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RETINAL GLIOMATA TREATED BY RADON SEEDS

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THE following cases are reported in detail as a means of treating a condition for which it can be said there has been no alternative to removal of the eye, and when, as is frequently the case, both eyes are affected, the only remedy available in the past has been removal of both eyes, a mutilation to which parents will often refuse to submit their children. From the year 1871 to the end of 1924 there have been reported at the Moorfields Eye Hospital 163 cases of glioma of the retina, and of these the proportion of bilateral to unilateral cases was 1 to 5.11. (*Proc. Roy. Soc. Med.*, 1929, Vol. XXII, No. 9, p. 951).

It is proposed in the first place to describe in detail the clinical features of the five cases here reported, and afterwards to describe the technique, the choice of case, the changes which were observed to take place in the growths and tissues of the eye, and the results obtained.

Mr. Stallard alone is responsible for the preparation of macroscopic as well as the microscopic specimens, and for the examination and report upon all of these.

In two only of these five cases was it possible to watch, for any considerable period, the disappearance of the growths and the subsequent changes which took place in them.

In February, 1929, one of us had treated a case of sarcoma of the

choroid by insertion of radon seeds into the growth (*Brit. Jl. of Ophthalmol.*, Vol. XIV., p. 145), and now, two and a half years after, this patient is well, the growth remains shrunken, there is no extra-ocular extension, and no glaucoma; and there is no discoverable evidence that dissemination has occurred.

In the light of the above experience we took the first available opportunity of treating a glioma in the same way when it seemed justifiable, and this opportunity was afforded in October, 1929.

A small boy, E.H., aged 5 months, was seen by Mr. Rupert Scott, at St. Bartholomew's Hospital, on April 6, 1925, on account of the unusual appearance of the left eye. Glioma of retina was diagnosed and, three days later, the eye was removed. The diagnosis was confirmed by pathological examination.

On October 30, 1929, the child was again brought to see Mr. Scott because there was more discharge from the left socket, and it was said there had been pain in the right eye. Mr. Scott again took the opportunity to examine the right eye, and found a glioma at the upper and inner part.

Six children of the family were well; the first child was found to have had bilateral glioma of the retina at the age of a year, and died six weeks afterwards, apparently of intracranial extension.

Two children died of convulsions; the father died of a "tuberculous throat" in 1929.

On examination of the right eye a growth, evidently a glioma, was found in the upper nasal quadrant; the lower limits of it were well defined and here it was between three and four discs' breadth from the edge of the papilla. The upper edge was not easily seen and was not so sharply limited, vessels were seen in the tumour, and one or two small haemorrhages were present on the surface of it (Fig. 1).

Having regard to the experience of the first child, the mother refused to have the only remaining eye of this boy removed and, in these circumstances, we were glad to have the opportunity of treating the growth by radium, and Mr. Scott was good enough to transfer him to our care for this purpose.

The first seed was inserted on November 15, 1929; it was of 3 millicuries strength and, on ophthalmoscopic examination afterwards, it was found that no vitreous haemorrhage had occurred to obscure the view; every detail was seen as clearly as before, the steely blue seed was seen to have traversed the growth, and its point was projecting from its lower end, it having tunnelled the mass of growth a little too far on the temporal side; had it been a millimetre more in the lower nasal direction it would have been buried completely in the glioma and would not have shown on ophthalmoscopic examination; the apex of the seed was a little nearer the disc than the nearest point of the growth (Fig. 2).

FIG. 2.

Observations of the growth and the changes that took place in it were easily made, and there has been no difficulty in this regard up to the present time; the changes will be referred to in detail under the appropriate head.

On November 26, *i.e.*, ten days after the insertion, the seed was removed: again the media remained clear and, immediately after the removal, the hole through which the seed had been introduced was clearly seen, as a dark grey crater, having a sharp cut falciform upper edge, and shelving off below to the level of the rest of the fundus, with a small fringe of haemorrhage attached to it (Fig. 3).

There was no retinal detachment or other gross change except in the immediate locality of the growth.

Detailed observations of the growth were made.

By December 3, it was clear that the growth was less bulky and was shrinking; this was particularly noticeable in that the point previously nearest to the disc had perceptibly receded.

The boy was discharged from hospital on December 8, 1929. He was shown at a clinical meeting of the Royal Society of Medicine on December 13, 1929 (*Proc. Roy. Soc. Med.*, Vol. XXIII, No. 4, February, 1930, p. 475). He was re-admitted for observation from January 17, 1930, to February 19. We were particularly anxious to assure ourselves as to whether there was any recrudescence of the growth. We, however, came to the conclusion that none was present, and he was discharged.

On July 6 he was re-admitted because we thought that there was a recurrence of the growth in the region of the hole of insertion;

there was no certain sign of this and, looking back, we think perhaps we were too apprehensive.

On July 8 a fresh seed of 5.3 millicuries strength was inserted through the same hole as the previous seed—there was no constitutional disturbance. On the next day it was found that the seed had slipped entirely within the globe, so that a further operation was necessary to fix it within the hole. Certain changes occurred in the retina at a distance from the hole, which are referred to later, as the result of this accident, but there was no haemorrhagic or other disturbances of the vitreous, and every detail of the fundus was as clearly seen as before.

This second seed was removed on July 15, *i.e.*, a week after its insertion. No difficulty was experienced in finding it and removing it and the intra-ocular appearances were little changed as a result, except that a hole replaced the seed (Fig. 3). The patient was seen on January 2, 1931, when the intra-ocular condition seemed to be stable, with no evidence of an active growth in it; he was attending school with other children, keeping well, and putting on weight.

He was next seen on March 13, 1931, when he was shown at a meeting of the section of the Royal Society of Medicine, and it then seemed certain that changes had occurred which were not of the nature of scarring, but were indicative of recrudescence at the edge. He was therefore re-admitted for further treatment, the method of which is described later.

He was examined on May 15, 1931; after this further treatment was completed. No alteration in the intra-ocular appearances was appreciable, his visual acuity was at least 6/12, the lens and media were unaltered. The retina had a faintly mottled appearance in places, but we could not be sure that it represented a pathological change. The mother spontaneously stated that so soon as it became at all dusk he saw less well than her other children. He was last examined by all of us on September 11, when it was evident that changes had occurred.

As regards the site of the growth; it was completely scarred and there was no sign of the neoplasm, so that it may be said with certainty that the original glioma had completely disappeared and remained scarred after so long as a year and ten months. One of us, however, was not quite sure that there was not a recurrence at the temporal edge.

Other changes had, however, developed in the optic disc. Its edges were blurred, a number of flame-shaped haemorrhages had developed around it, several pale areas were present, and the sight had deteriorated. The child was ill looking and frequently awoke at night in an attack of "terror."

It seems likely that the disc changes indicate an intra-cranial deposit although the appearances are not typical of papilloedema,

and alternatively they probably imply local retinal deposits: the future progress will probably make it clear which of these is the case. There still was a tendency to redness of the skin of the lids and lid margins.

Case 2.—Winifred B., aged 5 weeks. Two weeks after birth the mother noticed “a redness in the middle of the right eye.” Two weeks later the child attended Moorfields, under the care of Mr. P. G. Doyne, and was admitted for a staff opinion, and no doubt was expressed by any member of the staff that the condition was a glioma. Mr. Doyne, knowing of our interest in such cases, was good enough to transfer her to our care.

This child was the seventh child in the family and all the rest were normal. She was born at full term, and there was no history of glioma in the other children or the parents.

There was a white mass filling the vitreous chamber. It had a nodular surface with a number of dilated vessels on it, no normal fundus was visible, the cornea, iris, anterior chamber, and lens were normal. There was no clinical evidence of extra-ocular extension. The left fundus was examined under a general anaesthetic, and no growth was found in it.

On October 31, 1930, one radon seed of a strength of 3·5 millicuries was inserted into the growth, through the lower temporal quadrant and behind the equator: the wound healed without serious reaction and on the tenth day, after a further exploration of the left eye, and having made as certain as possible that no growth was there, it seemed best to remove the right eye.

This was done on November 11, together with the seed *in situ*, and four seeds of 3·5 millicuries strength were put into the orbital tissues at the same time, as a precautionary measure.

During the ten days that the seed was in the eye there was no appreciable change in the appearance of the growth, the lens and cornea remained clear, the anterior chamber was well formed, and the iris was normal.

For twelve hours after the operation the temperature was 100°F., P. 155, and R. 46, but they all subsided to normal: the lids were slightly swollen and reddened.

The seeds in the orbit were removed a week later: the socket continued to discharge a turbid, sanious fluid, and the surrounding skin was reddened. The detailed report is included later.

The child was examined again on March 3, 1931, under general anaesthesia, to be assured that no growth was present in the left eye, and none was found after a careful search. She was healthy and well and now making good progress.

Case 3.—Albert P., aged 3 months, was seen at the Royal Eye Hospital, Manchester, on September 8, 1930, by Mr. Milnes Bride, who diagnosed bilateral retinal glioma. He removed the left eye,

which was the worse of the two, and confirmed the diagnosis by pathological examination, and was then good enough to refer the child to us.

The patient was a healthy looking boy, the left socket was clean. The right cornea was clear, the pupil was active, and the iris normal: there was a large mass of glioma occupying the greater part of the temporal half of the fundus (*a* Fig. 4) and, what appeared to be a simple retinal detachment below (*b* Fig. 4).

On September 23, two seeds of a 4·8 millicuries strength were inserted into the glioma. There was a large mass of growth,

FIG. 4. October 23.

evidently sufficient to embrace completely the seeds. They were therefore inserted free into the mass of the growth, without any fixing collar.

After inserting the seeds it was found, on ophthalmoscopic examination, that one of them was too far forward, so that a considerable part of it was protruding beyond the growth into the vitreous; it was therefore removed and re-inserted further back, so as to be embedded almost completely within the growth.

There was a slight rise of pulse rate after the operation.

Ten days later, on October 3, the seeds were removed without trouble, and it was then noticed that changes had developed in the lens; these changes are referred to in detail under a separate head.

Two weeks later, on October 16, the eye was examined under a general anaesthetic. There was redness of the skin of the lids and

FIG. 1.

FIG. 3.

FIG. 6.

surrounding tissues, but of no marked degree. All fundus details were clearly seen, there appeared to be some loose fragments of growth below; the main mass of the growth was readily seen, and was believed to be smaller. The child continued to improve physically and to increase in weight, having gained 2 lbs. 2 oz. since admission, *i.e.*, five weeks.

Examination under general anaesthesia was again effected on November 18, when it was clear that the mass of growth was

FIG. 5. December 2.

shrinking (*a* Fig. 5); the detached portion of the retina had a degenerate appearance with pale pigmented areas in it (*b* Fig. 5), and three islets in outlying districts were present, which might well be gliomatous deposits (*c* Fig. 5).

On December 2, examination again revealed little alteration.

On January 2, 1931, the child was again examined under a general anaesthetic. It was not possible to appreciate any alteration in the islands of glioma, but it seemed that the main mass was increasing at one part.

A 3.5 millicuries seed was inserted through the old hole, using a rubber fixing shield to hold it in position. Next day the child appeared to be suffering from a chill, but the local progress was satisfactory till the 8th day after operation when, as explained later, panophthalmitis developed.

Case 4.—This child had both eyes so full of growth that no retina that was certainly normal could be seen in either eye. It has almost no value, except with regard to the technique of insertion, to

which reference has been made. The child died on the table, of massive collapse of the lungs, just after the insertion of seeds in both eyes was completed.

Case 5.—E. C., aged $1\frac{1}{2}$ years.

The parents had noticed at the age of two months that the left pupil was "light in colour," but did not seek advice till seven months later when they took the child to the Royal Eye Hospital where glioma was diagnosed and the eye removed.

Six months later the parents believed the sight of the right eye was not good, and glioma was again diagnosed, but it was suggested that, before sacrificing the second eye, they should obtain a confirmatory opinion and, with this in view, they attended Moorfields on June 25, 1931.

On examination under an anaesthetic it was evident that the eye was largely filled by growth, and a small area only of what appeared to be normal retina was visible. An endeavour was made to make the case clear to the parents, and at their request radium was used.

On June 27 four seeds of 3.5 millicuries were applied, as nearly as could be judged at equal distance from each other, two intra-ocularly and two in contact with the sclerotic.

On ophthalmoscopic examination immediately afterwards it was seen that the two intra-ocular seeds were successfully buried in the growth and the only disturbance produced by their insertion, as judged by the ophthalmoscope, was the presence of two or three small areas of haemorrhage.

All the seeds were removed ten days later. A good deal of reaction developed in the conjunctiva and in the substance of the lids, making examination of the eye unsatisfactory, and no certain change in the growth was observed with the ophthalmoscope.

The eye was removed on August 4. The child recovered and put on flesh, and when last seen on September 28 was in good condition; the swelling of the lids had almost completely subsided; the lids were, however, still very red.

For Mr. Stallard's report, see later.

It will be agreed that for so desperate a condition as bilateral glioma of the retina a form of treatment which may be considered experimental needs no justification as an alternative to enucleation of both eyes, if it offers any reasonable hope of success: indeed many parents will refuse to submit their children to so dreadful a mutilation, although no doubt such an individual, in after life, can have and can form no sort of idea of what it is that is missing to him.

In the *Proc. Roy. Soc. Med.*, Vol. XXII, No. 7, p. 951,

1929, one of us published two of the earliest possible cases of retinal glioma: in each the diameter of the growth was a little greater than that of the optic disc (Fig. 6).

In the one case, on the advice of colleagues at Moorfields, we told the parents that the best prospect, from the point of view of the child's life, was to have both eyes removed; and to this they submitted. In the second case treatment of any kind was refused.

In the light of our present experience we should not again entertain the immediate removal of such eyes, nor consider it a proper procedure.

Choice of Case.—In cases of bilateral glioma there will be no divergence of view, we think, with regard to the desirability of some form of radium treatment, for one eye at least, whenever there is any reasonable area of intact retina. In cases, however, like case 4, in which it is clear that even if it could be certain that the glioma would be cured, yet there is no chance of vision being obtained, enucleation is clearly called for.

The case, however, is quite different where, after the most careful search under general anaesthesia, the second eye is proved to be free of growth; and most surgeons would advise removal of the affected eye in such circumstances.

From the nature of things one seldom sees an early glioma of the retina, except where it is discovered in the second eye as a result of the child having been brought for a glioma, which has given rise to signs which have been observed by the parents in the first eye, signs which, therefore, imply at least a somewhat advanced growth.

It seems likely that, so long as it can be seen that the optic disc is not involved by the growth, there is little or no danger of dissemination, and experience may perhaps prove that the insertion of radon seeds in unilateral cases is a proper procedure if a considerable area of normal retina be present. This, however, remains for future decision.

Technique.—The seeds we have used have all been prepared for us by Prof. Hopwood, who is in charge of the radium department at St. Bartholomew's Hospital.

Strength of Seeds.—Forty seeds have been inserted in various ways—the weakest strength used has been 1 millicurie, and the strongest 5·3 millicuries, and in 11 instances the strength has been approximately 3·5 millicuries; all have been filtered through 0·5 mm. of platinum. Figure 7 shows a seed with the silk attached alongside a millimetre rule.

Technique of Insertion.—Our endeavour has been so to insert the seed that it is completely embedded in the growth, so that if possible no seed is seen on ophthalmoscopic examination afterwards; twice only have we succeeded in doing this, on the other occasions a part of the seed has been visible.

On two occasions we have used a local anaesthetic, a general anaesthetic has been the rule, but local injections are preferable when at all possible.

The first point of importance is to locate the growth, so that the seed is completely embedded in it; and for marking the radius along which it lies one can make use of the method employed for locating the hole in cases of detached retina. The distance from the limbus and from the disc can best be judged by means of a general survey and consideration of the position with respect to the disc and the

FIG. 7.

ora serrata. It will be found that the general tendency is to judge the growth to be further forward than it is.

Exposure of the Sclera.—There are several ways of reflecting the conjunctiva and Tenon's capsule for the exposure of the sclerotic, and there are two chief desiderata; first to give easy access, and secondly, we believe it is important that the reflection is so planned that the hole in the sclerotic is well distant from the incisions through the conjunctiva, so as to make the spread of infection into the globe along the track of the silk as unlikely as possible.

Where the incision into the eye is to be made at all in front of the equator (*b* Fig. 5), we believe the flap indicated in Fig. 8 is best, and it is a good plan to have the stitch at *a* put in beforehand, so that it is all ready for tying afterwards. When the point of the insertion is to be further back, a similar shaped incision, but placed further back, gives good exposure and good covering afterwards—in any case a large flap is best. A strabismus hook or a small double sharp hook form convenient retractors for the soft tissues, and the globe can be pulled into the desired position by means of a stitch

passed through the episcleral tissues at the requisite spot, or by means of a fine sharp double hook which catches on to the sclera; or a liberal and firm forceps grip of the deep surface of the soft tissues, where they have been reflected from the eye, may be taken as far back as possible; it will be found that these tissues can be dragged upon forcibly and the eye rotated into the desired position, by this means, without there being any pressure put upon the globe.

The Incision.—The incision through the sclera is made with a broad cutting needle; and sometimes one can get an indication as

FIG. 8.

to the best direction for the track, for clearly, in the case of a sarcoma at any rate, the ideal track will be a perpendicular directed inwards from the centre of the base of the growth and so an endeavour is made to insert the cutting needle in this direction and, with this in view, we have had needles made bent at right angles, and at an obtuse angle.

It has seemed best that the hole made in the sclerotic should be of such a size as just to transmit the seed and no larger, and Messrs. Weiss have therefore made the blade of the needle 3 mm. across, which width is suitable for the standard sized seed (Fig. 7); the needle is dipped into a solution of gentian violet and allowed to dry; by this means the cut edges of the incision are stained and so the point for the introduction of the seed is marked.

It seemed advisable that a track should be deliberately cut in the substance of the growth, into which the seed is to be introduced, otherwise on inserting the blunt pointed seed the growth may be pushed in front of it instead of being transfixed by it; this has happened in one case at least, and we believe that the end is best attained by inserting the needle well into the growth thereby cutting a track in it into which the seed is introduced.

The seed is now taken in the introducing forceps and inserted, with a slight wriggling motion, through the hole in the sclerotic. This forceps is made with blades at any angle corresponding with the angle of the needle which has been used, so that the seed is inserted in the line of the track made by the needle (Fig. 9).

If the growth is of considerable size the seed is pushed right home by means of the dimple made for the purpose on the side of the heel of the forceps, and the silk attached to the end of it is now

FIG. 9.

cut short leaving a length of about $1\frac{1}{4}$ inches, by means of which the seed is removed later.

The silk should be black in colour so as to facilitate the finding of it when the seed is to be removed.

The conjunctival flap is now replaced and sewn in position, the short piece of black silk being completely buried under it.

Some differing degree of difficulty may arise when it is necessary to insert the seed far back, a difficulty that varies with the prominence of the eye, with the width and looseness of the palpebral fissure, and especially with the point of insertion.

It may be said that there is no great difficulty in getting as far back as the equator anywhere in its circumference, except perhaps above, and that on the outer side one can get further back without difficulty.

In Case 1, the apex of the seed was within 3 disc breadths of the edge of the disc and there would have been no difficulty in getting it further back so as to be in contact with the disc.

In Case 4, the point of insertion was about 5.5 mm. from the disc, and Mr. Stallard has measured the nearest point to which the sclera had been cleared and it was 1.5 mm. from the disc.

We have avoided dividing a muscle as a preliminary because of the necessary disturbance of the replaced muscle at the subsequent

removal of the seed; we should not, however, hesitate to do it, and in some situations it would clearly be necessary and would be a great help; and, further, we fancy, it would not be difficult to replace the muscle after the insertion, bringing the silk attached to the seed through its substance so that the seed might be removed afterwards without a second resection.

In some cases the mass of growth may be insufficient to embrace the seed and hold it in position, so that it may fall loose inside the globe. This happened in Case 1 where the second seed was inserted as a precautionary measure when the bulk of the growth had disappeared, so there was insufficient mass to embrace it. In such a case we have used a very small rubber shield, which can be boiled, through the centre of which a small hole is made, and into which

FIG. 10.

the seed is inserted so that its hind end is held in the ring and, as an additional precaution, the silk of the seed is threaded through the substance of the rubber (Fig. 10).

The position of the part of the seed within the globe can be planned according to the direction of the track of the hole through the rubber washer.

Where it has seemed advisable to put in a second seed at a later date there has been no difficulty in finding the old hole of entry, by its dark colour and, in Case 1 even after seventeen months, it was quite easily identified.

Removal of the Seed.—It was planned to keep the seeds in for ten days in every case, and this rule has been carried out with very little variation.

The original conjunctival incision has been opened up, the conjunctival flap turned back again, the black silk found, the hole exposed, and the seed extracted by pulling on the thread.

In no case has there been any complication arising from this, such as haemorrhage into the eye or externally, nor any loss of vitreous,

and although one has felt a little apprehensive lest the silk should snap at its attachment to the metal, it has not happened.

Changes which occur as a result of the Seed.—On the first occasion that a seed was inserted in February, 1929, we wondered whether necrosis of the sclerotic might occur immediately around, but it, and all succeeding cases, have shown that there is no fear of this with the strongest seeds. After the introduction there has been reaction of the outer parts of the eye, but for the most part not of excessive degree, no undue chemosis and, apart from the case in which infection occurred, there has been very little evidence of intra-ocular reaction; in no case has there been evidence of cyclitis; in each of two cases a single posterior synechia has formed. A rather common occurrence, however, has been what perhaps may best be described as an eczematous condition of the lid margins and adjoining skin overlying the site of insertion, and this has been long persistent; it was severe in Case 5.

In four adult cases in which seeds have been inserted special inquiry has been made as to the occurrence of pain: one complained of some, one said he suffered short attacks of knocking sort of pain, at about twelve hour intervals, but of no particular severity; the third man said he at first had a bout of twenty minutes of pain a day, on the sixth day it became quite severe for some hours, and persisted after this period till the seed was removed. Following this there was no pain. The fourth man had a good deal of pain.

With these four cases in mind, and judging from the behaviour of the children who were operated upon, we think it probable that these children suffer no very severe pain from the procedure.

On examining with the ophthalmoscope, while the patient was still on the table, in no case so far has the view of the interior of the eye been spoiled or even obscured by haemorrhage; thus, in one case, it was not possible to see the slightest change of any kind, it was exactly as if nothing had been done. In other cases the light, steely blue apex of the seed has been seen protruding from the area of growth, or showing through the intact retina.

In Case 1, November 15, 1929, on examining with the ophthalmoscope immediately the seed was inserted a filmy sort of cloud was present, partly overlying the exposed part of the seed; this we took to be coagulated vitreous (*b* Fig. 2).

Nineteen hours later this had increased so as further to hide the seed, irregular streaks of blood were present on the surface, and a band of blood was present, apparently trickling along under the edge of the seed. Three days after the insertion all details were seen as clearly as before the operation, there was no evidence of infection, the exudate overlaying the seed became more solid looking, and the seed was still fringed by haemorrhage. On November 22 it seemed that the exudate was clearing, and the whole growth had

an opaque, white, rather woolly appearance, and four days later the exudate had almost gone.

The seed was removed on November 26, no vitreous haemorrhage or retinal detachment resulted, and the hole of entry was plainly seen as a clear-cut, greyish, deep recess (Fig 3).

By December 3, *i.e.*, eighteen days after insertion, it was possible to say that the growth was disappearing; the part protruding towards the disc had, in considerable measure, disappeared, an area of dark haemorrhage was still present, and there was a small patch of pigment to the outer edge of the hole, which has remained since.

The boy was discharged from hospital on December 8, 1929, and was re-admitted for observation on January 17, 1930, when the condition was as seen in Fig. 3.

On April 15, the note was, "I do not think that there is any fresh change except that it seems to me probable that the hole is filling up, and the edges are perhaps thickening as if from new growth, but I do not think the change is sufficient to be sure of it."

July 8. A fresh seed of a strength of 5.3 millicuries was inserted through the old hole, as there was a suspicion that a recurrence was taking place at the upper margin of the hole. This seed slipped free into the vitreous, but was recovered and fixed as described under the head of Technique.

July 23. There were some strands of vitreous opacity attached to the lower part of the hole. A little fresh haemorrhage occurred at the upper edge, and a little white exudate and strands of vitreous were observed attached to the seed. There was no constitutional disturbance, and the clarity of the vitreous was not impaired.

Four days after the insertion of this seed three small patches of exudate were present along the upper temporal vessels and one larger patch along the upper nasal; events seemed to substantiate the fact that these were a result of the seed dropping into the vitreous.

Next day two fresh areas were seen and Mr. Stallard observed that all these areas had shifted downwards, thus showing that they were in the vitreous.

This seed was removed on July 15. Eight days later the opacities in the vitreous had completely disappeared, a few haemorrhages were present at the edge of the hole and elsewhere, and strands were present in the vitreous.

Below the sharp falciform upper edge of the hole was a deep blue grey recess, and this shelved off below into the retina, which had a mottled appearance.

There was a small fluffy mass which was marked to be watched for recurrence, and as accurate and detailed drawing as possible was

made of the upper edge of the hole, also with a view of watching any change in it.

On November 2.—The note was: "a few bright dots in the surrounding retina, now no haemorrhages and indeed I should be unable to be sure of any change at all as compared with the appearances before the seed was put in in July."

December 30, 1930.—He was seen by Mr. Stallard, who noted that the hole was filling in, apparently by fibrous tissue. A strand of vessels was extending into the vitreous from the nasal edge of the hole, but the pigmented area of the retina was unaltered.

On March 13, 1931.—The boy was again shown at the Ophthalmological Section of the Royal Society of Medicine. He was in good health, was attending school, and had an acuity of $\frac{6}{9}$ for certain. The edges of the hole, above and to the temporal side, were more solid looking, and the vascular strand extending forward into the vitreous had increased, and we believed at these points there was a recurrence, although the changes were slight.

On March 20, therefore, under general anaesthesia, a conjunctival flap was reflected, as at the first operation, and the point of insertion through the sclerotic of the previous seeds was found. It was easily identified as a dark, broadly linear marking, quite flat and smooth, with no suggestion of any growth or other tissue protruding through it.

Four seeds of 3.5 millicuries strength were applied to the sclerotic in such a way that the hole was, approximately, in the centre of them.

We had a fine groove filed in the platinum coating around the middle, and around this groove fine silk was tied, by means of which the seed was sewn in position on the sclerotic (Figs. 11 and 12).

The conjunctival flap was replaced. The boy complained of no pain afterwards, nor was there any unusual degree of reaction; the lid margins and adjoining skin showed the rather common eczematous condition.

After ten days the four seeds were removed without difficulty, and the conjunctiva replaced in position.

Observations on the growth are continuing (see earlier). It may be that this, or some similar form of contact application, will prove as efficient as intra-ocular insertion. We have at present under observation two other cases in which seeds have been applied in this way, but for the time being we have no sufficient knowledge on this point.

In Case 2.—All that one can say about the appearance of the growth is that the insertion of the seed was carried out without at all obscuring the view of the intra-ocular tissues, and that, during the ten days that it was under observation, no appreciable change

was noticed in the growth, and that no lens changes or evidence of intra-ocular inflammation occurred, nor was there coagulation or other change in the vitreous.

It was hoped that some definite histological change might be demonstrated in the cells of the growth as a result of their ten days' exposure to the emanations, and Mr. Stallard's report, which follows, is of interest in this connection.

FIG. 11.

FIG. 12.

Case 2.—Pathological Report. Macroscopic Appearances. The glioma is mainly exophytum, the retina being completely detached and lying in a folded state just behind the lens. The radon seed (see Fig. 13) is embedded in the lower half of the glioma, and its point is apposed to the posterior aspect of the detached retina at six o'clock and in the same plane as the equator of the lens.

The neoplasm for 3 mm. around the seed shows macroscopic evidence of degenerative changes. This area is homogeneous and structureless and has several small scattered haemorrhages. The upper part of the glioma at a greater distance than 3 mm. from the

FIG. 13. CASE 2. Winifred B., aged 5 weeks.

Photograph of globe divided vertically and to the temporal side of the optic nerve. The globe is embedded in celloidin.
a Detached retina. *b* Glioma retinae. *c* Radon seed. *d* Degenerate area of growth in the vicinity of the radon seed.

seed retains the granular "cream-cheese" appearance which is characteristic of this neoplasm.

The choroid is oedematous and there is some exudate in the supra-choroidal lymph space and the anterior chamber.

There is no macroscopic evidence of extra-ocular extension of the glioma.

Microscopic Appearances. (Preparation—Zenker fixed. Embedded in celloidin. Serial sections down to the site of the radon seed. Stained with haematoxylin and eosin).

The retina is completely detached from the optic disc to the ora serrata, the line of cleavage extending a short way between the pigmented and non-pigmented epithelial layers of the pars plana. Degenerative changes, oedema and small haemorrhages are present in the retina. The retinal vessels are congested.

The glioma arises from the inner nuclear layer and extends into the sub-retinal space. Degenerative changes are more marked in the vicinity of the radon seed, but are also present throughout the whole neoplasm. The tumour cells are variable in size and shape; some are swollen and others shrunken and crenated. The chromatin network is broken up into minute spherules which are disposed in an irregular manner in the cells, and in some cases project from the periphery of the cell as minute excrescences. The cells in which degeneration is more advanced stain pink with eosin and the nuclear remains are represented by some faint blue dots (Fig. 14).

FIG. 14.

Diagram of some of the glioma cells which have undergone changes as a result of exposure to radium emanations. Necrobiosis, chromatolysis, granulation and vacuolation are represented.

Degenerative changes are present throughout the neoplasm, but in the upper part there are a few islands of glioma cells the viability of which is doubtful. As these islands do not possess a central capillary and are presumably cut off from any blood supply, it may be assumed that their destruction is in progress. The capillaries which permeate the growth are dilated and surrounded by a narrow zone of degenerate glioma cells. Glioma cells extend up to the edge of the optic disc, but have not infiltrated the optic nerve.

Irregular clumps of brown pigment are scattered sparsely through the neoplasm, and haemorrhages are also present.

All the vessels of the uveal tract and the capillaries in the optic nerve are congested. There is oedema of the choroid and exudate in the supra-choroidal lymph space and the anterior chamber. The

anterior two-thirds of the lens showed no change in structure (the posterior portion fell away in the process of section cutting.)

Conclusions.—The nature of the neoplasm was proved to be a glioma retinae exophytum. It is probable that the entire tumour was destroyed by the radium emanations and that growth was arrested. The destructive action is particularly well marked in a zone 3-4 mm. around the radon seed in all directions. Except for some localized oedema and congestion of the vessels of the uveal tract the radium emanations do not appear to have had an adverse effect on any of the other structures of the eye, so far as histological appearances are concerned.

Case 3.—In this case Mr. Milnes Bride had removed the worse eye and had confirmed the diagnosis. In the right eye was a large mass to the lower temporal side (Fig. 4), and into this two seeds were inserted on September 23, 1930; one about 15 degrees to the south of west, and one about 15 degrees to the west of south. On examining with the ophthalmoscope it was seen that the top seed was not well buried in the growth, a half of its length was protruding through into the vitreous. It was therefore removed straight away and without difficulty re-inserted further back.

The seeds were removed ten days later. The changes which occurred in the lens are discussed separately later. There was some general redness of the skin and surrounding tissues.

Examination was made under general anaesthesia on October 16, that is twenty three days after insertion of the seeds. Everything was clearly seen, the mass of growth was believed to be smaller, though one could not be sure of this, and some loose fragments of growth were scattered about on the retina.

On November 7, *i.e.*, forty-five days after insertion, the growth had altered in appearance, having a "cream cheese" sort of appearance; a single synechia had developed. The child still increased in weight.

On November 18, the glioma was shrinking, and the adjoining retina was taking on the degenerate appearance which occurred in Case 1. On December 2, the growth was further reduced in bulk, and the area of degenerate retina was increased (Fig. 5). The small outlying areas in the retina were little altered.

On December 12, the child was examined again under anaesthesia, and a small fragment which overlaid the point of insertion of the seed was removed for examination. It proved to be fibrous and granulation tissue only.

The isolated fragments did not increase in size, but it appeared that one part of the growth was increasing; a 3.5 millicurie seed was therefore inserted on January 21, 1931, held in position by a

rubber washer; and a new departure was to leave the silk attached to the seed long, bringing it out through the palpebral fissure and securing it to the cheek.

The next day the child showed signs of bronchial catarrh with nasal discharge, and soon became rather ill of it, and was too ill for anaesthesia to be advisable.

On the thirteenth day the seed was removed. *Streptococcus haemolyticus* was found in cultures of the conjunctival sac, and it soon became apparent that panophthalmitis was present, and

FIG. 15. Case 4. R.M., aged 6½ months.

Photograph of globe divided obliquely. The specimen is embedded in celloidin.

a Glioma. *b* Choroidal haemorrhage. *c* Radon seed inserted 5.5 mm. from the temporal edge of the optic disc. *d* is the most posterior point to which the sclera was exposed at operation. It is 1.5 mm. from the temporal edge of the optic disc. *e* Sub-retinal exudate.

ultimately the eye was removed. The child recovered and left hospital seemingly happy and well and in good health.

Case 4.—Fig. 15 shows one of the eyes with a seed *in situ* and, as will be seen, it was found possible to insert it at a point within 5.5 mm. of the optic disc. The sclera was found to have been cleared to a point 1.5 mm. from the disc, at which point a seed could easily have been put in, had it seemed advisable.

Case 5. Macroscopic Appearances.—The globe is small and shrunken.

There is a corneal ulcer which has perforated, and the remainder of the cornea is thin and ectatic. The sclera is thickened. There is no macroscopic evidence of extra-ocular extension of a neoplasm. The eye was divided horizontally, and the advance of the knife was arrested by a dense calcareous mass which occupied the vitreous

chamber. The anterior chamber is absent, the vitreous lying forward, and the retina detached.

Occupying the vitreous chamber is a neoplasm in which are calcareous deposits. The choroid is oedematous and congested.

Microscopic Appearances.—The corneal ulcer has perforated and the lens capsule is apposed to the posterior aspect of the cornea. The iris is converted into granulation tissue, and presents many new vessels which are congested. The vitreous has been forced forward and contains leucocytes, red blood corpuscles, and exudate.

The choroid is oedematous; the vessels are congested; there are some small haemorrhages and mild leucocytic infiltration is present. It is not invaded by the neoplasm.

The retina is detached and, except for a small strip at the ora serrata, is entirely destroyed by a neoplasm having the typical appearance of a glioma retinae.

The growth has extended into the subretinal space. Its diameters are 7.5×7.5 mm. It is degenerate; calcareous deposits are present; there is much fibrosis, and hyaline change. Haemorrhages, mild leucocytic infiltration, and congested blood vessels are in evidence. Except for twelve small islands of glioma cells, each measuring $1/10$ mm. in diameter, and arranged around the periphery of the main mass of the neoplasm, histological evidence points to its devitalisation and necrosis.

The retina is infiltrated by the neoplasm up to the optic disc, but there is no evidence of invasion of the optic nerve. The optic nerve is atrophic and shows an increase of neuroglial tissue and dilatation of the capillaries. There is no histological evidence of extra-ocular extension.

Pathological Diagnosis.—Glioma retinae.

Conclusion.—Except for the twelve small islands of glioma cells seen over a series of sections the neoplasm has been destroyed.

Lenticular Changes.—In a previous paper (*Brit. Jl. of Ophthal.*, Vol. XIV, p. 145, 1930), one of us showed that an unusual star-shaped opacity in the posterior cortex of the lens disappeared under the influence of radon seeds. Changes of especial interest took place in the lens of Case 3.

On September 23, 1930, two seeds of a strength of 4.8 millicuries were inserted into the eye. These were removed ten days later and it was then observed that three groups of what appeared as aggregated vacuoles were present in the posterior cortex of the lens.

Thirteen days later these changes had increased so that now there were seven of these groups and, exactly as before, they seemed to be aggregations of transparent vacuoles in the lens substance (Fig. 16).

On November 7, *i.e.*, twenty-two days after the last examination, and forty-five days after the insertion of the seeds, five groups only of vacuoles were left (Fig. 17).

FIG. 16. October 14, 1930.

FIG. 17. November 7.

On November 18, there were still five groups (Fig. 18).

On December 2, four groups could be identified, though they were very small (Fig. 19); and on January 2, 1931, the whole lens had returned to its former clear condition, except that one small group was discernible in the upper part of the lens (Fig. 20).

This was the last occasion of observations on the lens.

It is not obvious why lenticular changes should have developed in this and not in the other cases, but one may recall that two seeds of 4.8 millicuries were inserted and, as remarked elsewhere, one seed was at first too far forward, that is, rather close to the lens, but it was not retained in the position for more than ten minutes, at most, before its removal.

FIG. 18. November 18.

FIG. 19. December 2.

FIG. 20. January 2, 1931.

The increase in the opacities, which continued for some time after the seeds had been removed, is interesting, and especially also the fact that they disappeared practically completely within rather less than three months.

Conclusions.—It is evident that the data that are here presented are too scanty for much that can be properly set under the head of conclusions; sufficient, however, has been shown to guide us in further investigations, and enough it may be thought to justify further treatment along these lines, more especially in bilateral growths.

It is demonstrated that a seed of at least 5·3 millicuries may be inserted into the eye, and that at least five seeds, each of a strength of 3·5 millicuries, may be applied to the outside of the sclera without causing sloughing of any of the tissues.

The technique of insertion and subsequent removal of the seeds has been described and has been found to present no difficulties.

It is shown that a retinal glioma will disappear under the influence of radon seeds, and that in a concrete case a glioma of moderate size not only was not increased in size twenty-two months after the commencement of treatment, but was shrunk and seemed to be completely scarred; it is, however, premature to say that it is cured.

Histological changes in the glioma cells which have been exposed to the radon seeds have been demonstrated.

Opacities of a special type in the lens have been watched to develop and afterwards to disappear completely.

Further investigations with radon seeds on sarcomata as well as gliomata are being prosecuted, both intra-ocularly and as surface applications to the sclerotic.