TUMORS OF THE EYE

ALGERNON B. REESE
M.D., D.Sc. (Hon.), F.A.C.S.

Attending Ophthalmologist and Pathologist, Institute of Ophthalmology, Presbyterian Hospital, New York. Ophthalmologist to Memorial Center for Cancer and Allied Diseases, New York. Clinical Professor of Ophthalmology, College of Physicians and Surgeons, Columbia University

WITH 511 ILLUSTRATIONS,
122 IN FULL COLOR

CASSELL AND COMPANY LIMITED
LONDON, TORONTO, MELBOURNE, SYDNEY AND WELLINGTON

TUMORS OF THE EYE

Printed in the United States of America

Bound in Great Britain by The Leighton-Straker
Bookbinding Co., Ltd.

To J. L. R.

PREFACE

The subject of neoplasms was formerly incorporated in general medicine and surgery, but as our knowledge of tumors has advanced and the tendency to specialization has increased, it has emerged as a full-blown specialty. Progress in our understanding of ocular neoplasms has more or less kept pace with developments in oncology, but unfortunately no comprehensive effort to consolidate it has been made since LaGrange's publication in 1901. The present work was undertaken in an effort to fill this need for a review and evaluation of the advances in our knowledge of this particular subject. This book concerns the clinical and practical aspects of tumors of the eye, and is therefore intended for the practicing ophthalmologist. On the other hand, an effort has been made to make the book sufficiently comprehensive to be of value to the pathologist and to the tumor specialist. It covers all tumors and tumor-like lesions that directly and indirectly affect the eye, and it deals with the various types of lesions which must be considered in the differential diagnosis.

My own interest in neoplasms as a part of the pathology of the eye has been fostered by my 22-year association with Memorial Center for Cancer and Allied Diseases, where I have had the opportunity to study ocular tumors in relation to tumors found elsewhere in the body. The friendly and generous counsel of Dr. Arthur Purdy Stout of the Presbyterian Hospital has also been of inestimable value to me.

This book is not so much an attempt to present an unbiased and comparative account of all that has been written on ocular tumors as it is a monograph based on personal observations and convictions. In the discussion of many phases of the subject, I have found it necessary to supplement my own experience with that of other observers, but the reference material has been selected on the basis of my personal belief in its tenability.

In order to prevent repetition, it was decided that the best manner of presentation would be to discuss the various tumor groups affecting the eye and to point out in what manner each tumor affects various structures of the eye and adnexa. The general plan has been to present each group as extensively as its incidence demanded, and to discuss it in terms of pathology, diagnosis, prognosis, and treatment, with the emphasis always on the practical implications of the facts.

Errors are propagated and perpetuated in books because the authors have accepted without question what has previously been written. This I have tried to

avoid by using my own compilations of figures whenever possible, and by reporting the results of my own experience whenever it has seemed adequate.

Discussions of tumors are often complicated by the confusing terminology used in connection with them. In the interest of keeping the nomenclature simple, accurate, and consistent, I have chosen (often from among many synonyms for the same new-growth) that term which, in my opinion, is the most accurately descriptive of each condition. Although synonyms are given, the use of a single name to designate a tumor type has been adhered to throughout the text.

The illustrations are almost entirely original, and the few reproduced from publications were for the most part taken from material prepared or examined in our laboratory.

Miss Lilly Kneiske, our secretary in the Pathology Laboratory, has been of inestimable value to me in writing this book. Her excellent records and indices have made our material readily available for study, and her unfailing cooperation has helped immeasurably in the completion of the task.

I am grateful to Dr. Frederick Blodi for his valuable assistance in many directions, and particularly for his help in assembling the material on angiomatous tumors. The irradiation factors were furnished through the kindness of Dr. George Merriam. Doctor Osborne Perkins's help with the galleys is gratefully acknowledged.

I am indebted to Mr. Gustav Bethke for his painstaking care with the drawings; to Mr. Nicholas Ross for the preparation of sections; and to Mr. James Lafayette for his invaluable help with the photography.

The entire staff of the Institute of Ophthalmology has been most cooperative and generous. I am very grateful for the illustrations and case reports that have been lent me and have endeavored to accredit them properly.

New York City A.B.R.

TUMORS OF THE EYE

CONTENTS

CHAPTER 1

EPITHELIAL TUMORS OF THE LID, CONJUNCTIVA, AND CORNEA

BASAL CELL AND SQUAMOUS CELL EPITHELIOMA OF THE LID

Epitheliomas of the skin of the eyelids are the same as those occurring over the skin of the face in so far as the histologic characteristics and clinical course are concerned. When these lesions occur on the lids, however, they present a particular problem because their most frequent site is at the lid margin where, if they are excised, adequate plastic repair is required and, if irradiation is employed, certain hazards are encountered because of the proximity of the eye. Also, the possibility of orbital invasion, as well as invasion of the contiguous bone and sinuses, makes epithelioma of the eyelid a potentially destructive lesion locally and one in which the eye may be jeopardized.

In epithelioma of the face the nose is the site most often involved, and the eyelids are the next most frequently affected area. The topographic incidence of epithelioma of the lids given by Martin[12] is as follows:

Lower eyelid	54%
Inner canthus	28%
Upper eyelid	13%
Outer canthus	5%

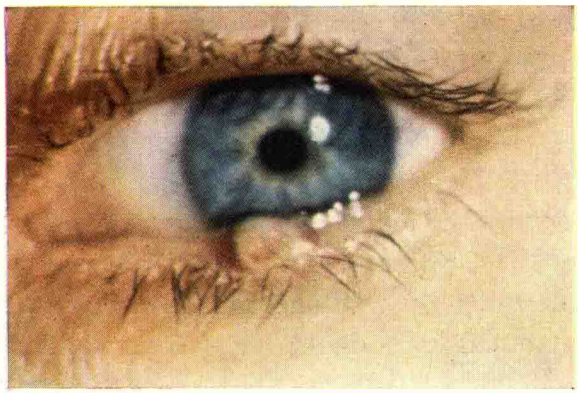
Epitheliomas are divided into two main groups, the basal cell and the squamous cell. There are subtypes which will be discussed in turn. Some of these tumors are entirely basal cell in type and others entirely squamous cell, but all gradations may occur so that some pathologists use the term basosquamous epithelioma when the two elements are mixed. The division, therefore, into the two main groups is somewhat arbitrary but it is definite enough to admit consideration of these tumors as two separate varieties. Certainly the basal cell variety is by far the more common: Martin[12]

quotes it as comprising 85 per cent of all epitheliomas of the eyelids, whereas the squamous cell type constitutes approximately 10 per cent, and the adenoidal basal cell epithelioma 5 per cent.

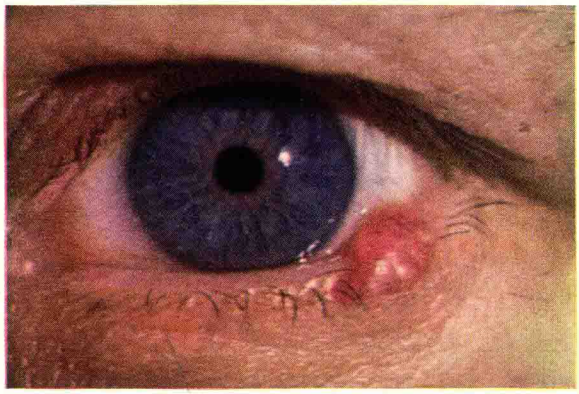
Broders[4] has pioneered in the grading of malignancy* and this has been particularly serviceable in regard to epitheliomas. His grading is briefly as follows: a Grade 1 epithelioma is one in which the differentiation ranges from almost 100 to 75 per cent and dedifferentiation from almost none to 25 per cent, a Grade 2 epithelioma one in which differentiation ranges from 75 to 50 per cent and dedifferentiation from 25 to 50 per cent, a Grade 3 epithelioma one in which differentiation ranges from 50 to 25 per cent and dedifferentiation from 50 to 75 per cent, and a Grade 4 epithelioma one in which differentiation ranges from 25 per cent to practically none and dedifferentiation from 75 to practically 100 per cent.

The average age at which epitheliomas occur is 50 to 55 years, and there is a somewhat higher incidence in men than in women. The lesion usually arises in an otherwise normal skin without any apparent etiologic factor. There is a general tendency for the tumor to occur at sites where the epithelium undergoes a transition and therefore the lid margin, the site of transition from epidermis to conjunctiva, is the place of predilection. Sometimes chronic irritation seems to be a precipitating factor, and when this occurs the lesions are often multiple over the skin of the face. The irritation may manifest itself as a natural aging process of the skin; as the result of long-continued and repeated exposure to the elements, particularly the sun; and in rare instances as the result of inadequately cleansing the skin with soap and water, particularly in those individuals whose faces are habitually soiled with mineral dust, ashes, grease, or oil. Martin[12] believes that precancerous keratosis and sometimes subsequent epithelioma of the skin of the face occur in women who attempt to preserve their complexions by a rigid abstinence from the use of soap and water. Also, the dermatitis consequent to blepharitis, conjunctivitis, or constant tearing may predispose to epithelioma. The senile keratosis from which an epithelioma may develop manifests itself as multiple, localized, slightly elevated areas of a dry, scaly character.

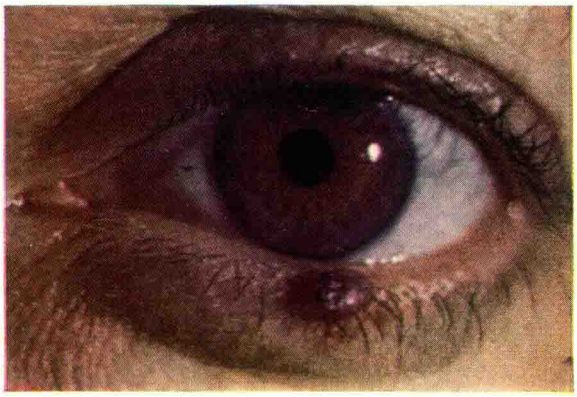
* It is possible to grade to some extent the degree of malignancy of cancer cells depending on their morphologic characteristics. There are many factors which may be taken into consideration in assessing cellular activity or unrest. These include mitosis and amitosis; variation in the size of the cells, and particularly the presence of large, spheroidal, irregular nuclei with or without prominent nucleoli; decrease in the cytoplasm of a cell in relation to the nucleus; hyperchromatosis with a particular avidity of the nuclei for the basic dyes; lack of polarity of the cells; invasive properties of the cells; and sparsity of cellular products laid down by the particular type of cell from which the tumor arises, such as fibers of various types (collagen, reticulin, elastin, myoglia, and the like), keratin, melanin, and similar substances. If the tumor is of a glandular structure, dedifferentiation is indicated by the degree of departure of the tumor cell from the parent cell, which has a spheroidal, oval, or spindle-shaped nucleus small in proportion to the cytoplasm and located at the base of a columnar or a cuboidal cell.



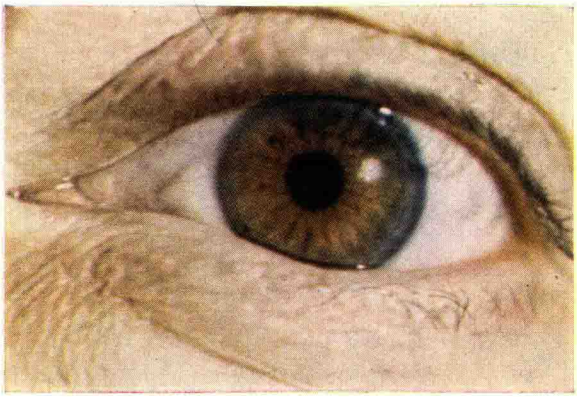
1.



2.



3A.



3B.

FIG. 1. SQUAMOUS CELL EPITHELIOMA OF THE LOWER LID.

FIG. 2. BASAL CELL EPITHELIOMA OF THE LOWER LID.

FIG. 3. PIGMENTED BASAL CELL EPITHELIOMA OF THE LOWER LID.

A, Before excision; *B*, After excision by the lesser resection (see Fig. 9, p. 12).

Clinical Appearance and Course

In their pure form the basal cell and squamous cell epitheliomas have essentially the same clinical appearance except that the squamous cell type shows whitish elements which are due to the production of keratin and which may give various degrees of a strikingly pearly-white translucency to the lesion (Fig. 1). In both types of tumors there appears, either at the lid margin or adja-

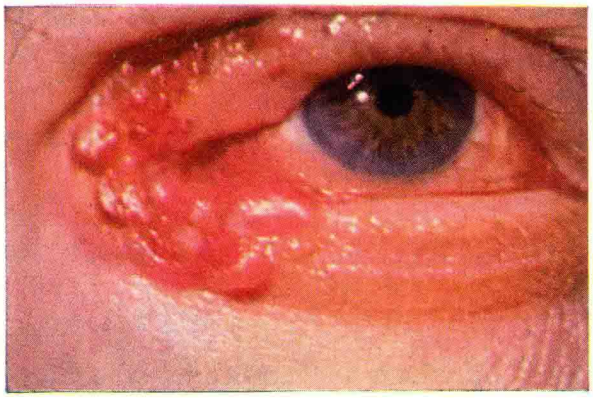


FIG. 4. BASAL CELL EPITHELIOMA OF THE INNER CANTHUS AND ADJACENT UPPER AND LOWER LIDS.

cent to it, an indurated, elevated, sharply demarcated nodule with irregular or undulating surface (Fig. 2). The lesion infiltrates the skin but is freely movable over the underlying tissue unless it is located directly at the lid margin. As the nodule enlarges, the overlying skin seems to become thin, appears more glossy, and develops telangiectases. Examined under high magnification, the lesion sometimes shows small, pearly, translucent foci embedded in it. Ulceration occurs as the lesion enlarges, or the ulceration may be present almost from the onset. Sometimes a papilloma with its somewhat cauliflowerlike surface may develop into an epithelioma. Also, the basal cell epithelioma, particularly in darkly pigmented individuals, may show pigment which in some instances is quite marked and may lead to the clinical diagnosis of nevus or malignant melanoma (Fig. 3).

In the more advanced stages an epithelioma of the eyelid may take one of several courses. It may grow outward as a bulky fungating tumor; it may invade and even erode the entire lid margin without producing any appreciable tumor mass; or it may penetrate the deeper structures of the orbit including the bone. A diffuse growth may cover a very wide area, and the extent of involvement must be appreciated when therapy is considered. Some epitheliomas show an early and marked propensity to invade the orbital structures without manifesting an ulcerative tendency.

The lesion not infrequently involves the inner canthus either primarily or from invasion. When this occurs (Fig. 4), either the punctum or canaliculus may become implicated, and an annoying epiphora results.

Adenoid Epitheliomas

There are various special types of adenomas or basal cell epitheliomas arising from the glandular appendages of the lid. As a group they are sometimes referred to as adenoid basal cell epitheliomas. They are usually localized and noninfiltrating and are composed of well-differentiated tissue resembling the gland from which they arise (adenomas), but they may manifest themselves as more dedifferentiated anaplastic carcinomas, the origin of which can merely be surmised. Among these are epitheliomas arising from the hair follicles, those originating from sweat glands, and those developing from meibomian glands.

Epithelioma Arising from Hair Follicles (Trico-Epithelioma or Adenoid Cystic Epithelioma) (Fig. 5). These tumors of hair-follicle origin are single or multiple, small, firm lesions of a yellowish color occurring in the skin not only of the eyelid but also of the forehead, of the side of the nose, of the cheeks, and less frequently of the neck, scalp, and shoulders. They are often noticed in early life, grow very slowly to the size of a pinhead or to that of a pea, and remain stationary.

The lesion can be viewed as a type of benign basal cell epithelioma. The tumor cells usually show great variation in the degree of differentiation toward hair follicle structure. Many immature follicles with rudimentary hair shafts may be present. There may be some keratinization and, also, cysts filled with keratin.

Keyes and Queen[8] have reported an interesting case of trico-epithelioma involving the lid margin. The tumor consisted of a localized nodule over the surface of which many abnormal, fine, blond hairs protruded. As a matter of fact, the presence of a tuft of abnormally light hairs or cilia which increased in number and length called the patient's attention to the lesion. The patient cut the hairs when they became noticeably longer than the surrounding cilia.

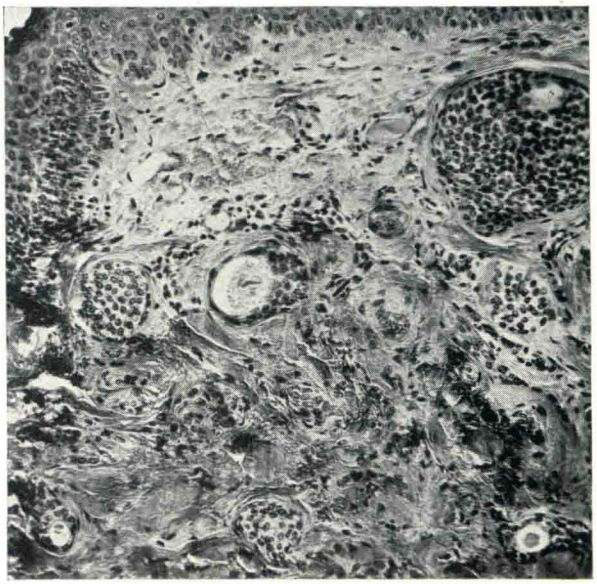


FIG. 5. HAIR-FOLLICLE EPITHELIOMA OF THE LID.

A woman, aged 58, had an elevated, slightly yellowish lesion of the skin of the lower lid measuring 4 mm. It had a smooth surface and resembled a xanthelasma.

The photograph shows the epithelial downgrowths in the nature of rudimentary hair follicles, some of which contain small hair shafts.

EPITHELIOMA ARISING FROM SWEAT GLANDS (SYRINGIOMA) (Fig. 6). These are single or multiple, pinhead- to pea-size, somewhat yellowish or waxy-appearing lesions usually occurring in young individuals. Histologically, the glandular acini resemble sweat glands in structure and have a tendency to form cysts filled with clear material.

EPITHELIOMA ARISING FROM MEIBOMIAN GLANDS (Fig. 7). Since the meibomian glands are viewed as modified sebaceous glands, tumors arising from them really represent a type of sebaceous gland epithelioma. The lesion may occur as a localized benign adenomatous growth, but not infrequently it manifests itself as a rapidly growing carcinoma. Because of its inflammatory nature it may be confused in the beginning with a chalazion or a hordeolum. Some product of the tumor growth seems to lead to inflammation which may mask the neoplastic nature of the lesion. In some instances I believe that the primary lesion is actually a chalazion with or without suppuration. Incision and curettage of the chalazion produce the usual friable granulation tissue with or without pus or liquefied tissue. The area remains somewhat inflamed and does not respond in the usual manner to the treatment.

At a later date at the same site a frank epithelioma develops. It is possible that the chronic inflammation occasioned by the chalazion precipitates the epithelioma. I think, therefore, that any chalazion which does not promptly regress should be observed at intervals for evidence of growth.

Knapp[9] mentions the tendency to confuse a meibomian gland epithelioma with a chalazion and cites such an instance in which the outcome was fatal.

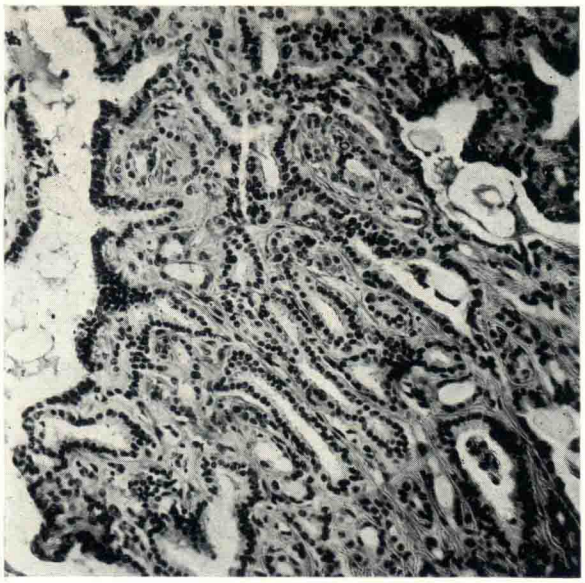


FIG. 6. SWEAT GLAND EPITHELIOMA OF THE LID.

A man, aged 53, had a slowly growing mass 5 × 8 mm. extending around the lid margin and involving the entire thickness of the lid.

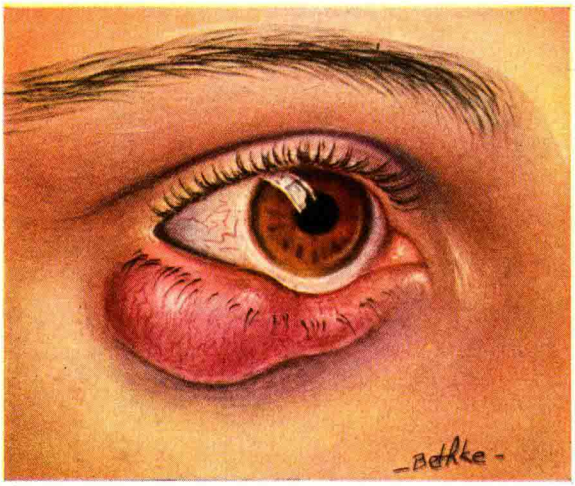
The photograph shows the epithelial structure resembling a sweat gland.

Differential Diagnosis

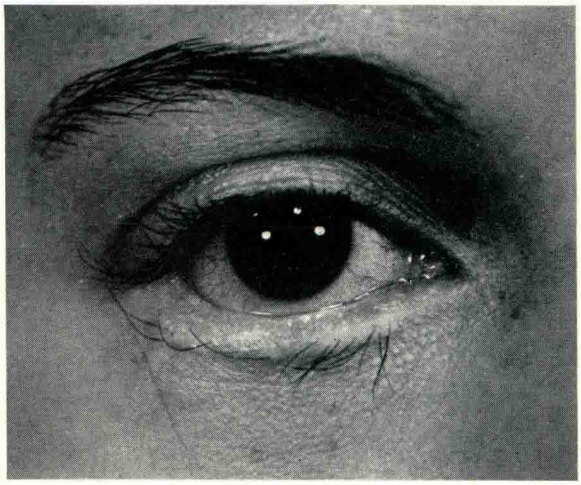
An epithelioma of the lid may be confused with a nonpigmented or pigmented nevus. This error is due particularly to the fact that some nevi have a papillomatous structure owing to the participation of the overlying epithelium in the form of extensive downgrowths. A basal cell epithelioma in a dark-skinned individual may be quite heavily pigmented and look like a nevus or a melanoma. Also a papilloma, when the cauliflower-like arrangement of the growth is not marked, may resemble an epithelioma or, as previously mentioned, a papilloma may undergo transition to an epithelioma. The umbilicated surface of a molluscum contagiosum may lead to its confusion with an epithelioma.

A sebaceous cyst, a sudoriferous cyst, a traumatic inclusion cyst, or a chalazion must be considered sometimes in the differential diagnosis, and, as discussed elsewhere, a chalazion or a hordeolum may provoke an epitheliomatous growth.

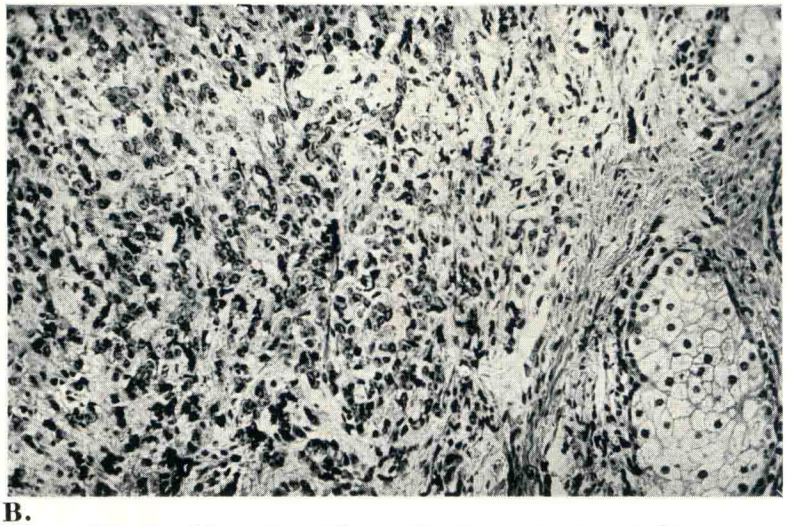
It must be remembered that the caruncle may be the seat of any tumor that occurs in the conjunctiva as well as any tumor that appears in and adjacent to the skin of the eyelid because, although its surface epithelium is a mucous membrane, it harbors all of the skin elements including hair follicles, sebaceous glands, and sweat glands. Therefore, at the caruncle, in contrast to the conjunctiva elsewhere, there may be a sebaceous or sweat gland cyst, or a sebaceous, sweat gland, and hair-follicle epithelioma.



A.



C.



B.

FIG. 7. MEIBOMIAN GLAND EPITHELIOMA OF THE LID.

A girl, aged 20, had a tumor of the lower lid which had been slowly growing for four years. *A,* Clinical appearance showing an inflammatory element and resembling somewhat a diffuse chalazion. *B,* Microscopic appearance. Some of the meibomian gland is seen at the right. *C,* The appearance of the eye after a Hughes operation and cilia graft.

Patient of Doctors J. H. Dunnington and Wendell Hughes.

Procaine hydrochloride (novocain) may lead to a localized subcutaneous nodule over the site of injection. Histologically these lesions show a granulomatous reaction with giant cells and are due either to sensitization or to an old decomposed, or possibly contaminated, solution. The lesion, conveniently referred to as a novocainoma,[15a] occurs gradually over a period of weeks following the injection and represents clinically a rather poorly demarcated indurated mass in the lid.

Prognosis

An untreated basal cell carcinoma of the eyelid tends to run a long chronic course with survival of the patient for, perhaps, ten to twenty years or more before the development of fatal complications such as deep invasion of the orbit, erosion of the bone, and intracranial extension. Squamous cell carcinoma of the eyelid usually runs a shorter course, and the disease, if not controlled, may terminate fatally owing to metastases. Epitheliomas of the lid may extend to the regional lymph nodes, the commonest site being that of the preauricular station, and the next in frequency being the upper and lower deep cervical nodes.

Epithelioma of the eyelid is seldom a fatal disease, because even the neglected lesions and those inadequately treated in the early stages can be controlled ultimately by therapy, which, however, in the advanced states is sometimes necessarily radical and therefore disfiguring. In the unneglected cases diagnosed early in which the indicated treatment is correctly given the lesion is very tractable, and a complete cure with a most satisfactory cosmetic result is to be expected.

The records of the Memorial Center for Cancer and Allied Diseases quoted by Martin[12] showed a mortality due to lid epithelioma of less than 6 per cent with the fatalities occurring mostly from metastases of squamous cell epithelioma and less frequently from complications of basal cell epithelioma.

Treatment

If merely curing the disease and the saving of life represented the entire problem it would be a simple one. However, in addition to these objectives the treatment must be given with due regard to the function of the eye and the cosmetic appearance. Therefore, selection of the proper method of treatment is very important.

There is no doubt that epithelioma can be cured by irradiation and probably a cure would be invariably secured provided an adequate amount were administered. Usually the problem is to give an amount sufficient to arrest the growth and at the same time produce a minimum of sequelae. Under the best of circumstances there are always sequelae of some degree. Following the treatment of epithelioma of the lid by irradiation the rule is that a localized loss of cilia and a break of some degree in the continuity of the lid margin are apparent. The latter usually represents a localized absorption of the elastic tissue which causes only a very slight marginal depression, but in some instances there may be an actual notch in the margin of the lid. Furthermore, there is atrophy of the adjacent skin with some bleaching of the pigment and usually telangiectasis. One of the most annoying complications, however, is a keratinization of the adjacent palpebral conjunctiva occasioning the constant desquamation of