Glioma retinae : with report of five cases / by Christian R. Holmes.

With the Author's Compliments

GLIOMA RETINÆ

With Report of Five Cases

BY

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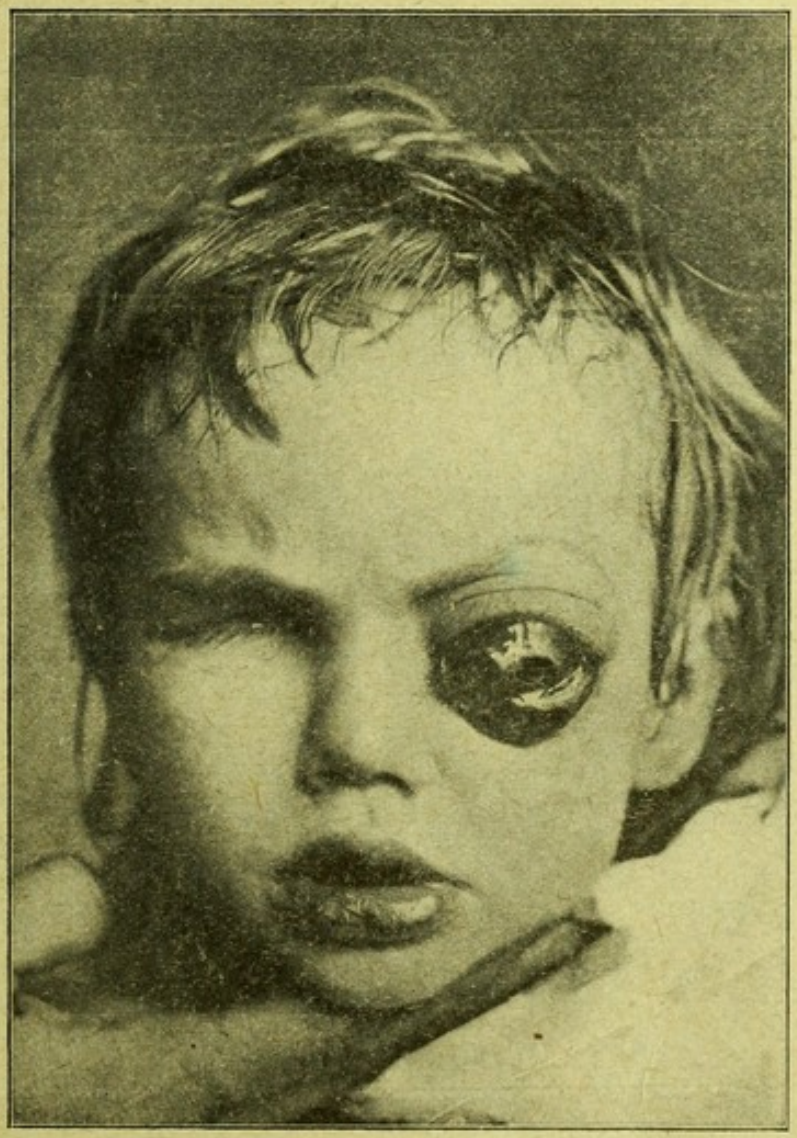
CINCINNATI, OHIO



With Fifteen Illustrations in the Text

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GLIOMA RETINÆ WITH REPORT OF FIVE CASES.*

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Glioma is a disease limited to childhood, and we may consider it the only true neoplasm developing in the retina. Its synonyms are: "Neuro-epithelioma" (Wintersteiner), "gliosarcoma" (Virchow), "glio-angio-sarcoma" and "tubular gliosarcoma" (De Gama Pinto).

H. Knapp, in 1867, appears to have been the first to give an accurate and thoroughly scientific description of this class of tumors. In 1868 appeared Hirschberg's classical work on this subject, with a report of 77 cases collected from different sources. Virchow believed the cells of this class of tumors to be derived from the supporting fibers of the retina (the glia), and hence gave it the name of glioma retinæ.

Iwanhoff, in 1869, described the structure of the glioma as follows: "The larger nodules are always very vascular, with a characteristic arrangement of the cells which are concentrically grouped around the blood vessels. On section the whole nodule appears to consist of closely arranged cell rings whose central spaces are filled with red blood corpuscles."

Wintersteiner has tabulated 500 cases from all sources, 31 of these being his own, which had been very thoroughly studied microscopically. The same author has tabulated the following cases, in which the origin of the gliomatous growth could positively be traced to one or more of the retinal layers with the following results:

* Read at the Fifty-third Annual Meeting of the American Medical Association, in the Section on Ophthalmology, and approved for publication by the Executive Committee: Drs. Frank Allport, H. V. Würdemann and J. A. Lippincott.

(a)	Origin in layer of optic nerve fibers	5 cases
	Origin in inner nuclear layer	19 cases
	Origin in any of the inner layers of retina	12 cases
	Total	36 cases
(b)	Origin in outer nuclear layer	9 cases
	Origin in outer layers of retina	3 cases
	Total	12 cases

From this we will observe that the origin is three times more frequent in the inner than in the outer layers. We must remember that the origin is not limited to one layer of the retina, but may spring from several layers in the same case. It has been observed that gliomata have their origin four times more frequently from the posterior than from the anterior half of the globe. The same author accepts Cohnheim's theory that tumors have their origin in the masses of embryonic cells which are at times left over in the building of the normal structure, these cells remaining dormant in their embryonic state until at some later period they may take on an active and perverted growth. Prof. Schöbl, who has observed a very large number of this class of tumors, concludes that glioma may start from the supporting fibers of any of the layers of the retina, but mostly from the inner nuclear layer. In this layer Da Gama Pinto found that the nuclei were mostly in process of division with karyokinetic figures. That glioma is a form of tumor independent of and different from sarcoma, was first doubted by Cornil and Ranvier; later they were termed small round-celled sarcomata by Delafield, and Nagel agreed in this opinion. From Virchow's standpoint the supporting tissue of the retina can not be considered identical with common connective tissue, and from the standpoint of Klebs the gliomata are derived even from a different germinal layer than that from which the sarcomata arise. The clinical picture of glioma also is so well defined that to confound it with sarcoma is against good judgment.

Becker thinks that there is a sufficient number of mesoderm cells in the blood cells to give rise to sarcomata. To this it must be answered that their origin

from the granules of the nuclear layer directly, especially of the inner one, can be observed, and that processes of division can be seen there, as Da Gama Pinto, Schöbl and others have witnessed, and that not a single observer has found a glioma starting from a retinal blood vessel, while with sarcomata this is nothing rare.

The most frequent mixed tumor of this kind is glio-sarcoma (Virchow). When spreading into the choroid and sclera and beyond the eye, gliomata may sometimes change their character in that their cells grow larger, up to 15 microns, while their nuclei remain comparatively small—6 to 10 microns; that is, the protoplasm is increased, or, in other words, the cells assume the character of small round-celled sarcoma. Berthold was the first who asserted that gliomata may assume a sarcomatous character, after having spread into the choroid, and that this membrane, irritated by the entering of the glioma cells, furnishes the sarcomatous elements. In a reverse way it may occur that sarcomata of the choroid take on a gliomatous character. This, perhaps, explains Von Graefe's two observations of gliomas in adults.

Prof. Schöbl's remarkable case of glio-fibro-sarco-myo-angioma confirms the statement that the character of the tumor often depends on whether or not it has invaded other tissues. In this case, the pure retinal glioma, when it spread into the sclera, produced proliferation with the formation of glio-fibroma; when the glioma cells spread into the orbital tissue they caused a proliferation in this locality, and sarcomatous (round and later spindle) cells were formed; and thus a glio-fibro-sarcoma resulted. The same process was repeated with the unstriped muscular tissue of the blood vessels, and thus the tumor formed a glio-fibro-sarco-myo-angioma.

Greef has examined fresh gliomata by the impregnation methods of Golgi and Cajal. By the latter method he succeeded in demonstrating the presence of differently shaped cells in retinal glioma. He found numerous oval

and star-shaped cells with free offshoots which were undoubtedly true neuroglia cells and the original cells of the tumor. From Greef's investigations, it appears certain that gliomata are not neoplasms of sarcomatous nature, since impregnation of the cells after Cajal's method could not take place. It is believed by some authors that neuro-epithelioma of the retina is always congenital, or at least that a predisposition exists through some disturbance in the process of development.

Glioma spreads in the retinal structure: 1, by enlargement of a single or the confluence of several smaller nodules, and 2, by metastasis within the retina.

The growth of the primary nodules takes place through division and multiplication of the cells next to the blood-vessels, whereby the older cells are constantly crowded farther back toward the periphery and become necrotic for want of nutrition.

The growth spreads in three ways: 1, through the inter-lamellar spaces; 2, through the lymph channels. and 3, through the blood-vessels.

It is characteristic of the development of glioma that the growth not alone displaces other structures by pressure but replaces them by neoplastic tissue. With the destruction and transformation of the retina by the rapidly developing gliomatous tissue come retinal detachment and an extension of the process to other structures, the choroid being generally and naturally the first to be involved. Beyond the retina and the choroid the extension of the neuro-epithelioma takes place most readily along the optic nerve, the cancer tissue replacing the nerve bundles and finally extending to and involving the chiasm and surrounding structures. Secondary tumors have been found in nearly all of the organs and even the bony structures are frequently involved.

In the second and third stages the growth replaces the orbital tissue, extending to and destroying the periosteum and bone by erosion.

The diagnosis between gliomata and other tumors is easily made, but the differentiation of the pseudo-glioma is fraught with many difficulties, but only when the disease is well advanced. We must differentiate from: 1, detachment or cysts of the retina; 2, tumors of the choroid and ciliary region; 3, masses of inflammatory exudate in the vitreous (pseudo-glioma), and 4, the combination of true glioma with any of the above.

The greatest difficulty in making a correct diagnosis occurs when the cornea, aqueous or lens have undergone such changes as to prevent inspection of the interior of the globe, cataract being the most frequent condition encountered. As a rule, we may state that inflammatory exudates into the vitreous give a yellowish reflex, with a metallic luster and smooth surface, while the color of glioma may be a light yellow, reddish or greenish-yellow and the growth is nodular.

The diagnosis may be complicated further by the formation of a post-inflammatory membrane or exudate upon the hyaloid membrane directly behind the lens, by chronic inflammation and fibrinous exudate into the vitreous, or by acute suppurative hyalitis. From detachment of the retina it should be readily differentiated by a careful ophthalmoscopic examination, and from tumors of the choroid by the fact that they are nearly all pigmented. Leucosarcoma of the choroid is rare and its growth is dissimilar to that of gliomata. It develops as a solitary half-round mass over which the retina may be atrophied, but does not form reduplications and thickened masses.

That there is often great difficulty in making a differential diagnosis between the true and the pseudo-glioma, is proved by the fact that Raab found in the collection of Otto Becker of Heidelberg twenty eyes that had been enucleated by various expert diagnosticians, after the diagnosis of glioma retinæ had been made, and yet in 25 per cent. of these no gliomatous or cancerous tissue was present, but only inflammatory changes in the uveal

tract. Treacher-Collins reports that out of 1020 eyes removed in Moorfield Hospital, London, from 1888 to 1892, the diagnosis of glioma had been made in 24 cases, and yet microscopic examination revealed that 7 of these were pseudo-glioma.

Fortunately, neuro-epithelioma of the retina is rare. Even in the largest clinics, six months to a year may pass without a child with glioma being presented. Twenty-two of the great clinics of the world reporting 498,057 patients, record 203 cases of glioma—one twenty-fifth of 1 per cent.—or one case of glioma out of every 2500 cases of diseases of the eye. But after reading the reports of Raab and Treacher-Collins, mentioned above, we are justified in concluding that no doubt many of these were cases of pseudo-glioma.

The disease is absolutely limited to childhood and is often well advanced at birth. The combined results of investigation by leading oculists of the world seem to prove conclusively that when glioma is reported as a primary growth in an individual over 16 years of age it is a mistaken diagnosis. Out of 467 cases, the growth was developed at birth in 34 cases to such an extent as to present the amaurotic cat's eye. Ophthalmoscopic examination would have shown a much larger number. Including these congenital cases, there developed during the first three years of life, 314 out of a total of 467 cases, or 67 per cent.

The percentage of involvement of both eyes is very large; out of 87 cases it occurred 16 times at birth, or in 18.4 per cent. Deducting these congenital cases from the 87 cases, it was found that both eyes were involved 65 times out of 71 cases during the first three years of life.

It is of interest to remember that the second eye appears never to have been found to become involved by an extension of the disease along the optic nerve and through the chiasm from the first eye. Where both eyes are affected, the disease always develops independently in each eye.

The disease may extend backward along the optic nerve to the chiasm, involving adjacent structures and causing death, but it has not been known to travel from the chiasm peripherally along the nerve of the sound eye; blindness of the non-affected eye due to atrophy may, however, result because of the destruction of the nerve fibers in the chiasm.

The influence of heredity has not been demonstrated; as yet we know of no case in which an individual who had an eye removed in childhood for glioma, has transmitted the disease to his offspring. There are, however, many cases on record where several members of one family have been affected, just as at times we find congenital cataract in some or all of the children of one family, where the parents are closely related. I have been unable to find whether there was consanguinity between the parents of the patients about to be cited.

Lerche, St. Petersburg, 1821, observed a family of 7 children, 4 of whom died from glioma; Sichel, in 1852, 4 cases in one family; Calderini, in 1867, 3 cases in one family; Knapp and Thompson, in 1874, 5 cases in one family; MacGregor, in 1885, 3 cases in one family, and Flexner, in 1871, 3 cases in one family. Wilson, in 1872, exhibited before the Pathological Society of Dublin, the photographs of 8 children of one family, four of whom had died from glioma and the remaining four being also afflicted with the same disease.

The disease may be divided into three stages of development:

1. Period of intra-ocular growth, without increased tension or inflammatory symptoms.

2. Glaucomatous or inflammatory period, which ends with rupture of the globe.

3. The period of extra-ocular growth and metastasis.

In some cases there is temporary arrest and even retrograde change, such as phthisis bulbi after rupture or violent inflammatory reaction of the globe, the tem-

porary arrest being probably due to destruction of the vessels of nutrition with degeneration of the glioma cells as a result of the suppurative process.

Death may result from:

1. Involvement of the brain.
2. Cachexia.
3. Pressure of the growth on the medulla oblongata.
4. Suffocation from extension of growth into the pharynx and larynx.
5. Pyemia or septicemia, with metastatic abscesses.

The duration of life when there is no surgical interference varies greatly, but from a few months to three years is the average. A few cases have been reported where the first period lasted five years from the time the disease was first discovered. The average duration of the second stage is from 2 to 21 months, while the third stage from the rupture of the cornea to the fatal termination is the shortest, varying from two weeks to one year, with an average of three months.

If there is no return in two years after enucleation the case may be regarded as cured so far as that side is concerned, but we must remember that the disease may occur in the other eye a considerable period after the first eye becomes affected, and we must then regard it as an independent attack in the same patient and not a recurrence of the primary growth.

The only treatment that can be considered as offering any chance of saving life is removal of the affected eye, with as much as possible of the optic nerve, at the earliest possible moment during the first stage. In operations undertaken during the second stage, before the rupture of the cornea, the chances of success are very slight, since the infection has often extended outside of the globe through the veins or lymph channels. But even then it is our duty to operate, and exenteration of the orbit should be added to the enucleation of the eye, if we hope to arrest the disease. In this stage I regard the use of pastes far superior to the use of cutting instru-

ments, because the liability of opening up new avenues of infection is much greater in the latter method.

When the case has once entered the third stage the rule is that, no matter how thoroughly exenteration is performed, there is always recurrence within a few weeks, and operation in this stage is only justifiable in order to afford temporary relief.

With the advent of serum-therapy it was hoped that this mode of treatment might be of service, and Nieden reported his observations upon this method at the meeting of the Ophthalmological Society at Heidelberg in 1896. The cancer serum was injected in a case of recurrent glioma. At first there appeared to be an arrest of the growth, but it soon broke forth with greater fury than before, and went on speedily to a fatal termination.

Shall we advise enucleation if both eyes are affected? Since cases of undoubted glioma—as proved by the microscope—have been cured after double enucleation, and as the disease springs from a separate and independent focus in each eye, we should answer this question in the affirmative, and urge the operation if the disease has not progressed beyond the first or second stage in either eye. For if life is saved, blindness to a child at this period is not a barrier to its acquiring an education and becoming a useful and independent citizen.

Case 1.—Baby M., female, white, aged 2 years, was first seen by me Feb. 7, 1894. Child was well-nourished and its general health good. Left eye normal; right pupil dilated, which caused the mother to seek consultation. External appearance of globe normal. The pupil appeared the normal black color. Tension normal. Ophthalmoscopic examination revealed that the dioptric media was clear, but there was a flat, yellowish, nodular mass to the outer side of disc; retina was intact outside of the affected area. A diagnosis of glioma retinæ was made, immediate enucleation advised, and the danger of delay fully explained to the mother. The family physician was informed of my opinion. He examined the eye superficially and said he could see nothing wrong, advised against the operation, and gave the mother little sugar pills for the child.

May 3, nearly three months later, the mother returned

with the child. It was emaciated, exhausted and fretful, frequently crying out in pain. The case was now well advanced into the second stage. Globe injected, tension +2, anterior chamber obliterated, pupillary area filled with a yellowish mass, slightly irregular, with a few fine vessels seen upon the surface. The family physician had now withdrawn his objection to operation. Left eye was still normal.

In order to give the child its only chance, and to relieve the suffering caused by the glaucomatous eye, I enucleated the globe and also removed a considerable piece of the optic nerve. Under similar conditions I should now make exenteration of the orbit. The operation was followed by marked improvement in the child's general condition, but on October 8, about five months after the operation, the mother returned with the child stating that it had vomited frequently during the previous week. Its appetite was poor, but it slept well. No other general symptoms were present. The orbital cavity was filled with a hard mass which did not appear to be attached to the bony walls, but was movable; the new growth appeared to spring from the optic nerve-end, which formed its pedicle. The tumor was removed to the very apex of the orbit and, as surmised, it sprang from that part of the optic nerve which had not been removed at the first operation. As I considered the case beyond hope, I did not wish to cause the child additional and useless suffering by the use of cautery or pastes.

The growth promptly recurred and soon developed into a large protruding mass. The child suffered most terrible agonies unless kept under the influence of opiates, 1½ grs. of morphia being administered hypodermatically every 4 or 6 hours.

The child died on Feb. 26, 1895. (Figs. 1 and 2 are sketches made after death, showing the appearance of the growth.)

Postmortem Notes.—Child greatly emaciated. Tumor 12 inches in circumference at the base, projecting from the right orbit about 4 inches. In shape, the tumor had much the appearance of a small cocoanut, and it was of a dark reddish color. The projecting surface was broken down in places and covered with nodules. The growth involved the bony structure and extended from the roots of the hair almost to the alveolar process. The meninges at the base of the right side and a portion of the brain, together with the optic nerve, were extensively invaded by the cancerous tissue which was partly necrotic. The meninges and brain of the left side, together with the left eye, appeared normal.

Microscopic Report of Globe.—Dr. Louis Stricker reports as follows: Unfortunately, the eye was cut through the equatorial region; hence, no complete sections of the entire globe could be made. Both halves were filled with a new growth, showing on its surface minute red spots—large ves-

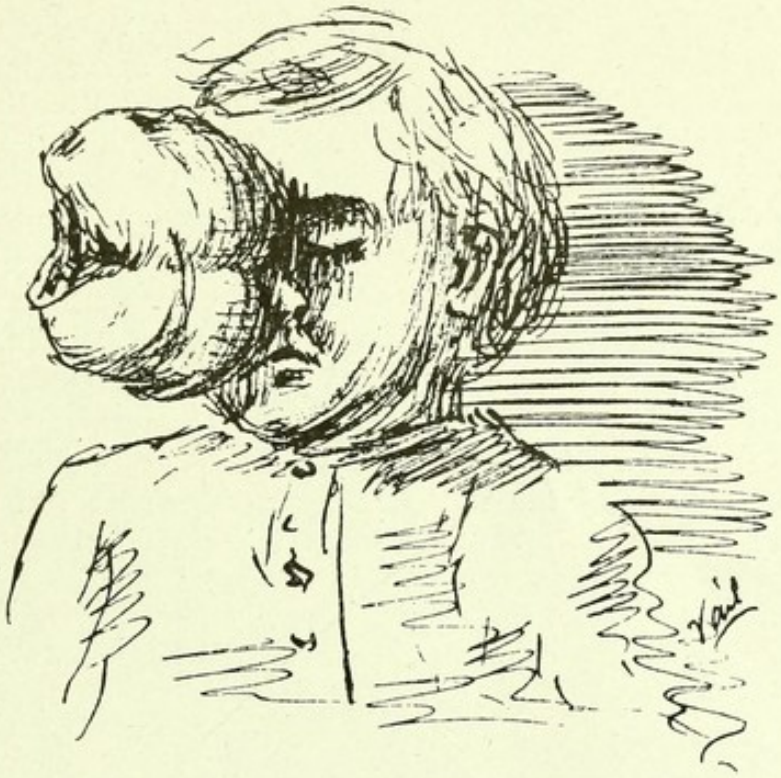

Fig. 1.—Case 1. Recurrent growth one year after neoplasm was first discovered ophthalmoscopically. Nine months after enucleation and five months after removing recurrent growth and all of optic nerve to apex of orbit.

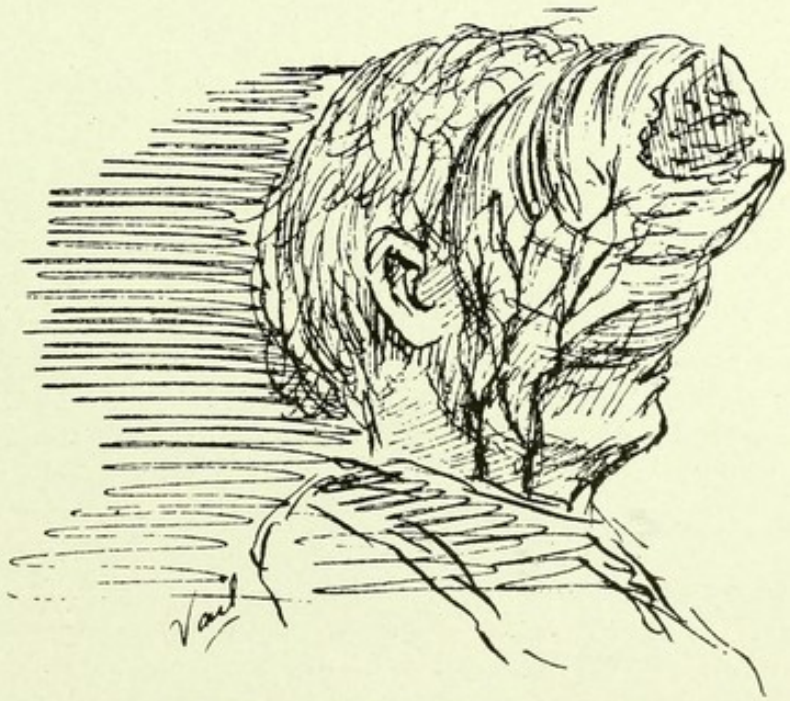

Fig. 2.—Side view of Fig. 1.

sels—and around these areas of a greenish color, whereas, at a distance from these the surface was white. The general contour of the globe was retained and at no point had the tumor perforated the sclera. The optic nerve, especially its nasal half, showed decided thickening. The anterior half of the globe was also filled with the tumor mass, and entirely hid from view the lens and ciliary body.

The specimen was carefully hardened in Mueller's fluid for 5 months, then washed out and gradually hardened in alcohol, finally imbedded in celloidin, and then cut in sections.

Without the use of a lens, the sections disclose that the optic nerve is infiltrated with the tumor up to the point of excision, necessarily having left behind some part of the new growth.

A general view of a section of the globe discloses a complete obliteration of the retina, not a vestige of its anatomic structure remaining, except here and there a few retinal pigment cells—a most widespread involvement of the choroid, which in many places is thickened to many times its normal size, and likewise, a complete involvement of the optic nerve, with total obliteration of nerve fibers.

All the sections disclosed a very marked involvement of the choroid. Anteriorly, for a very short distance, the choroid was found normal, but as it was followed around toward the optic nerve, its involvement in the tumor mass at once became apparent, and nodules begin to appear, until large areas are encountered completely infiltrated with round cells containing large nuclei. The stroma pigment cells of the choroid have entirely disappeared, but the vitreous lamella is in many places sharply outlined, giving the line of separation from the retina. In some places, however, the vitreous lamella has been eroded, and thus a point either of entrance or exit has been given for the tumor to invade this space between the choroid and the retinal layer of pigment cells which here and there exist and act as a barrier to invasion. At one point in the tumor the continuity of this vitreous lamella is broken, and here a distinct point of communication between choroid and interior of globe exists. In one section was found an enormous vessel extending directly from the choroid out into the tumor mass. The retinal detachment extended as far as the ora serrata, at this point the cystic degenerated retina can be followed forward for a short space, to be entirely obliterated in lobules of tumor.

The portions of the tumor confined strictly to the choroid are made up of round cells, which take the stain deeply, and to an equal degree, and though this is permeated by blood-vessels, they do not seem particularly more numerous or larger than usually encountered in the normal choroid. As soon, however, as the tumor is followed beyond the strict confines of the choroid, the vessels are much more numerous,

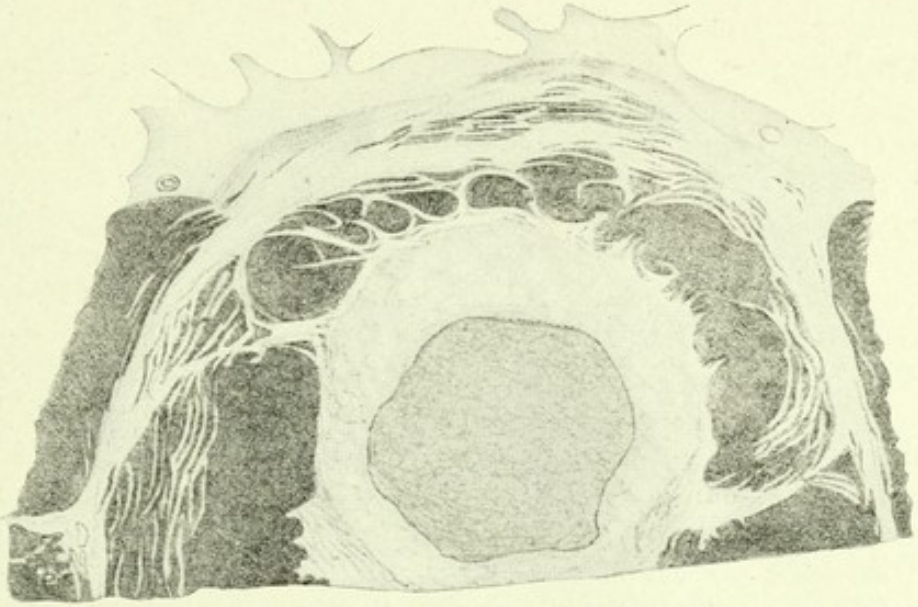

Fig. 3.—Section of optic nerve. The nerve fibers totally destroyed; also notice enormous thickening of the inner sheath, and infiltration of the subdural and subarachnoidal spaces with the tumor mass. (After Wintersteiner.)

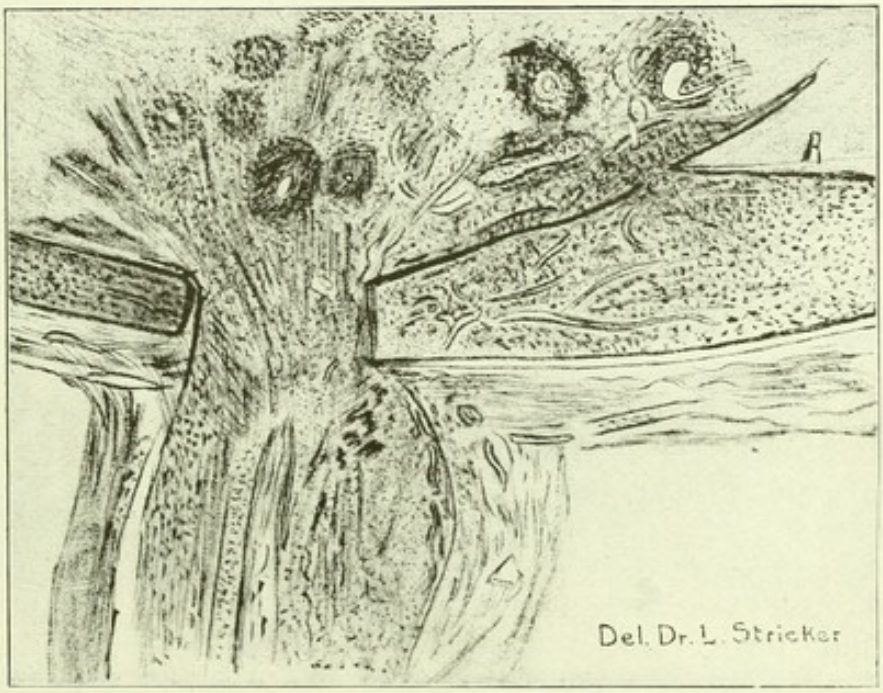

Fig. 4.—Case 1.—Showing new growth and infiltration of optic nerve.

widely dilated, some more than twice the size of the normal arteria centralis retinæ, and filled with blood cells. Around each one of the vessels the round cells of the tumor are closely pressed together, so that they often take on a polyhedral shape. They take the stain very deeply, whereas, at a distance, much less so, so that the tumor has a peculiar spotted or lobulated appearance. Nowhere did I find places where the tumor cells formed the walls of the vessels, but everywhere there are large vessels with thickened and distinctive vessel walls, showing the endothelial cells lining the vessel wall, the intima of the vessel, and around these grouped the cells of the tumor.

The choroid is distinctly and sharply demarcated from the optic nerve by connective tissue fibers. The fibers of the lamina cribrosa are especially sharply defined and pushed backward by the tumor, which has encroached on the nerve head, and finally invaded and thoroughly destroyed its fibers. Nevertheless, the line of demarcation between the choroid and nerve head is very sharply defined. The optic nerve itself is greatly thickened, its nerve fibers being entirely obliterated by the extreme infiltration. Both artery and vein intensely dilated and filled with blood cells. To the side of the artery this tissue is one mass of round cells, and all along the nerve sheath are new-formed and widely dilated blood-vessels. The lymph space is obliterated, due in part to the infiltration and swelling of the nerve and in part to the infiltration of the arachnoidal sheath and space, and also of the dural sheath (Figs. 3 and 4). The side nearest the vein is likewise infiltrated with round cells, as is also its dural sheath. These conditions exist to the very end of the nerve. In some of the sections the arteria centralis retinæ can be followed outward directly into the tumor mass, leaving no doubt that many of the large vessels permeating the tumor take their origin from the large central vessels.

The retina has been partly destroyed.

The sections of the anterior half of the globe (Fig. 5) show the retina detached to the ora serrata, from which point it was pushed anteriorly toward the lens, from both sides coming up close to the lens and then going backward toward the nerve head—a typical, total, umbrella detachment. In the triangular space between the lens and receding retinal framework are the connective tissue fibers of the vitreous. All the anterior sections of the choroid show this to be infiltrated. The ciliary body and its processes are atrophied, doubtless from pressure, and they likewise show slight infiltration.

The lens has not been affected and is perfectly normal, although the tumor mass with large blood-vessels is pressed up against its posterior surface. The lens shows the peculiar bulged edges always found in cases of tumor in the eyeball.

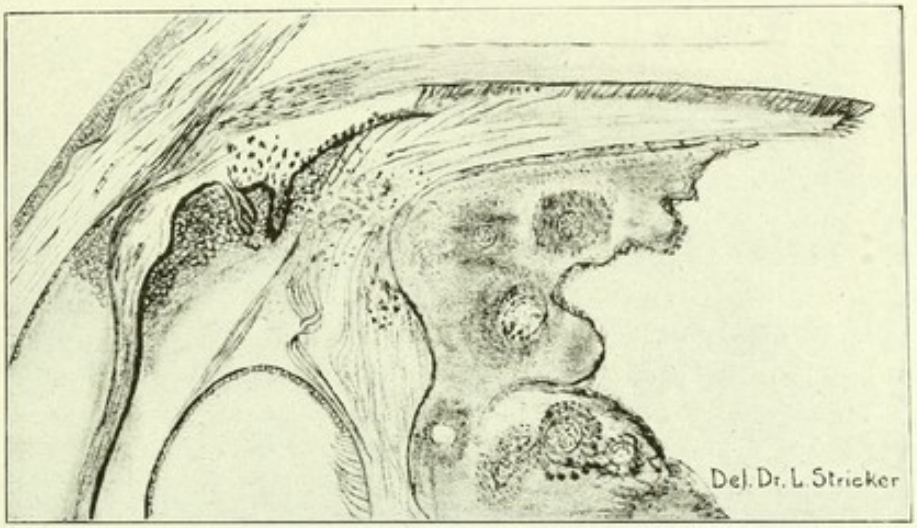

Fig. 5.—Section from anterior half of the globe, showing detached retina, atrophy of ciliary body and new growth pressing on the posterior surface of lens, which had remained perfectly transparent.

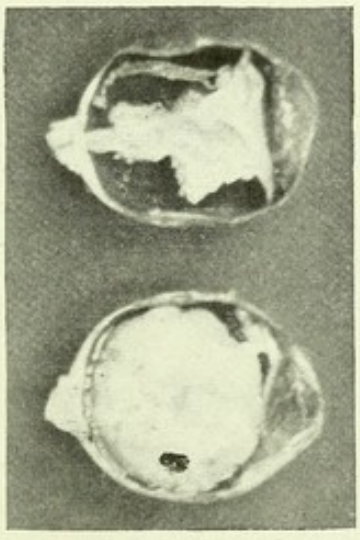

Fig. 6.—Case 2. Right eye, removed first. No recurrence three years and eight months afterwards.

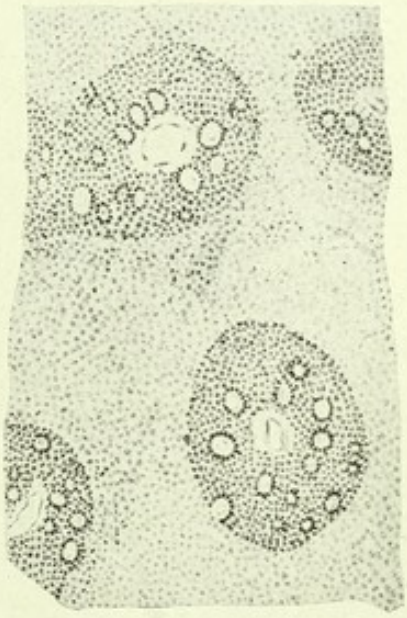

Fig. 7.—Neuroepithelial nests or "rosettes" surrounding a central blood vessel. (After Wintersteiner.)

On one side the tumor cells have worked their way through Petit's canal into the posterior chamber and forced the iris forward on that side, so as to produce a wide curvature, and a deepening of the posterior chamber. Some of the cells have found their way into the filtrating angle of the anterior chamber, which is not occluded.

The iris is atrophic, and near its insertion shows some widely dilated vessels. The cornea is normal. The sclera is attenuated owing to long intra-ocular pressure. Posteriorly, near the optic nerve entrance, it is traversed by vessels showing a large increase of nuclei in their vicinity.

This tumor is exceedingly vascular, the large size of the vessels being a prominent factor. Part of the tumor seems to be strictly confined to the choroid, and by a pedicle extends inward into the vitreous space, which is completely filled by the tumor mass. The large mass occupying the vitreous space has a characteristic appearance on section of deeply-stained portions around the vessels, and is less stained at more remote points, this being a result of removal of portions of the tumor from nutrition derived from the vessels. The growth of the tumor is likewise dependent on the growth of the vessels, around which the cells of the tumor arrange themselves, thus producing the alveolar or tubular form of tumor. The cells forming the tumor are all of the round-celled, non-pigmented variety.

The entire retina has been obliterated, save the cystic framework close to the ora serrata. That which originally—taking into consideration the age of the patient, 3 years—may have been a glioma, on spreading to the choroid—either by continuity of tissue or by direct introduction of cells of the tumor through the venous circulation—aroused this to excessive cellular activity, and so introduced the sarcomatous element which has completely masked the original picture, thus producing the glio-sarcoma of Virchow.

From this report the question might arise, whether or not this was a case of glioma, but the age of the patient, the rapidity of the growth, and above all, the early clinical picture, leave not the slightest doubt that the tumor primarily was a glioma, eventually assuming the sarcomatous type.*

Dr. H. J. Whitacre reported as follows upon the re-

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* The report, however, shows how very important it is to pull the globe well forward when enucleating, and to cut the nerve at the very apex of the orbit so that if possible, we may extend beyond that part of the nerve which may be infiltrated with cancer cells. In this case I resected the nerve far back, but the disease had extended further. Still, by subjecting the nerve to extra stretching, I might have secured more.

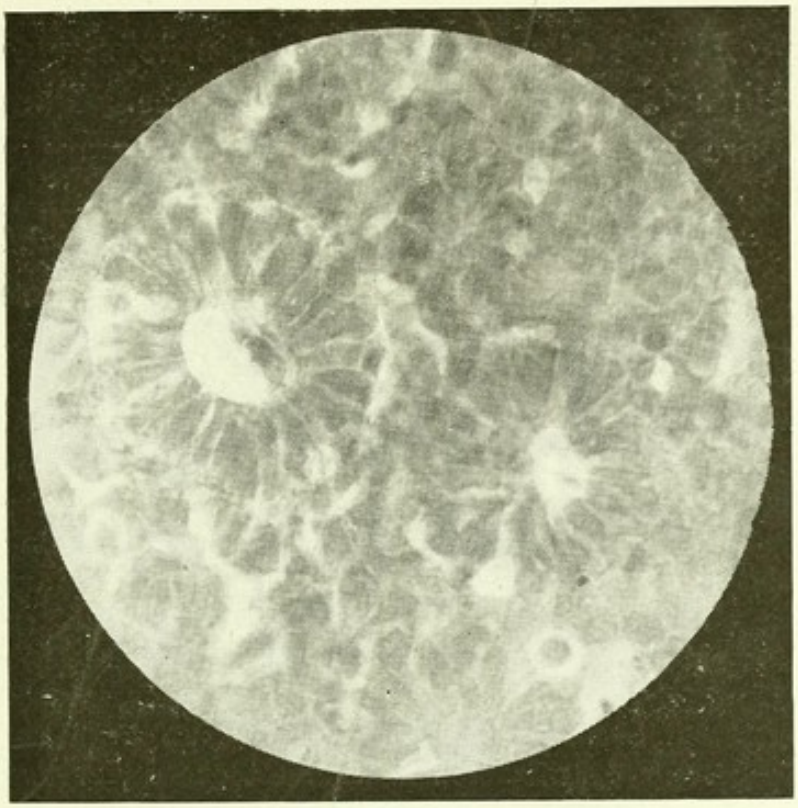

Fig. 8.—Photomicrograph showing the cells concentrically arranged around central vessels, forming "rosettes."

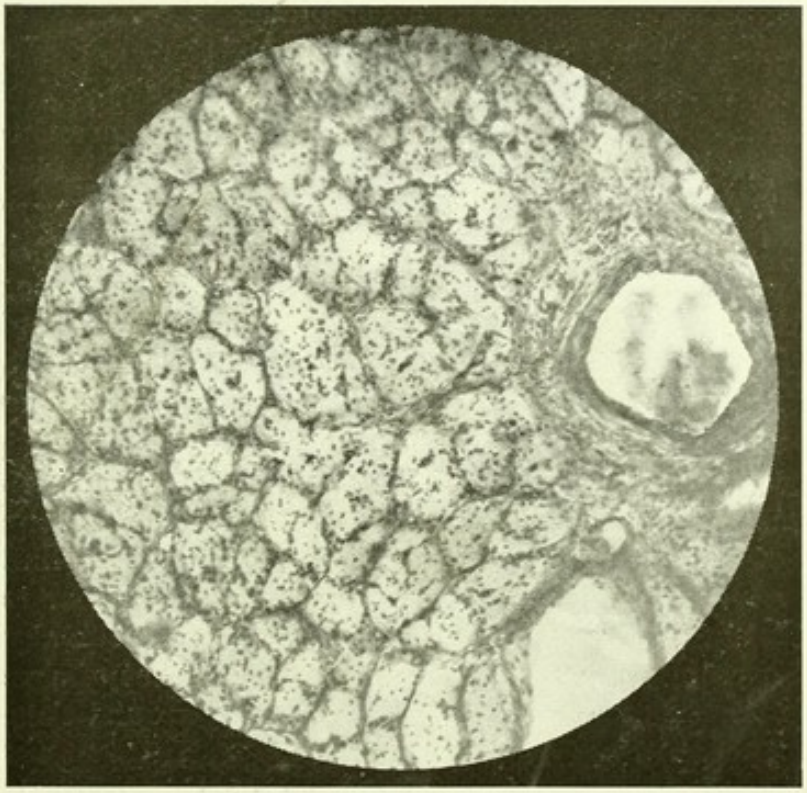

Fig. 9.—Case 2. Section of right optic nerve, removed with the globe. Nerve is normal, and there was no recurrence.

current growth springing from the optic nerve: The structure is that of small round cells in definite connection with a fibrous intercellular substance. The blood vessels are poorly formed and pigment granules are found in many parts. The tumor is a small round-celled sarcoma.

Case 2.—Baby R. E., aged 5 months, was brought to me Dec. 29, 1897. The child was well developed and nourished. Three weeks ago the parents noticed that the pupil of the right eye was dilated, and had a "silvery appearance which made the eye look dull." Dr. W. F. Shepherd was consulted, and promptly referred the case for consultation. The globe was congested; T.=+I; cornea clear; anterior chamber obliterated; lens and iris in contact with cornea; pupillary space filled with a mass of a reddish gray color, the surface being unusually vascular, the disease having advanced to the second stage. The appearance of the growth when examined under a strong light, gives a peculiar reflex not unlike a fire opal. Ophthalmoscopic examination of the left eye under mydriasis was negative. The child was admitted to my hospital; the same day enucleation with extensive resection of the optic nerve performed, and the specimen given to Dr. H. J. Whitacre for microscopic examination. The following is his report:

The specimen received was a complete right eye, which was placed in a 4 per cent. solution of formol for four days, and the hardening completed in 95 per cent. alcohol.

A sagittal section of the hardened specimen presented the appearance shown by the photograph (Fig. 6), and demonstrates a globular tumor occupying mainly the temporal half of the vitreous chamber. Posteriorly, the nasal half shows a pedicle attached to the point of entrance of the optic nerve. Anteriorly, the tumor presses against the posterior surface of the lens, and on each side of the detached retina can be seen a thin membrane extending from the tumor to the choroid.

The tumor, when half hardened, was very soft, and must have been almost gelatinous in its fresh state. Sections of the tumor were made with difficulty because of the multiple points of calcareous degeneration which dulled the knife and tore the sections. In general arrangement the tumor is made up of bands and circles of cells arranged regularly about the central opening (Fig. 7). The appearance is that of a vascular tumor with the cells concentrically arranged around the central vessel.

By higher magnification the lumen of this central vessel looks like the acinus of a gland surrounded by high columnar cells (Fig. 8); the other cells of the area have similar characteristics because of their origin by proliferation from these

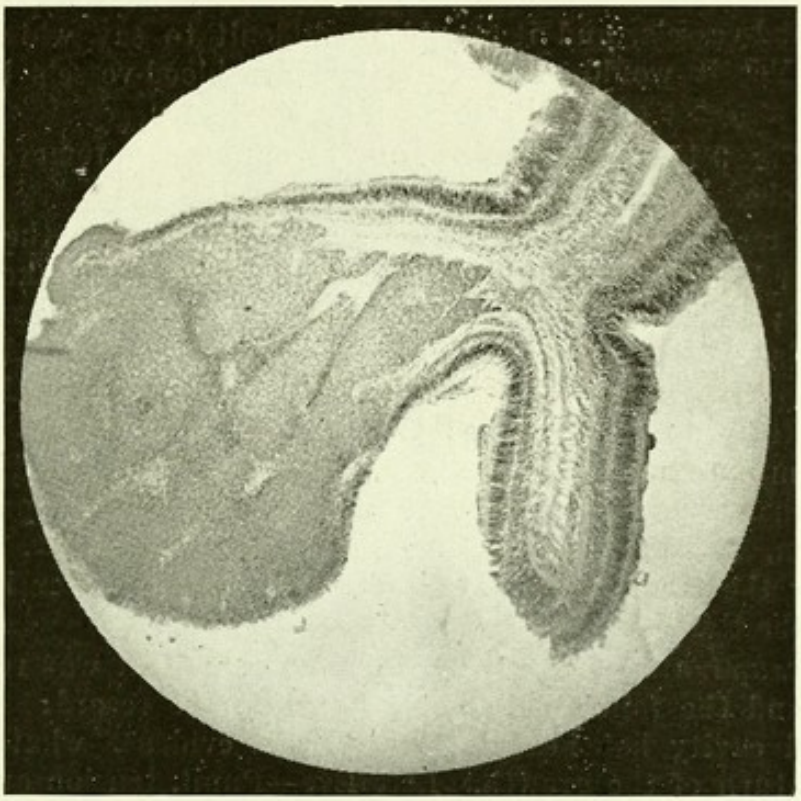

Fig. 10.—Glioma from right eye of Case 2, showing how the new growth sprang from the inner nuclear layer of retina.

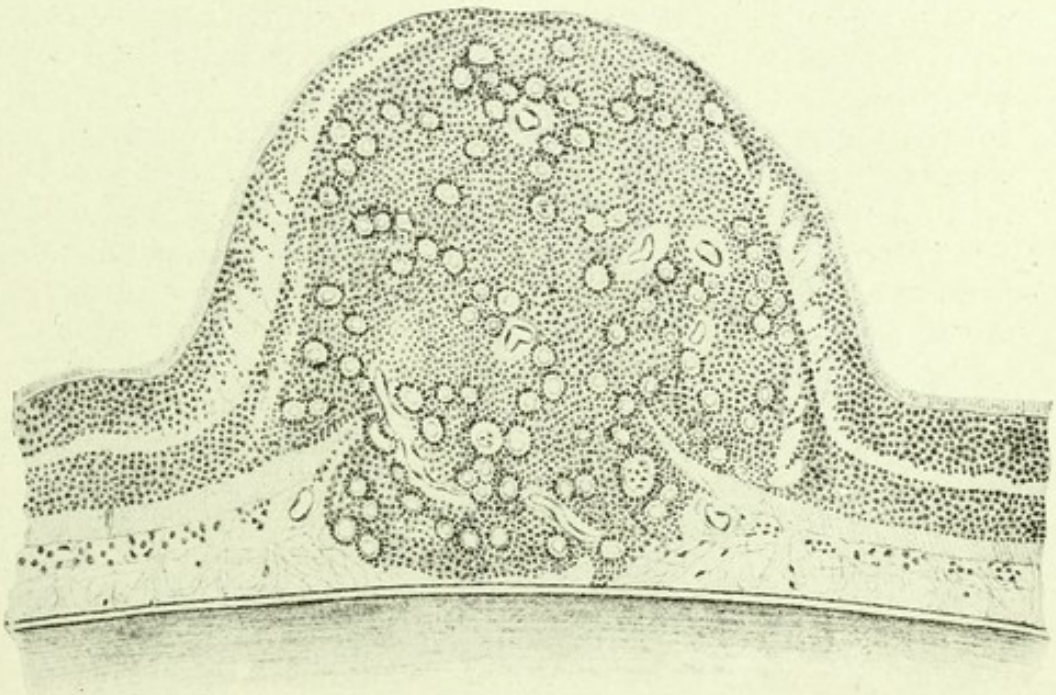

Fig. 11.—Miliary nodule (glioma) springing from the inner nuclear layer of retina, its location beautifully shown in Fig. 12, where a portion of the retina has been pressed against the posterior surface of the lens, the magnified growth shown here appearing as a minute nodule. (After Wintersteiner.)

central cells. These central openings may be either lymph or blood-vessels, and it would be difficult to say which they are. Yet it would seem that they are blood-vessels because of the presence of blood cells within their lumen.

In Fig. 9 is shown a section of the optic nerve removed with the globe.

The manner in which the glioma developed from the inner-nuclear layer is beautifully demonstrated in Fig. 10, taken from Case 2; and also shown in Fig. 11, copied from Wintersteiner; the relative size and location of this nodule is shown in Fig. 12. In this illustration we see three distinct gliomatous nodules in the totally detached retina; the one shown in Fig. 11 is seen as a minute pin-head swelling near the posterior surface of the lens. The second growth is in the upper and posterior portion, in shape resembling the lens, but smaller. While nearly the whole lower half of the vitreous chamber is filled with the third nodule.

Re-examination.—April 26, 1898. The patient was re-examined and the following note is found in the record: "Right orbital cavity has healed perfectly; no evidence whatever of any return of the growth. Left Eye—Pupil, tension and general appearance, normal. Ophthalmoscopic examination negative." In January, 1900, I sent a communication to the parents asking if the child was still living and if so to bring it to the office, which they did February 7. Child in excellent physical condition; the right orbit from which the eye had been removed 2 years and 2 months before, was in perfect condition, the conjunctival sac smooth and pale. The left eye appeared normal; the pupil was dilated with a mydriatic, a careful ophthalmoscopic examination made, and the fundus found normal.

On March 7 the mother returned, bringing another child who had complained of its eyes, as she feared that a similar growth might be developed in this child; this, however, proved not to be the case. I made another examination of the baby which she had brought with her and found to my great surprise that there was a small, whitish-yellow, irregular patch, appearing as a slight thickening of the retina, its edges not being sharply defined. It had an area of about one-half the diameter of the disc and was located outwards from the same about two diameters. The mother was told to bring the child again in one week, when it was found that the infiltration had spread, and near it could be detected a small fresh area of a similar nature.

There could now be no doubt about the diagnosis. The mother was informed that the eye was affected and was requested to return March 21 and bring the father, which she did. The areas of infiltration had increased both in area and thickness, and the parents were informed of the true

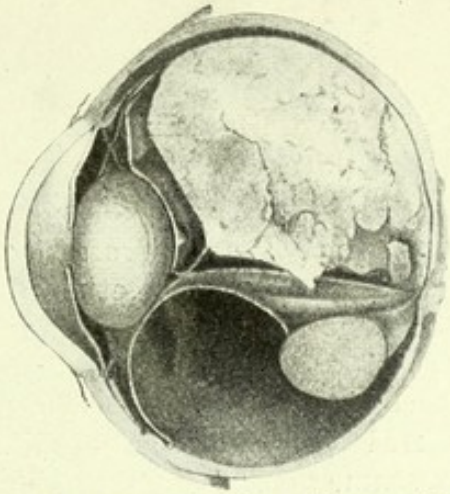

Fig. 12.—Section of globe, showing three gliomatous nodules in the totally detached retina, the third being very minute and seen near the posterior pole of the lens on which a part of the retina has been reflected. This nodule shown much magnified in Fig. 11. (After Wintersteiner.)

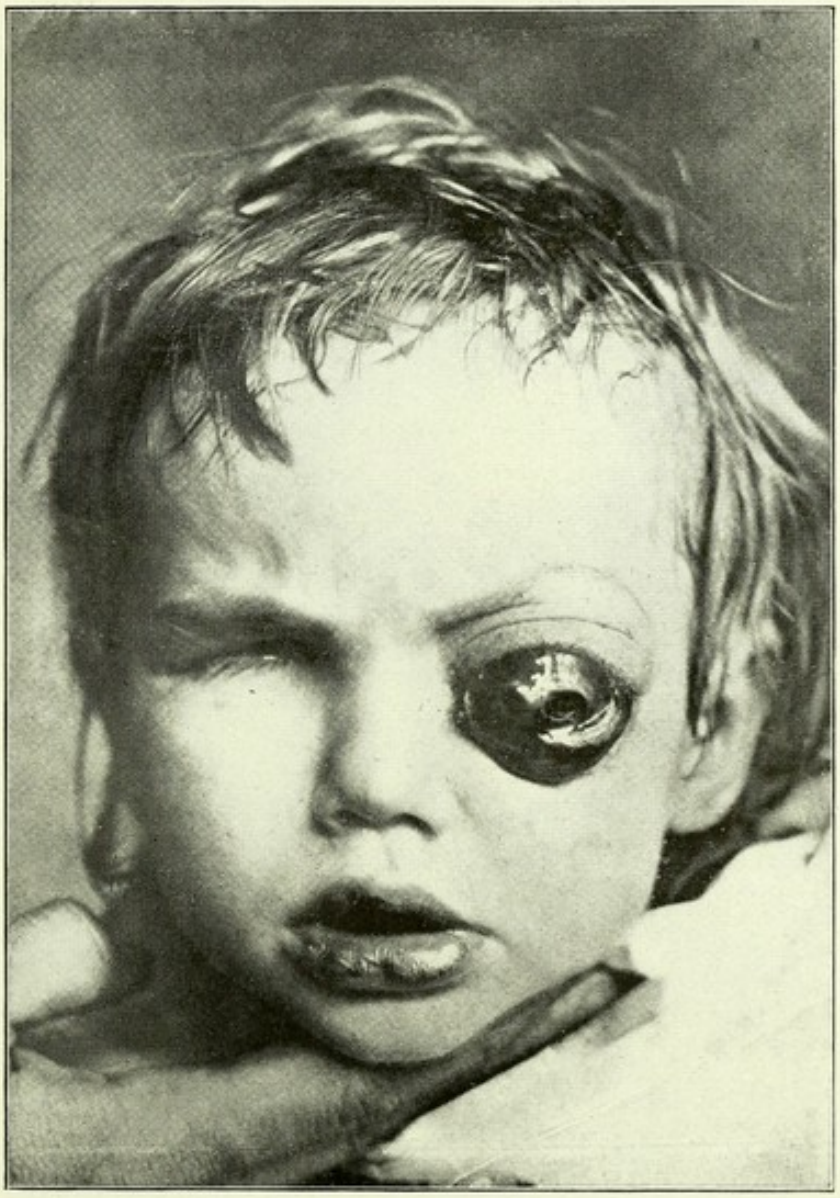

Fig. 13.—Baby Edwards.—Right eye removed three years before this picture was taken. No recurrence, nor was there any sign of it at the time of death, about eight months later. The left eye protruding and globe ruptured from extension of growth, beginning primarily in this eye.

state of affairs. To save life enucleation was urged; that was refused, and the patient disappeared. Dr. S. C. Ayres was consulted and confirmed my diagnosis.

The child received no further professional attention till April 17, 1901, when the parents returned, asking that an operation be made, if only to relieve the sufferings of the child, as it now cried or moaned constantly, refused to eat, and was rapidly becoming emaciated. The globe was protruding and had ruptured (Fig. 13). The child was readmitted to the hospital the same day and under chloroform, exenteration of the orbit was performed solely to afford temporary relief from pain. The growth filled the orbit, the optic nerve having become enlarged so that its diameter was almost equal to that of the globe (Figs. 14 and 15). Caustics were not applied on account of the hopelessness of the case.

In three days the child had again become playful and free from pain. June 3 the cavity had healed. The child has gained in flesh and is very bright and happy.

In a recent communication the family physician, Dr. Sheppard, states that in September the patient began to suffer again and was seized with convulsions, which gradually increased in frequency and severity and could be controlled only by the administration of chloroform. The pain was never a "marked feature." The child died Nov. 7, 1901. No autopsy could be obtained..

Case 3.—H. M., aged 2 years, was brought to me by her parents for a final opinion. I found it to be a typical case of neuro-epithelioma retinæ of the left eye at the end of the first stage, and advised immediate enucleation. They then informed me that this coincided with the opinion given by Drs. Ayres and Sattler. The operation was performed by them, and with their permission I merely state the condition of the patient as I saw her, and also her present condition as ascertained by a letter from the father, under date of Feb. 6, 1901, wherein he states that the child is in excellent health and attending school. A recent examination by an oculist showed the right eye to be perfect, excepting that it required a glass for correcting a moderate error of refraction, the vision becoming normal.

It is now 9 years since the operation, and as failure to recur after two years means a cure for the operated side, and the present age of the child (11 years) brings it almost absolutely beyond the period of development, we may consider the child's life saved.

Case 4.—L. L., aged 18 months, was examined Jan. 18, 1897. His parents and grand-parents are all living and well; no history of cancer, tuberculosis or consanguinity. He had chicken-pox at the age of six months, but no other diseases. About a month previous, the mother first noticed a glistening

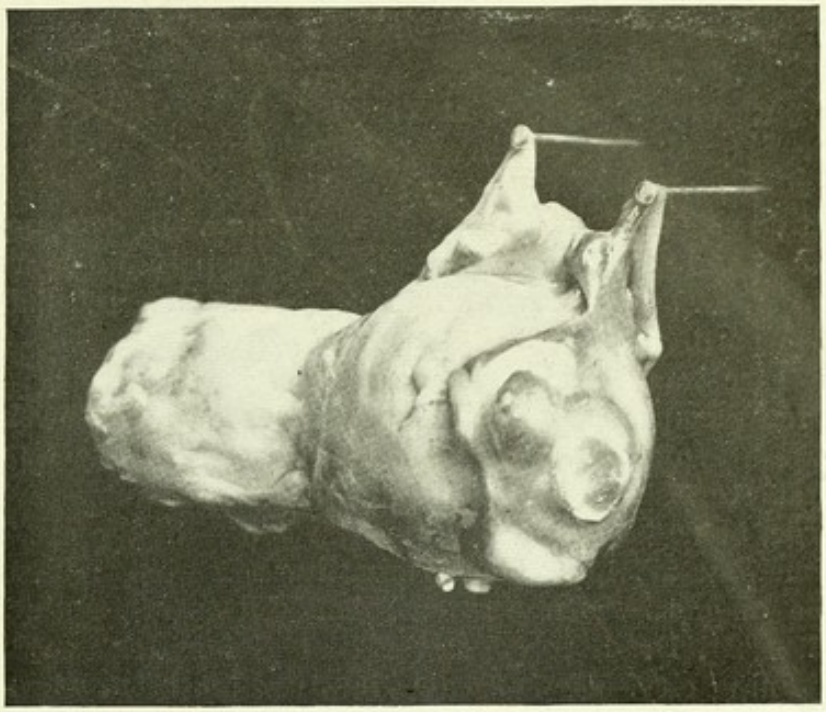

Fig. 14.—Baby Edwards. Left eye, showing also enormous infiltration of optic nerve.

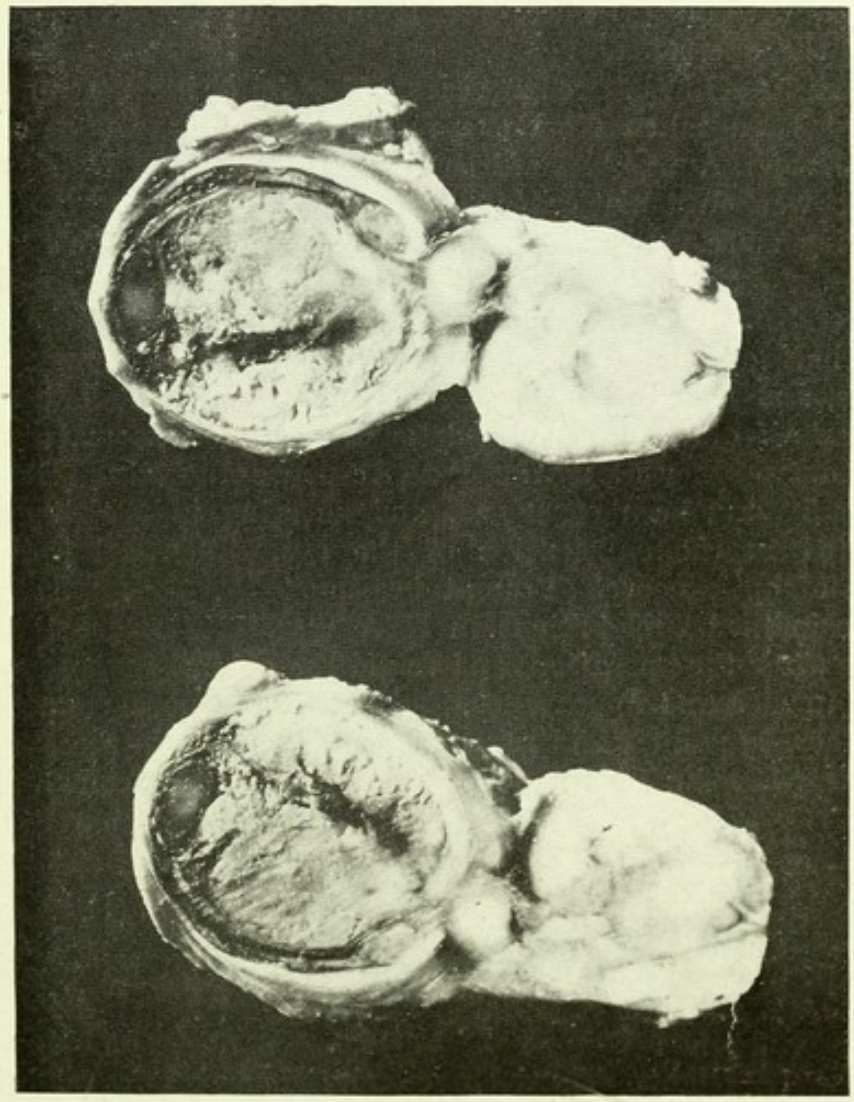

Fig. 15.—Baby Edwards. Section of left eye and portion of enormously infiltrated optic nerve. The lens was still clear.

appearance of the left eye, at first toward the inner part, but it spread quickly, involving almost the whole of the pupil. On bandaging up the well eye, the child acted as if blind, and tried to remove the bandage. He sleeps well, has not lost any in weight, and apparently suffers no pain. The mother has three children older and in perfect health and has had one still-born.

This case was referred to me by Dr. F. G. Stueber, Lima, Ohio, for an opinion as to the character of the growth. As this was a typical case of glioma retinæ, in the latter part of the first stage, I could only confirm the Doctor's diagnosis, and urge, as he had done, the speedy removal of the eye, which was done Jan. 27, 1897, the examination after removal confirming the diagnosis. In answer to my letter of inquiry, sent Feb. 6, 1901, Dr. Stueber stated that the patient resided in an adjoining city. He last saw him June 25, 1897, when there was no evidence of return, and that he has since heard that he is still in perfect health.

In answer to a letter of inquiry, the mother answered, under date of Feb. 19, 1901, that the boy was in perfect health, with no evidence of a return of the growth, 4 years after the operation.

Case 5.—H. W., aged 2 years. The following notes of this case I have taken from the record of my former associate, Dr. Joseph Aub: "About two weeks ago a yellowish-white reflex was first noticed in the right eye, which has been growing more perceptible daily, with deviation of the eye outwards. June 9, 1887.—The eye was examined to-day under chloroform. The entire inner and lower portion of the anterior half of the eye is taken up by a tumor, irregular in shape, and rich in blood vessels upon its surface. The entire outer half of the retina is detached; tension normal; deviation outwards well marked; no response to light. Dr. S.C. Ayres having been consulted, and agreeing in the diagnosis, assisted in the enucleation of the eye. Removed a liberal piece of optic nerve. Prompt healing."

I examined this patient in November, 1901, more than 14 years after the operation, and found the orbital cavity normal, both in size and appearance, and absolutely no asymmetry of the face, a point of interest in connection with the removal of the globe during infancy. The left eye was normal.

RESUME OF THE CASES.

Counting each eye as a case we have six operations. In speaking of a cure, I refer only to the operated eye.

Case 1.—Right. Third stage. Optic nerve affected beyond point of section. Recurrence and death.

Case 2.—Right. Beginning of second stage. Optic nerve normal beyond point of section. Three years and two months since operation. Cured.

Case 3.—Left. Beginning of third stage. Optic nerve affected beyond point of section. Recurrence and death.

Case 4.—Left. End of first stage. Nine years since operation. Cured.

Case 5.—Left. End of first stage. Four years since operation. Cured.

Case 6.—Right. End of first stage. Fourteen years since operation. Cured.

Three cases, or 50 per cent., were operated on during the first stage and all were cured; one case operated on in the second stage was cured. Two cases operated on in the third stage were fatal.

While the number of cases is very small, yet there can be no doubt that operations during the first stage with extensive resection of the optic nerve will give us a large percentage of recoveries for the operated side. We must also remember that in a great many of these cases the affection will involve the other eye sooner or later; by early removal of the second eye, however, the patient's life may be saved.

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