völkers (1878), and the intimate association of the pupillo-constriction with the internal rectus was further demonstrated.

Henke (1860) put forward the view that the reverse effect, relaxation of accommodation for distance, was accompanied by active dilatation through the sympathetic. However this may be, Hensen and Völkers found that stimulation of the slightly more lateral sixth nucleus was accompanied by some pupillo-dilatation. This is probably an active pupillo-dilator *divergence synkinesis.*

Curious cases are on record in which pupillo-constriction accompanied outward movements of the eye (Adamük, Weiss, Sichel, v. Graefe, Schiff).

The Sensory Reflex is a dilator reflex induced by tactile, pathic and other sensory stimuli. It is a complex effect exhibiting a primary rapid dilatation due to augmentation of the dilator tone through the cervical sympathetic, followed by a second dilatation, rapid in onset but very slow in its disappearance, due to inhibition of the constrictor tone. When originated through spinal sensory nerves, the afferent impulses are carried up in the posterior columns of the cord.

In dealing with the course of the pupillo-dilator path we have seen that Chauveau (1861) first obtained the sensory reflex experimentally by stimulating the posterior columns of the cord. He found that if the cord was cut above the inferior cilio-spinal centre the effect was abolished, except in one experiment on an ass, in which a very small effect was produced. Claude Bernard (1862) showed that the sensory reflex might be obtained on stimulation of the central end of any sensory nerve.

Reference has already been made in the same section to the work of Salkowski (1867), Balogh (1869), Hurwitz (1878), Schiff and Foa (1875), François-Franck, Luchsinger, Bellarminow, and Braunstein. Balogh (1861), however, was

the first to obtain the sensory reflex after section of the ordinary dilator path in his experiment after excision of the superior cervical ganglion. Hurwitz, as we have seen, found that the effect was very slow after the cervical sympathetic had been cut. Vulpian (1878) observed reflex dilatation after removal of both the superior cervical and stellate ganglia. v. Bechterew (1883) contended that the sensory reflex was entirely due to inhibition of the light reflex, *i.e.*, of the tonic action of the third centre. He based this view largely upon the findings of neuro-pathology, the light and pain reflexes being almost invariably abolished together. He also supported it by further experiments. Thus, if one optic nerve is cut, no further dilatation was caused in the eye of that side by pathic stimuli unless the opposite eye was open, and contraction thereby excited consensually in the sphincter on the side of the lesion. Secondly, the dilatation was inconsiderable when the eyes were examined in a dim light. Thirdly, the degree of dilatation did not exceed that which followed the withdrawal of the light. These experiments were confirmed by Mayer and Pribram (1884), and later by Braunstein (1894). The last-named author found that after section of the third nerve inside the skull, stimulation of the central end of the sciatic nerve with strong and weak currents at periods varying from 12 days to 7 months after the operation caused no reflex movements of the pupil. He observed no change in the size of the pupil between the operation and the final experiment, though during the latter he obtained dilatation from stimulation of the cervical sympathetic.

The subject has received attention from this point of view recently by Anderson (1903). As the result of five experiments in which the pupillo-constrictor tract was divided in some part of its course, he found that well-marked dilatation could be obtained by stimulating the sciatic nerve, pinching the skin, or stroking the hairs. The effect was accompanied by all the usual effects of exciting the cervical sympathetic, and all were abolished if this was cut in addition to the third nerve.

The converse aspect of the subject has also been disputed. Luchsinger (1880) and Guillebeau and Luchsinger (1882) obtained the sensory reflex after the cervical cord had been cut above the inferior cilio-spinal centre. Kowalewski (1886) failed to obtain this result, and similarly Braunstein. Anderson obtained a positive result in the only experiment specially directed to the point; the effect was slow, and was accompanied by slight retraction of the nictitating membrane and eyelids. Second stimulation was ineffectual unless an interval of some minutes was allowed to elapse. The effect continued after destruction of the brain and medulla, and hence cannot have been due to inhibition of constrictor tone.

Anderson considers that the ordinary sensory reflex is of two-fold origin:—(1) reflex augmentation of the dilator tone, causing relatively rapid and short dilatation; (2) reflex inhibition of the constrictor tone, causing a second rapid dilatation which only slowly and gradually subsides.

Hippus.—Anderson makes a valuable contribution to the obscure question of hippus. He found that this occurred not uncommonly after section of the third nerve, but ceased immediately on cutting the sympathetic. It was excited by tactile stimulation, or by a certain state of anæsthetisation. It might be accompanied by rhythmic movements of the eyelids and nictitating membrane.

The Cerebral Synkinesis is also a complex phenomenon, and cannot be considered a simple reflex. It is induced by psychic stimuli, *e.g.*, fear, etc., and also by concentration of thought upon a bright light or a dark room. It is also largely an associated movement, accompanying eye movements which may be themselves due to sensory impulses.

The pure psychic reaction, entirely caused by ideas of light and shade, was described by Haab (1886), though Beer had long before discovered that he was himself able to alter the size of his pupils in this manner; it may account for some cases in which persons have apparently been able to alter their pupils at will. The phenomenon is unaccompanied

by any obvious movement of the eyes, and, therefore, cannot be called a synkinesis ; it is, in fact, a *psycho-kinesis.* The reaction has recently been called in question by Bumke (1903), and it must be admitted that it is very difficult to exclude the many sources of error, of which accommodation is the most probable and difficult to avoid.

I propose now to discuss in detail my observations on the relationship of the cerebral cortex to the movements of the pupil.

Fontana, as long ago as 1770, showed that in the cat, even under the strongest light stimulus, the pupils dilated widely if the animal was frightened by a loud noise. A child's pupil can also be made to dilate, even during ophthalmoscopic examination of the macula, by a loud sound, such as clapping of the hands. Raehlmann and Witkowski consider that psychic impulses assist in maintaining the tone of the dilator centre, accounting for the constriction of the pupil during sleep by their absence.

Schiff and Foa (1869) first stimulated the cerebrum by electricity, and obtained dilatation of the pupils from stimulation of the anterior four-fifths, and of the cerebellum only by strong stimuli. They attributed the effect to the sensibility of the brain.

Hitzig (1871) sometimes obtained constriction of both pupils, but generally dilatation, rarely only one pupil reacted.

Similar experiments have been carried out by Bochfontaine (1875), Danilewski (1876), Luciani and Tamburini, Grünhagen, Bessau, Ferrier, Horsley and Schäfer, Schäfer, Beevor and Horsley, Grünhagen and Cohn, Katschanowski, François-Franck and Pitres, Mislawski, Bechterew and Mislawski, and Braunstein. In most of these cases the observations were incidental during research directed to some other object. In all, dilatation was much more easily induced than constriction, and no accurate localisation was effected.

Most observers have regarded the effects as inconstant, and but little attention has been specially directed to them.

Thus Ferrier includes dilatation of the pupil with salivation from the submaxillary gland, changes in pulse and blood pressure, and "other indications of general reverberation throughout the organism." He regards them as "merely complications and not as results of localised cortical stimulation." On the other hand, Bechterew and Mislawski conclude that "stimulation of the given regions of the cortex and of the optic thalami has hit off the central endings (Verlangerungen) of the cervical sympathetic," and that "the chief reflex centre for the secretion of tears lies in the optic thalami, and that there, too, are found the central tracts of the cervical sympathetic, their prolongations (Fortsetzungen) being continued thence to the cortex." François-Franck is careful to distinguish between two causes of dilatation of the pupil resulting from cortical stimulation. One is a special and localised effect following excitation of definite foci in the cortex, and also obtained from excitation of the underlying fibres of the corona radiata and internal capsule. The other accompanies epileptoid convulsions resulting from stimulation of any and every part of the motor areas, and is never obtained from the underlying white matter, which does not induce the epileptic state. To the latter he attributes the dilatation after administration of curare which was observed by Bochfontaine. He perhaps lays too much stress upon this as a fundamental distinction, for it applies equally to other motor effects induced through the cortex.

My experiments were made principally upon cats; a few dogs and one monkey were also used. The animals were anæsthetised with ether, the degree of anæsthesia varying, but always being amply sufficient to cause insensitiveness to pain. The qualifying terms used apply to the condition of excitability of the motor areas of the cortex to stimuli of moderate severity, as shown by movements of the limbs of the contra-lateral side. "Epileptoid convulsions" is the term used to express the violent general movements which often follow stimulation of the motor area after exposure of

the brain to air, or prolonged or frequently repeated excitation. This condition is quite compatible with complete anæsthesia.

The cervical sympathetics were either cut or isolated on one or both sides. In the dog the vago-sympathetic was treated as a whole. This was also done in the cat to insure the complete division of all sympathetic fibres. In some experiments the superior cervical ganglion was extirpated to eliminate any dilator fibres which might reach the ganglion by any hitherto unknown course. Section of the sympathetic was usually followed by a distinct moderate constriction of the corresponding pupil, but this was certainly not invariably the case. Absence of a tonic dilator influence is probably under these circumstances due to the condition of anæsthesia of the animal.

I need not enter into further details of the operative procedures, which were those usually employed in cerebral physiology. It was important to keep the light falling upon the eyes as constant as possible throughout the experiment.

It is easy in the cat's eye to direct one's attention to the horizontal meridian. The constricted pupil being a vertical slit, the distance from the centre to the periphery can be divided into four imaginary parts, the pupil being said to be a quarter, a half, three-quarters, or fully dilated.

I have not paid much attention to any movements other than those of the eyes and pupils. Dilatation of the pupils is often obtained without any movement of the eyes or body. I have usually found that a slightly stronger stimulus is necessary to evoke it than that which is required to produce movement from excitation of the arm or leg areas; or the same strength of stimulus may suffice if the animal be slightly less under the influence of the anæsthetic.

(A) *Cat.*—In the cat dilatation of the pupil can be obtained from a considerable area in the neighbourhood of the crucial sulcus and from a considerable area of the occipital region. As the result of many experiments it is

found that the mesial surface of the hemisphere near the crucial sulcus (prorean and presplenial convolutions) gives the most marked effect, but I have also found that the anterior part of the third or median convolution (coronal or anterior supra-Sylvian) gives a very constant effect. In one or two instances there was a transitory constriction of the pupils before the dilatation from this area. Ferrier obtained constriction of the pupils and divergence of the eyeballs from this spot in the dog, but I have not observed the latter effect in the cat.

In the occipital region, what may be called the focal spot is in the posterior part of the third or median convolution (posterior supra-Sylvian convolution). I have not observed any constriction of the pupil here, as described by Ferrier. François-Franck, however, obtained a transitory constriction from this spot, followed by dilatation, exactly like that which I describe for the coronal gyrus. It is, therefore probable that there are foci for pupil constriction both in the frontal and occipital areas, but that they are masked by the dilator effects, which are much more readily produced. One may compare with this the greater representation of lateral eye movements over any other eye movements in the cortex.

Only the results which are deduced from a large number of carefully planned experiments can be considered trustworthy, more particularly in deciding between areas which give a positive result independently of epileptoid convulsions. These are very readily brought about by repeated excitation of the same or closely neighbouring areas, owing to the increased excitability of the cortex which is thereby induced. The condition of anæsthesia is also of the utmost importance. If this is deep, the pupils remain immobile. If it is too light, dilatation is obtained from almost every part of the cortex, at any rate when bodily movements occur. The results are only reliable when the anæsthesia is moderate.

(B) *Dog.*—The areas are very much the same in the dog as

in the cat. This animal is less suited for the purpose because of the rarity of dogs with light-coloured irides, and a round pupil is less easy to detect slight variations upon than the slit-like one of the cat. In the dog I obtained a very marked effect from the precrucial gyrus, but I failed to observe any convergence of the optic axes as noted by Ferrier.

(c) *Monkey.*—I have done only one experiment of this nature upon the monkey. I found it much the easiest animal to work with, and it gave very definite results.

We conclude, therefore, that previous section of the cervical sympathetic diminishes the effect, but by no means abolishes it. When both cervical sympathetics are intact, the dilatation of the pupil, when well marked, is accompanied by all the usual effects of excitation of the nerves themselves, viz., retraction of the nictitating membrane, widening of the palpebral aperture and projection of the eyeball; to these, Bechterew and Mislawski add secretion of the lacrymal gland, but this I am unable definitely to confirm. All these effects are abolished by previous section of the sympathetics except the dilatation of the pupils, and this is diminished. Whereas when the nerves are intact full dilatation of the pupils may occur, especially during epileptoid convulsions; after they are divided, the pupils rarely become more than three-fourths dilated. The effect is very well seen if one nerve is divided, the other being intact. In this case the two pupils move synchronously and apparently to the same extent, except that they start unequal, the one on the divided side being the smaller. François-Franck is, therefore, certainly wrong in asserting that the pupillary dilatation is unilateral if one sympathetic has been cut. He certainly admits a slight degree of dilatation, which he attributes to dilator fibres running another course, probably in the trigeminal. I have eliminated this possibility by dividing the fifth nerve intracranially, and still obtaining the undiminished effect. To eliminate the possibility of other dilator fibres reaching the superior cervical ganglion I have, as already stated, extirpated it. The pupil on the side from which the ganglion was

removed was slightly but appreciably smaller than on the side on which the vago-sympathetic was cut.

I have found that section of the third nerve intracranially after previous division of the cervical sympathetic causes the pupil to become immobile, about three-fourths dilated. Stimulation of the cortex has then no effect upon it.

Complete section of the corpus callosum has no effect upon the result of exciting the cortex. The bilateral effect is, therefore, not due to the stimulus acting through the opposite cortical areas, but to its acting upon lower centres, but whether the optic thalami or the superior colliculi, or the sub-collicular nuclei I am not prepared to say, but probably upon the last mentioned.

Stimulation of the anterior and posterior parts of the corona radiata and internal capsule containing the fibres derived from the cells of the frontal and occipital areas leads to bilateral dilatation of the pupils. I have generally found a stronger excitation necessary, but this may be due to the fact that stimulation took place at the end of prolonged experiments. In one case I obtained a very marked constriction of the pupils, with strong convergence of the eyeballs from stimulation of the posterior part of the internal capsule.

A point of great interest arising from these experiments is the question of the mechanism whereby dilatation of the pupils can occur in the absence of the usual dilator tract. Two explanations offer themselves, viz., inhibition of the tonic action of the third nuclei, and dilatation brought about by vascular changes in the iris. An extremely interesting observation by Sherrington may be mentioned in this connection. In bringing physiological experiment to bear upon current theories of the emotions, he performed "appropriate spinal and vagal transection" in the dog to eliminate "the sensation of all the viscera and muscles below the shoulder." He says:—"The eyes were well opened, and the pupil distinctly dilated in the paroxysm of anger. Since the brain had been, by transection, shut out from discharging impulses

viâ the cervical sympathetic, the dilatation of the pupil must have occurred by inhibition of the action of the oculo-motor centre."

It is said that after the optic nerves have been cut, dilatation of the pupil is not obtained upon section of the third nerve, and hence tonic action of the third nuclei has sometimes been denied. There can be no question, however, that it exists when the optic nerves are intact, as in my experiments.

The immobility which follows section of both the third and the sympathetic is strong evidence in favour of the inhibition theory. It must be noted, however, that the blood pressure was probably very low at this stage of the experiment.

We have seen that dilatation of the pupil is still obtained after section of the sympathetic. No vaso-motor fibres are known to run to the iris, except by way of the sympathetic, and even if such exist, the experiments of Langley and Anderson tend to show that vascular effects are inefficient to bring about the dilatation observed. Moreover, it is well known that changes in blood pressure may occur from stimulation of various parts of the cortex, whereas pupil dilatation only occurs from certain localised spots in the absence of the epileptoid state.

It seems justifiable from these considerations to regard the effect as another example of direct inhibition of the oculo-motor nerves from the cortex.

There is no lack of evidence as to the presence of fibres connecting the cortex with the mesencephalon, and some of these must be regarded as the ones concerned in the pupillary effects. We may leave out of the question the dilatation of the pupil which accompanies the epileptoid state, for this is undoubtedly of an extremely complex nature, requiring special investigation. Confining our attention to the more specialised results obtained from the oculo-motor area in the posterior part of the frontal convolutions, which are to be looked upon as part of the fronto-parietal motor or kinæsthetic

area and quite distinct from the more anterior or so-called pre-frontal area, and to the results obtained from the oculo-sensory or visual area in the occipital convolutions, we find definite anatomical connections with the lower centres.

The pallio-tectal or cortico-mesencephalic system of fibres has recently been thoroughly investigated by Dr. Beevor and Sir Victor Horsley. It is noteworthy that no fibres were found passing to the mesencephalon from the frontal region, *i.e.*, from the area of cortex in front of the excitable cortex. From lesions of this part there was marked degeneration of the fronto-thalamic fibres previously described by Déjerine; the only mesencephalic centre to which fibres could be traced was the upper or anterior part of the locus niger. No fibres, therefore, go to the tectum.

A large number of fibres could be traced from the excitable cortex to the corpora quadrigemina and mesencephalon, especially to the superior colliculus. This was very marked in the cat, much less so in the monkey. The fibres from the oculo-motor areas have not yet been specially investigated.

The results from lesions of the occipital lobes were particularly striking, and confirmed Edinger's researches on birds. In proportion as more of the area of the cortex containing Gennari's streak is involved in the lesion the number of degenerated fibres passing to the colliculus increases. The fibres are large, and stand out distinctly from the medium-sized occipito-thalamic and occipito-geniculate fibres, and from the small callosal fibres and fine collaterals which enter the corona radiata in large numbers. Some of the occipito-tectal fibres pass among the fibres of Gratiolet's radiation, others run through the mesial region of the inferior longitudinal bundle. All the fibres are distributed to the whole breadth of the stratum griseum profundum of the superior colliculus.

Which of these fibres are concerned in the pupillary phenomena, and whether they pass, any of them, directly to the superior pupillo-dilator centre or to the pupillo-

constrictor centre, or only by intermediate connections, must be left for future research to determine. We have already shown that the cortical pupillo-dilatation is a complex event, strikingly resembling the ordinary sensory dilator reflex in that it is accompanied by all the usual effects of stimulation of the cervical sympathetic as long as that path is intact, but that it also occurs, deprived of the other sympathetic effects, when this nerve is divided. The evidence is, therefore, in favour of a more circuitous course, or at any rate of multiple and complicated interconnections.

There is evidence that pupillo-constriction can also be elicited from stimulation of the cortex. Ferrier obtained it from stimulation of the anterior and posterior limbs of the angular gyrus in the monkey, but this observation is probably incorrect. I have already stated that, apart from a transitory constriction (*cf.* François Franck and Pitres), I failed to confirm the same observer's results from the third external or coronal convolution in dogs. In pigeons, Ferrier found intense constriction of the pupil from excitation of the middle of the convexity of the hemisphere. Schäfer obtained marked constriction of the pupil from stimulation of the quadrate lobule in monkeys.

This brings us to the consideration of the exact nature of the phenomena. The view of Bechterew and Mislawski that we have here the central prolongations of the cervical sympathetic, is, *à priori*, highly improbable, or at any rate a misleading explanation of the results. Indeed, the continuance of the dilatation after section of the cervical sympathetic proves that it can only be partially true.

So, too, it is unlikely that we are dealing with "centres" for the pupils, in the ordinary sense of the term. We have found that the effect is most specifically obtained from the areas which are most concerned with ocular movements, whether from the motor or the sensory side. Moreover, it would seem that the effect is indissolubly connected with those movements, and does not occur in their absence. Hence it is most reasonable to conclude that the phe-

nomenon is an associated effect. As regards the so-called sensory areas, *i.e.*, the visual centres in the occipital cortex, it is probable that the attention plays some part. We produce, by artificial excitation, some strong, but probably ill-defined, visual sensation, which arouses the attention, and leads to the appropriate movement of the head and eyes towards the direction from which the stimulus seems to procede. The sensation is strong and sudden, and is accompanied by dilatation of the pupils in no physiological sense other than the expression of emotion.

Bibliography.

The Dilatator Pupillæ.

Maunoir. See Drouin. La Pupille. Paris, 1876.
Valentin. Repertorium f. Anat. u. Phys., ii, 1837.
Krohn. Müller's Arch., 1837.
Bruch. Zur Kentniss des körnigen Pigmentes der Wirbelthiere. Zürich, 1844.
Brücke. Anat. des menschlichen Augapfels. Berlin, 1847.
Kölliker. Zeitschrift f. wissensch. Zoologie, i, 1849.
Henle. Handbuch der systemat. Anat. des Menschen, ii, 1866.
Luschka. Anat. des menschlichen Kopfes. Tübingen, 1867.
Merkel. Zeitschrift f. rat. Med., xxxi, 1868.
v. Hüttenbrenner. Sitzungsbericht d. kaiserl. Acad., Math. naturw. Klasse, lvii. Wien, 1868.
Faber. Der Bau der Iris des Menschen und der Wirbelthiere. Gekronte Preisschrift. Leipzig, 1869.
Hulke. Monthly Microscopical Journal, 1869.
Dogiel. Arch. f. mikr. Anat., vi, 1870.
Jeropheeff. Stricker's Handbuch, ii, 1871.
Merkel. Die Muskulatur der menschlichen Iris. Rostock, 1873.
Iwanoff. Graefe-Saemisch Handbuch, i, 1874.
Michel. Die histologische Structur des Irisstroma. Erlangen, 1875.
Arnold. Physiologie, i.
Hall. Edin. Med. and Surg. Journal, 1849.
Hampeln. Ein Beitag zur Anat. der Iris. Inaug. Diss. Dorpat, 1869.
Michel. Arch. f. Ophth., xxvii, 2, 1881.
Schwalbe. Lehrbuch der Anat. des Auges, 1883.
Koganei. Arch. f. mikr. Anat., xxxv, 1885.
Fuchs. Arch. f. Ophth., xxxi, 3, 1885.
Eversbusch. Zeitschrift. f. vergleichende Augenheilkunde, iii, 1885.

Retzius. Biologische Untersuchungen, v, 7, 1893.
Juler. VIII International Ophth. Congress. Edinburgh, 1894.
L. Müller. Wiener klinische Wochenschrift, 1895.
Gabriélidès. Arch. d'Ophth., xv, 1895.
Grunert. Arch. f. Augenheilkunde, xxxvi, 1898.
Verhoeff. R. L. O. H. Rep., xv, 4, 1903.
Szili, Jr. Arch. f. Ophth., liii, 3, 1902.
Crimelli. Memorie della Med., contemp., 1840.
Rouget. Gazette méd. de Paris, 1846.
Zeglinski. Arch. f. Anat. u. Phys., Phys. Abtheilung, 1885.
Heese. Pflüger's Arch., lii, 1892.
Grünhagen. Virchow's Arch., xxx, 1864. Zeitschr. f. rat. Med., xxviii, 1866; xxxi, 1868; xxxvi, 1869. Arch. f. mikr. Anat., ix, 1873.
Grünhagen and Samkowi. Pflüger's Arch., x, 1875.
Grünhagen. Pflüger's Arch., liii, 1893.
Budge and Waller. Comptes rendus de l'Acad. des Sciences, xxxiii, 1851.
Budge. Ueber d. Bewegung der Iris. Braunschweig, 1855.
Waller. Comptes rendus, xliii, 1856.
Brown-Séquard. Journal de la Physiologie, ii, 1859.
Mosso. Hofmann and Schwalbe's Jahresbericht, ii, 1875.
François-Franck. Travaux du Laboratoire de M. Marey, iv, 1880.
Claude Bernard. Comptes rendus, 1852.
Waller. Comptes rendus, xxxvi, 1853.
Kuyper. In Donders, Accommodation and Refraction of the Eye. London, 1864.
Salkowski. Zeitschrift f. rat. Med., xxix, 1867.
Becker. Stellwag (von Carion's) Ophthalmologie.
Sinitzin. See Rembold.
Arlt, Jr. Arch. f. Ophth., xv, 1869.
Langley and Anderson. Journal of Physiology, xiii, 1892.
Claude Bernard. Journal de la Physiologie, v, 1862.
Schiff. See François-Franck.
Jegorow. Arch. f. Anat. u. Phys., Phys. Abth., 1886.
Waller. Comptes rendus, xliii, 1856.
Vulpian. See François-Franck.
Langley and Dickinson. Journal of Physiology, xi, 1890.
Gaskell. Journal of Physiology, vii, 1886.
Bernstein and Dogiel. Verhandl. d. naturhist.-med. Verein zu Heidelberg, vi, 2, 1865.
Bernstein. Zeitschr. f. rat. Med., xxix, 1867.
Engelhardt. Untersuch. a. d. phys. Lab. in Würzburg, iv, 1869.
Hensen and Völkers. Experimentaluntersuchungen ü. d. Mechanik der Accommodation. Kiel, 1868.

The Efferent Pupillo-Constrictor Path.

Romberg. Nervous Diseases, ii. London, 1853.
v. Trautvetter. Arch. f. Ophth., xii, 1, 1866.

SCHIFF. Giornale di Scienze naturali ed economiche, iv. Palermo, 1868.
ADAMÜK. Centralbl. f. d. med. Wissensch., 1870.
HENSEN and VÖLKERS. Arch. f. Ophth., xxiv, 1, 1878.
LANGLEY and ANDERSON. Journal of Physiology, xiii, 1892.
APOLANT. Arch. f. mikr. Anat., xlvii, 1896.
BIDDER and VOLKMANN. Die Selbstständigkeit des sympathischen Nervensystems. Leipzig, 1842.
MARINA. Deutsch. Zeitschrift f. Nervenheilkunde, xiv, 1899; xx, 1901.
BACH. Arch. f. Ophth., xlvii, 1899.
BUMM. Neurol. Centralbl., xxi, 1902.
SHERRINGTON. Journal of Physiology, xxiii, Supplement, 1898.

PARADOXICAL PUPILLO-CONSTRICTION.

ANDERSON. Proc. Phys. Soc., Journal of Physiology, xxviii, 1902.

THE EFFERENT PUPILLO-DILATOR PATH.

PARFOUR DU PETIT. Mem. de l'Acad. des Sciences, 1727.
MOLINELLI. See Braunstein.
ARNOLD. See Braunstein.
STILLING. See Braunstein.
VALENTIN. De Functione Nervorum.
BIFFI. Inaug. Diss. Paris, 1846.
REID. Physiological, Anatomical, and Pathological Researches. Edinburgh, 1848.
BUDGE. Ueber die Bewegung der Iris. Braunschweig, 1855.
SCHIFF. Untersuch. zur Phys. des Nervensys. mit Berücksichtigung der Pathologie. Frankfurt, 1855.
CHAUVEAU. Journal de Phys., 1861.
NOTTA. Arch. gén. de Méd., 1854.
CLAUDE BERNARD. Journal de Phys., 1862.
BALOGH. Moleschott's Untersuchungen, viii, 1862.
OEHL. Meissner's Jahresbericht, 1862.
GUTTMAN. Centralbl. f. d. med. Wissensch., 1864.
SALKOWSKI. Zeitschr. f. rat. Med., xxix, 1867.
NAWALICHIN. See Braunstein.
VULPIAN. Journal de Phys., 1874.
HURWITZ. Inaug. Diss. Erlangen, 1878. See Nagel's Jahresbericht, 1878.
SCHIFF and FOA. La Pupilla come Estesiometro, L'Imparziale, 1874. Trans. by Dr. R. Guichard de Choisity, 1875.
FRANÇOIS-FRANCK. Comptes rendus, lxxxvii, 1878. Gaz. des Hopitaux, 1878. Travaux du Laboratoire de M. Marey, iv, 1880.
LANGLEY and ANDERSON. Journal of Physiology, xiii, 1892.
GUILLEBEAU and LUCHSINGER. Pflüger's Archiv, xxii, 1880.
LUCHSINGER. Pflüger's Archiv, xxii, 1880.
TUWIM. Pflüger's Archiv, xxiv, 1881.

Guillebeau and Luchsinger. Pflüger's Archiv, xxviii, 1882.
Ott. Journal of Nervous and Mental Diseases, viii, 1882. Journal of Physiology, ii, 1880.
Sheglinski. Inaug. Diss. Kasan, 1885. See Braunstein.
Grünhagen. Pflüger's Archiv, xl, 1886.
Langley. Journal of Physiology, xxx, 1903.
Jegorow. Pflüger's Archiv, xli, 1886.
Bellarminow. Dissertation. St. Petersburg, 1886. See Braunstein.
Schipilow. Pflüger's Archiv, xxxviii, 1886.
Nawrocki and Przybyiski. Pflüger's Archiv, l, 1891.
Braunstein. Zur Lehre von der Innervation der Pupillenbewegung. Wiesbaden, 1894.
Langley. Phil. Trans., clxxxiii, 1892.
Sherrington. Journal of Physiology, xiii, 1892.
Langley. Journal of Physiology, xxii, 1897. In Schäfer's Physiology, ii, 1900.
Tuckett. Journal of Physiology, xix, 1896.
Marina. Deutsch. Zeitschr. f. Nervenheilkunde, xiv, 1899.
Magendie. Journal de Physiologie, iv, 1824.
Longet. Anat. u. Phys. du Système nerveux, ii, 1842.
Valentin. Lehrbuch der Physiologie, ii, 2, 1848.
Claude Bernard. Leçons sur la Physiologie et Pathologie du Système nerveux, ii.
Schiff. Untersuchungen zur Naturlehre, x, 1867.
Rembold. Ueber Pupillarbewegung und deren Bedeutung bei den Krankheiten des Centralnervensystems, 1880.
Eckhard. Centralblatt für Physiologie, 1892.
Langley. Journal of Physiology, xxv, 1900.
Anderson. Journal of Physiology, xxx, 1903.
Parsons. Journal of Physiology, xxvi, 1901.

Paradoxical Pupillo-Dilatation.

Budge. Ueber die Bewegung der Iris. Braunschweig, 1855.
Schiff. Giornale di Scienze naturali ed economiche, iv. Palermo, 1868. Gesammelte Beiträge, iii. Lausanne, 1896.
Surminski, Zeit. f. rat. Med., xxxvi, 1869.
Tuwim. Pflüger's Archiv, xxiv, 1881.
Kowalewski. Arch. slav. de Biol., i, 1886.
Braunstein. Zur Lehre v. d. Innerv. d. Pupillenbewegung. Braunschweig, 1894.
Tuckett. Journal of Physiology, xix, 1896.
Langendorff. Klin. Monatsbl. f. Augenheilkunde, xxxviii, 1900.
Lewandowski. Sitz. d. k. preuss. Akad. d. Wiss. zu Berlin, 1900.
Langley. Journal of Physiology, xxvii, 1901.
Levinsohn. Arch. f. Ophth., lv, 1902.
Anderson. Journal of Physiology, xxx, 1903.
Waymouth Reid. Journal of Physiology, xvii, 1895.

Light Reflex.

Lambert. Photometria, 1760. See Leeser, Die Pupillarbewegung in physiol. und path. Beziehung. Wiesbaden, 1881.
E. H. Weber. De Motu Iridis. Lipsiæ, 1851.
Mayo. See Leeser.
Flourens. Récherches experimentales sur les Propriétés et les Fonctions du Système nerveux. Paris, 1824.
Knoll. Dissertation. Giessen, 1869. See Leeser.
v. Bechterew. Pflüger's Archiv, 1884.
Ferrier and Turner. Brain, xxiv, 1901.

The Afferent Pupillo-Constrictor Path.

v. Bechterew. Pflüger's Archiv, xxxi, 1883.
Henschen. Klin. u. anat. Beiträge zur Path. des Gehirns. Upsala, 1892.
Bogroff and Flechsig. Neurol. Centralbl., v, 1886.
v. Bechterew. Deutsch. Zeit. f. Nervenheilkunde, xvi, 1900.
Darkschewitsch. Arch. f. Anat. u. Phys., Anat. Abth., 1886.
v. Bechterew. Die Leitungsbahnen im Gehirn und Rückenmark, Leipzig, 1899.
Bellonci. Zeit. f. Wiss. Zool., lxxiv.
Bernheimer. Arch. f. Ophth., xlvii, 1899.
Bach. Deutsch. Zeit. f. Nervenheilkunde, xvii, 1900.
Barker. The Nervous System. London, 1900.

The Pupillo-Constrictor Centre.

Bernheimer. In Graefe-Saemisch Handbuch, 2nd Edition, 1899 (Bibliography).
Bach. Zeitschrift für Augenheilkunde, xi, 1904 (Bibliography).
Argyll Robertson. Edinburgh Med. Journal, 1869.
Wolff. Arch. f. Psychiatrie, xxxii, 1899.
Sacki and Schmaus. Vorlesungen ü. d. path. Anat. d. Rückenmark, 1901.
Schaffer. Anat. u. klin. Vorträge, 1901.
Ruge. Arch. f. Ophth., liv, 1902.
Marina. Deutsch. Zeit. f. Nervenheilkunde, xx, 1901 ; xxiv, 1903.

The Accommodation Synkinesis.

Scheiner. Oculus, 1619.
v. Trautveiter. Arch. f. Ophth., xii, 1, 1866.
Hensen and Völkers. Experimentaluntersuchungen ü. d. Mech. d. Accom. Kiel, 1868. Arch. f. Ophth., xxiv, 1, 1878.
Kaiser. Arch. f. Anat. u. Phys., 1868.
Adamük and Woinow. Arch. f. Ophth., xvii, 1, 1871.

Olbers. Inaug. Diss. Göttingen, 1780. See Leeser.
E. H. Weber. De Motu Iridis. Lipsæ, 1851.
Hering. Lehre von binoc. Sehen, 1868.
Verwoort. Arch. f. Ophth., xlix, 1899.
Adamük. Centralbl. f. d. med. Wiss., 1870.
Henke. Arch. f. Ophth., vi, 2, 1860.
Weiss. Arch. f. Ophth., xxi, 2, 1875.
Sichel. Gas. des Hôpitaux, 1876.
v. Graefe. Arch. f. Ophth., iii, 2, 1856.
Schiff. Lehrbuch der Phys., 1859.

The Sensory Reflex.

(See the Efferent Pupillo-Dilator Path.)

v. Bechterew. Pflüger's Archiv, xxxi, 1883.
Mayer and Pribram. Zeit. f. Heilkunde, v, 1884.
Anderson. Journal of Physiology, xxx, 1903.

The Cerebral Synkinesis.

Haab. Korrespondenzblatt der Schweizer Aerzte, 1886.
Bumke. Neurol. Centralbl., 1903.
Fontana. Dei Moti dell'Iride. Lucca, 1770. See Leeser.
Raehlmann and Witkowski. Arch. f. Phys., 1878.
Hitzig. Arch. f. Anat. u. Phys., 1871.
Danilewski. See Braunstein.
Luciani and Tamburini. Sui Centri Psico-motori corticali, 1878–9.
Bochfontaine. Comptes rendus de la Soc. de Biol., 1875.
Bochfontaine. Arch. de la Phys. nor. et path., iii, 1876.
Grünhagen. Berliner klin. Woch., 1879.
Bessau. Inaug. Diss. Königsberg. See Braunstein.
Ferrier. The Functions of the Brain, 1886.
Horsley and Schäfer. Phil. Trans., clxxix.
Beevor and Horsley. Phil. Trans., clxxix, clxxxi.
Schäfer. Brain, xi, 1888.
Grünhagen and Cohn. Centralbl. f. prakt. Augenheilkunde, 1884.
Katschanowski. Med. Jahrb., 1885.
François-Franck. Leçons sur les Fonctions motrices du Cerveau. Paris, 1887.
Mislawski. Comptes rendus de la Soc. de Biol., 1887. Journal of Physiology (xxix), 1903.
v. Bechterew and Mislawski. Neurol. Centralbl., 1891.
Braunstein. *Loc. cit.*
Parsons. Journal of Physiology, xxvi, 1901.

By the same Author.

THE PATHOLOGY OF THE EYE.

(In 4 vols., with over 700 Illustrations.)

Vol. I.—Histology. Part 1. (*Now Ready.*)

Vol. II.—Histology. Part 2.

Vols. III and IV.—General Pathology.

The price of each volume will be 15*s.* net. To those who subscribe in advance for the complete work the price will be £2, payable 10*s.* net on receipt of each volume.

LONDON:
HODDER AND STOUGHTON,
27, Paternoster Row.

TRACHOMA.

By Dr. J. BOLDT,

Translated by

J. Herbert Parsons and Thomas Snowball,

With an Introductory Chapter by

E. Treacher Collins.

LONDON:
HODDER AND STOUGHTON,
27, Paternoster Row.