So that we may regard our case as a developmental, or inherent fault, showing arrest and aberration; macular arrest and abnormal development of pigment as a somatic mutation. We know little of the laws that govern mutation. Experimentally the gene constitution can be altered by X-rays in Drosophila to produce white facets in the eyes of an insect which would otherwise be uniformly red. The toxins of disease may on occasion be the initiators of somatic mutations in actively differentiating tissues. Alternatively, one may simply regard this case as a foetal choroiditis, having the main characters of any patch of old choroiditis, namely, atrophy at the centre of the lesion and pigment proliferation at the periphery, the pattern of the peripheral pigmentation being subsequently altered by growth of the globe. The grouped pigmentation was unusually well-marked being present in all quadrants of both eyes. It might be suggested that a foetal inflammation had destroyed the macula and given rise to the surrounding pigmented changes, these changes assuming the characteristics of grouped pigmentation with further growth of the globe.

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SECONDARY CARCINOMA IN THE ANTERIOR CHAMBER*

BY

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FROM THE PATHOLOGICAL DEPARTMENT, MOORFIELDS

Secondary carcinomatous deposits within the eye probably occur with greater frequency than the literature would lead one to suppose. Stallard (1933) gave a ratio of 1:140,000 in the Moorfields records. There is little doubt that if routine examinations were

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made of those dying of generalised metastases, many cases would be found, a point made by Devereux Marshall (1897) who made the first collection, of 24 cases, from the literature. Enough have, however, been recorded for the salient clinical and pathological features to be assessed. Surveys of the sites of the primary growths, and of the regions of the eye affected have been made by Ask (1934) and by Lemoine and McLeod (1936) and the condition has been described and the literature collected by Duke-Elder (1940).

In only one case verified by pathology has the retina alone among the intra-ocular structures been invaded, that reported by Smoleroff and Agatston (1934) in which the primary growth was a gastro-oesophageal carcinoma. Otherwise in all recorded cases intra-ocular metastases have been in the uveal tract, the choroid being by far the most frequently implicated. In the series of histologically proved cases collected by Ask and later added to by Lemoine and McLeod there were 156 of choroidal metastasis. In 8 of these 156, growth was also present in the iris or ciliary body or both, having arisen there either as a result of direct extension forwards from the anterior choroid, or in some cases apparently from separate emboli. In 8 further cases only growth was confined to the anterior part of the uveal tract, the ciliary body, or ciliary body and iris. Involvement of the iris alone is rarer still. The only two examples in which such limitation has been proved by histological examination of the whole eye are those of Proctor and Verhoeff (1907), and Sanders (1938).

This apparent selective affinity for the choroid probably depends on the vascular arrangements, since the malignant cells reach the eye as an embolic process. Of the cases in Ask’s, and in Lemoine and McLeod’s series in which clinical and pathological data are adequate, metastases in the eyes were bilateral in 137 per cent., right sided in 40.5 per cent., and in the left eye in 45.8 per cent. Thus as in cerebral and retinal embolism, and for the same reason, the left side is slightly more often involved than the right, and the anatomical arrangements and number of vessels favour the travel of emboli along the short posterior, rather than the long posterior or anterior ciliary vessels, thereby determining the higher incidence in the posterior half of the eye. The vascularity of their eventual resting place may also play some part; the area temporal to the disc in which secondary deposits are most often found is the region of the choroid not only with the largest number of afferent vessels, but also with the richest capillary network.

Following the lodgment of the embolus, proliferation of the malignant cells takes place, and after perforation of the blood vessel wall the tumour spreads along the line of least resistance, laterally in the choroid, forming the flattened plaque with rounded
edges giving the characteristic clinical appearance. The extent of spread will depend on the rate of growth, the amount of reactionary-fibrous tissue formed, and the period of survival of the patient. Perforation of Bruch’s membrane, invasion of the sclera, and extra-ocular extension are rare. A retinal separation may occur at any time, probably as a result of exudate from the choroid. The histology of the deposit depends on the nature of the primary growth. In many cases, particularly those of anaplastic type, it may be difficult or impossible to give a definite opinion as to the primary focus from the appearance of the secondary, but in all cases the tendency is for spread to take place by direct lateral extension.

This case is reported because it shows a condition not hitherto described, the presence of carcinomatous deposits free in the anterior chamber, as well as in the root of the iris, in the ciliary body, choroid and sclera.

The patient, a woman aged 64 years, attended Moorfields in December, 1943, giving a rather vague history of progressive failure of vision in the right eye over a period of about a year. She had seen an ophthalmic surgeon in October, 1943, and had been given miotic drops. When seen at Moorfields the right eye was injected, the cornea was so oedematous that no deeper structures could be clearly seen, the tension was markedly increased, and there was no perception of light. In the left eye the corrected vision was 6/6, and the fundus was normal. She had had a left radical mastectomy for carcinoma (confirmed by histological examination) a year previously, and at the time of ocular examination there were no obvious metastases. The possibility of secondary carcinoma in the eye was considered and she was advised to have it removed. This was done. A letter from her doctor in July, 1944, stated that apart from arterial hypertension and slight symptoms referable thereto, she was well and showed no clinical evidence of recurrence.

The enucleated eye was fixed in Zenker's solution, divided horizontally, embedded in celloidin, and stained with haematoxylin and eosin. Macroscopically it was noted that the lens and retina were in situ, and that there was some cupping of the disc, and a little thickening of the choroid on the temporal side. Microscopically the salient feature is the presence of secondary carcinomatous deposits, composed of spheroidal cells showing some variation in size and staining, a few mitotic figures, and no attempt at tubule formation. Deposits are present:—

(a) In the choroid. The main mass is on the temporal side where it extends from near the disc as far forwards as the equator (Fig. 1). A few small foci of growth are also present on the nasal side, indicating multiple emboli.
FIG. 1.

Infiltration of the choroid by spheroidal celled carcinoma. The photograph shows the posterior edge of the deposit on the temporal side close to the disc. (X64).

FIG. 2.

Showing one of the ciliary nerves lying in its canal and surrounded by secondary carcinoma. (X64).
Fig 3.
The region of the angle of the anterior chamber, showing deposits of growth in the root of the iris, and proliferation of carcinoma cells in the anterior chamber. (×64).

Fig 4.
Showing part of a nodule lying on the surface of the iris, demonstrating the type of cell, and lack of vascular or connective tissue connection between the iris stroma (below) and the growth. (×360).
(b) In the sclera. Here growth is extending along the canal of one of the ciliary nerves close to the disc. In the photomicrograph (Fig. 2) it can be seen surrounding the nerve fibres.

(c) In the ciliary body and root of the iris on the temporal side. (Fig. 3.) A small nodule of growth can also be seen 'in the intermediate portion of the iris.

(d) In the anterior chamber. In the angle malignant cells have burst through the iris root and are proliferating into the anterior chamber where they form a plaque lying on the surface of the iris, but not intimately connected with, and deriving no blood supply from it (Fig. 3). A few isolated malignant cells are lying on the posterior surface of the cornea, and, towards the pupillary border of the iris quite large isolated masses of growth are present on the iris surface (Fig. 4). These again derive no connective tissue support, and no blood supply from the iris stroma. Serial sections were cut to ascertain if these apparently isolated masses were part of the head of a "mushroom" growth with its "stalk" rooted in the iris, but such is not the case and the masses are in fact isolated and without visible means of sustenance.

On the nasal side of the anterior chamber (not pictured) there is no growth in the iris root nor in the ciliary body; but there are peripheral anterior synechiae of the iris, and the false angle is filled, and almost the whole of the anterior surface of the iris covered by a thick layer of carcinoma cells, again having no connection with the iris stroma. The amount of growth in the anterior chamber is considerable, and there seems to be no doubt that, once having gained access to it by bursting through the root of the iris, rapid proliferation of the cells took place, and that their nutriment must have been derived from the aqueous fluid. The conditions of growth must therefore have been similar to those obtaining in tissue culture experiments. The isolated nodules towards the pupillary border of the iris may have grown from the terminations of tongue shaped extensions from the main mass in the angle with subsequent disappearance of the connecting bridge. It appears more likely, however, that they have developed from detached malignant cells floating in the aqueous and eventually lodging in the iris crypts.

The remainder of the eye shows no features of particular interest. There is some oedema of the corneal epithelium, corresponding to the clinical observations. The retinal vessels and those of the uveal tract show slight arteriosclerosis (seen in Fig. 3), and the disc is cupped.

Discussion

The spread of secondary carcinoma in the eye is usually by a process of direct extension between the tissue planes as a result
of the original location of the embolus, and the appearance of proliferation into, and metastasis across the fluid-containing chambers of the eye has not hitherto been described. Such phenomena are common in the case of neuro-epithelial retinal tumours, in which "seedling" deposits of varying size and activity are often seen on the surfaces of the pigment epithelium, the unaffected part of the retina, the ciliary processes, the lens, or in the anterior chamber. The manner of their formation is clear; owing to its situation the retinal tumour must project at an early stage into either the vitreous or inter-retinal space, and malignant cells are easily separated and distributed as in carcinomatosis of the pleura or peritoneum. Cells from this type of growth are readily viable, and able to grow in a culture medium of the intra-ocular fluids, it being by no means unusual to find a clump of them thriving on the posterior surface of the cornea.

Secondary carcinoma does not behave in this way, either because the cells are less viable, or, more probably, because its situation does not usually permit of free access to the spaces containing intra-ocular fluid. That the latter is the true explanation is suggested by the findings in the present case, and in that of Smoleroff and Agatston to which reference has already been made. In their case a metastasis from a gastro-oesophageal carcinoma had caused an extensive retinal separation and the photo-micrographs show, in addition to the main deposit in the retina, small seedlings on the surface of the pigment epithelium. These must have grown from cells detached from the main mass which had floated through the fluid filling the inter-retinal space.

It has been shown in experimental cancer research work that carcinoma can be inoculated into, and will grow in, the anterior chamber of the homologous animal (Greene and Saxton, 1938). Heterologous transplants have also been successful, examples being the implant of a human schirrus breast carcinoma (Greene, 1938), and of a human fibrosarcoma (Greene, 1942 a), into the anterior chamber of rabbits' eyes. Other interesting, if conflicting, work suggests that the blood-aqueous barrier may be impermeable to circulating antibodies, and that the experimental animal may be susceptible to anterior chamber inoculation while being resistant elsewhere (Saphir, Appel and Strauss, 1941. Cheever and Morgan, 1942. Greene, 1942 b, and others). As pointed out by Freeman and Zimmerman (1944), and demonstrated by a series of colour photographs of eyes containing implanted brain and other tumours, the anterior chamber is a most favourable site for studying the growth of transplants, the clear cornea allowing of direct observation under magnification.
SULPHONAMIDE IN THE TREATMENT OF
OPHTHALMIA NEONATORUM

Summary

A hitherto undescribed condition is described, in which secondary carcinoma is growing in the anterior chamber after the manner of a tissue culture.

Attention is drawn to the differences in manner of intra-ocular extension between neuro-epithelial retinal tumours and secondary carcinoma within the eye, and it is suggested that these are largely the result of the different sites in which the two types of growth originate.

Attention is also briefly drawn to the use made in experimental cancer research of the capacity of the aqueous fluid to act as a tissue culture medium.

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CHOICE OF SULPHONAMIDE IN THE TREATMENT
OF OPHTHALMIA NEONATORUM*

BY

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The value of the oral administration of sulphapyridine in the treatment of ophthalmia neonatorum was established in an earlier communication (Sorsby, Hoffa and Smellie, 1942). In a series of 273 cases clinical cure of the affection was obtained within 8 days in 61.9 per cent, as against cure in 15.2 per cent. in a control series of 46 cases treated by the classical local methods. It was also pointed out that the results were actually better than these figures indicated, for this series contained many cases treated—during the earlier stages of the investigation—with an inadequate dosage. A subsequent communication (Sorsby and Hoffa, 1944) confirmed and extended these findings. In a series of 133 cases treated to a conclusion with sulphapyridine 88.7 per cent. showed clinical cure

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