the accommodation of additional radon seeds. For instance, in a case in which there was a large mass of glioma extending above and below the macula the posterior extremity of the Stent strip could be bifurcated, each division carrying a radon seed, one passing above the insertion of the inferior oblique muscle and the other below and between the muscle and the globe.

Summary

This paper describes a method of applying radon seeds to the posterior part of the sclera by means of embedding the seed or seeds in a strip of Stent dental wax moulded to the sclera at the desired site. The Stent strip is secured in place by sutures traversing the superficial layers of the sclera in front of and behind the equator.

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CATARACT ASSOCIATED WITH AN HEREDITARY RETINAL LESION IN RATS

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ABOUT three years ago our attention was called to the occurrence of cataract in a colony of rats kept by a research laboratory.* It had been observed that from time to time mature bilateral cataract appeared in a healthy animal, which had been kept for breeding purposes and had never been subjected to any experimental procedure or dietary deficiency. The cataract was not the result of an injury; the animals grew well, reproduced reasonably well, and, apart from the cataract, showed no pathological symptoms. Since there was no obvious explanation for the appearance of this cataract, we concluded that an hereditary factor might be involved.

We received in the first instance a cataractous female rat with

* We are greatly indebted to Messrs. Vitamins, Ltd., for drawing our attention to this cataract and for presenting us with affected animals.

Rat from the affected stock showing mature cataract.

a litter of eleven. Subsequently we received seven other cataractous animals from the same source, and from these, six generations of rats (200 animals) were bred.

The original animals were pink-eyed piebald agouti, a variety of *Rattus Norvegicus*. By interbreeding many albinos were produced, and in the piebald offspring the colour of the hood varied from pale grey to deep fawn; in two litters piebald agouti with pigmented eyes appeared (3 rats). All of the animals bred by us were apparently healthy; a few (0.2 per cent.) died with middle ear disease or "rat pneumonia," conditions which are known to occur in rat colonies. The diet was at all times adequate with respect to composition and to the amount of food supplies; the animals were well housed and cared for. The cataract appeared in successive generations, and we were satisfied that some hereditary factor was concerned in its production. Many of our animals were observed for as long as two years, and no obvious or characteristic pathological conditions appeared, except in the eyes.

Histological examination of the eyes of 115 animals showed that, although the iris and ciliary body were normal, cataractous changes in the lens were invariably associated with a typical form of retinal degeneration. In this paper we wish to describe the cataract; the retinal lesion is fully described in the following paper (p. 613).

Ophthalmoscopic Observation.—The cataract was found to have a characteristic form and course of development. The typical course as observed ophthalmoscopically was as follows: The lens remained clear for a period varying from five weeks to three months after birth. The first change that could be seen was the appearance of a patch of dust-like opacities in the posterior cortex. These opacities gradually increased in number and in density, taking the form of a disc of stippled opacities. The area of this

disc slowly increased, spreading to involve the whole of the posterior cortex, and at the same time a shadowy ring formed around the nucleus. Gradually the whole lens became shadowy, and finally opaque, milky white. Apparently degeneration of lens tissue began in isolated areas in the posterior cortex, the degenerative changes spreading gradually to involve the whole of the posterior, and finally, the anterior cortex.

The chief variations from this typical form were: (1) The first lens changes sometimes took the form of small vacuoles scattered over the back of the lens. (2) The nuclear ring was absent in many cases. (3) The position of the disc of stippled opacities varied; in some cases it appeared at the posterior pole, but usually it was a little below and on the nasal side.

The age at which the lens changes first became apparent varied in different animals from five weeks to three months, the usual time was at about the age of nine weeks. The rate at which the cataract developed also varied greatly in different animals and even in the two eyes of the same animal. Sometimes the cataract developed rapidly in one eye while in the other eye the lens opacities remained stationary or progressed very slowly. In one animal mature cataract developed in one eye, while the other lens remained perfectly clear until the animal was killed at the age of 11 months. In a number of animals the lens changes progressed so slowly that mature cataract did not develop although the animals lived as long as 21 months.

Apart from the characteristic lens opacities, the only other abnormality observed with the ophthalmoscope was the occasional persistence of remnants of the hyaloid artery, and the appearance of a marked shagreen. In some cases these were associated with typical cataractous changes, but in other cases in which they were observed cataract did not develop.

Histological Examination of the Lens.—The lens capsule showed some interesting changes. Up to the age of 10 weeks it remained very thin and of equal thickness throughout, but in older animals, both with normal and abnormal retinae, it became much thicker anteriorly. Some actual measurements showed that the anterior capsule had an average thickness of 9μ in the young animal and 20μ in the adult (Figs. 1 and 2), and with the development of mature cataract the anterior capsule usually reached a thickness of 45μ (Figs. 3 and 4). In comparison, normal eyes from other stocks and various ages showed a lens capsule of about 10μ in thickness (Fig. 5). The posterior capsule was thin and was always disrupted when the cataract had fully matured. The broken ends of the capsule could be seen coiled like a spiral spring at the equator (Figs. 6 and 7).

The difficulty of obtaining unbroken thin sections of the lens

FIG. 1.

Lens from a rat, aged 7 weeks, belonging to the affected stock, but with a normal retina. Anterior capsule (7μ) and cortex are normal. $\frac{3}{4}$ Bouin.

Haematoxylin and eosin. ($\times 150$.)

FIG. 2

Lens from a rat, aged 21 months. Retina was degenerate. The lens appeared cloudy ophthalmoscopically, but on section showed only slight vacuolation of the cortex. The anterior capsule was thickened (21μ). $\frac{3}{4}$ Bouin.

Haematoxylin and eosin. ($\times 150$.)

FIG. 3.

Lens from a rat 21 months old, with very degenerate retina and almost mature cataract. The cortical fibres are swollen and vacuolated. The anterior capsule is much thickened (35μ). $\frac{3}{4}$ Bouin.

Haematoxylin and eosin. ($\times 150$)

FIG. 4.

Lens from a rat, 17 months old, with hypermature cataract. There is a total loss of cortical structure, and new fibrous tissue formation inside the grossly thickened anterior capsule (51μ). Advanced degeneration of the retina, and intra-ocular haemorrhages were present. $\frac{3}{4}$ Bouin.

Haematoxylin and eosin. ($\times 150$.)

FIG. 5.

Normal lens capsule (6μ) from a black and white rat, aged 6 months, of normal stock. $\frac{3}{4}$ Bouin.

Haematoxylin and eosin. ($\times 150$.)

FIG. 6.

Eyeball from a rat, aged 11 months, showing a mature cataract. The posterior capsule has disrupted, the coiled up ends of the capsule can be seen (*a* and *b*). The posterior cortex has absorbed; the anterior cortex (*c*) is a flocculent mass. The nucleus (*n*) is palely stained, and the retina (*r*) is very degenerate. A hyaloid remnant (*h*) can be seen extending from the retina to the lens. $\frac{3}{4}$ Bouin.

Haematoxylin and eosin. ($\times 15$.)

FIG. 7.

A high power view of the coiled-up capsule (*a*) in Fig. 6
 ‡ Bouin.

Haematoxylin and eosin. (X150.)

FIG. 8.

Eye of a rat, aged 17 months, in final stage of degeneration. There is a mature cataract and the posterior capsule has disrupted. The posterior chamber is full of haemorrhages (*h*) and an accumulation of lens debris (*l*). There is fibrous tissue formation (*f*) behind the iris (*i*) and inside the anterior lens capsule (*a*) which is much thickened. The retina (*r*) has entirely lost its normal structure.
 ‡ Bouin.

Haematoxylin and eosin. (X15.)

is well known to histologists. We experimented with a large number of fixatives and found that Zenker, which was in sufficient strength to fix the retina, hardened the lens, while formol caused a vacuolation of the cortex which was a most deceptive artifact. Orth's fluid proved unsatisfactory, but with Bouin's solution ($\frac{3}{4}$ strength) it was possible to cut whole sections of the lens and at the same time to obtain a good fixation of both lens and retina.

In the young animals the cortex of the lens had a normal appearance with numerous nuclei and growing fibres at the equator (Fig. 1). The earliest discernible histological change in the cortex occurred immediately under the capsule. The fibres swelled and became homogeneous (Fig. 3), while the vacuoles occurred patchily in both the anterior and posterior parts of the lens. No direct relation between this vacuolation and the "stippling" observed with the ophthalmoscope could be established, although both occurred at about the same time. It is highly probable that the stipples may be vacuoles caused by osmotic changes such as occur in the early stages of diabetic cataract, and that subsequently fixation and staining would cause them to disappear.

The nuclear outline was usually distinct, particularly in sections fixed with Zenker. In a cataractous lens the nucleus stained palely. With maturation of the cataract the cortical fibres broke into globular masses. This softening was most marked in the anterior cortex where a flocculent mass remained inside the thickened capsule. The posterior cortex seemed to absorb and, after the capsule disrupted, lens debris escaped into the vitreous (Fig. 8). Finally, a fibrosis occurred immediately inside the capsule and the same process occurred in the vitreous particularly in the region between the ciliary body and the lens. In a few cases the cataract evidently absorbed and a shrunken remnant of the lens was left, surrounded by a much thickened capsule.

It has already been mentioned that in the affected rats an occasional hyaloid remnant was seen with the ophthalmoscope and this was also apparent on section as a fibrous plaque on the back of the lens. In some cases also there was a persistence of fibrils in the vitreous which passed from the optic disc in such a manner as to suggest that they were remnants of the primary vitreous (Fig. 6).

Genetics.—Breeding experiments showed that the retinal lesion is inherited as a Mendelian recessive factor. The evidence may be summarised as follows: The offspring resulting from crossing an affected male with a normal female* all had normal retinæ; in the back-cross of females of this mating with an affected male, the

* London Strain Wistar Rat purchased from Glaxo Laboratories, Limited.

lesion appeared in 50 per cent. of the offspring; when both parents were affected the lesion appeared in 100 per cent. of the offspring. There was no evidence of sex-linkage.

The cataract is not inherited as a simple recessive factor since when both parents were cataractous only 69 per cent. of the offspring developed cataract. If the cataract is directly inherited the mode of inheritance is complex, involving more than one factor; it is more probable that the cataract is a secondary phenomenon associated with the retinal degeneration or some other developmental defect. The inheritance of the retinal lesion and of the cataract are more fully discussed in a separate communication (Bourne and Gruneberg).

Discussion

The immediate cause of this cataract has not been identified. The fact that animals of this strain with normal retinae showed no lens abnormalities of any kind and the lens changes described were never found without the retinal lesion indicates that the two conditions are closely associated; probably a single hereditary factor (gene) is responsible for both. The variations in the time of onset and in the rate of development of the lens changes in different animals and in the two eyes of the same animal suggest that the cataract is a secondary phenomenon, but we cannot regard it as being simply a "terminal complication" resulting from the retinal disintegration. In the first place the lens changes begin at an early age, and can be seen with the ophthalmoscope when the animal is about nine weeks old, in a few cases they were visible as early as the fifth week; and it was found that at this age the retina is not grossly degenerate, only the outer nuclear and rod layers being affected (see page 616). Furthermore, the retinal degeneration was not invariably associated with lens changes; a number of animals in which the retinal degeneration had progressed to an advanced stage failed to show any lens changes at all, although they were observed for as long as eighteen months. Therefore, although there is a close genetical association between the retinal degeneration and the cataract, a further search must be made for the factors which affect the lens directly.

The persistence of hyaloid remnants and of fibrous strands in the vitreous, together with the abnormal thickness of the anterior capsule and the early rupture of the very thin posterior capsule, are prominent features of this lesion. This suggests that, associated with the hereditary retinal defect, there may be also a defective development of the vitreous and lens capsule. It is possible that some abnormality in the vitreous body or in the lens capsule may be more directly related to the production of the

cataract than the retinal lesion itself. This point is being more fully investigated.

The cataract is not due to a disturbance in the blood supply to the eye; the vessels of the retina and choroid were found to be healthy at the time of onset of the lens changes; the iris and ciliary body were found to be normal. Nor is it likely that the cataract results from some general metabolic disturbance, since the two eyes of an animal are not always affected to the same extent. The animals appear to be healthy and their diet is adequate in all known dietary essentials.

It is interesting to note that Jess (1925) described an hereditary and congenital cataract occurring in a colony of white rats. Thirty-four per cent. of the 300 eyes examined by him were affected. The cataract consisted of granular opacities in the anterior cortex; the number, size and density of these opacities varied greatly, often appearing as a thick "bee-swarm" in an otherwise clear lens. From this description it appears that Jess's cataract is different from the one described here.

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HEREDITARY DEGENERATION OF THE RAT RETINA

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IN the preceding paper (p. 608) a form of cataract occurring in rats and associated with a particular form of retinal degeneration was described. It was shown that the retinal defect is hereditary and that the mode of inheritance is that of a Mendelian recessive factor. The purpose of the present communication is to describe