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SPONTANEOUS ANOPHTHALMIA AND MICROPHTHALMIA IN WHITE-TAILED DEER*

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INTRODUCTION

Observations of anomalous organs provide insight into the normal development of an animal. In the eye, common clinical anomalies such as Mittendorf's dot or typical colobomas, bring attention to the development of the hyaloid system or closure of the embryonic cleft. However, extensive ocular anomalies have been best studied in animals, where a variety of stages and degrees of severity have allowed the sequence of events leading to the anomaly to be deduced, as in von Szily's studies of closure of the embryonic cleft (von Szily, 1924).

Since 1974, 7 white-tailed fawns (*Odocoileus virginianus*) have been found with abnormal eyes but with no apparent abnormalities of other organs. In 1970 another animal with similar eye abnormalities had been studied (Wyand, Lahav, Albert and Stone, 1972). The severity of the eye abnormalities of these 8 animals ranged from complete anophthalmia to microphthalmia with a massive, benign, intra-ocular inclusion to microphthalmia with a more normal arrangement of the intra-ocular structures. The configuration of the elements of the tumour and the variable severity of the abnormality, representing a variety of stages, have suggested a course of development of the ectodermal structures in the eye.

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MATERIALS AND METHODS

Each of the animals was observed in captivity for several days. Physical examination revealed them to be well and of normal development except for conspicuous visual difficulties. They were killed with an overdose of intravenous sodium pentobarbital. The globes, or orbital contents of the anophthalmic animals were removed immediately and the tissue fixed in 10 per cent formalin. These tissues were embedded in paraffin and sectioned at 6 μm; representative sections of each specimen were stained by haematoxylin and eosin (HE), and by Schiff's periodic acid technique. Alcian blue stain with and without diastase and Masson's Trichrome stain were used to demonstrate the composition of the intra-ocular tumours. A 3-in-thick horizontal section of the skull was taken at the level of the orbits of animal 2. This section was fixed in formalin, decalcified and embedded in celloidin. Sections 12-μm-thick were cut in the horizontal plane and stained with HE.

RESULTS

The 8 animals were found in the upstate New York counties of Dutches, Columbia, Greene, Ulster, Delaware and Allegheny. All the animals appeared to be nursing fawns. They demonstrated the conspicuous, peculiar behaviour of blind animals, running in circles and colliding with objects. The animals were maintained under observation for varying periods by two of the authors (D. S. W. and W. B. S.). Two of the animals appeared anophthalmic; the others were microphthalmic. The animals were otherwise without obvious deformity.

Systemic Pathology

Routine gross and microscopical examination revealed no significant systemic anomalies. Bacteria were not isolated from lung, liver, and heart blood.

Eye Pathology

Abnormalities were confined to the eyes and involved every eye. Details of the eye findings are given in Table 1.

Anophthalmic Eyes

The 2 animals which appeared anophthalmic were found on gross and microscopic examination to have true anophthalmia (Fig. 1) in one fawn and congenital cystic eye (Fig. 2) in the other animal. One of the cysts contained cartilage and embryonal retina and pigmented epithelium. No optic nerve was identifiable. Normal appearing ciliary nerve fibre bundles, striated muscles, adipose tissue and lacrimal gland surrounded the cysts.

Microphthalmic Eyes

The other eyes were microphthalmic ranging in size from $10 \times 12 \times 10$ mm to $19 \times 19 \times 16$ mm. The right eye of animal 8 was $21 \times 23 \times 20$ mm, which is

TABLE I

SUMMARY OF MAIN EYE FINDINGS

Animal number	*Age*	*Sex*	*Orbital contents or globe*	*Gross findings*	*Microscopical findings*
1	2 wks	F	19 × 32 × 44 mm	Anophthalmia	True anophthalmia
2	4 mths	F	Orbits and adjacent skull prepared for histological examination	Anophthalmia	Congenital cystic eye
3	2 mths	M	18 × 18 × 17 mm 16 × 17 × 18 mm	Microphthalmia Pupil not identifiable	Failure of cleavage of angle structures Intra-ocular dermoid Dysplasia of ciliary epithelium Aphakia Retinal dysplasia Hyperplasia and dysplasia of retinal pigment epithelium Hypoplasia of optic nerve
4	4 mths	F	13 × 14 × 15 mm 13 × 13 × 12 mm	Microphthalmia Pupil not identifiable Did not transilluminate light	Immature angle structures Dermoid cysts incarcerated in iris and ciliary body Intra-ocular cartilage Foci of lens cortex Pigmented epithelial cells mixed with dysplastic retina and other ectodermal derivatives Hypoplasia of optic nerve
5	6 mths	M	15 × 14 × 14 mm 13 × 14 × 14 mm	Microphthalmia Pupil not identifiable Did not transilluminate light	Immature angle structures Dermoid cysts incarcerated in iris and ciliary body Intra-ocular cartilage Foci of lens cortex Pigmented epithelial cells mixed with dysplastic retina and other ectodermal derivatives Hypoplasia of optic nerve
6	7 mths	?	10 × 12 × 11 mm	Microphthalmia Pupil not identifiable Did not transilluminate light	(Same as Animal 5)
7	?	?	12 × 13 × 12 mm 13 × 13 × 13 mm	Microphthalmia Transilluminated light poorly	Immature angle structures Iris and ciliary epithelium form cysts and adenoid structures Aphakia Retinal dysplasia Hypoplasia of optic nerve
8	6 wks	F	21 × 23 × 20 mm 19 × 19 × 16 mm	Left eye--(L) Microphthalmia Transilluminated light	Right eye within normal limits except gliosis of retina

approximately normal. The microphthalmic eyes all had abnormal development of the anterior segment. The angle structures, when identifiable, were poorly differentiated and incompletely cleaved. The anterior chambers were shallow or absent; in place of the chamber were cysts lined by cuboidal and columnar epithelium with numerous goblet cells (Fig. 3). Dysplastic or hypoplastic retina and hypoplastic nerve were present in every case.

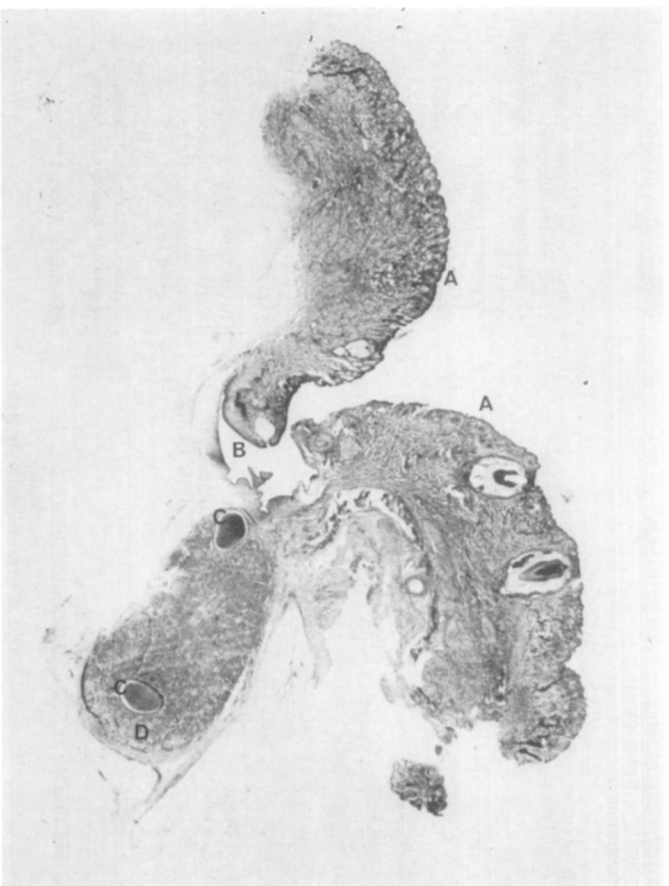

Fig. 1. Photomicrograph of orbital contents of animal with anophthalmia (case 1). A, eye lids; B, conjunctival lined recess; C, island of cartilage; D, adenoid tissue. HE. × 2·1.

In the left eye of animal 8, an eye with more normal architecture, the ciliary and non-pigmented iris epithelium were hyperplastic in places and formed a few cysts (Fig. 4). In more severely affected animal 7, the iris and ciliary epithelium formed cysts and, in addition, adenoid structures (Fig. 5). In more abnormal eyes (animals 4, 5, 6) cystic choristomas incarcerated in the iris and ciliary body were seen. The cysts contained dysplastic retina and other ectodermal derivatives (Fig. 6). The ectodermal elements and dysplastic retina were blended with pigmented epithelial cells (Fig. 7). In the mass were foci of eosinophilic material resembling lens cortex and islands of cartilage

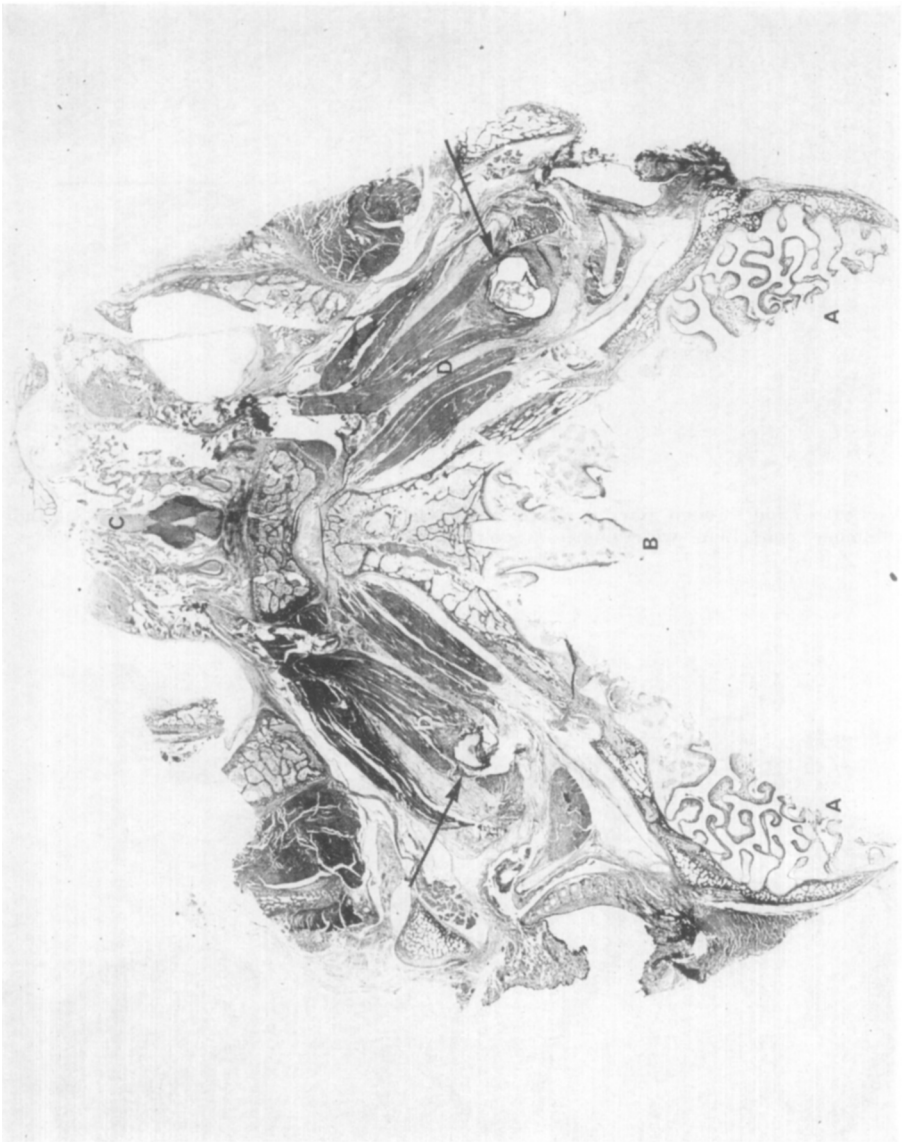

Fig. 2. Transverse section through head of animal 2. A, nasal turbinate; B, nasal septum; C, pituitary; D, extraocular muscle, cystic eye (arrow). HE. × 0·9.

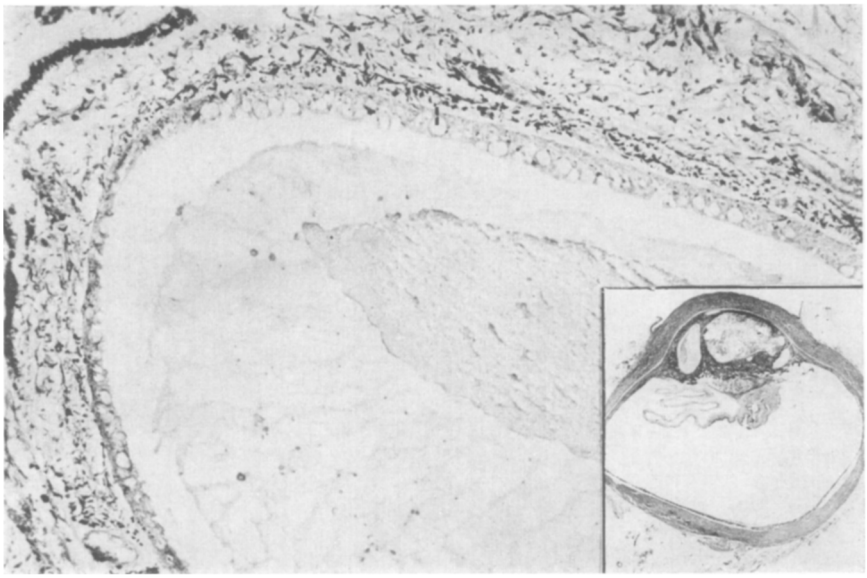

Fig. 3. Vertical section through anterior chamber of animal 5 to show cyst lined by cuboidal and columnar epithelium with numerous goblet cells. HE. × 40. Inset shows entire globe. HE. × 3·5.

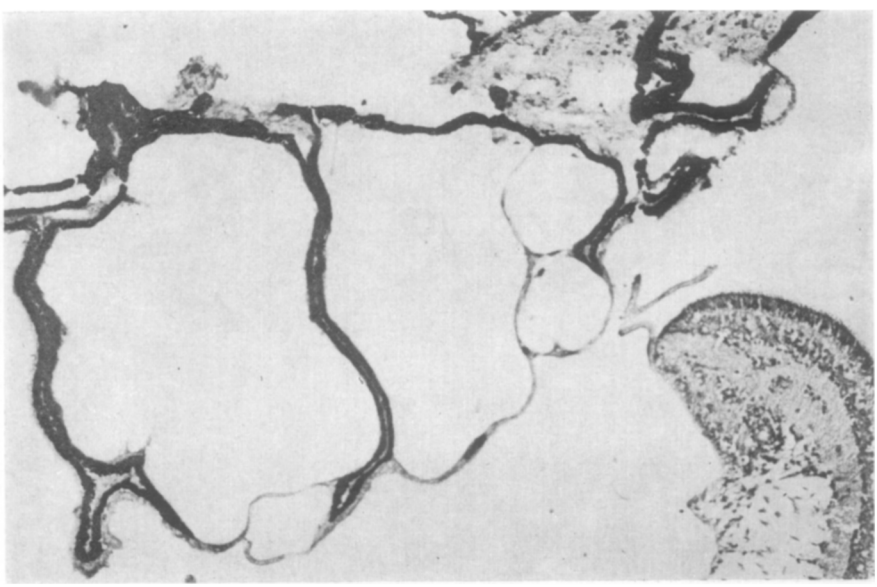

Fig. 4. Ciliary and iris epithelium forming cysts in the milder form of the anomaly (case 7). HE. × 25

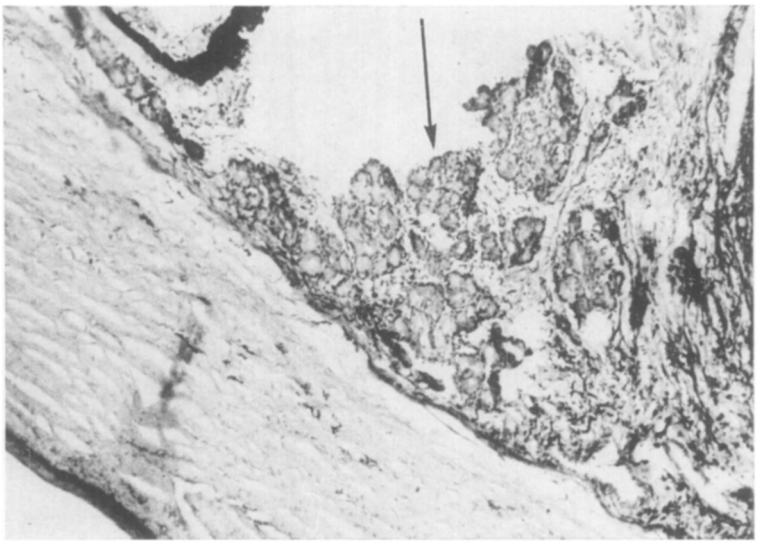

Fig. 5. Iris and ciliary epithelium forming adenoid structures (arrow) in a more severely affected eye (case 6). HE. × 39.

surrounded by fibrovascular connective tissue, adenoid structures and nests of epithelial cells (Fig. 7).

Animal 3 had a similar intra-ocular mass with glandular structures and cysts. The ciliary body and iris showed marked dysplasia. There were numerous processes extending posteriorly. These processes had a dense fibrovascular core and were lined by pigmented epithelium which was in turn lined by non-pigmented epithelium (Fig. 8). The non-pigmented epithelium formed spaces

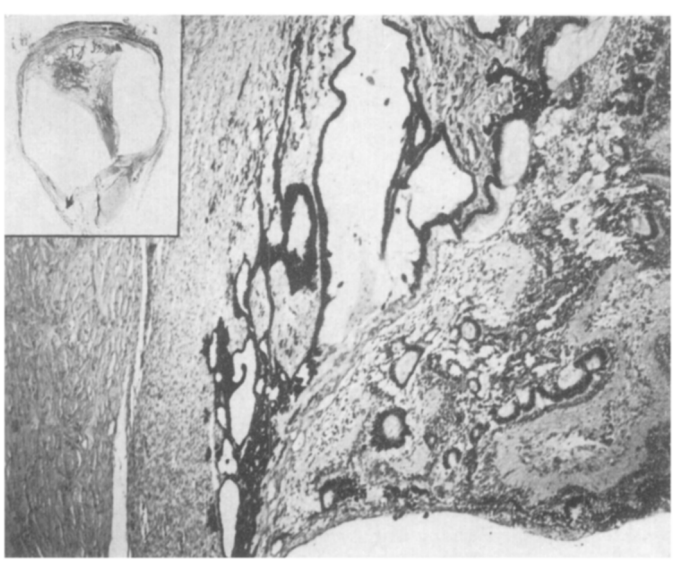

Fig. 6. The tumours contain dysplastic retina (case 5). HE. × 17·5. Inset (× 2·5) to show section of entire eye.

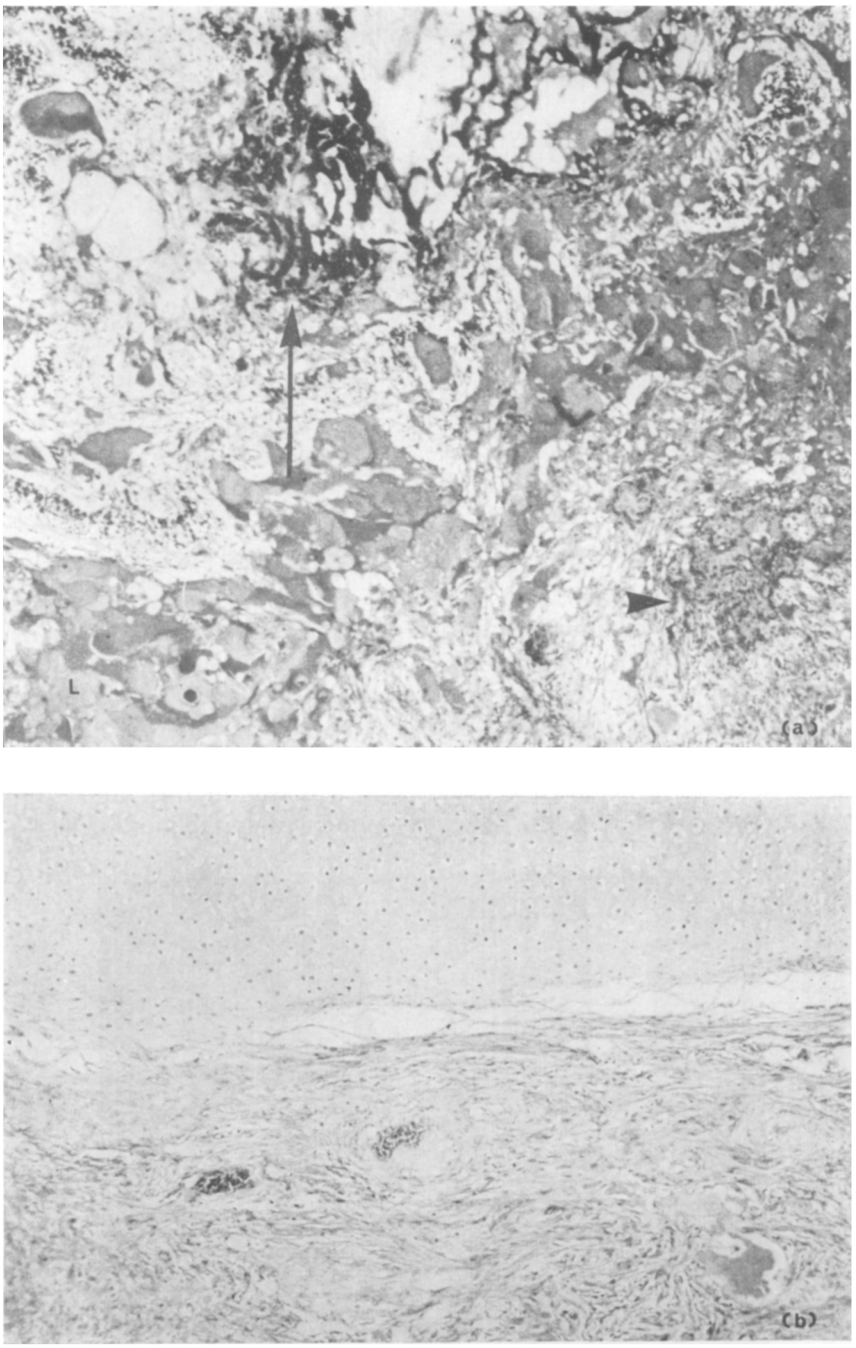

Fig. 7. Sections of eye of Animal 5 showing features of the intra-ocular choristoma. (a) in the tumour are foci of eosinophilic material resembling lens cortex (L) and ectodermal elements (arrow head) blended with pigmented epithelial cells (arrow). (b) Fibrovascular tissue surrounding islands of cartilage similar to that found in human trisomy 13 eyes. HE. × 65.

which contained an Alcian-blue-positive material sensitive to hyaluronidase. No lens could be identified on gross or microscopical examination. Retinal dysplasia, hyperplasia, and dysplasia of the retinal pigment epithelium and hypoplasia of the optic nerve were also present.

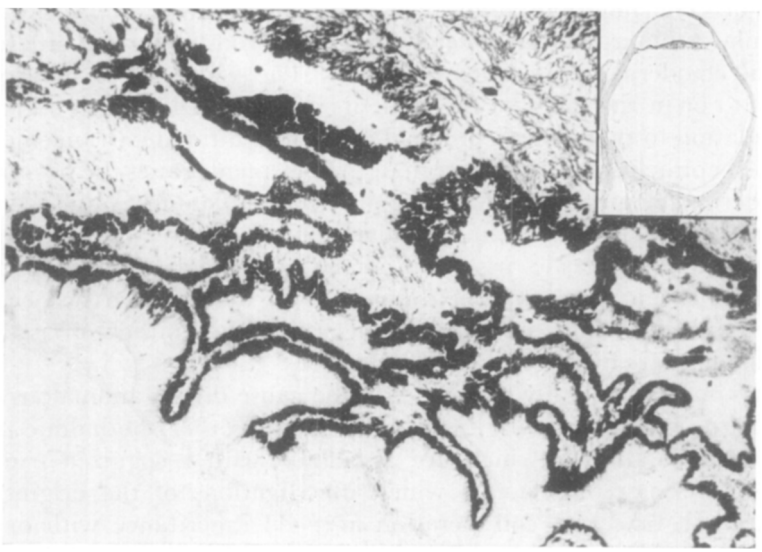

Fig. 8. Eye of Case 3 showing marked dysplasia of the anterior uveal tissue. HE. × 39. Inset shows overall view of eye. × 2·1.

Lymphocytes and fibroblasts were obtained for chromosomal studies which were carried out independently by Dr Doris H. Wurster-Hill and Dr Sang-Nam Kim. The modal number was found to be 70, which is normal for white-tailed deer (Wurster and Benirschke, 1965; Hsu and Benirschke, 1967). The material was not adequate to permit banding techniques to rule out less obvious chromosomal abnormalities.

DISCUSSION

Anophthalmia and microphthalmia in human eyes has been associated with chromosomal defects of the 13 to 15 group (Patau, Smith, Therman, Inhorn and Wagner, 1960) and a variety of hereditary patterns (Hoefnagel, Keenan and Allen, 1963; Joseph, 1957). Induced microphthalmos and anophthalmos in animals has been described (Hicks, 1954). Little is known about spontaneous anophthalmia and microphthalmia in animals, and has been little studied in white-tailed deer (Wobeser and Runge, 1973; Barrett and Chalmers, 1975; Howard, Krehbiel, Fay, Stuht and Whitenalk, 1976).

In the true anophthalmic eyes there has been failure of development of the primary optic vesicle. The clinically anophthalmic eyes, which, in fact, were found to have cystic optic primordia are interpreted to be due to failure of the optic vesicle to invaginate normally. Such a defect must occur early in

embryonic development. Similar abnormalities in the human eye are stated to develop when the embryo is at the 2 to 7 mm stage (Duke-Elder, 1963a).

In the microphthalmic eyes, invagination of the vesicle has occurred. Invagination has been complete in the more normal eyes (animal 8) with evidence that the immature neurosensory retina has joined the pigment epithelium. The microphthalmic eyes with more severe anomalies have an intra-ocular tumour including elements derived from abnormal differentiation of neural ectoderm and surface ectoderm. The glandular structures closely adjacent to or in the midst of the tumours of animals 4, 5, and 6 are in close approximation to pigmented epithelial cells. This intimate arrangement of the pigmented epithelial cells and the ectodermal elements raises the possibility that the ectodermal elements arise from the pigment epithelium. Animal 3, in which no lens material is found, has intra-ocular acini similar to lacrimal gland mixed with markedly dysplastic iris and ciliary epithelium. This configuration, although different from that in animals 4, 5, and 6, also has ectodermal elements and epithelium juxtaposed, suggesting the epithelium as the origin of the ectodermal elements.

At this time we can only speculate on the cause of this anomalous development. There are certain similarities reported here to other ophthalmic anomalies in man and in animals which are associated with recognized causes. The categories of instigating factors which investigations of the origins of deer anomalies will take into consideration are: (1) inheritance with or without demonstrable chromosomal abnormalities, (2) intra-uterine infection with viral or other agent and (3) environmental factors such as exposure to naturally occurring or man-made toxins.

Human cases of trisomy 13 (Ginsberg and Perrin, 1965) have an intra-ocular mass with islands of cartilage surrounded by fibrovascular tissue, not unlike the intra-ocular inclusion found in a human infant. As yet we have not had an opportunity to obtain viral cultures or antibody titres on these animals. Although these similarities lead one to consider viral or other infective agents among the causes of the abnormalities in deer, the apparent limitation of the anomalies to the eyes might be against this view.

The production of congenital ocular deformities by maternal ingestion of various naturally occurring toxins such as *Veratrum californicum* (Burns, James, Shupe and Thacher, 1962; Keeler and Binns, 1967) or plants containing high levels of selenium salts (Franke, Moxon, Poley and Tully, 1936) has been well documented. Ocular anomalies have been induced in experimental animals by numerous chemical agents including many classes of compounds (Duke-Elder, 1963b). No naturally occurring toxin has been recognized in the farming areas where these animals were found. Insecticides and herbicides which are apt to be used in these areas would be included among the suspect causative agents. However, it should be pointed out that none of the commonly used herbicides have been reported to cause ocular defects (Johnson, Van Kampen and Binns, 1972; Dickinson, 1972; Palmer, Haulfler, Hunt, Schlinke and Gates, 1972; Palmer, 1972; Courtney *et al.*, 1970) but most of these workers have investigated acute poisoning.

SUMMARY

Extensive ocular anomalies of 8 white-tailed deer are described. The abnormalities include true anophthalmia, congenital cystic eyes, and microphthalmic eyes with choristoma containing ectodermal derivatives including dysplastic retina mixed with pigment epithelial cells. The intimate association of the epithelial cells and ectodermal elements suggests that the ectodermal elements are derived from the pigment epithelium. The animals' chromosome counts were normal. Possible causes of the abnormalities are considered.

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