TUMORS OF THE IRIS: CLASSIFICATION AND CLINICAL FOLLOW-UP

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THE MATERIAL FOR THIS STUDY consists of upwards of two hundred and thirty examples of tumors of the iris from the collection of the Massachusetts Eye and Ear Infirmary and from specimens contributed with case histories from physicians and other agencies. Study of this panorama of histopathology has permitted a classification of tumors according to tissues of origin and the nature of the growths—benign or malignant. Statistics have been compiled which furnish approximate estimates of frequency of type, and of incidence in relation to age, sex, and other factors. A special clinical follow-up of ninety patients has supplied data concerning extensions, recurrences, and suggestions about treatment.

The methods used were study by light microscope of variously stained and bleached specimens coupled with clinical findings from biomicroscopy and gonioscopy in some instances and photography.

PROLIFERATIONS AND HYPERPLASIAS OF IRIS TISSUES

The various tissues of the iris undergo proliferations and hyperplasias of limited degree. Pigmented and unpigmented nodular masses form commonly. Small collections of cells apparently arise from the adventitia of anteriorly placed vessels and have a limited growth (Figure 1). Either end of the dilator myoid at its anchor line may show collections of benign cells possibly of neural origin (Figure 2). Senile hyperplasias occasionally form hyalin plaques under the sphincter pushing the latter anteriorly (Figure 3). The posterior pigmented layer will proliferate uncommonly into small solid nodules or small cysts at the pupil border (Figures 4 and 5).

PRIMARY BENIGN TUMORS AND CYSTS OF THE IRIS

Primary tumors of mesodermal origin include angiomas showing capillary, cavernous, or racemose patterns. These lie on the surface or

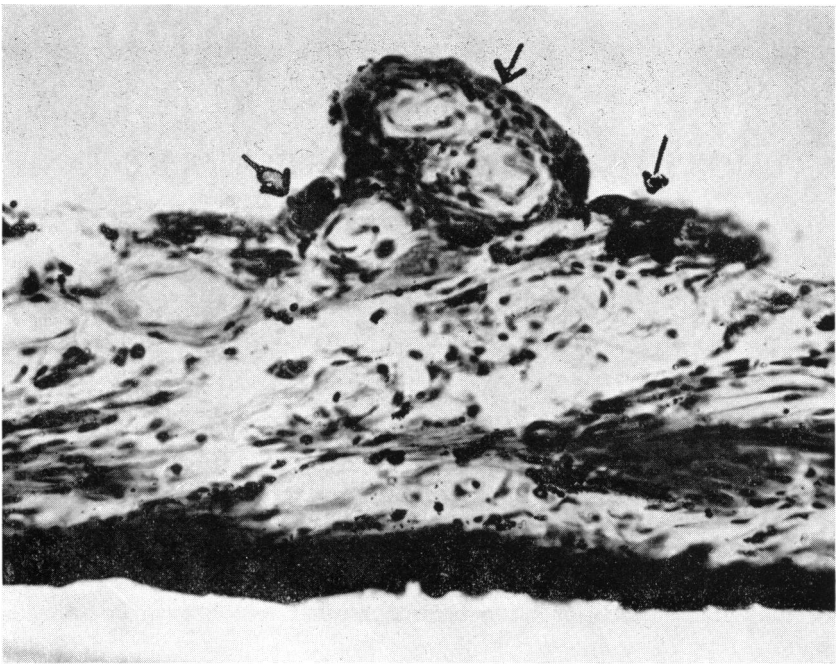

FIGURE 1. ANTERIOR BORDER TISSUE HYPERPLASIA, ARROWS. 312×

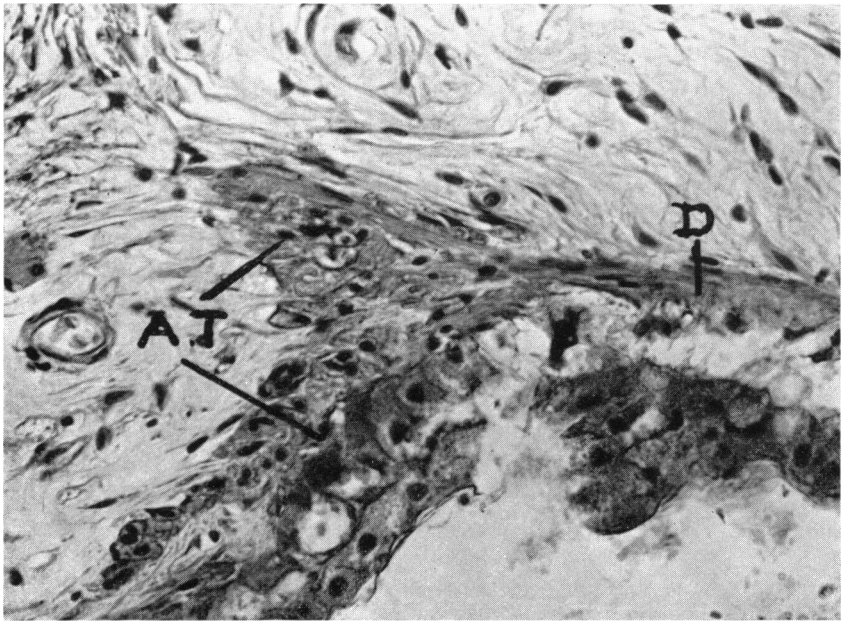

FIGURE 2. HYPERPLASIA OF THE ANCHOR TISSUE OF THE DILATOR MUSCLE.
D, dilator; AT, anchor tissue. 300×

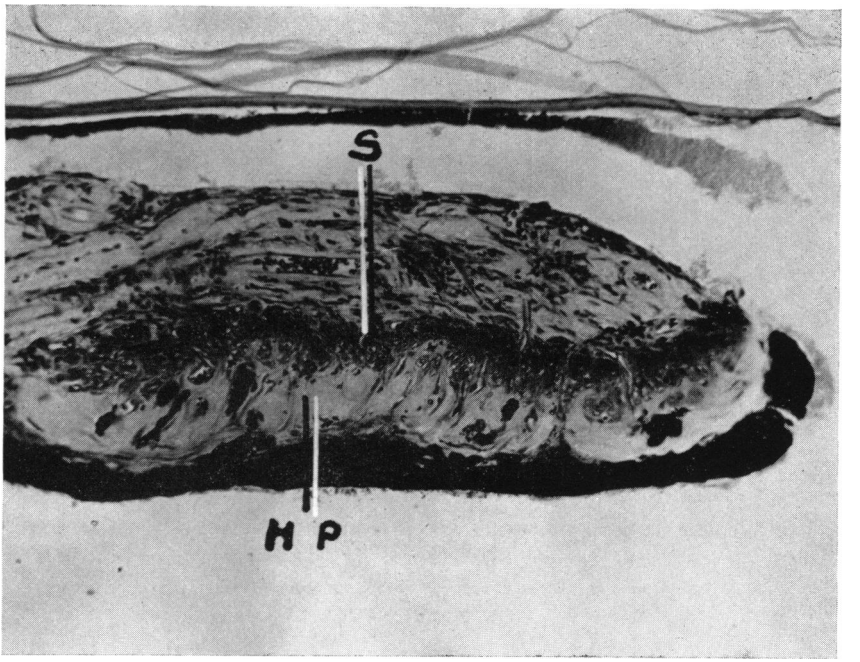

FIGURE 3
Senile hyaline plaque, HP, pushing sphincter, S, anteriorly.

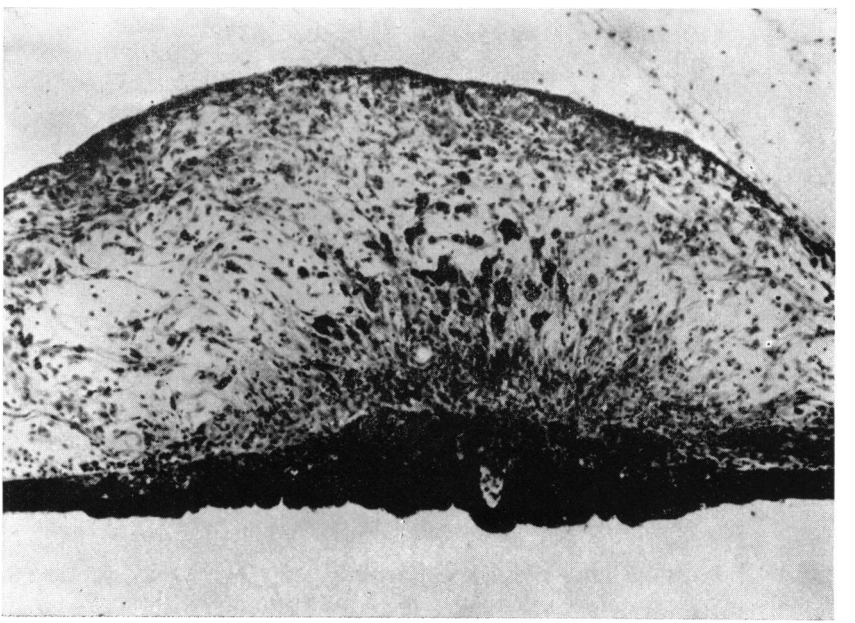

FIGURE 4. NODULE FROM POSTERIOR PIGMENT LAYER. 43×

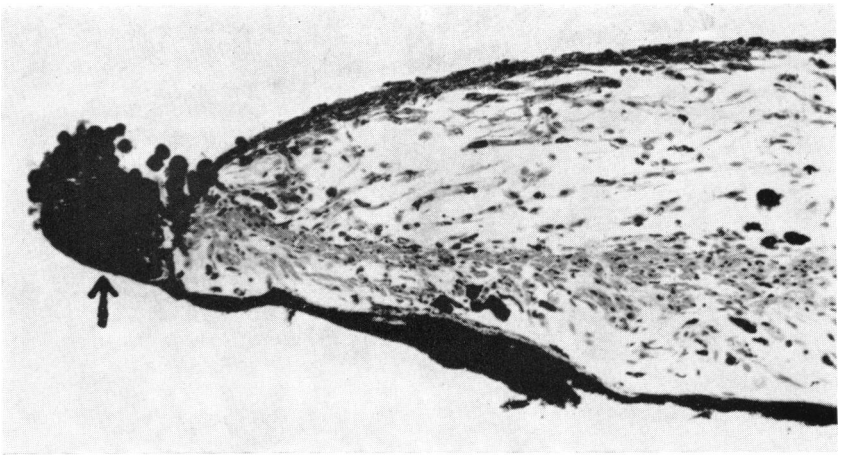

FIGURE 5. FOCUS OF BENIGN HYPERPLASIA OF POSTERIOR PIGMENT LAYER AT PUPIL BORDER. 150×

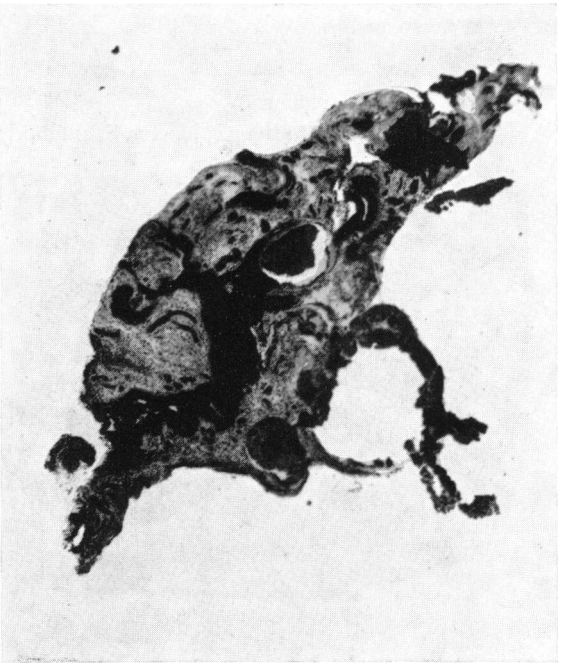

FIGURE 6. HEMANGIOMA OF IRIS, AS REMOVED. 24×

within the stroma and avoid the posterior iris. They may represent hamartomas, vascular remnants, or combinations with congenital remnants of teratoid nature (Figures 6 and 7). Occasionally they show

activity coupled with recurrent hemorrhages. Aberrant vascular structures rarely may separate off and lie free in the anterior chamber or remain connected to the iris by a strand. The fibroma is an exceedingly rare primary tumor of the iris although fibrous changes related to inflammation are common.

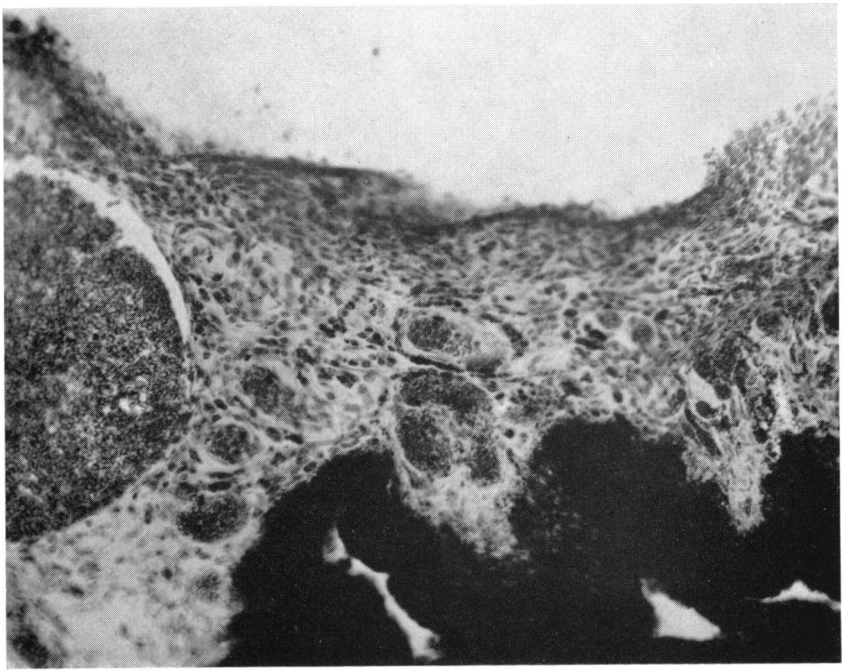

FIGURE 7. HEMANGIOMA, CAPILLARIES, AND MEDIUM-SIZED VESSELS. 156×

The commonest primary benign tumors of the iris are those of the melanotic nevi (Figures 8–10). These may occupy any part of the iris stroma, usually in the temporal quadrant. They are accepted as an innocent part of the iris coloring pattern and do not change over the years. Size increase of nevi sometimes follows inflammations and also can occur as a satellite reaction to malignant growth. Malignant conversion is possible, but very rare. The longest authentic interval in this collection is thirty-five years between an apparent benign state and malignant growth. The posterior pigment layer not uncommonly proliferates and forms a heavily pigmented cyst (Figure 11). A diffuse melanosis also known as melanosis oculi may be in the iris from the beginning or slowly infiltrate from adjacent structures. It is uncommon (1.32 per cent), chiefly seen in brunettes, and usually

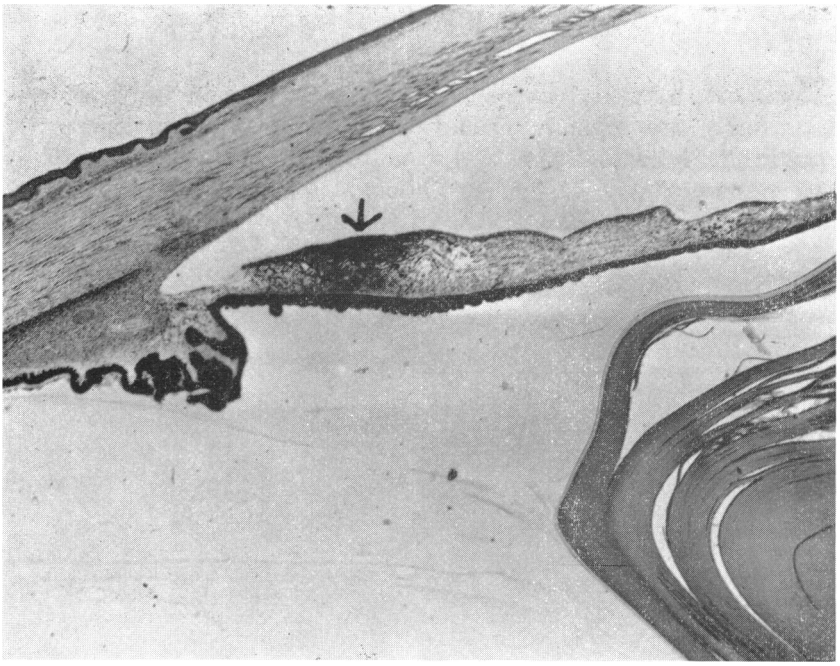

FIGURE 8. BENIGN NEVUS. 24×

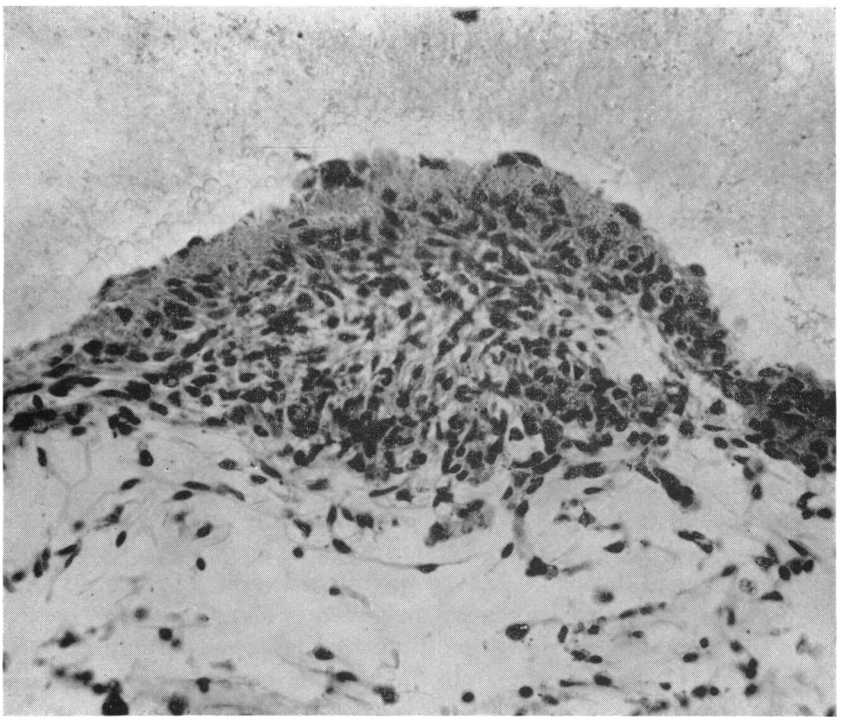

FIGURE 9. NEVUS, ELEVATED AND STATIONARY IN ANTERIOR STROMA. 312×

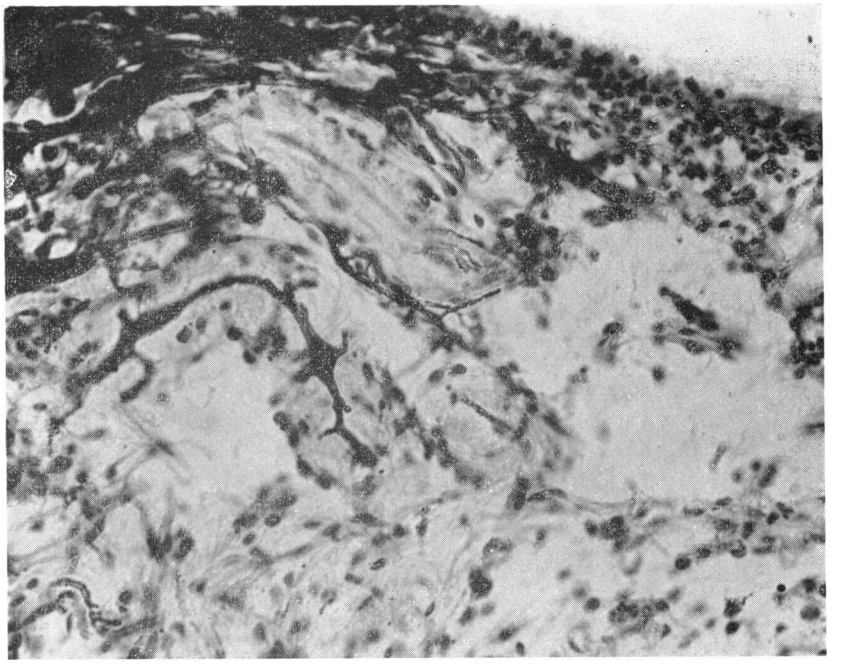

FIGURE 10. BENIGN NEVUS; CELL TYPES. 312×

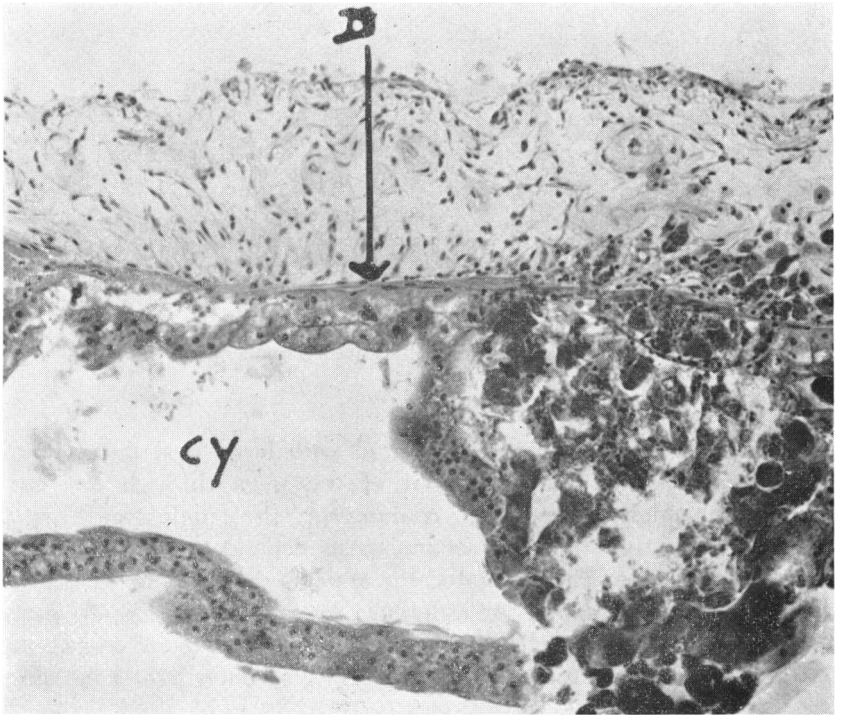

FIGURE 11. PROLIFERATION OF POSTERIOR PIGMENT LAYER WITH CYST FORMATION. Bleached; D, dilator; CY, cyst.

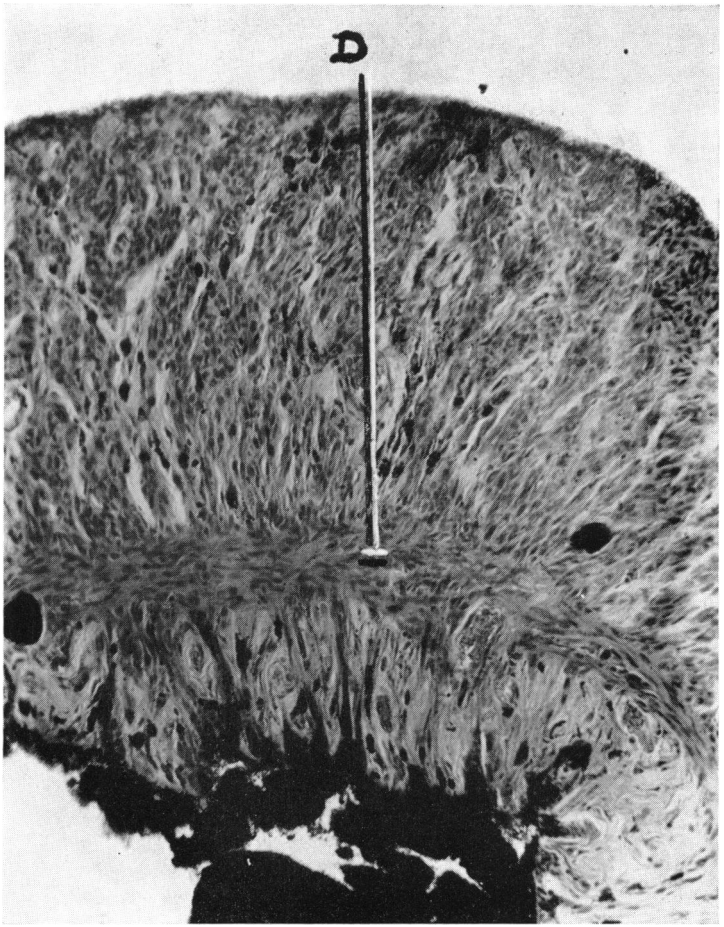

FIGURE 12. DILATOR LEIOMYOMA, ORIGIN OF TUMOR SHOWN.
Section made on oblique plane; pigmentation moderate; D, dilator. 156×

unilateral. The uvea becomes infiltrated with large oval deeply pigmented cells which may spill out of the uvea through emissary vascular channels into sclera, conjunctiva, the angle, and nerve sheaths. When the large cells of melanosis oculi enter the iris, color changes take place. The infiltrated iris appears darker than its fellow. The term "heterochromia," or difference in color, may refer to parts of the same eye. Heterochromia is a feature of certain inflammations of the uveal tract wherein the iris, if affected, becomes lighter in color;

this is also true of some metastatic new growths in the iris. The end results of the slow infiltrative flat growth are obstructive angle glaucoma and heterochromia. Much searching in some cases reveals giant tumor cells containing typical mitotic figures which suggest that the process is of a quasi-benign nature.

Neuroectodermal growths arise from the sphincter and dilator muscles. The sphincter leiomyoma is well differentiated, grows slowly and not circumferentially at the pupil margin; colors are light gray, yellow, or pink. The dilator leiomyoma is usually pigmented and arises between the pupil margin and the iris base; it is sometimes found in young children. The cell types and arrangement often are variegated[6] (Figures 12 and 13).

Rare tumors in the iris are the neurofibroma and the ganglioma. The cells and arrangements are typical in each type. The posterior pigmented retinal layer of the iris or the ciliary body may form cysts within the stroma. The design is that of coiled strands of pigmented cells.

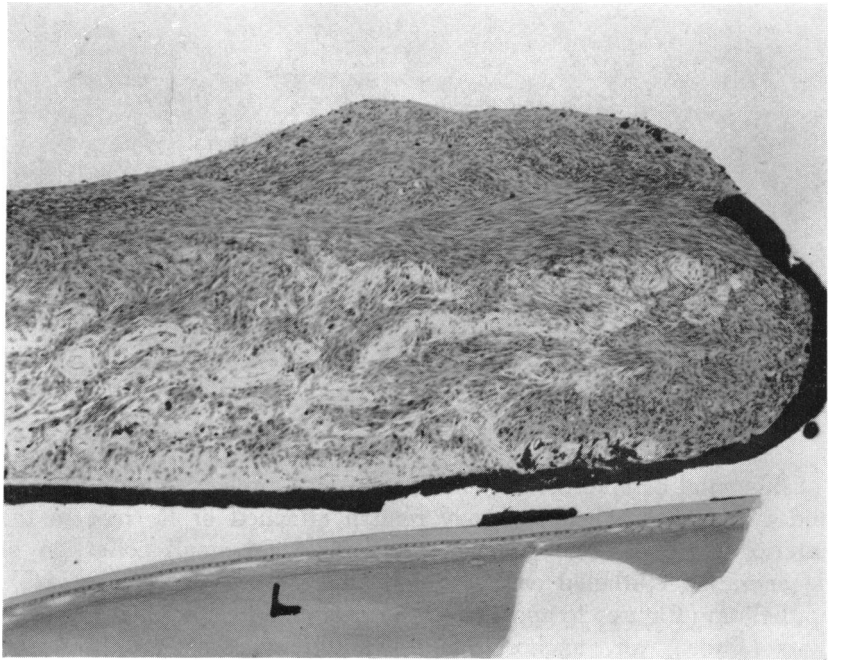

FIGURE 13. SPHINCTER LEIOMYOMA INVOLVING IRIS TIP.
Nearly free from pigmentation; L, lens. 60×

A rare growth in the iris is contributed by the reticuloendothelium and classified as benign—the xanthogranuloma or nevoxantho-endothelioma. This appears in the iris of infants and young children as massive collections of histiocytes and abortive endothelial structures accompanied by Touton giant cells and is similar to this growth in the skin. Recurrent hemorrhages in the anterior chamber and secondary glaucoma are characteristic[5] (Figures 14 and 15).

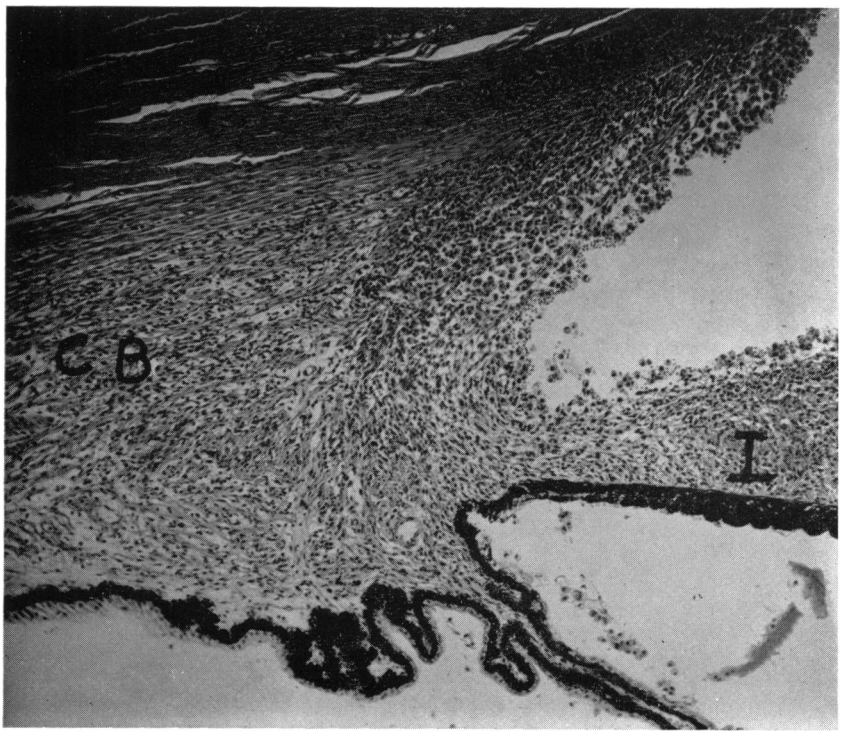

FIGURE 14. NEVOXANTHO-ENDOTHELIOMA.
CB, ciliary body; I, iris and angle infiltrated with xanthoma cells. 70×

Congenital ectopic tissue (choristoma) is found in the iris in solid and cystic form. The cysts may remain attached or lie free in the anterior chamber. The pearl variety is a solid small collection of degenerating epithelial cells within a thin capsule containing viable epithelium (Figures 16 and 17). Other examples of epithelial inclusion cysts (three) were anchored in the anterior stroma and possessed a cuboidal and columnar epithelial covering. Although classified as benign they have undesirable qualities in some cases. The epithelium

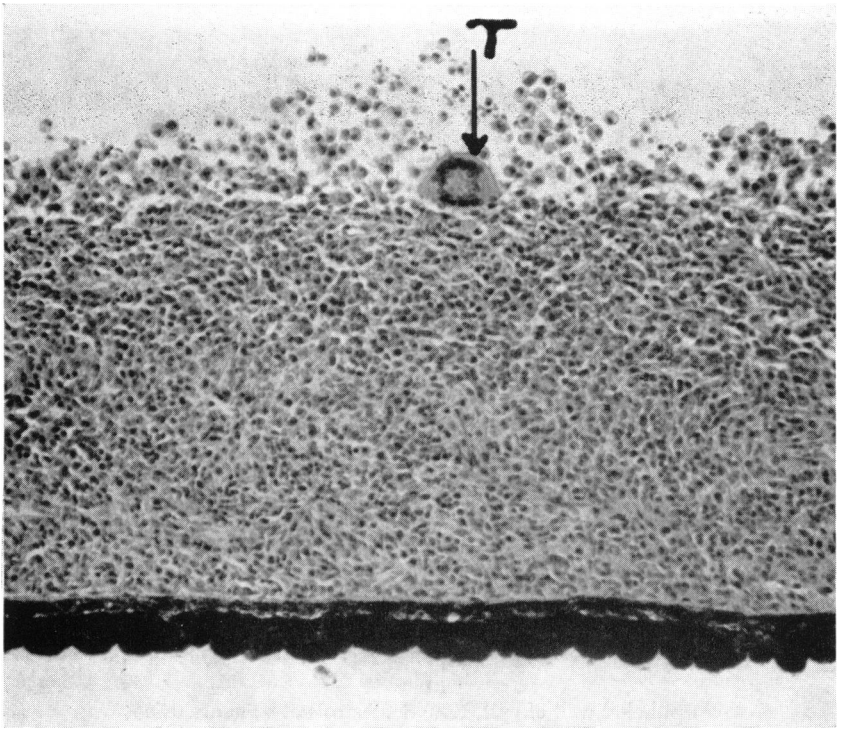

FIGURE 15. XANTHOMA CELLS IN IRIS.
T, Touton giant cell. 115×

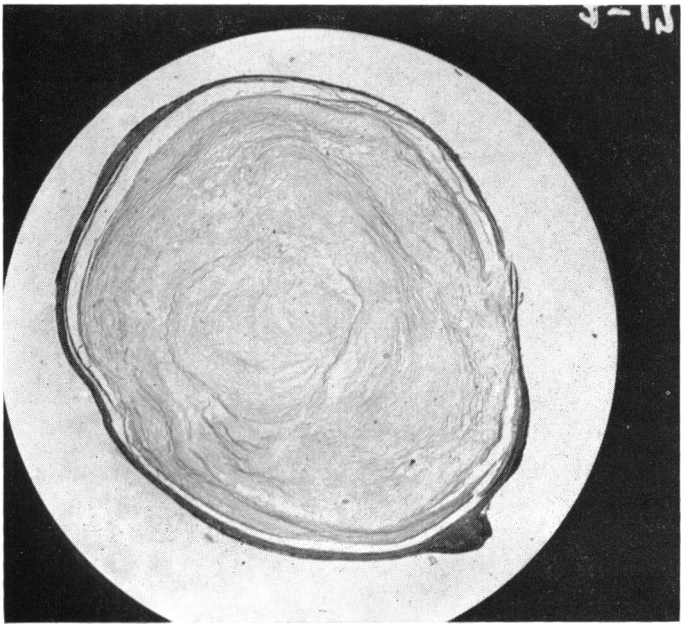

FIGURE 16. "PEARL" CYST OF IRIS AS REMOVED AND SECTIONED, CHOLESTEATOMA.

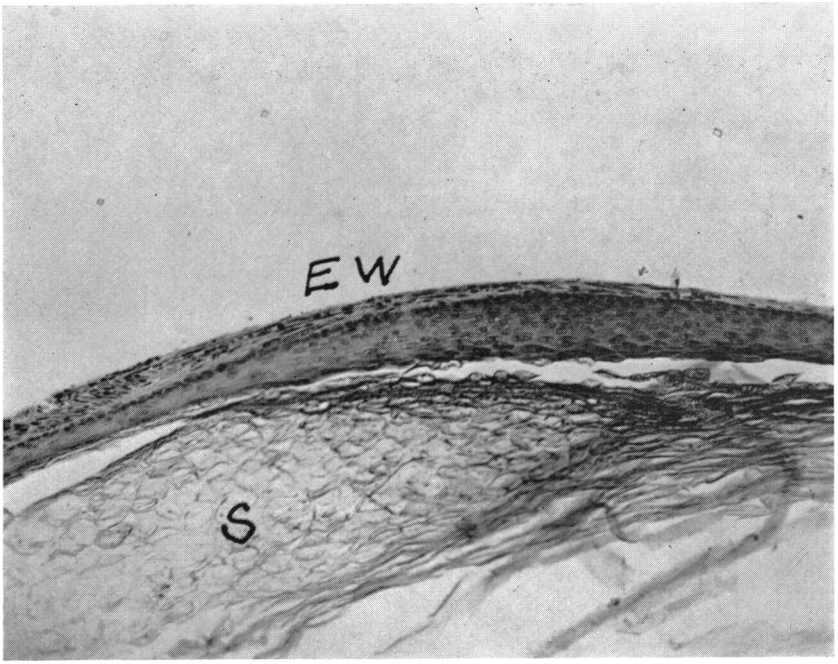

FIGURE 17
Epithelial wall of cyst, EW; S, steatosis of contents. 156×

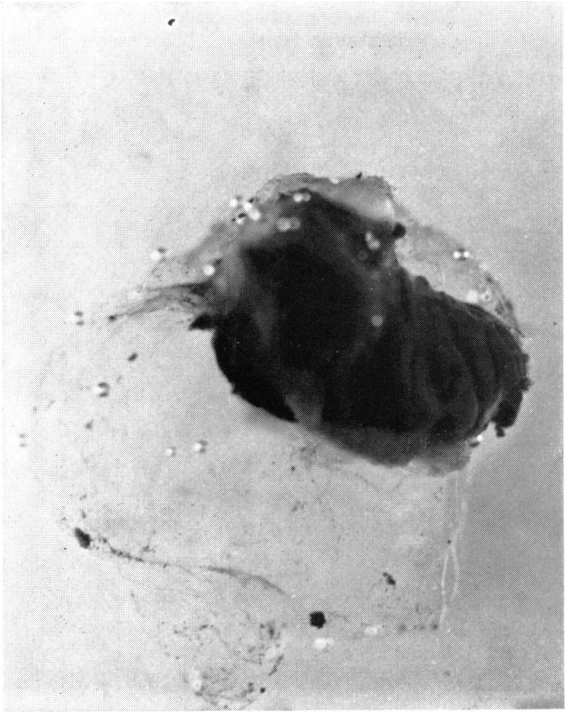

FIGURE 18. GLOBULAR EPITHELIAL CYST, PARTLY PIGMENTED, GROSS APPEARANCE RESEMBLING A MELANOMA.

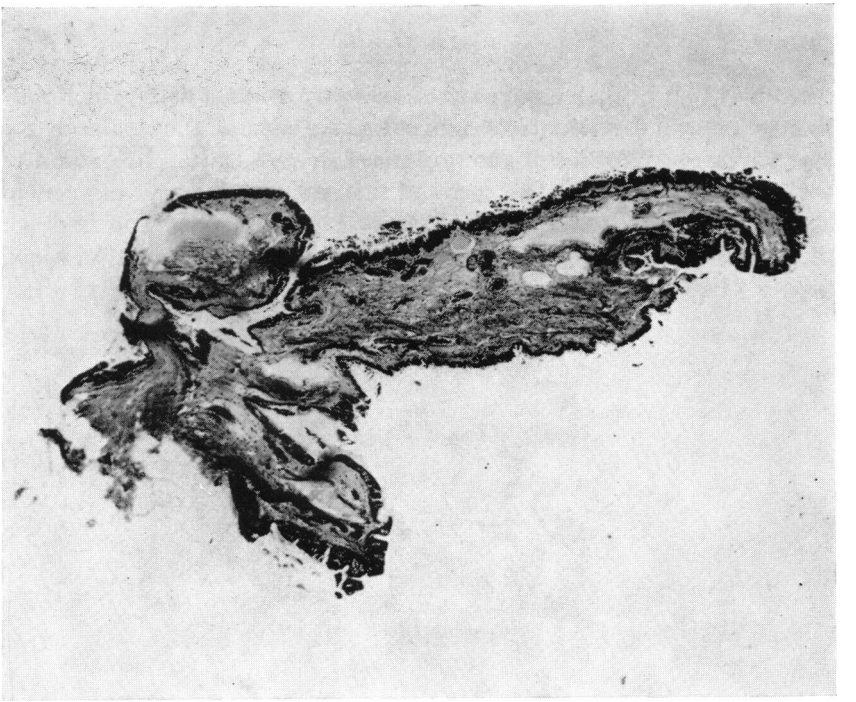

FIGURE 19. CONGENITAL EPITHELIAL INCLUSION CYST AS REMOVED. 25×

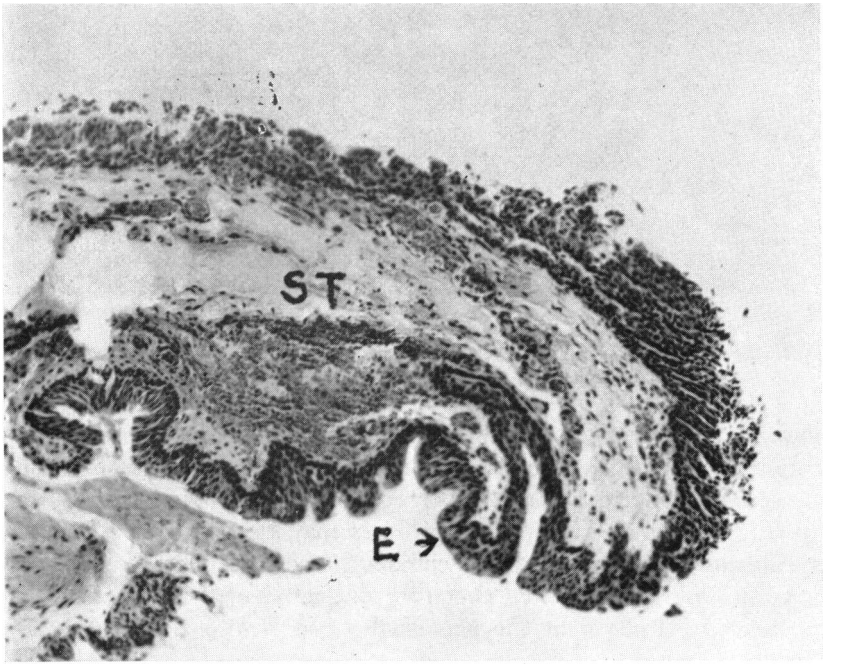

FIGURE 20. EPITHELIAL CYST.

E, cuboidal and columnar epithelium containing goblet cells; vascular matrix, ST. 156×

resembles that of the conjunctiva, containing mucous cells which may secrete bountiful amounts of mucoid material and thus enlarge the cyst, or be set free in the anterior chamber and cause obstruction to outflow and glaucoma. The secreted material can become pigmented and mark the underlying growth or cyst (Figure 18). The body of the cyst is fibrous and the stalk vascular-areolar with a plentiful blood supply (Figures 19–22). Several explanations for the source of these

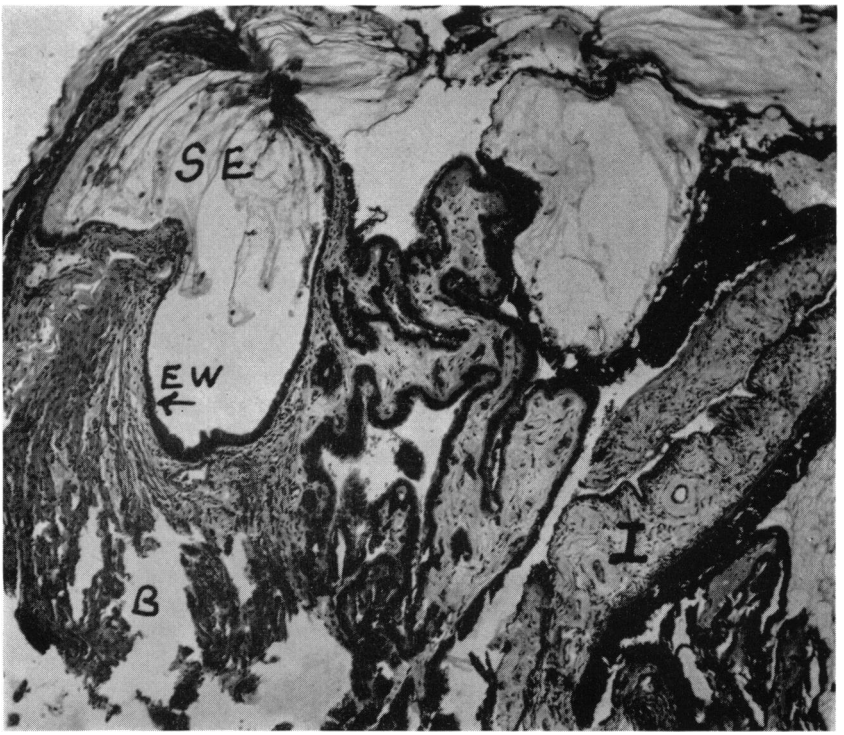

FIGURE 21

Cyst attached to iris, I: base, B; rich vascular stroma; active secretion from epithelial wall, EW; secretion, SE. 70×

nomad cysts have been postulated. An origin from the lens has been suggested, but this is not likely since the lens in each case studied showed no abnormality and other congenital anomalies were absent. An origin from aberrant ciliary process may be considered, but this is a'so unlikely since no derangements in the iris suggested this relationship. Mann[11] suggested that the congenital cyst could arise from the neural ectoderm of the rim of the cup before the ingrowth of

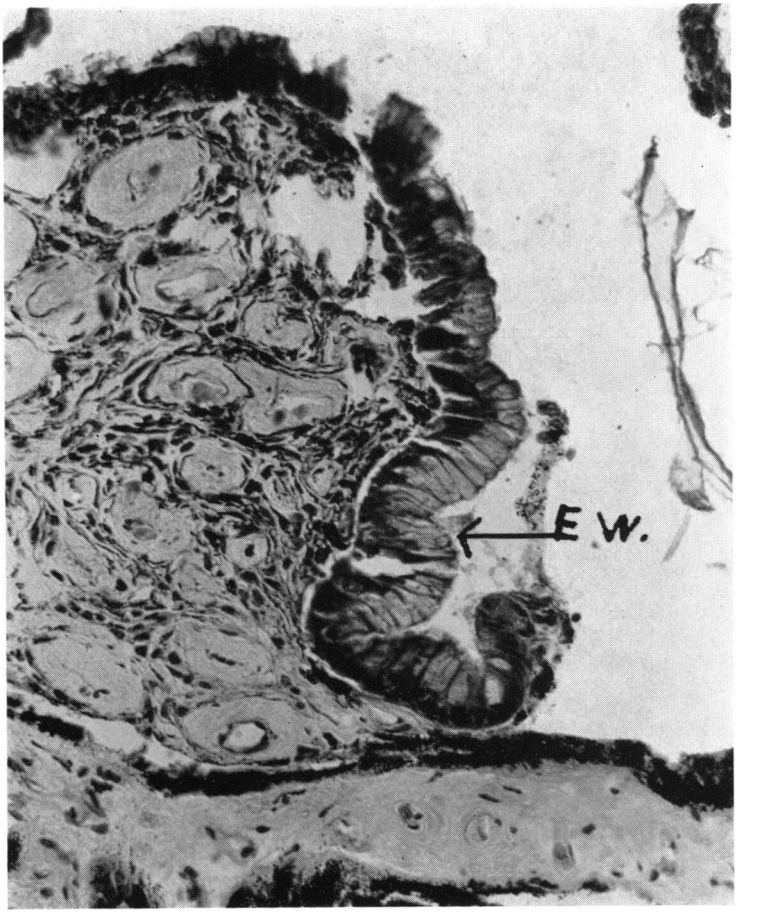

FIGURE 22
Epithelial wall, EW.

the iris begins. This theoretical consideration seems unlikely since in experimental studies the presence of a lens inhibits such a development. A possibility of de-differentiation from neural epithelium exists. But the absence of transitional forms and the great rarity of the congenital cysts argue against this. A relatively normal tissue may be found widely out of position—heterotopic. Such tissue is caught in the shifts and twists of developmental fate and becomes a foreign colony with potentials for atypical growth on the adopted site. Normal acini of the lacrimal gland may be found in the iris. As a rule epithelial

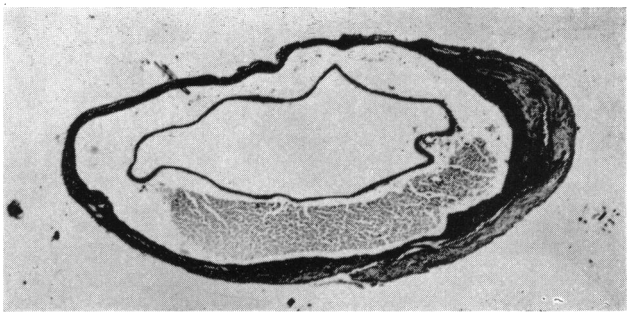

FIGURE 23. DOUBLE WALL EPITHELIAL CYST AS REMOVED FROM IRIS. 25×

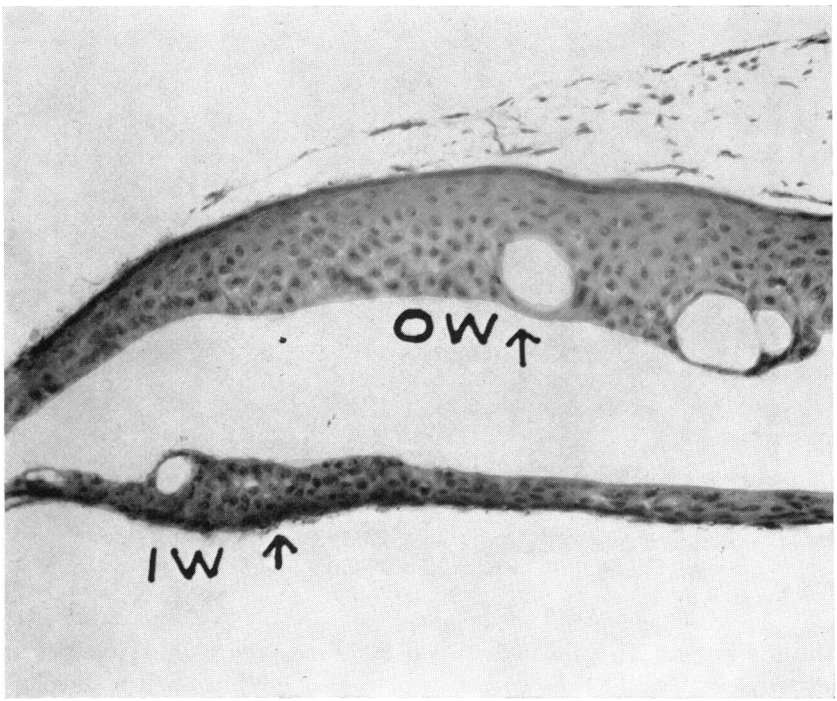

FIGURE 24. DOUBLE WALL CYST, CYST WITHIN A CYST.
OW, outer wall of epithelium containing mucous cells on inner surface; inner wall, IW, containing mucous cells on the outer surface. 212×

congenital cysts in the iris remain quiet over periods of years, but a fair number show rapid growth in later life and may destroy the eye through glaucoma.

SECONDARY BENIGN CYSTS AND TUMORS OF THE IRIS

Secondary benign tumors are fed to the iris from blood and lymph channels and by traceable extensions from contiguous or related structures. They commonly arise from the epithelium and endothelium of the cornea and rarely exhibit a fixed and limited growth. Other origins by extension or implantation may derive from the choroid, ciliary body, and lens in flat, globular, cystic, or solid forms. One example is a cyst within a cyst (Figures 23 and 24). In this series of cases a surprising number of secondary growths on the iris by corneal epithelium occurred (Figures 25 and 26).

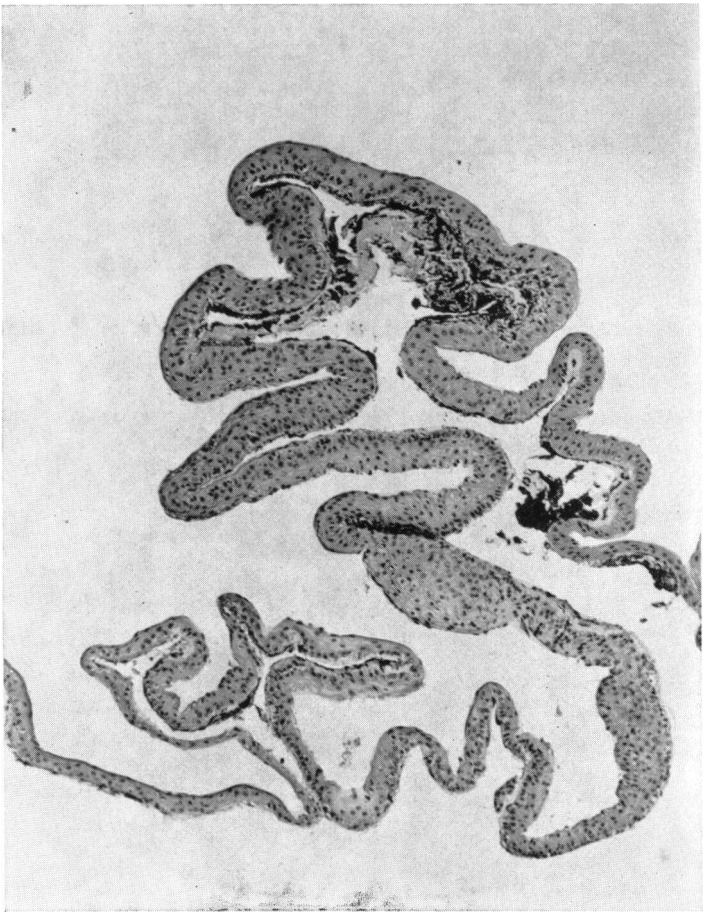

FIGURE 25. EPITHELIAL EXTENSION FROM CORNEA, STRIPPED FROM IRIS AND ANGLE SURGICALLY. 70×

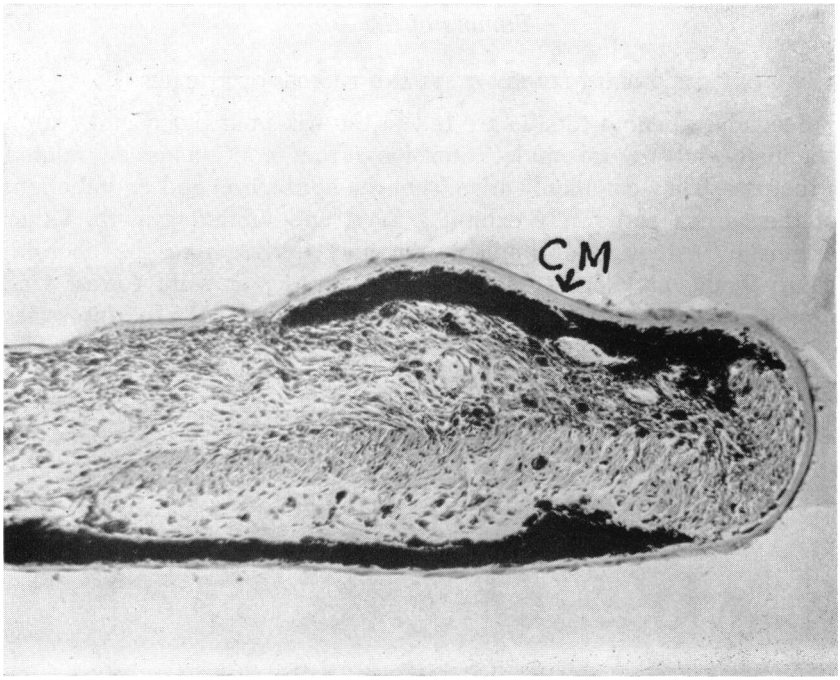

FIGURE 26

Endothelial cuticular membrane, CM; a secondary extension on the iris. 300×

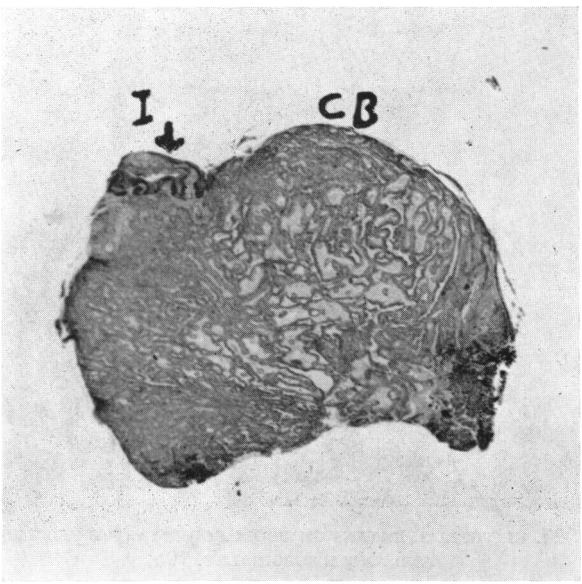

FIGURE 27. CYSTADENOMA OF CILIARY BODY EXTENDING INTO IRIS. 25×

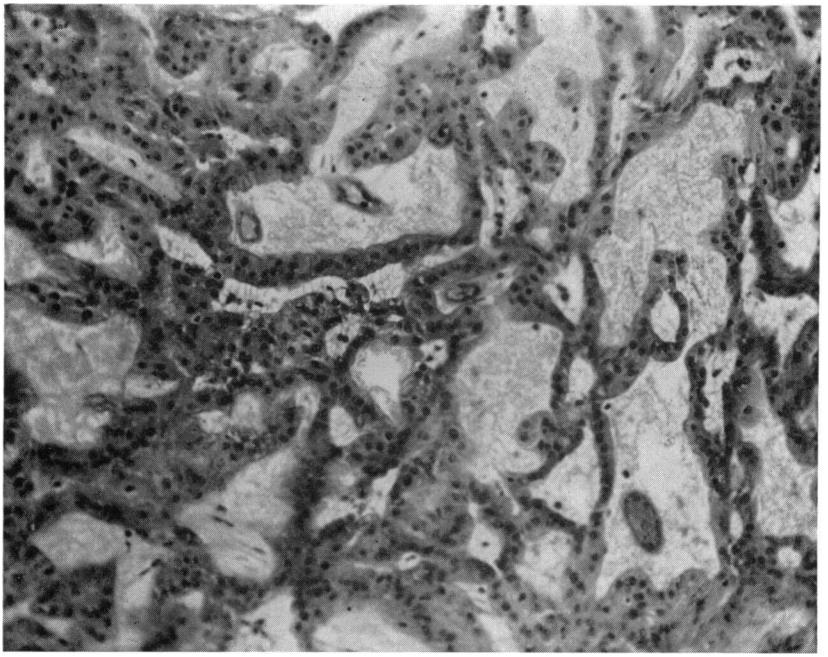

FIGURE 28. DETAIL OF CYSTADENOMA; STRANDS OF UNPIGMENTED CILIARY EPITHELIUM. 156×

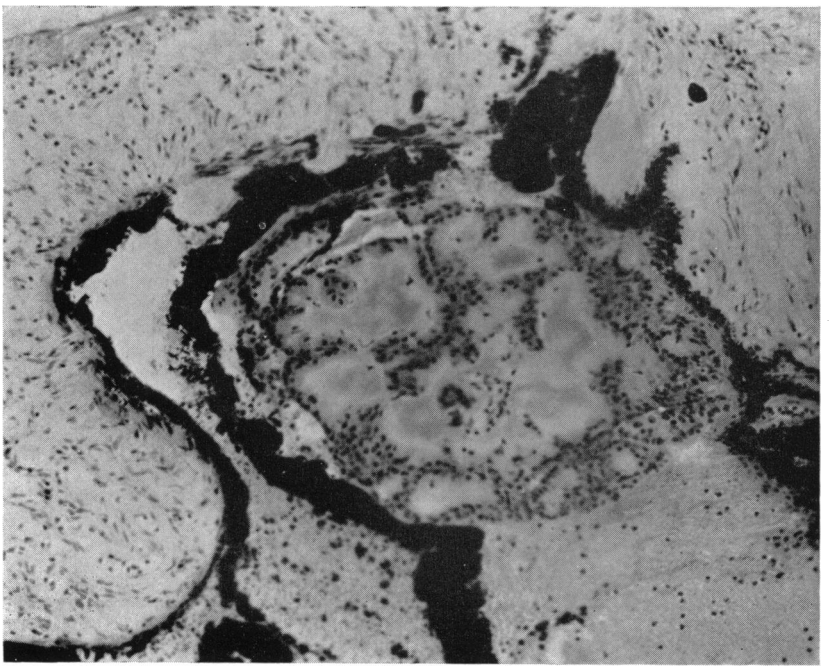

FIGURE 29. PSEUDOADENOMA, BENIGN HYPERPLASIA OF ATTACHED CILIARY EPITHELIUM IN IRIS. 113×

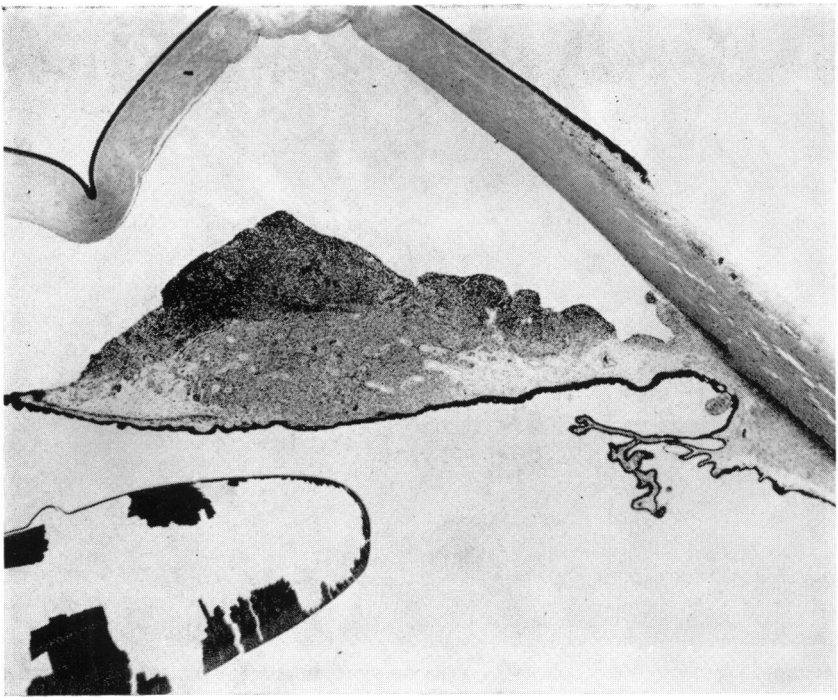

FIGURE 30. MALIGNANT MELANOMA.

Thirteen-year-old boy; epithelioid cell type; has entered trabeculum and also has established multiple seeding of the iris. 15×

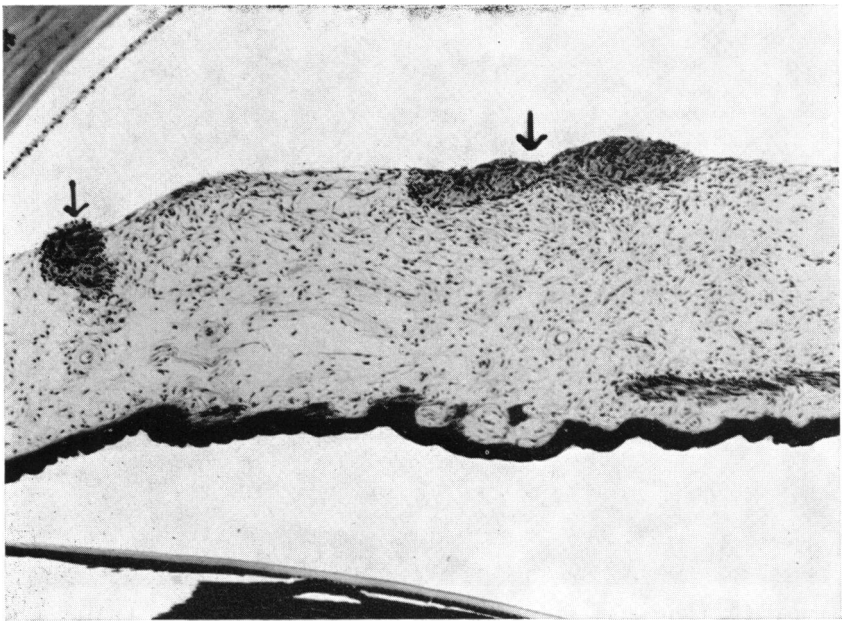

FIGURE 31. SEEDINGS IN THE IRIS FROM PRIMARY TUMOR. 60×

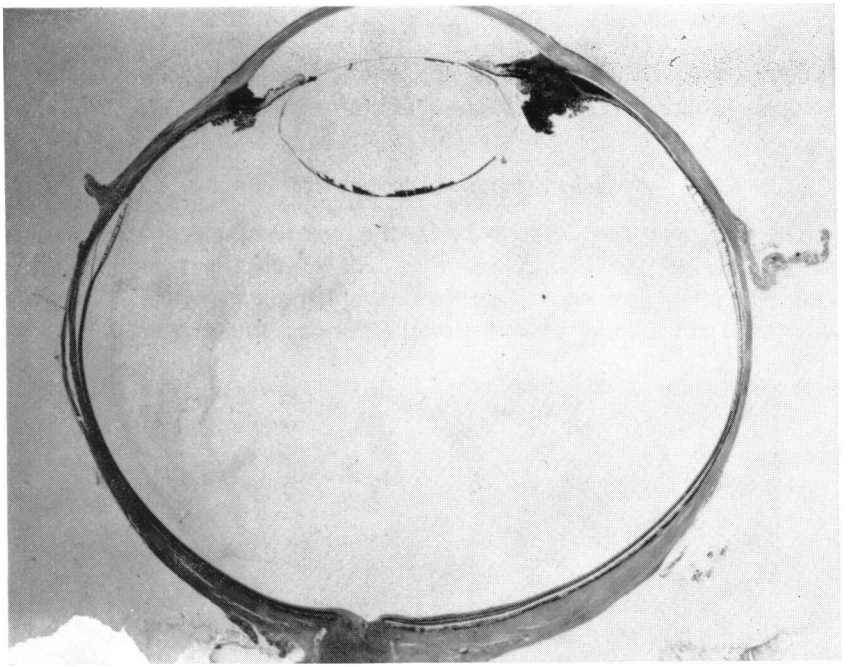

FIGURE 32. MALIGNANT MELANOMA.

Ring growth, early extension externally through vascular channels in angle; mixed epithelioid cell and spindle B.

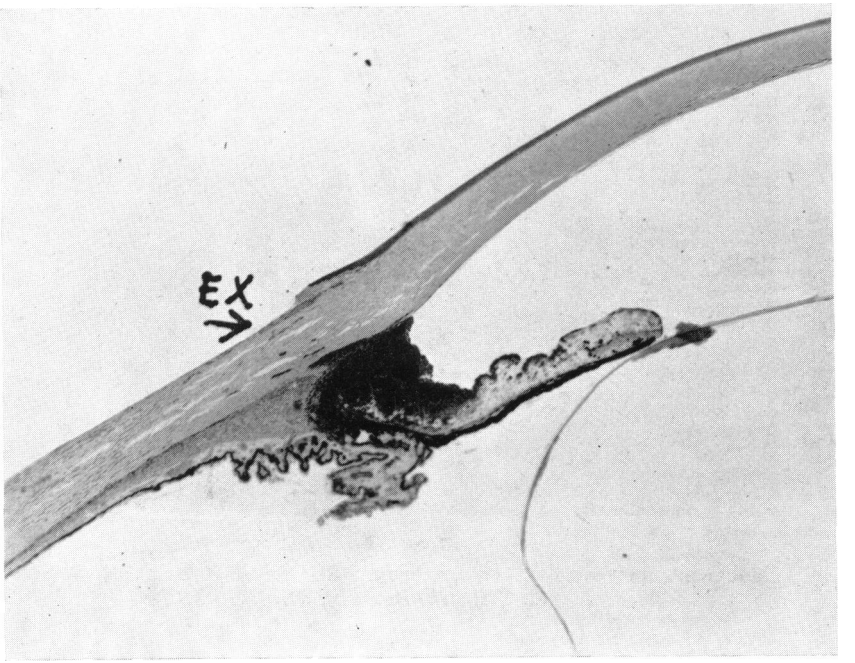

FIGURE 33. CIRCUMFERENTIALLY EXTENSION AND EARLY EXTERNALLY, EX. 25×

Senile hyperplasias of iris-attached ciliary processes constitute secondary tumorous manifestations (Figures 25–29).

PRIMARY MALIGNANT TUMORS OF THE IRIS

The malignant melanoma is by far the most common primary malignant tumor of the iris—constituting half of all the tumors studied and a much higher percentage of the malignant growths. In the iris these tumors are invasive and spread according to cell type but unlike

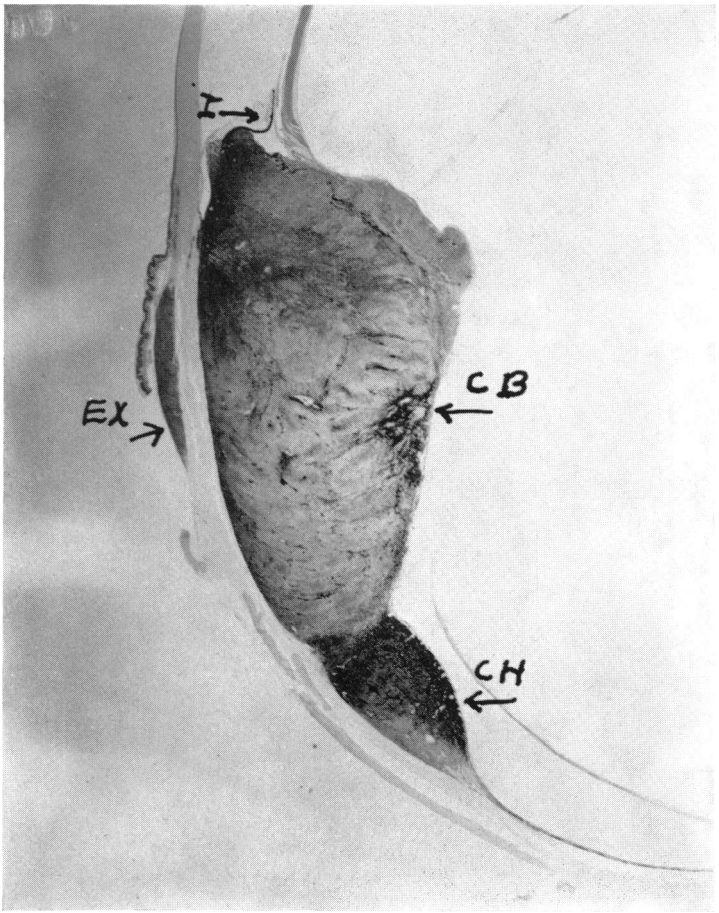

FIGURE 34
Malignant melanoma of ciliary body, CB; extended into iris, I; choroid, CH; and externally, EX. 8×

similar tumors of the choroid are slow to metastasize.[1] The growth habits may be slow, sometimes are diffuse, from multiple centers, are flat, or elevated, or spread along the iris base ringing the eye here or in the ciliary body (Figure 30). Extension occurs in some cases through the angle drainage apparatus to the exterior. Necrosis and bleeding tendency from high vascularity may be features of certain cases. Early seeding is more likely from the epithelioid cell tumors because these cells are less adhesive to the main tumor mass and tend to float free (Figure 31). Deformity of the pupil or the dilator function is typical except in those cases whose tumors begin at the iris base, or ciliary body. The tendency then is to ring growth, circumferential, along the ciliary body and iris base, or angle. Clinical discovery of the ring form of growth may depend upon thorough use of the gonioscope. Other comments upon clinical problems of the malignant melanomas are discussed later (Figures 32–36).

Malignant tumors of the neuroectoderm are exceedingly rare but they do exist (Figure 37). Malignant leiomyoma and leiomyoidoma are suggested terminologies for the muscle tumors, and teratoneuroma or teratomyoma when teratoid elements are included. Medullary epithelioma has been suggested as a term for malignant ciliary epithelium in the iris.

Malignant vascular tumors such as hemangio-endothelioma are very rare. The lymphoma is another rare tumor when prime in the iris; it generally is secondary or associated with this neoplasm elsewhere in the body.[2] Fibrosarcoma is a rare possibility in the iris.

SECONDARY MALIGNANT TUMORS OF THE IRIS

Secondary malignant tumors of the iris may arise from intraocular structures, as, carcinoma from the cornea, medullo-epithelioma from the ciliary body, malignant melanoma from the ciliary body choroid, retinoblastoma from the retina. Distant extraocular sources supply a considerable variety from viscera by means of blood and lymph channels (Figure 38). These growths may cause heterochromia.

A WORKING OUTLINE OF TUMORS, GROWTHS, AND CYSTS OF THE IRIS

I. PROLIFERATIONS AND HYPERPLASIAS OF IRIS TISSUE

A. Anterior border tissues

B. Stromal melanocytes, nevi

C. Dilator muscle anchor tissue

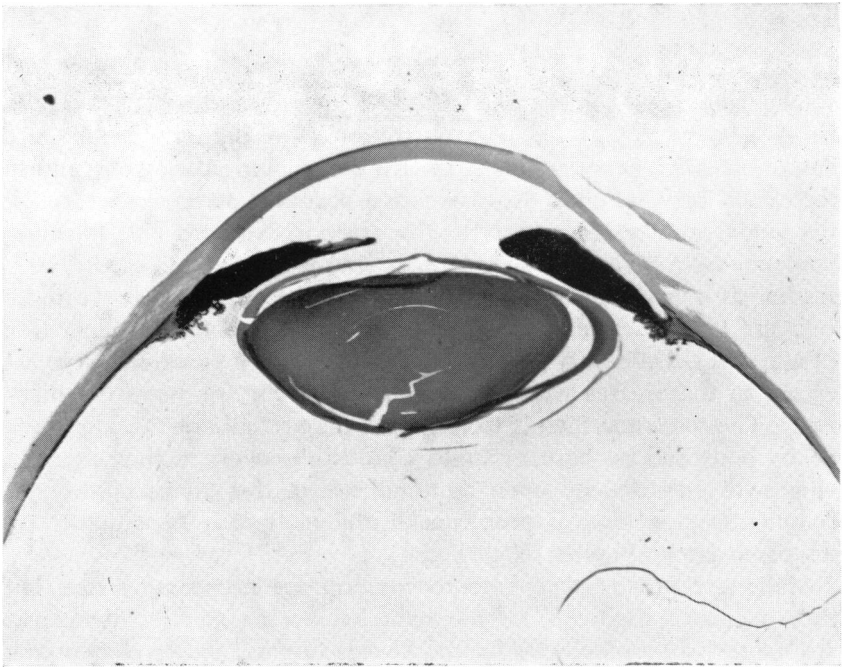

FIGURE 35. MALIGNANT MELANOMA OF IRIS.
Spindle cell A type; slow infiltrative flat growth over period of years; extended posteriorly. 4×

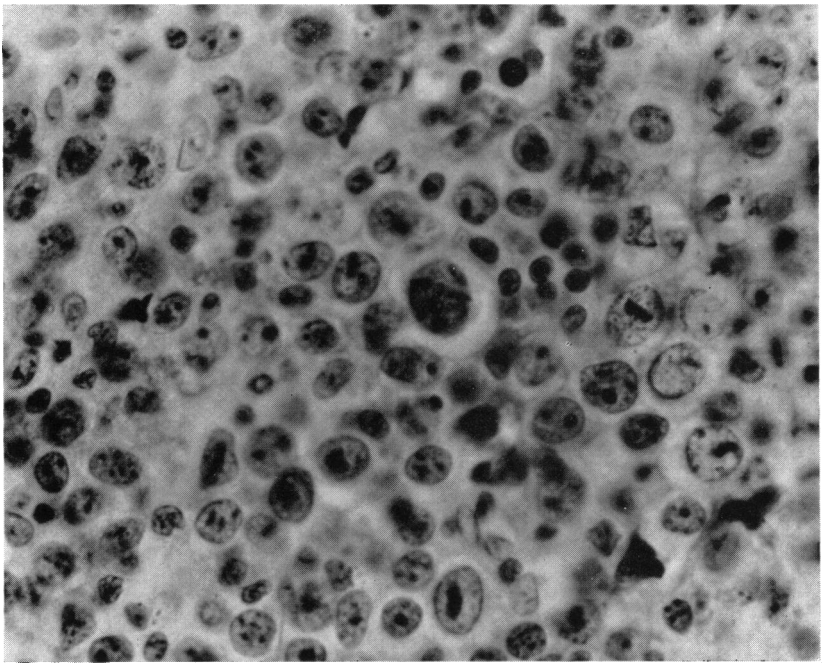

FIGURE 36. UNUSUAL POLYMORPHOUS VARIETY OF EPITHELIAL CELLS WITH NUMEROUS MITOTIC FIGURES. 650×

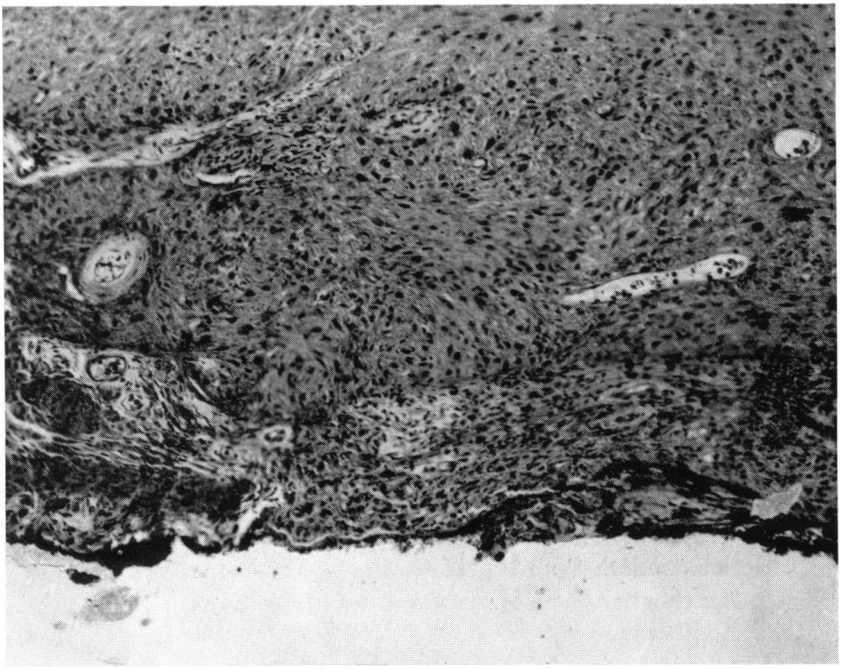

FIGURE 37. NEUROECTODERMAL MYOBLASTOMA ARISING FROM DILATOR, WITH SHEET AND STRAND ARRANGEMENT. 113×

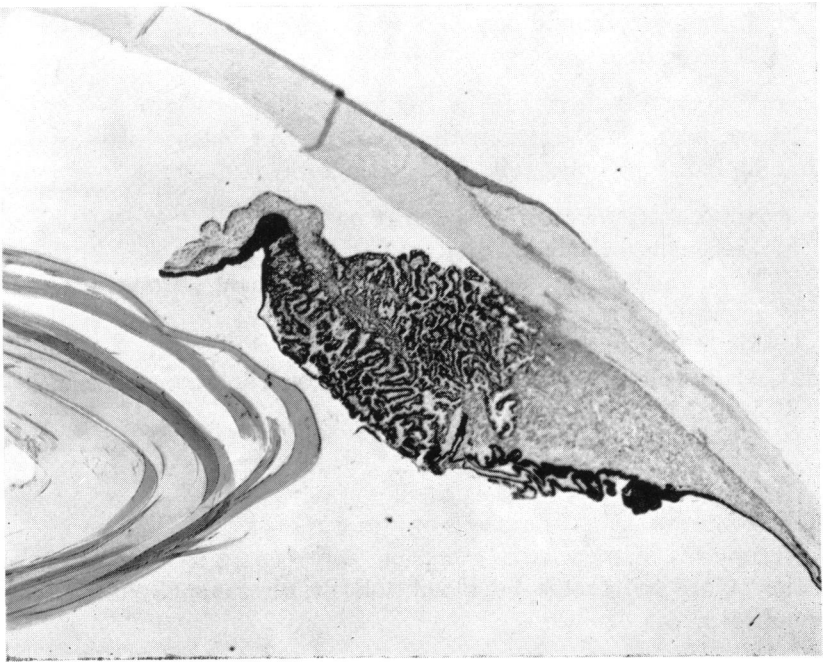

FIGURE 38. METASTATIC ADENOCARCINOMA TO IRIS. 20×

D. Posterior pigment layer hyperplasia, with and without cysts
E. Senile hyperplasias

II. PRIMARY BENIGN TUMORS AND CYSTS OF THE IRIS

A. Mesodermal origin
   1. Angioma; capillary, cavernous, racemose types, hamartoma, congenital vascular remnants, and teratoid growth
   2. Fibroma
B. Neural origin
   1. Stationary nevi, benign melanocytoma
   2. Melanosis oculi
   3. Neuroectodermal neoplasia, sphincter and dilator leiomyoma
   4. Neurofibroma
   5. Ganglioma
   6. Retinal pigment layer cysts
C. Reticuloendothelium
   1. Xanthogranuloma or nevoxantho-endothelioma
   2. Xanthoma
D. Congenital ectopic tissue, choristoma, in the iris
   1. Stationary epithelial cysts
   2. Lacrimal gland
   3. Ciliary processes
   4. Conjunctiva
   5. Benign teratoids, dermoids, and cholesteatomas
   6. Serous and pearl cysts

III. SECONDARY BENIGN TUMORS OF THE IRIS

Extensions or implantations from cornea, lens, ciliary body, retina, choroid; in flat, globular, solid, and cystic forms

IV. PRIMARY MALIGNANT TUMORS OF THE IRIS

A. Malignant melanoma
B. From malignant neuroectoderm; malignant leiomyoma and leiomyoidoma
C. Medullary epithelioma
D. Malignant teratoid tumors (teratoneuroma and teratomyoma)
E. Malignant vascular growth
F. Lymphoma
G. Fibrosarcoma

V. SECONDARY MALIGNANT TUMORS OF THE IRIS

Occupy iris by metastasis, extension, and seeding from other ocular tissue or are fed to iris by blood and lymph channels, often from remote sources

STATISTICAL SUMMARIES

MALIGNANT MELANOMA: 49 per cent (113)

Spindle cell A, 26; spindle cell B, 36; epithelioid or mixed cell, 46; special: giant, polymorphous, and small cell, 5. Ten per cent with glaucoma, of all malignant melanomas.

IRIS ACQUIRED CYSTS: 21.6 per cent

Flat or globular: implant, transplant, ingrowth

EXTENSIONS INTO IRIS FROM ALL SOURCES: 30.8 per cent (70)

Cornea, 49; ciliary body, 8; choroid, 7; retina, 4; lid, 1; lens epithelium, 1. About half of epithelial extensions showed glaucoma.

LEIOMYOMA: 2.2 per cent (5)

METASTATIC TUMORS: 2.96 per cent (6)

VASCULAR TUMORS: 1.32 per cent (3)

VERY RARE IRIS TUMORS: 0.44 per cent (7)

Teratoma, 1; congenital ectodermal cyst, 1; pearl cyst, 1; nevoxanthoendothelioma, 1; myoid leiomyoblastoma, 1; medullo-epithelioma, 1; congenital racemose artery, 1.

BENIGN TUMORS SURGICALLY REMOVED: 8.81 per cent (20)

Frequency according to sex, equal
Single iridectomies, 84
Iridectomies with recurrence, 10
Iridectomy plus enucleation, 16
Iridectomy plus exenteration, 3
Enucleations, 112 (primary 96)
Exenterations of orbit, 5

PROGNOSIS RELATING TO IRIS TUMORS

From this series of cases 90 were followed after initial diagnosis and surgical treatment for an average period of over six years. Among the 90, 23 deaths occurred—12 from unknown causes, 7 from tumor, and 4 from unrelated new growths. Of the 7 dead from malignant growth, the iris may have been the primary source in 5. Of the 5 the tumor involved the iris primarily or with parts of the uvea (5.55 per cent). Unlike those in the choroid, tumors of the iris therefore have significantly low mortality rates. Metastases are rare. Why is this so?

It seems a fair generalization that iris tumors are discovered early, are readily inspectable, and receive early surgical treatment. The blood vessels of the iris are composed of an inner endothelial tube surrounded by a space and another tube supported by a loose spongy stroma with low tissue pressure.[9,10] Tumor cells are not commonly found in blood channels. Involvements along with the iris of the angle, Schlemm's intrascleral connections, anterior external extension, and deep and wide penetration of the ciliary body call for enucleation. Thus a common form of treatment is early enucleation of the whole structure containing a small tumor. Congenital inclusion cysts may be removed surgically with a good prognosis. Epithelial downgrowth, flat or globular, offers a poor prognosis from surgical treatment alone. In the first place it is difficult to isolate and remove all the epithelium and, secondly, the globe may become incapacitated in the process. Surgical treatments of small or moderate-sized angiomas do well after

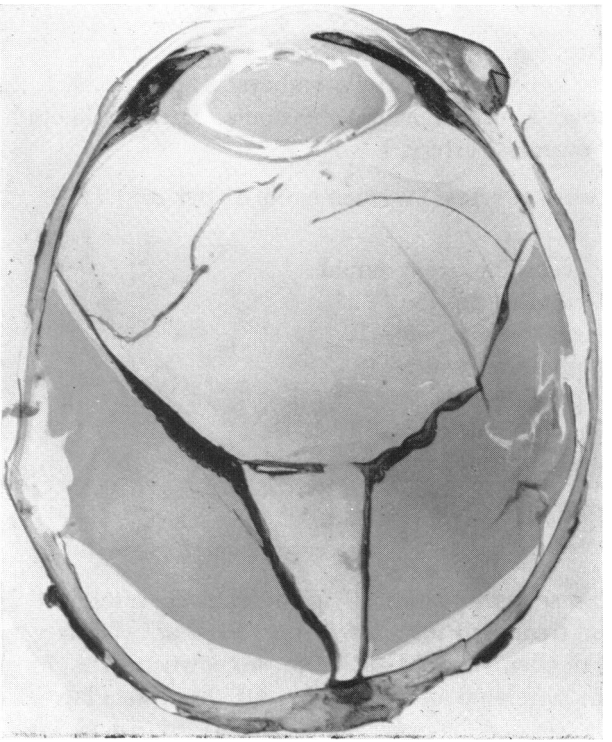

FIGURE 39. MALIGNANT MELANOMA OF DIFFUSE GROWTH.
Epithelial cell; glaucoma; trephine operation. 4×

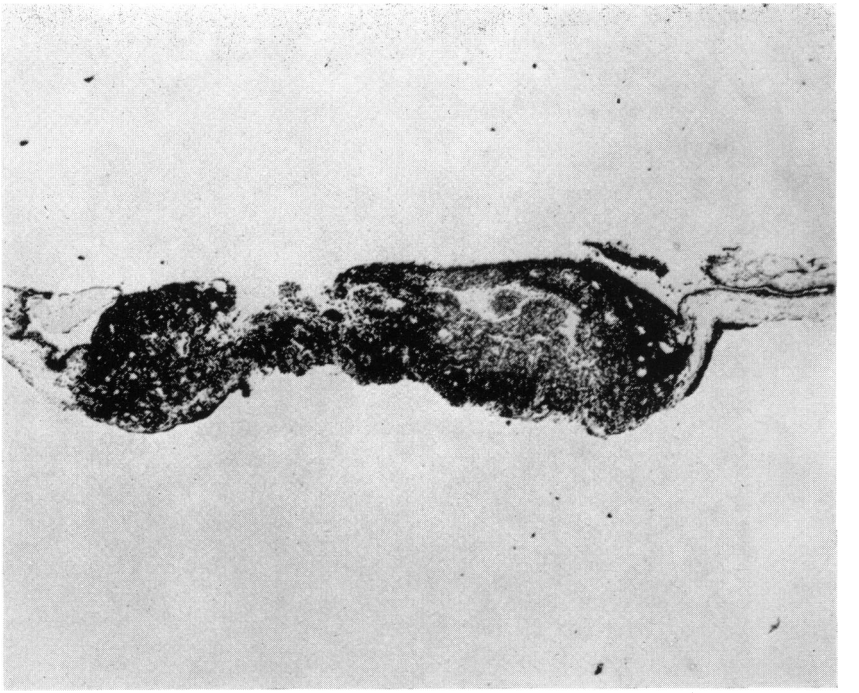

FIGURE 40. MALIGNANT MELANOMA.
Iridectomy specimen grasped in the middle, twisted, and squeezed. 20×

iridectomy. The bleeding points should be closed by cautery or freezing therapy.

Secondary malignant tumors of the iris may have palliative X-ray with or after diagnostic biopsy.

NOTES REGARDING TREATMENT

Good treatment is closely related to accurate diagnosis and classification. Biomicroscopy including gonioscopy is an important diagnostic technique.[7] Glaucoma commonly is a complication of intraocular growths (Figure 39). After establishing a diagnosis the cardinal method of treating iris tumors is local removal. This is best accomplished by a definite preoperative plan of exposure which will permit as easy a direct attack as possible. The plan should vary with the position and extent of involvement. When the iris and its base are free and there is no involvement of the ciliary body the solution of the problem is an adequate iridectomy. When it is established that

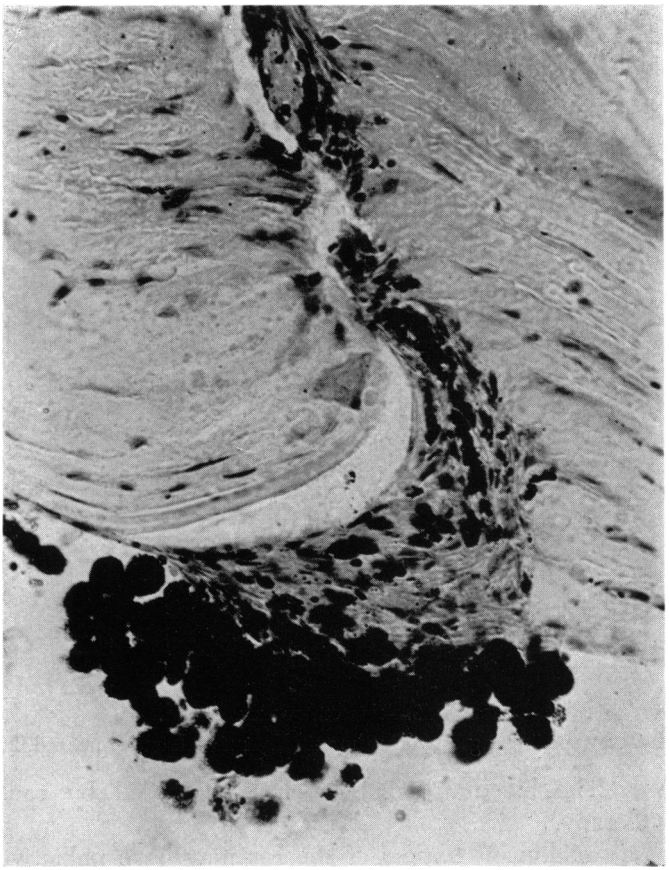

FIGURE 41. SEEDING OF OPERATIVE WOUND BY DRAGGING IRIS ACROSS LIPS OF THE WOUND. 312×

the iris alone is involved, and that the tumor is malignant and expanding, the best approach is a full hemi-section of the cornea at the limbus, under a conjunctival flap, as in cataract surgery, using preplace sutures. Then the corneal flap is held everted over the growth so the surgeon can work freely, directly over the iris. The tumor is not seized but instead adjacent tissue is grasped and held without release or twisting. Traction near the tumor permits it to be lifted out cleanly without contact with other ocular tissue. Transplanting of tumor cells is possible when the iris and tumor are dragged across the lips of the wound. A probable cure is thus converted into a recurrence and has appeared in this collection several times (Figures 40 and 41).

General anesthesia is often advisable, and completely tight closure of the wound desirable.

When careful appraisal has shown involvement of the ciliary body the patient should be advised of the likely need of an enucleation although he may be given a trial of iridectomy and partial cyclectomy. The plan of attack is to make a large conjunctival flap and to place sclerolimbic and also scleral sutures for a scleral flap. Limbic section then is done. The incisions for the scleral flap are made separating the sclera somewhat from the muscle ring; these are made at right angles to the limbus on either side of the suspected zone. This permits hinging the flap at its base away from the limbus and thus allows direct observation. The decision is then made for further dissection or enucleation. When extensive malignant involvement of the iris includes the angle or seems to be extensive in the ciliary body enucleation is the treatment of choice. Sections made on the spot from removed tissue sometimes enable the surgeon to decide his course. Justification for trying to save an eye that harbors a malignant melanoma by extensive intraocular surgery is based upon the low mortality rate and rare metastasis from this neoplasm in the iris. The possibility exists that what is left, after complete removal of the iris tumor and involved parts of the globe, may not be visually effective. The best hope for the patient is early treatment and complete removal of the growth under the most favorable circumstances. Extensive involvement of the ciliary body, the angle with glaucoma, and extraocular extension require enucleation or exenteration.[4,8]

Epithelial downgrowth in the form of sheets or cysts supplies, as we have noted, a very difficult problem for therapy. Combined surgical and chemical therapy with cryotherapy may offer some hope.

Radiation therapy is of palliative benefit to some patients with metastatic tumors. The secondary or associative lymphomas in the iris usually respond locally to low dosage.

Endocrine therapy benefits certain patients afflicted with metastatic growths, especially those arising from the breast. Ordinarily the metastatic ocular tumor is treated by radiation or left undisturbed. If, however, it is accompanied by pain or disfigurement, enucleation may be indicated as palliative treatment.

SUMMARY AND CONCLUSIONS

From microscopic and clinical study of a collection of over 230 iris tumors a working classification has been constructed based upon tissue

of origin and clinical traits. The types and frequency of iris tumors are indicated statistically. Examples of all those catalogued are in this collection.

The proliferations, cysts, and tumors are grouped in five classes as listed below and briefly discussed: benign proliferations and hyperplasias; primary benign iris tumors; secondary benign iris tumors; primary malignant iris tumors; secondary malignant iris tumors. In this series of patients the predominate new growth is the malignant melanoma, with an incidence of 49 per cent, including several types. The lower age limit is about 15 years, although one example occurred at age nine. The upper ages may run over 90. The malignant growth of this neoplasm is frequently accompanied by benign satellite proliferations. Sex distribution is nearly equal.

The slow diffuse growth, known as melanosis oculi, shows some of the properties of neoplasm and may be properly classified as a low order of infiltrative growth. An interesting high incidence (21.6 per cent) of secondary ingrowth, chiefly from corneal epithelium was found.

Hypothetical origins of congenital epithelial inclusion cysts are discussed. The prognosis of primary new growths in the iris compared with similar tumors elsewhere in the eye and body is found to be markedly favorable. Some hypotheses for this difference are discussed.

Methods and techniques of treatment are discussed briefly.

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DISCUSSION

DR. T. E. SANDERS. Considering the relative rarity of iris tumors this report of 232 cases is a large and significant series. From the standpoint of pathology such a series is useful in ascertaining the incidence and nature of these lesions. Of more importance is the clinical information regarding the accurate recognition, clinical course, and proper management of iris neoplasms.

This series of iris tumors is not a continuous clinical series as it is collected not only from the cases of the Massachusetts Eye and Ear Infirmary but also from an unspecified number of specimens referred from outside sources for diagnosis and opinion. These specimens sent for such diagnosis and opinion are normally the more unusual types of tumors and, therefore, there is naturally some distortion as to the actual incidence of the various lesions. The author includes in this series acquired epithelial cysts involving the iris both by implantation and by ingrowth. These lesions, which make up 21 per cent of the series, are not true neoplasms. Also included in this series are extensions into the iris from neoplasms at other sites. These are also not primary iris neoplasms and often the primary site is clinically evident. Proper management is dependent on the primary tumor. This group of secondary tumors includes 70 cases, some 30 per cent of the total series. Some 6 per cent of the series is made up of the rarer tumors, such as leiomyoma, metastatic tumors, vascular tumors, and six other single unusual lesions. In the total series about half are malignant melanomas. However, if we delete the 21 per cent of cysts and the 30 per cent of secondary invasive tumors, the ratio becomes some 113 malignant melanomas to 21 rarer tumors, making the incidence of malignant melanomas over 82 per cent of the total primary group. Thus a malignant melanoma is by far the most important tumor to consider in the recognition and clinical course of these lesions. This is particularly true if we consider that the rarer tumors are usually clinically different than the pigmented malignant melanomas and the clinical diagnosis can be often suspected.

Unfortunately in the past the term malignant melanoma has suggested that these tumors are similar in their nature and clinical course to those malignant melanomas arising elsewhere in the uvea. Recently there has been much evidence that the malignancy of these tumors is quite different from that of tumors in the choroid and ciliary body. In the follow-up of the 110 malignant melanomas in this series only five have proved fatal, giving a mortality of around 4 per cent. This figure is quite comparable to that recently reported by Rones and Zimmerman,[1] and also to that of Reese[2] (p. 315). In a series of over 100 cases, Ashton[3] has noted no metastasis. The reasons for this low mortality are not even yet entirely clear. As Dr. Heath pointed out these tumors are usually discovered early, are readily inspectable, and often receive relatively early surgical treatment. He

suggests that the iris stroma is such that tumors in this site might not metastasize easily and that the blood vessels in the iris are very thick-walled, thus being less susceptible to invasion by the lesion. However, it seems evident that there must be other factors present because in other sites in the uvea rather small tumors can often give rise to early metastasis.

The commonest pigmented lesion of the iris is the ordinary, benign melanoma, or freckle. It is possible that many of the iris malignant melanomas arise from this completely benign source (Reese,[2] p. 300). The cytology of the iris tumors in many cases is quite similar to that of tumors elsewhere in the uvea but the interpretation of this cytology is often difficult. The majority of these iris tumors tend to be chiefly spindle cells of the mature type, both of the spindle A and spindle B variety. There is often an element of true nevus cells in the iris melanoma (Reese,[2] p. 300). Zimmerman[4] suggests that some of the spindle cell iris tumors should be considered to be spindle cell nevi. Although there are often so-called epithelioid cells present in iris tumors, the markedly predominant tumor of epithelial type is uncommon in the iris. Therefore, from a study of their possible source, their cytology, their environment, and their clinical course, it is probable that the iris malignant melanoma, in a very great majority of the cases, represents a different type of tumor from those seen elsewhere in the uvea.

Although these tumors apparently do not tend to metastasize as frequently as do other uveal tumors, with a resultant low mortality, they are definitely invasive and at times will grow rather rapidly. Of great importance in the management of these tumors is the extent of this invasion. In this regard the increased use of gonioscopy has proved invaluable in localization of extension of these tumors peripherally into the iris base and ciliary body. In the management of these tumors it would seem that the invasive element is much more important from the clinical standpoint than is the possibility of metastasis.

In the management of iris tumors there are only three possible clinical courses available: enucleation, iridectomy, and clinical observation. In this series there were single iridectomies in 84 cases and primary enucleation in 96. It is probable in the future, with the better understanding of these lesions, that many more eyes can be salvaged by iridectomy and observation. Recently Reese[2] (p. 315) has shown that in carefully selected cases the prognosis both as to life and retention of the globe is about the same with enucleation, iridectomy, or continued observation.

Choice of the proper method of treatment depends on the character, the size, and the site of the tumor, the rapidity of growth, and the extent of the invasion. As shown by Rones and Zimmerman[1] the diffuse, darkly pigmented tumors causing heterochromia usually with severe glaucoma are very malignant with a high rate of metastasis. It is generally agreed that eyes harboring this type of iris tumor should be enucleated immediately. Enucleation is also indicated in those iris tumors in which the invasion of surrounding

structures, particularly the iris base and face of ciliary body, is such that complete removal of the tumor by iridectomy is impossible. The presence of glaucoma is an indication for enucleation as involvement of the trabeculum must be assumed, indicating that complete removal of the tumor is impossible. In those tumors in which there is apparently rather rapid growth and the iris base is uninvolved, excisional iridectomy is indicated as delay will give rise to invasion that would make complete removal impossible. After iridectomy, if incomplete removal is evident either clinically or by histologic examination, secondary enucleation may be indicated. However, many eyes may be safely retained under observation if the tumor is histologically benign. With tumors near the pupil, particularly those flat, dense, plaque-like tumors in which there is apparently little invasive growth, continued observation is usually the best course. By observing these indications for surgical attack many eyes with iris tumors can be salvaged by iridectomy while many other eyes will be safely retained under observation for long periods of time.

Thus it is obvious that we are greatly indebted to Dr. Heath for presenting this very large series of iris neoplasms. From it we can gain an excellent idea of the broad spectrum of tumors arising in or invading the iris. He also emphasizes the relative high frequency of malignant melanoma, with further evidence that these malignant melanomas of the iris are different from those elsewhere in the uvea and that they have a relatively low rate of metastasis. With this evidence we are able to become much more conservative in the surgical management of these lesions, with the retention of many globes that would have been enucleated in the past because of the fearful diagnosis of malignant melanoma.

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