RETINOBLASTOMA

REPORT ON 19 PATIENTS TREATED WITH RADIOOTHERAPY

BY

M. W. PATERSON† AND A. A. CHARTERIS‡

From the Department of Ophthalmology, University of Glasgow and the Radiotherapy and National Radium Centre, Western Infirmary, Glasgow

RETINOBLASTOMA is usually diagnosed when it has already severely affected one eye to the extent of producing a visible change in the pupil or a squint. If it is present in both eyes, the more affected eye is usually enucleated, and if the diagnosis is confirmed histologically the decision has to be made either to attempt to destroy the tumour in the remaining eye while preserving useful sight, or to remove the second eye in the effort to save the child’s life. If extra-ocular spread is already present the child will not survive, and treatment can be only palliative.

The decision to attempt to preserve the eye is justified if a method is available of completely and permanently inactivating the tumour, and if there is some retina which is unaffected by the disease and will remain unharmed by the treatment. In general, the likelihood of preserving useful sight becomes very small if more than one-third of the fundus (some would say one-quarter) is involved.

Radiotherapy in some form is the most reliable of the methods available, with chemotherapy coming into use as a valuable adjuvant. Diathermy has been used for tumours less than one disc diameter across. The possibilities of light-coagulation are under investigation and Meyer-Schwickerath (1960) has claimed the same degree of success for this method as other workers have reported using X-irradiation combined with chemotherapy.

Successful radiotherapy depends on having a localized and reasonably sensitive lesion in such a position that an effective dose of radiation can be administered uniformly in a time depending upon the total dose required. The normal tissues in the vicinity should have a good blood supply, and the differential action of irradiation enables one to deal with the tumour while causing minimal disturbance to normal tissue.

These requirements are not easy to achieve in dealing with so delicate an organ as the eye, upon which the effects of high irradiation levels are well known, while the sclera proper is almost avascular. In some instances the tumour is multifocal and the sites can be very diverse within the one eye.

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† Present address: Glasgow Eye Infirmary.
‡ Late Director, Radiotherapy and National Radium Centre, Western Infirmary, Glasgow.
One possible method is to place radio-active material on the exterior of the globe at the required position, and this has been done using radon seeds. For one patient in this series, the seeds were fixed on a small mould made of dental compound, but this was found difficult to work with. For other patients the seeds were stitched in place in an appropriate arrangement, but later, plastic envelopes containing the seeds arranged in the desired pattern were attached, again by stitches, and this seemed easier. In all these applications the seeds must, of necessity, be very near the sclera, so that the incident dose is very high and above normal therapeutic levels if an adequate dose is to be received by the tumour. The anatomy is such that the achievement of a distance between the seeds and the sclera sufficient to even out the dose seems impossible. On the other hand, the treatment area is very localized and this is important as far as the eye dose is concerned. Cases with multiple lesions, or those in which the growth is near or opposite the optic nerve, can hardly be dealt with in this way and X-ray therapy was therefore tried. By using small-angle fields converging behind the lens such tumours can be treated, and in this instance there is no point subjected to abnormally high dose as opposed to “tumour dose”. The accurate direction of such fields is not difficult to achieve, though the application of radium to the same position would call for some form of directional shell as well as an anaesthetic.

The difficulties of satisfying the usual conditions for radiotherapy are therefore very great, but it seemed essential to make the effort in an attempt to preserve sight or, in many cases, merely to diminish suffering. The measure of success may not appear very great, but this seems to us to reflect the magnitude of the problem and, of course, even the most unfavourable cases have been included in this review. Obviously those with extension of the tumour beyond the eye, or with metastases, could not receive effective radiotherapy. It should be noted that the resources of the radiotherapeutic department were very meagre at the time in question and there may now be new possibilities from the use of supervoltage therapy. The linear accelerator, with its isocentric mounting, would be easier to handle and its beam, which could be as small as desired, would be much better defined than is the case with conventional therapy. It also seems likely that the two converging fields, modified by wedge filters, could give a well-localized tumour dose area, and work along these lines seems desirable.

The use of X-rays has been fully described, and the results obtained in a large series of patients reported at intervals, by Reese, Hyman, Merriam, Forrest, and Kligerman (1955). The dosage they applied has been gradually reduced. Originally they made three applications a week to alternate portals over a period of three and a half months to a total of 8,000 r/air × 2. This was reduced to 4,400 r/air to each of two portals. Of 148 patients, 43 died of the disease, 26 were lost to follow-up (19 doing well when last seen, 7 not doing well), and 79 survived; of these survivors, 19 (23·7 per cent.) had useful vision, 10 (12·5 per cent.) had limited vision, and 51 (63·8 per cent.) had no vision. Late haemorrhage into the vitreous, which might occur as long as one and a half years after the completion of treatment, was a complication which could mar an apparently successful visual result.

Following Alan Woods’s demonstration of a patient in whom a remarkable regression of a retinoblastoma occurred after the use of triethylene melamine
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(T.E.M.) (Kupfer, 1953), Reese and his colleagues treated 34 eyes with T.E.M. plus radiotherapy and satisfactory regression was obtained in 19. This method has not been used by us.

Dollfus and Auvert (1953), whose monograph surveys all the available reports up to that date, give details of 46 patients treated by radiotherapy and personally followed up. Of these 9 were treated for orbital recurrence after enucleation and 10 were given “prophylactic” irradiation of the orbit. Twenty-seven were treated for intra-ocular tumour, almost all in the second eye of a bilateral case. Of these 10 had died, 5 had had the second eye enucleated, 2 were living but blind, 1 was living, with vision, over five years after treatment, 1 was living, with vision, over three years after treatment, 2 were living, with vision of at least 1/10, over two years after treatment, and 6 had been treated for less than two years at the time of the report.

The authors point out the advantage that X-ray therapy can be practised in any well-equipped centre with an experienced radiotherapist.

Stallard (1962) has reviewed the subject in detail in his Doyne Memorial Lecture to the Oxford Ophthalmological Congress. He considers that treatment by means of X-rays has the disadvantage that it is impossible to direct a sufficiently narrow pencil of rays to strike accurately a neoplasm in an eye which cannot be completely immobilized, and that there is therefore a danger of scattered rays affecting the lens, skin, conjunctiva, cornea, and the eye as a whole in a manner which may lead to glaucoma.

He used radon seeds in his first series of 16 children. In 10 the neoplasm was destroyed and useful vision retained; in 5 no useful vision was retained; and one child died from metastasis from the opposite orbit.

In his second series of 104 children he has preferred to use $^{60}$Co contained in curved metal applicators sewn to the sclera over the site of the neoplasm. The applicators are usually circular, but crescentic when the neoplasm is close to the optic nerve, and semicircular when it is near the ora serrata. He considers that radiotherapy is so effective for retinoblastoma less than 10 mm. in diameter that there is no case for excising a unilaterally affected eye containing one of this size. If more than two islands are present, irradiation with $^{60}$Co should be combined with synergetic chemotherapy. In this series 85 children survived, 62 retaining useful vision (6/18 or better in 48).

The 19 patients in the series here reported are those treated during the period 1947 to 1962. All except one had the more severely affected eye removed and the diagnosis confirmed histologically in the first place. The exception had radiotherapy to both eyes, but one eye was thereafter removed. Five patients were treated by means of radon seeds alone, 3 had radon seeds and X-ray therapy, 11 had X-ray therapy alone. Thirteen patients survive at the time of writing, the minimum period since completion of treatment being three years. Of these, 5 have vision of 6/12 or better, 3 have vision of less than 6/12, in 1 the vision is not known but certainly poor, and 4 have had the second eye removed; 5 patients have died of the disease, and 1 patient has died of intercurrent disease. These figures are set out in the following Table.

Detailed records of the 19 cases comprising this present series follow.
TABLE
RESULTS IN 19 CASES OF RETINOBLASTOMA TREATED BETWEEN 1947 AND 1962

<table>
<thead>
<tr>
<th>Result</th>
<th>Vision</th>
<th>Radon Seeds only</th>
<th>Radon Seeds + X-rays</th>
<th>X-rays only</th>
<th>Totals</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surviving</td>
<td>6/12 or better</td>
<td>2</td>
<td>—</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>Less than 6/12</td>
<td>—</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Very poor</td>
<td>1</td>
<td>—</td>
<td>—</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Both eyes removed</td>
<td>2</td>
<td>—</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Died of the disease</td>
<td>—</td>
<td>1</td>
<td>—</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Died of intercurrent disease</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>5</td>
<td>3</td>
<td>11</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

Case Reports

Case 1. The right eye was removed in January, 1939, from a 2-year-old girl, and retinoblastoma was confirmed. Fifteen months later a whitish tumour was seen in the left eye on the nasal side of the disc and towards the lower nasal quadrant. The anterior edge was some 6 mm. behind the limbus and the tumour extended from 7 to 9.30 o’clock. The diameter was not more than 8 mm.

Four radon seeds, each 1 mc. in 0.5 mm. Pt, were applied in a 1 cm. square arrangement in a mould stitched to the sclera for 10 days, giving a dose of 11,000 r at 1 mm. depth and 9,600 r at 3 mm. depth, the probable limit of the growth.

Nine weeks later the sclera was sloughed slightly at the site of irradiation. Ten days later the cornea was slightly steamy and there was cloudiness in the anterior chamber. The growth was wrinkled and possibly slightly less in volume.

Two months later the sclera was healing rapidly; the cornea was clear; the tumour was present but small. The child was active and apparently seeing quite well. The right orbit was now found to contain a hard sub-conjunctival mass, considered to be a metastasis in the optic nerve stump. The right orbit was exenterated and 3 radon seeds, each 0.6 mc. were inserted, one into the optic foramen and one into each fissure.

Seven weeks later the sclera of the left eye had healed, with thinning, so that the choroidal pigment could be seen. Two months later there was bulging at the irradiated site. In a further month acute intra-ocular inflammation occurred and the eye became blind, shrunken, and soft. It was removed because of pain ten months later, the girl then being aged 6. She was alive and in good general health in May, 1961, at the age of 24.

Case 2. (Patient of Dr. John A. Mortimer and Dr. Dorothy Primrose; did not come under the continued observation of either of the present authors.)

This girl’s right eye was enucleated at the age of 15 months, in April, 1942, and the diagnosis of retinoblastoma was confirmed.

Three radon seeds of 1 mc. and 1 seed of 0.5 mc. were sutured to the sclera of the left eye and left in position for 7 days. Two months later slight shrivelling of the growth had occurred and it then had the appearance of a degenerative choroiditis.

The left eye was removed at the age of 2 years. The patient was alive and in good general health in 1963, and was doing a full week’s work as a shorthand typist.

Case 3. Palliative therapy after extra-ocular spread. (Patient of Dr. Urquhart and Dr. J. Pendleton White.)

This boy’s left eye was removed in August, 1946, at the age of 2 years. Five months later there was marked proptosis (2 cm.) of the right eye, with injected swollen conjunctiva, hypopyon, papilloedema, and infiltration of the orbital margin.
Palliative X-ray therapy was given in 11 treatments over 15 days, through a direct field of area 5 cm. diameter, distance 50 cm., 200 kV., M.A. 8, filters Cu 0·5 mm., Al 1 mm., H.V.L. mm. Cu 1·1 per cent. Dose delivered by portal of entry: skin 2,000 r, tumour 1,000 r.

The patient was discharged home at his parents’ request, and died two months later, unconsciousness and fits having developed. Dr. Urquhart reported that there had been no apparent benefit from the treatment, and large secondary deposits were present in cervical glands on the right side, in the ribs, and in the liver.

Case 4. Palliative therapy after extra-ocular extension. (Patient of Dr. S. Meighan.)

This girl’s right eye was removed in December, 1946, at the age of 11 months, the tumour filling the globe in continuity with extra-ocular limbal sub-conjunctival extension. Tumour cells were also found in the sub-arachnoid space around the optic nerve. The left eye appeared to be unaffected.

In January, 1947, X-ray therapy was applied as a palliative measure to the right orbit in 9 treatments over 21 days (200 kV., M.A. 8, field 1 area 5 cm. diameter, filtered by 0·5 mm. Cu, 1·0 mm. Al. Dose delivered by portal of entry: skin 3,000 r, tumour 2,040 r.).

Three months later mild fits began and for three days the patient was almost continuously asleep before she died in the Royal Hospital for Sick Children. Necropsy showed the cause of death to be diffuse pneumonia. There was no evidence of increased intracranial pressure, or any sign of tumour in the orbit.

Case 5. Palliative and placebo therapy to a large intra-ocular tumour. (Patient of Dr. J. S. Conway.)

This girl’s left eye was removed in 1943 at the age of 1 year and retinoblastoma was confirmed.

In 1947 the right eye was found to contain a tumour which filled the lower half of the globe and extended upwards on the temporal and nasal sides, presenting a solid appearance.

In April, 1947, X-ray therapy was given in 15 applications over 21 days (200 kV., 15 M.A., two fields—right and left lateral oblique—aimed at the posterior portion of the globe. Skin dose delivered to each field: 2,650 r; tumour dose obtained: 3,000 r.).

The lesion appeared to regress and vision improved for two months (after a visit to Lourdes), but within a further three months the eye became totally blind and extension of the tumour was observed, with intra-ocular haemorrhage; six months later a new mass appeared.

In April, 1948, X-ray therapy was given as a palliative and placebo. In the first two applications the skin dose delivered to each field was 348 r and the tumour dose obtained was 393 r. A change was made because of a skin reaction, and 19 applications were then made over 25 days, using frontal, infra-orbital, and right inferior oblique fields. The skin dose delivered to each field was 3,000 r and the tumour dose obtained was 4,000 r. A further course of 5 applications was then given over 7 days through a medial field to the right eye. The skin dose delivered was 1,250 r and the tumour dose obtained was 625 r.

In December, 1948, spasmodic pain began to occur in the right eye, accompanied by vomiting, and the child was admitted to Killearn Hospital under the care of Mr. J. E. Paterson, who made a transfrontal exploration, displaying an optic nerve and chiasma of normal appearance; the optic nerve was excised. Fourteen days later the right orbit was exenterated. Encephalography thereafter showed a filling defect in the chiasmal cistern, suggesting the spread of tumour into this cavity.

In June, 1949, a small cherry-like tumour was seen in the right orbit and the child was admitted to the Victoria Infirmary, Glasgow, where X-ray therapy was given in 15 applications over 21 days (200 kV., 10 M.A., filters 0·5 mm. Cu, 1 mm. Al, giving 3,000 r). The tumour regressed rapidly towards the end of the treatment, but the patient’s condition was poor, though with no definite symptoms. On the last day of treatment she had two short convulsions and died without presenting further neurological signs. Necropsy showed extensive metastases in the right frontal lobe of the brain.

Case 6. (Patient of Dr. J. Marshall and Prof. W. J. B. Riddell.)

This girl’s left eye was enucleated in September, 1947, at the age of 6 months, and shown to contain retinoblastoma. The right eye had a massive tumour in the lower inner part, about four times the size of the optic disc A, a white area on the macula B, and a small white area above the macula C (see Fig. 1).
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In October, 1947, X-ray therapy was given in 15 treatments over 21 days (2 fields: right temporal and right nasal glancing and avoiding the lens, the fields being located by a mould; 200 kV., 8 M.A., filters 0·5 mm. Cu, 1 mm. Al, 50 cm. F.S.D., skin dose 3,000 r, tumour dose 3,120 r).

At the end of the treatment, A looked "deflated", with craggy ill-defined edges; B was a white area, flatter and broken up, with pigment mottling, and C was unchanged; two weeks later C appeared to be a hard white mass.

Fifteen years later (1962), A and B appeared dense and opaque as if calcified, and C had disappeared. The optical media were clear and the retinal vessels healthy. There was slight darkness of the macular area. Vision with correction was 6/9. A photograph of the fundus is shown in Fig. 1.

Family History.—A younger sister has had both eyes removed for retinoblastoma.

Case 7. (Patient of Dr. J. Pendleton White.)

In July, 1948, an abnormality was seen in the right eye, the patient, a girl, being 4 weeks old, and a tumour 8 mm. in diameter was found. In the left eye there was a raised area 1–2 mm. in diameter, 2 disc diameters from the macula.

The right eye was treated in July, 1948, by the suture of 4 radon seeds, each 1 mc. in 0·5 mm. Pt, to the sclera, in square form, giving an estimated total dose of 6,000 r at 0·5 cm. in 7 days. Fourteen days later the tumour had a "crumpled look".

In August, 1948, the left eye was given X-ray therapy in 15 treatments over 21 days (140 kV., filters 0·25 mm. Cu, 1 mm. Al., two fields being located by a mould. F.S.D. 15 cm. Skin dose 2,600 r. Tumour dose 3,000–3,300 r.)

Three months later the right eye appeared to be satisfactory. In the left eye the tumour appeared to be increasing in thickness; 4 radon seeds, each 1 mc. in 0·5 mm. Pt, were therefore sutured.
to the sclera of the left eye in square form in relation to the tumour, giving 6,000 r at 0.5 cm. in 7 days. Two weeks later the tumour area appeared to be fibrosed and there was no sign of extension.

In July, 1954, there appeared to be no growth at the primary sites, nor any evidence of metastases, but in October, 1954, a balloon detachment of the retina was found in the upper nasal quadrant of the left eye, while some white areas and haemorrhages were visible on the temporal side. The left eye was therefore removed after section of the optic nerve at the chiasma and definite tumour was found to be present.

In July, 1962, at 1 years of age, the right eye was quiet. A small posterior lens opacity was present and vision was 3/60.

**Family History.**—The patient is a sister of Cases 11 and 19.

**Further Note.**—We are indebted to Dr. N. L. Stokoe and Dr. R. J. McWilliam for the following details:


Two large choroidal scars are visible, in the horizontal meridian at the temporal side, and down and out from the disc. In the lower scar, below some necrotic pigment and in the 8 o'clock meridian, there is a cheesy-white prominent mass coming forwards. There are some haemorrhages in the neighbourhood. The possibility of recurring activity even at this long interval has to be considered.

**Case 8.** (Patient of Dr. J. S. Conway and Prof. W. J. B. Riddell.)

In April, 1951, when this boy was 7 months of age, an abnormality was seen in the right eye, which was enucleated at 13 months. A mass of retinoblastoma was found in the vitreous. In the left eye three blue-grey elevated areas were seen in the fundus, designated for convenience of description A, B, C: A at 12, B at 3, and C at 6 o'clock.

In February, 1952, X-ray therapy was given to the eyeball in 9 treatments over 21 days in right and left lateral fields 1 and 2 directed by means of a mould (220 kV., filters 1 mm. Cu, 1 mm. Al, 50 cm. F.S.D., O.S.D. each field 2,720 r, mid-point dose 2,420 r). Three weeks later A appeared unchanged, B might have regressed, and C was more difficult to see. Four months later A was considerably flatter, B not definitely seen, and C was broken into three parts. Five months later A and C had enlarged. In December, 1952, X-ray therapy was repeated to the eyeball in 3 treatments over 11 days in lateral and medial fields 3 and 4, the fields being at right angles, and the eyeball rotated laterally by a suture (140 kV., filters 1 mm. Al, 0.25 mm. Cu, 15 cm. F.S.D., I.S.D. each field 1,086 r, mid-point dose 1,500 r). Some months later A appeared smaller, grey, and elevated, with a clear-cut outline; B and C were diffuse, grey, and stationary.

In January, 1962, at the age of 11, vision was recorded as 6/6 partly. A faint posterior subcapsular opacity was visible in the lowest one-third of the lens.

**Family History.**—This boy's father had one eye removed for retinoblastoma in infancy.

**Case 9.** (Patient of Dr. McLellan and Dr. Turner.)

In May, 1952, when this girl was 2 years old, the right eye was enucleated for a retinoblastoma which filled the greater part of the eyeball. The left eye showed a small greyish elevation, 1/4 disc diameter in size, at the periphery from 4.30 to 5.30 o'clock.

Radon seeds were sutured to the sclera in the infero-lateral quadrant, 1 cm. square being formed by 4 seeds of 1.3 mc. The dose 0.5 cm. from the centre of the seeds was 7,000 r in 7 days of application.

Four months later a pigment disturbance was seen in the lower outer quadrant, and three circular areas of choroidoretinal atrophy in relation to the site of the radon seeds.

In May, 1962, at 12 years of age, the corrected vision was 6/9, N. 5. There was a triangle of posterior subcapsular disturbance in the lens at 6 o'clock; the rest of the lens was clear.

**Case 10.** (Patient of Dr. A. M. Wright Thomson.)

In June, 1951, this boy's right eye was removed at the age of 7 months, and retinoblastoma was confirmed, affecting practically the whole retina, with early involvement of the choroid and optic nerve; the section of the nerve appeared to be beyond the tumour.

In the left eye a raised white swelling was seen in the retina at the periphery on the nasal side.
In January, 1952, 4 radon seeds, each of 1·3 mc., filtered with 0·3 mm. gold and 0·15 mm. Pt were applied in the form of a square of 1 cm. side, giving a dose, at 0·5 cm. from the plane, of 7,700 r at 168 hours. Five months later the growth appeared to be stationary, and in a further seven months the irradiated area had become quite white and atrophic. A year later, increasing lens opacity was observed, and peripheral spread of the tumour was suspected. Haemorrhage then occurred and a detachment of the retina and a white tumour mass were seen.

X-ray therapy was then given as a palliative measure, in 2 applications over 8 days (140 kV., filter 0·25 mm. Cu, 1 mm. Al, 15 cm. F.S.D., fields 1 and 2 left eyeball lateral and medial, O.S.D. each field 501 r, mid-point dose 402 r). The detachment of the retina and the tumour increased, and enucleation was advised but was refused. Three months later there was spread into the orbit, with proptosis. After a further three months the nerve was divided at the chiasma, but the tumour had spread into the antrum. The patient died in August, 1955, with enormous growth at the primary site and probably lumbar metastases.

Case 11. (Patient of Dr. J. Pendleton White.) In September, 1943, at the age of 6 months, this girl's right eye was enucleated for retinoblastoma. The left eye was seen to be affected at that time. Radon seeds were applied to an area to the nasal side of the optic disc (6 x 1·0 mc. and 2 x 0·5 mc.) (Dr. Abernethy, Royal Cancer Hospital (now the Beatson Memorial Hospital, Glasgow), and Dr. White). Fourteen months later radon seeds were again applied (6 x 1 mc.). The patient was very well until nine years later, when activity was again seen in the eye. A dense scar was visible to the nasal side of the disc, and four or five active whitish buds of tumour to the inner aspect. There was slight evidence of early posterior polar cataract. Radon seeds were applied to this new field (A.A.C. and Dr. White). Exposure was difficult on account of dense fibrous tissue. A polythene envelope giving between 1 and 2 mm. distance was used as support for 6 radon seeds, each 1 mc., with filtration 0·3 mm. Calculated dose at 0·5 cm.: 7,000 r in 7 days.

In this case of recurrence at the edge of the original tumour there was reduced vascularity from the previous treatment; repeated treatment was possible only because the previous application was so localized and it was possible also to localize the final treatment. One year later it was considered that the last application of radon seeds had been successful in arresting the growth of the tumour. Five years later, at age 16, vision with correction was 6/12. A small lens opacity was present. The fundus lesion did not appear to have increased. The patient had done well at school and had been dux of the joint homecraft and commercial section.

Family History.—This girl's mother had an eye removed in childhood for tumour; two younger sisters developed bilateral retinoblastoma (Cases 7 and 19).

Case 12. This boy's eye was removed at the age of 1 year and 10 months with a large tumour mass, shown to be retinoblastoma.

In the right eye the retina was detached on the temporal side, and a mass about 6 x 10 mm. filled the lower one-third of the fundus from 5 to 8 o'clock; some globules overlay the main mass.

In June, 1955, 4 radon seeds, each 1·25 mc. with filtration 0·3 mm. gold, were sutured over an area 11 x 8 mm., giving 6,000 r in 1 week at 0·5 cm.

Eight months later the major part of the growth was greyish-white and calcareous in appearance. The upper edge of the growth was buff-coloured and rounded and did not appear to be shrinking or calcareous, but showed no great change since the previous examination. There were horizontal lines of tension in the retina between this part of the tumour and the disc and macula.

Four months later (under the observation of Dr. H. Bentley) the buff-coloured mass appeared pigmented and the tumour appeared to be arrested. Vision was poor and the child bumped into objects.

Two years later (under the observation of Mr. H. Ridley) the tumour appeared to be active; a small area near the disc appeared to have escaped adequate irradiation.

Case 13. (Patient of Dr. Brown and Dr. Turner.) This boy's right eye was noticed to squint at birth (December, 1955). A white mass was seen at 3 months of age and medical advice was sought at 10 months of age as it was getting worse. The
right eye was enucleated and shown to contain retinoblastoma with well-formed rosettes. In the left eye a white mass about 4 disc diameters across was seen lateral to the disc, from 2 to 5.30 o'clock, with 6 D prominence.

In September, 1956, X-ray therapy was given in 14 treatments over 21 days (right and left lateral fields, 4 cm. square, 250 kV., 15 M.A., filters 1 mm. Cu, 1 mm. Al, F.S.D. 50, H.V.L. 1.7 cm., incident dose 3,310 r, tumour dose 3,240 r).

Fourteen days later the main mass appeared craggy and glistening, white in the upper part, duller in the lower part, and shading off into the rest of the fundus, the adjacent part of which showed speckled pigmentation.

Seven months later there was no sign of activity, but in a further five months (October, 1957) the inferior one-third of the tumour was seen to have changed, a buoyy swelling coming forward, while the remainder of the tumour was craggy and glistening.

Ten radon seeds in a container 20 × 10 mm. were sewn to the sclera in relation to the tumour, giving a total dose of 5,000 r at 0.5 cm. in 17 days.

One month later some improvement was recorded. In a further five months the vessels round the tumour were seen to have changed considerably, having become tortuous and irregular in calibre. Some superficial haemorrhages had broken through into the vitreous.

In May, 1961, when the child was 5 years old, there was no sign of activity. An atrophic area was present just below the macula, and the macula itself showed pigmented change. Vision was "counting fingers" at 2 metres, and a coin could be recognized at 1 metre.

Case 14. (Patient of Dr. J. Mellick.)

In August, 1956, this girl's right eye was removed when she was 2½ years old, and retinoblastoma confirmed. The section showed no true rosette formation. The sclera was invaded but not perforated. Two months later the right orbit was filled with reddish active-looking tumour.

In October, 1956, X-ray therapy was given as palliative and placebo for this orbital extension, in 1 treatment (220 kV., filter 1 mm. Cu, F.S.D. 50 cm., I.S.D. 600 + 8 per cent. = 648 r). Two days later there was considerable regression and evidently less pain.

Two weeks later X-ray showed the right optic foramen to be larger than the left, but opinion was divided on the significance of this as the ostium was well defined.

Further X-ray therapy was then given to the right orbit, in 12 treatments over 4 weeks (220 kV., 4 cm. square, 2 fields 50 cm. distance, filtration 1 mm. Cu, 1 mm. Al, incident dose 3,200 r and tumour dose 4,320 r).

Two months later projectile vomiting occurred and intracranial metastases were diagnosed. The patient died six months later with evidence of growth at the primary site.

Case 15. (Patient of Dr. A. M. Wright Thomson.)

A convergent squint of the left eye was observed in this girl at the age of 5 months. At the age of 8 months the left eye was enucleated, retinoblastoma nearly filling the globe.

A rounded lesion occupied most of the lower inner quadrant of the retina of the right eye. X-ray therapy was chosen because of the proximity of the tumour to the optic disc, and this was given in March, 1957, the child being then 10 months old (9 treatments over 21 days, 220 kV., filters 1 mm. Cu, 1 mm. Al, 56 cm. F.S.D., fields 1 and 2 lateral and oblique, L.S.D. 3,000 r, tumour dose 3,240 r).

Three months later the tumour was dead white with adjacent pigmentary disturbance.

Four years later the mass was noted to be smaller and the appearance satisfactory.

At 7 years of age vision of the right eye was 6/9 partly and N 5, unaided. A small posterior cortical lens opacity was present. A photograph of the fundus is shown in Fig. 2.

Case 16. The girl's mother noticed a squint at the age of 7 months; her family doctor "thought it would require treatment at a later date". Soon afterwards redness of the right eye developed and the pupil became dilated. The left eye then became inflamed and the child appeared to be blind. In October and November, at the age of 16 months, both eyes were enucleated and retinoblastoma confirmed.

Ten months later the left orbit would no longer retain the prosthesis and it was found to be filled with tumour. A "doubtful" nodule was present in the right orbit. There was no radiological sign of bony involvement.

In November, 1957, palliative and placebo X-ray therapy was applied by opposed fields treating
both orbits (220 kV., 2 6 x 4 cm. fields, 50 cm. distance, filtered 1 mm. Cu; incident dose 3,300 r, tumour dose 4,750 r maximum, in 4 weeks).

Treatment was stopped because of reaction, which took the form of marked erythema of the irradiated areas and purulent discharge from the orbits. Two glands were palpable in the upper deep cervical region. The reaction settled down and one year later the child appeared to be well and no significant nodes were found.

Five months later swellings appeared in the left thigh, the neck, and the left side of the face. No treatment was advised and the child died three months later with extensive bony metastases, but nothing at the primary sites.

Case 17. (Patient of Dr. W. O. G. Taylor.)

This boy's right eye was removed in January, 1958, at the age of 1 year and 7 months, squint having been noticed at the age of 6 or 7 months. Retinoblastoma was confirmed histologically; the cut end of the optic nerve was free of tumour, but there was almost complete penetration of the sclera close to the optic nerve.

In the left eye a large growth protruded into the vitreous on the nasal side of the disc, with a smaller growth rather further forward, most of the nasal half of the eye being involved.

In February, 1958, X-ray therapy was given in 9 treatments over 21 days (220 kV., filters 1 mm. Cu, 1 mm. Al, 55 cm. F.S.D., fields 1 and 2 left lateral and left nasal, I.S.D. 3,682 r, tumour dose 3,257 r).

At the end of this treatment the vitreous appeared to be hazier. There were many floating opacities and daughter tumour masses. The main mass appeared to have shrunk and was dead white. The blood vessels were engorged and tortuous near the disc.

Four months later the vitreous was hazy, the growth appeared larger, and the main blood vessels were no longer visible. The eye was still able to fix a light. The optic foramina were radiologically normal.

Three weeks later the left eye was enucleated on account of the progressive condition of the tumour.

In April, 1962, the patient was alive and well and the sockets appeared healthy.
Case 18. (Patient of Dr. J. Dunlop and Dr. R. J. McWilliam.)
A growth was observed in this boy's right eye when he was in hospital with pneumonia at the age of 6 months. There was complete detachment of the retina, the outer part appearing solid. The right eye was enucleated in March, 1958, and retinoblastoma confirmed.
In the left eye a tumour mass, about 4 disc diameters in width and 5.5 disc diameters vertically, occupied the macular area. The eye could follow a light.
In April, 1958, X-ray therapy was given to the left eye in 15 treatments over 21 days (250 kV., filters 1 mm. Cu, 1 mm. Al, 50 cm. F.S.D., fields 4 cm. square, incident dose 2,730 r, average tumour dose 4,300 r).
One week later the tumour was noted to be regressing well. Six weeks later the larger mass was whiter and harder but a smaller mass superior to this was still slightly fluffy.
Two and a half years later there was no sign of activity.
Five years later in July, 1963, vision was 6/36 (E test). There was some central cataract but a fairly good view of the fundus was obtained; no projecting masses were seen nor any seeding.
Family History.—The patient's mother had the left eye removed for a tumour in infancy.

Case 19. (Patient of Dr. J. Pendleton White.)
When this girl was about 5 months of age tumours were noticed by her mother. A course of vitamin B₁₂ was given for two weeks without benefit.
The left eye was removed in August, 1959, and retinoblastoma confirmed, a large tumour completely detaching the retina, showing calcification and few and imperfect rosettes.
In September, 1959, at 8 months of age, X-ray therapy was given to the right eye in 15 treatments over 21 days, through 3 fields by beam-directed shell, 2.5 cm. circles (220 kV., filters 1 mm. Cu, 1 mm. Al, incident dose 2,370 r, total tumour dose 4,200–4,500 r).
Five weeks later the tumour appeared to have regressed to some extent, but much was still present. Further irradiation was not considered justifiable and as there was no vision the eye was enucleated.
Three years later the girl was alive and well and there was no evidence of disease.
Family History.—The patient is a sister of Cases 7 and 11.

Commentary
In 4 patients the first abnormality noticed was squint, and in one of these the family doctor told the parents that "it would probably require treatment at a later date". This child died. The moral is obvious.
The application of therapy presented no particular difficulties, but in one case X-ray therapy was preferred because of the expected difficulty and risk of suturing radon seeds close to the optic nerve.
General anaesthesia was used for the repeated X-ray treatments, usually by means of rectal pentothal.
No severe erythema or other general or local reaction occurred. In Case 13, however, there was sloughing of the sclera, which may have been the result of the large dose of irradiation in the immediate neighbourhood of radon seeds.
Case 8 had two courses of X-ray therapy with a successful result. Case 11 had three applications of radon seeds with a successful result. Case 7 had the larger of two tumours, in the right eye, treated by radon seeds with success. The smaller tumour, in the left eye, was initially treated with X-ray therapy, and when it recurred radon seeds were applied. The growth was not arrested and the eye was enucleated.
In Case 18 the tumour occupied the macular area, so central vision was lost, but useful peripheral vision has been retained. In Cases 3, 4, 14, and 16 palliative treatment only was given in the hope of arresting extra-ocular extensions which had
already occurred. In Case 10 therapy failed to cure the condition. As the outlook for vision was poor, it is a question whether enucleation might have saved the child's life. In Case 5 the tumour was large initially, and therapy failed to cure.

The series of patients here reported formed a record of work and experience in one provincial radiotherapy centre, and is not to be considered as a source of statistical material, in which respect it falls far short of the studies of Reese and others (1955), Stallard (1962), and others.

It does show, we believe, that it is possible to treat favourable cases with a considerable measure of success, using the ordinary apparatus and personal skills available in a radiotherapy centre, with close co-operation between the consultant in radiotherapy and the ophthalmologist.

Unfavourable cases are unfavourable because of the extent of the tumour at the time of diagnosis. These have been treated palliatively or by way of placebo.

Summary

Nineteen patients with bilateral retinoblastoma were treated by radiotherapy, using the facilities ordinarily available. Of the 13 survivors, 5 had vision of 6/12 or better, 3 had vision of less than 6/12, in 1 the latest vision is not recorded but is very poor, and 2 had both eyes removed; 5 died of the disease and 1 died of intercurrent disease. Details of radiotherapy are given in each case.

We thank the surgeons who referred their patients for treatment for permission to report on them: Prof. W. J. B. Riddell, in charge of the ophthalmic side of the work, which was carried out in the Tennent Memorial Institute (Cases 6, 8, 9, 12); Dr. J. S. Conway (Case 8); Dr. John Marshall (Case 6); Dr. D. Turner (Cases 9, 13); Dr. A. M. Wright Thomson (Cases 10, 15); Dr. R. Leishman (Case 9); Dr. W. O. G. Taylor (Case 17); Dr. R. J. McWilliam (Cases 7, 11, 18, 19).

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REFERENCES


