COMMUNICATIONS

SPONTANEOUS REGRESSION OF RETINOBLASTOMA*

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BECAUSE children with tumours of the eye form such a small proportion of patients attending ophthalmic clinics the true incidence of cancer in childhood may not be realized by many ophthalmologists. With the steady decrease in deaths from bacterial infections, malignant disease has assumed a relatively greater importance in paediatric practice, and is now the third commonest cause of death in children over the age of one year, being exceeded only by accidents and respiratory infections (Registrar-General, 1954).

The place of retinoblastoma amongst the tumours of childhood may be judged by a study of the Table which shows the frequency of the various types of neoplasm in 165 cases recorded by the Children's Tumour Registry of the Departments of Child Health and Pathology, Manchester University, during the 2 years ending September 1, 1955. All these patients were under 15 years old and lived in a region containing approximately one million children.

TABLE

Leukaemia	46
Central nervous system tumours ...	24
Sympathetic nervous system tumours ...	21
Lymphoid tumours	14
Sarcomata (other than lymphoid) ...	12
Wilms's tumours	12
Teratomata	9
Retinoblastomata	8
Miscellaneous	19
Total	165

Only two of the eight children who had retinoblastomas had a family history of the disease; these two were brothers and this communication is concerned with them and with the occurrence of the disease in their relatives.

Case Reports

Case 1, a boy aged 2 was stated to have been well until September, 1954, when he was noticed to have a squint. 3 weeks later the following observations were made:

Examination

Right Fundus: A large yellowish mass on the temporal side.
Left Fundus: A small nodule in the upper nasal quadrant of the retina.

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On September 30, 1954, the right eye was enucleated. Since then two more foci have appeared in his left eye, and these have been treated with radon and diathermy.

Histological Findings.—The specimen comprised a right globe with a small white tumour mass floating in the anterior chamber. There was a funnel-shaped retinal detachment with a large underlying coagulum containing small seedling nodules. Microscopically the latter were composed of typical retinoblastoma cells. In the retina a diffuse neoplasia had left little surviving normal tissue but had not produced localized tumour masses of any size. Several detached tumour nodules were present in the vitreous and a few in the anterior and posterior chambers. Rosettes were *not* evident. The optic nerve appeared to be free from tumour.

Case 2, an infant 4 days old (brother of Case 1), was first seen on January 17, 1955.

Examination

Right Fundus: Two greyish masses were observed, the larger almost obscuring the disc, the smaller a short distance below, adjacent to the temporal vessels.

Left Fundus: Normal.

He was admitted to the Manchester Royal Eye Hospital on March 19, 1955, when it was found that the tumours in the right eye had increased in size and that a small growth was present in the left retina. On March 28, 1955, the right eye was enucleated and the growth in the left eye was treated with diathermy.

Histological Findings.—There was a shallow, incomplete retinal detachment, mainly posterior. Adjacent to the optic nerve were two small oval nodules of retinoblastoma, while a third independent nodule lay on the nasal equator in the main horizontal meridian. Rosettes were plentiful.

Family History

The parents stated that several relatives on the father's side had been affected by the disease. Two reports on this family, one by Griffith (1917) and the other by Bride (1923) have appeared in the literature, and it was also cited by Griffith and Sorsby (1944). In addition, we interviewed a great-aunt who had cared for the family and an aunt who was unaffected by the disease but had seen several of her siblings suffer from it. The family tree brought up to date is shown in Fig. 1 (opposite) ; the second generation (as shown by us) omits one stillbirth.

It will be noted that the disease apparently started in the paternal grandmother (I, 2), who had only one eye affected. The other members of the family who inherited the disease had bilateral growths. The family tree indicates that the predisposition to retinoblastoma was inherited as a dominant characteristic—the grandmother being heterozygous in that respect. The noxious gene was passed on to five of her children (II, 1, 3, 4, 5, 7), but almost certainly missed one of her daughters (II, 2) who has five surviving unaffected children (III, 1, 3, 5, 6, 7). One cannot be so sure about a son (II, 6) as he has only one child (III, 8).

In interpreting the inheritance in this family, the experience of Falls and Neel (1951) is relevant. They showed that members of a retinoblastomatous family, even though their fundi are normal, may pass the disease on to their children.

The eyes of all surviving descendants were examined by us, and three showed ocular abnormalities:

Case 3, a boy aged 9 (III, 6), has a right marginal lens coloboma.

Case 4, a man aged 38 (II, 6), has a left total cataract. Projection of light is only

FIG. 1.—Family tree showing the inheritance of retinoblastoma.

moderate, suggesting the possibility of a retinal defect. The cataract is stated to have been present for many years. Bride (1923) records that at the age of 5 his eyes were normal apart from a squint.

Case 5, a man aged 37 (II, 7), father of Cases 1 and 2, was a full-term infant; at the age of 2 weeks it was noticed by his sister that his pupils were of different colours and that the right pupil had a white spot in it. When he was a few months old he was seen by Bride who found a typical retinoblastoma in the right eye, and some months later the left eye also contained a tumour. During the child's first year of life the right eye watered and gradually shrivelled up, but it was never acutely inflamed. The case was demonstrated by Bride to the North of England Ophthalmological Society in 1922 when the child was just 3 years old; by that time the left eye had been quiescent for 21 months. No x-ray treatment was given.

He was admitted to Henshaw's Institute for the Blind when he was 5 years old as his sight was so poor that he required special training. He was examined by an ophthalmologist at the age of 6 and it was noted that he had atrophy of his right eye and his left fundus showed "central choroiditis". He was re-examined at the age of 14 when it was again noticed that the right eye was atrophied and the left fundus showed "central choroiditis with disseminated choroiditis".

He married and had a daughter; she is now 11 years old and her fundi are normal. He subsequently married again—this time a woman who had two normal children by her first husband—and his two children by this second marriage are Cases 1 and 2.

Examination.—He was first seen by us in October, 1954, when he was 35 years old.

Right Eye: Phthisis bulbi.

Left Eye: Vision 6/60 not improved. Nystagmus. Anterior chamber no abnormality. Media clear.

The fundus showed a large clear-cut area of chorio-retinal atrophy adjacent to the disc on the temporal side. This was apparently flat, apart from a few small pigmented patches in the lower part which appeared to be excavated. The only other feature in the atrophic area was in the upper temporal quadrant where the choroidal vessel pattern could be seen; at its lowest point the vessels showed slight dilatation as they converged. Normal retinal vessels passed across on the front of the dead white surface. In the upper nasal quadrant there was a circular raised mass greyish-yellow in colour with a smooth outline. This was bordered below by the upper nasal retinal vessels. There was a vessel passing up on to the surface of the mass at its peripheral border. Between these two lesions was a discrete chalky-white clump of material, lobulated and protruding forwards. In some parts the outline was clear-cut, in others indistinct. It appeared to be a small mass of calcification. The remainder of the fundus was normal. The appearance of the eyes is shown in Fig. 2, and the left fundus in Fig. 3 (opposite).

FIG. 2.—Case 5, aged 35, showing right phthisis bulbi.

Several attempts to detect calcification in the left eye by *x* rays were unsuccessful, though a small amount of calcification would have been difficult to detect owing to the coarse nystagmus. *X* rays of the skull also failed to show any calcification.

As the right eye was useless and unsightly, it was enucleated on December 7, 1954.

Histological Findings.—The globe was markedly shrunk with an elliptical cornea which measured only 4 mm. vertically. Occupying the centre of the globe, internal to the choroid, were scattered clumps of calcified tumour cells. They lay in fibrous tissue and near a few of them some bone formation had occurred. In the clumps, especially towards their peripheries, the individual cell elements were clearly recognizable. One could even appreciate the nuclear pattern in some pyknotic cells. A caricature of the rather erratic system of small spaces normally seen in these tumours (the result of individual cell necrosis) could still be clearly made out (Fig. 4, opposite).

FIG. 3.—Left fundus of Case 5, aged 35 years.

FIG. 4.—Phthisical right eye of Case 5, showing scattered groups of calcified retinoblastoma cell and some bone formation. $\times 45$.

Review of the Literature

We have found in the literature fifteen cases of spontaneous regression of retinoblastoma in which the evidence both for the diagnosis and for the regression appears satisfactory.

Knieper (1911) reported a boy in whom a diagnosis of bilateral retinoblastoma was made in 1899, when he was 10 weeks old. The right eye was glaucomatous and was removed immediately. Histological examination confirmed the presence of a retinoblastoma. The parents refused permission for the left eye to be removed and the child was not seen again until 1910 when he was found in a home for the blind. His parents stated that 2 months after enucleation of the right eye the left began to enlarge and the child was in continual pain. One morning they noticed that the eye had got much smaller overnight. It discharged for several days and then became dry. From the age of 5 months to 11 years its condition remained unchanged, apart from an intermittent discharge of pus. When Knieper examined the patient in 1910, she found no evidence of growth in the right orbit. On the left side there was a shrunken globe, the cornea was opaque, and the child was blind. The parents refused permission for this eye to be removed. Martin and Reese (1936) stated that permission for enucleation of the phthisical eye was obtained, but there is no mention of this in Knieper's article.

De Kleijn (1911) recorded the case of a girl first seen at the age of 8 months when a diagnosis of right-sided retinoblastoma was made. This eye was enucleated and showed retinoblastoma histologically, the tumour having invaded the optic nerve as far as the line of section. Retinoblastoma in the left eye was diagnosed 5 months later, but no treatment was given as the prognosis was considered hopeless. During the next 5 years the left eye became blind without pain or inflammation. At the end of that time de Kleijn examined the patient and found no sign of growth in the right orbit. The left eye was shrunken and was therefore enucleated. It contained darkly-staining heaps of necrotic calcified tissue, in places partly surrounded by bone. In the periphery of these heaps the original structure of small cells could be seen though the centres were formed by fused compact masses. The photomicrographs of this eye correspond to those of the eye removed from our Case 5 (see Fig. 4).

Siegrist (1912) reported a boy who had his right eye enucleated in 1910 at the age of $3\frac{1}{2}$ years. This eye was examined histologically and showed a retinoblastoma with extensive necrosis and calcification. The left fundus showed a dark grey area of five disc diameters in the macular region, in which there were prominent white shiny masses, lobulated below but map-like above. The child appeared able to see but his visual acuity could not be accurately determined. By 1912 there had been little change apart from the fact that the white areas had atrophied somewhat and become more intensely white. The macular area could now be seen as a weak ring reflex and an intensive central punctate reddening corresponded to the fovea. The visual acuity was 0.6. This patient was referred to by Axenfeld (1918) and again by Siegrist (1920); he had remained well and his fundus was unaltered. Siegrist's original article contains colour pictures of the fundus.

Purtscher (1915) described a family in which there were three children who died of retinoblastoma in two generations. In addition, two members of the family, a woman of 30 and a boy of 5 years, showed abnormalities of the fundi. The woman's left eye had a large central lesion, somewhat raised and of a yellowish-white colour. A temporal vein disappeared beneath it while several vessels emerged from it, giving the impression sometimes of arising in pits. A second opinion by Prof. Fuchs, whom Purtscher consulted, was "choroidal atrophy after complete regression of glioma". In the right eye a small atrophic area was situated on the course of the inferior vein towards the periphery. In the boy's left eye there was a large defect of the central fundus occupied by an opaque, grey-

yellow swelling with a girdle of chorio-retinal atrophy. The right eye showed a smaller grey lesion above and nasal to the disc, lying between the vein and artery.

In 1917 Salzmann examined a woman whose left eye had been removed for retinoblastoma when she was 2 months old. There is no mention of any histological confirmation of the diagnosis. At the age of 23 years her right eye showed a peripheral area of choroidal atrophy bearing a central dark green patch on which there were flecks of calcification (Fuchs and Salzmann, 1933).

The case of von Hippel (1928) was that of a boy who had his right eye removed in 1891 when he was 5 years old. A clinical diagnosis of retinoblastoma was made but there is no record of any pathological examination of the enucleated eye. The boy's left eye was said to be normal in 1891, but apparently he did not have an examination under an anaesthetic. At a further examination in 1925 there was a vitreous haze and the retina showed, below the macula, an oval discoloured zone from which projected a shiny white structure with a knobbly surface on which there were some red spots; some of these were seen to be due to collections of small vessels.

Stallard (1936a) reported the case of a man born in 1903 whose left eye had been removed for retinoblastoma at the age of 14 months—the diagnosis being confirmed histologically. The right eye had been similarly affected but operation had been refused. During an attack of scarlet fever at 4 years of age the right eye gradually cleared. In 1934 the fundus showed two irregularly-shaped pale areas of retinal atrophy along the course of the upper and lower nasal branches of the central retinal vessels. There was some pigmentary disturbance. This man's two sons developed bilateral retinoblastoma: the elder was treated with radon seeds and in 1955 was alive and well; the younger had extensive bilateral growths. Attempts were made to inoculate the younger boy with scarlatinal streptococci when he was 5 months old, but he failed to develop the disease. He was then given a course of injections of Globenil* and after each injection an inflammatory reaction developed in the right conjunctiva. During this time the left eye gradually collapsed, but the course of the disease did not seem to be altered and the patient eventually died of intracranial extension.

Hine (1937) described two cases—father and son. The father had had his left eye removed for retinoblastoma at 2 years of age, and at that time his parents refused enucleation of the other eye. When he was 42 years old his right eye showed a patch of choroidal atrophy in the centre of which was an indistinct raised pink area. No calcification was seen. He had five sons, three of whom were known to have retinoblastoma. A fourth son was thought to be unaffected until, at the age of 16, Hine found an area of choroidal atrophy in both eyes; in the centre of each was a raised grey area and in the right eye this grey area contained calcified deposits. Hine (1944) gave an account of the subsequent history of this patient; he had married and one of his children had developed bilateral retinoblastoma. Hine's original article contains excellent illustrations of these fundus appearances.

Fuchs (1943) saw an 8-year-old boy who had had one eye removed for retinoblastoma 6 years previously; in the periphery of the fundus of the remaining eye there was a discoloured area containing crumbly white masses.

Wüstenberg (1950) reported two cases. The first was that of a boy who, at the age of 3 years, had his left eye enucleated for retinoblastoma, the diagnosis being confirmed histologically. The right eye contained two typical nodules but received no treatment. One of these nodules was flat and the other projected into the vitreous. 8 years later the spherical nodule had become more translucent and a fleck appeared to be breaking away from it; the other was unchanged. The second case was that of a boy born in 1938. At the age of 9 months a diagnosis of bilateral retinoblastoma was made. The right eye contained a spherical prominence extending far into the vitreous. At 22 months the

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left eye was removed for glaucoma and the diagnosis proved histologically. Examination 9 years later showed no change in the remaining eye except for a chalk-like deposit at the tip of the prominence.

Seuss and Stutz (1951) described the case of a boy in whom bilateral retinoblastoma was diagnosed when he was $3\frac{1}{2}$ years old. The blind right eye was enucleated and shown to contain a cellular retinoblastoma with many mitoses; the left eye exhibited a nodule of three discs diameter in the upper nasal quadrant. The child was well and the socket healthy 7 years later. In the upper peripheral fundus of the left eye lay a well-demarcated, glaring white area of slight prominence looking like a small cloud cumulus and mimicking a healed choroiditis. It was surrounded by a bluish-grey zone which could not be seen to its peripheral limits and which contained a second bright white disc-shaped area in its lower part. This latter was about three dioptres prominent and temporally it joined with several smaller, partly confluent, grey-white areas of lesser prominence. Between these two main areas ran a large tortuous vessel. A further vessel climbed up directly from the papilla to branch in a tortuous fashion over the raised region. The whole occupied an area of some six to eight discs diameter and was irregularly demarcated, the transitional zone being formed by very small chalky flecks. In the nasal periphery was a second, smaller area, 2 dioptres prominent, made up of small white discoloured areas; a delicate vessel, slightly tortuous, branched over the region.

Sovik (1952) reported a family of nine, six of whom had bilateral retinoblastoma. They were the children of a poor white farmer in Ohio. Their mother had a shrunken left eye, blind since childhood, and the grandmother had been told that this was due to "cancer" in the eye. Unfortunately, examination of the mother proved impossible, her refusal to co-operate being emphasized by threats supported by a shotgun.

Discussion

In the cases described the diagnosis of spontaneously regressed retinoblastoma has been based on four types of evidence:

- (a) A family history of the disease.
- (b) A clinical diagnosis of bilateral retinoblastoma with removal of one eye only (usually with histological proof) followed by arrest of the growth in the other.
- (c) A fundus picture corresponding to that of verified cases.
- (d) Calcified tumour cells in phthisical eyes.

It will be appreciated that (a) and (b) or a combination of them, can only be available in exceptional circumstances. A family history is relatively rare in retinoblastoma—probably less than 5 per cent. of all cases (Vogel, 1954). If enucleation of a second eye is refused, recourse to irradiation or diathermy will modify the natural history of the disease.

One can recognize three main elements in the fundus appearances:

- (1) Discoloured raised areas in the retina, sometimes showing a lobulated or map-like pattern.
- (2) Chalky-white patches indicative of calcification.
- (3) Areas of chorio-retinal atrophy, usually forming a background for the tumour remains.

These three elements may be superimposed (as in Hine's second case) or separate (as in our case). Thus one must envisage the possibility that certain of these neoplasms, even of considerable size, may heal, leaving a

clinical picture indistinguishable from a patch of old choroiditis. However, the disappearance of retinal vessels over part of their course, and their emergence, apparently *de novo*, in the middle of an atrophic area, as occurred in Purtscher's case (Fig. 5), would seem to be peculiar to healed retinoblastoma. The difficulty of making the diagnosis after the tumour has regressed (especially in the non-familial unilateral growth) may partly account for the small number of reported cases. It may well be that this phenomenon is more common than has hitherto been supposed. Twelve of the patients in whom the growth regressed were boys and four were girls. Most series show that retinoblastomas occur approximately equally in the two sexes. It would be very difficult to say whether this sex disproportion in arrested cases was significant, not only because of the small numbers recorded but also since they are all in a selected minority of retinoblastomas, *i.e.* the bilateral and/or familial cases.

FIG. 5.—Left fundus of case described by Purtscher (1915), showing disappearance and emergence of vessels in large central lesion.

The prognosis in retinoblastomas treated by irradiation and/or enucleation

is better than in any other malignant disease in childhood. Hope of spontaneous regression, therefore, should never influence our treatment, as one cannot foretell in any particular case whether there is a chance of this occurring. Although four of the reported cases of regression (Hine, 1937; Purtscher, 1915) occurred in two families, this cannot be interpreted as evidence that the ability to overcome the tumour is an inherited characteristic. Two brothers of our Case 5 (II, 1 and 4) died of a recurrence of the growth, and there are several other instances of death from the disease in the relatives of those in whom it has regressed.

The knowledge that the growth may be destroyed by some unknown factor is of considerable theoretical interest. This interest is increased by the knowledge that neuroblastoma sympatheticum (a tumour showing histological and histogenetic similarity to retinoblastoma) may also undergo spontaneous regression (Cushing and Wolbach, 1927; Gross, 1953; Bodian, White, and Jaco, 1955).

The role of x rays as a curative agent in retinoblastoma is incontrovertible. However, in a few children in whom the growth has regressed after irradiation, one cannot be certain how much the treatment contributed to the favourable result. The following three cases received doses of x rays, apparently less than is generally considered necessary for a cure.

(1) Meller (1915) described the history of a boy who presented signs of bilateral retinoblastoma at the age of 4 years. Enucleation being refused, only two treatments with x rays were given (dose not stated), and 2 months later glaucoma necessitated removal of the right eye, which contained an exophytic growth without rosettes. Three nodules in the other eye continued to increase slightly during the next 2 years. When the patient was 9 years old the nodules had become flattened and looked like atrophic patches of choroiditis but contained calcified masses. The child could see and was in good health.

(2) Seefelder (1926) reported a child whose right eye was enucleated at the age of $1\frac{1}{2}$ years and found to contain a tumour with rosettes. The left eye was treated with three doses of x rays, and 7 years later the child was alive and well with a chalky-white mass over the disc.

Neither Meller nor Seefelder considered that the irradiation had contributed to the final result.

(3) The well-known case of Verhoeff (1952) was that of a man who had had his right eye removed in 1917 when he was 17 months old. The tumour contained many rosettes. The left eye contained three nodules and was treated with eight sub-erythema doses of x rays; 34 years later, the patient, who had developed a limited posterior polar cataract subsequent to treatment, had good central vision. Verhoeff put his case forward in support of the use of small doses of x rays.

One must recognize, therefore, that the growth of some retinoblastomas may be arrested after small doses of irradiation, and that these may be examples of spontaneous cure. In the above three cases which received

small doses of x rays the histology of the contralateral eye suggested that the tumours were of neuro-epitheliomatous type or, at any rate, of focal character and predominantly exophytic—a triad of features tending to be found in combination. Of the cases which regressed without irradiation, only those of Knieper (1911) and de Kleijn (1911) had detailed histological descriptions; in each, rosettes were present in the tumour of the other eye.

The age at which arrest occurred may be roughly estimated in some of the recorded instances. In de Kleijn's patient regression took place some time between the ages of 1 and 6 years. The case of Siegrist (1912) showed very little change between the ages of $3\frac{1}{2}$ and 5 years, remaining stationary thereafter. In the two patients reported by Wüstenberg (1950) the growth remained stationary from the ages of 9 months and 3 years respectively. In our case growth had almost certainly ceased by the age of 15 months. In those cases observed while regression was occurring, the fundus picture continued to alter slowly over a few years. Most of these changes must, however, be attributed to the processes of repair.

The vast majority of retinoblastomas are diagnosed in the first 4 years of life, and are not uncommonly present at birth (our Case 2 had a definite tumour when he was 4 days old). As we have seen, in all cases of spontaneous regression where it was possible to estimate the time of arrest, the growth had become static by the age of 6. Since the cells of these neoplasms are of embryonic type, conditions may perhaps become less favourable as the body develops so that the tumours cease to grow. However, hypotheses on these lines cannot provide a complete explanation. Retinoblastomas behave differently in the same patient as regards their rate of growth and also in their time of appearance. In the cases of Lindenfeld (1913) and O'Connor (1917) the tumours regressed in one eye and continued to grow and eventually fungate in the other. Hosch (1888) gave an account of a $3\frac{1}{2}$ -year-old boy with advanced retinoblastoma in the right eye and a small area of neoplasm round the left disc; the latter appeared to remain static during 6 months of observation prior to death from exhaustion. The eyes were removed immediately after death: the right globe was full of tumour which had spread widely in the orbit; in the left eye the tumour was confined to the region of the papilla and the adjacent portion of the optic nerve. Evidence of this kind would indicate that the growth potential is in large measure a function of the individual tumour.

The fact that these tumours may occur later in life is of some significance in considering the mechanism of regression. Rychener (1948) reported a woman who developed a retinoblastoma when she was 33 years old. The growth developed on the scar of an old choroiditis. Schreck, in the discussion following a paper by Meisner (1951), cited the case of a patient who developed a retinoblastoma in the right eye at the age of 2 years. The left eye remained apparently normal until she was 19 years old when severe visual disturbance drew attention to a retinoblastoma in it. One wonders

if these late neoplasms are not examples of arrested growths which have become re-activated: particularly such cases as Rychener's, which arose on an old choroidal scar.

Since the arrest of the growth may occur in both eyes, it is unlikely to be due merely to accidental ischaemia or reactive inflammation. In some cases of spontaneous regression phthisis bulbi resulted, while in others some sight was preserved without shrinkage of the eye. To the best of our knowledge our Case 5 is the first patient to be reported in whom bilateral regression has led to one phthisical and one sighted eye. Assuming the same mechanism in both eyes, the final result must be related to the degree of ocular disorganization at the time of arrest; it is unlikely that the destruction of the tumour is secondary to the phthisis bulbi. In de Kleijn's case some tumour had been left in the proximal cut end of the optic nerve, but regression occurred even after the growth had escaped from the eye.

The possibility that an acute febrile illness could cause arrest of the growth is suggested by the history of Stallard's case. The sister of our Case 5 stated, on direct questioning, that he had had no such illness during the first year of life.

There is some evidence to support the hypothesis that regression may be caused by the development in the patient of a humoral resistance to the tumour, and that this resistance is not merely a function of the eye but is a more generalized tendency. This would account for regression in bilateral growths and also, as in de Kleijn's patient, in tumour tissue which had escaped into the orbit. It is more difficult to see how this hypothesis could explain cases in which the tumour in one eye regressed while that in the other later grew and fungated (*vide supra*). One would have to postulate either that the resistance waned or that one of the growths had the power to overcome it. We have used the word "resistance" rather than "immunity" because the latter might imply that retinoblastoma could stimulate the production of oncolytic antibodies. This is a possible explanation, but as far as we know, one that lacks support. If the hypothesis of a humoral resistance to the growth is the correct one it seemed possible that the electrophoretic pattern of plasma proteins in our Case 5 might be altered. However, we found this to be normal.

Much experimental work in animals has been done to try to elucidate the mechanism of induced immunity to various neoplasms. Animals normally susceptible to tumour transplants may be made resistant to them. Snell (1953) gives a review of the subject. It would be difficult to prophesy whether these experiments will ever provide the explanation of regression of human growths. They do, however, show that induced immunity to tumours is not such a rare phenomenon as the study of neoplasia in man might suggest.

Summary

Two brothers suffering from retinoblastoma are described and the inheritance of this disease in their family is traced. Evidence is brought forward to show that their father suffered in infancy from bilateral retinoblastoma which regressed spontaneously.

The literature of the spontaneous regression of retinoblastoma is reviewed. The mode of regression is discussed.

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