HISTOLOGY AND HISTOPATHOLOGY OF THE EYE AND ITS ADNEXA

By

I. G. SOMMERS, M.D.

Assistant Professor (Ophthalmology), College of Medical Evangelists; Medical Officer (E.E.N.T.), U.S. Public Health Service, Los Angeles, California

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PREFACE

For many years it has been my opportunity to examine eyes, first clinically, and, if enucleation became necessary, also pathologically in various clinics and laboratories. Both European and American hospitals have made available to me for study a vast amount of eye section material. During this time, too, I have instructed a number of physicians specializing in ophthalmology or doing postgraduate work toward specialization in histology and histopathology of the eye, and for some years I taught histology and histopathology in general to undergraduate medical students.

This book is an elaboration of the instruction courses I gave, and has grown out of the desire expressed by my students to have the lectures in more permanent form.

The material presented here is divided into three parts. As introduction, the normal histology of the eye is outlined. Next follows a section on general pathology, the emphasis being placed on its application to pathology of the eye, with a brief report on the bacteriology and parasitology of the eye included. The main body of the book deals with the histopathology of the eye, and in this third and very important part it has been my attempt to describe the findings which lead to the pathologic diagnosis of the sectioned eye.

For a subject so complex, clarity of presentation must be a prime consideration. The text, then, has been arranged as continuous and simple description, omitting as much as possible cross references to other chapters or to previously noted data. Rather, when necessary, I have repeated such facts in brief form, this repetition, it is hoped, enabling the inexperienced student to grasp the material more easily and fix it more firmly in his mind. The book may serve not only the beginner but, indeed, the practicing ophthalmologist as well; it may also help the student who wishes to compare his findings in a section of an eye with an authoritative text. Finally, I hope, too,

that the book in this form will offer a valuable guide to the hospital and laboratory pathologist who is not already trained in the specialty of eye pathology.

As a further aid to clarity of presentation, rather than interrupt the main current of discussion with constant references to the names of the many hundreds of authors who have contributed to our knowledge and whose opinions are so often contradictory, I have omitted these from the text and reserved special sections for the literature. Following each of the first two parts and each chapter of the third part, the reader will find a separate discussion of published works arranged in the same sequence as the chapter is subdivided in the text. This rather complete outline of the current world literature on the pertinent subjects covers the years 1920 to 1947, and is followed in each instance by a detailed bibliography of the material discussed. These annexes may be of value to those scientific workers who possibly may not be able to orient themselves quickly in the extensive material already published.

The literature of the years previous to 1920 may be found in quite complete form in the volumes on the eye in Henke and Lubarsch's comprehensive work listed below. The following list of handbooks, textbooks and monographs contains material of importance for more than one chapter of the present book.

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I am indebted and very grateful to Dr. Edgar O. Breakstone of Chicago, Illinois, and Dr. Victor Marshall of Los Angeles, California, who have studied with the greatest care the text of the manuscript, corrected it thoroughly and improved it by their valuable advice. They helped also in reading the proofs to make the book as free of errors as possible.

I should like to express my thanks, too, to my publisher, Mr. Henry M. Stratton, who has shown the greatest interest in the progress of this extensive work, and who has done all possible to give the book its attractive form.

Finally, I would not have been able to begin this great task, continue and carry it to completion if my good wife Vita had not helped and advised me continuously during the many hours I spent with the work. I want to express my deep gratitude to her.

I. G. SOMMERS, M.D.

Los Angeles, California
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Chapter I

NORMAL HISTOLOGY OF THE EYE

The eye has three tunics: (1) An external tunic consisting of cornea and sclera; this is the fibrous tunic. (2) A middle tunic consisting of the uvea; this is the vascular tunic. (3) An inner tunic consisting of the retina and the optic nerve; this is the nervous tunic.

1. The Cornea

The cornea consists of five layers, from without inward: (1) the epithelium, (2) Bowman's membrane, (3) substantia propria, (4) Descemet's membrane, and (5) endothelium.

The epithelium is a stratified squamous cell epithelium and is very regular. The basal layer consists of cylindrical cells with oval nuclei, covered by two layers of prickle cells, on top of which are two layers of flat cells. The epithelial cells are connected with one another by tonofibrils. A few migratory cells are found in the epithelium.

Bowman's membrane is a homogeneous lamella with a smooth anterior surface. Fibers extend from its posterior surface to the corneal lamella. Bowman's membrane is therefore easily separated from the epithelium, but only with difficulty from the propria. The membrane contains many pores for the passage of corneal nerves which end in the epithelium. It ends abruptly at the limbus. The membrane does not regenerate when injured.

The substantia propria is composed of lamellae which are very regular and arranged parallel to the surface. The lamellae consist of collagenous fibers connected by cement. Fine spaces between the lamellae serve as lymph spaces. They contain flat fixed cells (corneal corpuscles), which form a syncytium, and a few compressed migratory cells. The substantia propria constitutes about 90 per cent of the thickness of the cornea.

Descemet's membrane is a thin, homogeneous elastic membrane. When injured, it curls up and readily regenerates.

The endothelium is attached to Descemet's membrane, consisting of a single layer of flat epithelium-like cells lining the anterior chamber. Their oval nuclei bulge the cells somewhat toward the anterior chamber.

2. The Sclera

The sclera consists of the episclera, the substantia propria, and the lamina fusca.

The episclera is composed of loose connective tissue mixed with elastic fibers surrounding many blood vessels. Its deeper

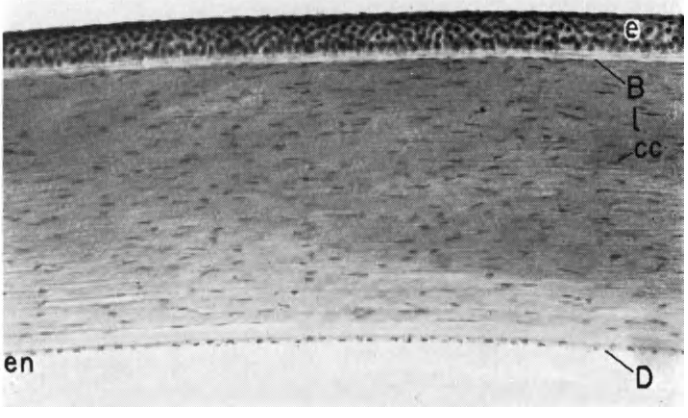

Fig. 1.—Cornea. B, Bowman's membrane; cc, corneal corpuscles; D, Descemet's membrane; e, epithelium; en, endothelium; l, lamellae. 105×.

layers contain heavier connective tissue bundles which fuse into the propria.

The substantia propria has coarse connective tissue bundles which show lamellar structure. The lamellae are composed of fibers. Near the limbus, the bundles are arranged for the most part in circular fashion; otherwise they lie meridionally, interwoven with bundles which run in an equatorial direction. A few flat fix cells lie between the bundles. The sclera has only a few of its own blood vessels and nerves but is penetrated by many channels for arteries, veins, and nerves near the limbus, on the equator, and around the optic nerve. The channels penetrate obliquely and are lined by tissue of the suprachoroid. The anterior ciliary

veins leave the eye, carrying the fluid from Schlemm's canal, and the anterior ciliary arteries enter the eye and proceed to the large iris circle. At the equator, the vortex veins leave the eye, carrying the blood from the uvea. The short and long posterior ciliary arteries enter posteriorly, carrying blood to the uvea. Only a few small branches of the short posterior ciliary arteries enter the sclera, but a few branches go off which anastomose with one another and form a ring around the optic nerve.

The lamina fusca is the innermost layer of the sclera next to the choroid. Its bundles are smaller than those of the propria, and contain more elastic fibers and chromatophores.

The sclera is connected with the cornea at the limbus; it has posteriorly a large canal through which the optic nerve leaves the eye.

3. The Limbus

At the limbus cornea, conjunctiva, episclera, and sclera meet. The anterior layers of the limbus consist of epithelium and loose connective tissue with blood vessels and nerves.

The epithelium is a stratified squamous cell epithelium of the type of the conjunctival epithelium; it shows flat papillae and is higher and more irregular than the corneal epithelium. The basement cells are narrower and more closely packed, while the prickle cells and the flat cells are more numerous than in the corneal epithelium.

The loose connective tissue of the limbus flows together from the mucosa of the conjunctiva, Tenon's capsule, and episclera. The tissue converges at the end of Bowman's membrane. The blood vessels have thin walls and are surrounded by lymph spaces. Branches of the ciliary nerves enter the sclera from the suprachoroid and reach the cornea from the limbus. After losing their medullary sheaths, they enter into the anterior cornea and go vertically up to Bowman's membrane, which they pass to enter the epithelium. Nerves of the conjunctiva and episclera form a pericorneal plexus which anastomoses with the corneal nerves.

The irregularly arranged lamellae of the sclera continue at the limbus into the regularly arranged lamellae of the cornea.

4. The Uvea

The uvea is the pigmented vascular tunic of the eye, composed of the iris, the ciliary body, and the choroid.

In the iris, several layers can be distinguished histologically. They are, anterio-posteriorly: (1) endothelium, (2) anterior border layer, (3) stroma with blood vessels and sphincter muscle, (4) dilator muscle, and (5) pigment epithelium.

Some assert and some deny that the iris has an endothelium. On the anterior surface of the iris may be found flat cells with oval nuclei which project over the surface. These cells are considered by some as a continuation of the corneal endothelium.

The anterior border layer consists of several layers of cells lying very close to each other with only a little collagenous fibrous tissue between. Their nuclei are oval and are arranged parallel to the surface. These cells are considered as densely arranged chromatophores which are loaded with pigment granules in brown eyes, but have no pigment in blue eyes. The endothelium and anterior border layer are missing in the iris crypts, and are more developed in the ciliary zone of the iris than in the pupillary zone. In the depth of the crypt, the iris stroma is open to the aqueous humor of the anterior chamber.

The stroma consists of a meshwork of fine collagenous fibers mixed with a few elastic fibers and has large spaces filled with fluid. The stroma cells are represented by nonpigmented cells with fusiform nuclei, fine processes, and starlike chromatophores containing pigment granules. The chromatophores appear as spider-shaped formations in sections parallel to the surface of the membrane. The processes are few; they are connected with processes of adjacent chromatophores to form a syncytium. The cell body around the oval nucleus is also oval. The pigment (melanin) appears as fine granules and is dark brown to black in color. The normal stroma has few migratory cells, occasional plasma cells with acidophil granules, and so-called clump cells found mostly around the sphincter. They are round, heavily pigmented cells without processes and are apparently pushed out of the pigment epithelium into the stroma. The stroma contains a plexus of nerves and ganglion cells.

The blood vessels of the stroma originate in the greater circle of the iris. Arteries branch off, course radially between the

crypts of the iris root, and anastomose in the region of the collaret with vessels forming the inner circle. The collaret is formed by a large iris crypt corresponding with the ciliary margin of the sphincter. The adventitia of the arteries appears as a homogenous thick ring, and the media is reduced to a few cells surrounding a single layer of endothelial cells. The veins have a perivascular sheath.

The sphincter muscle surrounds the pupil like a ring and consists of parallel circularly arranged bundles of typical plain muscle fibers. The pupillary margin of the muscle is close to the pupil and touches the pigment epithelium. The sphincter muscle is considered by some as ectodermal, originating from the anterior margin of the eye cup, by others as mesodermal.

The dilator muscle appears histologically as a more or less broken band in front of the pigment epithelium. But one can see in bleached eyes and eyes of albinos that the dilator is in reality a part of the epithelial cells. The epithelium cell itself is pigmented and is oval with an oval nucleus. It has a non-pigmented long process which is contractile. These processes are arranged in a tile-shaped pattern to form the band of the muscle. The dilator extends into the ciliary margin of the sphincter and is thicker at the root of the iris-forming processes which extend to the ciliary muscle and the trabeculae and which lend a tendon-like grip to the muscle.

The pigment epithelium consists of two layers of densely pigmented epithelial cells. The anterior layer has smaller cells which aid in making up the dilator. The posterior layer has high and wide cells with round nuclei. The epithelium shows several spurlike protrusions toward the stroma, especially distinct in the region where the pigment epithelium of the iris turns at a right angle to the anterior surface of the most anterior of the large ciliary processes. Other spurs can be seen in the region of the sphincter. The pigment epithelium extends beyond the sphincter and the stroma into the pupil (physiologic ectropion). Sometimes a fine, homogeneous membrane can be made out on the inner surface of the pigment epithelium which is considered to be an inner limiting membrane.

The iris is seen to have its greatest width in the area of the sphincter and is usually equally wide throughout the

ciliary zone, but it thins out suddenly in the root in the chamber angle where it has several crypts. The root of the iris frequently has only little stroma in front of the dilator and pigment epithelium. The stroma of the iris continues in the loose tissue of the ciliary body, which is situated anterior to the ciliary muscle in various thicknesses, and also in the adjacent part of the anterior ciliary process, which is the largest and branches off from the iris root and has on its anterior surface both

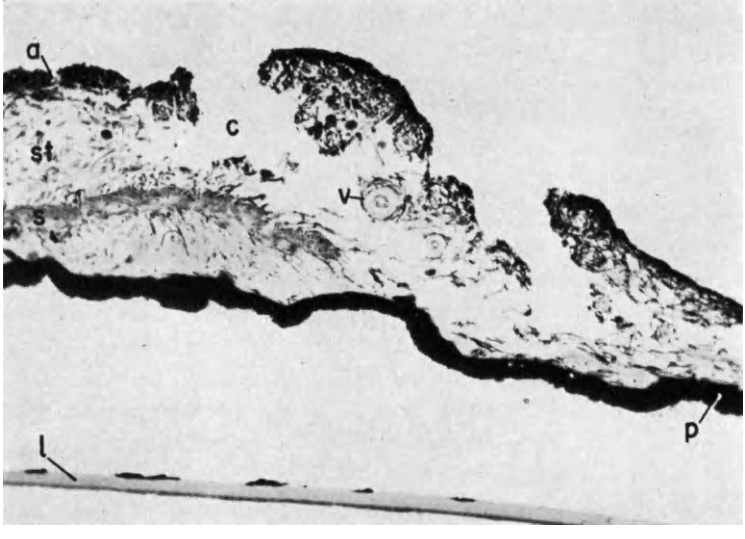

FIG. 2.—IRIS WITH CRYPTS. a, anterior border layer; c, crypt; l, lens capsule; p, pigmentary epithelium; s, sphincter muscle; st, stroma; v, vessel. 65×.

epithelial layers pigmented the same as the iris. On the crest of this process, the inner layer is nonpigmented.

The ciliary body consists of two parts: one adjacent to the iris with radially arranged projecting processes, the so-called corona ciliaris or pars plicata; the second adjacent to the retina, the so-called orbiculus ciliaris or pars plana. Both consist of a uveal and retinal portion. The uveal portion has four layers: (1) the suprachoroid, (2) the ciliary muscle, (3) the vessel layer, and (4) Bruch's membrane. The retinal portion is the

anterior continuation of the retina proper and has three layers: (1) the pigment epithelium, (2) the ciliary epithelium, and (3) the inner limiting membrane.

The suprachoroid consists of elastic lamellae which are less numerous anteriorly, submerge into the ciliary muscle, and disappear entirely near the scleral spur.

The ciliary muscle is most voluminous anteriorly, thins out posteriorly, and extends into the choroid. It consists of three

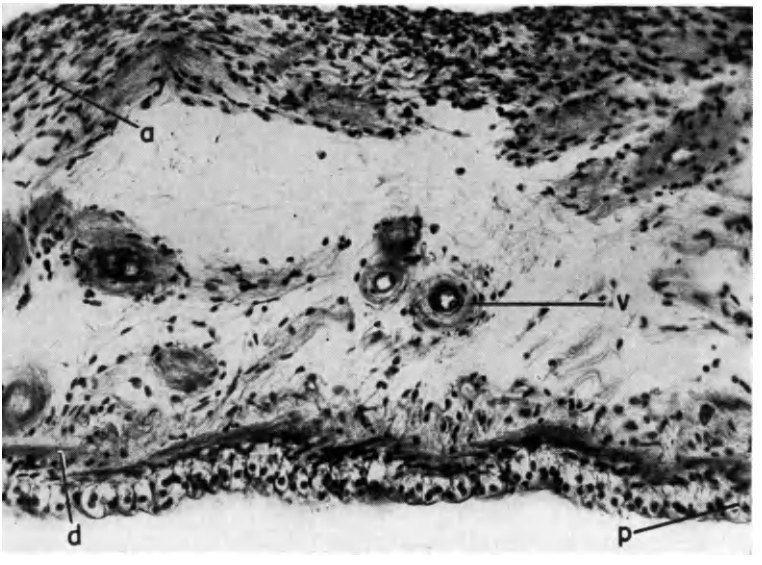

FIG. 3.—IRIS OF ALBINO. a, anterior border layer; d, dilator muscle; p, pigmentary epithelium; v, vessels. 115×.

sections: (1) fibers which extend along the sclera in a meridional direction, the so-called meridional fibers; (2) fibers which lie further in and extend from the scleral spur fanlike toward the pars plana and the ciliary processes, the so-called radial fibers; (3) a group of bundles arranged like a ring in the anterior part of the ciliary body, the so-called circular fibers.

The meridional fibers are bundles of plain muscle cells arranged in rows one behind the other. There is only little connective tissue and fine lamellae of the suprachoroid between

the bundles. The fibers insert on the scleral spur on some connective tissue and elastic fibers there as on a tendon. This tissue embraces the circularly arranged coarse connective tissue bundles of the scleral spur. The muscle fibers increase in number posteriorly in the area of the ciliated part of the ciliary body and decrease again in the area of the pars plana and toward the choroid. Further posteriorly, they connect with the elastic lamellae of the suprachoroid.

The radial fibers extend from the scleral spur toward the vessel layer of the ciliary body and the epithelium of the pars plana. Trabeculae of the chamber angle can be followed to the radial fibers. Connective tissue in varying amounts lies between the muscle bundles, frequently containing chromatophores.

The circular fibers consist of muscle bundles of varying number and width situated near the anterior free margin of the ciliary body in loose connective tissue. A relatively large artery lies close to this bundle which also runs circularly, the so-called circulus arteriosus iridis major. Large anterior ciliary arteries pass at regular intervals through the sclera and through the ciliary muscle to the first-mentioned artery.

The vessel layer is made up of veins. It extends through the entire ciliary body between the muscle and the epithelium and continues into the choroid. The ciliary processes contain arteries which originate in the larger circle and give off capillaries. They continue into the veins which run through the vessel layer, finally carrying the blood to the vortex veins. There is loose connective tissue with many cells in the ciliary processes and in the vessel layer which might also contain chromatophores.

Bruch's membrane has three layers in the ciliary body: (1) an elastic lamina, (2) an intermediate connective tissue layer consisting of fine collagenous fibers and a few cell nuclei, and (3) a cuticular layer which forms branched ridges in the pars plana, the so-called reticulum of Mueller.

The retina continues into the ciliary body in two layers: (1) The outer layer is formed by the pigment epithelium, the cells of which are cylindrical and densely filled with pigment granules which they lose on the crest of the ciliary processes. (2) The inner layer consists of a row of cylindrical cells which

are higher in the pars plana than in the pars plicata and which increase in height toward the ora serrata. Both layers are joined rather tightly by cement. The inner limiting membrane is homogeneous, without structure and not distinct throughout.

The choroid has four layers: (1) the suprachoroid, (2) the vascular layer, (3) choriocapillaris, and (4) lamina elastica (Bruch's membrane).

The suprachoroid consists of thin lamellae supported by a network of elastic fibers. The lamellae are covered with flat endothelial cells and are nearly parallel to the sclera, lying about six to eight deep. There is a potential space between the lamellae, which may be filled with fluid and cells. Normally, there are few migratory cells here. Starlike chromatophores, forming a syncytium, lie on the lamellae beside the endothelial cells; they are heavily pigmented with melanin granules. The shape and number of their processes vary somewhat and they are generally larger than those of the iris. Plain muscle fibers, arranged singly and in groups, hang on to the lamellae, beginning on the equator and becoming more and more numerous toward the anterior. The long posterior ciliary nerves and arteries are situated in the suprachoroid in the horizontal meridian. The nerves give off fine branches which are associated with large multipolar ganglion cells and which probably innervate the contractile chromatophores also. Suprachoroidal tissue accompanies vessels and nerves through the scleral channels.

The vascular layer takes up the largest part of the width of the choroid. It is composed, for the most part, of veins which cross each other and have perivascular spaces. The larger vessels lie in the external layers of the choroid; the smaller ones in the inner layers. The arteries occupy most of the external layers between the veins. The veins flow together to form four large vortex veins, two superiorly and two inferiorly, which lead through scleral canals out of the eye. The vessels of the choroid are separated from each other by a stroma which consists of collagenous fibers, connective tissue cells, chromatophores, a few migratory cells, a few nerve fibers, and ganglion cells.

The choriocapillaris is a network of large capillaries which come from the arteries of the choroid and continue into the

veins of the choroid. The largest and the greatest number of capillaries are at the fovea centralis. The nuclei of the endothelial cells are on the side of the capillaries opposite the pigment epithelium. The capillaries are surrounded by fine collagenous and elastic fibers. They nourish the external retinal layers.

Bruch's membrane consists of an outer elastic layer, thin and highly refractile, and an inner cuticular layer which is a homogeneous product of the pigment epithelium cell.

FIG. 4.—CHOROID, VORTEX VEIN. c, canal in sclera; cc, choriocapillaris; cv, choroidal veins; p, pigmentary epithelium; s, sclera; sc, suprachoroid; v, vortex vein. 65×.

5. THE CHAMBER ANGLE

The chamber angle is enclosed by the cornea, the meshwork of the trabeculae, the ciliary body and the iris. It contains the canal of Schlemm, an important structure, which serves for the outflow of the aqueous humor. Therefore, the chamber angle is also called the filtration angle. Descemet's membrane tapers out and ends together with the endothelium. In this region, there is, between the lamellae of the cornea and Descemet's membrane, a circularly arranged bundle of connective tissue and elastic fibers with a number of cells, the so-called anterior border ring. The corneo-scleral trabeculae insert here (scleral meshwork). These should be considered as plates and bands which increase in number antero-posteriorly. This meshwork appears triangular in cross section.

The trabeculae consist of (1) a basis made up of collagenous fibers representing a lamella, (2) elastic fibers surrounding the basis, (3) a homogeneous layer which goes all around the lamella and represents a continuation of Descemet's membrane, and (4) endothelial cells which surround the homogeneous layer completely and are continued from the endothelium of the cornea. The elements of the cornea thus continue into the trabeculae which represent a miniature cornea. The plates and bands of the trabeculae intercross and anastomose, forming a spatial network with anastomosing spaces, the so-called intertrabecular spaces.

A much finer and looser network of trabeculae lies on the inner side of the corneo-scleral trabeculae, the so-called uveocorneal trabeculae (ligamentum pectinatum). These extend in an arc from the iris root across the anterior surface of the ciliary body along the corneo-scleral trabeculae. On cross section, the uveocorneal trabeculae appear spherical and contain the same parts as the corneo-scleral trabeculae except for the elastic fibers. This network represents the rudiment of the spongelike ligamentum pectinatum which fills out the chamber angle in many animal eyes and in the eye of the human embryo, and has spaces which are called the spaces of Fontana. Occasionally, iris processes extend directly from the iris surface across the chamber to the trabecular network.

The corneo-scleral trabeculae continue, in their outer portion, directly into the scleral spur, the lamellae of which are, like the trabeculae, arranged circularly. It appears as though the trabeculae become larger and rounded, lose the homogeneous layer and endothelium, and move closer together. The inner portion of the trabeculae continues into the stroma of the ciliary body and on toward the radial fibers of the ciliary muscle.

The stroma of the anterior part of the ciliary body, anterior to the ciliary muscle, consists of loose connective tissue with relatively more cells and contains many tissue spaces which apparently are open toward the anterior chamber. The stroma continues directly into the anterior ciliary processes which shows nearer the crest denser connective tissue with fewer cells.

The iris root, from which the anterior ciliary processes continue, is very thin; from here, the iris becomes abruptly

much thicker (toward the pupil) and lies nearer to the posterior surface of the cornea. The pupillary part of the iris comes closer and closer to the posterior surface of the cornea, as the iris rests on the interior surface of the lens which increases in diameter toward the pupil. These circumstances and the arrangement of the trabeculae explain the fact that the iris root lies in a recess of the chamber angle which is directed posteriorly.

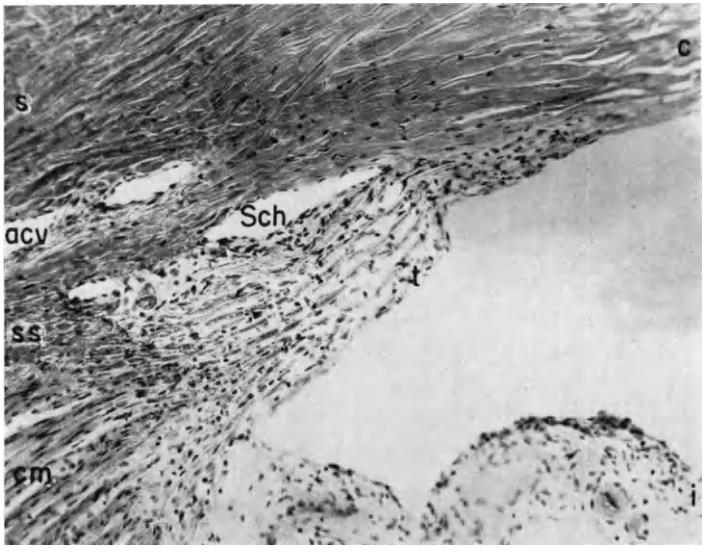

FIG. 5.—CHAMBER ANGLE. acv, anterior ciliary veins; c, cornea; cm, ciliary muscle; i, iris; s, sclera; Sch, Schlemm's canal; ss, scleral spur; t, trabeculae. 105×.

The trabecular network of the chamber angle, the scleral spur, and the corneo-scleral junction surround the canal of Schlemm. This canal is lined with a single layer of endothelium and is connected with the sclera anteriorly and the spur posteriorly by a thin layer of fine connective tissue. The endothelium lies inward directly on the trabeculae. The intertrabecular spaces are separated from the lumen by the endothelium and fluid has to filter through the thin membrane of the endothelium. The canal represents an irregular lumen with many branches

and is often divided by tissue islands into several lumina. Small vessels leave the canal at intervals. These vessels, which are provided with a kind of valve, empty into a plexus in the sclera, from which the anterior ciliary veins stem. The discussion as to whether the canal of Schlemm, during life, contains blood or only the lymphlike aqueous humor, presents considerable evidence for the latter view.

6. The Retina

For the study of the finer anatomy of the retina, well-preserved tissue and special methods of staining and examination are necessary. Through these methods, the interrelation of the various cell structures were discovered.

Histologically, the retina shows ten layers. They are, from the inside out: (1) the internal limiting membrane which separates the retina from the vitreous body, (2) the nerve fiber layer, (3) the ganglion cells layer, (4) the inner plexiform layer, (5) the inner nuclear layer, (6) the outer plexiform layer, (7) the outer nuclear layer, (8) the external limiting membrane, (9) the layer of rods and cones, and (10) the pigment epithelium.

The inner limiting membrane appears as a highly refractile line. It is common to the vitreous and retina and therefore represents also the hyaloid membrane. Normally, it cannot be divided into separate membranes, one for the vitreous body and the other for the retina. If two lines appear on section, this is considered an artifact caused by folding of the tissue. The membrane can be followed up to the ora serrata and into the disc to the physiologic cupping. The footplates of Mueller's fibers are connected with the membrane. It is said that they form the membrane, but in sections they also can be seen separated from the membrane, and the membrane itself continues unaltered onto the vitreous body.

The nerve fiber layer contains the nonmedullated nerve fibers of the optic nerve. They run centripetally, mostly in radial arrangement, to the papilla and on to the brain along the path of the optic nerve. A small number of thin centrifugal fibers are intermixed, which end in the amacrine cells in the inner

nuclear layer. The nerve fiber layer is composed of fine parallel fibers and contains glial cells. It increases in width from the periphery of the retina toward the papilla.

The ganglion cells are multipolar cells of various sizes. Their axon cylinders form the nerve fiber layer. They have a large nucleus with a distinct nucleolus and contain Nissl's bodies in their cytoplasm. Their dendrites branch out in the plexiform layer. The ganglion cells are surrounded by glial cells (spider cells) and in the peripheral retina are situated further apart from each other than in the central retina. Approaching the pole of the globe, they increase in number, lie closer together, and are smaller in size. The fibrils of the glial cells form a membrane-like layer in which the ganglion cells are embedded. The cells and the nerve fibers form the inner neuron of the retina.

The inner plexiform layer is the synapse between the ganglion cells and bipolar cells. This layer appears histologically as a fine meshwork with a grouping of layers by way of fiber systems parallel to the surface. The dendrites of the ganglion cells end either diffusely throughout the plexiform layer or in one or another of the sublayers. Here they connect with dendrites and axon cylinders of cells of the inner nuclear layer.

The inner nuclear layer consists of nuclei of various forms and sizes. They are mostly round, but a few are oval in shape. They contain considerable chromatin and a distinct nucleolus. The cells themselves have little cytoplasm. The innermost part of the inner nuclear layer contains so-called amacrine cells. Most of the cells of the layer are bipolar and between them are the cell bodies of Mueller's fibers. The external part of the layer is characterized by horizontal cells.

The bipolar cells constitute the middle neuron of the retina. They are connected with the ganglion cells in the inner plexiform layer and with the rod and cone cells in the outer plexiform layer. The amacrine cells, like the horizontal cells, are association cells, connecting various parts of the retina. The function of the neuron generally is to connect peripheral parts with the central nervous system, in this case, the retina with the brain. The dendrites and nerve fibers of the amacrine cells extend

into the inner plexiform layer and are joined here with the ganglion cells. The dendrites of the horizontal cells join the terminal plates of the rod or cone cells in the outer plexiform layer, and their axon cylinder extends in the outer plexiform layer to a distant rod or cone cell. The amacrine cells not only connect ganglion cells with each other, and bipolar cells with distant ganglion cells; in addition they also probably receive stimuli through centrifugal nerve fibers. The horizontal cells connect distant rod and cone cells with each other. Mueller's fibers, which have their nuclei in the inner nuclear layer between the bipolar cells, extend through nearly all the layers of the retina from the inner to the outer limiting membrane. Their nuclei are surrounded by much cytoplasm, which appears granulated. The rest of the cells appear as a fiber, standing perpendicular to the inner and outer limiting membrane and in contact with the membranes which it helps to support. The fibers are V-shaped at the inner limiting membrane, forming arcades. They extend through the outer limiting membrane in the form of brushlike fibrils along the rods. The fibers give off wing-shaped plates in the nuclear layer and fibrils in the plexiform layer.

The outer plexiform layer contains the synapse of the rod and cone cells with the bipolar cells. The outer, wider layer shows parallel fibers; the inner, smaller layer contains an irregular network of fibers. The parallel fibers are the rod and cone fibers. The rest is a meshwork consisting of axon cylinders and dendrites of bipolar and amacrine cells. The rod and cone fibers end on the boundary of these two layers, the rod fibers in a small end knob, the cone fibers in the cone foot.

The outer nuclear layer appears uniform as the nuclei are spherical and contain chromatin granules. The nuclei of the cone cells are somewhat larger than those of the rod cells and are surrounded by more cytoplasm. The rod and cone cells are the neuroepithelial elements of the retina, representing the sensory epithelium which receives the light stimulus. The stimulus is carried from here through the neurons of the retina and the primary optic centers to the cortex of the occipital lobe. The rod and cone cells are the outer neuron of the retina.

The outer limiting membrane appears as a refractile continuous layer. It is perforated by the rod and cone fibers which cannot be differentiated from the membrane itself under ordinary methods of preparation.

The rods and cones are the receptors in which the transformation of the light stimulus into the nervous stimulus takes place. They are parallel cell processes and can be compared to modified sense hairs in other sense organs, as the ear or the taste organ. These processes have a lighter stained outer segment, with longitudinal and cross striation, and a darker stained homogeneous inner segment. The rods are thinner and longer than the cones which appear wider and shorter. The rods contain a pigment, the so-called visual purple. Its presence in cones is still a matter of discussion. Occasionally, displaced nuclei are found in this layer, most frequently temporally, close to the papilla.

The pigment epithelium consists of a single layer of hexagonal regular cells. Cement connects these cells with one another and with Bruch's membrane. The visibility of the nucleus depends on the amount of the pigment in the cell. The nucleus is spherical and lies close to the basic membrane. The yellowish brown pigment lies more in the inner side of the cell and is granular melanin, also called fuscin. Closer to the rods and cones there is a more crystalline needle-shaped pigment. The rods, and probably also the cones, are in contact with the pigment cells which have very fine processes between them. Small droplets of lipoid seem to exist already in the normal pigment epithelium cell. The pigment epithelium of the retina is often called the pigment epithelium of the choroid also. Embryologically, it belongs to the retina, but it is more adherent to the choroid than to the retina which often separates from the pigment epithelium in the cadaver eye and in the fixed eye.

We can conclude that the retina has three neurons: the outer neuron, the sensory epithelium, which extends from the rod and cone layer through the external nuclear layer into the outer plexiform layer (neuro-epithelial layer); the middle neuron, represented by the bipolar cells, which extends from the external plexiform layer through the inner nuclear layer into the inner

plexiform layer; and the inner neuron, represented by the ganglion cells, which extends from the inner plexiform layer through the layer of the ganglion cells into the nerve fiber layer and from there into the optic nerve, chiasm and optic tract, to the primary optic ganglia (external geniculate body and anterior colliculus). The middle and inner neuron represent the cerebral layer of the retina.

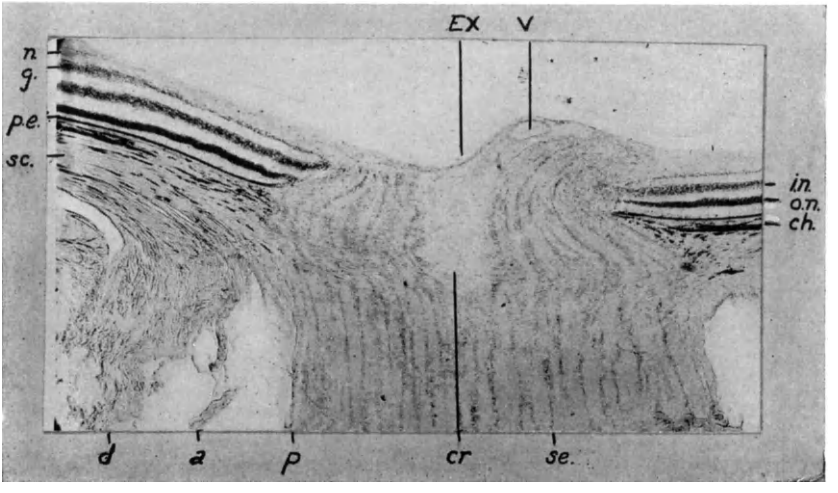

FIG. 6.—RETINA AND OPTIC DISK. a, arachnoid; ch, choroid; cr, lamina cribrosa; d, dura; EX, physiologic excavation; g, ganglion cell layer; in, inner nuclear layer; n, layer of nerve fibers; on, outer nuclear layer; p, pia; pe, pigment epithelium; sc, sclera; se, septa; V, vessel.

The structure of the retina changes completely in the macula and in the most peripheral part in the region of the ora serrata. In the macular region the ganglion cells are in a wider layer in five to seven rows and their nuclei are round. Here the entire retina seems to thicken slightly, then thins out obliquely against the center of the macula which represents the fovea. The layer of the ganglion cells and nerve fibers, and the inner plexiform and inner nuclear layer, too, thin out and finally disappear entirely toward the fovea. The bottom of the fovea is covered by a thin meshwork of the outer plexiform layer, by the inner limiting membrane, the outer nuclear layer, the outer limiting

membrane, and the cones, which are longer and thinner than in the extramacular part of the retina. The rods disappear in the region of the macula. As the cones are longer here, the outer limiting membrane is slightly convex anteriorly. The outer plexiform layer takes on a structure different from the rest of the retina. The cone fibers have to go in an oblique direction from the center cones to the bipolar cells, as the inner nuclear layer ends on the margin of the fovea. In this way the entire outer plexiform layer appears composed of rows of oblique fibers (fiber layer of Henle).

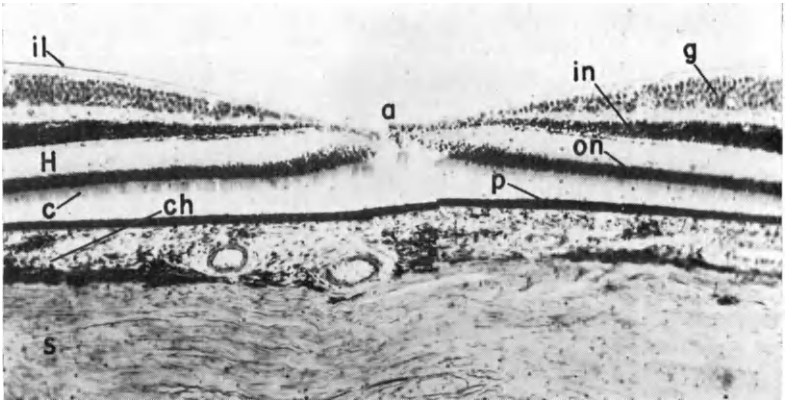

FIG. 7.—MACULA WITH FOVEA. a, artifact; c, cones; ch, choroid; g, layer of ganglion cells; H, Henle's fiber layer; il, inner limiting membrane; in, inner nuclear layer; on, outer nuclear layer; p, pigment epithelium; s, sclera. 65×.

The retina ends on the ora serrata, showing here a continuous transition into the nonpigmented epithelium of the pars plana of the ciliary body or appearing hanging over the epithelium. The inner limiting membrane follows until the end of the retina. It probably continues over the ciliary epithelium. The nerve fibers and ganglion cells end at a variable distance from the ora serrata and more and more glia appears. The outer limiting membrane extends beyond the ora serrata between the two epithelial layers of the pars plana. The rods disappear some distance from the ora serrata, and only irregularly formed cones

reach the end of the retina. The retina shows small and large cystic spaces in varying number (Blessig's cysts, Iwanoff's retinal edema, cystoid degeneration) which appear empty or contain debris of fibers. The cysts are, for the most part, located in the area of the nuclear layer, but may also extend from the inner to the outer limiting membrane.

The blood vessels of the retina are the central artery and central vein. The artery emerges from the optic nerve through the papilla and divides dichotomically in the retina. In the papilla the vein submerges into the optic nerve. The vessels distribute exclusively in the inner layers of the retina, the so-called cerebral layer. Larger vessels of the retina extend from the inner limiting membrane into the inner nuclear layer. The smaller vessels are situated chiefly among the ganglion cells and give off a plexus of capillaries to the nerve fiber layer and another to the inner nuclear layer. The capillaries and larger vessels are surrounded by a glial perivascular limiting membrane (membrana limitans perivascularis), which is formed by the bodies and processes of glial cells. A perivascular space lies between the loose adventitia and this perivascular membrane, which takes the place of lymph vessels. Arteries and veins can be easily distinguished, as in other parts of the body.

7. The Optic Nerve

The nerve fibers of the retina are collected in the papilla where the optic nerve begins. The optic nerve continues through the scleral canal into the orbit and optic canal to the chiasm, and after semidecussation through the tractus to the primary optic ganglia.

The optic nerve can be divided into (1) the intra-ocular part with (a) the papilla and (b) the intrascleral part, and (2) the extra-ocular part in the orbit and optic canal.

The papilla consists of nonmedullated nerve fibers which turn almost at a right angle from their course in the retina parallel to its inner surface into the optic nerve. The nerve fibers are arranged in bundles divided by rows of glial cells. The inner limiting membrane continues to the papilla and on to the physiologic cup. Here the vitreous body touches the nerve

tissue directly. A varying amount of glial fibers and connective tissue covers the cup (connective tissue meniscus, Kuhnt). Here vestiges of the embryonal papilla and hyaloid artery persist. Sometimes the vitreous body extends further into the intrascleral part of the optic nerve. The central retinal vessels are located on the nasal side of the physiologic cup. The individual layers of the retina and the choroid extend for various distances toward the papilla. The nuclear and plexiform layers end first, and an intermediary tissue lies between retina and optic nerve. We see as variations: (1) the pigment epithelium and Bruch's membrane extend further into the optic nerve (pigment ring of the ophthalmoscopic picture); (2) the pigment epithelium stops before the thin choroid covered by Bruch's membrane (choroidal crescent); (3) the pigment epithelium and choroid stop at the same point and only Bruch's membrane extends further toward the optic nerve (scleral ring). In general, the outer elastic portion of Bruch's membrane extends the furthest into the optic nerve and there splits into fine fibers. The inner cuticular portion of Bruch's membrane ends with the pigment epithelium.

The intrascleral portion of the optic nerve passes through perforations in the lamina cribrosa sclerae. The nerve fibers on the one side and the choroid and sclera on the other are separated by a thin layer of fibrous and elastic tissue which is lined on the inside by glia (border tissue, Elschnig). The lamina cribrosa sclerae consists of bundles of interwoven collagenous and elastic fibers, tissue from the choroid, sclera, border tissue, the glia and connective tissue septa of the optic nerve, which are filled with many vessels of the annulus of Zinn. The central vessels penetrate the center of the lamina cribrosa sclerae and are surrounded by the perivascular limiting membrane.

The scleral canal varies in different eyes and in different sections of the same eye with respect to size, shape, and direction of its lateral walls. Depending on the size of the scleral canal, the extension of the physiologic cup may vary, and is usually larger in larger canals. The direction of the wall may be vertical through the sclera or oblique. Usually with an obliquely directed canal, the retina and choroid stop earlier (conus). The opening of the canal may be larger anteriorly or posteriorly.

The structure of the nerve fibers changes posterior to the lamina cribrosa sclerae. Here the fibers become medullated but have no Schwann's sheath. The structure of the optic nerve can be studied only by employing special staining methods, of which there are a number designed specifically for use on the myelin sheaths of the nerve and on the glial tissues. As the optic nerve has no Schwann's sheath, it is similar to a nervous tract in the central nervous system.

The optic nerve has fibers of different widths. Whether the difference in width is related to a difference in function is still unsettled. Some scientists believe that the wider fibers serve the vision, the thinner ones, the conduction of the pupillary reflex, and the finest are centrifugal fibers of unknown function. The fibers of the optic nerve are separated by many septa into large bundles, which are subdivided by finer septa. The septa of the first order, originating from the pia in an oblique direction, subdivide into septa of the second, third order and so on. The septa consist of coarse connective tissue containing blood vessels and are lined by neuroglia.

The glia cells send fibrillar processes between the nerve fibers. The glia septa of the disc continue through the lamina cribrosa sclerae into the extra-ocular optic nerve. Here also between the nerve fibers are fine glia septa. The glia cells of the optic nerve are oligodendroglia, which have relatively much cytoplasm and few processes, and microglia, which have little cytoplasm and many processes.

The pia is the inner sheath of the optic nerve. It is formed by fine collagenous and elastic fibers and contains small vessels and nerves. It is lined on its outer side by an endothelium and on its inner side by a glia mantle. Thus, as in the retina, the optic nerve fibers, which are ectodermal, are separated by glia from the mesodermal connective tissue. Along the glia mantle there is a potential space that is continuous with the suprachoroid space.

Like the brain, the optic nerve has three meninges which continue through the optic canal directly from the intracranial cavity. The pia is surrounded by the arachnoid, composed of fine and coarse connective tissue trabeculae, which have an

endothelial lining. The heavier trabeculae cross the subarachnoidal space, which lies between pia and arachnoid. The arachnoid is surrounded by the thick dura, which consists of heavy connective tissue bundles similar to the sclera. The dura also has an endothelial layer on its inner side and on its outer side is separated by a fascial layer from the fat of the orbit. The subdural space lies between arachnoid and dura. Both spaces, the subarachnoidal and the subdural, are filled with cerebrospinal fluid. Both end blindly in the area of the lamina cribrosa sclerae where pia, arachnoid, and dura merge with the sclera.

The central retinal vessels enter through the sheaths of the optic nerve perpendicular to the nerve fibers into the optic nerve and turn on its axis at a right angle anteriorly toward the disc. These vessels are surrounded by the axial connective tissue strand in which a fine sympathetic plexus also lies. The axial strand is separated from the nerve by glia. The artery and the vein have their own adventitia; only when they pass through the lamina cribrosa sclerae do they share a common adventitia. Recurrent branches leave these vessels to the nerve fibers and have anastomoses with the circle of Zinn.

8. The Lens

Structurally, the lens consists of three parts: (1) capsule, (2) epithelium, and (3) lens substance. The homogeneous lens capsule is elastic and resistant. It consists of a fine outer lamella which continues into the zonule (zonular lamella) and the capsule proper.

The epithelium lies beneath the anterior capsule and extends to the lens equator. The posterior capsule normally has no epithelium. The cells at the anterior pole (central cells) are cuboid, have intercellular bridges, and an oval nucleus. Toward the equator, the cells are more cylindrical (peripheral cells) and the nuclei spherical. At the equator, the cells grow out to form long fibers (equatorial cells). At the same time, their posterior ends remain in contact with the lens capsule, but their anterior ends settle beneath the cells of the anterior capsule. The cells which move toward the center of the lens grow out to form long prismatic lens fibers, appearing hexagonal in cross section, and their nuclei become fusiform.

The lens substance consists of lens fibers which are arranged regularly at the equator and have a honeycomb appearance on cross section. They grow more and more irregular toward the center of the lens where they lose their nuclei. At the equator, the lens fibers are arranged radially, and toward the center more in an antero-posterior direction. The inner fibers fuse more and more as the lens scleroses with age. In this way they form the central nucleus as lens fibers continuously grow at the equator, the peripheral layer (cortex) becoming thicker. At the same time the nucleus also increases as the lamellae which are pushed toward the center sclerose. The nuclear substance appears homogeneous as the cell borders disappear. Histologically, the nucleus is split into lamellae which are often stained differently. However, they must be differentiated from the various nuclei (embryonic, fetal, juvenile, and adult) which can be discerned by bands of discontinuity with the slit lamp microscope. The lens fibers meet each other anteriorly and posteriorly with their anterior and posterior ends, forming the lens sutures.

9. The Zonule

The zonule consists of membranes which are stretched from the ciliary body to the lens. These membranes pass through the slit between the pars plana of the ciliary body and the vitreous body; they lie in the valleys between the ciliary processes and extend through the circumlental space to the equator of the lens. They insert on the pars plana of the ciliary body, in the crevices of the ciliary processes, and on the lens capsule.

Histologically, the membranes are composed of fine and heavy round fibers which are easily stained and which are connected by a nonstained homogeneous transparent gel-like substance. Some fibers extend to the ora serrata. The greater part pass from the pars plana of the ciliary body in a meridional direction through the space between the orbiculus ciliaris and the vitreous body. The finer fibers are closer to the ciliary epithelium, the heavier to the vitreous body. They originate chiefly from the pars plana of the ciliary body in front of the ora serrata, but some fibers come from the inner surface of the ciliary body in the region of the base of the vitreous, some from the vitreous

body, and others from the retina. A small number of cells, oval for the most part, are situated singly or in groups between the fibers. They originate, apparently, from the ciliary epithelium. A smaller number of mostly finer fibers originate along the pars plana of the ciliary body up to the region of the ciliary processes. One portion of these fibers runs in an oblique direction anterior to the major part of the fibers and unites with them, another portion in an oblique direction coursing backward, and suspends the major group of the fibers. These two groups of shorter oblique fibers come largely from the anterior part of the pars plana and form crossings (supporting fibers). Fine fibers lie on the anterior surface of the vitreous body (innermost fibers), probably coming out of the vitreous body, and pass to the posterior surface of the lens.

We do not yet know the exact origin of the fibers in the ciliary body. They may come from the inner limiting membrane of the ciliary body, or they may come out of the cells of the ciliary epithelium or from between the cells. They may have their anchorage in the cuticular part of Bruch's membrane, or in the cement ridge between the pigmented and nonpigmented epithelium. The fibers which submerge into the vitreous body cannot be followed to any formation there. Perhaps they unite with the fibrils of the vitreous body.

On transversal section, the fibers are seen coursing anteriorly in the valleys between the ciliary processes. Fibers originate also from the ciliary processes and extend from one to another (interciliary fibers), or run perpendicularly to the meridional fibers and support them, or extend toward the vitreous body. These fibers extend to the anterior border layer of the vitreous body, dividing into meridional fibers and into fibers which lie along the anterior border layer equatorially (circular). Anterior to the ciliary processes, the zonule membrane splits in two, the anterior and the posterior zonular leaf. These contain the anterior and posterior fibers which extend into the anterior and posterior capsule of the lens and insert poleward from the equator of the lens. The fibers split fanwise and merge into the zonular lamella of the capsule. Fine fibers lie between both leaves and insert directly on the equator of the lens (middle

or equatorial fibers). The space between both leaves is Hannover's canal.

The space between the iris, ciliary body, anterior zonular lamella and lens is the posterior chamber. Strictly speaking, this space is also called the prezonular space, as often the entire space between iris, lens, ciliary body and vitreous is considered the posterior chamber. Consequently, the circumlental space—which lies between lens and ciliary body, has no definite border, and also contains Hannover's canal—is part of the posterior chamber. The circumlental space is also called the zonular space as far as it contains Hannover's canal.

The orbicular space is the cleft between the vitreous body and the pars plana of the ciliary body; the greater part is filled with zonule fibers and vitreous fibrillae. It continues through the ciliary valleys into the circumlental space.

The retrozonular space (canal of Petit) lies between the zonular lamella and the anterior border layer of the vitreous body, which continues into the inner part of the ciliary valleys. It therefore passes continuously over into the orbicular space.

10. The Vitreous Body

This transparent gel, the vitreous body, is difficult to fix and prepare in histologic section. The usual methods cannot be applied; special methods must be used to study its histologic structure. We have learned a great deal about the vitreous body through the slit lamp examination of the living eye and examination under the ultramicroscope.

The vitreous body apparently consists of a meshwork of fibrils containing fluid. The densest accumulation of fibers is found in front of the ora serrata where zonule fibers seem to enter. Here the vitreous body is fixed to the ciliary body (base of the vitreous) at the point where the vitreous is connected with the inner limiting membrane of the ciliary body. From here a thick layer of slightly wavy lamellar arranged fibers runs parallel to the inner surface of the retina (posterior border layer) and is connected with the inner limiting membrane which at the same time is the membrana hyaloidea. It is densest on the ora serrata, thinning out posteriorly. It ends on the margin of the physio-

logic cup into which the vitreous extends and is here attached to the optic nerve. The posterior border layer also stops with the membrane, and the structure appears here to consist of much finer fibers. The part of the papilla not covered by the inner limiting membrane represents the entrance of Cloquett's canal, which is funnel-shaped anteriorly and which cannot be seen in histologic section but can be demonstrated by injection with dyes. The entrance is the area Martegiani. The canal itself lies in the axis of the vitreous body, extending toward the posterior pole of the lens and is considered as a lymph space.

Anterior to the base of the vitreous, there is a zone where the fibrils are fine and loose, and through which zonule fibers seem to pass (zonular cleft). Anterior to this, there is a layer of lamellae containing stronger fibers which lie parallel to the surface of the vitreous body (anterior border layer). This layer continues on the posterior surface of the lens in the fossa patellaris. Fibrils of the vitreous body extend into the lens capsule at the equator of the lens (ligamentum hyaloideocapsulare). The anterior border layer appears as a condensed membrane of the vitreous body, but different from the inner limiting membrane of the retina, which is more like the inner limiting membrane of the ciliary body. Inside the border layer, is the main body of the vitreous, consisting of the finest fibers lying farther apart from each other (body of the vitreous or nucleus) than in the border layer. These fibrils are interwoven with one another to form a network. In addition, granules are visible. Isolated cells can be seen on the inner limiting membrane of the retina and occasionally at the base of the vitreous. They are oval and for the most part have few processes. Apparently, they are migratory cells.

11. The Conjunctiva

The conjunctiva covers as a mucosa the inner surface of the lids, turns in the fornix onto the bulb, covers the anterior sclera, and ends at the limbus.

It consists of (a) epithelium, (b) substantia propria, and (c) subconjunctiva.

The epithelium has a different character in different regions. At the lid margin, it is a stratified squamous epithelium like the epidermis, but without hornification. Over the tarsus, it changes to an epithelium, most of which has two rows of cells. The superficial layer contains cylindrical cells with spherical and vertical oval nuclei and a basal layer of cuboidal cells with spherical or horizontal oval nuclei. Toward the fornix and over it on the bulb a third layer of polygonal cells appears between the cylindrical and cuboid layer. In this area, depressions of the epithelium are found in the form of furrows and tubuli which on section often appear glandlike. The epithelium becomes more irregularly stratified on the bulb and contains goblet cells with a mucous content. At the limbus, again higher stratified squamous epithelium with papillae is found. Pigment granules in varying amounts fill the basal cells.

The thin layer of the propria consists subepithelially of loose connective tissue and small vessels. This layer is filled with lymphocytes which accumulate in the fornix sometimes to form lymphatic nodules. A nerve plexus and end organs (tactile corpuscles of Krause) lie subepithelially.

The subconjunctival layer beneath the propria, consisting of coarser fibrous and elastic tissue, is lacking over the tarsus. It contains the larger vessels and the nerves. The arteries and veins are connected with the arteries and veins of the lids and of the anterior ciliary vessels. Lymph vessels are also found.

The conjunctiva of the upper fornix has serous glands of the type of the lacrimal gland (accessory tear glands, glands of Krause) at the fornix and the glands of Wolfring close to the upper margin of the tarsus. In the fornix the conjunctiva is surrounded by fat which is connected with the orbital fat.

12. The Plica Semilunaris

The conjunctiva forms, in the inner canthus, a crescent-shaped fold the construction of which is similar to that of the conjunctiva. The epithelium contains many goblet cells, and the subepithelial tissue has smooth muscles, fat tissue, and, in rare instances, cartilage. It may also have accessory tear glands.

13. The Caruncle

The caruncle, a round nodule, lies medially to the semilunar fold in the inner canthus and is covered by stratified squamous epithelium which does not hornify. Large sebaceous glands are situated beneath the epithelium in connective tissue. They have their own efferent ducts, such as the meibomian glands. Besides, there are smaller sebaceous glands which open into hair follicles. Occasionally, rudimentary accessory tear glands are present. Fat tissue and smooth muscles are also found.

14. The Eyelids

Histologically, the eyelids consist of (1) cutaneous layer, (2) muscle layer, (3) tarsus and orbital septum, and (4) conjunctival layer.

The integument of the lids is similar in structure to the skin in general, but it is finer and some of its formations appear rudimentary. It is made up of epidermis (cuticle). Under it lies the corium (cutis), and in the depth the subcutaneous tissue.

The epidermis has (1) a stratum germinativum, (2) an intermediary layer not everywhere distinct, and (3) a stratum corneum.

The stratum germinativum is a stratified squamous epithelium with a cylindrical cell basal layer containing some pigmented cells. It is covered by layers of prickle cells which become more and more fusiform the closer they are to the surface. These horizontal lying spindle-shaped cells change further into cells filled with keratohyalin granules (stratum granulosum) which belong to the intermediary layer. To the intermediary layer also belongs the stratum lucidum which lies immediately above it. The stratum lucidum is formed by the liquefaction and coalescence of the keratohyalin which changes into eleidin. The cells of this layer have no nuclei, are homogeneous, transparent, and have no distinct cell borders.

The surface of the epithelium is covered by the stratum corneum in which the nucleus-free cells coalesce into flat lamellae and scales in which the eleidin is transformed into keratin. In this way, the cells are keratinized or cornified. In the lid proper, only the stratum germinativum and corneum can be distin-

guished, but in the areas where the skin becomes thicker, as toward the eyebrow, the nasal root and the cheek, the intermediary layer appears more evident, in which the living cells, coming from underneath, are continuously transformed into necrobiotic cells, and finally, into a necrotic form of structure.

The cutis, also known as corium or derma, beneath the epithelium, consists of connective and elastic tissue and is elevated at the border of the epidermis into papillae which thin out the covering epithelium; consequently, its under surface appears wavy. The cutis contains small arteries and veins, capillaries and lymph vessels, fine nerve bundles, branched pigment cells, a few plasma and mast cells, rudimentary hairs, sebaceous and sweat glands. The latter increase in number and development toward the eyebrow. The subcutaneous tissue of the lid is not distinctly differentiated from the cutis. It is situated between the cutis and the orbicularis muscle and consists of connective tissue and elastic tissue with larger vessels and also has considerable fat tissue in the area of the eyebrow.

The structure of the skin is somewhat different at the lid margin. Here the cutis has (1) the rows of cilia, (2) the sebaceous glands of Zeis, and (3) the modified sweat glands of Moll. The cilia, like other hairs, consist of shaft and root. The shaft is that part of the hair which extends above the surface of the epidermis and can be followed beneath the surface some of the way to the root. That part of the hair which lies beneath the epidermis is the hair follicle which originates from the epithelium as a tubular invagination of the epidermis and cutis and penetrates deeply into the tissue of the lid. The cutis surrounds the hair, which originates from the epithelium, in a layer of longitudinal and circularly arranged collagenous and elastic fibers. At the bottom of the hair follicle, the epithelial formation of the root of the hair is pushed upwards to give place to a projection of connective tissue, the hair papilla, which carries the capillary loops into close relation with the cells most active in the production of the hair (hair matrix).

The hair follicle consists of an inner root sheath and of an outer root sheath which is continuous with the invaginated epidermis. The central cells above the papilla hornify to form

the hair shaft. The sebaceous glands of the cilia are the glands of Zeis. They are relatively large and lie in close association and surround the hair follicle as acinous glands with an epithelial wall and fatty epithelial cells toward the center. The glands open into the hair follicle. Peculiar sweat glands (Moll) lie between the hair follicles. They are tubular in form, lined by a single layer of cylindrical, conical, or flat cells with a basement

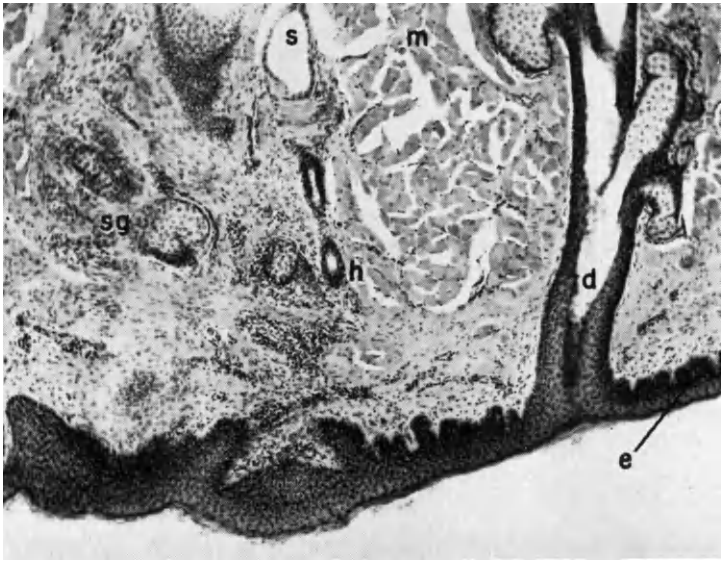

FIG. 8.—EYELID. d, duct of meibomian glands; e, stratified squamous epithelium; h, hair follicle; m, musculus orbicularis; s, sweat gland; sg, sebaceous glands. 65×.

membrane, and are surrounded by smooth muscle. Their ducts open into the hair follicles. Between the rows of the cilia and the end piece of the secretory duct of the meibomian glands which open freely at the lid margin lies the pars marginalis of the orbicular muscle. The pars subtarsalis of the orbicular muscle is situated between the efferent ducts of the meibomian glands and the conjunctiva.

The muscle layer consists of thin striated fibers of the orbicular muscle. Nerves lie underneath the orbicular muscle, which they

perforate, and distribute in the skin. Others run to the tarsus to form a plexus there. They enter the tarsus, send out branches to the conjunctiva and also form a plexus on the lid margin. Between the muscle and the tarsus of the upper lid lies connective tissue, which continues from the tendon of the musculus levator palpebrae, and fat. The superior arterial arcade lies on the inner side of the tendon, and there are veins, too, in the same layer. Fibrous bundles of the orbital septum extend into the upper and lower lid. Smooth muscle fibers (Mueller's muscle) lie at some distance from the margin of the tarsus in the upper and lower fornix.

The tarsus is a plate of dense connective tissue, containing embedded in its substance the meibomian glands. These are lobated alveolar sebaceous glands. Their terminal portions have short ducts which, from all sides and in all layers, enter into a long central excretory duct lined with stratified squamous epithelium. The central duct ends at the lid margin. Arteries and veins lie on both the dermal and conjunctival sides of the tarsus. Lymph vessels are also found in this layer.

The conjunctiva covers the inner side of the lid. Its stratified squamous epithelium continues into the lid margin where it becomes higher and shows hornification.

15. The Lacrimal Organs

The tear gland is a serous gland of the tubulo-alveolar type. The lumen of its terminal portion is surrounded by a layer of cylindrical cells with spherical nuclei, which contain small and large secretion granules. Between these cells and the basement membrane are myoepithelial cells. The end pieces are arranged in lobules and have intralobular excretory ducts lined with cuboid epithelial cells. The larger interlobular ducts, which have two rows of epithelium of flat outer cells and cylindrical inner cells, end at the conjunctiva above the fornix. Connective tissue septa with vessels and nerves separate the lobules. A fine reticulum surrounds the end pieces. In addition to elastic fibers, the septa have lymphocytes and plasma cells in small number.

The lacrimal passages consist of (1) the lacrimal canaliculi, (2) the lacrimal sac, and (3) the naso-lacrimal duct.

The lacrimal canaliculi continue from the conjunctiva. They begin in the ostia of the lacrimal puncta. They are lined by stratified squamous cell epithelium which rests on connective tissue and elastic tissue, and are surrounded by striated muscle fibers. They unite shortly before their entrance into the tear sac.

The tear sac is lined by columnar epithelium which has a basal membrane. This epithelium is similar to the epithelium of the nose, but it is not yet settled whether it, too, is ciliated. Goblet cells are present. The subepithelial connective tissue contains lymphocytes. The submucous tissue is more densely fibrous and has many elastic fibers, numerous venous plexuses, arteries, and lymph vessels.

The naso-lacrimal duct has a structure similar to that of the tear sac; it is surrounded on all sides by bone, and continues in the lower nasal meatus directly into the nasal mucosa.

16. The Orbit

The orbit has (1) bony walls, (2) periosteum (periorbita), (3) muscles, (4) fascia, (5) fat, (6) nerves, and (7) vessels.

The bone of the walls is cancellous. It consists of trabeculae which surround marrow spaces. The trabeculae show parallel lamellae composed of fibrils and oval osteocytes with many fine projections (bone corpuscles). The lamellae are arranged in parallel bands or represent concentric cylinders which surround the Haversian canals. The bone marrow is composed of cellular elements (myeloid cells) or occasionally of fibrous vascular tissue. Strands of marrow may extend from the periosteum of the orbit to the mucosa of the paranasal sinus, which surround the orbit above, especially medially and also below.

The periosteum consists of connective tissue and is identical with the dura in the canalis opticus. At the end of the canal the connective tissue separates into a periosteal layer which follows the bone and the dura proper surrounding the optic nerve. In the angle between these two lies a tendon-like ring (annulus of Zinn), onto which the extrinsic eye muscles insert. The periosteum has a layer of dense connective tissue toward the bone; the latter has rows of osteoblasts. The periorbita is

also connected with the orbital septum, the palpebral ligaments, and with the fascia of the tear sac.

The muscles of the orbit are both striated and smooth. The striated muscles have fine muscle fibers which are not uniform but contain a varying number of fibrils and vary in width. The connective tissue between the fibers and bundles have much elastic tissue. The muscles have typical terminal plates. Smooth muscles bridge the inferior orbital fissure beneath the annulus of Zinn. They are also found on the anterior capsule of Tenon and extend into the lids.

Sheaths consisting of loose connective tissue surround the eyeball (Tenon's capsule) and muscle (muscle sheaths). Tenon's capsule adheres to the episclera. The episcleral space between both is bridged by a loose meshwork of fibers. The muscle sheaths continue from Tenon's capsule and are thicker than the latter. They surround the muscle on all sides. Anteriorly, they give off heavy check-ligaments which insert on the palpebral ligaments or bony walls. They contain smooth muscle fiber.

The larger part of the orbit contains fat, which fills the spaces between the structures of the orbit. It consists of fat cells and of connective tissue which forms small and large septa and contains blood vessels and nerves. In addition to the optic nerve, the orbit contains medullated nerve fibers, especially those of the motor eye muscle nerves which end on the numerous end plates of the motor muscles of the eye and those of the ciliary nerves and branches of the ophthalmic division of the trigeminal nerve. The orbit also has nonmedullated nerve fibers which are found in the eye muscle nerves and which are connected with the finer muscle fibers. They are considered to be centripetal sensory nerve fibers. There also are nonmedullated nerve fibers which belong to the sympathetic nerve.

The branches of the ophthalmic artery and the ophthalmic vein are numerous and have typical structure. The veins are surrounded by perivascular spaces which continue into the lymph vessels of the neck and of the pterygomaxillary fossa. These spaces serve to collect the lymph of the orbit which has neither lymph vessels nor lymph nodes of its own.

Chapter II

EMBRYOLOGY OF THE EYE

The eye develops from the anterior end of the ectodermal neural tube evaginating symmetrically on both sides to form a vesicle (primary optic vesicle). This vesicle grows, surrounded by mesoderm, toward the surface ectoderm of the embryo. It remains connected with the neural tube by an epithelial optic stalk. The vesicle invaginates just beneath the surface ectoderm and forms a cup (optic cup) or secondary optic vesicle. The invagination continues a short way into the stalk. Thus a fissure is formed (fetal fissure or cleft) into which enter connective tissue and blood vessels.

The optic cup consists of two layers of epithelium. The outer layer, composed of a single row of cells in which pigment granules appear, becomes the pigment epithelium. The inner layer develops into the retina and soon shows differentiation by cell increase. It forms an outer zone with many rows of cells (primitive neuroepithelium) and an inner zone with fibers and a few nuclei; in the latter, capillaries develop. Layers of cells of different shapes are formed by proliferation from within and differentiation of the cells of the primitive neuroepithelium. First the ganglion cells are differentiated in the innermost layer; later the various elements of the inner nuclear layer are formed (bipolar, amacrine, and horizontal cells); the supporting elements of Mueller's fibers are visible earlier. At the beginning, the outer layer of the retina has cilia which disappear to make place for the rods and cones. The outer epithelial layer is transformed into the cells of the rods and cones (outer nuclear layer). Between the layers of the ganglion cells and the inner and outer nuclear layers, fibrillar strata appear (molecular layers). At the beginning, the cells in the macular region increase and differentiate more than in the rest of the retina so that the macula appears thicker. Later it slowly thins out by the spreading of the ganglion cells and the inner nuclear layer,

and on the end a fovea-like depression appears. The process of thinning is not yet finished at the time of birth, but continues through the first four months of the postfetal life.

The fetal fissure closes early in the development of the eye, disappearing entirely as both layers of the optic cup close and become continuous. Only a small part remains open where the central retinal artery enters the disc.

The nerve fibers grow from the ganglion cells at the inner surface of the retina and radiate toward the optic stalk which has on its inner side, at the end of the fetal fissure, a primitive epithelial papilla. The nerve fibers grow through these cells into the inner layer of the stalk. In this way, cells are separated from the retina and form a cone-shaped accumulation (Bergmeister's papilla). The nerve fibers invade the cells of the invaginating layer of the stalk, which vacuolize and disappear. Cells of the stalk also persist; they are arranged in longitudinal rows and become glial septa. The fissure in the stalk closes and thus the hyaloid artery, which lies in it, becomes enclosed. At the end of the fissure a small slit remains open through which the hyaloid artery, which branches off as the main branch of the ophthalmic artery, enters from the surrounding mesoderm into the stalk. The nerve fibers leave the stalk as they grow further toward the brain and reach the hypophysis, where they form the chiasm. In a later stage of development, myelinization appears.

As the optic cup forms, a thickening appears in the surface ectoderm. This is the lens plate, which is soon transformed into the lens pit by invagination. Then by closure it becomes the lens vesicle. The anterior layer of its cells remains simple; the cells of the posterior layer elongate forward into fiber-shaped cells which, in a later stage, occlude the lumen of the vesicle. The lens zone is closed off from its surroundings by the formation of a cuticula (lens capsule).

The epithelium which remains above the lens vesicle after its separation from the surface epithelium becomes the corneal epithelium.

Protoplasmic fibrils extend from the lens vesicle to the primitive neuroepithelium of the optic cup, bridging the space between

these two formations (primary vitreous). Mueller's fibers, which, through their footplates, help form the inner limiting membrane, are in contact with these fibrils through the membrane. Mesodermal elements enter through the fetal fissure and are mixed with the ectodermal elements. The hyaloid artery extends through the stalk into the primary vitreous and proceeds to the posterior lens capsule; on its way, it gives off many branches in the primary vitreous and on the posterior surface of the lens where it forms a meshwork of capillaries (posterior portion of the tunica vasculosa lentis). Near the equator of the lens, in the region of the margin of the optic cup, these vessels are connected with a vessel which here runs circularly to form the lateral or capsulo-pupillary portion of the tunica vasculosa lentis. Later in the fetal development, buds originate from here and form a meshwork on the anterior surface of the lens (anterior or pupillary portion of the tunica vasculosa lentis).

The blood vessels in the primary vitreous atrophy relatively early, and a secondary avascular vitreous is deposited, formed by the inner layer of the optic cup. It compresses the primary vitreous and pushes it toward the center and behind the lens; in all probability this is what remains as Cloquet's canal. The retina becomes closed off from the vitreous by the cuticular limiting membrane.

In the third month, when the anterior end of the optic cup grows forward and forms the ciliary body, vitreous is secreted from its inner surface and fibers grow out from its cells (tertiary vitreous). At the same time, the most anterior part of the secondary vitreous atrophies up to the ora serrata, where it forms the base of the vitreous. Anterior to it, more and more fibers develop, which now extend to the lens capsule, forming the zonule in the tertiary vitreous.

The hyaloid artery, which finally disappears entirely in the vitreous, remains only in the optic nerve and sends off branches into the retina (arteria centralis retinae). During its development, it forms a bulbar swelling in Bergmeister's papilla, from which vessels ensheathed in glia start to ramify into the nerve fiber layer of the retina. These extend peripherally toward

the ora serrata and into the depth up to the inner nuclear layer. The central retinal vein appears later.

The margin of the cup, consisting of two layers of epithelium, the outer pigmented and the inner nonpigmented, early grows anteriorly into the mesoderm. Both epithelial layers ultimately adhere except at their anterior end where the cavity of the primary optic vesicle remains to form the marginal sinus. As the epithelium grows anteriorly, it starts to fold to form the ciliary processes. The layers increase slowly, and mesoderm with blood vessels grows into them. The most anterior part of the epithelium grows linearly. Probably in the fourth month it forms the sphincter muscle, which finally appears separated from the epithelium by mesoderm, and in the sixth month the dilator muscle, which always remains in contact with the epithelium. The mesoderm with blood vessels grows with the epithelium over the surface of the lens and continues beyond the epithelium, covering the entire anterior lens surface. This lamina iridopupillaris has a thick peripheral portion which forms the stroma of the iris; it has a thin central portion, the pupillary membrane, which finally disappears. Both the lamina and the pupillary membrane are connected with the tunica vasculosa lentis.

The cornea develops relatively early from the mesoderm, which lies between the lens vesicle and the surface ectoderm which also forms the corneal epithelium. The mesoderm forms fibrils and lamellae (substantia propria). In a later stage, Descemet's and Bowman's membranes differentiate. A cleft appears in the mesoderm, becoming the anterior chamber. The mesoderm cells lining the cleft anteriorly arrange themselves into a row to form the layer of the endothelium. The mesoderm, which lies on the lens, contributes to the formation of the iris.

The anterior chamber is formed by the enlargement of the cleft and the atrophy of the mesoderm in an early stage of the development when the anterior end of the optic cup has not yet advanced far anteriorly. When the anterior end starts to form the ectodermal portion of the iris, Schlemm's canal is already present, lying in the deepest part of the chamber angle. Posterior to Schlemm's canal, the scleral spur and the ciliary muscle

appear as a condensation of the mesodermal tissue between the optic cup and the scleral condensation. The recess of the chamber angle is formed by deepening of the angle during the course of the embryonic growth of the eye and is filled with loose tissue which is entirely reabsorbed by the time of birth.

In the earliest stage of the development, when the optic cup is formed, it is surrounded by capillaries forming the chorio-capillaris. Soon a basement membrane appears which separates the capillaries from the pigment epithelium to become Bruch's membrane. The layer of the veins appears later as a loose mesh-work, acquiring larger venous channels in the third month. The arteries develop only later; in the fifth month all the layers of the choroid are formed, and the first chromatophores appear.

The sclera is formed by condensation of the mesoderm surrounding the optic cup, first in the region of the insertion of the extrinsic eye muscles and further on anterior to the chamber angle and the corneoscleral junction. Later the mesoderm condensates on the posterior pole; in the fourth month, the sclera grows from there and is well differentiated by the end of the fifth month.

The eyelids appear in the second month as folds of the surface ectoderm. The outer surface of the folds becomes epidermis and the inner surface the epithelium of the conjunctiva. Mesoderm grows into the folds and forms the tarsus, connective tissue of cutis and subcutis and musculature. The folds elongate quickly and cover the eye. The ectoderm of the margins of the lids adheres. As long as the lids are closed, the caruncle develops by a cutting off of a margin of the lower lid, and the cilia first appear as pits of the epithelium. From the hair follicles, the epithelium evaginates to form sweat and sebaceous glands. The glands of the conjunctiva are formed by invagination of the epithelium, and the accessory tear glands and the tear gland proper by outgrowth of the epithelium. The first solid tubuli are later canalized. In the sixth month, the lids open again as the epithelial adhesions between them loosen as a result of disintegration of cells.

During the growth of the maxillary process of the face from below and the lateral nasal process from above, which enclose

the optic cup from the inside, a fold of ectoderm is displaced into the depth as a solid strand of cells as anlage of the excretory lacrimal organs. The growing lids also displace ectoderm into the depth and in this way form the canaliculi. These first solid epithelial strands open up, through disintegration of the central cells, into channels and form the canaliculi which open on the puncta toward the cul-de-sac, the tear sac, and the naso-lacrimal duct.

The extrinsic eye muscles are early formed by condensation of mesoderm surrounding the optic cup. The first undifferentiated layer separates antero-posteriorly into the muscle bellies of the recti and the obliques. The levator of the upper lid separates from fibers at the medial side of the superior rectus. Tenon's capsule develops as a mesodermal sheet at the insertion of the recti. Its posterior part forms much later.

Chapter III

SENESCENCE OF THE EYE

In old age, the tissue of the eye and its adnexa degenerate. The arcus senilis appears in the cornea in the form of small fat droplets in Bowman's membrane and in the stroma. Descemet's membrane shows warts in increasing numbers—the Hassal-Henle excrescences. The circumscribed wartlike thickenings of Descemet's membrane give rise to the condition known as the cornea guttata. The sclera shows fatty infiltration and calcium deposits.

In the uvea the collagenous tissue is enlarged and thickened and undergoes hyaline changes.

The iris root widens on account of progressive tissue sclerosis. The pigment margin around the pupil atrophies.

The limitans interna ciliaris becomes thicker. The ciliary epithelium shows nodular excrescences of nonpigmented epithelium on the crests of the ciliary processes. The connective tissue in the ciliary processes and also between the bundles of the ciliary muscle becomes thicker. The circumlental space may be greatly narrowed by enlargement of the ciliary processes and the lens.

Senile warts (verrucae) appear in the elastic membrane of the choroid. They are stained like the cuticular lamella and the elastic membrane continues beneath the warts. Frequently the warts are surrounded by cuticular substance. They are apparently secretion products of the pigment epithelium. The pigment epithelium continues above the warts, and its cells are thin over them. Sometimes the pigment epithelium on the warts disappears entirely. The warts are frequently found in the periphery of the fundus, rarely in the macular region where they appear ophthalmoscopically as round, yellow spots. The warts may show calcareus deposits in the form of fine granules. The choriocapillaris has fewer nuclei.

The pigment epithelium of the retina atrophies diffusely, and as a result the tasselation of the fundus appears in the ophthal-

moscopic picture. The atrophy of the pigment epithelium around the papilla produces the halo senilis. Cystic degeneration appears in the peripheral retina.

The lens capsule thickens and the lens itself shows sclerosis of the nucleus, which increases progressively. The lens may enlarge in toto.

The anterior and posterior chambers become smaller owing to the enlargement of the lens and the widening of the iris and ciliary body.

The border layer of the vitreous becomes thicker; the inner part of the vitreous more and more liquid. The zonule fibers become heavier.

The conjunctiva shows degeneration of connective tissue and elastic fibers.

The skin of the lids shows decrease of elastic tissue. The connective tissue becomes heavier and hyalinizes. The epithelium atrophies.

In all tissues, the vessels may become sclerotic.

PART I. READING OF SOURCE MATERIAL

Tonofibrils extending through all layers of the corneal epithelium are described by Frieboes, Mans.

Panico finds the sclera the thickest at the optico-sclerotic canal and the thinnest at the equator and behind the insertion of the extrinsic eye muscles.

Reiser could show in the sclera with the help of the staining method of Bielschowsky, nerve plexuses of first and second order and a preterminal network from which the end nerves branch off.

Fischer describes loops of the ciliary nerves in the posterior sclera.

Redslob finds in the deep layers of the limbus epithelium potential melanoblasts corresponding to the Langerhans cells of the epithelium of the skin; Winkler Prims finds few pigment granules subepithelially.

Alexander describes in detail the various elastic tissues of the eye and the structures of the chamber angle.

The pigment of the uvea originates from the pigment epithelium, according to Dawson, Spencer; Redslob believes that cells derived from the neuroepithelium may be enclosed in the choroid, produce pigment and may even form the pigmented cells of the malignant melanoma.

Wolfrum believes like others that the clump cells of the iris are derived from the pigmentary epithelium.

Reese describes spherical and branching pigmented cells in generalized melanomatosis of the uvea.

Wolfrum believes that the chromatophors of the uvea contain contractile substance and that each stroma cell and chromatophor have their own nerves.

The nerve plexus of the iris contains medullated and nonmedullated nerve fibers and ganglion cells (Jirman).

The dilator muscle sends processes consisting of muscle cells and connective tissue into the ciliary muscle and into the trabeculæ and thus has a fixed attachment (Berner).

Lauber describes the normal histology of the ciliary body; Fuchs the structure and shape of the ciliary muscle in various age groups and refractions.

Gartner describes abnormal ciliary processes arising from the posterior surface of the iris.

Fortin believes that the pull of the ciliary muscle displaces the scleral spur posteriorly and regulates the outflow of the aqueous humor.

Saba finds that the meridional bundles of the ciliary muscle insert as a whole on the scleral spur if the spur is developed strongly, on the corneoscleral trabeculæ if it is developed weakly.

Herbert finds a cement substance in the intra-ocular eye muscles which is probably related to the hyaline and glass substances of the eye.

Albrich, Carrère conclude from the presence of granules and vacuoles in the ciliary epithelium a glandular function, Duke-Elder considers this rather as passive edema caused by formation of intra-ocular fluid in great quantity.

The muscle layer of the anterior ciliary arteries rapidly decreases in thickness after they have perforated the sclera (Fuchs).

Schaly finds Rouget's cells (contractile cells situated on a membrane) on the endothelium of capillaries of the uvea, the most numerous on the choriocapillaris of the macula.

Meller finds occasionally in the region of the ora serrata blood vessels between the pigment epithelium and the elastic lamella of Bruch's membrane. The vessels appear here during the early embryonic life and may persist, or are the result of a past inflammation.

Bruno, Cattaneo, Maggiore contribute to the normal histology of the retina.

Fortin observed on fresh sections of the retina a layer of irregularly arranged half-spherical structures between the external plexiform layer and internal nuclear layer. From these formations fine fibers extend into the inner nuclear layer.

Scullica explains variations in the size of the blind spot from the various anatomic appearances of the peripapillary retinal layers. The sensory cells reach to the margin of the papilla, the degree of closeness varying in different cases. In glaucoma, papilledema and myopia the blind spot is enlarged; in glaucoma due to damage to the peripapillary retina, in papilledema due to displacement of the retina from the papilla and in myopia due to absence of sensory cells in the conus.

Redslob believes that the retinal pigment is first amorphous and later becomes crystalline.

Lo Cascio finds small droplets of lipoid in the pigmentary epithelium.

Evans described a sphincter-like narrowing of the capillaries of the retina where they branch from the precapillary vessels.

The fovea is described in great detail by Fortin, Fortin and Balado.

Rønne believes that the course of the macular fibers of the retina is determined by the passive displacement of the nerve fibers due to the development of the fovea.

Grimminger finds, in a small percentage of anatomically examined eyes, the fovea hypo- or aplastic. Such eyes are usually small and hyperop.

The topography of the nerve fibers in the optic nerve is described by Balado and Fortin.

Marchesani divides the glia of the optic nerve into two groups: in cells with much cytoplasm and few processes (protoplasmic astrocytes and oligodendroglia) and in cells with little cytoplasm and many processes (fibrous astrocytes, Hortega's microglia). According Lopez Enriquez, the former are more numerous axially, and the latter peripherally.

Favaloro finds that each nerve fiber of the optic nerve is surrounded by a double row of irregular glial network, and from it a few fine radial glial fibrils spread out toward the myelin sheath, forming a peculiar perimyelinic reticulum.

Bulac contributes also to the morphology of the normal neuroglia in the optic nerve.

Behr describes in detail the anatomy of the septal system and the arterial blood supply of the optic nerve and finds that the lamina cribrosa and the anterior third of the optic nerve is supplied by the posterior ciliary vessels.

Beauvieux and Ristich injected the central retinal vessels in the optic nerve and made serial sections. They did not find any anastomoses with the ciliary vessels and believe them to be end vessels like the cerebral vessels and that they also supply the optic nerve and the pia.

The central retinal artery and vein show in their course in the optic nerve manifold variation (Beauvieux and Gouelmino), and according to Fry, the entrance of the artery is more anterior than the exit of the vein.

Uveal chromatophors can be found physiologically in the lamina cribrosa and in the septa of the optic nerve (Scheerer).

Reese describes pigmentations of the papilla which may be produced by chromatophors, extensions of the pigment epithelium, hematogenous granules and siderosis.

The optic nerve sheaths are supplied by numerous fine nerve fibers which are partly sensory and partly vasomotor (Stoehr).

Sanna finds the dural sheath of the optic nerve thicker on the temporal side. He finds here an inner compact layer which continues into the inner scleral layers and into the pia and an outer loose layer continuing into the outer scleral layers. The middle scleral layers cease abruptly and form a ring.

The chambers and the vessels of the eye were studied by Kiss, who injected them with india ink.

According to Busacca, there are tonofibrils in the epithelium of the lens.

Elschnig calls the superficial layer of the lens capsule into which the zonule fibers enter and which surrounds the capsule proper, the zonule lamella, which can be distinguished, according to Beauvieux, by staining with aniline blue.

Klein also believes that the zonule fibers do not insert on the lens capsule itself, but on the zonule lamella.

Dejean distinguishes in the zonule four layers: (1) a fine membrane covering the anterior surface of the zonule; (2) a system of meridionally directed lamellæ; (3) a system of frontal lamellæ; (4) a limitans intervitrealis corresponding to the anterior border layer of the vitreous.

Duke-Elder believes that the fibers of the zonule are imbedded in a clear, nonstainable gel-like substance.

Beauvieux, Carrère, Dejean, Mann, are of the opinion that the zonule fibers develop from the ciliary epithelium, probably extracellularly.

Castroviejo, Wolff describe the histology of the zonule.

Verhoeff finds in the histologic examination of eyes after intracapsular cataract extraction the hyaloid membrane intact and the ciliary epithelium and the retina uninjured. The zonule fibers rupture close to the surface of the lens.

Goldsmith believes that the zonule fibers insert entirely on the orbiculus ciliaris, that there are no zonule fibers in the vitreous body and that the anterior border layer of the vitreous is a membrane.

Heesch and Leboucq describe the structure of the vitreous body; Baurmann reports about ultramicroscopic studies of the vitreous body.

Dejean, Fracassi, Howard, Mann believe that mesoderm contributes to the formation of the ectodermally formed vitreous.

Cowan and Fry defend the existence of an anterior hyaloid membrane, Dejean insists that the hyaloid membrane represents a separate mesodermal formation, but Mann believes that the vitreous body and the zonule form a continuity and that there is no hyaloid membrane between them.

Wolff finds ghost-rings on the internal limiting membrane of the retina which represent disintegrating mononuclears originating from the ciliary body and the retina which disappear from the vitreous body.

Baurmann finds in ultramicroscopic examinations of the vitreous body that already in adolescence, disintegration sets in and fluid-filled spaces appear, which enlarge with age. The central parts are affected earlier and more extensively than the peripheral. The disintegration is more marked in high myopia than in normal eyes.

Comberg and Duke-Elder describe the vitreous as true gel without any microscopic structure.

Greeff denies the existence of the so-called glia cell of Contino in the vitreous body.

Scalinci denies the existence of fibrils in the living vitreous body.

The central canal of the vitreous body was injected by Dejean, Redslob; Wildi established the presence of the central canal of the vitreous body microscopically.

Goldstein and Wexler describe histologically a preretinal artery arising from the papilla and returning through the vitreous body into an artery of the retina.

Reitsch describes the histology of fornix, semilunar fold and caruncle.

Gallenga describes various fasciscles of Horner's portion of the orbicularis oculi: (1) a bundle directly to the lower lid; (2) scattered bundles which continue with the muscle to the lower lid; (3) bundles directed to the caruncle; (4) bundles directed to the upper lid; (5) a few fibers uniting

with the muscles of the upper lid; (6) a few bundles continuing to the conjunctiva.

Mamoli finds normally accumulations of lymphocytes in the lacrimal gland, occasionally forming follicles.

Aliquò-Mazzei never found glands in normal tear sacs, but Iwata finds small serous glands in the wall of the tear sac but none in the naso-lacrimal duct.

Serra describes in the wall of normal tear sacs; (1) deep tubulo-alveolar glands; (2) subepithelial tubulo-alveolar glands; (3) tubulo-alveolar glands in the surrounding tissue; (4) submucous simple and branching tubular glands; (5) simple and sebum containing alveolar glands in the fornix of the tear sac.

Wolland describes in the extrinsic eye muscles two types of muscle fibers, thick and thin ones.

Schwartz describes circular fibrils situated beneath the sarcolemma of the muscle fibers in the cross-striated extrinsic eye muscles which, according to his opinion, oppose the muscle tonus and make a very exact fixation of the eyes possible.

Daniel finds that the fibers of the oculomotor nerve with thick myelin sheaths are arranged as simple or multiple spirals, winding in three to eight turns around the muscle fibers and ending in a finger-like process in the motor end plate of a fiber of an extrinsic eye muscle. Thin nerve fibers divide in two or more fibrils, encircling the muscle fibers in multiple spirals and ending in fine dots along a nucleus. These spirals might be present for proprioceptive sensations.

The histology of the ciliary ganglion is described by Pines.

Kiss observed in the ciliary ganglion: (1) multipolar cells belonging to the autonomous system, and (2) bipolar cells belonging to the sensory system.

Dewey finds only clefts in the orbital tissue containing lymph, but no true lymph vessels.

Israel describes the development of the cornea in human embryo.

Sondermann finds that the arching of the cornea is caused by pressure of the growing lens. Sondermann's opinion is that the corneal endothelium is of ectodermal origin. The ectodermal layer in front of the lens vesicle is split parallel to the anterior surface by fibers from the sclera.

Sondermann finds that Schlemm's canal develops from radial blood vessels which distend in circumscribed areas. These dilatations become connected by dilated capillaries and as the vessels obliterate, the dilatations form the circular canal.

Sondermann, in describing the development of the chamber angle, states that the corneo-scleral trabecular network is formed from the uvea and to a small degree from the sclera.

Development and histology of the dilator muscle is described by Speciale-Cirincione.

The development of the retina is studied by Cattaneo.

Seefelder observed that in a certain period of the development of the retina in the fetus, mitosis of cells stops and that in the new-born many more cells are present in the same area than in the later age.

Haden describes the development of the lamina cribrosa which first is glial and in a later stage mesodermal.

Fischer describes the budding-off of the lens from the ectoderm in embryos of 7 to 9 mm. length. The opening of the lens sac narrows gradually until finally the center of the junction separates or the outer ectodermal layer closes this part of the opening.

The Meibomian glands develop as ectodermal ingrowth from the inner part of the fused margins of the lids (Klee).

Iwata, Speciale-Cirincione contributed to the knowledge of the development of the lacrimal passages.

Tenon's capsule, which appears as mesodermal condensation with the insertion of the eye muscle, differentiates slowly from anterior posteriorly (Goldstein).

Fischer describes the development of the mesodermal layers of the eye.

Mann, Versari, Wolfrum report about the embryonal circulatory system of the eye (hyaloid artery and tunica vasculosa lentis) which disappear during the development.

Sondermann describes the development of the vascular system of the eye and finds in the early stage irido-scleral veins and lentico-ciliary veins independent of each other. The former form the anterior ciliary veins, and the latter the vortex veins. The arteries grow into the eye when the tissue pressure is the lowest and the veins grow out of the eye when the tissue pressure is the highest.

Studies of the fetal fissure and its closure are reported by Mann, v. Szily.

Hagedoorn contributes to the study of development of the eye.

Microphthalmos can be inherited: (a) dominant (Usher), (b) recessive (Macklin), (c) sex-linked (Ash).

Wessely reports about correlation of the growth of the eye and its adjacent organs.

Larsen and Osterlind found as causes of the senile miosis and rigidity of the pupil, depigmentation of the epithelium and stroma of the iris, hyaline and calcareous degeneration of the iris vessels, hyaline deposits between pigmentary epithelium and the sphincter and atrophy of the sphincter and dilator muscles.

Fine connective tissue fibers appear in the subendothelial tissue, the elastica thickens and the adventitia becomes hyaline in senile changes of the ciliary vessels (Fuchs).

Reichling and Klemens describe as senile change a newly formed connective tissue layer containing capillaries, between the pigmentary epithelium and Bruch's membrane, starting at the ora serrata and progressing posteriorly. They assume that the choriocapillaris becomes more permeable and the nutritional fluid changes its composition, stimulating the new formation of the tissue.

Loewenstein and McGregor find in scarlet-red stain of the retina lipoid granules in ganglion cells appearing with increasing age, and sometimes also a brownish pigment.

Kolen finds lipoid deposits starting in the tenth year of age in the cornea, sclera, ciliary body, Bruch's membrane and pigmentary epithelium. The fatty deposition goes parallel with such in other organs.

Jaensch believes that senile changes of the eye depend on heredity, but also environmental influences play a role.

Berens reports about the aging process in the eye and its adnexa.

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CHAPTER IV

GENERAL PATHOLOGY IN RELATION TO THE EYE

1. DEGENERATIVE PROCESSES AND DISTURBANCES OF METABOLISM

DEGENERATIVE processes are the result of disease and disturbed metabolism of the cell and tissue and of their wear and tear.

In *fatty degeneration,* the cell or the tissue is filled with a large fat droplet or many small ones. They consist either of neutral fat or lipoid. They are extracted in the usual fixation and staining methods of the tissue and holes remain. But fat can be easily stained by special staining methods. Thus, fat is stained red with Scharlach R or sudan III in frozen sections or the entire tissue is impregnated with osmic acid, embedded and sectioned and as a result fat appears as dark spots.

Fatty degeneration and fatty infiltration are distinguished. Neutral fats appear in large quantity in both. The cytoplasm normally contains fat in finest distribution fixed to the protein and is histologically invisible. In fatty degeneration, the fat appears freed from the cytoplasm in the form of droplets (fat phanerosis—visibility of fat). In fatty infiltration a pathologic change of the metabolism of the cytoplasm exists. More fat is taken in and hoarded than is normal.

Fatty degeneration is caused by toxins and deficiency of oxygen. Inorganic and organic poisons are responsible: for instance, phosphor, alcohol, bacterial toxins, metabolic products of the protein. Deficiency of oxygen appears in the venous congestion and in senile atrophy. Fatty plaques appear in arteriosclerotic arteries. Fatty degeneration is found in the cornea and sclera of old people, in corneal scars, in atrophic eyes, in different retinopathies (renal retinopathy, retinitis circinata). Fatty infiltration is caused by too great intake of fat and carbohydrate, further by disturbances of glands of inner secre-

tion, especially of the hypophysis. It is rarely seen in the eye itself, but chiefly in striated muscles.

If medullated nerve fibers degenerate by any cause—primarily in degenerative processes or secondarily by severing or inflammation—the myelin disintegrates in fatty droplets (wallerian degeneration).

Lipoidal degeneration. Lipoid and especially cholesterol are present invisibly in the tissue. If the tissue undergoes autolysis, cholesterol is freed and is visible in the tissue as needle-shaped crystals or flat plates. Cholesterol crystals appear in old hemorrhages, in hemorrhagic infarct, in dermoidcyst and cholesteatoma, which are both seen also as orbital tumors. In xanthomatosis, in various retinopathies, free cholesterol in the tissue can be surrounded by giant cells or is absorbed by phagocytes which appear in sections prepared by the usual methods filled with vacuoles (so-called foam cells). Lipoid is stored in the body in the reticulo-endothelial cells in certain diseases (lipoidoses) in which the lipoid metabolism is disturbed. To these belong Gaucher's disease, amaurotic family idiocy (Tay-Sachs) in which the ganglion cells of the retina are filled with lipoid, Niemann-Pick's disease in which lipoid is stored in inner organs and also in the retina, Christian-Hand-Schueller's disease in which foam cells are found in the bones of the skull and also in the orbit, in severe diabetes and obstructive jaundice in which xanthoma multiplex can be seen. Circumscribed lipoidal degeneration is seen in the eyelid as xanthelasma. Lipoidosis of the bulb exists if a larger amount of cholesterol is free in the aqueous humor and in the vitreous body (synchisis scintillans) or is fixed to cells (asteroid hyalitis).

Lipemia. In lipemia, fatty substances are increased in the circulating blood. Neutral fats are rarely increased, mostly cholesterol. The latter condition is called hypercholeresteremia. Lipoids in the blood are often increased in diabetes, chronic alcoholism and nephritis. The retina is mostly affected in this case. Fat globules can appear in the blood circulation from the bone marrow in fractures and can fill blood vessels and also occlude them (fat embolism), as in vessels of the retina and choroid.

Hydropic degeneration. In hydropic degeneration, clear fluid can accumulate in the cell through change of the osmotic pressure of the cytoplasm. This happens in the corneal epithelium in an increased intra-ocular pressure, in the pigment epithelium of the iris in diabetes, in the ciliary epithelium in inflammation or glaucoma.

Hyaline degeneration. Hyaline appears in the form of transparent substances in the tissue which stain intensively with acid dyes. Collagenous connective tissue of the blood vessels degenerates hyaline most frequently and appears homogeneously swollen. This happens especially in arteriosclerosis. The subendothelial layer and the media show homogeneous hyaline thickening in arteriosclerotic arteries. Scar tissue inclines to hyaline degeneration, especially corneal scars. Thrombi in blood vessels can be hyaline if the platelets degenerate hyaline and coalesce. Corpora amylacea which are found in the senile central nervous system and occasionally also in the optic nerve are hyaline spherical masses. They represent degenerated cells or excretory products of cells. Striated muscles can show in severe infectious diseases, especially in typhoid fever, hyaline degeneration (Zenker's degeneration). In this case, muscle fibers are necrotic, coagulate, lose their striation and appear as swollen homogeneous hyaline masses. It seems that the cell as well as the extracellular substance can degenerate hyaline, the cell nucleus as well as the cytoplasm.

Amyloid degeneration. Amyloid is a substance composed of protein and chondroitin sulphuric acid and appears as waxy and homogeneous masses compressing the original tissue. It stains mahogany brown with Lugol's solution and metachromatic pink with methyl violet. It is seen either as general or local amyloidosis, and is found often, chiefly in severe bone diseases, as in tuberculosis of the bones and joints or long-lasting suppurations of the bone, in severe suppurations of other organs, further in syphilis, malaria, dysentery, Hodgkin's disease. Localized amyloidosis is to be noted occasionally in eyelids, cornea, and especially in the conjunctiva, where it is found in cases of trachoma and in connection with intensive plasma cell infiltration.

Mucoid degeneration. Mucin is secreted normally by epithelial cells of the mucosa, as by goblet cells of the conjunctiva. The secretion is increased in inflammation and is combined with mucoid degeneration of the cell. Mucin is stained with basic dyes, metachromatic purplish with toluidin blue, and is precipitated by acetic acid. Not only epithelial cells, but also connective tissue can produce mucin (myxomatous degeneration). The connective tissue of the cornea can become gelatinous in certain degenerations and contain mucin. Connective tissue tumors can show mucoid degeneration sometimes (myxoma). Mucoid degeneration appears in undernourishment. The skin shows myxedema due to underfunction of the thyroid.

Calcification. Calcium is necessary for the life of the tissue and it is present in the cytoplasm histologically invisible. The normal calcium metabolism is regulated by vitamin D and the secretion of the parathyroid. In pathologic processes, visible quantities of calcium are deposited in the tissue in the form of calcium salts, mostly in the relation of nine parts calcium phosphate to one part calcium carbonate. They are deposited mostly in dying or dead tissue. Calcium is found in granules and clumps, circumscribed and diffused and is noticeable by its intensive blue staining with hematoxylin. Parathyroid deficiency leads to hypocalcemia and further to tetany and cataract formation.

The mechanism of the deposition of calcium is a double one: (a) fatty degeneration precedes. Fatty acids are formed which produce calcium soaps through intake of calcium. The fatty acids are finally substituted in these soaps by carbonic acid and phosphoric acid. Calcareous patches can develop in the intima of arteriosclerotic vessels, vascular thrombi can calcify, old tubercles appear calcified. (b) Calcium salts diffuse from living into less active or dying tissue. Under certain circumstances, Bowman's membrane can contain calcium. Calcium can be deposited in cataractous lenses and cyclitic membranes. The senile sclera can show deposits of calcium.

Both pathologic processes can be combined in the same tissue.

Gout. In gout, sodium urate is deposited in the tissue without known cause and is surrounded by necrosis (tophi). The disease

attacks mostly cartilage of joints and periarticular tissue. Deposits of uric acid are found occasionally in cornea and sclera, and tophi are seen in the eyelids. Gout may cause iritis.

Necrosis. Necrosis means changes of the tissue after it is dead but remaining in the living organism. If the tissue is observed in the state of dying, this state is called necrobiosis (stage between life and death). Necrosis is caused by occlusion of blood supply, by bacterial toxins, trauma, physical and chemical agents (as heat or cold), x-ray or radium, acids or alkalies. The cytoplasm of the necrotic cell is hardly stained and homogeneous and the cell boundaries are indistinct. The nucleus is dissolved and its chromatin diffuses (karyolysis) or the nucleus breaks up in fragments (karyorrhexis) or the nucleus shrinks to an irregular dense intensely stained mass (pyknosis). Necrosis is seen in the tissue as coagulation necrosis or liquefaction necrosis. In the first, the structural outlines remain, but the cytoplasm is coagulated and the nuclei show signs of necrosis or are gone. The tissue can finally calcify or polymorphonuclear cells enter from the circulation and absorb the dead tissue. In the latter, the dead tissue softens and changes into liquid material which slowly is absorbed. Cystlike spaces can appear, as we find them often in degenerated retinae. Severe injuries can lead to necrosis of parts of the eye and its adnexa. The cornea is necrotic in ring abscess; necrotic choroidal tumors are toxic and may cause necrosis of the uvea and cornea. Intra-ocular metallic foreign bodies like iron and copper can produce necrosis of the retina.

Caseation. A dry caseous granular amorphous mass remains from the original tissue in this form of necrosis. It is typical for tuberculosis and can be found also sometimes in syphilis. The caseous tissue does not attract polymorphonuclears, but can easily calcify.

Traumatic fat necrosis. Induration of the fat tissue may be produced by trauma. The necrotic fat cell appears opaque and as its content does not dissolve in the usual fixation fluid, it is cloudy in contrast to the normally empty appearing fat cell and is usually smaller. Usually, necrotic and inflammatory processes are mixed and, therefore, infiltration with inflamma-

tory cells takes place and foreign body giant cells appear. The traumatic fat necrosis might in some cases be the cause of traumatic enophthalmus.

Pathologic pigmentation. Pigments originate inside the body (endogenous) or enter the body from outside (exogenous). The endogenous pigments are (a) melanin, (b) lipochrome, (c) derivatives of the hemoglobin, (d) malarial pigmentation.

Increase of the melanin inside the body or the organ leads to melanosis. Decrease of melanin leads to albinism. Melanin is present in the form of granules in the basal cells of the skin, in the cells of the pigment epithelium of the eye, in the chromatophores of the uvea, in the hairs. It originates from the protein. The aromatic compounds of the protein, tyrosin, phenylalanine, and tryptophane can be transformed in dark dyes by oxidation. Certain cells contain an oxidizing enzyme, tyrosinase, which acts on the liberated compound and deposits melanin granules in the cell body. In the layer of the basal cells of the epidermis, cells are present which possess such a ferment and are able to transform a stainless aromatic compound of the blood into melanin. They are called melanoblasts. In the deeper layer of the stratified squamous epithelium are branched cells (Langerhans) which also possess this ferment. Melanin is structurally related to adrenalin and both derive perhaps from the same original substance. If the adrenal is unable to produce adrenalin as in Addison's disease, the original substance is exclusively transformed into melanin and abnormal pigmentations appear, as in the form of fine granules in the epithelium and subepithelial tissue in the conjunctiva, at the limbus and in the cornea. It is the opinion of some authors that connective tissue cells can overtake the pigment from the melanoblasts and in this way become chromatophores; they express the opinion that the pigment migrates from the pigment epithelium of the retina to the chromatophores of the uvea. This migration has never actually been seen in normal eyes, but one can see that the pigment in the uveal elements develops independently from the ectodermal element, as in the rests of the mesodermal pupillary membrane on the anterior lens capsule which normally has already disappeared during the embryonal life before the pigment epithelium reaches the pupil. Melanogen can be found

in the choroidal cells of the embryo with the method of Masson. The majority of the authors believe that pigmentation can take place in ectodermal and mesodermal tissue.

The "Dopa" reaction (Bloch) imitates the natural process of the formation of melanin. Dihydrooxyphenylalanine (shortened to "Dopa") reacts with an oxydase in certain cells with the formation of a dark stain. This reaction performed on frozen sections shows cells as melanoblasts when they are dark stained—"Dopa"-positive. Chromatophores are not stained with this reaction and are "Dopa"-negative. Another method to detect melanoblasts is the silver impregnation (Masson), in which the stainless mother substance (melanogen) is oxidized to melanin.

Melanotic tumors are nevus and malignant melanoma which both contain melanoblasts. If a malignant melanoma grows rapidly, pigment can enter the blood and appear in the urine. The pigment can appear stainless in the urine but darkens on contact with air by oxidation. It is thought that a pigment which is deposited in the rare disease, ochronosis, in large quantities in cartilage, muscles, skin, conjunctiva, and sclera also is melanin or a closely related substance. Most cases of ochronosis show alkapton in the urine (alkaptonuria).

Lipochromes. These are called the "wear-and-tear" pigments. They are formed in the protoplasm in the process of wear. They appear as brown granules in the cell body.

Derivatives of the hemoglobin. If hemoglobin is broken up in the course of the destruction of erythrocytes, it splits into an iron-free substance (hematoidin) and an iron-containing substance (hemosiderin). Hematoidin is identical with bilirubin of the bile. Hematoidin is deposited extracellularly in brown rhomboid crystals or amorphous granules in the surrounding tissues of old hemorrhages or stains the tissue, e.g., the sclera, diffusely yellow. This is the case if large numbers of erythrocytes are continuously destroyed (for instance in hemolytic jaundice). Hemosiderin is stained blue with potassium ferrocyanide and hydrochloric acid (prussian blue reaction for iron). It usually appears as brown crystals which are phagocytosed by histiocytes. It is formed in hemorrhages or hemolysis.

Malarial pigmentation. The malaria parasite inside the erythrocytes destroys them and produces a dark pigment from the hemoglobin (hemozoin) which may also be deposited in the conjunctiva. This pigment contains iron but does not give the prussian blue reaction.

Biliary pigmentation. Bilirubin is formed from the hemoglobin in the Kupfer cells of the liver. It is formed, as already mentioned, in excess in hemolysis. Bilirubin cannot be excreted from the liver if the bile passages are blocked and appears in great quantity in the blood (obstructive jaundice) and passes from here into the tissue. The sclera is also stained yellow in this case, as in hemolytic icterus.

Exogenous pigments. These enter the body through skin or mucosa and can be carried by way of the tissue-, lymph- and blood current. Substances entering the body are deposited as such or undergo first a chemical transformation and can be deposited as stained matter. Continuous occupation with silver, as in silver plating or in treatment with silver salts for a long time, may produce argyria. Silver is deposited in this case as albuminate in the skin, conjunctiva or posterior surface of the cornea (argyrosis). Iron and copper of intra-ocular foreign bodies diffuse through the fluids of the eye and are deposited in cornea, lens, ciliary body, or retina as brown substance (siderosis, chalkosis).

Postmortem decomposition. The destruction of the retina sets in rapidly after death due to postmortem softening from autolysis. The choroid and retina are soon detached. It is therefore necessary to fix the enucleated eye and biopsy material immediately after surgery. Cadaver material removed from the body many hours after death often shows many cadaverous changes in uvea, retina and optic nerve.

2. Abnormalities of Growth

Growth is brought about by multiplication of the cells. The less the cell is differentiated the more it is able to multiply. The nondifferentiated cancer cell multiplies readily, the highly differentiated nerve cell loses the power of reproduction.

Tissue culture. It is possible to remove tissue from the body, thus also tissue from the eye, and to let it grow in artificial medium. Corneal epithelium grows freely, but not so much the highly differentiated nervous tissue of the eye. On the other hand, frequently the anterior chamber of animal eyes is used as a bed for the implantation of foreign tissue where the latter often grows readily; such a procedure can be important for diagnostic purposes, as, for instance, in tuberculosis.

Melaplasia. Here tissue is transformed with change of the type. The columnar cylindrical epithelium of the tear sac may change under the influence of irritation or inflammation in stratified squamous epithelium. The nonhornifying epithelium of the cornea and conjunctiva may be transformed under circumstances in hornifying epithelium, as in avitaminosis or ectropion of the lid. The connective tissue of the lid may change into myxomatous tissue. Bone may be formed in striated muscle (myositis ossificans). In a chronically inflamed choroid and in a cyclitic membrane, fibrous tissue may change into bone.

Atrophy. Cell tissue or an entire organ may shrink and become atrophic. Senility, undernourishment, toxin, disuse, pressure, may be the cause. The skin of the lids loses its elasticity in old age and shrinks; the ciliary muscle and the iris stroma rarify. Undernourishment leads to disappearance of fat, so that lids and eye recede. Toxins and chronic infection lead to lack of glandular elements. If the normal function is missing, atrophy of disuse is present, as atrophy of the tear gland after removal of the tear sac. Pressure of a tumor on the optic nerve produces circumscribed atrophy of the nerve fibers at the place of pressure. Increased intra-ocular tension brings about degeneration of the nervous elements. If the nerve supply to a tissue is severed, neurotrophic atrophy sets in, as atrophy of the musculus orbicularis after severing of the facial nerve. The bulk becomes smaller in toto in severe chronic uveitis (atrophia bulbi).

Hypoplasia. Parts of an organ or entire organs do not develop fully. Microcornea, aniridia, absence of fovea, microphthalmos, are examples.

Anaplasia. This is the reversion of a more highly differentiated tissue into a less differentiated. In cases of defect in the tissue due to ulcer or injury, young fibroblasts are formed from connective tissue cells. In malignant tumors, nondifferentiated embryonic cells appear, as in carcinoma.

Hypertrophy. Hypertrophy means the increase in size of the individual cell or of the entire tissue, without increase of the elements. Muscle fibers become thicker the more the muscle is used.

Hyperplasia. By this we mean the increase in the number of the cells and of the tissue. Corneal facette is an example. In this case, a small defect of the corneal surface is entirely filled by a higher epithelium from increase of its cells. In irritation, but also without apparent cause, tissue can increase and thus hyperplasia merges gradually into neoplasm.

But the two expressions are often used interchangeably. We speak of a papillary hypertrophy as we occasionally find it in the limbus epithelium; actually, a papillary hyperplasia has appeared, the epithelium is much higher, and the papilla elongated, but the cell elements are not enlarged. Without doubt, however, both can appear at the same time that the tissue elements are increased in number and are enlarged.

Malformation. In maldevelopments, remnants of fetal structures may remain, which normally disappear. Pupillary membrane, tunica vasculosa lentis, or arteria hyaloidea may persist. Parts of an organ can be displaced during the development (heterotopia). Retina can be misplaced into the orbit if the fetal cleft remains open and an orbital cyst is formed, or the lens may be luxated by abnormal development of the zonule (congenital ectopia lentis). Local malformation takes place if grooves and fissures remain open which would normally close during the development. A well known example for it is the coloboma of the iris and choroid. If the nasal cleft remains open, both eyes may be united in the middle line to one eye, on which one can still recognize histologically the unification of two separate organs (cyclops). If twins develop and the formation of the one is arrested, this twin formation may remain in connection with the other otherwise normally developing twin, and

congenital teratoma is formed. From the second twin an indefinite mass remains, consisting of skin tissue, bone, cartilage, teeth or glands. Teratomata may also appear in the orbit.

3. Heredity and Constitution

Both heredity and constitution must be considered together, inasmuch as hereditary diseases on the one hand, and constitution and constitutional abnormalities on the other, are inherited in the germ plasma.

Heredity. Abnormalities can be inherited in families. Hereditary diseases are manifest at birth (congenital) or appear first during the extra-uterine life. The inheritance can be (a) dominant; (b) recessive; (c) sex-linked.

In dominant inheritance, an abnormal organ character (D equals dominant) is transmitted to the offspring. The rule is that this character is present beside normal qualities if, in such a mating, one of the parents is a normal individual (N). The offspring then contains dominant abnormal and normal characters (DN equals heterozygous individual). Such an individual shows the abnormal character inasmuch as this is dominant. If such a person has children with a normal individual (NN), according to the mendelian rule half of the offspring is affected and half normal. If two heterozygous individuals of a mating have children, part of these children will have only the abnormal character (DD equals homozygous). In this type of inheritance, the defect usually appears regularly in each generation. One parent is usually normal.

In recessive inheritance, the abnormal character (RR) is often covered and is transmitted as a latent condition. If mating of a person (RR) with a normal individual (NN) takes place, the heterozygous offspring (RN) is a carrier, but the abnormal quality is covered. Only if two heterozygous individuals of this group mate will a part of the children be homozygous (RR) and then the abnormal quality will become manifest in this group. In this type of inheritance, sporadically a defective child appears when both parents are apparently normal. If both parents are affected, then most of the children are also

affected. Therefore, marriage of relatives in this group would seem eugenically inadvisable.

In sex-linked inheritance, the abnormality is usually passed from the father to the daughter, who is recessive heterozygous. If the daughter marries a normal man, and has sons, then the sons show the abnormality, which is dominant in them.

One and the same disease may be dominant, recessive or sex-linked in different families. Thus, for instance, night blindness, aniridia, blue sclerotics, coloboma, microphthalmos, congenital cataract, are examples of dominant inheritance. Retinitis pigmentosa, anophthalmos, albinism, total color blindness, are examples of recessive inheritance. Leber's disease, and red-green color blindness are sex-linked, but the best known sex-linked disease is hemophilia.

Constitution. Constitution is the sum of hereditary physical and psychologic characteristics of the individual. It is influenced by the surroundings of the individual, which condition him. The congenital constitution and the conditions of the surroundings influence each other continuously from the beginning of the individual life. Heredity takes an important role in this interplay of influences. The constitution gives to an individual the ability to react to environmental stress and very often influences the result. It provides congenital immunities against certain diseases and, on the other hand, also susceptibilities which express themselves especially in allergies. The constitution may be abnormal and constitutional anomalies may be the etiologic factor in diseases. The "inborn errors of metabolism" and "abiotrophy" belong in this group. Thus individuals are seen having congenital alkaptonuria, which is associated with ochronosis with abnormal pigmentation on the body and also on the eye. Or we may see porphyrinuria, which leads to hydroa aestivale with affection of the lids and conjunctiva. Certain organs have a congenital imperfection and are prematurely worn out and age earlier than normally, as it is seen in presenile macular degeneration or presenile cataract, and also in Leber's disease.

Constitutional and environmental factors influence each other often. Weak external stimuli may produce disease if the indi-

vidual constitution permits a reaction and constitutional factors predispose to certain diseases (diabetes, gout, essential hypertension). Organs may show as expression of abnormal constitution inferiority. The inclination of the blue eye in heterochromia of the iris to iridocyclitis and cataract is well-known.

4. Circulatory Disturbances

Introduction: The Intra-ocular Blood Circulation and the Intra-ocular Fluid in Normal and Pathologic States

The eye has two circulatory systems independent of each other: (1) that of the uvea which is provided by the anterior and posterior ciliary vessels which communicate with each other; (2) that of the retina which is provided by the central retinal vessels. The intra-ocular arterial and venous pressure in both systems seem to be approximately equal, the arterial pressure surpasses by far the intra-ocular pressure, but the venous pressure only slightly and the pressure of the capillaries lies between both. The pressure in Schlemm's canal and the intrascleral efferent veins is slightly higher than the pressure in the anterior chamber, but in the extrascleral efferent veins it is about seven mm. lower than the intra-ocular pressure. The canal of Schlemm acts as safety valve if the intra-ocular pressure increases, in that if the pressure is lower in the canal than in the anterior chamber, intra-ocular fluid can easily enter the canal and flow from here into the intrascleral veins. If the intra-ocular pressure increases, first the pressure rises in the intra-ocular veins and is always somewhat above the intra-ocular pressure; this makes it certain that the intra-ocular blood circulation continues. The pressure in Schlemm's canal, which normally is somewhat above the intra-ocular pressure, remains now somewhat below it.

The intra-ocular blood circulation is ruled, as in the rest of the body, by nervous and chemical control. Vasoconstrictor nerves originating from the cervical sympathetic nerve can be followed to the vessels of the uvea. It is questionable if the retinal vessels also have vasoconstrictor nerves and apparently the eye does not have vaso-dilating nerves. But it seems that

the trigeminus innervates, by axon reflexes, dilatation of vessels. When sensory nerve fibers are innervated, the stimulus flows centripetally to the central nervous system and returns antidromically as axon reflex into the vascular nerve branches. With this, histamine-like substances seem to be liberated by changes of the cell metabolism and first cause the dilatation of the vessels. Substances formed in the metabolism of the body cause changes of the lumen of the blood vessels; e.g., vasoconstrictors such as the hormones pituitrin and adrenalin which act chemically, and the vaso-dilator histamine which is produced by tissue cells. Disturbances of the circulation in the body in general may produce also circulatory disturbances which appear in the eye, but the intra-ocular blood circulation is, like the blood circulation in other organs of the body, to a certain degree independent from the general circulation as the local circulation shows to some extent an independent activity of its own. The capillaries of the eye are relatively impermeable and the intra-ocular fluid is poor in protein, salts and other substances originating from the blood. If the capillaries become permeable by pathologic changes or dilated, colloidal substances enter more readily the intra-ocular fluid and, with them, also immune bodies.

The intra-ocular fluid contains more than 99 Gm. water in 100 cc. The small quantity of substances dissolved in it are protein, sugar, urea, organic acids and inorganic salts of sodium, potassium, calcium and magnesium and gases (oxygen and carbon dioxide). The fluid gives a slightly alkaline reaction. Immune bodies, such as agglutinins and hemolysins, are present in small quantity.

Changes in the permeability of the capillary wall and changes in the constitution of the blood lead to abnormalities of the intra-ocular fluid. If the permeability of the capillaries is increased, it contains more protein (plasmoid intra-ocular fluid) and also more immune bodies. Increase of the proteins of the blood increases the protein content of the intra-ocular fluid slightly, but the increase of the sugar and the introduction of other substances into the blood (e.g., acid dyes, drugs or salts) results in their passage into the intra-ocular fluid.

It is assumed that the intra-ocular fluid originates from the capillaries of the uvea and especially from those of the ciliary body. The origin of the fluid was chiefly studied by injections of dyes into the blood circulation and by observation of their appearance in the eye during life and in anatomic specimens. The origin was found in the ciliary body but also in the iris and choroid. The fluid is either (1) a dialysate of the capillaries, as the dialyzing semipermeable membrane is represented by the walls of the capillaries, or (2) a dialysate in which electrical potentials between the fluid in the chamber and the blood plasma play a role, as a difference exists in their polarity, the fluid being positive and the blood negative, or (3) a transudate which is formed by pressure filtration from the blood, or (4) a secretion formed by a secretory activity of the ciliary epithelium. There exists a circulation of the intra-ocular fluid inasmuch as it is continuously renewed and has a metabolism. It originates from the ciliary body under high pressure, undergoes pressure changes due to pulse beat, respiration and muscle action, is moved from the posterior chamber into the anterior chamber through the pupil and is excreted from Schlemm's canal under low pressure (pressure circulation). In the anterior chamber, there exists a thermal circulation, as the iris is warmer than the cornea and the fluid goes up along the iris and down along the posterior wall of the cornea. The intra-ocular fluid leaves the eye through the chamber angle and Schlemm's canal, and probably also through iris, ciliary body, vitreous body, optic nerve and peri-choroidal spaces.

Hyperemia is usually seen as active dilatation of small arteries, arterioles, and capillaries, which are filled with much blood. This active hyperemia is part of an acute inflammation. Toxins may act directly on the vessel wall and may produce relaxation of the smooth muscles of the vessel wall by vasomotor paralysis. Hyperemia is found in infiammations of the conjunctiva and the iris.

Venous congestion is usually seen as passive dilatation of the veins. This happens especially when a vein is obstructed. The obstruction can be acute or chronic. An acute obstruction is the sequela of thrombosis or of sudden compression of the vein

from the outside. The smaller veins, the venules and capillaries are very engorged by stasis and blood leaves them by diapedesis through holes or a rupture of the wall. If a vein is obstructed slowly by a chronic process, and collateral circulation exists, no hemorrhages appear and the collateral veins are dilated. Obstruction of the central retinal vein or its branches is always accompanied by hemorrhages, as no collateral circulation exists, but this is not the case in veins of the orbit, the lids and conjunctiva.

Ischemia is present in cases of acute or chronic obstruction of the arterial blood supply. Sudden closure of the artery takes place in embolism or thrombosis. The outcome depends on the existence of a collateral circulation which can readily assume the function. If the obstruction is sudden and there is no collateral circulation, necrosis sets in through anemia. The central artery of the retina is an end artery, and its closure is accompanied by destruction of the retinal layers which are supplied by it. Gradual obstruction, as it is produced especially through arteriosclerosis on account of a narrowing of the lumen by endothelial proliferation or prolonged arterial spasm, leads to atrophy of the supplied area where no collateral circulation is established.

Hemorrhage occurs when blood leaves the blood vessels for any cause and appears on the surface of the organ or in the surrounding tissue. Hemorrhage sets in through break of a vessel or blood passing through the unbroken wall (diapedesis). Hemorrhage may be spontaneous or due to trauma, and can reach different extensions. Spontaneous hemorrhage is produced through rupture of the diseased vessel wall due to atheromatous ulcer or aneurism, through damage of the endothelium by toxins in infectious diseases, by reason of obstruction of vessels, and, finally, by disease of the blood itself, as in leukemia or pernicious anemia. Hemorrhages are frequently seen in the conjunctiva, further in the retina and in the choroid, and sometimes in the orbit. The blood entering the tissue is removed partly by phagocytes; the erythrocytes break up, hemoglobin is set free and breaks up into hematoidin and hemosiderin. Hematoidin is deposited in the form of granules and crystals in the tissue; hemosiderin is usually taken up by phagocytes and is removed.

Thrombosis. A thrombus may be formed from the circulating blood, especially when the endothelium is damaged. Platelets adhere in masses on the injured vessel wall and liberate thrombokinase which inhibits the antithrombin present in the blood and produces thrombin from prothrombin under support of calcium salts. Thrombin is a ferment which changes fibrinogen into fibrin. Fibrin is deposited on the platelets and masses so formed together can finally obstruct the lumen. Erythrocytes and white blood corpuscles are deposited between the layers of fibrin and blood platelets. The thrombus can grow on both ends by apposition of these layers. If platelets and fibrin prevail in the thrombus, one speaks of a pale thrombus; if many erythrocytes are between the meshes of the fibrin, it is called a red thrombus. Frequently the thrombus is partly pale, partly red, and is called mixed thrombus. If the thrombus contains pathogenic bacteria, it is called a septic thrombus. A septic thrombus very often becomes suppurative and contributes to the propagation of the infection (pyemia).

Thrombosis takes place more frequently in veins than in arteries, as thrombi tend to form in the slower flowing blood. Stases of the current in itself can lead to thrombosis. The vascular endothelium can be damaged in arteries by atheromatous ulcer, but this happens infrequently. The endothelium is often injured by inflammation of the vessel wall and this frequently happens in veins (thrombophlebitis). If the outflow of blood in veins is obstructed, venous thrombosis takes place. The effect of the thrombosis depends mostly on the speed of the development of the thrombus and if the vascular area has collaterals. An aseptic thrombus is partly attacked by polymorphonuclears and absorbed, but mostly it is organized. Capillaries and fibroblasts besides lymphocytes grow in from the vessel wall and the thus newly formed tissue is transformed into dense connective tissue. The ingrowing capillaries may dilate, or channels may be formed in the fibrous masses and lined by new endothelium. In this way, the blood circulation may be opened again (canalization). Thrombosis can take place in the retina as well in the arteries as also in the veins, but more frequently in the latter, and is accompanied by severe changes through lack of collateral circulation. Thrombosis of

the central artery brings about ischemia of the retina; thrombosis of the central vein is accompanied by extensive hemorrhages of the retina. Sclerosis of the vessels is a frequent cause. The blood current is often slowed by thickening of the wall at the place of the arterio-venous crossing.

Embolism is a process in which a vessel is obstructed by a substance which is brought there from a distant part of the circulation. The substance is the embolus and is chiefly a part of a thrombus, but can also represent fat, tumor cells, clumps of bacteria and air bubbles. An embolus can come from vegetations of the valves of the heart in endocarditis, or from a thrombus in the auricle and ventricle of the heart, or from a thrombosed vein. If the embolus is septic, it can produce suppuration on the site of the embolism. This happens in septic retinitis and in cases of acute chorioditis. If the embolus is bland and obstructs the central artery of the retina, ischemic necrosis of the inner retinal layer sets in as no collateral circulation is present. We can compare this with the pale infarct of other organs such as heart or kidney, in which case coagulation necrosis sets in. But if anastomoses exist which can establish a collateral circulation, hemorrhages are formed from the dilated anastomotic vessels and the infarct is red. Similar pathologic changes happen sometimes in the choroid in case of obstruction or rupture of a posterior ciliary artery. Bone fracture is the most frequent cause of fat emboli; however, in osteomyelitis, burn of the skin, or suppuration of fat tissue, small fat particles can pass through the capillaries of the lung into the major circulation and produce fat emboli in arteries. It is mostly observed in cerebral arteries. Fat emboli can also appear in choroidal and retinal vessels and can be proved by special staining methods.

Edema represents abnormal accumulation of fluid in tissue spaces. Either free water or albuminous fluid is present. The tissue elements are, in edematous tissue, histologically separated by fluid which sometimes appears in fixation through coagulation as fine and granular. The cells themselves may become hydropic and swollen. The edema is either inflammatory, obstructive, cardiac, renal, angioneurotic, or produced by chronic

starvation. Edema sets in (1) if the wall of the capillaries becomes permeable for protein by toxic influence or lack of oxygen; (2) if the colloid osmotic pressure of the plasma protein decreases as in severe loss of albumin from the blood in albuminuria of nephrosis; (3) in increase of the capillary blood pressure as by occlusion of a larger vein or through venous congestion in cardiac failure; (4) in lymphatic obstruction, if lymph vessels are closed by parasites, inflammation, tumor, or after erysipelas. The edema may be general or local. Inflammations of the lid, conjunctiva or orbit may be accompanied by edema of the lid or chemosis. Lid edema is present in renal and cardiac edema.

5. Inflammation

Inflammation is the local reaction to an irritation; it is the effort to eliminate the irritant by a moving of migratory cells of mesodermal origin from the blood and tissue to the area of irritation. These cells represent the exudation, combined with a small or great amount of plasma, which produces fibrin and originates from blood- and lymph-vessels. The cells infiltrate the tissue spaces. Finally, also, fixed cells of the tissue proliferate and thus prepare for repair of the damaged tissue. The mesodermal wandering cells which move to the area of the irritation are mostly polymorphonuclear cells which have a phagocytic quality. They come chiefly from the circulation but also from the fixed cells of the tissue as it can be seen in the avascular cornea. These fixed cells are called resting wandering cells, but probably in the cornea many of these cells migrate from the marginal circulation. In this way, the exudate at the place of the irritation comes partly from the blood (hematogenous), partly from the tissue (histogenous). The irritant producing inflammation may be living or nonliving. Living irritants are bacteria and parasites, nonliving irritants are of physical or chemical nature. Of physical nature are injury, light, electricity, x-rays; of chemical nature are acids and alkalis and other substances.

The inflammation may be acute, subacute, or chronic.

In acute inflammation, vessels dilate and white and red blood corpuscles emigrate from veins and capillaries (diapedesis).

The polymorphonuclears pass through the wall by an active process in the form of ameboid movements and the erythrocytes are pressed through holes of the endothelium. The polymorphonuclears migrate through tissue spaces such as the interlamellar spaces of the cornea. The vessels dilate, capillaries are newly formed, endothelial cells of the vessels swell (especially by influence of toxins), their contact becomes looser and the vessel walls are more permeable. The blood circulation slackens and thrombosis can take place with subsequent necrosis of the surrounding tissue. The polymorphonuclears are attracted by chemotaxis to the irritant and can ingest in their cell bodies living and nonliving substances. In addition, fixed cells have the ability to phagocytose, especially the cells which belong to the reticuloendothelial system. But possibly also endothelial, epithelial and fixed connective tissue cells are able to phagocytose. Frequently in the exudate and infiltrate of inflammations, large cells with round nuclei are found, which are called macrophages and which represent the scavenger cells of the system. They remove tissue particles, erythrocytes, dead cells. If the substance which should be removed is too large, many macrophages flow together to form a cytoplasmic syncytium which represents a foreign body giant cell and appears as a very large cell with many nuclei.

Cells which can be found in an exudate of inflammation are (1) polymorphonuclear leukocytes, (2) eosinophil leukocytes, (3) mast cells, (4) lymphocytes, (5) plasma cells, (6) macrophages, and (7) giant cells.

The polymorphonuclears appear as round cells with lobulated nuclei of various shapes. They form the pus and are found mostly in acute inflammations. They fill the vessels at the site of the inflammation and are found extravascularly in large amount. They are attracted mostly by chemical influence (chemotaxis). The action of bacteria and their toxins, disintegrated tissue and foreign bodies is chemotactic. These polymorphonuclears are the microphages and can ingest bacteria. If they disintegrate, they liberate a proteolytic ferment which can dissolve dead tissue.

Eosinophil leukocytes are characterized by coarse eosinophil granules in the cytoplasm. They are found in large numbers

in the tissue in which a parasite harbors and in allergic conditions. They represent perhaps a reaction toward foreign protein.

Mast cells are rarely found. They contain coarse basophil granules and an indented polymorph nucleus and are found in subacute inflammations.

Lymphocytes have small, round nuclei and little cytoplasm. The nucleus contains chromatin in the form of dots which frequently have a wheel-like arrangement. They are found in chronic inflammations.

Plasma cells have a nucleus similar to that of the lymphocytes, which is situated peripherally in the oval cell. They probably grow out from lymphocytes and appear in chronic inflammation.

Macrophages are large monocytes and originate probably in the tissue from cells of the reticulo-endothelial system. They are also called histiocytes. They appear as large, round cells with relatively small nucleus and contain phagocytosed cells or diverse substances. They are the epithelioid cells of the tubercle, the large bladder cells of the retina in retinopathies.

Giant cells as a rule appear as very large cells with many nuclei around foreign bodies. They mostly originate by coalescence of many mononuclear cells. The foreign body giant cells are irregular in shape and their nuclei are different in size and irregularly arranged. However, they can accept a special form, as, for instance, the so-called Langhans giant cell which is characteristic for tuberculosis. These very large cells have oval nuclei in their periphery on one or both poles. Giant cells are found also in syphilis, sympathetic ophthalmia, chalazion.

Lymph collects in large amounts in the inflamed tissue. Capillaries are more permeable and albuminous fluid appears in the tissue and forms the inflammatory edema. Fibrinogen passes with the fluid through the vessel wall and coagulates to fibrin which appears as fine fibrillar network. In acute inflammation, the chamber of the eye may be filled with albuminous fluid and fibrin. The looser the tissue, the more intensive is the edema, as in the iris, suprachoroid, conjunctiva. The fibrin sometimes catches the infecting organisms and becomes the scaffold in which the regenerating tissue newly forms. Often it forms the precursor of adhesions, e.g., between iris and cornea as

anterior synechia, and between iris and lens as posterior synechia.

The inflamed tissue itself can show degenerative or destructive and proliferating processes. Toxins of bacteria may produce necrosis and the proteolytic ferments of the leukocytes may liquefy the destroyed tissue and form the pus. If the covering tissue also becomes necrotic and melts away, an ulcer appears. This happens in suppurative inflammation of the cornea. If the suppuration remains circumscribed in the tissue, an abscess is formed, which represents a cavity filled with pus. Its walls contain many polymorphonuclear cells and macrophages and frequently the connective tissue proliferates (pyogenic membrane). Abscesses are found in the lids, orbit and sclera. If an abscess breaks through toward the skin or mucosa, in the form of a sinus, a fistula appears. A suppurative inflammation of the periorbit can perforate through the lid. If the suppuration spreads through the tissue, the process is called cellulitis, which can be found in the orbit.

The histologic picture can be characteristic for a certain inflammation, so that we can conclude from it the nature of the infecting micro-organism, but in most cases it is nonspecific. The pneumococcus can produce an exudate of much fibrin and fluid, as it is found in the conjunctiva. In the beginning of the inflammation, gonococci are found intracellularly in epithelial cells and in polymorphonuclears, as in gonoblenorrhea. The bacillus diphtheriae produces an intensive necrosis and exudation of fibrin. If the conjunctiva is infected by diphtheria, its surface is covered by necrotic tissue mixed with much fibrin and polymorphonuclear cells.

Inflammations show different forms depending on the preponderance of one or the other tissue alteration, the nature and intensity of the irritant, the kind of affected tissue and duration of the inflammation. If only albuminous fluid is secreted, it is called a serous inflammation. Detachment of the retina may be produced if such a fluid is exuded beneath the retina. If much fibrin is produced, it is called fibrinous inflammation. Considerable fibrin can be found on the surface of the conjunctiva in certain types of conjunctivitis or in the

anterior chamber in acute iritis. Catarrhal inflammation is present if mucus-producing cells secrete mucus onto the surface of the tissue and epithelial cells are desquamated. This is found in some chronic conjunctivitides. Suppurative inflammation is characterized by presence of polymorphonuclears in the tissue with simultaneous necrosis and liquefaction of tissue. Membranous or diphtheritic inflammation is formed by surface necrosis with simultaneous production of fibrin. The necrotic material is bound by fibrin to the underlying tissue ("false membrane, pseudomembrane"). This can also happen in the conjunctiva, as already mentioned above.

The fibrinous and the diphtheritic inflammations form membranes on the surface of the mucosa. In the fibrinous inflammation, fibrin is deposited on the epithelium with leukocytes and other products of the exudate entangled in its meshes. In the diphtheritic inflammation, fibrin is poured into the necrotic cells of the epithelium and on its surface and is also filled with wandering cells. The membrane in fibrinous inflammation is easily peeled off, but in diphtheritic inflammation it adheres to the underlying tissue which forms granulations, and leaves a bleeding surface if pulled off with force. Often the former is called pseudomembrane and the latter true membrane, but inasmuch as sometimes the reverse terminology is employed, it would seem more accurate to speak of fibrinous and diphtheritic inflammation as forms of the membranous inflammation.

The various inflammations may take an acute or subacute course and appear suddenly, show several local and general changes and take a rather rapid course. On the other hand, they may show a slow onset, produce mild or severe local and general symptoms and take a protracted course, such as the serous and catarrhal inflammations.

Chronic inflammations appear in various forms. Much less exudation is present than infiltration and proliferation. The chronic inflammation may start from the beginning as a chronic inflammation or develop from acute inflammation that will not heal. Bacteria, virus, fungi, animal parasites, toxins, or foreign bodies may produce chronic inflammations. The chronic inflamed tissue frequently takes a specific form called

specific granuloma, as in tuberculosis, syphilis, sympathetic ophthalmia, leprosy and actinomycosis. In other cases, the histologic picture of the infiltration and proliferation is not characteristic and represents the nonspecific chronic inflammations. Inclusion bodies as expression of a virus infection are found in chronic conjunctivitides. Larvae and cysticercus as parasites may produce a chronic inflammation of the conjunctiva and the inner eye. Toxins are causes of chronic inflammation of the outer layers of the eye, the uvea and the retina. Intra-ocular foreign bodies cause chronic inflammation with proliferation of tissue. Glia cells proliferate in chronic inflammation in the retina and in the optic nerve, fibroblasts in other eye tissues. A productive fibrosis or gliosis is produced either by the stimulation of the inflammation, or a replacement fibrosis or gliosis in which connective tissue or glia substitutes the destroyed tissue. Mostly lymphocytes are found in the infiltration of chronic inflammation, further plasma cells in some of its forms, as especially in syphilitic lesions. Large mononuclears may be present. Histiocytes proliferate and may form epithelioid cells which are especially numerous in miliary tubercles. If histiocytes coalesce, giant cells appear. If an acute inflammation becomes subacute or chronic, eosinophils appear in large numbers. These are seen in vernal catarrh and in pemphigus of the conjunctiva.

Allergic inflammations appear in organisms developing hypersensitivity toward certain living or nonliving organic substances, if the hypersensitivity is not inherited. These substances form, after one or repeated intake, antigens which produce antibodies in the cells of the organism. If antigen and antibody meet inside the cell, a hypothetic hystamin-like substance is liberated which damages cells and tissue, producing anaphylaxis and inflammation. The inflammation is characterized by considerable exudate and necrosis of tissue. The anaphylaxis is a musculospasmodic reaction. Allergy is cellular, not humoral. If the organism is infected with bacteria and survives the infection, hypersensitivity toward these bacteria may persist. If the organism is reinfected with the same bacteria, or if enclosed

bacteria remaining from the original infection proliferate due to decreased resistance of the organism, a severe inflammation may set in if the tissue cells are sensitized toward these bacteria. We find this in tuberculosis. Ocular tissues can be sensitized experimentally toward protein and can suffer a severe allergic reaction. Instillation of tuberculin into the conjunctival sac of a tuberculosensitive patient can produce phlyctenules and keratoconjunctivitis. Chronic conjunctivitis may be produced by sensitization toward toxins of staphylococci and streptococci.

6. Repair

If a defect is produced in tissue, proliferation of cells and tissue is stimulated by chemical irritation. The more highly differentiated a cell is, the less readily it will proliferate; the less differentiated a cell is, the more readily it will proliferate. Nerve cells proliferate but little, connective tissue or glia cells proliferate readily. Highly differentiated tissue is, when destroyed, replaced by connective tissue. If a wound is set so that its margins are not dehiscent and it remains clean, healing by first intention or primary union will be accomplished. The wound is filled with plasma, fibrin, few blood cells, the vessels on the margin of the wound dilate and connective tissue and endothelial cells proliferate. The fibrocytes of the ripe connective tissue have but little cytoplasm and a small, rodlike nucleus. They are transformed into fibroblasts, the nuclei of which become oval and bigger and the cytoplasm of which becomes enlarged, with oval-shaped cells with processes resulting. The fibroblasts move into the defect filled with plasma and fibrin. They now start to produce collagenous fibers, which originate in the cytoplasm of the cell. The more fibers formed, the smaller becomes the cell body and the narrower the nucleus. The collagenous fibers form bundles and the fibrocytes separate. In this way, scar tissue is formed. Finally, the fibrous bundles shrink. The proliferating endothelial cells form buds in which always one endothelial cell lies opposite another one. These buds which enter between the fibroblasts open a lumen by separation of the endothelial cells and form vessels. As soon as the scar tissue

is formed, the vessels again regress. The epithelium of the surface immediately moves over the plasma and fibrin before the fibroblasts start their proliferation.

But if the defect in the tissue is large, healing by granulation sets in. The surface defect represents an ulcer which is covered with coagulated blood, fibrin, inflammatory exudate. The epithelium moves over it from the margin. From the bottom, young vascular granulation tissue grows upward, containing, besides fibroblasts and endothelial buds, migratory cells, which in the beginning are chiefly polymorphonuclears, later lymphocytes and macrophages. Finally the granulation tissue becomes organized. The fibroblasts produce more and more collagenous fibers, the vessels and also the wandering cells disappear and finally fibrous tissue remains. This process is called cicatrization.

The process of wound healing takes place in lids, conjunctiva and uvea in the above described manner. But the cornea is avascular, and wounds and ulcers can heal without participation of vessels. Fixed cells of the cornea move toward the wound filled with plasma and fibrin; they are transformed into fibroblasts forming collagenous fibers which are arranged into bundles and finally into lamellae.

An abscess can also heal by granulation, which forms a scar, filling the cavity entirely. If the cavity is very large, the granulation tissue forms dense fibrous walls around a cavity often filled with fluid. A thrombus, for instance, in the central retinal artery or vein, can also be organized in time. Fibroblasts grow from the wall of the vessel into the thrombus, accompanied by capillaries, and finally new connective tissue is formed.

Epithelium and connective tissue are soon completely repaired. Elastic tissue heals slowly. Descemet's and Bruch's membranes are slowly formed again. If fat cells are entirely destroyed, they are not replaced. The eye ball may sink in if the orbital fat disappears. Smooth muscles do not regenerate. Striated muscles if severed show proliferation of the sarcolemma with closure of the wound. Tendons are avascular and heal very slowly. Mucosa is formed rapidly and entirely. Nerve cells of the retina do not regenerate, but are replaced by glia. Fibers of the optic nerve do not regenerate and a glial scar is formed, but peripheral nerves are well able to regenerate.

7. Infection and Resistance

The body is invaded in infection by pathogenic micro-organisms or animal parasites, with a local or general reaction of the body resulting. The invasion is followed either by more or less acute inflammation or a slowly progressing chronic inflammation at the site of entrance or in distant areas. The entering organisms can be killed by leukocytes on the site, or remain there alive and perhaps produce a reaction later, or they may spread through tissue spaces and lymph vessels. The subsequent reaction depends upon the infecting organism, its virulence and the resistance of the patient.

The eye is chiefly infected primarily from the surface of the skin and mucosa, or secondarily by way of the blood circulation after the infecting organism has been taken in through the skin at a distant place or by inhalation or ingestion. The syphilis spirochete enters through the skin; tubercle bacilli establish themselves in the lungs after inhalation; parasites are usually ingested with food into the gastrointestinal tract.

There is also a normal bacterial flora on the surface of the conjunctiva consisting of Xerosis bacilli, staphylococci, pneumococci in individual variation. These saprophytes can become parasites under certain circumstances.

The bacteria entering the tissue in infection can be fixed locally at the port of entrance or can progress into the deep tissues. The local fixation depends on several factors: bacteria can be caught in exuded fibrin or the infected organism possesses immunity, in which case the bacteria are clumped together by antibodies (opsonins and agglutinins), are retained at the point of entrance and can be eliminated relatively easily by phagocytes. On the other hand, bacteria may possess tissue-dissolving substances which facilitate their progression into the tissues.

If bacteria circulate in the blood, they enter the tissues (depending on the permeability of the capillaries). If the tissue is damaged, the capillaries, being dilated, allow blood and bacteria to pass easily through their walls. The entrance area of the bacteria into the body is called the primary focus, and the production of a secondary infection in distant areas the focal infection. For instance, the tubercle bacillus is inhaled

into the lungs, producing there a primary lesion. If tubercle bacilli enter the blood circulation from this focus and are deposited in the choroid, a focal infection is formed here. The focal infection depends partly upon the infecting organism which has a predilection for a certain localization (such as the tubercle bacillus for the uvea), and upon local conditions of the tissue which favor the deposition of the bacteria.

In pyemia and septicemia, bacteria circulate in great quantities in the blood, frequently originating from infected thrombi. The patient is severely sick, has chills and high temperature and petechiae of the skin. The bacteria stop in various organs, forming small and large abscesses, as in liver, kidney, lungs, heart. The bacteria are brought into the eye either through the central retinal artery or ciliary arteries and infect choroid or retina, forming acute choroiditis or septic retinitis with the same end result in their further course; namely, endophthalmitis or panophthalmitis. This can be the case in meningococcemia, puerperal sepsis, or sinus thrombosis.

In toxemia, bacteria remain fixed at the point of entrance but their toxins enter the blood circulation and damage distant organs, such as liver, kidney, heart. The eye also can be affected by toxins, e.g., choroiditis can be produced by the toxins of the tubercle bacillus.

Resistance of the body against infection depends: (1) on antibodies, (2) phagocytosis, and (3) tissue immunity. The antibodies are (a) antitoxins, which neutralize the toxins of the bacteria; (b) bacteriolysins, which attack the bacteria themselves and destroy them by lysis; (c) opsonins, which sensitize the bacteria so that they can be ingested by phagocytes; (d) agglutinins, which clump the bacteria, and (e) precipitins which precipitate soluble foreign proteins.

Phagocytes are polymorphonuclears and macrophages of the tissue which originate from the reticulo-endothelial system. This system is represented especially in liver, spleen, bone marrow, but also in the eye.

If there is tissue immunity, toxins or bacteria cannot find affinity to cells and cannot damage them, or are destroyed by antibodies immediately. The immunity as a whole can be general

immunity in which the entire organism is resistant against a certain infection or local immunity in which a circumscribed area of the body cannot be infected, e.g., the skin. Immunity is natural or acquired. The acquired is either active or passive, depending upon whether the individual has produced his own antibodies or received them as serum injections.

The immunity of the eye is minimal, as the capillaries are relatively impermeable and antibodies enter the aqueous humor with difficulty. Dilatation of the capillaries in inflammation, or after paracentesis of the cornea, facilitates their entrance into the aqueous humor. Antibodies are found experimentally in the aqueous, and even in the avascular cornea in active immunization.

8. Bacterial Infections

Two groups of bacterial infection are to be distinguished: (a) those bacteria affecting the eye directly and producing local inflammation, as is the case in many conjunctivitides and keratitides, or entering at the eye and producing generalized symptoms in addition to local symptoms as in tularemia; (b) those affecting other parts of the body first, and the eye and its adnexa secondarily in direct continuation or by way of the lymph current or blood circulation. Further, there are many bacteria which infect the eye directly and by way of the blood circulation, as, for instance, the gonococcus, which can be transmitted from the genitalia to the eye by the hand, producing severe conjunctivitis, or can enter the eye by way of the blood circulation, causing severe uveitis.

The bacteria found in eye infections, in the majority of cases in conjunctivitis, can, with sufficient certainty, as a rule be classified without special culture in simple staining methods such as staining with methylene blue or Gram's stain.

Staphylococci are found frequently in blepharitis. They are often saprophytes, but can also produce suppurative inflammation. Various types of staphylococci are distinguished according to the color which appears when they are cultivated on agar, and on their ability to dissolve blood on blood agar. They are gram-positive cocci appearing in irregular clusters.

Streptococci are gram-positive, growing in small or long chains. Depending on their ability to dissolve blood on blood agar, they are distinguished as hemolytic and nonhemolytic. The hemolytic streptococci are dangerous for the eye, especially if they enter it in perforating injury or in septicemia. They can produce by their exotoxin a severe conjunctivitis. Erysipelas is an acute inflammation of the lymph vessels of the skin caused by hemolytic streptococci and can be found also in the eyelids. Lymphocytes and monocytes usually appear in the subcutaneous tissue. Streptococci are found in infected apical granulomata, puerperal sepsis, endocarditis. The organisms can be carried from these lesions into the eye, producing severe suppurative inflammation which frequently affects cornea and conjunctiva.

Rheumatic fever is thought to be caused by streptococci. As acute or chronic disease, it especially affects fibrous tissue. Hypersensitivity of the organism to streptococcal infection or to autolytic products of the bacteria may play a special role. The characteristic lesion of the rheumatic infection is the Aschoff body which appears in typical form in the interstitial tissue of the myocardium. It contains (1) large epithelioid cells, many of them multinucleated, which probably are derived from the reticulo-endothelial system; (2) lymphocytes and plasma cells; (3) proliferating fibroblasts which lead to fibrosis, and (4) in the center, necrotic material. The pharynx and the tonsils seem to be the port of entrance for the infection where rheumatic nodules are found in the acute stage. Rheumatism, in which sometimes exudation, sometimes proliferation prevails, often affects the eye and produces especially acute iridocyclytis and scleritis.

Pneumococcus (Fraenkel) or diplococcus pneumoniae is lance-shaped, gram-positive and is often found in the normal conjunctiva. It causes severe conjunctival suppuration and is associated especially with dacryocystitis.

Gonococcus (Neisser) is a gram-negative diplococcus which is found typically intracellular in polymorphonuclears, but proliferates also on epithelia. It produces especially severe suppurative conjunctivitis.

Meningococcus (Weichselbaum) is also gram-negative and is found intracellular. It occasionally affects the conjunctiva, but produces also metastatic ophthalmia in cases of meningococcic meningitis.

Sarcina is characteristically arranged to four spherical cocci. It is found in the conjunctiva and is usually not pathogenic.

Diplobacillus of Morax-Axenfeld is a gram-negative relatively thick and short bacillus, two of which are enclosed in a capsule. It grows in the normal conjunctiva and produces especially angular eczema with conjunctivitis.

Bacillus Koch-Weecks is a gram-negative, slender rod, producing epidemics of acute conjunctivitis by contact infection.

Bacillus diphtheria (Klebs-Loeffler) is a fine rod with thickened edges. It frequently shows spores and produces a virulent exotoxin which has strong affinity to nerve fibers. It produces necrosis of the superficial layers of the conjunctiva. It enters the conjunctiva by autoinfection, usually from other infected areas of the body, especially from throat and nose.

Xerosis bacillus is gram-positive and granular and proliferates on desquamated epithelial cells. It is found in great numbers in xerosis of the conjunctiva.

Bacillus subtilis is gram-positive and is found occasionally as saprophyte in the conjunctiva. It can sometimes produce very severe intra-ocular inflammations (ring abscess or panophthalmia).

Bacillus anthracis is a gram-positive, thick rod, forming malignant anthrax edema of the lids. It is transmitted from animal to man by infected wool, skins, brushes.

Bacillus pyocyaneous can produce membranous conjunctivitis and corneal ulcers, but often grows on the normal skin.

Bacterium tularense is gram-negative and small, and produces severe conjunctivitis and lymphadenitis (preauricular, submaxillary and cervical) with necrosis, suppuration and ulceration. It is transmitted from a rodent.

The tubercle bacillus, a thin rod, sometimes beaded, produces a chronic, specific infective granuloma. The bacillus is acid-fast, difficult to grow on culture media and difficult to stain in the

tissue. It can grow on potatoes. The bacillus can be demonstrated by special staining method (Ziehl-Neelsen), occasionally from the secretion of an ulcer of the conjunctiva. It can be demonstrated by injection into guinea pigs in which it produces caseated lymph nodes and specific granulation tissue.

Tuberculosis is characterized in the tissue by formation of typical tubercles, which show (a) lymphocytes, (b) epithelioids, (c) giant cells of Langhans type, and (d) caseation. These structures have a characteristic arrangement, as the lymphocytes are peripheral, surrounding epithelioid and giant cells and caseation obtains in the center. This type of reaction of the body is the proliferative one. The bacillus rarely infects by contact, as by way of the conjunctiva where it produces a primary infection. Nearly always it enters the body by inhalation of infected dust or droplets. It establishes itself in bronchi and lungs and regionary lymph nodes, or enters by ingestion through the gastrointestinal tract by drinking of infected milk and establishes itself in the regional abdominal lymph nodes. From these primary foci, the eye is infected secondarily through the blood circulation, and thus conjunctiva, uvea, retina, optic nerve and orbit can be affected. The bacillus is carried away from the site of infection (1) by phagocytes, with spread to the regional lymph nodes; (2) by spread along natural passages, as from conjunctival ulcers by way of the canaliculi into the lacrimal sac; (3) very frequently by passage through the lymph vessels into the regional lymph nodes, especially the bronchial lymph nodes, where it is arrested or from where it infects, through the capillaries, the blood circulation and thus distant organs; (4) or by massive outpouring into the blood circulation when the wall of a larger vessel is affected by the tuberculous process. If the eye is affected by tuberculosis, in the majority of cases there is a primary lesion in the lungs which usually appears healed. The primary lesion of the lungs develops as a small caseous focus, mostly in the periphery of the lower lobe, frequently subpleural. A chain of tubercles extends from the primary lesion to the regional lymph nodes. This lesion heals with fibrosis and calcification but enclosed bacilli can survive for a considerable time. Allergy toward the product of the

bacillus (tuberculoprotein) and immunity against the living bacillus can develop in such persons. Bacilli can enter the blood circulation from time to time from the primary lesion and can be deposited in the eye, especially if the eye is made sensitive by injury or intercurrent disease. Less frequently, an individual with a primary lesion is reinfected if his immunity has disappeared or is broken down by massive new infection (reinfection occurs especially in the lungs, but also in other organs) and bacteria are poured into the blood circulation from these foci. If tubercle bacilli enter a nonimmune organ, first polymorphonuclears appear which phagocytose the bacilli but do not kill them, and later monocytes appear which originate partly from the histiocytes and partly from the blood. They change into epithelioid cells, perhaps under the influence of lipoids which are liberated from phagocytosed and destroyed bacilli. The epithelioid cells often form a syncytium through their anastomosing cell processes. Confluent epithelioid cells form giant cells with numerous nuclei peripheral and a caseous substance in the center. Lymphocytes surround the epithelioid and giant cells. Bacilli, especially those enclosed in the caseous material, to the extent that they are not destroyed are carried away by phagocytes into the periphery of the tubercle and cause here new proliferation and tubercle formation. The tuberculous granulation tissue is avascular and the absence of vessels apparently is the cause of the caseation. The softening and liquefaction of the caseous substance facilitates the increase of the bacilli. In contrast to this proliferative inflammation, there is the exudative reaction which sometimes can be observed in the eye also, in which only polymorphonuclears and fibrinoserous fluid appear. This happens especially as an allergic reaction against tuberculoprotein or in reinfection. The bacilli can spread rapidly in the latter case and form tubercles if they are only slightly virulent and extensive caseation if they are very virulent.

The leprosy bacillus, an acid-fast bacillus, resembles the tubercle bacillus. It does not grow in culture media and is not infectious for animals. The mode of infection in man is unknown. The bacilli form a chronic specific granulation tissue in which large mononuclear cells with foaming cytoplasm are

prominent (lepra cells). These cells are loaded with bacilli-producing lipoid which causes the foamy appearance. These cells can aggregate into multinuclear giant cells. The infected tissue shows lymphocytes and proliferation of connective tissue and blood vessels. Finally, fibrosis sets in. The granulation tissue appears nodular (nodular or tubercular type) or grows in the nerve sheaths (anesthetic or nervous type). Leprosy bacilli are also found in lepers with otherwise normal eye tissues, but frequently they are found in lesions of the cornea, sclera and uvea.

Spirochaeta pallida (treponema pallidum) causes syphilis. The spirochete is a delicate, very motile spiral-like formation, best seen in dark field illumination. It can be shown in smears with Giemsa stain or by india ink and in tissue by silver impregnation. It grows in culture media and animals can be infected experimentally. The spirochete which cannot penetrate the intact skin can enter the mucosa. In the area of the inoculation, the primary lesion is established. The spirochete enters perivascular lymph spaces and produces reaction here. Lymphocytes and plasma cells accumulate and the endothelium swells after a latent period of three to four weeks following the inoculation, forming the primary lesion (chancre). Dense infiltration of the connective tissue is noted, especially perivascularly with lymphocytes and mainly with plasma cells, proliferation of fibroblasts, intensive vascularization. The endothelial cells of the vessels swell and proliferate, sometimes obliterating the lumen. The surface epithelium desquamates and a shallow ulcer is formed. The tissue fluid contains numerous spirochetes. The regional lymph nodes show diffuse hyperplasia and contain spirochetes in large numbers. The disease heals locally, but the spirochetes are already poured into the blood circulation and after a latent period, in which the spirochetes infect without clinical symptoms nearly every organ, local reactions in various organs appear. The skin especially is affected, but also mucosae such as the conjunctiva, further inner organs as the uvea (iritis), the optic nerve and eye muscle nerves as part of a generalized infection of the central nervous system, bones and joints and the lymph nodes of the body (secondary lesions). These lesions can consist of small nodules containing epithelioid and giant

cells. They heal without necrosis and without scars but spirochetes produce recurrent lesions in other parts of the body again and again. A long, quiet period follows after the cessation of the secondary lesions. Finally, tertiary lesions appear which contain only few spirochetes and which are seen (a) as circumscribed reaction (gumma) or (b) as diffuse inflammation. The gumma consists partly of necrotic tissue in which tissue structure and destroyed cell nuclei are seen as shadows. The necrotic tissue is surrounded by proliferating fibroblasts, lymphocytes and plasma cells and numerous blood vessels are present, showing peri- and endovasculitis. The gumma is considered as an allergic phenomenon due to changed reactivity of the tissue. Gummata can be found in the lid, conjunctiva, uvea and optic nerve. The diffuse, chronic inflammatory reaction appears in the form of accumulations of lymphocytes and plasma cells, frequently perivascular with degeneration of the parenchyma and its substitution with fibrous tissue. The cardiovascular system is frequently affected, as is also the central nervous—the meninges in the form of syphilitic meningitis, the cerebrum in the form of general paresis of the insane and the spinal cord in the form of tabes dorsalis. Optic atrophy, affection of eye muscle nerves and pupillary disturbances are often accompanying symptoms. Congenital syphilis is transmitted from father or mother to the child. It does not show primary lesion but secondary and tertiary lesions. The latter affect the eye in the form of gummata or diffuse inflammation. The cornea especially is diffusely inflamed in interstitial keratitis which is also considered as an allergic reaction; further the uvea and retina in various forms of chorioiditis and retinitis.

Mycoses are caused by higher fungi. They frequently produce granulation tissue in the affected organ. The eye, and more frequently its adnexa, are sometimes the seat of this disease. Organisms of this group affecting the eye are streptothrix (actinomyces), leptothrix, sporotrichum, rhinosporidium, blastomyces; rarely trichophyton, thrush and favus.

Streptothricosis is caused by streptothrix, a filamentous fungus with branchings which is gram-positive and anaerobic. A special form is actinomyces bovi (Ray fungus), showing radiate

arrangement of the threads with spores and club-shaped bodies at the periphery. The nodular lesion caused by these fungi shows histologically accumulation of polymorphonuclears around the colonies of the fungi and, distant from them, fibroblasts, epithelioid- and giant cells with lymphocytes in between. The fungi probably enter through cracks of the epithelium and produce local lesions which rupture into blood vessels, causing spread of the infection through the blood circulation. Streptothrix proliferates in lacrimal canaliculi, producing mycotic canaliculitis, and grows also in the conjunctiva. Actinomycosis affects especially the periosteum.

Leptothricosis is caused by leptothrix, a filamentous organism with spores, but without branchings. A granulation tissue is formed around the fungus which consists of polymorphonuclears, fibroblasts, epithelioid and giant cells. It affects the conjunctiva.

Sporotrichosis is caused by sporotrichum which grows in culture medium as branching mycelia. Its gram-positive spores are found inside of macrophages of the granulation tissue which contains histiocytes and giant cells and polymorphonuclears in small abscesses. Lid, skin and conjunctiva can be affected.

Rhinosporidiosis is caused by rhinosporidium seeberi, producing a polypoid granulation tissue. It consists of connective tissue with fibroblasts and lymphocytes into which stratified epithelium proliferates from the surface and which contains numerous cysts representing the organism which can grow out to enormous size. The cysts contain many nuclei and spores. Tear sac and conjunctiva are affected.

Blastomycosis is caused by blastomyces which belongs in the group of yeastlike fungi. The spherical organism is characterized by clear double contour and budding. It produces granulation tissue consisting of lymphocytes, monocytes and giant cells which contain the organisms in large numbers. Lid, skin and conjunctiva are affected.

Thrush is caused by oidium albicans (monilia albicans), a yeastlike organism which affects adults only in a state of extreme debility. It produces proliferation of lymphocytes and monocytes, occasionally of polymorphonuclears. Lid skin and rarely conjunctiva can be affected.

Trichophyton grows in branching threads on epithelial cells and brings about infiltration with plasma cells. It grows on the lid skin and rarely on the conjunctiva.

Favus is caused by acherion schoenleinii and is related to trichophyton. Branching mycelia grow in large numbers on the epithelium and destroy hair follicles. Eyebrow and lid skin and infrequently the conjunctiva are affected.

Virus diseases. The viruses are filtrable ultramicroscopic infectious agents. Filters which retain bacteria let them pass and the filtrate inoculated produces disease. They cannot be seen in the ordinary microscope except in their large forms (elementary bodies), but they can be made visible in the ultramicroscope in which otherwise invisible particles can be seen as they scatter light in intensive illumination or they can be brought to visibility in ultraviolet light photography. They can be brought to visibility also in the electron microscope. Viruses do not grow in culture media but only on living cells. They are considered as very small organisms which can ingest only as parasites already digested nutriment from the host, but they are also thought of as inanimate proteins. Perhaps they represent a stage between living and nonliving formations. Viruses produce specific inclusion bodies situated in cytoplasm or nucleus (cyctoplasmic or intranuclear inclusion bodies). The inclusion bodies are spherical, oval, or irregular, acidophilic or basophilic, homogeneous or granulated, and are somehow in relation to the organisms of the virus if they do not actually represent the organisms themselves. There is discussion as to whether the inclusion bodies actually represent viruses, or specific changes of the affected cells due to the activity of the viruses, or disintegrated phagocytosed bacteria. Viruses produce immunity, especially a cellular one. It seems that the virus stays fixed to the cell and that therefore reinfection is not possible. Viruses produce cellular changes in the form of hyperplasia or degeneration. Hyperplasia is seen in molluscum contagiosum, degeneration in herpes. These primary changes are followed by secondary inflammatory changes. Frequently lymphocytes and monocytes appear, rarely polymorphonuclears. Viruses usually attack only a certain cell type or certain tissue. The epithelium of the skin is affected in

smallpox or molluscum contagiosum (dermatropic type), the nervous system and especially ganglion cells in herpes zoster or poliomyelitis (neurotropic type), glands in mumps (glandular type).

Viruses affect the eye and its adnexa primarily or secondarily when other organs or the entire body is infected by virus; e.g., in virus affections of the central nervous system, besides other nerves and nuclei the optic nerve and eye muscle nerves are also affected. Virus infections affecting the eye are trachoma, inclusion blennorrhoea, follicular conjunctivitis of swimming baths, herpes, molluscum contagiosum, smallpox, poliomyelitis, measles, influenza.

In trachoma, basophilic inclusion bodies are found in scrapings of the conjunctival epithelium stained with Giemsa; they are found in the epithelial cells close to the nuclei as large granular, spherical formations (trachoma bodies, Halberstaedter-Prowazek corpuscles). They are called chlamydozoa, as they are surrounded with an envelope of clear substance. These granular formations contain peripherally duplicated bodies (initial corpuscles) and centrally simple bodies (elementary corpuscles). When the cell breaks up, these bodies become free.

Inclusion-body conjunctivitis (inclusion blennorrhoea of the new-born) and follicular conjunctivitis of swimming baths also show basophilic inclusion bodies similar to trachoma.

Herpes appears in two different forms, as herpes simplex and herpes zoster. It is characterized by acidophilic inclusion bodies in the nucleus which are homogeneous or granular and are surrounded with a clear zone (Lipschütz bodies). They appear in the epithelial cells of the conjunctiva and cornea and in the nervous cells of ganglia and of the central nervous system. Perineuritic round-cell infiltration can appear. Also uvea and eye muscle nerves are affected.

Molluscum contagiosum shows large acidophil homogeneous inclusion bodies, which enlarge enormously the affected epithelium cells and usually push the nucleus to one side (molluscum bodies). The epidermis of the lid skin is affected, with the epithelium first proliferating and later degenerating and chronic conjunctivitis of long duration as the sequela.

In smallpox (variola), spherical homogeneous acidophilic inclusion bodies appear in the cytoplasm of the epithelial cells of the skin (Guarneri bodies). The lesion of the skin starts with papules which in a few days become vesicles which soon are converted into pustules. Lid skin and lid margin are affected primarily and conjunctiva and cornea secondarily. Similar lesions arise in vaccinia.

Poliomyelitis has intranuclear inclusion bodies in motor cells of the central nervous system. Also eye muscle nuclei can be affected.

Rickettsial diseases. Rickettsia are gram-negative, intracellular, minute organisms which are found in arthropoda (lice, ticks, bugs). They are transmitted from those onto humans. Typhus fever, for instance, which also produces eye symptoms, is caused by rickettsia prowacecki. Rickettsia are also described in the epithelial cells of the conjunctiva in trachoma.

9. Animal Parasites

Animal parasites affecting man and producing also eye symptoms can be grouped as: (a) protozoa, (b) worms or helminthes which appear as (1) nemathelminthes or roundworms and (2) as platyhelminthes or flatworms, and (c) arthropoda.

Protozoa producing eye symptoms are (a) plasmodium malariae, (b) Leishmania and (c) toxoplasma. Plasmodium malariae is transmitted to men by the bite of an infected anopheles mosquito. It injects with the bite rod-shaped parasites (sporozoites) into the blood circulation. They enter erythrocytes and change here to round forms consisting of cytoplasm and a peripheral nucleus. They ingest hemoglobin from which they produce dark brown pigment granules (malaria pigment). Their nucleus splits by asexual partition into 18 fragments forming a rosette. This breaks up and around each nuclear fragment cytoplasm collects, and 18 new cells are formed (merozoites) which are discharged freely from the erythrocytes into the blood current. Each merozoite enters a new erythrocyte and the process repeats. Between the merozoites there are always some which are transformed into sexual cells (gametocytes) which are male and female. If these come into the stomach of a female

anopheles, then from a male gametocyte oblong formations are detached (male gametes) and the female gametocyte loses nuclear chromatin and becomes a female gamete. A male gamete enters a female gamete and the impregnated cell becomes after the conjugation a zygote, which perforates the epithelium of the intestine of the host and forms a cyst, in which the cell nucleus divides in hundreds of rodlike bodies (sporozoites). These are carried into the salivary gland of the mosquito and if this bites a man, they enter the blood circulation of the human host. Malaria produces anemia of high degree by destruction of numerous erythrocytes. The eye can be affected in malaria, as malaria pigment is deposited in the conjunctiva and blood vessels of the uvea and retina.

Leishmania is a flagellate, but under certain circumstances loses its flagellum and is transformed into an oval cell with two nuclei. The flagellate form is found in insects which have bitten an infected man, the oval form (Leishmania form, Leishman-Donovan bodies) is found in man free in the tissue or in swollen macrophages. The parasite is deposited in the skin of the face and produces the tropical sore (Delhi sore, Aleppo boil) and affects the conjunctiva.

Toxoplasma, the classification of which is still in discussion, is related to the plasmodia and is found as a spherical body in reticulo-endothelial cells and leukocytes, in the blood and spleen of man, and produces spores. It causes toxoplasmic encephalomyelitis and chorioretinitis.

Of the nemathelminthes (nematodes, roundworms), the following are of importance: (a) filaria, (b) Dracunculus medinensis, (c) Onchocerca volvulus, (d) thelazia callipoeda, (e) Habronema, (f) Ascaris lumbricoides, (g) trichina spiralis.

Filaria (threadworms) live as adult worms in the lymphatic system and their larvae circulate in blood vessels (microfilaria, filaria sanguinis hominis). The male and female live together and the ova develop in the uterus into larvae which enter the blood circulation. They are ingested from here by an insect (mosquito, fly) when it bites the infected man and develop to maturation inside of the insect. If the insect bites a man again, it injects the parasite into him; sexual development is obtained then in the human host and reproduction takes place.

Filaria loa (filaria oculi) is found in West Africa. Its intermediate host is the Mangrove fly (chrysops). It sucks during the day and the larvae are thrown into the blood circulation during the day (microfilaria diurna). Filaria bancrofti is found especially in China and India. Its larvae enter the blood circulation during night (microfilaria nocturna) as the mosquitoes bite only at night. Filaria inermis (filaria palpebralis, filaria conjunctivae) is found in Southern Europe. There are no microfilaria present in the blood. If Filaria bancrofti block lymphatics, elephantiasis appears, which may occur also in eyelids. Filaria loa can be situated subconjunctivally and produce inflammation. Filaria inermis forms small cysts in the subconjunctival tissue. But filaria can also affect the inner eye and be situated in anterior chamber, lens, vitreous body, and subretinal space. They are either tolerated without irritation or produce inflammations like keratitis and iridocyclitis.

Dracunculus medinensis (filaria medinensis, vena medinensis, guinea worm) is found in Africa, India and South America, and its intermediate host is a crustacean (cyclops). The male is small, the female very long and consists nearly exclusively of uterus from which the larvae are emptied in enormous quantity into water. The larvae enter in the water the intermediate host and develop further until they are ingested by man. They perforate the wall of the stomach of the infected man, copulate in the retroperitoneal tissue, the males die and the females traverse to the surface of the body from which they return to the water. The parasite can appear in lid or subconjunctival tissue.

Onchocerca volvulus (onchocerca caecutiens) is an inhabitant of Africa and Central America. A biting fly (simulium) transmits the parasite. Subcutaneous fibrous nodules develop, containing males and females. From here, microfilaria pervade the skin and appear also in the eye (onchocerciasis). They locate in conjunctiva, cornea, ciliary body, iris, choroid, in the chambers and vitreous body. They produce deep punctate keratitis with much vascularization and cyclitis with keratic precipitates; further, retinochoroiditis and optic atrophy.

Thelazia callipoeda (filaria circumocularis, filaria lacrimalis) lives in the lacrimal organ of animals as short worm and is

occasionally also found in man in China. It forms papillomatous lid tumors.

Habronema, found in Australia, affects the conjunctiva. The larva is carried into the conjunctival sac by flies. There is extensive cellular infiltration, proliferation of endothelial cells, and migratory cells containing yellow pigment. Small tumor-like granulations of the conjunctiva contain the worm.

Ascaris lumbricoides is a long, round worm rather commonly found in small intestines of children where it lives freely in large quantities. Its ova, eliminated with the feces, stay alive in moist earth and are ingested with uncooked vegetables. The larvae, developing in the intestines, perforate the intestinal wall, enter the blood circulation, are carried into the lungs, are filtered out here into the trachea, pass it up and the esophagus down into the intestines, where they maturate. Larvae can also migrate through tissue and appear also in the eye, producing severe iridocyclitis.

Trichina spiralis (trichinella spiralis) is a tiny round worm which infects rat, hog and man. The hog eats the infected rat and infects the man if he eats imperfectly cooked pork. The curled up larvae of the trichina are situated in the muscle fibers of the pork where they are encapsulated. When the infected meat is ingested by man, the capsule is dissolved in his intestine and the larvae develop to mature worms in several days. The males die after copulation and the females bore into intestinal villi. Their ova become larvae in the uterus and are discharged into the lymphatics, from which they enter the blood circulation and pass, as they are smaller in diameter than erythrocytes, through the pulmonary circulation into the major circulation. They perforate the walls of capillaries and pass into the striated muscles in which sites they survive. The muscle fibers entered by the larvae degenerate, and acute myositis with infiltration of polymorphonuclears, eosinophils, lymphocytes and giant cells develops. The larvae become coiled up in the muscle fibers and surrounded by a hyaline capsule. Like the other voluntary muscles of the body, the eye muscles, too, can be affected.

The platyhelminthes (flatworms) are subdivided into the flukes (trematodes) and tapeworms (cestodes), both of which can also cause ocular diseases.

In the fluke group, schistosoma haematobium (Bilharzia hematobia, distomum haematobium) is to be mentioned. The parasite is habitant in Egypt and surrounding countries. The small, flat adult worm lives in the distributions of the portal vein of the liver. The females migrate into the pelvic veins and their ova are deposited into the wall of the bladder and the rectum where they produce inflammation, polypoid tissue reaction and even carcinoma. Ova pass into the outer world through the urethra and rectum and are ingested by a water snail as an intermediate host in which the larvae develop. These escape into the water and can penetrate the skin of bathing persons. However, the ova can pass also into pulmonary arterioles, producing necrotizing arteriolitis, and into the lungs. They infect also the conjunctiva, where they produce granulomatous tumors.

In the tapeworm group belong (a) Taenia solium, (b) Taenia ecchinococcus and (c) sparganum mansoni.

The universal Taenia solium (pork tapeworm) consists of a small head (scolex) with a double row of hooklets and four disc-like suckers, and an infinite number of segments (proglottides). The ova of the worm are ingested by the pig as intermediate host and are carried by lymph or blood current into striated muscles in which they grow out to larvae (cysticercus cellulosae). If man eats imperfectly cooked pork, the larvae grow in his intestine to the adult form of the segmented Taenia, the scolex of which adheres by the hooklets to the wall of the intestine. If, owing to self infection, ova are swallowed by man and are deposited in the stomach, larvae developing from them pass into the body. They form in his organs the cystic forms of the cysticercus cellulosae and the man becomes the intermediate host. They are found in this case in great numbers in the brain, meninges, eye and striated muscles. Cysticercus cellulosae affects eyelids and conjunctiva, but is chiefly seen intraocularly to be subretinal, in vitreous body, anterior chamber or even in the lens. The universal Taenia echinococcus prevails in sheep-raising countries like Australia and South America and lives in its adult form in the intestine of the dog, which is infected when he eats the flesh of infected sheep, as a very small flatworm with a scolex with two rows of hooklets and four suckers and only three segments. Its ova pass with the excreta

of the dog to the outside and if man eats unboiled vegetable soiled by these excreta, the swallowed ova develop in the intestine to larvae which are carried by the portal circulation to the liver and from there to all parts of the body. The larvae are deposited in various organs and soon surrounded with a thin chitinous membrane and a fluid rich in salts and albumin is collected inside of the membrane. These larval cysts (hydatid cysts) are most common in the liver but they are also found in the brain and eye. The larvae multiply inside the cyst to numerous clusters of stalked scolices, originating as buds from the inner lining of the membrane (inner, or germinal layer) which become hollowed. Externally, this membrane is densely enclosed in a capsule which has laminated structure (outer layer or ectocyst). The hollowed buds form daughter cysts and the scolices contained in them have their four suckers and thirty to fifty hooklets invaginated. They are evaginated when they come into the intestine of an infected dog, where they adhere to the intestinal wall. Hyatid cysts appear rarely in the subconjunctival tissue and inner eye, as in the subretinal space or vitreous body, but relatively frequently in the orbit.

Sparganum mansoni is found in the Orient, its adult form living in the dog and its motile larvae in a fresh-water crustacean (cyclops) as intermediate host. However, many other animals are intermediate hosts: mammals, birds and reptiliae, which, eaten by the dogs, infect him. Man is infected as intermediate host by drinking of water or eating imperfectly cooked flesh. The long, flat and narrow larvae have a globular and spinous head. Ocular adnexa, the conjunctiva, eyelids and orbit are infected, and subconjunctival nodules develop, containing the coiled-up larvae.

Arthropoda in great numbers affect the eye and its adnexa. Pediculi and especially flies belong in this group. Pediculus capitis (head louse) produces eczematous kerato-conjunctivitis. Pediculus pubis adheres to eye lashes (phthiriasis palbebrarum). Flies commonly cause conjunctival diseases (external ophthalmomyiasis), and only rarely do they enter the inner eye (ophthalmomyiasis interna, intra-ocular myiasis).

Of interest among the flies are the families (1) of the muscidae, the representative of which is the house fly, (2) of the oestridae, (3) sarcophagidae, (4) anthomyeidae. Flies deposit ova in the conjunctival sac and the larvae (maggots) produce a larval conjunctivitis. The larvae can produce small cystic tumors in the conjunctiva, they can pass into the lacrimal passages and can also enter the eye and the orbit, where they cause severe destruction. The larvae of the hypoderma bovis of the family of the oestridae can perforate the sclera and enter the anterior chamber (ophthalmomyiasis anterior), or into the vitreous or the subretinal space (ophthalmomyiasis posterior). In every case, severe exudative uveitis with infiltration with lymphocytes, eosinophils and with perivasculitis sets in. The end result may be atrophia bulbi, but the eye can be destroyed entirely, and also the structures of the orbit, including bony walls and the meninges.

10. Injuries Caused by Physical Irritants

Among physical agents causing tissue damage are to be mentioned heat (infra-red rays), cold, light, electricity, radium and x-rays, increased atmospheric pressure, and trauma.

Heat causes burns of various degrees, depending on the severity of a single exposure or repeated and long-lasting thermal attacks of relatively small intensity. The eyelids can be affected, showing in burn of first degree hyperemia, in second degree vesication, in third degree necrosis of the skin and in fourth degree charring of the tissue. The burn of the eye is usually part of a burn of the face and the rest of the body. If the protecting eyelids do not function for some reason, conjunctiva, cornea and deep parts of the eye are burned. The conjunctiva is hyperemic, shows vesicles and coagulation with thrombosis in blood vessels. The corneal epithelium shows vesiculation and desquamation, the stroma coagulation causing opacities, the iris congestion and hemorrhages, the lens capsule exfoliation, the lens substance coagulation and the retina necrosis. Lens and retina are usually affected when they are exposed for a long time to heat waves. This happens especially in such workers as glass blowers, but

also in persons looking directly into the sun with unprotected eyes.

Cold scarcely affects the eye itself, only the eyelids and conjunctiva. Should the temperature of the body fall so low that the eye itself would be affected, rather death from freezing would occur. The eyelids are hyperemic and edematous and the epidermis shows vesicles and necrosis.

Very intense light may irritate like heat but acts photochemically when it consists more of rays of the spectrum toward the ultraviolet which give little heat. Ultraviolet light produces hyperemia and edema, but its action appears often long after the exposure. Ultraviolet causes intensive pigmentation of the lids. The corneal epithelium shows desquamation and proliferation and nuclei change into homogeneous structures. The conjunctiva swells and becomes hyperemic (photophthalmia), cataractous changes can appear and ganglion cells of the retina are especially damaged. Damage by light can be occupational. Severe changes set in if the individual is light hypersensitive, e.g., in xeroderma pigmentosum in which abnormal pigmentation, keratosis and finally cancerous degeneration appear. Hypersensitivity to light is present in congenital hematoporphyria in which hematoporphyrin is in the blood and appears in the urine. It is a sensitizer in the sense that when the sensitized tissue is exposed to ordinary light, severe damage and eventual necrosis occur.

Electric current of great intensity and strong voltage produces a local effect in the form of a burn where the current enters the body and where it leaves. The eye is rarely the place of entrance and never the place of exit. The eye is mostly injured by the passing current which especially causes thrombosis and hemorrhage, cataract formation, degeneration of the retina and atrophy of the optic nerve.

Radium and x-rays are destructive in different form in the alpha, beta and gamma rays, of which the first two are absorbed from the surface and only the gamma penetrate. The cell nuclei, and to a lesser degree the cytoplasm, are affected, the former especially in the stage of mitosis. Embryonal tissue is also vulnerable. The superficial tissue shows burns with little

tendency for healing. Arteries undergo hyaline degeneration, occlusion of their lumen occurring with frequent thrombosis, and capillaries are dilated. Cornea, lens and retina can be damaged. An embryo exposed to the rays often shows malformations of the eye later on.

Caisson laborers, who work under increased atmospheric pressure, develop, if they are decompressed too fast, hemorrhages in various organs (hence also in the retina) and paralysis of muscles (e.g., eye muscles). When the worker must undergo high pressure, much air with considerable nitrogen is dissolved in the blood plasma. With fast decompression, this is released in the form of bubbles, forming emboli in the vessels.

Trauma in general is not uncommon, such as blow, stab, cut and foreign body, and produces great variations of pathologic changes. Trauma may also be considered in relation to infection; e.g., bacteria circulating in the blood often settle in injured organs.

11. Injuries Caused by Chemical Irritants

Poisons are brought into the eye from the outside or affect it internally by way of the blood circulation. The exogenous poisons enter the eye by accident, especially in industrial occupation, in self infliction (as in psychopaths), by plant and animal parasites. Endogenous poisons enter the eye through the blood circulation in a generalized intoxication, when poisons are resorbed from the gastrointestinal tract or are inhaled or are injected directly into the blood circulation, by accident in occupations or self infliction, or further as the result of abnormal metabolism or production by bacteria (toxins). A great variety of matter affects the eye. Such corrosive acids as sulfuric, nitric, hydrochloric burn the eye, their damage depending on their concentration. They produce necrosis of the tissue of the lids, the conjunctiva and cornea and if they enter the intrinsic eye in sufficient concentration, they excite a severe inflammation of all parts of the eye with formation of cataract. Carbolic acid (phenol) fixes the tissue in strong concentration and produces intensive hemorrhagic inflammation when diluted. Caustic alkalis, like lime and lyes, dehydrate cells and tissue and cause

coagulation of the protein and saponification of the fat. The tissues are soft and show acute inflammation. Conjunctiva and cornea are often damaged.

Arsenic causes, in chronic poisoning, neuritic degeneration of the optic nerve besides other damage of the central nervous system. Lead poisoning usually occurs as occupational disease and causes peripheral neuritis, encephalopathy and blue lead-lining of the gums; further, endarteritic changes, hyaline degeneration and tissue proliferation in the retina and inflammation, hemorrhages and degeneration in the optic nerve may develop. Methyl alcohol (wood alcohol) causes degeneration of the optic nerve. Ethyl alcohol rarely affects the optic nerve, electively degenerating the papillo-macular bundle besides showing marked edema of the brain and degeneration of inner organs. Thallium produces inflammation of the optic nerve and cataract. Retention of urea in the blood due to renal failure brings about severe changes of the retina and the optic nerve besides edema of the brain. The appearance of acetone in diabetes mellitus is said to be responsible for retinopathy and cataract. Botulism is caused by a bacterial poison produced by the bacillus botulinus which grows in spoiled food. Cerebral damage other than ophthalmoplegia interna and paralysis of other cranial nerves is found.

12. Disorders of the Regulators of the Body

Hormones and vitamins regulate the various functions and the metabolism of the body. Hormones are secreted from endocrine or ductless glands directly into the blood circulation. They regulate growth, sexual function, functions of the autonomous nervous system, metabolism of calcium and sugar. Vitamins are food factors necessary in addition to the adequate supply of protein, carbohydrate, fat and mineral salts to sustain life.

Disturbances of the endocrine glands in the sense of hyper- or hypofunction often lead to ocular symptoms. Hyperfunction of the thyroid (hyperthyroidism) produces Graves' disease (exophthalmic goiter) with exophthalmus and wide interpalpebral fissure. Hypofunction of the thyroid leads, when congenital, to cretinism which frequently is associated with myopia

and lenticular opacities; when appearing later in life, to myxedema. Overactivity of the adrenals results in boys in premature development of the sexual organs (virilism), and in girls appearance of hair on face and body (hirsutism); insufficiency of the adrenals in Addison's disease results in abnormal pigmentation of the skin and mucosae, also of the conjunctiva, besides asthenia. Hyperfunction of the parathyroid glands (hyperparathyroidism) which normally regulates the calcium metabolism, causes mobilization of calcium in the body and thus decalcification of bones, insufficiency of the glands (hypoparathyroidism), depletion of the tissue of calcium with hyperexcitability of the nerves and muscles (tetany) and cataractous changes of the lens. Overactivity of the pituitary gland (hyperpituitarism) produces in growing individuals gigantism and in adults acromegaly besides disturbances of the sexual function. Underactivity of the pituitary gland (hypopituitarism) leads to manifold symptoms (depending on which cells of the gland are deficient in their secretion), generally to dwarfism, infantilism, and sexual underfunction. The various types of the symptoms in hypopituitarism are (1) the Froehlich type with the special variation, the Moon-Laurence-Biedl syndrome, (2) the Simmond's type and (3) the Loran type. The Froehlich type (dystrophia adiposogenitalis) shows decrease of the sexual function, atrophy of the skin and conjunctiva, adiposity of various degrees and mental dullness. In the hereditary familial Moon-Laurence-Biedl syndrome, there is retinitis pigmentosa, adiposity, sexual disfunction and polydactylism. Simmond's type (Simmond's cachexia) is associated with premature aging, the inner organs are small and there is sexual hypofunction. In the Loran type (pituitary dwarfism, nanosomia pituitaria, Paltauf's dwarfism) the individual is small and sexually undeveloped but mentally alert. To the extent that tumors of the hypophysis are associated with the symptom of hyper- and hypofunction, frequently additional symptoms result from pressure of the tumor on the neighboring chiasm and the formations of the third ventricle (e.g., hypothalamus). If the chiasm is affected, defects in the visual field and atrophy of the optic nerve and rarely papilledema result. The thymus, which is partly epithelial and partly lymph-

oid, is an endocrine gland as well as lymphoid structure. Hyperplasia of the thymus is found in myasthenia gravis which frequently affects extrinsic eye muscles. The pancreas consists of a gland which secretes externally into a duct, and of an endocrine gland in the form of the islets of Langerhans which regulate the carbohydrate metabolism. If they are disturbed, diabetes mellitus develops which occasionally damages retina and optic nerve, the lens and extrinsic eye muscles.

The main vitamins synthesized in nature by plants are known as six different substances: vitamins A, B, C, D, E, K. Deficiency of these various vitamins produces characteristic symptoms, which almost always include ocular symptoms. The fat-soluble vitamin A is of especial importance to the eye as it is necessary for the formation of the visual purple. Vitamin A deficiency produces keratinizing metaplasia. Columnar and non-hornifying squamous epithelium are changed into hornifying squamous epithelium. This can be seen also in the conjunctiva and cornea which show keratinization (xerosis) besides similar changes in the respiratory, alimentary and urinary tracts. The corneal parenchyma can become atrophic and necrotic (keratomalacia). Deficiency of regeneration of visual purple is combined with night blindness. This vitamin further protects against infection (anti-infectious vitamin) and its deficiency can facilitate local infection.

The water-soluble vitamin B consists of several components (vitamin B complex), of vitamin B_1 (thiamin), B_2 (riboflavin, vitamin G), B_6 (pyridoxin), nicotinic acid and pantothenic acid. Deficiency of vitamin B_1 (antineuritic vitamin) produces polyneuritis and is responsible for the neuritis of chronic alcoholism, diabetes and pregnancy and produces beriberi in countries in which the population eats polished rice exclusively. Its deficiency is associated with affections of the conjunctiva and cornea, paresis of eye muscles and retrobulbar neuritis. Vitamin B_2 deficiency (ariboflavinosis) is associated with keratoconjunctivitis, showing erosions of the skin of the lids, perhaps cataract, fissures at the corners of the mouth (cheilosis) and of the nares. Deficiency of nicotinic acid (pellagra-preventing factor) pro-

duces pellagra with pigmentation and hyperkeratosis of the skin, desquamation of face, muscular weakness and nervous disorders.

The water-soluble vitamin C (ascorbic acid, antiscorbutic vitamin) is destroyed easily in heat. Its deficiency produces scurvy (scorbutus) in the adult with suffusions in skin and mucosa, in muscles and nerves, in periosteum and joints. Secondary anemia is found and bones are rarified. It produces in children infantile scurvy (Barlow's disease) with subperiosteal hemorrhages and cessation of the growth of the bone and hemorrhages of the gum. The eye is affected in the form of keratoconjunctivitis with ulceration and decrease of tear-secretion and hemorrhages in lid, conjunctiva and retina.

The fat-soluble vitamin D is an isomer of ergosterol, from which it is formed under the influence of ultraviolet light. It controls calcium metabolism and its deficiency produces in children rickets, dental caries and zonular cataract.

Deficiency of the fat-soluble vitamin E (antisterility vitamin) causes destruction of the spermatozoa and death of the fetus. There are no ocular symptoms present.

The fat-soluble vitamin K (coagulation vitamin) participates in the formation of prothrombin. It is deficient in the new-born when the bile ducts are closed. Its deficiency produces hemorrhages, perhaps also hemorrhages in the eye.

13. Tumors (Neoplasms)

Tumors or neoplasms are characterized by new growths of cells which proliferate without control and do not serve any useful function. But there are borderline cases in which the decision as to whether there is a neoplasm present or not is difficult or impossible. In inflammations, there is also a proliferation of cells and sometimes it may be difficult to decide if hyperplasia of a chronic inflammation exists, or even if tumor growth is already present. Furthermore, there are those tumors which continue the function of normal tissue; e.g., tumors of the thyroid.

We distinguish tumors as malignant or benign, this differential diagnosis being made mostly from histologic appearance. They are characterized as follows.

Malignant tumors: (a) They proliferate and infiltrate the surrounding tissue and replace it. (b) They show many mitotic figures as they grow rapidly. In this case, one sees the chromatin as a dark band across the nucleus, or it is already divided into opposite lying rows of loops (chromosomes). Atypical mitosis exists also as chromosomes appear in three groups. Incomplete divisions of the nucleus are seen or the nuclei may divide without division of the cell. In this way, multinuclear cells (giant cells) are created. (c) After removal of a tumor, recurrence appears on the same place or in distant organs. Either tumor cells remained in the tissue after removal and started to grow, or the tumor commenced to grow from cells which were not yet tumor cells at the time that the primary tumor was removed, or tumor cells were carried to distant organs where they proliferate even after years of quiescence. (d) The cells of the tumor are more undifferentiated and appear as young or rather degenerated forms, different from the differentiated cells of their origin. They are anaplastic. (e) The cells lose their normal relationship to the neighboring cells. Their cell borders are indistinct and they separate from the cell complex. In this way, they show loss of polarity. (f) The nucleus of the malignant cell is large, hyperchromatic, as the chromatin stains deeper. The nucleolus becomes much larger in relation to the nucleus, and is surrounded by a clear halo. (g) The cells have a larger variation than those of the normal tissue. They are polymorphic and show more differences in size. Pleomorphism is present. (h) Secondary tumors appear in lymph nodes and distant organs (metastases). (i) In the majority of cases, they are fatal for the individual. However, not in every malignant tumor are all these characteristics present; usually only some of them.

Benign tumors: (a) They grow by expansion, often on the surface, and are surrounded by a capsule. (b) They usually show the structure of the surrounding tissue. (c) The cells are well differentiated, of normal size and have normal nuclear structure.

Four stages are distinguished in malignant tumors of the eye: (1) the growth of the tumors at the place of origin; (2) the infiltration of the surrounding tissue; (3) the perforation of eye

ball, from within outward, or from without inward, and (4) the formation of metastases.

The benign and malignant tumors are distinguished according to their origin from germinal layers in (a) ectodermal (epithelial, neuro-ectodermal) and (b) mesodermal (originating from connective tissue, muscles or the blood system).

The connective tissue stroma and blood vessels of the tumor are formed either from its cells, as in fibroma and fibrosarcoma, or from the surrounding tissue. The more malignant the tumor is, the more cells and less stroma is present. In very malignant sarcoma, the stroma is extremely fine and can be presented only by special staining with silver. In epithelial tumors, the stroma increases with the growing of the tumor. We must assume that the growing epithelial cells stimulate the stroma to proliferation, as they themselves are not able to produce connective tissue. In papilloma, the connective tissue of the papillae increase, and also in carcinoma can a considerable increase in the connective tissue be noted.

Broder's grading of tumors according to their malignancy has validity for epithelial tumors of the eye, but can hardly be used for sarcoma of the uvea and retinoblastoma. The malignancy is graded in regard to anaplasia, hyperchromatism and number of mitoses. Four grades are distinguished. Grade 1 is a tumor with the least and Grade 4 with highest malignancy. In Grade 1, the tumor resembles normal tissue the most, with the differentiation of the cells complete and the number of the anaplastic cells with hyperchromatic nuclei and the number of the mitoses small in relation to the normal cells. In Grade 2, half the cells are anaplastic, this becoming more pronounced in Grade 3 until in Grade 4, almost none but anaplastic cells and numerous mitoses appear. The grading is not of great importance in the pathology of the eye, as in general the epithelial tumors of the eye are rarely malignant and the intra-ocular tumors are very malignant.

Carcinoma spread is: (1) rarely intraepithelial, (2) by infiltration into the surrounding connective tissue and lymphatics, (3) by emboli in lymph- and blood vessels and (4) by implantation. Sarcoma spreads: (1) by infiltration into the surrounding tissue and (2) by embolism in blood vessels.

Intra-epithelial spread of the carcinoma is rare as the epithelium resists it. The carcinoma originates inside the epithelium and spreads in it, or it is situated beneath the epithelium and protrudes between the normal epithelial cells. The normal cells may undergo precancerous changes before the carcinoma reaches them, but frequently the carcinoma destroys the epithelium and substitutes for it.

The usual spread of the carcinoma is the infiltration into the connective tissue, or any other surrounding tissue (cornea, sclera, muscle). It penetrates into connective tissue spaces and lymphatics, permeates them and spreads far out and destroys and substitutes the connective tissue. This is the usual spread of the carcinoma in the region of the eye. The tissue may show reaction, as lymphocytes proliferate and connective tissue cells increase and form a wall against the carcinoma cells. The lymphatics, too, may show inflammatory reaction and fibrosis and the vessels may obliterate. The tumor cells become choked in this way and their penetration is stopped.

Carcinoma cell emboli are found in lymph and blood vessels. They are carried through the lymph vessels into regional lymph nodes, are deposited and grow here (regional metastases). Through the blood vessels, they are carried to distant organs and grow there (distant metastases). Carcinoma may grow into blood vessels, and carcinoma cells are carried, singly or in clumps, away by the current. The carcinoma cells must find a proper place to grow in the distant organs, otherwise they degenerate; therefore, they show predilection for certain organs. The metastasis may be similar to the primary tumor from which it originates or may be different. Carcinoma in the region of the eye seldom produces regional or distant metastases; more often metastases develop in the eye from surrounding or distant organs. Carcinoma of the nose may metastasize in the orbit, carcinoma of the breast in the uvea. Implantation plays a smaller role in the spread of the carcinoma of the eye; e.g., carcinoma of the conjunctiva or of the lid may spread onto the surface of the eye bulb.

Sarcoma spreads mostly by infiltration of the surrounding tissue, the connective tissue, sclera, muscles, and nerves, and destroys and substitutes for them. Seldom does it grow into lym-

phatics, and the appearance of a reaction of the surrounding tissue in form of lymphatic infiltration is infrequent. Sarcoma cell emboli are found relatively early in blood vessels and therefore they usually form distant metastases in organs of their predilection.

Multiple tumors may exist and then it is difficult to distinguish them from primary tumor and metastasis. Multiple myeloma sometimes affects the orbit.

The effects of tumors of the eye are different according to their seat and their type. Even benign tumors may lead to destruction of the organ. When they are located in the orbit and protrude the bulb, they may produce suppurative keratitis with perforation and suppuration of the entire eye. Benign tumors of the orbit may lead to pressure atrophy of the optic nerve and to blindness. Benign tumors grow to a certain degree and then usually stop. Carcinoma of the lids and of the cornea may ulcerate and may be infected secondarily. Malignant tumors such as glioma and sarcoma can destroy the entire eye and grow eventually into the optic nerve also; death finally intervenes through malignant cachexia and exhaustion. Malignant tumors very rarely show regression or spontaneous healing which is seen occasionally in retinoblastoma.

Little is known about the etiology of the malignant tumors of the eye. Three factors are generally mentioned in the origin of tumors: (1) The carcinogenic agents (exogenous and endogenous), (2) susceptibility (especially heredity), and (3) time. Of the exogenous factors, chiefly chronic irritation is mentioned. Continuous exposure to intensive sunlight is said to produce carcinoma of the skin. Chronic irritation may produce hyperplasia of tissue which changes into malignant tumors. A trauma may perhaps do the same, or an until then unobserved malignant tumor may be stimulated by the trauma to rapid growth. Experimentally, tar ingredients have been used successfully for the production of malignant tumors in superficial application or injection. Sex hormones have a relation to formation of carcinoma. It is not known to what extent these exogenous or endogenous agents take part in the development of malignant tumors in the region of the eye. It is assumed that these agents produce

in the mechanism of the origin of the cancer a precancerous state, as many cells suddenly show the character of the malignancy. These cells then spread the malignancy in the tissue of the affected area. It seems that these cancerous cells thus produce enzymes which act on the normal cells and change them into malignant cells. However, filtrable viruses have also been found in certain animal tumors which were able to produce the same tumor in transmission to other animals. Further, heredity plays a role as is seen in the appearance of malignant tumors in certain families, and such tumors can show organ susceptibility as they affect always the same organ. Heredity has a part in such eye tumors which appear in early age. Retinoblastoma appears at an early age and sometimes in several members of the same family. Age plays a role in the appearance of malignant tumors. Carcinoma of the lids or the conjunctiva and also melanosarcoma are seen mostly in middle or old age. There is further the question of misplaced cells producing malignant tumors. It is assumed that such cells, misplaced in the development of the embryo, can, under certain circumstances, begin to grow in their abnormal surroundings and finally form malignant tumors. Furthermore, congenital benign tumors such as nevi, or at a later age such benign tumors as papilloma, may change into malignant ones. On the other hand, there seems to exist immunity against carcinoma so that either it does not develop at all, or, if an organ is affected by carcinoma, no other carcinoma can grow at the same time in another organ. The time factor plays a role insofar as certain malignant tumors arise only at a certain age and that malignant tumors need a certain time to appear. It is assumed that the stronger the stimulus and the more sensitive the organ, the shorter the time lapse before the appearance of the malignancy. It is interesting that transplantation of a malignant tumor until now has been successful only in the same species, with the exception that in the anterior chamber of the animal eye any malignant tumor may grow as in a tissue culture.

It is the rule that a tumor has to be destroyed wherever it appears in the body, either malignant or benign, if there is a possibility that it may destroy an organ or may be fatal by

pressure on a vital organ. Malignant tumors of the eye usually destroy the vision and are fatal by spread to the brain or by metastasis, but benign tumors, too, frequently destroy the vision, either by covering the cornea, growing in the interior of the eye and eventually producing glaucoma or destroying the eye by protrusion when they develop in the orbit. Tumors of the eye are removed, as a rule, surgically, sometimes without removal of the eye, but chiefly by enucleation of the eye or exenteration of the orbit, but under certain conditions they may be destroyed by radium or x-rays. Not all tumors are radiosensitive and radiosensitive tumors show different degrees of sensitivity. The gamma rays of radium and x-rays act on the tumor cells and on the stroma. The rays act especially on the dividing cells and arrest their activity (growth restraint). Therefore, the more the tumor is sensitive to rays the more mitoses are present. Further, they act on the nuclei, produce chromatolysis and in this way destruction of the cells, and vacuolization of the cytoplasm (autolytic degeneration). The rays, in addition, act on the stroma, especially on the blood vessels. The vessel walls hyalinize, the lumen narrows by intima-proliferation and thrombi are formed. Lymphatics, too, may show obliteration by endothelial proliferation. In this way, the nourishment of the tumor, especially its respiration, is affected, which on the other hand is also decreased as the rays damage the cytoplasm directly. The closure of blood and lymph vessels also decreases the spread of the tumor. Furthermore, the rays act also on other elements of the tissue and, as an irritant, cause inflammatory reaction. Exudation of serum, polymorphonuclear cells, lymphocytes, plasma cells and eosinophils sets in and fibroblasts and fibrils proliferate. The inflammation is a defense reaction of the tissue against the tumor and the resulting fibrosis opposes the infiltration of the tumor. In general, one can say that the less the tumor is differentiated, the more it is radiosensitive. Basal cell carcinoma, especially rodent ulcer, is more sensitive than squamous cell carcinoma. Nondifferentiated sarcomata, especially lymphosarcoma or multiple myeloma, are often more radiosensitive than differentiated ones. Benign tumors are therefore in general radioresistant, but there

are exceptions. The anaplastic and nondifferentiated retinoblastoma, malignant melanoma, and neurogenic sarcoma, are mostly radioresistant. In general, the neurogenic tumors are resistant, the tumors of the blood system sensitive. The radiosensitivity further depends on the stroma in which the tumor is embedded. Tumors inside the sclera are rather radioresistant. Also, infected tumors become more radioresistant; e.g., exulcerated and infected carcinoma of the limbus. Inadequately treated tumors or recurrences of treated tumors acquire resistance.

The diagnosis of the type of tumor and the determination of its malignancy is often not difficult in histologic examination, but under certain circumstances it becomes very difficult. It may be hard to distinguish between inflammatory fibrous tissue and sarcoma. Carcinoma in situ, e.g., in a papilloma of the conjunctiva or in a papillary hypertrophy of the limbus, is often difficult to distinguish if there are, inside the epithelium, without invasion of the surroundings, hyperchromatic cells and cells irregular in size and shape. On the other hand, epithelium may grow into the depth without malignancy, as, for instance, in implantation of epithelium in the anterior chamber. Of importance is the biopsy examination, which is to be recommended on the eye only in superficially growing tumors. Generally speaking, frozen sections are not necessary and the specimen may be fixed in 10 per cent formalin and sectioned in paraffin. Diagnosis of the type of malignant tumor can be made clinically on the eyelid, conjunctiva and surface of the eye; also, the ophthalmoscopic examination together with diascleral transillumination and slit lamp examination aids the diagnosis. The diagnosis is rather doubtful in tumors of the orbit. In intraocular tumors from which a biopsy can not be taken, sometimes the trans-scleral aspiration of tumor material can be used successfully.

Tumors are classified histologically according to the tissue from which they originate and the cells which they contain. Tumors may originate from one germinal layer (ectoderm, mesoderm or entoderm), or may originate from several germinal layers. Tumors originate: (1) from epithelium and are papilloma and

adenoma as benign, and carcinoma as malignant tumors. A special form of the epithelial tumors is hypernephroma. (2) There are also tumors of the nervous tissue, and as such chiefly malignant; they are glioma, retinoblastoma, neuroblastoma and ganglioneuroma. (3) Tumors also originate from connective tissue and its derivatives, and are fibroma, lipoma, chondroma and osteoma as benign, and sarcoma as malignant tumors. (4) There are tumors of the muscle tissue and are leiomyoma and rhabdomyoma as benign, and leiomyosarcoma and rhabdomyosarcoma as malignant tumors. (5) Tumors of the blood and lymph vessels (angioma) occur and are hemangioma and lymphangioma as benign, and angiosarcoma as malignant tumors. Closely related to them is the endothelioma. (6) Tumors of the hemopoietic system are benign lymphoma and malignant lymphoma, to which latter belong lymphosarcoma, multiple myeloma and leukemia. (7) There are pigmented tumors: benign naevus and melanoma and malignant melanoma. (8) Some tumors contain mixed tissue from two or three germinal layers, as the dermoid and teratoma.

Epithelial tumors are characterized histologically by the cells lying close to each other without interstitial tissue. They are frequently arranged in groups surrounded by connective tissue (alveolar arrangement). The benign papilloma arises from a surface epithelium carrying on the surface an epithelial cover, and beneath, branching papillary connective tissue with vessels. They are distinguished as they grow from stratified or columnar epithelium as (a) squamous (hard) and (b) mucous (soft) papilloma. But papilloma is classified by some as mesodermal tumor, inasmuch as the connective tissue papilla is considered the seat of the pathologic growth and the proliferation of the epithelium as secondary. Papilloma of the lid (wart, verruca) has a thick stratified squamous epithelium which is mostly hornified. Papilloma is found also on the conjunctiva, caruncle and plica semilunaris and on the limbus, carrying nonhornifying squamous epithelium. The benign adenomata originate from the epithelium of glandular tissue and are similar in texture to glands; they are adenoma of the sebaceous, sweat or tear glands found in the lid, conjunctiva and caruncle. The adenomata show

tubular growth and solid (pseudo solid) strands. Sometimes, glandular structures in the tumor distend and form cysts, as in the accessory tear gland or in the tear gland itself (cystic adenoma, cyst adenoma). Papillomata and adenomata may become malignant.

The malignant epithelial tumor is carcinoma originating from the epithelium of the skin or a mucosa as (a) squamousal carcinoma and (b) basal carcinoma, or originating from the epithelium of a gland as (c) adenocarcinoma. The squamousal carcinoma (epidermoid carcinoma, epithelioma) frequently shows characteristic hornification inside of columns of epithelial cells growing into the depth. Granules appear inside the cytoplasm and finally the entire cell becomes a structureless keratin in which the nucleus often is still present. The hornified cells grow in concentric circular, onion-shaped lamellae (epithelial pearls). The columns are composed of prickle cells, have no basement membrane and are therefore ill defined, and in the surrounding connective tissue there is frequently accumulation of lymphocytes in different density. Carcinoma can show various grades of differentiation. They sometimes have many anaplastic cells which infiltrate the surroundings singly and in groups, substituting for infiltrated tissue, and which have little or no hornification. The skin of the lids, conjunctiva, limbus and cornea can be affected primarily, or tear sac and orbit can be affected secondarily, mostly from the paranasal sinus. The basal cell carcinoma (rodent ulcer) consists of solid masses of epithelial cells which branch into the depth. They consist of basal cells of the epidermis which are distinctly cylindrical on the margin and appear in rows, and which are more spindle shaped towards the center. This carcinoma grows occasionally in narrow columns, sometimes only in two rows of cylindrical cells surrounded by connective tissue of various widths (cylindroma, cylindromatous type). Especially the lids, nose and cheeks are affected, and the orbit may be invaded, in which case large destructions arise. The adenocarcinoma may show various types according to the origin and growth of its cells. A frequent type consists of columnar epithelium lining a lumen with cells and showing

irregular growth, hyperchromatism, mitosis and anaplasia. The epithelium usually has several layers and grows irregularly in branching processes into the depth without basement membrane. The epithelium may appear acinotubular or grow in solid strands. In the latter case, we usually find spheroidal or polyhedral cells in solid columns (carcinoma simplex). The latter may appear in two forms: (1) as scirrhus carcinoma, in which only one to several rows of cells are surrounded by much dense connective tissue; (2) as medullary carcinoma, in which large masses of cells are surrounded by little connective tissue. When the cells of the adenocarcinoma contain much mucin, the cells are distended and appear clear (mucoid carcinoma). This type is found especially in the large bowel, but also in the stomach, breast and bronchi. Adenocarcinoma in the region of the eye are rarely primary in the lid and the tarsus. Adenocarcinoma of the tear gland is seen mostly in the form of a mixed tumor in which not only glandular tissue proliferates carcinomatously but also connective tissue and myxomatous tissue. Otherwise it is chiefly metastatic, especially in the uvea, with the primary tumor in breast or intestines, rarely in the bronchi. The special type of hypernephroma is also metastatic in the uvea and primary in the kidney, where it is said to originate either from displaced suprarenal elements or from tubuli of the kidney itself. This tumor is easily recognized by its rows of large epithelial cells, clear or vacuolized as they contain much lipoid and glycogen, which is dissolved in the usual preparation of the tissue. The cells appear arranged in solid cords or in tubuli, between which are small connective tissue septa.

Tumors originating from nervous tissue are derived from the supporting tissue (neuroglia) or from the parenchymatous tissue. Gliomata originating from the supporting tissue are multiform, have spindle-shaped or round nuclei and a different amount of fibrillar tissue. They are chiefly found in the optic nerve. Tumors originating from the parenchymatous tissue have their origin mostly in embryonal nerve cells and are frequently congenital or appear in early childhood. The retinoblastoma consists of small, round nondifferentiated embryonal

cells. The neuroblastoma originates from the neuroblasts of the medulla of the adrenal and consists of small round cells, some imperfect ganglion cells and fibrils, which are arranged in long bundles, or small rounded masses; it metastasizes typically in the orbit. Very rarely, ganglion-neuroma originates from the ganglion cells of the retina, containing imperfectly developed nerve cells and nerve fibers.

The benign connective tissue tumors are very manifold in their histologic appearance. The fibroma consists of fusiform fibroblasts and bundles of collagenous fibers. If the fibroma has numerous cells, it is a soft fibroma. If fibrous tissue prevails in the tumor, then it is a hard fibroma. It is distinguished: (1) as a neurofibroma of the nerves of the skin (multiple neurofibromata or Recklinghausen's disease); (2) as neurofibroma of the deeper nerves, which appears as plexiform neuroma and sometimes becomes a neurogenic sarcoma. Fibroma and neurofibroma are found on the lids, conjunctiva, sclera, ciliary nerves and sheaths of the optic nerve.

Lipoma consists of encapsulated fat tissue. It is found in the lids, conjunctiva and orbit. Chondroma consists of hyaline cartilage with cells arranged singly, although in normal cartilage its cells form groups. Osteoma consists of compact or cancellous bone. Both may be found in the orbit.

The muscle tissue is plain or striated, and accordingly the tumors originating from it are distinguished: (1) as leiomyoma and (2) as rhabdomyoma. Leiomyoma is microscopically characterized by interlacing bundles of smooth muscle fibers with rodlike nuclei, separated by connective tissue fibers. Rhabdomyoma consists of large polygonal cells with small processes and some striation. Eyelid and orbit may be affected.

Vascular tumors (angioma) are (a) hemangioma and (b) lymphangioma. Hemangioma are (1) capillary and (2) cavernous. In capillary angioma, a network of blood-filled capillaries is found, closed capillaries with swollen endothelial cells, sometimes appearing in several layers, and solid masses of endothelial cells. It is congenital in lid, conjunctiva and orbit. The cavernous angioma shows large sinusoids which communicate

with each other and may infiltrate surrounding tissue. It is found in the orbit. The lymphangioma consists of capillary and cavernous spaces which are filled with lymph. Lid or conjunctiva may be affected. Tumors which originate solely from endothelial cells of vessels, perhaps also from those of the adventitia or from reticulo-endothelial cells, are called endotheliomata, which are malignant. Its cells are arranged epithelial-like, have small nuclei and much cytoplasm and lie in cords and cylinders. Histologically, they are often difficult to distinguish from some types of sarcoma and certain forms of epithelioma. They are found in conjunctiva and orbit.

Tumors of the hemopoietic system consist of cells which originate from the blood-forming organs. They are often difficult to differentiate from each other or from hyperplasia. Thus, the benign lymphoma (lymphoblastoma) and the malignant lymphoma (lymphosarcoma) are difficult to differentiate from each other in the tissue. Both consist of accumulation of lymphocytes with fine connective tissue reticulum. In the latter, larger reticulum cells are interspersed between the lymphocytes which have larger hyperchromatic nuclei and more cytoplasm. The malignant tumor has a tendency to infiltrate the surrounding tissue. Both forms are found in conjunctiva and orbit. The benign lymphoma can appear by itself without evidence of constitutional disease, but it can also be the expression of a lymphatic leukemia in which almost exclusively lymphocytes in very large number are found in the blood, and lymph nodes are universally enlarged. To the group of the malignant lymphoma also belongs multiple myeloma, which, too, affects the orbit. It develops in bone marrow and lymph nodes and consists of diffusely arranged round or polyhedral cells with round nuclei, without intercellular substance and sometimes with preponderance of plasma cells. Further, some include in this group the leukemias, in which myeloid and lymphoid cells proliferate enormously, but others believe that they are of inflammatory nature. Leukemia may be acute or chronic and may be myelogenous (in which the myeloid cells are more numerous in the blood picture), lymphatic (in which the lymphoid

cells are increased), or monocytic (in which the monocytes are increased). Myelogenous leukemia produces infiltration of the retina and uvea.

In sarcoma, the cells are uniformly distributed and always have a stroma between the single cells in different density, sometimes very distinctly or sometimes of such fine fibers that they can be shown only by special staining methods. The cell forms vary considerably, depending upon how far the differentiation of the sarcoma has progressed. Its differentiated forms are rare or nonexistent in the region of the eye; they are fibrosarcoma, neurogenic sarcoma, osteosarcoma, chondrosarcoma, angiosarcoma, myosarcoma, or liposarcoma as their stroma shows the origin of the tumors from connective tissue, from the fibrous envelopes of nerves (perineurium) characterized by their intertwining bundles forming fasciculi and whorls, from bone, cartilage, blood vessels and muscles, or as their cells show the origin as large polyhedral cells with fat granules. The nondifferentiated sarcomata have either round cells (round cell sarcoma) or fusiform cells (spindle cell sarcoma). Other sarcomata are polymorph and contain also giant cells and scant stroma.

Pigmented tumors are (a) nevus (innocent melanoma) and (b) malignant melanoma (melanotic sarcoma, melanosarcoma). The nevus is a congenital pigmented or nonpigmented tumor which is composed of groups of nevus cells. They lie in rows and strands of various size, and consist of round or polygonal closely packed cells which extend beneath the epithelium into the depth. The marginal cells of the groups are more oval and filled with melanin (melanoblasts). The origin of the nevus cells is still in question, i.e., whether they are epithelial or of mesodermal origin. They are often seen in continuation of the surface epithelium which also contains pigmented cells, apparently originating from it. Some consider the pigmented cell of the nevus as mesodermal chromatophor. As its cells simulate in their arrangement endothelial tumors, they were also considered of endothelial nature. Recently, the theory was put forward (Masson) that the nevi originate from sensory end organs (Meissner's corpuscles) and therefore are neuroecto-

dermal (neuronevus). There exist also tactile end organs inside the surface epithelium (corpuscles of Merkel-Ranvier) from which cells may proliferate into the subepithelial tissue and so form a nevus. The nonpigmented nevus cells which originate from the cells of the ectodermal end organ are surrounded by cells which are able to form pigment (melanoblasts) and these occur also intra-epithelially as the so-called Langerhans cells. Nevi are found typically in the lid skin but also at the limbus, in the lacrimal caruncle and plica semilunaris. On the other hand, but histologically distinctly different from the typical nevus, circumscribed dense accumulations of chromatophors in the choroid are called melanomata of the choroid and accumulations of pigmented cells of the anterior border layer of the iris are called nevi. Malignant melanoma may or may not develop from a benign lesion and is often multiform according to the place of the origin and the tissue from which it originates. It may simulate carcinoma, sarcoma or endothelioma and may appear nonpigmented or may show little pigmentation; on the other hand, however, very densely pigmented tumors may be seen. In a melanoma similar to carcinoma, the cells are large, oval, polygonal and are arranged in alveolar groups which are separated by little stroma. In melanoma similar to sarcoma, spindle cells often preponderate. Free pigment may also be found in the tissue, after breaking up of pigmented cells, or inside of histiocytes. Malignant melanoma is found in the area of the eye most frequently in the uvea but also in the conjunctiva and on the eyelid. The melanoma of the uvea forms metastases directly through the blood circulation; the melanoma of the conjunctiva and lid skin spreads first in the lymph vessels to regional lymph nodes and from here into the blood vessels.

Dermoids are congenital and are found on the eyelids and on the bulbus surface, especially at the limbus, and they contain elements of the skin, hornified stratified squamous epithelium, hair follicles, sebaceous and sweat glands, nerve fibers, smooth muscles and occasionally cartilage. They consist of two germinal layers, ectodermal and mesodermal. They are formed chiefly by inclusion of dermal tissue during the closure of embryonic fissures and clefts of the face (sequestration dermoid). Teratoma

is in reality an undertaking of nature to form a new individual in the tissues. It develops from a primitive germinal cell or represents a malformed twin. It contains tissues of all three germinal layers without order and forms frequently malignant tumors of carcinomatous or sarcomatous type. It may be found in the orbit.

PART II. READING OF SOURCE MATERIAL

Engelking, Heath, Kurz report on lipoid deposition in the tissues of the eye.

Jaensch describes lipoidosis in corneal scars, following keratitis neuroparalytica, serpigenous ulcer and keratoconjunctivitis eczematosa, absolute glaucoma and hydrophthalmos, lipoidophages in the anterior chamber and fat granules in Schlemm's canal and iris in cases of glioma, pseudoglioma and vitreous abscess, fatty degeneration in blood vessels and histiocytes loaded with fat granules in the tissue in secondary glaucoma, inflammations and intraocular tumors.

Depositions of lipoid are found by Seefelder in the retina in retinitis circinata and albuminurica, by Verhoeff as floating particles in the form of crystals in the vitreous body.

Fatty degeneration of the retinal ganglion cells in amaurotic idiocy is reported by Bielschowsky, Hamburger, Jaffe.

Heath, Rowland describe xanthomatous deposits in the orbit in Christian-Schueller disease associated with diabetes insipidus.

Wolff describes hyalin-like bodies found in the intra-ocular fluid and the tissue as so-called hemoglobin-bodies, formed by clumping of about 25 erythrocytes, and fibrin, bodies which are deposited as spherical protrusions on the inner limiting membrane appearing in inflammations.

Mandicevski describes calcareous deposits in the form of thin plates and needles in the anterior and posterior chambers.

Depositions of crystals of bi-urate of sodium in the cornea in gout is reported by Weve, in the sclera by Wood.

Fuchs finds as consequence of the softening of the eyeball the posterior corneal layers folded, the anterior sclera bale-shape and the posterior part of the iris lies in an anterior plane in comparison to the anterior part of the iris. The outer retinal layers are folded and edema of the papilla sets in due to a great difference between intra-ocular and intra-cranial pressure.

According to Collins, fibrous tissue develops in the eye around foreign bodies, neoplasms, parasitic cysts to encapsulate them and in trachoma and vernal catarrh due to down-growth of the epithelium.

Duke-Elder reports about measurements of the pressure in arteries, veins, and capillaries of the eye.

Pollock describes the terminal plexuses containing many ganglion cells disseminated over the uvea and attributes them to self-determination.

Cohen and Bothman, Magitot and Bailliart found in animal experiments constriction of the retinal vessels in stimulation of the cervical sympathetic nerve.

Magitot found in stimulation of the cervical sympathetic constriction of the uveal vessels accompanied by the decrease of the intra-ocular pressure.

Links states that severing of the sympathetic nerve produces an increased permeability of the capillaries of the eye.

The dilation of the capillaries in the eye does not go parallel with their permeability; the permeability of the capillaries is decreased in spite of their dilation after severing of the cervical ganglion of the sympathetic nerve (Asher).

Adrenalin, histamin, dionin, cholin, atropin, and pilocarpin increase the permeability of the capillaries in the eye (Adler and Landis, Duke-Elder, Kikai, Szasz.)

It seems that axon reflexes of the sensory nerves in the eye liberate in their stimulation histamin from the cells and produce dilatation of blood vessels as this finds its expression in trauma of the cornea (Colle, Duke-Elder and Duke-Elder), in iris wounds (Magitot), or contusion of the eye (Larsson, Leplat).

Scheerer finds in the central vessels of the optic nerve in cadaver eyes blood coagula resembling emboli. He believes that some formations described as emboli in reality are postmortal blood coagula.

Loewenstein and Garrow describe cases with multiple thromboses in vessels of retina, choroid and optic nerve. There are chains of aneurysms with fatty walls and vessels are newly formed (rete mirabile). Hemorrhages originate through rupture of vessel walls.

Rintelen finds in comparing arteriosclerotic changes of the brain, the heart, kidney and large vessels with those of the eye that the vascular sclerosis in one organ can exist without being found in another and that also not all the vessels of the eye show equal changes. There is a parallelism only between the sclerosis of the vessels of the retina and the kidney.

Uyama describes as thromboangiitis obliterans in the eye proliferation of the intima in arteries and veins and occlusion of their lumina by a fibrin-like substance.

Fuchs finds in chronic inflammation with plasma cells sometimes multinuclear plasma cells and Russell bodies present. Some of the Russell bodies can be seen still inside of the cells.

Weiss describes spread of eye infections, especially of those appearing in sub-tropical and tropical countries.

Babel found in a 35-year old man with arthritis panophthalmitis which showed histologically typical nodules with micronecrosis, edema, histiocytes with clear cytoplasm and occasional giant cells.

Blank finds similar germs on normal corneae as in normal conjunctivae, especially staphylococci, xerosis bacillus and pneumococci.

Various types of pneumococci can produce ocular infection, according Fodor and Vlastis, Lobeck.

Salvati observed cases of panophthalmitis caused by micrococcus catarrhalis.

Diplobacillus Morax-Axenfeld is frequently found in normal conjunctiva by Pillat.

Knorr is of the opinion that influenza- and Koch-Weeks bacilli are identical.

Mayou finds xerosis bacillus already early in the eye of the infant and believes that it is identical with a bacillus found in the vagina.

Krueckmann finds that in ocular tuberculosis an active pulmonary tuberculosis cannot be proved, but that the infection probably originates from bronchial lymph nodes.

Pasternak describes cases of tuberculous panophthalmitis.

Meller, Urbanek report about frequent appearance of tubercle bacilli in the blood in various ocular diseases.

Harley, Naar, Plingst report on histologic changes in ocular leprosy.

Fernandez, Fuchs, Gyotoku found lepra bacilli in various parts of the eye which apparently were normal.

Cattaneo finds in fetuses with congenital lues nearly always spirochetes in all ocular tissues except lens, vitreous and retina. Some tissues show lymphocyte and plasmacell infiltration, most frequently the choroid.

Stock describes a metastatic opthalmia with necrotic masses in the vitreous surrounded by polymorphonuclears and giant cells and mycelia probably of aspergillus fumigatus.

Gots, Thygeson and Waisman find in seborrhoic blepharitis a yeastlike organism, pityrosporum ovale.

Thygeson gives a resume of the virus diseases of the eye.

Inclusion bodies are the virus itself, according to Howard, Thygeson; specific protoplasmatic changes caused by the virus, according to Lumbroso; nonspecific formations in the cytoplasm, according to Gifford and Lazar.

Basophilic inclusion bodies are found in trachoma by Nagy, Rohrschneider, further in inclusion blenorrhea of the newborn by Hamburger, Roetth.

Lindner describes intracellular and extracellular basophilic inclusion bodies containing initial bodies peripherally and elementary bodies in their center.

Thygeson succeeded in producing inclusion blenorrhea by inoculation of inclusion bodies.

Friendenwald, Fuchs and Lauda, Loewenstein, find acidophilic inclusion bodies in the epithelium of conjunctiva and cornea in herpes.

Neame finds histologically in herpes zoster opthalmicus subconjunctivae round cell infiltration, new fibrous tissue underneath the irregular corneal epithelium and vascularization of the stroma. There are accumulations of epithelioid cells surrounded by lymphocytes in the cornea and choroid.

Bland describes the infecting organism of trachoma as agent in intermediate position as link between virus and rickettsia infection.

Busacca, Cuenod and Nataf, describe Rickettsia bodies in the epithelium of the conjunctiva in trachoma.

Filariæ in the anterior chamber were seen by Gabrielides, Mayou, in whose case the worm was calcified, Laignier-Terasse, Muehlens and Mylius.

Johnstone found loa loa in the eye. Fernando, Wright report on filaria Bancrofti in the eye. Quevedo, Silva report ocular onchocerciasis.

Semadini found microfilaria of onchocerca volvulus situated in the epithelium of the conjunctiva, parenchyma of the cornea, iris, ciliary body, sheaths of the optic nerve and between sclera and muscles.

Cysticercus cellulosae is found in the anterior chamber by Guliakov, in the posterior segment by Lewitzky, Michail.

Ocular sparganosis produced by the larvae of a tape-worm (dibothriocephalus mansoni) shows periorbital fibrosis, diffuse or pseudo-cystic as a result of the encystment of the larvae (Collin).

Contardo and Peralta report on the findings of larvae of cochliomya Americana or hominivorax in an injured eye and orbit of an 82 year old man.

Barczinski reports larvae of hypoderma bovis in the anterior chamber of a 6 year old boy.

Maggots can perforate through the sclera into the eye (Archangelsky and Braunstein, Behr), through corneal scar (Weisz).

Ophthalmomyiasis anterior is reported by Balod, Bietti, Borsello, Derer, Hartmann, Kuriks, Maggiore, Spanyol, Weisz.

Ophthalmomyiasis posterior is reported by Archangelsky and Braunstein, Behr.

Suurkuela gives a resume of ophthalmomyiasis.

Schmidtke finds as expression of the hypovitaminosis A neurotrophic lesion in conjunctiva and cornea, keratoconjunctivis sicca, conjunctival pigmentation, congenital lesions and night blindness.

Reese gives a resume of pigmented tumors of the eyes which are of ectodermal and mesodermal origin.

Heyl describes various intra-ocular tumors.

Nitsch found a neurofibromatosis of the eye with changes in the episclera, sclera, cornea, iris, ciliary body and choroid.

Pascheff calls phacomata of the eye nevus flammeus, plexiform neurofibroma and elephantiasis neuromatodes of the lid, heterochromic pigmentation of the iris with absolute glaucoma and meningoblastoma of the optic nerve sheaths.

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CHAPTER V

PATHOLOGY OF THE CORNEA

1. INFLAMMATIONS OF THE CORNEA (KERATITIS)

GENERAL CONSIDERATIONS: The cornea is avascular. It has therefore been of great interest to the pathologist to find the source of the inflammatory cells of the cornea. The question has been whether the migratory cells appearing in the cornea in inflammations arise from the fixed cells or from the blood circulation. If, through chemical or thermal irritation, bacteria or toxins, an inflammation of the cornea is produced, polymorphonuclears or lymphocytes appear, depending on the type and intensity of the stimulus. In the beginning of the inflammation, polymorphonuclears (microphages) migrate from the marginal loops into the cornea. Later, histiocytes (macrophages) proliferate which originate from the corneal corpuscles. Soon the cornea may be filled with infiltrating cells which lie in the interlamellar spaces and block them. In these narrow spaces, the cell nuclei take on bizarre forms. They are mostly flat, compressed and elongated. If, because of damage to the lamellae from the inflammatory irritant, or because of blocking of the fluid spaces and malnutrition, the lamellae disintegrate and larger spaces are formed, the cell nuclei attain a shape resembling that of the polymorphonuclears and monocytes.

The usual classifications of corneal diseases are unsatisfactory as they are based sometimes on clinical appearance or clinical course and at other times on etiology.

Suppurative (Acute) Keratitis (Corneal Ulcer)

This condition is characterized histologically as follows: (1) Infiltration of the cornea with polymorphonuclears, (2) necrosis of the corneal tissue with the formation of ulcers, (3) avascularity of the cornea, and (4) secondary iritis with exudation of polymorphonuclears into the anterior chamber.

In addition, reparations of various kinds are found, depending on the severity of the corneal defect.

Suppurative keratitis includes: (1) mycotic keratitis, (2) serpiginous ulcer, (3) diplobacillary ulcer, (4) posterior abscess of the cornea, (5) ring abscess, (6) keratitis e lagophthalmo, (7) keratitis neuroparalytica, (8) keratomalacia, (9) keratitis pustuliformis profunda, (10) atheromatous ulcer, and (11) suppurative corneal inflammations in infected injuries and secondary to conjunctivitis.

Mycotic keratitis (keratomycosis). Parts of the cornea are necrotic, permeated by mycelium, and surrounded by infiltration rings of polymorphonuclears and lymphocytes. The anterior chamber contains polymorphonuclears and fibrin, and the iris and ciliary body are infiltrated with round cells. An ulcer is formed, and the mycelium may perforate Descemet's membrane and appear in the anterior chamber. In the noninfiltrated parts of the cornea, the lamellae appear normal, but nuclei are no longer stained. The infecting organism is the aspergillus fumigatus (aspergillus keratitis, aspergillosis). Streptothrix infection is also seen, but has not been examined histologically, and there are only a few rare cases of yeast- and botryomycosis-infection reported.

Ulcus serpens (serpiginous ulcer, pneumococcal ulcer, hypopyon ulcer). Ulcus serpens is characterized by dense, flat-shaped infiltration of the middle layers of the central cornea, parallel to the surface, with polymorphonuclears, hypopyon, and infiltration of the iris with polymorphonuclears. The corneal lamellae over the infiltration may appear normal in the beginning or may become necrotic and disintegrate with the appearance of an ulcer. At first, the ulcer is covered with necrotic debris of polymorphonuclears and destroyed lamellae. As soon as the necrotic material is removed, the thickened epithelium grows over the clean ulcer. The epithelium is irregular, shows mitoses, and is detached in areas. Usually, the infiltration extends beyond the ulcer beneath the nonaffected lamellae. In the area of infiltration, the lamellae are swollen and disintegrated. In addition to the infiltration in the center of the cornea, there is usually a second area of infiltration in front of Descemet's membrane.

Accumulations of bacteria (pneumococci) are sometimes on the margin of the ulcer and are also found further away between the corneal lamellae. The hypopyon is sterile as long as the cornea is not perforated. Descemet's membrane may be perforated in the early stages of the corneal infection through histolysis from the side of the cornea or the chamber. The pus cells of the hypopyon which stick to the posterior surface of the cornea may erode Descemet's membrane and infiltrate the posterior corneal lamellae (early perforation of Descemet's membrane).

Just anterior to Descemet's membrane a posterior abscess will be formed, sometimes splitting the membrane and projecting into the anterior chamber. The endothelium is sometimes detached and disintegrated. Toxins diffuse into the chamber and produce an acute inflammation of the iris and ciliary body with exudation of polymorphonuclears and fibrin into the chamber, forming the hypopyon which also may contain eosinophils, mast cells, lymphocytes, large monocytes, and phagocytes filled with pigment granules. A serpiginous ulcer arises if pus-forming organisms enter the corneal stroma through a defect in the epithelium. In the majority of cases a pneumococcus causes the ulcer, but other bacteria also may form very similar ulcers, especially the diplobacillus and bacillus pyocyaneus. Occasionally, a traumatic or chemical agent may have a greater effect than the introduced bacteria. Frequently, bacteria, such as pneumococci, are already present in the conjunctival sac, especially in the presence of dacryocystitis, when the cornea is injured by pieces of stone or carbon, plant hairs, grains of corn, leaves or twigs. Usually, a corneal erosion precedes the ulcer. Reduced tissue resistance plays a role in the formation of the ulcer. Consequently, it appears especially in older persons and in arteriosclerotics, cachectics and alcoholics. Predisposing local factors are absolute glaucoma, herpes of the cornea, trachomatous pannus, leukoma. After perforation of the cornea, bacteria enter the eye, and endophthalmitis is the sequela.

Diplobacillary ulcer. Histologically, the diplobacillary ulcer appears similar to the serpiginous ulcer. Polymorphonuclears enter between the epithelium and Bowman's membrane. The

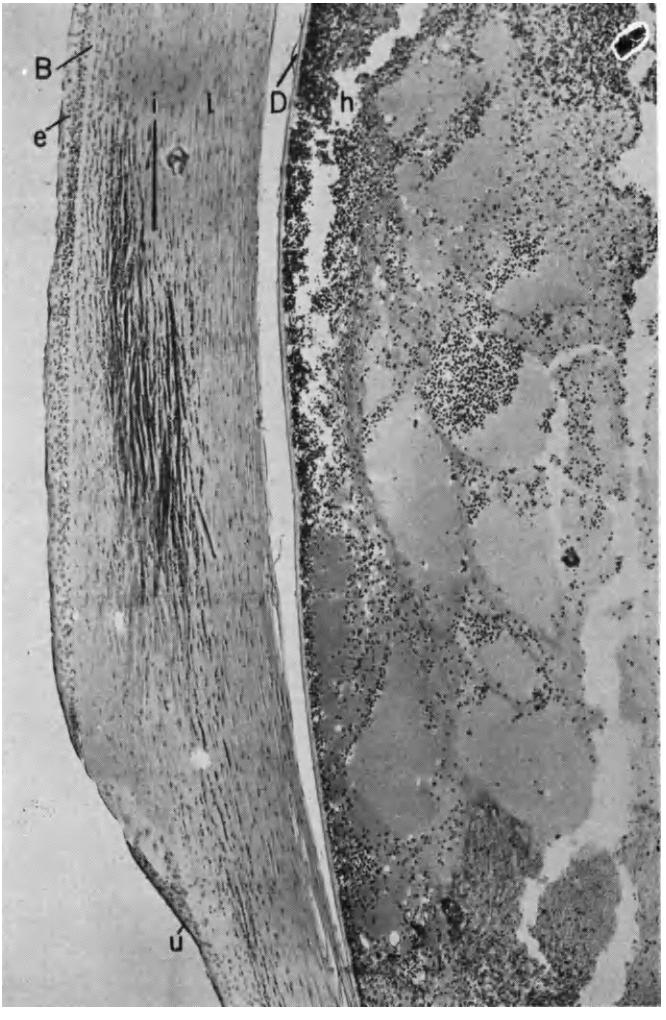

FIG. 8-a.—SERPIGINOUS ULCER. B, Bowman's membrane; D, Descemet's membrane artificially detached; e, epithelium; h, hypopyon consisting of polymorphonuclears, fibrin and serum; i, infiltration of lamellae with polymorphonuclears; l, corneal lamellae; u, cleaned ulcer. 45×.

central middle layers show infiltration with polymorphonuclears; an ulcer is formed, and in the deep layers in front of Descemet's membrane polymorphonuclears are accumulated. The periphery of the cornea remains intact. Hypopyon is present. Corneal lamellae are necrotic in the area of infiltration. Diplobacilli are found between the polymorphonuclears, epithelial cells, and lamellae, and are arranged in long rows, never in heaps. The cornea may perforate. The diplobacillus affects the cornea especially in cachectics.

Posterior abscess (internal ulcer). This affection is either secondary to serpiginous ulcer and trauma, in which cases bacteria grow in the anterior chamber or in the corneal stroma, or primary, as a metastatic infection. When toxins diffuse through the cornea, or bacteria grow in the deep layers of the cornea, or toxins enter the cornea from the anterior chamber through Descemet's membrane, chemotaxis acts on the deep anterior ciliary vessels from which pus cells migrate anterior to Descemet's membrane. They form an accumulation of cells between the deep corneal lamellae which necrotize. Thus, an abscess is formed. Descemet's membrane may be split and polymorphonuclears infiltrate it. If Descemet's membrane is destroyed, a posterior corneal ulcer exists. Pus cells may also enter the cornea from an hypopyon through the endothelium and Descemet's membrane.

Primary posterior ulcer. This affection has various etiologies. During the fetal period, inflammation of the posterior corneal layers may arise, probably through endogenous infection by way of the placenta. Tuberculosis and syphilis may produce pussy infiltration in the posterior corneal layers and perforation into the anterior chamber with the formation of hypopyon. The posterior abscess is found in acquired syphilis (luetic hypopyon keratitis); it is questionable if it is also found in congenital syphilis. In interstitial keratitis also, occasionally Descemet's membrane is perforated, but no pus is formed and hypopyon is scarcely ever seen. Internal ulcer is sometimes complicated by endophthalmitis.

Ring abscess (peripheral annular infiltration). This type shows a typical histologic picture. The central cornea is necrotic

and shows pyknotic nuclei, shadows of nuclei, or absence of nuclei; the lamellae are barely stained, indistinct and swollen; the limbus region is circularly infiltrated with polymorphonuclears which are grouped in an anterior and posterior zone. Epithelium and endothelium are fallen off. Hypopyon is present. A ring abscess may appear after perforation of the eye with infection of the anterior chamber in case of a necrotizing intra-ocular tumor or may be metastatic. Bacteria may enter

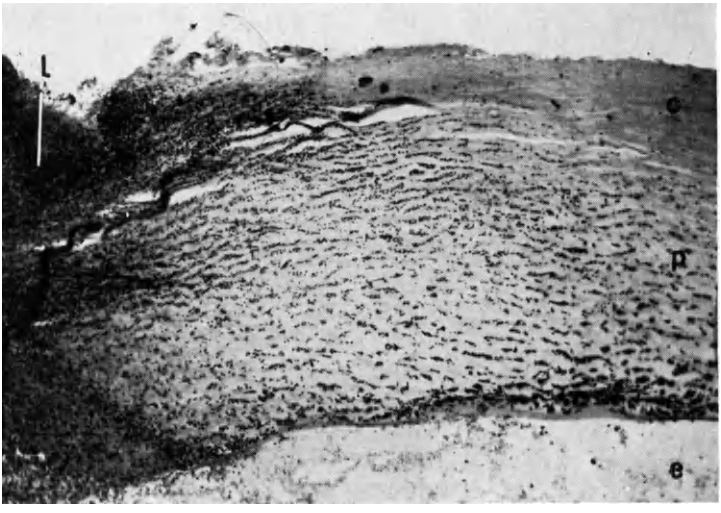

FIG. 9.—RING ABSCESS. c, necrotic cornea; e, exudate in anterior chamber; l, limbus; p, polymorphonuclears. 65×.

the anterior chamber; their toxins spread to the avascular cornea from the chamber, causing necrosis. In the case of a necrotic tumor, toxic products of the tumor diffuse in the intra-ocular fluid and cause necrosis of the cornea. The ring abscess is followed by endophthalmitis. Pneumococci, streptococci, staphylococci, Bacillus subtilis, Bacillus pyocyaneus, and Bacillus proteus are the producing organisms. A ring abscess may be found to be metastatic in endocarditis, pneumonia, otogenous sinus thrombosis, purpura, and diabetic carbuncles.

Keratitis e lagophthalmo. In this form, epithelial defects appear in the exposed peripheral part of the cornea. In the

beginning, Bowman's membrane is intact, and beneath the epithelial defect the interlamellar spaces are filled with polymorphonuclears and broken-up nuclei, usually most densely in the interior and decreasingly in the posterior corneal layers. As the inflammation progresses perpendicularly into the deeper corneal layers, there are, in front of Descemet's membrane, many polymorphonuclears which sometimes lie almost between Descemet's membrane and the endothelium. As a result of necrosis of the infected corneal stroma an ulcer is formed destroying Bowman's membrane and lamellae, and the cornea may finally be perforated, causing endophthalmitis. The anterior chamber contains fibrin and polymorphonuclears. Primary is the desiccation of the noncovered exposed cornea and secondary is the infection with pus-producing bacteria. When, for any reason, the interpalpebral fissure cannot be closed, this form of keratitis may appear. This is the case in (1) severe proptosis, as in orbital tumor, Graves' disease, and in a relatively short orbit in oxycephaly; (2) cachexia of malignant tumors and long lasting coma from any cause; and (3) ectropion through paralysis of the orbicularis muscle, spasm of the elevator of the upper lid, or traction of scars.

Keratitis neuroparalytica. In neuroparalytic keratitis, the center of the cornea shows a flat ulcer, on the margin of which epithelium may have already proliferated. The epithelium may be thickened epidermis-like and filled with migratory cells. In some cases, desquamation of epithelium may be marked. The lamellae beneath the ulcer are necrotic and studded with polymorphonuclears. Many are gathered in front of Descemet's membrane. Endothelium may be missing in some areas and proliferate in others. The hypopyon is rich in fibrin. In addition to infiltration and destruction there is proliferation of fixed cells in the middle and deeper corneal layers. The keratitis is caused by a lesion of the trigeminus, mostly when the ganglion Gasseri is destroyed by operation or disease, but also by disease of the trigeminus nucleus in the pons cerebri and the supraganglionic trigeminus root. It is considered to be neurotrophic keratitis, as the damage to the corneal nerves apparently deprives the corneal surface of its protection. With the absence of the

normal sensory stimuli of the cornea, abnormal stimuli appear in it; furthermore, the insensitive surface of the cornea is more easily traumatized and organisms may enter more easily and infect the cornea secondarily. Because of the absence of normal sensibility, disturbances of the cellular metabolism probably take place, and abnormal metabolites are accumulated in the epithelial cells, inducing epithelial edema and exfoliation of the epithelium. In consequence, trauma, desiccation, and infection contribute to the pussy inflammation.

Keratomalacia. In keratomalacia, the corneal epithelium is transformed into stratified hornifying epithelium which becomes defective in areas. Bowman's membrane is destroyed, the superficial corneal lamellae are necrotic, and an ulcer is formed. The surrounding area of the ulcer is infiltrated with polymorphonuclears, which also form a zone of heavy infiltration in front of Descemet's membrane. The anterior chamber contains polymorphonuclears. Descemet's membrane perforates early, resulting in endophthalmitis. Pneumococci and streptococci may be found in the cornea. The conjunctiva may show xerosis, the primary cause of which is vitamin A deficiency, due to lack of the vitamin in the diet or failure to absorb it because of digestive disturbances. Frequently, severe enteritis in infants is complicated by keratomalacia, the affection being common in countries suffering from famine and malnutrition. Primarily, the epithelium is diseased, the corneal stroma only secondarily through immigration of pathogenic bacteria.

Keratitis pustuliformis profunda. In this type, there is an infiltration with polymorphonuclears of the posterior corneal layers, a defect of Descemet's membrane and endothelium, and proliferation of the fixed cells, or the latter may be diminished and polymorphonuclears fill the anterior chamber. Abscess of the posterior cornea may be single or multiple. The cause is syphilis, which appears either primarily in the cornea and produces here suppurative inflammation or is deposited primarily in the iris and from here affects the cornea secondarily.

Atheromatous ulcer. In this ulcer, the cornea shows superficial scars with hyaline and calcareous deposits. The scar is necrotic, the epithelium partly desquamated and proliferating

into the depth between the loosened masses of hyaline and calcium and the intact cornea. The necrotic area is surrounded by polymorphonuclears which also appear in the anterior chamber. The primary condition is the sequestration of the degenerated scar (sequestrating cicatricial keratitis). The secondary infection leads to suppuration and eventually to perforation of the cornea, subsequently to endophthalmitis which may also occur without perforation through the adherent iris in adherent leukoma.

Suppurative keratitis. Suppurative keratitis in injury gives various pictures depending on whether or not the cornea is perforated. From the wound canal, zones of infiltration of varying shape and extent spread into the parenchyma. Lamellae are necrotic and hypopyon may appear.

In suppurative keratitis secondary to conjunctivitis, the corneal parenchyma shows suppurative infiltration, destruction of Bowman's membrane and necrosis of lamellae, but there is no hypopyon present, and pus may appear in the anterior chamber only following perforation of the cornea; vascularization of the cornea may be present. Severe suppurative infiltration of the cornea is seen especially in gonococcic conjunctivitis, also in conjunctivitis caused by diphtheria and streptococci.

Nonsuppurative Superficial and Deep Corneal Inflammations

To this group belong: (1) herpes corneae, (2) keratitis superficialis punctata, (3) nummular keratitis, (4) keratitis superficialis diffusa, (5) superficial linear keratitis, (6) traumatic corneal opacity, and (7) disciform keratitis. The pathologic pictures vary. In superficial keratitides, the epithelium and Bowman's membrane are affected but in the deep forms remain intact. The infiltrating cells are lymphocytes and plasma cells, rarely polymorphonuclears. The cornea remains avascular and the iris only infrequently is affected with the inflammation.

Herpes corneae shows pathologic changes, in the beginning restricted to the epithelium and extending at a later stage into the stroma. At first, the nuclei are affected. The nuclear membrane is thickened, and the chromatin is clumped together and adheres to it. In the center of the nucleus, homogeneous

acidophil masses appear (Lipschütz' bodies). The nuclei swell more and more and may eventually undergo balloon degeneration. Finally, the epithelium necrotizes with swelling and vacuolation of the cells; the necrotic epithelium is then desquamated and the surrounding epithelium thickened. Bowman's membrane also may necrotize. The superficial lamellae become infiltrated with polymorphonuclears. Finally, the necrotic foci are surrounded by scar tissue and superficial lymphocytic infiltration is apparent. Herpes corneae is caused by the herpes virus, an ultramicroscopic filter-passing organism which can produce manifold clinical appearances on the cornea: the vesicles of the herpes simplex, herpetic superficial punctate keratitis, dendritic keratitis, extensive separation of the epithelium from Bowman's membrane (epitheliolysis), and stellate keratitis. The virus is related to herpes zoster which also may produce superficial round corneal opacities. Perhaps the virus of the herpes simplex and the herpes zoster are strains of the same virus, the herpes simplex being a dermotropic and the herpes zoster a neurotropic strain.

In *superficial punctate keratitis,* the changes take place in the epithelium and superficial lamellae of the cornea. The epithelium and superficial corneal lamellae show edema with swelling and necrosis of epithelial cells and fibrin threads, which may undergo hyalin degeneration and lie in front of and beneath Bowman's membrane. Lymphocytes may appear between the epithelium and lamellae; while beneath Bowman's membrane, necrotic areas may appear which contain polymorphonuclears and debris of chromatin and cytoplasm. Sometimes degenerative, sometimes inflammatory processes are more marked. There is probably a virus infection present, but a bacterial origin has been assumed and a neurotropic theory (affection of the Gasserian ganglion) is also suggested. The superficial punctate keratitis, however, is not a disease entity; it indicates only discrete superficial opacities due to degenerative or inflammatory processes. Many forms are symptomatic, associated with other diseases of the eye or the body, and are examined clinically only, not histologically. It may appear in several febrile diseases, like measles, influenza, chickenpox; also in eczematous diseases, in leprosy, epidemic

keratoconjunctivitis, herpes, in iridocyclitis, snow blindness, ophthalmia electrica; and as keratitis epithelialis vesiculosa disseminata and multiple epithelial erosions.

Nummular keratitis is apparently an occupational disease occurring in young farmers. It is seldom examined histologically. It may show large round opacities beneath Bowman's membrane in addition to a superficial and deep vascularization. Its etiology is unknown. The lamellae disintegrate and are surrounded by infiltrating cells as the keratoblasts proliferate.

In *diffuse superficial keratitis*, there is essentially an edema of the basal cells and an accumulation of infiltrating cells between the basal cells and Bowman's membrane which is wavy and thin and may be split or even destroyed. The epithelium is irregular and of varying thickness; the superficial lamellae may show edema and infiltration. The condition is apparently due to a deficient and disturbed metabolism, perhaps caused by a deficiency of vitamin B_2.

In *superficial linear keratitis* (letter-shaped keratitis), the main characteristic is the many folds of Bowman's membrane over which the epithelium may be normal or eroded and under which fibroblasts and fibrils proliferate. The affection is always associated with decreased intra-ocular tension and appears in perforated eyes and atrophia bulbi. Though there are inflammatory changes in these bulbi, similar folds of the Bowman's membrane appear after operation (e.g., cataract operation) and trauma; also, where no inflammation arises (superficial striate opacities, lattice-like keratitis).

Traumatic corneal opacities appearing after severe contusion of the globe show edema and necrosis of lamellae with circumscribed splitting up into fibrils karyorrhexis and karyolysis in corneal corpuscles. At the same time, the surrounding keratoblasts proliferate and cells wander in.

In *disciform keratitis*, there is inflammation of central corneal lamellae with a swelling of the fibrils, edema, necrosis, and loss of corneal corpuscles. This central disclike area is surrounded by lymphocytic infiltration of varying density, decreasing in intensity antero-posteriorly. The anterior chamber may contain fibrin and blood. Trauma and ectogenous infection are held

to be the cause. Perhaps it is a virus infection. The condition may develop in the course of superficial punctate keratitis or herpes corneae when the disease extends from the surface into the deeper parenchyma.

Corneal involvements of vernal conjunctivitis are secondary to changes in the conjunctiva. They are: (a) direct extension of the limbus changes into the surface of the cornea, and (b) dystrophies caused by the decrease in nourishment of the cornea through changes in the limbus. The epithelium is affected; the epithelial cells degenerate and may completely necrotize; finally, formless detritus remains. Or the epithelium shows small round papilloma-like proliferations with thickened hornifying stratified epithelium, the cells of which have darkly stained granules and the base of which is fine connective tissue with destruction of Bowman's membrane beneath.

Phlyctenular (eczematous, scrofulous) keratitis shows: (a) nodules of lymphocytes between the epithelium and Bowman's membrane, or beneath Bowman's membrane; (b) infiltration of the epithelium; (c) destruction of Bowman's membrane; (d) superficial vascularization; (e) formation of ulcers through destruction of the epithelium and the superficial lamellae; (f) formation of connective tissue replacing the superficial vessels; and (g) infiltration of the superficial and deeper lamellae with polymorphonuclears in the case of secondary infection. It is a part of the eczematous keratoconjunctivitis.

As sequel, nodular dystrophy (Salzmann) may appear as a slowly progressing degeneration. The epithelium is thickened and degenerated. Bowman's membrane is destroyed. The superficial corneal lamellae split up into fibrils and vacuolize, and the nuclei become pyknotic. Cellular infiltration appears and vessels grow into the cornea.

Rodent ulcer (Moorens' ulcer) has some characteristic features such as: (1) extensive necrosis of the epithelium and Bowman's membrane, necrosis of the lamellae to a considerable depth, and thinning of the cornea without perforation; (2) by this necrosis, a marginal ulcer being formed with undermining edges; (3) epithelial strands proliferating into the depth; (4) granulation forming on the floor of the ulcer and incomplete reparation

setting in; (5) scanty infiltration of the tissue appearing in comparison to the intensity of the ulcerating process; and (6) numerous small blood vessels growing in. The ulcer begins on the margin of the cornea and extends toward the center. The overhanging tissue consists of thickened epithelium which grows around the margin, and infiltrated fibrous tissue containing blood vessels. The epithelium proliferating into the depth appears, depending on the sectioning, as epithelial islands in the tissue.

The infiltrating cells are mostly lymphocytes, but there are also polymorphonuclears, plasma cells, and eosinophils. Furthermore, hemorrhages are present. The thinned cornea contains fairly normal lamellae with few vessels and an increased number of nuclei. Descemet's membrane and endothelium are unchanged. On the floor of the ulcer are islands of epithelium, part of Bowman's membrane and a few remnants of lamellae, and granulations. Little scar tissue is formed. The limbus and episclera are very hyperemic and infiltrated. The etiology of this chronic ulcer is unknown; bacilli have been considered a cause, and malnutrition and necrosis of nervous origin may also be contributing factors. It has also been assumed that an episcleritis or scleritis should be the primary source, and from here granulation tissue extends over the cornea.

Interstitial keratitis (parenchymatous keratitis) takes a different course in the fetus and newborn, on the one hand, and in the child and adult, on the other hand. In the former, the epithelium is disintegrated; Bowman's membrane is intact; between the lamellae are polymorphonuclears and necrotic nuclei; corneal fixed cells proliferate. Descemet's membrane and endothelium are intact. In the latter there is: (1) necrosis of corneal corpuscles and lamellae; (2) secondary immigration of lymphocytes which lie in the interlamellar spaces; (3) rows of plasma cells and polymorphonuclears fill the interlamellar spaces; (4) deep blood vessels appear in the form of endothelial tubes, accompanied by lymphocytes and plasma cells interlamellarly; (5) the interlamellar spaces are dilated and the lamellae swollen; (6) giant cells may appear, especially in the depth in front of Descemet's membrane; (7) fixed cells and connective tissue fibrils

proliferate; (8) the epithelium may become atrophic and Bowman's membrane may be eroded; (9) the cornea, especially in the center, is markedly thickened through swelling of the lamellae and infiltration and proliferation of young connective tissue, which may cause permanent scars; (10) Descemet's membrane may be folded, is occasionally perforated, and the endothelium desquamated.

The posterior surface of the cornea may be covered by keratic precipitates. Infiltrated fibrous tissue containing giant cells also may bulge the corneal center toward the anterior chamber through the perforated Descemet's membrane. The connective tissue, proliferating into the anterior chamber, may remain attached to the endothelium, eventually undergoing hyaline degeneration and forming a hyaline network and membranes in the anterior chamber. The endothelium may also deposit hyaline material around the exuded fibrin which is coagulated in fine fibers.

(11) The limbus, episclera, anterior sclera, and especially Schlemm's canal are densely infiltrated with lymphocytes, and the vessels may be obliterated. From here granulation tissue, consisting of lymphocytes, endothelial buds, and young connective tissue, may extend into the cornea. (12) The iris is infiltrated with lymphocytes, which aggregate in nodules, and lymphocytes may also be found in the ciliary body and anterior choroid. Giant cells may also accompany the infiltration. Occasionally gummatous changes may exist in the ciliary body.

The interstitial keratitis of the fetus and newborn is always produced by congenital syphilis; spirochetes are also found in the cornea of congenital syphilitics. Interstitial keratitis in child and adult also results, in the majority of cases from congenital syphilis, rarely from acquired syphilis, tuberculosis or other causes. Histologic changes are the same in all cases, varying only according to the severity of the disease process. Avascular forms also exist. It is not yet certain, however, in what way the spirochetes affect the cornea. Although spirochetes are often found in corneae of congenital syphilitics without keratitis, they may be found more rarely in the corneae with keratitis. Consequently, interstitial keratitis is often considered of allergic origin, similar to the experimentally produced ana-

phylactic keratitis of Wessely, which appears, after repeated injection of foreign serum into the cornea, as severe interstitial keratitis, and in which the corneal lamellae necrotize, the interstitial spaces are filled with polymorphonuclears and monocytes, and numerous vessels appear in the posterior layers. Spirochetes deposited in the cornea produce toxins which cause sensitivity, and if, later on, toxins of spirochetes diffuse from other areas of the body into the cornea by way of the circulation, keratitis

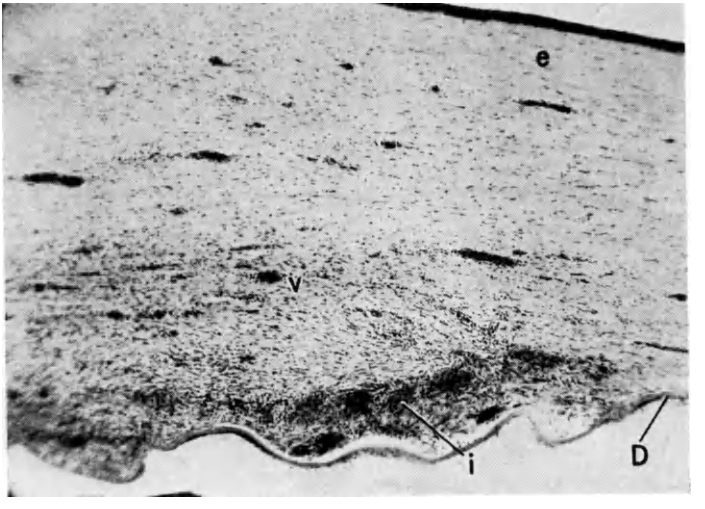

FIG. 10.—INTERSTITIAL KERATITIS. D, folded Descemet's membrane; e, epithelium; i, infiltration with lymphocytes and proliferation of fibroblasts; v, deep vessel and infiltration. 65×.

may appear. In tuberculous interstitial keratitis the tubercle bacillus is only rarely found in the cornea. The majority of cases seem to indicate an allergic reaction to tuberculin. Occasionally, endocrine disturbances and trauma may be factors in the outbreak of the keratitis.

2. WOUND HEALING, REGENERATION, KERATOPLASTY

If the cornea is severed, healing may be seen accompanied by the formation of a transparent cornea, and the cornea may remain avascular.

If the defect is not too large, is not the result of an ulceration, and no infection has set in, the wound closes by primary intention. In a short while, the defect is filled by fibrin and serum, and the epithelium grows over it, proliferating a short way into the depth of the defect. First, the epithelium covers the defect so that the epithelial cells stretch horizontally and the entire epithelium becomes thinner. But soon mitoses appear, and the number of cells increases. Fixed cells of the cornea are mobilized, and are transformed into spindle-shaped cells with larger and wider oval nuclei, and appear as fibroblasts (keratoblasts). They migrate toward the margin of the wound and start to produce fibrils, which proliferate through the scaffold of the fibrin and unite the lamellae firmly. Bowman's membrane does not regenerate. The defect is filled with scar tissue. Descemet's membrane has a tendency to roll into a spiral shape anteriorly. The endothelium covers the defect in a short time by proliferation, and the endothelial cells start to secrete a new cuticular membrane which either unites with the original Descemet's membrane at the margin of the defect or remains ununited. Sometimes, several layers of a new Descemet are formed. The fibrils which bridge the defect in the corneal lamellae are first arranged in bundles, which later start to form the lamellar structures. At first they are irregular, but subsequently they begin to assume a direction parallel to the surface and in this way simulate histologically the original corneal lamellae.

If the corneal wound is perforating, and especially if the defect is dehiscent, healing by secondary intention takes place. The iris prolapses into the wound. The free surface of the iris becomes hyperemic through irritation and pours out fibrin. Briefly, granulations grow out of the iris, consisting of young fibrous tissue filled with vascular buds and densely infiltrated with lymphocytes. The epithelium and the cornea itself, as far as it is not covered by iris, act as already described in healing by primary intention. The granulations organize, and the newly formed scar tissue is slowly transformed into lamellar tissue.

Keratoplasty is the grafting of a transparent corneal tissue into a nontransparent cornea. The transplants include: (1) the

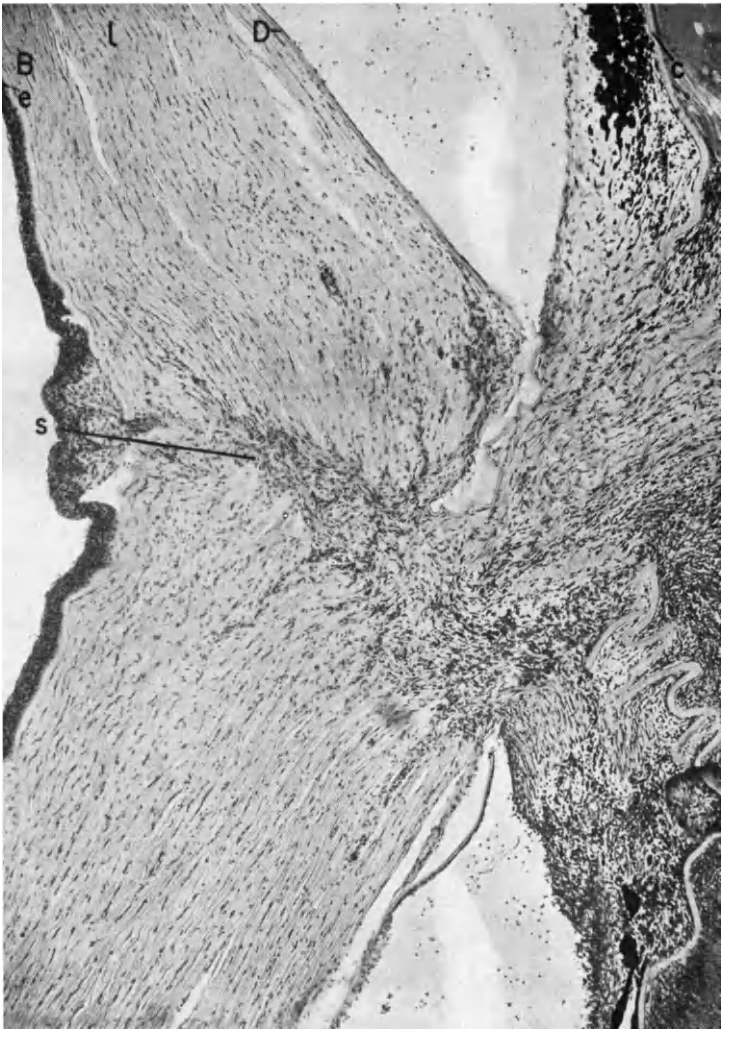

FIG. 11.—WOUNDHEALING OF CORNEA. B, Bowman's membrane; c, lens capsule; D, Descemet's membrane; e, epithelium; i, iris; l, lamellae; s, scar of perforation of the cornea formed anteriorly by cornea and posteriorly by iris. 40×.

entire cornea (total keratoplasty); (2) the anterior lamellae only (superficial lamellar keratoplasty, incomplete keratoplasty); and (3) the entire thickness of a circumscribed corneal piece (penetrating circumscribed keratoplasty, complete keratoplasty). The latter is used almost exclusively, and in many cases gives good results, depending on the nature of the corneal opacity. Cases of permanent corneal opacities following interstitial keratitis, lime burn, or superficial inflammation are relatively favorable; however, dense leukoma after a deep ulcer or perforating injuries are less favorable. In complete keratoplasty, an angular or round portion is dissected from the opaque cornea, and a congruent transplant taken from a transparent cornea is implanted in its place. Histologic examination of cases of keratoplasty shows that Bowman's and Descemet's membrane of the transplants are preserved and are united finally by scar tissue with the membranes of the host. The epithelium, endothelium, and lamellae may also survive. However, blood vessels often grow into the transplant and lamellae are newly formed, substituting the disintegrating tissue of the transplant. Infiltrating cells may appear together with the vessels. If nonliving material is implanted, it is permeated with cells from the living cornea, and these cells in the end form new lamellae.

3. Corneal Scars

If a defect in the cornea extends through the epithelium, Bowman's membrane, and a few superficial lamellae, the newly formed epithelium fills up the entire defect, as it has a tendency to level the surface. This results in a corneal facet. The epithelium is several layers thicker than the surrounding area and dips in waves under the surface beneath the level of Bowman's membrane. A superficial opacity after a defect may be fine (nebula) or dense (macula). First, the defect is traversed by epithelium which partially fills the defect. Keratoblasts proliferate, producing fibrils which unite into bundles to form irregular lamellae, which in the course of time are arranged more and more parallel with the surface. If the defect is large and the scar is dense and whitish, it is called leukoma. The epithelium is irregular and sends downgrowth into the underlying tissue. Bowman's

membrane is lacking, and the tissue consists of more or less numerous irregular nuclei, fibers, fiber bundles, and thin and thick irregular lamellae. Vessels may be present and from the vessels, regeneration may take place into more transparent tissue, which may appear clinically as Fuchs' lines of clearing.

The scar tissue may show deposits of lipoid and hyaline. It is often thinner and less resistant than the normal cornea and

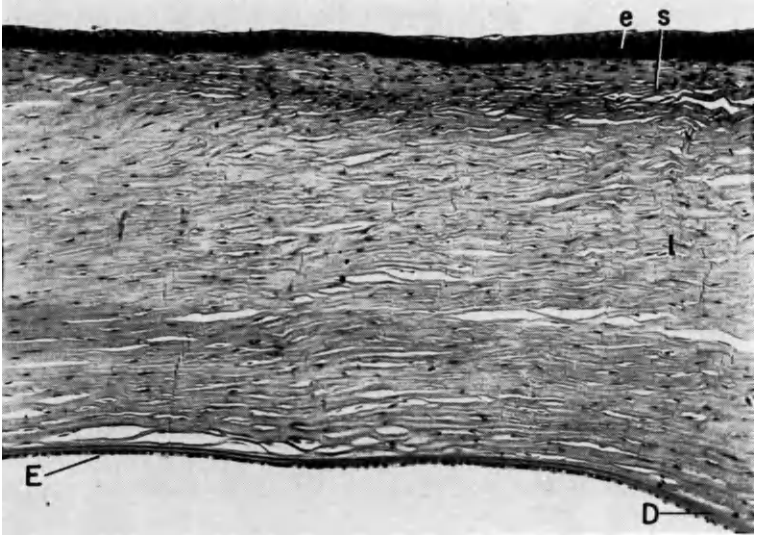

FIG. 12.—CORNEAL SCAR. D, Descemet's membrane; E, endothelium; e, epithelium; l, lamellae; s, small irregular lamellae of scar. 65×.

bulges under the relatively strong intra-ocular pressure to produce a corneal ectasia, which, depending on its extension and the situation of the scar, may include a circumscribed marginal or central area of the cornea, or even the greater part. If the defect in an ulcer reaches the resistant Descemet's membrane, a descemetocele results, around which scar tissue slowly forms, and which may persist for a long time if perforation does not take place. As already mentioned, if the cornea perforates, the iris is usually incarcerated in the wound and assists in the formation of the corneal scar. Anterior synechia takes place. If the

iris protrudes above the surface, prolapse of the iris exists. After perforation of the cornea and incarceration of the iris, a dense scar is formed which is called adherent leukoma. The epithelium is irregular and Bowman's membrane is not present. The lamellae are irregular, or there is only irregular fibrillar tissue with many nuclei, into which the iris extends. In the area of the adhesion, the iris has less stroma or no stroma at all any longer and only the pigment epithelium may be left. If the iris adheres to the wound without participating in the construction of the scar, aqueous humor seeps through the loose tissue of the corneal scar and causes it to bulge (cystoid cicatrix).

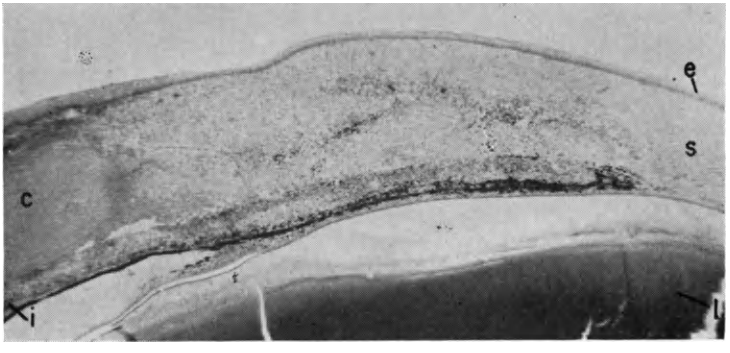

FIG. 13.—RECENT STAPHYLOMA CORNEAE. c, cornea; e, epithelium; i, iris; l, lens; s, staphyloma. 50×.

4. CORNEAL STAPHYLOMA (ANTERIOR STAPHYLOMA)

Corneal staphyloma is formed when the perforating defect of the cornea is large and is regenerated entirely from the iris. Histologically it shows: (1) irregular stratified squamous epithelium; (2) no Bowman's membrane; (3) irregular lamellar tissue with relatively few variously shaped nuclei and probably degenerative changes, such as hyaline plaques, fatty and calcareous deposits; (4) no Descemet's membrane; and (5) the posterior surface formed by irregular pigment epithelium. The staphyloma may be partial or total, depending on whether the entire cornea or a large part of it is substituted by scar tissue

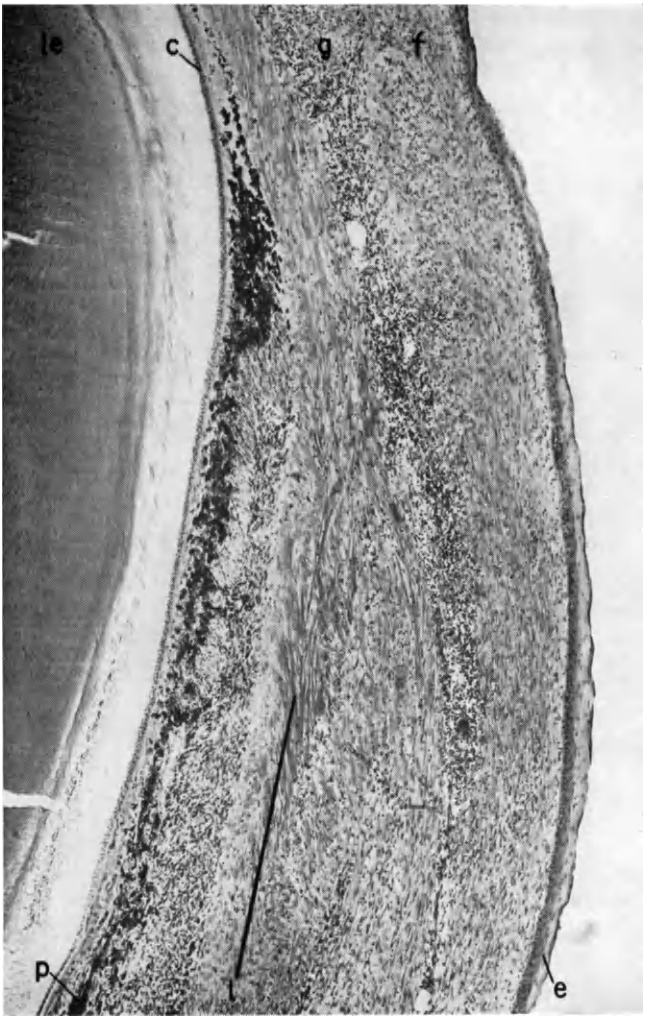

FIG. 14.—RECENT CORNEAL STAPHYLOMA. c, lens capsule; e, epithelium; f, fibrous tissue; g, granulation tissue consisting of lymphocytes and vessels; l, newly formed lamellae; le, lens; p, disintegrating pigmentary epithelium of the iris. 45×.

formed from the iris. If a large defect of the cornea exists, the iris prolapses and closes the defect. In contact with the air, the iris undergoes inflammatory changes through irritation and pours out fibrin onto the surface; the blood vessels dilate; and lymphocytes infiltrate in great numbers. The epithelium soon crosses over the fibrin. The inflamed iris forms granulation tissue as the vessels produce endothelial buds; the lymphocytes

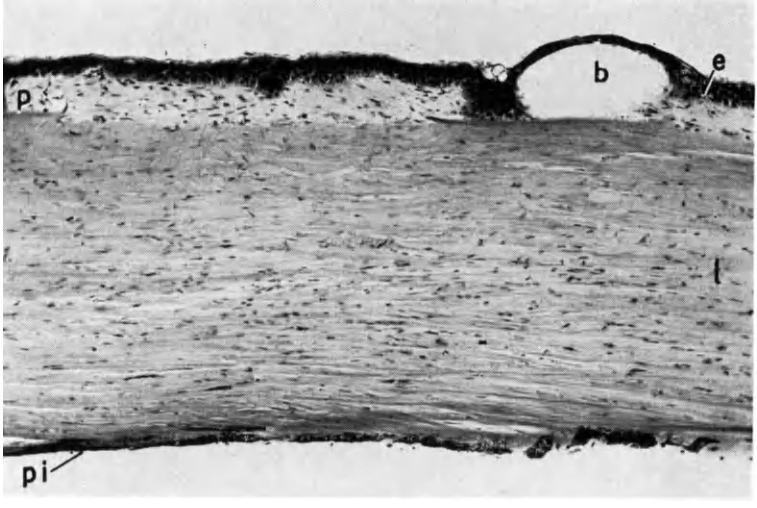

FIG. 15.—STAPHYLOMA CORNEAE, KERATITIS BULLOSA. b, bulla; e, epithelium; l, irregular lamellae; p, pannus degenerativus; pi, irregular pigment epithelium. 65×.

increase; the stroma cells become fibroblasts after the loss of pigment and produce fibrils. The granulation tissue organizes and eventually forms irregular lamellae. Finally, only disintegrated pigment epithelium remains of the iris, and its pigment may be carried into the stroma of the staphyloma. Fluid may enter between the lamellae and separate them.

From this description, it is obvious that there is no anterior chamber in the region of the staphyloma. As the chamber angle is, for the most part, occluded, secondary glaucoma sets in, with bulging of the staphyloma. If the staphyloma is thin, it may break. Sometimes a thin area of the staphyloma bulges (cystoid

cicatrix). In this case, beneath the thin epithelium there is a thin layer of fine connective tissue lined on its posterior surface by the pigment epithelium of the iris. If, at the time of the perforation, the lens is also injured, fragments of the lens, the lens capsule, or the vitreous may heal into the staphyloma.

5. Cysts of the Cornea

These cysts may be (1) intracorneal, (2) retrocorneal, (3) precorneal, or (4) endothelial.

Intracorneal cysts are (a) implantation cysts and (b) pseudocysts. The corneal or conjunctival epithelium may start an ingrowth after perforating injury or operative section. The epithelium displaced into the depth proliferates and finally includes a space lined by stratified squamous epithelium. Such cysts may also be included in the corneo-scleral junction, or sometimes may be confined entirely to the sclera. Pseudocysts may exist congenitally if clefts are formed in the stroma by disturbance of the development of the embryonal cornea. These clefts have no epithelial or endothelial lining but are surrounded by embryonal connective tissue.

Retrocorneal cysts are really cysts of the anterior chamber and the iris, originating from the implantation of the surface epithelium into the anterior chamber, and are united with the corneal substance. Multiple cysts can exist simultaneously in the cornea, anterior chamber, and sclera. They may also be connected with the outer surface of the globe by the sinus.

Precorneal cysts are formed by a deposit of conjunctival epithelium on the corneal epithelium. They are formed, for the most part, through the obliteration of a pterygium on the corneal surface, but may also occur if the conjunctiva adheres to the cornea in the case of an ulcer or a superficial injury.

Endothelial cysts may form if Descemet's membrane ruptures and the endothelium proliferates. In the posterior portion of the cornea, an endothelium-lined space exists.

6. Corneal Fistula

As already mentioned, this is a duct lined with epithelium, which may form after perforation of the cornea, uniting the

anterior chamber with the conjunctival sac. In some cases, there is a preceding cystoid scar. Aqueous seeps into the loose corneal scar, forming lacunae and vesicles, elevating the corneal epithelium; finally, it bursts and the fluid is emptied. Epithelium may grow in secondarily in such a fistula and make it a permanent one.

7. Pannus

Pannus represents a vascular connective tissue, containing lymphocytes in varying quantities which grows in from the limbus of the cornea across its surface. It may be in front of or behind Bowman's membrane. Its etiology varies. It is differentiated as: (1) pannus trachomatosus, (2) pannus scrofulosus, (3) degenerative pannus, and (4) leprotic pannus.

Trachomatous pannus shows (a) irregular epithelium, which sends buds and glandular-like tubules into the depth, and is infiltrated with polymorphonuclears; (b) infiltration with lymphocytes and plasma cells beneath the epithelium and between the most superficial lamellae of the cornea; (c) perforation and absence of Bowman's membrane; (d) appearance of typical follicles; and (e) vessels with thin walls.

The epithelium may show edema, and its nuclei an acidophil degeneration and inclusion bodies. The pannus formation may start in front of or behind Bowman's membrane, with ingrowth of fine vessels and connective tissue and an accumulation of infiltrating cells. Plasma cells are sometimes accumulated in dense masses to form a plasmoma. Ulcers may occur after loss of the epithelium. The pannus may organize into a layer of fine connective tissue. Amyloid or hyaline degeneration may appear in the pannus and can also affect vessel walls; fat may form. In pannus crassus, the anterior two thirds of the corneal lamellae are replaced by granulation tissue. The pannus is the result of an infection of the cornea, in most cases from the bulbar conjunctiva.

Scrofulous pannus (eczematous, phlyctenular) shows: (a) lymphocytic nodules between the epithelium and Bowman's membrane; (b) ingrowth of vessels from the episclera behind Bowman's membrane; (c) proliferation of fibroblasts; (d) nod-

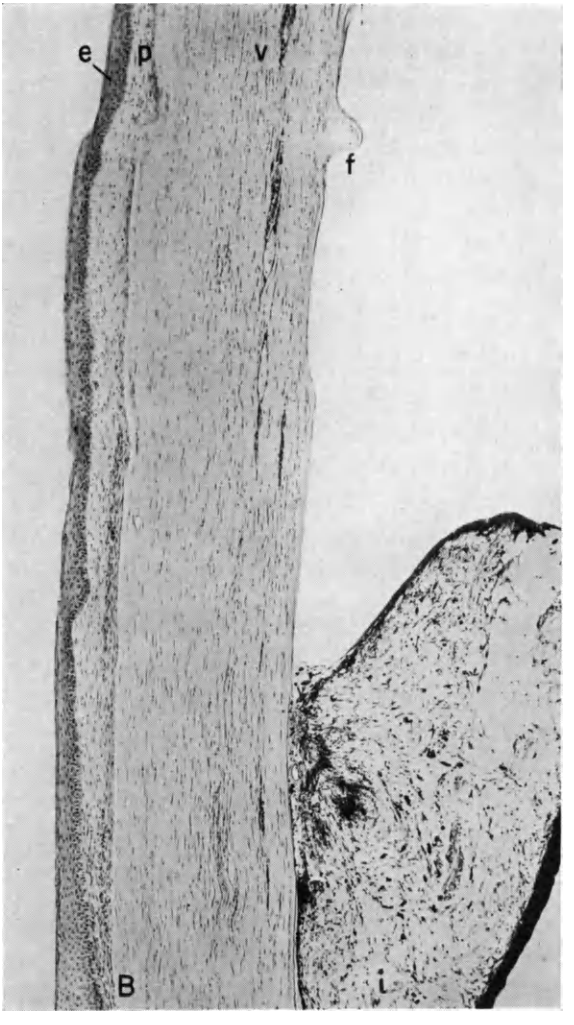

FIG. 16.—DEGENERATIVE PANNUS. B, Bowman's membrane; e, epithelium; f, fold of Descemet's membrane; i, adherent iris; p, pannus degenerativus; v, deep vessels and infiltration. 45×.

ular accumulation of polymorphonuclears beneath Bowman's membrane; (e) at times destruction of Bowman's membrane; (f) formation of ulcers due to necrosis of the epithelium.

This condition is found in phlyctenular kerato-conjunctivitis.

Degenerative pannus shows newly formed vascular connective tissue in different thicknesses between the irregular epithelium and Bowman's membrane. Bowman's membrane is sometimes destroyed. Amyloid and hyaline degeneration may be present. Degenerative pannus is found in blind eyes with primary or secondary glaucoma. It is preceded by the formation of vesicles in the corneal epithelium (keratitis bullosa). The vesicles burst, and Bowman's membrane is denuded (sometimes for a long period) of the epithelium. This is said to act as an irritation to produce the proliferation of fine protective connective tissue from the limbus.

Leprotic pannus shows nodules with round cells and large vacuolated histiocytes, destruction of Bowman's membrane, ingrowth of vessels and connective tissue, and infiltration of the corneal lamellae.

8. Degenerative Processes

In this category are grouped entirely different pathologic processes of various etiologies having one characteristic in common: absence of inflammation but showing degeneration of cells or tissues of different types. These processes include: (1) nodular dystrophy, (2) band-shaped opacity, (3) marginal degeneration, (4) pterygium, (5) epithelial dystrophy, (6) endothelial dystrophy, (7) fatty, hyaline, amyloid, calcareous degeneration of the cornea, (8) lamellar stratification, (9) arcus senilis, (10) myxomatous dystrophy, (11) sclerosis of the cornea, (12) dimples of the cornea, and (13) keratoconus.

Nodular dystrophy (Groenouw) is a hereditary familial degeneration and is related to the lattice-like corneal degeneration. It is characterized by: (a) flattening of the epithelium, (b) disintegration of Bowman's membrane, (c) deposit of hyaline between the corneal lamellae which disintegrate and in some cases show hyaline degeneration, (d) disintegration and proliferation of corneal corpuscles, and (e) appearance of basophil

granules in the epithelium, Bowman's membrane, corneal corpuscles, and migratory cells. There are variations of these changes, as occasionally hyaline appears between the epithelium and Bowman's membrane or the epithelium thickens and proliferates downward.

The etiology is unknown; it may be a dystrophy of the nerves of the cornea of a type of abiotrophy.

Band-shaped opacity is characterized by the deposit of very fine calcareous granules in Bowman's membrane, which appear as bluish dust when stained with hemalum. This condition is a primary deposit of calcium phosphate and carbonate. It is assumed that the tissue fluid is rich in calcium and, on evaporating on the corneal surface, precipitates the calcium. Bowman's membrane is irregularly thickened, brittle and broken up with displacement of the parts which occasionally extend into the irregular epithelium. The irregular epithelium may extend buds into the depth. Bowman's membrane may be covered with lamellar, homogeneous masses. In front of and under Bowman's membrane, much connective tissue is formed, which may undergo hyaline degeneration. The opacity may be primary, but is usually secondary in eyes with severe chronic iridocyclitis. In rare cases, it appears after long exposure to irritating substances, such as animal hairs or fumes.

Marginal degeneration of the cornea shows, beneath an intact epithelium, loss of Bowman's membrane, substitution of the anterior corneal lamellae by fine fibrillary connective tissue with numerous nuclei and fine vessels, fatty deposits in and between the lamellae, and Descemet's membrane torn or thickened and split in layers. The diseased corneal area may be very ectatic. The etiology is unknown; it may be a fatty degeneration or it may be caused by an inner secretory disturbance.

The *pterygium* is covered with stratified, often pigmented conjunctival epithelium, containing goblet cells, and having bud-like ingrowths and glandular-like invaginations lined with cylindrical cells. Cysts may be formed by obliteration of these invaginations. The stroma is a fibrous tissue containing elastic fibers showing hyaline degeneration. It contains vessels with fibrous and hyaline degeneration of the walls. Bowman's mem-

brane is destroyed in the area of the pterygium. The superficial corneal lamellae are substituted for by fibrous tissue in the area of the pterygium and beyond it they are curved and pushed together. The pterygium probably originates as a superficial degeneration of Bowman's membrane and the superficial corneal lamellae, and as sequel newly formed tissue appears. The true pterygium represents a pocket-like invagination which is covered by epithelium except where it is adherent to the cornea. At its apex, it progresses farther into the cornea. The adherence to the cornea is of various extent. The pseudopterygium is of inflammatory origin in ulcers and burns of the cornea. The swollen conjunctiva may fill the corneal defect and remain adherent there. The conjunctival tissue shows lymphocytic infiltration, is covered by epithelium on its upper and under surface, and adheres, to a large extent, to corneal lamellae.

Epithelial dystrophy (Fuchs). The epithelium is thinned and a lamellar deposit, with a few vessels, spindle shaped and some giant cells, lies on the atrophic Bowman's membrane. It seems to follow endothelial dystrophy, which causes the entrance of intraocular fluid into the cornea and may finally affect the epithelium.

Endothelial dystrophy (cornea guttata). Descemet's membrane shows many drusen, and the endothelium is degenerated and contains pigment. It may finally desquamate entirely.

Fatty, hyaline, amyloid, and calcareous degeneration. The fatty degeneration is either primary or secondary.

In the primary form, the epithelium, Bowman's membrane, lamellae, and endothelium have fatty deposits. Especially in and between lamellae there are fat droplets and needle-shaped crystals. Large fat-loaded histiocytes appear (foam cells). Staining with sudan III and osmic acid shows the deposits as neutral fats or lipoids. The condition indicates a disturbance of the fat metabolism, the cause of which is largely unknown. The secondary form appears in tissue which has been previously affected, as in injuries, scars, ulcers, keratomalacia, interstitial keratitis, glaucoma, and trachoma. Fat droplets are found in the cells and tissues. Also the white ring (Coats) consists, histologically, of an accumulation of lipoid material.

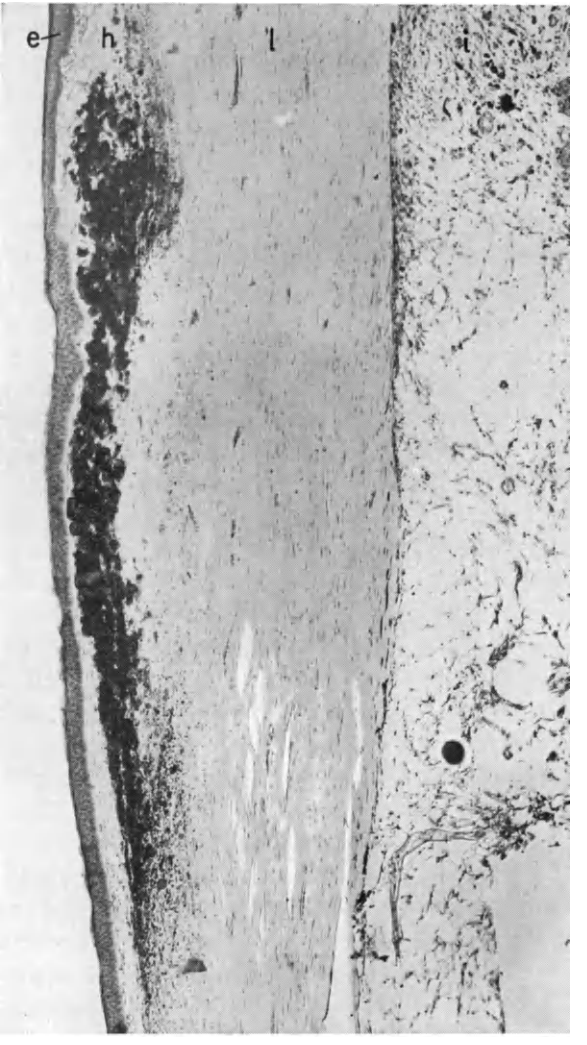

FIG. 17.—HYALINE DEGENERATION IN CORNEAL SCAR. e, epithelium; h, hyaline; i, adherent iris; l, lamellae. 45×.

In hyaline and amyloid degeneration, spherical homogeneous, strongly stained plaques of hyaline and amyloid appear in varying sizes and quantities, extracellularly, mostly in scars and staphyloma. They may coalesce. It is uncertain whether they are secreted from the cytoplasm or are the product of degenerated necrotic cells. They may appear in the epithelium in and between the lamellae, and especially in the connective tissue of the scar.

In calcareous degeneration, calcium in the form of fine granules or irregular nodules may be deposited, especially in scars in its secondary form, and may be encapsulated by connective tissue containing giant cells. Primary calcareous degeneration of the cornea may also appear.

Lamellar stratification is characterized by the formation of new lamellar tissue beneath the epithelium. In the center of the cornea, as a rule in front of Bowman's membrane, is an insular area consisting of lamellar tissue and nuclei. It increases in thickness progressively and may become as thick as the entire cornea. The nuclei disappear finally and the mass becomes more homogeneous. It may undergo hyaline, calcareous, or fatty degeneration. It is formed in eyes which have become blind through iridocyclitis or glaucoma and appears to have some relation to vesicles of the epithelium in keratitis bullosa. As a result of irritation of the denuded Bowman's membrane, cells seem to proliferate through dehiscenses in Bowman's membrane, accumulate beneath the epithelium, and form there the lamellar stratification.

In *arcus senilis*, lipoid droplets appear intracellularly and extracellularly in the marginal cornea. They are found in Bowman's membrane, in and between the lamellae, in corneal corpuscles, and in large foam cells. Also, the surrounding sclera may show a fatty infiltration. It is probably a lipoid infiltration and not a formation of a lipoid substance as a product of degeneration in the area. It seems possible, too, that hyaline granules also may be able to form an arcus senilis.

In *myxomatous (mucinous) dystrophy,* mucinous material is deposited in broken-up lamellae.

Sclerosis of the cornea shows swollen corneal lamellae, and the fibers, which are wavy and irregular, are split up. As a result, the cornea becomes whitish, nontransparent, and sclera-like.

Dimples of the cornea. Where the epithelium, Bowman's membrane, and the superficial lamellae are very thin, dimples of the cornea appear near the limbus. They are largely temporal. Dimples are found in swelling of the limbal tissue from inflammation or tumor formation, after advancement of an eye muscle, cataract operation or lagophthalmos, and in sclerosis of the limbal vessels.

In *keratoconus*, the cornea is thinned at the apex of the conus, and in the epithelium hemosiderin may be deposited which represents Fleischer's brown ring. Bowman's membrane may show holes which are filled with newly formed fibrillar tissue. The lamellae may be wavy and show fibrillary degeneration, and hyaline masses may be present. Cell nuclei may accumulate locally. Descemet's membrane may show tears. The etiology is unknown; inner secretory disturbances are mentioned as factors.

9. Pigmentation of the Cornea

A great variety of causes may lead to pigmentary deposits in the layers of the cornea, and a number of substances may produce staining. Some of these substances originate in the body and in the eye; others are introduced externally into the cornea and into the interior of the eye. Pigmentation is found as (1) blood staining of the cornea, (2) siderosis, (3) chalkosis, (4) tattooing, (5) epithelial melanosis, (6) endothelial melanosis, (7) pigmented line of the cornea, and (8) Kayser-Fleischer ring.

In *blood staining*, pigmented granules are found in the cytoplasm of the corneal corpuscles, which are believed to be hemosiderin (hematogenous siderosis). These may also produce a diffuse staining. Stainless rod-shaped, oval or spherical deposits may likewise appear between the lamellae and between Bowman's membrane and the epithelium. They are considered to be iron-free derivations of the hemoglobin and are perhaps albumin or fibrin. In addition, erythrocytes may be deposited in the periphery of the cornea where they may enter from extensive

subconjunctival hemorrhages. In general, blood staining of the cornea appears when severe hemorrhages have taken place in the anterior chamber. The erythrocytes are broken up in the anterior chamber and the blood pigment is absorbed through Descemet's membrane into the cornea.

In *siderosis,* too, pigmented granules are found, especially in the corneal corpuscles, between the lamellae and in the epi-

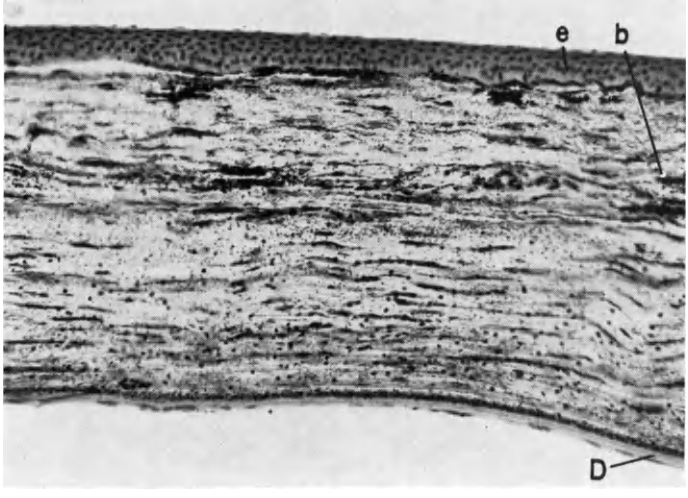

FIG. 18.—BLOODSTAINING OF CORNEA. b, blood pigment; D, Descemet's membrane; e, epithelium. 65×.

thelium; they can be demonstrated to be iron-containing by specific staining (Perlia's stain). In the presence of an intra-ocular iron foreign body, iron-containing fluid diffuses mainly through the chamber angle into the cornea, and iron is deposited there (xenogenous siderosis).

Chalkosis shows granular deposits of copper in the endothelium, Descemet's membrane, and posterior lamellae of the cornea. It comes from a copper foreign body in the interior of the eye which dissolves under severe inflammatory changes in the intra-ocular fluid.

Tattooing, used frequently on corneal scars for cosmetic or optical reasons, is done with either india ink or chemicals (gold

chloride or platinum chloride). Ink particles are deposited in the epithelium, in the corneal corpuscles, and in the intralamellar spaces. Metal is deposited in the corneal corpuscles and between the lamellae and also fills the epithelial cells.

Epithelial melanosis. In cases of melanotic tumor of the limbus, and in congenital melanosis of the bulb, melanin granules are found in the epithelial cells.

In *endothelial melanosis,* melanin is on, in, and between the endothelial cells, and pigment granules may also be deposited on the trabeculae of the chamber angle. Pigment is deposited frequently if the pigment epithelium of the uvea is disintegrated. In senile degeneration, in atrophic and inflammatory processes, and in intra-ocular melanotic tumors, pigment may be liberated and deposited in the endothelium. Myopia, glaucoma, diabetes, intra-ocular operations, and trauma have been found to be causes. The pigment deposit occasionally takes the form of a spindle (Krukenberg's pigment spindle).

The *pigmentary line* appears (a) in senile eyes as ruptures of Bowman's membrane (Hudson's brown line, Staehli's line), and (b) in old scars as a deposit of hemosiderin in the epithelium.

The *Kayser-Fleischer ring* is characterized by numerous fine granules beneath the endothelium and in Descemet's membrane. Their composition is uncertain. They are thought to be hematogenous, but they are also considered urobilin, lipochrome, and metal compounds as silver albuminate. The ring is found in hepatolenticular degeneration.

10. Pathology of the Epithelium

Sometimes the epithelium alone, in whole or in large part, is diseased, but sometimes its changes constitute only one aspect of a general change in the cornea. Epithelial changes are found (1) in edema of the cornea, (2) as keratitis bullosa, (3) as filamentary keratitis, (4) in recurrent erosion, and (5) in keratosis.

Edema of the epithelium is part of a general disease of the bulb and is always present in edema of the cornea. Small and large fluid droplets are found between and in the basement cells, which are vacuolated. The prickle cells are separated and some-

times also contain fluid droplets; the superficial cells, too, are separated and detached. In edema of the cornea, the lamellae are swollen and fluid, and granules fill the interlamellar spaces. The endothelium shows intercellular slits and fluid in the cytoplasm. The most frequent cause of corneal edema is increase in intra-ocular pressure. In such cases, intra-ocular fluid is probably pressed into the cornea. Further causes are trauma, inflammation, and degenerative changes.

In *keratitis bullosa,* the intercellular spaces are dilated, the epithelial cells are flattened, and the irregular epithelium is to a large extent detached in vesicles from Bowman's membrane. The blisters may contain epithelial cells and white and red blood cells. The epithelial cells may show mucoid degeneration. The keratitis is found mostly in eyes with increased tension and may have some relationship to degenerative pannus and lamellar stratification.

Filamentary keratitis is characterized by the outgrowth of an epithelial filament from a triangular elevation of the corneal epithelium. This thread shows various changes in the cells: (1) large cells of distinct contour, with two or more nuclei, are present; (2) large cells have marginal nuclei and homogeneous content; (3) large cells have fine granular content and round dark-stained inclusions; (4) distinctly outlined formations have centrally located cells with extensive hyaline plates; (5) heaps of disintegrating cells are present; (6) cytoplasmic syncytia with fifty to sixty nuclei are present; and (7) near the root of the filament are tortuous band- and spindle-shaped cells. The filament originates from corneal wounds, edema, herpetic lesions, and recurrent erosions, and is also found as an idiopathic disease.

Recurrent erosion (epithelial disjunction, von Szily; balloon degeneration, Franke) shows edema and necrosis of the epithelium which is separated from Bowman's membrane. Trauma and erosion sometimes precede by a considerable period. In some cases, an endothelial disorder and the entrance of aqueous humor into the cornea is the primary cause. Neurotrophic disturbance through trauma on the nerve endings of the epithelium as well as a hereditary factor are also assumed to be causes.

Keratosis presents hornification of the epithelium, which is thickened and contains many balloon-shaped cells. The superficial epithelial layers form keratohyaline and hornify. This condition is frequently part of a circumscribed or general xerosis of the conjunctiva (xerosis parenchymatosa, xerosis epithelialis) or circumscribed affection of the cornea, which frequently appears on the limbus (epithelial plaques), or over a dense leukoma or in staphyloma.

11. Pathology of the Endothelium and Keratic Precipitates

Changes of the endothelium vary. The cells may be edematous and vacuolated; they may be detached, proliferate, form several cell layers or fall off into the chamber; they may shrink and become necrotic. Polymorphonuclear cells may migrate between endothelium and Descemet's membrane. Under certain circumstances, the endothelium may deposit homogeneous or lamellar tissue. The endothelial cells secrete a substance which is regarded as newly formed Descemet's membrane. Endothelial changes accompany suppurative ulcers and the deep infiltration in chemical burns of the surface. The endothelium may be damaged from the chamber in cases of endophthalmitis or necrotic intra-ocular tumors and may proliferate in traumatic iridocyclitis. Proliferating endothelium sometimes appears as folds, reaching into the anterior chamber and there forming hyaline networks. If the chamber angle is blocked by peripheral anterior synechia or newly formed connective tissue, the endothelium may also proliferate onto the iris (which, in such cases, is covered with newly formed connective tissue), and deposit a new Descemet's membrane on the anterior surface of the iris. If keratic deposits appear, the endothelium becomes defective. Deposits on the posterior surface of the cornea include pseudo-precipitates (precipitation), which form a uniformly thick cell layer with several elevations, and true precipitates, which are preformed in the aqueous humor and lie isolated on the posterior surface. Precipitates contain lymphocytes, monocytes, and polymorphonuclears embedded in fibrin, and pigment granules are

found intra- and extracellularly. Hyaline and fatty degeneration may appear in the precipitates.

12. Pathologic Changes of Bowman's and Descemet's Membranes

We find in Bowman's membrane dilatation of the perforations of the corneal nerves in shrunken eye balls, and in such eyes and in eyes with low intra-ocular tension there are also wavelike folds of the membrane, which are leveled on the surface by the epithelium (superficial striate opacity). In inflamed eyes, anteriorly elevated folds appear, over which the epithelium is usually eroded (lattice-like opacities, letter-shaped keratitis). The superficial lamellae participate only slightly in the folding, and occasionally loose fibrous tissue is deposited in the folds. Increased tension may, in the eyes of young persons, produce breaks in the membrane having jagged margins; the holes are filled with round and spindle cells. Sometimes, in circumscribed areas, the membrane bulges toward the epithelium in drusen-like, half spherical formations. These half spherical deposits are made up of a hyaline substance secreted from the epithelium.

Descemet's membrane shows folds in low tension, especially after cataract extraction, sometimes after a perforating injury and in shrinking eye balls (deep striate opacity). The deep lamellae follow the folds; sometimes they are separated by fluid and infiltrating cells or the lamellae do not follow the folds and fibrillar tissue and spindle-shaped cells fill the spaces of the fold. In inflamed corneae, such as in interstitial keratitis, but also in herpes corneae, folds may be formed which occasionally bulge far into the anterior chamber as thick ridges and into which are deposited fibrin and fibrin-producing cells and layers of newly formed homogeneous material secreted from the endothelial cells (hyaline networks). As already mentioned, this hyaline network originates from various formations: (1) from folded proliferating endothelium through a deposit of an homogeneous substance which forms the scaffold and makes the folds permanent; (2) fine threads of fibrin secreted into the anterior chamber, which adhere to the posterior surface of the cornea and over which endothelium grows secreting a

Descemet-like substance; (3) folds of endothelium-covered Descemet's membrane enforced by secreted material; or (4) ruptured pieces of Descemet's membrane hanging freely into the anterior chamber and becoming surrounded by endothelium. They are enforced by secreted material and thus become permanent.

If fibrous, membranous deposits are formed on the iris, which bridge the chamber angle and adhere on the posterior surface of the cornea, Descemet's membrane may be extensively separated from the cornea by traction of the shrinking membranes. Ruptures in Descemet's membrane appear in young children if the cornea is stretched by an increased intra-ocular pressure or on account of an inherited weakness, as in hydrophthalmos, keratoconus, and myopia; in young and old alike it occurs as the result of injury, as in contusion and compression (birth injury). Ruptured Descemet's membrane has a tendency to curl up in spirals anteriorly. The defect is crossed by endothelium which usually secretes a new membrane. The new membrane may appear doubled if the endothelium proliferates on large defects and a new membrane is secreted, or if the broken-off piece of Descemet's membrane extends freely into the anterior chamber and the endothelium proliferates on the posterior surface deprived of Descemet's membrane and there forms a new membrane. As already mentioned, if an anterior peripheral synechia exists, the membrane may occasionally proliferate around the chamber angle onto the anterior surface of the iris. Lamellar stratified tissue with oval nuclei may be formed, produced, as already noted, by the endothelium (endothelogenous connective tissue, Wagenmann). Homogeneous layering of considerable thickness on the posterior surface of the cornea (Fuchs) may be found occasionally. It is composed of endothelial cells, pigment granules, and hyaline masses. This layering is considered a deposit of protein into the anterior chamber in cases of increased tension and is said to re-enforce Descemet's membrane.

13. Corneal Lesions Caused by Chemical and Physical Agents

Lime burns. Opacities caused by lime burns are frequently seen. In these (1) the epithelium is defective; (2) the corneal

corpuscles are destroyed; (3) the corneal lamellae become homogeneous and split up; (4) deposits of calcium carbonate and organic calcium compounds appear; and (5) diffuse infiltrations with lymphocytes are seen. In severe cases, the cornea becomes extensively necrotic into the deep layers, and the endothelium may be desquamated.

Bee sting of the cornea is occasionally observed and shows (1) epithelium and Bowman's membrane desquamated; (2) necrotic anterior lamellae filled with polymorphonuclears; (3) anterior chamber containing fibrinous, suppurative exudate; (4) a deep abscess may be present.

In *x-ray and radium damage* of the cornea, (1) the epithelium loses nuclei; epithelial cells become pleomorphic and break up; (2) the cornea may be covered by connective tissue with vessels showing swollen endothelium; (3) lamellae disintegrate and connective tissue appears between the lamellae; and (4) the deep layers contain only a few swollen nuclei.

14. Tuberculosis of the Cornea

This condition is characterized by typical tuberculous granulation tissue consisting of lymphocytes, epithelioid cells, giant cells, and caseation of varying extent in typical arrangement. This specific infiltration of the cornea in tuberculosis must be distinguished from nonspecific infiltration. The nonspecific types are phlyctenular keratitis (of allergic origin) and interstitial keratitis, which is either primary or secondary following inflammation of the iris or sclera. Specific infiltration of the cornea may appear (1) as primary in the form of an ulcer and deep infiltration; (2) as secondary, being continuous from tubercles of the conjunctiva, sclera, iris, and chamber angle; (3) produced by dissemination of tubercle bacilli into the anterior chamber in tuberculosis of the iris; in this case, deposits may appear on Descemet's membrane consisting of epithelioid cells and giant cells; or (4) as tuberculoma of the limbus extending into the cornea.

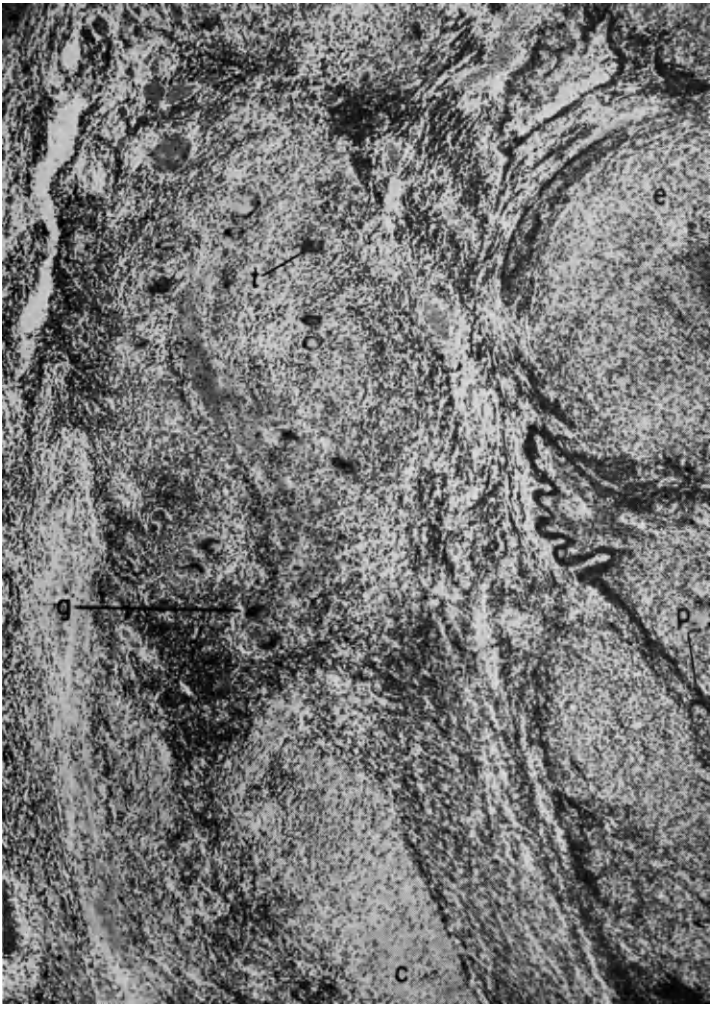

FIG. 19.—TUBERCULOSIS OF CORNEA AND UVEA. e, caseation; e, epithelioid cells; g, giant cells; p, pigment epithelium; t, tubercle. 40×.

15. Leprosy of the Cornea

The characteristic feature is the presence of lepra cells in the form of relatively large vacuolated mono- or multinucleated cells containing numerous lepra bacilli. In cases of leprosy of the cornea, bacilli are also found between unaltered lamellae, and in leprotics, frequently even between the lamellae of a non-affected cornea. Leprosy of the cornea appears as (1) superficial punctate keratitis, (2) leprotic pannus, (3) diffuse interstitial keratitis, (4) lepromata of the limbus, and (5) large tumor replacing the cornea.

Superficial punctate keratitis shows, beneath Bowman's membrane, nodules consisting of lepra cells, and accumulations of bacteria surrounded by polymorphonuclears. The most superficial lamellae are disintegrated, and corneal corpuscles are irregularly increased. Bowman's membrane may be eroded from the posterior position. In pannus, which may follow this keratitis or limbus nodules, Bowman's membrane is destroyed, and blood vessels and connective tissue appear in addition to lepra cells. In interstitial keratitis the epithelium is vacuolated, and many lepra cells and dense lymphocytic infiltration fill the middle layers of the cornea. The lepromata of the limbus are either miliary nodules consisting of lepra cells or large nodes reaching into the cornea which show lymphocytic infiltration, large nests of lepra cells, and newly formed vessels and fibroblasts. The covering epithelium may present accumulations of yellow pigment while Bowman's membrane reveals holes in it. The large tumor has connective tissue parenchyma containing nests of spindle-shaped and epithelioid cells, and may show partly mucoid softening. The iris and ciliary body are affected along with the more severe corneal lesions.

16. Congenital Corneal Opacities

A persistent pupillary membrane may be adherent on the posterior corneal surface showing defects of Descemet's membrane in the area of the adhesion. This may be due to either a developmental anomaly or to an inner ulcer caused by an intra-uterine inflammation. In addition, congenital central

defects of Descemet's membrane are found and the posterior corneal lamellae with and without adhesion of the iris. In these cases, the cells are increased in the anterior layers and the lamellae are swollen. Sometimes, inflammatory changes are present which indicate intra-uterine inflammation. In many cases, however, inflammatory changes are not present, but other disturbances of the development are additionally found, such as microphthalmos or coloboma of the uvea. Consequently, the lesion is attributed to developmental disturbances, such as delay in the separation of the lens vesicle, or apposition of the lens to the posterior surface of the cornea for too long a time, or developmental disturbance of the corneal endothelium.

In congenital corneal staphyloma, Bowman's membrane is absent entirely or is present only in the peripheral parts. The lamellae appear irregular, or irregular dense connective tissue bundles are present with blood vessels and pigment may be seen. Descemet's membrane is absent, and the atrophic iris adheres to the posterior surface of the cornea or its pigment epithelium covers the posterior surface. The cornea may contain an infiltration with lymphocytes or polymorphonuclears; a dermoid may sit on the staphyloma; iris cysts may be present at the same time. The rest of the eye may also show pathologic changes. The lens may be absent or present, and may be cataractous, small and disintegrated, and adhere to the posterior surface of the cornea. The retina may show arcuate arcade or rosette formation of the outer layers. The papilla may present glaucomatous cupping. Perivascular infiltrates are seen; also exudates into the posterior chamber and lymphocytic infiltration of the choroid and suprachoroid. The staphyloma may follow an intra-uterine inflammation, producing a perforating ulcer of the cornea, or it may be the result of malformation if the lens vesicle is not separated from the surface epithelium.

17. Neoplasms

These are almost exclusively tumors of the limbus or of the adjacent conjunctiva, which grow into the cornea. Tumors originating from the cornea itself are extremely rare. Tumors may be described as (1) mesodermal, (2) epithelial, (3) con-

genital, (4) metastatic. They are either benign or malignant.

Mesodermal tumors include (a) fibroma and fibromyxoma, which are benign, and (b) sarcoma, which is malignant.

The fibroma consists of fibroblasts and fibrillar connective tissue of varying density. Occasionally, the cells appear with anastomosing processes, and the parenchyma contains homogeneous masses which give mucous reaction in special staining (fibromyxoma). Most of these tumors are formed in scars

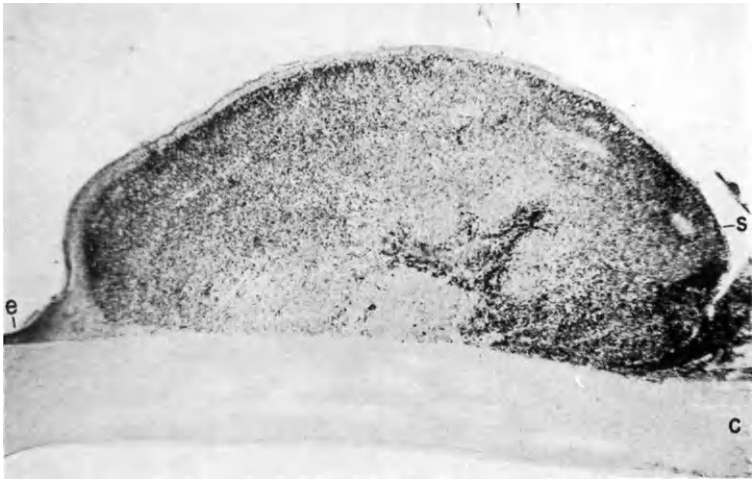

FIG. 20.—SARCOMA OF LIMBUS. c, cornea; e, epithelium; s, sarcoma consisting of spindle shaped cells. 60×.

of the cornea, and it is a question whether they are proliferating inflammatory products or real new growths.

Sarcoma consists of spindle cells having a relatively large oval nucleus with a distinct nucleolus, between which is found only scant reticulum. Sarcomas are also seen which contain round cells. Besides, there are sarcomas which show large cells filled with pigment. They originate either from pigmented spots of the limbus or are primary from the cornea, the latter being very rare. If they originate from a true nevus, they should be called malignant melanoma. Sarcoma may perforate into the anterior chamber or erode Bowman's membrane and proliferate into the epithelium.

Epithelial tumors include (a) papilloma and corneal horn, which are benign, and (b) carcinoma, which is malignant.

Papilloma is an overgrowth of the stratified squamous epithelium and the papillae. If the epithelium grows high and the primary papillae become wider and higher, epithelial hyperplasia exists. If the epithelium and the papillae are elevated over the surface, secondary papillae are formed and a tumor develops containing wide irregular stratified squamous epithelium, eventually with mitoses and a central core of connective tissue and blood vessels. The papillae appear as folded, leaflike, branched formations on longitudinal sections. A papilloma is usually located at the limbus, but may also develop from a trachomatous pannus or pterygium. It frequently precedes carcinoma.

Corneal horn is a high conical formation of horn substance. Occasionally, the proliferating papillae remain small, but the surface of the stratified squamous epithelium forms an extensive apposition of hornified layers.

Bowen's disease (a precancerous dermatosis) may be grouped between the benign and malignant epithelial tumors. Bowen's disease occasionally affects the cornea and adjacent conjunctiva and is characterized by dyskeratotic cells, large vesicular cells with clear nuclei, irregularity of the epithelial cells and a dense, subepithelial lymphocytic infiltration. The epithelium may proliferate into the underlying tissue as squamous or basal cell carcinoma.

Carcinoma appears as squamous cell epithelioma with an infiltration of the corneal stroma of prickle cells singly and in groups. The cells show hyperchromatic nuclei; and polymorphism, and anaplastic cells are seen in addition to mitosis. This tumor grows almost exclusively from the limbus; it is questionable whether it ever originates in the corneal epithelium proper. It grows into the corneal epithelium, destroys Bowman's membrane, infiltrates and replaces the lamellae, and may perforate in the form of cell nests along the anterior ciliary vessels into the anterior chamber. It may spread intra-ocularly to the uvea and extra-ocularly to regional lymph nodes.

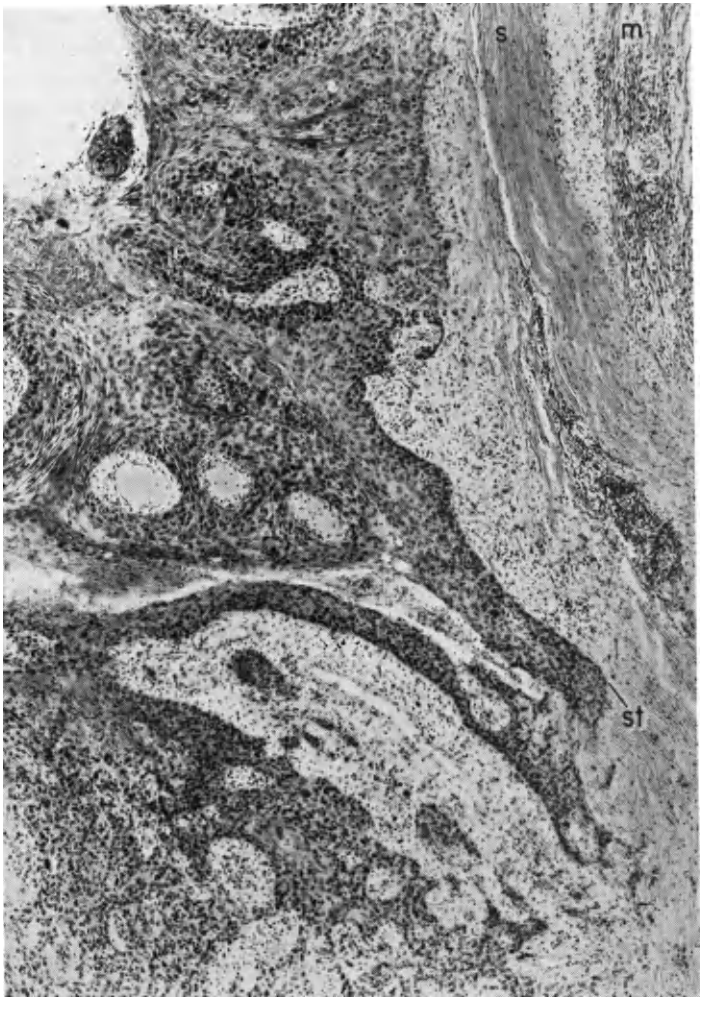

FIG. 21.—SQUAMOUS CELL CARCINOMA OF LIMBUS. m, ciliary muscle; s, sclera; st, infiltrating epithelial strands. 45×.

Congenital tumors are dermoid, lipodermoid, and teratoma. They contain epithelial and mesodermal elements.

A dermoid most frequently occurs at the limbus but in rare cases may extend over a large area of the cornea. The surface is epidermis, and the substance of the tumor consists of a meshwork of coarse connective tissue bundles containing hair follicles, sebaceous and sweat glands, smooth and striated muscles. The rest of the eye may be normal; if it shows malformations, the anterior chamber is undeveloped, or the chamber angle remains fetal. Choroid and retina are abnormal, depending on whether the dermoid develops before the lens vesicle separates and the mesoderm forms the cornea and uvea, or whether this takes place in a later stage. If the lids do not close during the development, the surface of the cornea remains exposed and develops with all the characteristics of skin. But it is also possible that the dermoid represents the remains of an amniotic band.

Dermo-lipoma (lipodermoid). The surface is epidermis with hair follicles, sebaceous and sweat glands, and beneath is a thick layer of fat tissue. The deep layers of the cornea appear normal.

Teratoma, also, contains elements of the skin; in addition there are acinous glands, fat, and hyaline cartilage.

Metastatic tumors. Metastatic tumor of the cornea is retinoblastoma. It grows, after destruction of Descemet's membrane, directly from the anterior chamber into the cornea, or extends along the anterior ciliary vessels leading into it.

READING OF SOURCE MATERIAL

Loehlein finds that cells immigrate in inflammation into the cornea and appear as granular polymorphonuclears and that the fixed cells show little increase, but Busse believes that the cells of inflammation in the cornea are formed there. He does not believe that there are tissue spaces open to cellular migration.

Nakamura finds neutrophil polymorphonuclears in the scrapings of suppurative ulcers of the cornea and monocytes in non suppurative inflammation.

Chefik found in the scrapings of an affected cornea microgametocytes of coccidia.

Aspergillus in a corneal ulcer was found by Castroviejo and Muñoz Urra, glenospora graphii by Wright, periconia by Fazakas; Bedell found a fungus

in the cornea after an injury and calls the inflammation cephalosporium keratitis.

Lindner describes in a fulminating serpiginous ulcer fine bacilli which belong in the hemorrhagic septicemia group.

Hypopyon ulcer caused by bacillus pyocyaneus is reported by Garretson and Cosgrove, Safar, Shearer, but the great majority of cases of hypopyon ulcer are caused by pneumococci (Gasteiger, Schmelzer).

Planta reports a case of bilateral serpiginous ulcer which he considers as expression of constitutional inferiority.

Posterior abscess of the cornea in ulcus serpens is described by Fuchs; Stanka finds frequently in serpiginous ulcer Descemet's membrane early split by polymorphonuclears in several lamellae and perforated.

Samuels believes that the cells of the posterior abscess in ulcus serpens come from the iris by way of the aqueous humor or from the deep blood vessels.

Metastatic opthalmia with internal ulcer of the cornea is reported by Alten.

Flieringa, Gifford and Hunt report about ring abscess of the cornea.

Jaensch found in keratomalacia of the infant necrosis and fine lipoid granules and droplets, intracellular and extracellular, between the corneal lamellae, which occasionally are transformed in structureless fatty masses.

Igersheimer, Klien found histologically in keratitis pustuliformis profunda dense infiltration of polymorphonuclears in the deep layers of the cornea with some defects in Descemet's membrane.

Thygeson finds in scrapings from marginal corneal infiltrations and ulcers accompanying chronic conjunctivitis mostly pathogen staphylococci.

In herpes corneae, the cells of the corneal epithelium are decreased, the nuclei become flat, the intercellular spaces widen, vacuoles appear in the cells, the basal cells show ballooning, Bowman's membrane is destroyed and round cell infiltration appears between the lamellae (Berger).

Fuchs and Lauda inoculated corneae of eyes which had to be enucleated with herpes virus. The result was keratitis dendritica. The chromatin of the nucleus is disintegrated and is finally substituted by a homogeneous acidophil mass and the nuclear membrane becomes thickened.

Fuchs described herpes of the cornea.

Doerr considers herpes simplex and herpes zoster affecting the eye as different types of virus.

Lee reports about a keratitis accompanying molluscum contagiosum and Redslob, Sysi saw molluscum contagiosum of the cornea.

Wright finds in superficial punctate keratitis degenerative changes of uncertain nature.

Guenther describes in epidemic keratitis microscopically accumulation of lymphocytes, fibroblasts and histiocytes between the normal epithelium and the disintegrated Bowman's membrane.

Miyashita describes superficial diffuse keratitis with edema between the basal cells of the irregular corneal epithelium. Cell infiltration appears beneath the epithelium and Bowman's membrane is split. The superficial lamellae are edematous and sometimes infiltrated.

Aust describes in numular keratitis, disintegration of the lamellae with few infiltrating cells and proliferation of keratoblasts.

Junius, Knapp report histologic findings in keratitis disciformis.

Beigelman found vacuolation, intercellular clefts and disintegration of the nuclei of the corneal epithelium in vernal catarrh.

Zondek, Landau and Bromberg could show by active intracutaneous examination that cases of keratitis rosacea are hypersensitive to their own hormones.

Leser finds in Mooren's ulcer histologically at the limbus, venous thromboses, hemorrhages, round cell infiltration and proliferation of the epithelium into the depth, and in the ulcer, plasma cells and vascular granulation tissue.

Bussola, Feingold, Heintz report the histology of the rodent ulcer.

Junius, Suganuma consider the rodent ulcer of neurogen origin.

Interstitial keratitis in lues is histologically examined by Gilbert, Jaeger, Spicer.

Kunze describes a case of interstitial keratitis with perforation of Descemet's membrane and retro-corneal cell proliferation containing giant cells. Anterior retino-chorioditis is present.

Ling saw in a histologically examined case of interstitial keratitis diffuse infiltration of the choroid with occasional nodules consisting of epithelioid and giant cells.

Spirochetes in interstitial keratitis were found by v. Hippel, Weve.

Weve could find spirochetes in the smear from superficial granulomata of a case of keratitis parenchymatosa. The granuloma showed edematous infiltrated tissue with some karyorrhexis and pyknosis and many capillaries with endothelial proliferation (papula luetica).

Igersheimer describes in extenso experimental metastatic interstitial keratitis after inoculation with spirochetes.

Sommer reports a case of interstitial keratitis of apparent tuberculous origin.

Aylesworth found in a case of lymphatic leukemia the cornea densely infiltrated and lymphocytes in limbus and episclera.

Levkoeva finds essentially proliferation of the fixed cells of the cornea and sclera at the edges of a wound. These cells may proliferate into the aqueous humor and the vitreous body without inflammatory changes.

Ascher, Sommer, find that the transplant in keratoplasty preserves Bowman's and Descemet's membrane and frequently also lamellae. Castroviejo, Filatov, Frieberg find that nerves grow from the host cornea into the transplant. Further, Imre reports histologic findings in keratoplasty.

Fieandt finds in a transplant in keratoplasty histologically all layers intact including Bowman's and Descemet's membrane.

Franceschetti and Babel describe a transparent graft in keratoplasty and found only one fine subepithelial nervous filament. They believe that only the epithelial innervation keeps the transplant transparent.

Babel finds in the graft of keratoplasty Bowman's and Descemet's membranes persisting and in some grafts vessels growing in the cornea and adherent iris.

Babel and Campos believe that grafts become opaque in keratoplasty due to faulty metabolism caused by abnormal innervation. They could find with silver impregnation degeneration and incomplete regeneration of nerve filaments in the graft.

Scars and hyaline masses are seen in keratitis due to smallpox (Carmi).

Fileti describes pseudocysts of the cornea arising in scar from lymph vessels or by dissociation of the tissue by traction of the scar.

Gallemaerts describes the cysts of the cornea as epithelial, interstitial and endothelial.

Epithelial ingrowth in corneal wounds, resp. ulcers with formation of implantation cysts are described by Custodis, Fazakas, Levine, Michail, Moore, Papolczy, Radnot, Salus, Speciale-Cirincione, Vail.

Vrolijk reports congenital cysts of the limbus, probably arising from vestiges of embryonic, not entirely obliterated veins.

Fileti describes a cyst of the cornea lined with endothelium as "lymph-cyst." He considers it as cleft formation lined with modified corneal corpuscles.

Cattaneo describes cysts partly lined with endothelium.

In Jacobelli's case there was a cystic space in the cornea without epithelial or endothelial lining. The iris was incarcerated into the traumatic defect of the deep corneal layers. Aqueous humor had entered and formed the space.

Pastore describes a small cyst inside the cornea in an atrophic eyebulb, communicating with a large subconjunctival cyst.

Corneal fistula is described by Sattler.

Piesbregen's opinion is that exogenous stimuli from the epithelium produce in scrofolous pannus immigration of lymphocytes from the limbus to this center of attraction. The lymphocytes collect beneath Bowman's membrane, which resists perforation.

Levkoeva found in a case of primary degeneration of the cornea microscopically beneath the epithelium granulation tissue displacing corneal lamellae and a homogeneous amyloid like substance.

Hiwatari describes typical follicles near the limbus in trachoma.

Szasz saw in a case of trachoma the cornea thickened, containing granulation tissue with many lymphocytes, fibroblasts, mast cells and macrophages containing fatty droplets.

Huber reports on the histology of trachomatous pannus.

Cange considers only pannus crassus with follicles as specific in trachoma, not the pannus vasculosus. He distinguishes the trachomatous pannus as (1) traumatic caused by irritation of the granular conjunctiva; (2) granular due to spread of the infection from conjunctiva onto cornea; (3) mixed. It begins with many migratory cells in the corneal epithelium. He found follicles with germinative centers in pannus crassus of trachoma.

Pascheff finds the pannus in trachoma rich in follicles and calls it a lymphatic reticulo-endothelial hyperplasia ("pannus follicularis.") He describes the center of the follicles of the pannus consisting of lymphocytes, histiocytes, endothelial cells, many macrophages and phagocytes.

Busacca describes avascular keratitis in early trachoma with edema of the epithelium and infiltration with polymorphonuclears and absence of Bowman's membrane. Some epithelial cells show inclusion bodies. It is followed by a secondary infiltration with lymphocytes, histiocytes and blood vessels. Pannus represents a special granulation tissue as defense of the vascular tissue.

Franceschetti and Babel classify anatomically the familial degeneration of the cornea and find (1) a progressive noncongenital form of dominant

or recessive type and (2) a congenital stationary group. In the first group the superficial corneal lamellae show hyaline degeneration and subepithelial deposition of a basophil hyaline substance. In the second group there is besides hyaline degeneration a granular albuminous substance in the epithelium, in the fix cells of the cornea and in the endothelium.

Meesmann and Wilke describe a dominant form of hereditary corneal dystrophy with punctate lesions in the center of the cornea. The epithelium is irregularly thickened and contains vacuoles filled with glycogen; superficial scars contain elastidin.

The histology of familial nodular keratitis is described by Car, Chon, Brown and Katz, Collins, Ellis, Goar, Judd, Ladekarl, Salzmann, Wirth; they find the epithelium vacuolated, irregular and partly substituted by homogeneous hyaline masses, masses of amorphous substances spherically lying on Bowman's membrane with the membrane disintegrating or disappeared in places, many superficial lamellae split or destroyed, hyaline substance deposited between the most superficial lamellae of the cornea and migratory cells and foreign body giant cells.

Loewenstein finds in the lattice-like opacity of the cornea acidophil deposits on Bruch's membrane and basophil granular masses beneath the membrane.

Yoshida describes a diffuse form of nodular keratitis with great irregularity of the epithelium, hornification of the superficial cells, occasional thickening of Bowman's membrane, deposition of hyaline beneath Bowman's membrane, fibrillar transformation of the superficial lamellae with some capillaries and giant cells.

Herrmann describes familial degenerative reticulo-corneal dystrophy consisting microscopically of acidophil intralamellar concretions and basophil intra- and extralamellar concretions.

Salzmann describes a nodular dystrophy of the cornea following keratoconjunctivitis. The nodules are situated beneath scars and show dark-staining swollen fibrils and granules.

Bischler, Muir found in cases of Salzmann's nodular corneal dystrophy microscopically Bowman's membrane destroyed, clumps of lymphocytes and fibroblasts, or absence of cells, disintegration of lamellae and hyalin-like material in the interlamellar spaces.

Streiff and Zwahlen report a hereditary band-shaped degeneration of the cornea showing absence of Bowman's membrane and acidophil granules in the superficial lamellae.

Shihinasvili describes cases of ribbon-shaped degeneration of the cornea in which calcareous depositions were present not only in Bowman's membrane but also in the lamellae, the fix cells and the endothelium.

Gifford describes the histology of the band-shaped opacity of the cornea.

Loewenstein finds deposits of calcium phosphate due to decreased metabolism in Bowman's membrane when the diseased membrane does not permit exchange of fluid from the anterior chamber to the epithelium and vice-versa. In cases of glaucoma, hemispherical bodies can be formed in the membrane.

Schieck finds histologically in marginal degeneration of the cornea the peripheral lamellae split into fibers and finally replaced by granulation tissue.

Gifford reports histologic findings in marginal dystrophy of the cornea.

Schoeniger places the beginning of the pterygium in the cornea. Changes appear in Bowman's membrane in the places where the nerves pass; the membrane is soon destroyed here and the most superficial corneal lamellae degenerate. Dense connective tissue is formed beneath the epithelium.

Claes found a pterygium containing nevus tissue with cysts and blood-vessels, and also Bistis describes formation of cysts in the pterygium. Triossi describes the histology of pterygium. Kamel believes that pterygium forms after keratoconjunctivitis.

v. Hippel found in dystrophia epithelialis corneae (Fuchs) absence of the endothelium of the cornea and the corneal epithelium thin and elevated.

Epithelial dystrophy appears histologically as generalized atrophy of the epithelium and Bowman's membrane; they are substituted by a thick layer of connective tissue (Filatow and Kalfa, Thiel, Uhthoff).

Pfingst and Townes report on a girl with generalized endarteritis obliterans whose cornea became completely necrotic, appearing histologically without any inflammation.

East and Savin discovered foam cells in the pinguecula of a 59 year old man with Gaucher's disease.

Blanchi, Denti, Elschnig, Hanssen, Meesmann, Meyer, Satanowsky, Verderame report primary and secondary fatty degeneration of the cornea.

Dystrophia adiposa corneae consists of fatty infiltration of the epithelium and the lamellae of the cornea in the form of fat droplets and needle-like crystals and of lipoid in fix cells and large macrophages (Davidson, Ivanova, Katz and Delaney, Kusama, Meyer, Shapira, Vannas, Wright).

Bachstetz finds in fatty degeneration of the cornea in Sudan-stain fat in and between epithelial cells, in and between corneal lamellae and in fix cells. Bowman's membrane is split into finest fibrils.

Covitz describes lipid dystrophy of the cornea with many calcific granules, cholesterol crystals and cells distended with lipoid granules in a 29 year old woman. The central cornea is infiltrated with lymphocytes and shows blood vessels and giant cells surround cholesterol crystals. He considers the disease as primary lipid dystrophy of the cornea due to faulty fat metabolism.

Versé ascribes to a slight increase of cholesterol content of the blood an important role in the deposition of fat in the cornea.

Ivanowa found in primary fatty degeneration of the cornea subfunction of the adrenal.

Examination of cadaver corneae reveal fatty deposition beginning in the third decade, becoming constant with sixty years (Rohrschneider). The fatty deposition starts in Descemet's membrane peripherally and progresses towards the center. The fatty deposition starts in Bowman's membrane peripherally and affects later the entire periphery of the cornea.

White rings (Coats) of the cornea are made up of clusters of globules in Bowman's membrane and its close surroundings, consisting of calcium phosphate, lipoids and other substances according to Ballantyne, Jacoby and Dominguez, Nyano.

Hogan and Cordes, Rochat, Zeeman saw in gargoylism (dysostosis multiplex, Hurler's disease), which is caused by a faulty lipoid metabolism and produces similar changes in the central nervous system as in amaurotic family idiocy, in silver impregnation on Bowman's membrane, a marked cleavage and vacuolation and the fissures filled with large, oval cells contain-

ing a fine granular substance which is also present in many cells between the lamellae of the cornea.

Valerio saw, in a case showing a juvenile disciform opacity of the cornea, greyish polygonal elements in Bowman's membrane in the form of a mosaic and crystalloid depositions in the parenchyma.

Crystalline deposits of urea and sodium urate in the cornea are described by Axenfeld, Scheffels, Weve.

Peppmueller found in a case of ostitis deformans (Paget) brownish subepithelial deposits of the cornea consisting of hyaline material and spherulae elaiodes. There is a question as to whether the adenoma of the parathyroid is their cause.

Levkojewa describes primary degenerative amyloidosis of the cornea. An amyloid tumor of the surface of the cornea can contain giant cells, hyalinized vessel walls and amorphous masses (Pollack).

Meesmann found deposition of homogeneous dense substances in the cornea which represented histologically Bence-Jones albuminous bodies.

Joel reports arcus juvenilis. Aubineau, Kaiser report arcus senilis.

Rohrschneider finds that the first trace of fat in Descemet's membrane appears in puberty and the fatty degeneration progresses slowly. The arcus senilis appears in two zones of fatty degeneration, one in the lamellae beneath the peripheral edge of Bowman's membrane and the second in the lamellae close to the margin of Descemet's membrane. There is a relationship between the intensity of the fatty degeneration and arteriosclerosis.

Thiel describes histologically lamellar stratification with hyaline, fatty, mucoid and calcareous degeneration.

Axenfeld describes deposition of mucinous material in the cornea besides lamellar fibrillation.

Seale describes an interstitial degeneration of the central portion of the cornea in the form of an interstitial edema following choroidal hemorrhage.

Dimples of the cornea show anatomically the deep layers of the epithelium irregular and migratory cells between the basal cells; there is a slight infiltration between the superficial lamellae and proliferation of corneal corpuscles and the endothelium has been cast off in some places (Fuchs.)

The pathology of keratoconus is reported by Wolfrum and Boehmig.

Vogt describes as substrate of the lines at the apex of the keratoconus distinctly outlined vertical folds in the middle and deep layers of the cornea.

Bichelonne, Maghy describe in blood staining of the cornea very small refractile inter-lamellar bodies and many spindle-shaped pigment masses.

Manschot finds in blood staining of the cornea the substance entering the cornea between its lamellae as structureless masses from a hyphemia. They become granular and are taken in by the lamellae as numerous small highly refractile granules, consisting of a crystalline precipitation of the protein body of the hemoglobin; some pigment granules appear in the fix cells of the cornea, containing iron and fat.

Grimminger explains the highly refractile depositions as hematoidin crystals; Potechina finds histologically hemosiderotic pigment and pigment originated from the albumen of the hemoglobin.

Klien-Moncreiff describes an atypical pigment line of the cornea in a perforated eye consisting histologically of blood pigment which passed through a dehiscence of Bowman's membrane.

Moncreiff found a pigment line in a leukoma consisting of hemosiderin deposited in the epithelium.

Matsuoka, Sallmann report siderosis of the cornea.

Loddoni describes a ring at the posterior surface of the cornea produced by depositions of copper.

Tattooed corneae are histologically examined by Baratta, El-Tobgy and Wilson, Pischel, Spinelli.

Fuchs finds the india ink in tattooing of the cornea interlamellar extracellular.

Sallmann finds, after tattooing of the cornea with gold chloride, deposits of apparent colloidal gold in the middle and deep layers. The gold is pushed by newly formed connective tissue from the epithelium into the depth.

Steiner found pigment between the deep epithelial cells of the cornea at the limbus of the trachomatous eyes.

In Kruckenberg's spindle, the endothelial cells are filled densely with fine pigment granules. The chamber angle is infiltrated with pigment and the edges of Descemet's membrane are pigmented (Hanssen).

Pigment is found in endothelial melanosis histologically in, on and between endothelial cells with simultaneous proliferative and degenerative changes in iris and ciliary body (Korobova).

Endothelial dystrophy in the form of degeneration of the cytoplasm and appearance of pigment may be combined with drusen in Descemet's membrane (Everett, Goar).

Sallmann describes a case of dystrophy of the corneal endothelium which had absorbed much pigment due to its increased absorptive power.

Henderson and Gillespie found a scattered degeneration of the corneal endothelium with pigmentation causing corneal opacities in cases of infectious hepatitis in soldiers in New Guinea.

Grueninger, Vogt consider the senile pigmented line (Staehli's line) of the cornea caused by ruptures of Bowman's membrane.

Stocker and Prindle describe a pigmented line in the cornea of a blind eye with nonspecific uveitis in the form of a fine, brownish line crossing from limbus to limbus. Histologically, the cells of the cornea are filled with brown pigment which probably is melanin.

Kaiser-Fleischer ring appears pathologically as fine pigment granules densely aggregated beneath the endothelium, reaching into Descemet's membrane (Archangelsky, Hall, Jess, Kubik, Rohrschneider, Vogt).

Jess considers the Fleischer pigment ring as deposition of copper. Kubik found pigment in the Kaiser-Fleischer ring which he considers as pigment of catabolic origin. Corneae with Kaiser-Fleischer ring contain besides the normally present sodium, calcium and magnesium zinc, copper, iron, silver, and alumen (Eckhardt, Stolzer, Adam and Johnson).

Meighan, Nicoletti, describe the recurring epithelial vesicles in keratitis bullosa.

Epithelial streaks in the cornea (v. Szily) resemble recurrent erosion and are microscopically dehiscences of the most superficial epithelial cells (Schulte).

Pillat describes a mummification of the corneal epithelium due to vitamin-A deficiency consisting of dehydrated cells with preserved cell membranes and pigment in the rest of the cytoplasma.

Hanssen finds changes of the tonofibrils of the epithelium of the cornea and conjunctiva which are considered by some of mesenchymal origin in various pathologic conditions. They degenerate in nevus, pterygium and glaucoma and hypertrophy in chronic conjunctivitis and in corneal scars.

The endothelium of the cornea may proliferate in suppurative keratitis and lie free in the anterior chamber and on the iris as endothelial precipitates (Fuchs).

Mayou describes the pathology of keratic precipitates and finds them consisting of agglutinated lymphocytes, plasma cells and phagocytes originating from the endothelium.

Fuchs finds that the firmness of the cornea depends on Descemet's membrane reinforced by the anterior and posterior marginal ring, of which the anterior shows great variations in its development, but the posterior appears always strong. The cornea bulges when the membrane is defective.

Reis brings histologic findings of ruptures of Bowman's membrane in increased intra-ocular pressure.

Van Veelen saw in a 32 year old imbecile a primary spontaneous rupture of Descemet's membrane with a heavy edema of the stroma and formation of cavities.

Vogt finds in cornea guttata fungiform, angular or trapezoid warts of Descemet's membrane.

Siegrist finds the cornea becomes involved in tuberculous iridocyclitis: (1) as keratic precipitates damage endothelium and Descemet's membrane, and erode the cornea; (2) as the tuberculous iris becomes attached to the posterior surface of the cornea and tuberculous tissue proliferates into the latter; (3) as tuberculous granulation tissue proliferates from the root of the iris and the ciliary body into Schlemm's canal and into the cornea and (4) as the tuberculosis of the ciliary body extends into the sclera and from here into the cornea.

Koyanagi describes a primary tuberculous ulcer of the cornea containing epithelioid and giant cells; tuberculous ulcerations of the cornea spreading to the inner eye are histologically examined by Key, Nicolato.

Carboni describes a tuberculoma of the limbus in an 11 year old boy.

Rollet and Colrat, Schulz report tuberculous interstitial keratitis.

Pillat, Pinkerton found lepra bacilli in the scrapings of the cornea in lepers.

Hagedoorn describes keratitis subepithelialis of leprosy.

Colvin, Meyerhof and Sobhy Bey describe lepromata of the cornea.

Fibromata of the cornea are reported by Favoloro, Hammetter, Lamb, Nano, Tallei.

Bussy describes as myxoma of the cornea a tumor consisting of branching anastomosing cells and granular mucoid substance.

Montanelli found capillary angioma of the cornea following an injury.

Galeazzi, Manzutto report about plasmoma of the cornea.

Towbin reports leukosarcoma of the limbus in a 55 year old woman.

Rosenstein observed fast progressing sarcomatous changes of a nevus of the limbus following Koch-Weeks conjunctivitis.

Cange and Duboucher, Derby, Roy, Schmidt report melanosarcoma of the limbus.

Loewenstein and Foster report a malignant melanoma of the limbus with pigmentation of the neighboring sclera, cornea and chamber angle and a spontaneous cyst of the pigmented layers of the iris in the same sector as result of a fetal inflammation in an early stage of development preventing complete closure of the cleft between the two layers of the optic vesicle and producing a melanoma by displacement of the pigment-storing cells of the outer germinal layer.

Azny el Kattan describes endothelioma of the cornea. The malignant tumors show polymorphism, alveolar and tubular structure, hyaline degeneration, concentric arrangement of the cells and relation to blood- and lymph vessels.

Barletta describes a perithelioma of the limbus.

Dejean, Poleff, Lo Russo describe epithelial tumors of the cornea.

Dame found an accessory lacrimal gland on the cornea.

Drak reports tubulous adenoma of the limbus.

Drak reports a case of cystadenoma of the limbus of a 19 year old man and believes that it originated in a displaced gland.

Ash and Wilder believe that the epithelial tumors of the limbus are simple leukoplaquic metaplasia of the conjunctival epithelium. Papilloma and squamous cell carcinoma develop secondarily from it.

Polev describes epithelial hyperplasia of the limbus with transition into papilloma and carcinoma.

Lopes de Andrade, Lowther describe bilateral epithelioma of the limbus.

Papillomata of the cornea are reported by Belgeri and Pavia, Boehm, Garraghan, Heymans, Lo Russo, Saba, Zappalà who calls the tumor fibroepithelioma papillare.

Berger found in cases of cornea- and limbus epitheliomata islands and strands consisting of basal cells and containing spindle-shaped cells.

Balding saw a papilloma of the limbus with intraepithelial carcinomatous changes.

Gourfein observed at a perforating wound of the limbus a papillomatous growth with carcinomatous degeneration.

Weskamp describes Bowen's disease (precancerous dermatosis) of the cornea showing dyskeratotic cells in the epithelium, irregularity of the epithelial cells and subepithelial inflammatory infiltrates.

Bowen's disease of the cornea is further reported by Esterman, Laval and Okrainetz, McGavic, Paulo Filho and Sebas, Wise.

Weymann describes a flat papilloma of the limbus containing cells of Bowen's type.

Judd, Papolczy describe cases of primary carcinoma of the cornea.

Squamous cell carcinomata of the limbus are reported by Bedell, Bilger, van Duyse, Freeman, de Schweinitz, Sédan.

Fejer reports a case of papillary basal cell carcinoma at the limbus.

Ballacco described a papillomatous carcinoma of the limbus in a 65 year old woman. It perforated the cornea and papillomatous growth appeared on the surface of the iris.

Nevo-carcinomata of the cornea of alveolar structure are reported by Castroviejo and Castroviejo, Veil.

Del Duca describes as nevus of the limbus an epithelial tumor with infiltration of eosinophils, lymphocytes, polymorphonuclears and erythrocytes.

Nevus cysticus non pigmentosus develops from proliferation of the basement layer of the epithelium (van Duyse).

Graves, Luedde, Moscardi describe melanotic nevi of the limbus, Cridland a vascular nevus of the limbus.

Rumbaur reports on dermoid of the cornea, Farina, Wood and Scott on dermolipoma of the cornea.

Rosen found several bilateral teratoid tumors of the limbus.

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Chapter VI

PATHOLOGY OF THE SCLERA

1. Wound Healing

The wound in the sclera itself has little tendency to heal and frequently does not heal from the sclera, but rather from the episclera and uvea. The wound is filled with fibrin into which polymorphonuclears immigrate from the surrounding vascular tissue. The polymorphonuclears absorb the necrotic tissue when it is present. Soon granulation tissue proliferates out of the surrounding tissues, consisting of newly formed blood vessels, fibroblasts, numerous lymphocytes, and many phagocytes. The oval nuclei of the fibroblasts are arranged in parallel rows, and the cells produce fibrils which at first have an irregular, but finally a parallel, arrangement. In this way, the granulation tissue organizes and the fibers develop more and more to form lamellae. Frequently, chromatophores and pigment granules are enclosed in the scar.

2. Rupture of the Sclera

Rupture of the sclera takes place typically on the corneo-scleral border through blunt trauma, rarely spontaneously, and the sclera ruptures from within outward. Sometimes only the inner layers are ruptured. The corneo-scleral trabeculae are frequently torn and Schlemm's canal opened. If the rupture is complete, the uvea may prolapse.

3. Ectasia, Scleral Staphyloma

Ectasia is an excavation of the sclera, total if it is ectatic in its entire circumference, or partial if it is ectatic in a circumscribed area. Scleral staphyloma would really be a substitution of a destroyed part of the sclera through scar formed from the uvea which becomes ectatic because of its softness, forming sclera-like lamellae lined inwardly only by pigmentary epithelium. How-

ever, both expressions are used interchangeably by the clinician as well as by the pathologist. Total ectasia is found in hydrophthalmos; partial ectasia takes place in areas where the sclera is weakened naturally by penetrating channels, as at the anterior ciliary vessels, at the equator in the region of the vortex veins, in the area of the posterior pole, or elsewhere where the sclera is thinned by disease or injury. Ectasia may sometimes rupture and lead to atypical rupture of the sclera. It is caused through increased intra-ocular pressure in glaucoma, through constitutional weakness of the sclera in myopia, through thinning due to congenital coloboma, scleritis, tuberculoma, gumma, tumor, or injury. The sclera appears thin in all cases, the lamellae are stretched and few in number in cross section and the uvea is degenerated. The thinning and protrusion of the sclera in the region of the limbus is called anterior scleral staphyloma, and ring staphyloma if such anterior scleral staphylomata coalesce all around the limbus. In the case of an intercalary staphyloma, the iris is adherent to the posterior surface of the cornea and the staphyloma is situated in the region of the iris root. Here the sclera is very stretched and thin, and on its inside it is lined by pigment epithelium. Posteriorly, this staphyloma is bordered by the ciliary body. In the case of a ciliary staphyloma, the sclera above the ciliary body is very thin, and on the inside atrophic, long, stretched ciliary processes are attached. The equatorial staphyloma is situated in the region of a vortex vein and the staphyloma posticum at the posterior pole.

4. Congenital Changes

Congenital changes include (a) melanosis, (b) blue sclera, (c) cartilage in the sclera, (d) pseudocornea, (e) coloboma, and (f) cysts.

In *melanosis sclerae,* pigmented cells with long processes and occasionally extracellular pigment granules lie between the superficial lamellae of the otherwise normal sclera, and in the tissue of the episclera. They may be chromatophores which originate from the suprachoroidal tissue, accompanying the perforating scleral channels and are probably of mesodermal origin. The

melanosis is sometimes a part of the melanosis bulbi which besides the sclera affects cornea, uvea, retina, and optic disc.

Blue sclera. In some cases of blue sclerotics the sclera is apparently thinned; in others the thinness is not certain but the scleral fibers are less in number and in this way the sclera is perhaps abnormally translucent. This congenital anomaly combined with fragility of the bones and otosclerosis is apparently hereditary.

Hyaline cartilage in the sclera is rarely found in eyes which otherwise show congenital changes similar to those in dermoid growths. It is perhaps an atavistic tendency as lower animals normally have cartilage in the sclera.

Pseudocornea is formed occasionally when scleral lamellae arrange themselves at the side of a corneal staphyloma parallel to the surface, and oval nuclei appear between the lamellae. The ciliary body underneath may be an irregular structure. As the corneal staphyloma appears sclera-like, the adjacent sclera appears cornea-like. One speaks in such a case also of heterotopia of the cornea.

In *coloboma,* the sclera is either thinned through the absence of inner lamellae or shows a defect which is filled with cystic glial tissue.

Cysts. In scleral cyst there is, beneath the conjunctiva of the limbus, a thin layer of scleral tissue and beneath this, a space lined by flat, stratified epithelium of two to five layers of cells. Its basal layer is cylindric, similar to conjunctival epithelium. Presumably, it originates from evaginations of the surface epithelium, but there is also the theory that it represents a diverticulum of the anterior chamber and the rest of Schlemm's canal which extends in the embryo far into the sclera, and that this part did not disappear in the case of a congenital cyst. But it is difficult to explain the presence of the stratified epithelium. Similar to the congenital cysts appear the traumatic cysts. They represent a space in the sclera lined with stratified epithelium containing fluid and cell debris. In the majority of cases they are found at the limbus. They are unilocular or multilocular. They develop from corneal or conjunctival epithelium which extends in a case of injury into the depth of the sclera; more

rarely, they develop from proliferating epithelium of the ciliary body. Sometimes they communicate with the chambers of the eye.

5. Necrosis and Degeneration

Necrosis takes place in circumscribed patches in the case of malnutrition of old age, especially in the region of pathologic anterior ciliary vessels. Calcareous deposits are found in necrobiotic, nuclear-free parts of the sclera. Calcium may be deposited in any layer of the sclera, frequently where the sclera is exposed to traction; e.g., at the insertion of the lateral rectus muscle. It is found in senile degeneration and after inflammation, especially in excessive fibrous replacement of the infiltration (hyperplastic scleritis). It may be the precursor of bone formation. Fatty degeneration appears in old age after inflammation and in old scars. In old age, hyaline degeneration may occur after inflammation.

6. Inflammation of the Sclera

We find nonspecific and specific inflammations. They may affect the episclera as well as the sclera. The sclera is affected primarily, and in severe cases the inflammation extends into the uvea or the scleritis is secondary to inflammation of the uvea. If the inflammation of the sclera extends to the limbus, it continues frequently into the cornea (sclerosing keratitis), and the histologic picture is similar in both the sclera and cornea. Many types of scleritis are examined clinically only and histologic examination is conducted only in severe cases in which the extension of the inflammation and complications urge the enucleation of the eye. In nonspecific inflammations, the fiber bundles of the episclera are separated by edema, blood and lymph vessels are dilated, and infiltrations with lymphocytes, polymorphonuclears and monocytes appear. The lamellae of the sclera are swollen, small blood vessels proliferate, and nodules of lymphocytes appear. Lymphocytes may infiltrate diffusely and polymorphonuclears are also present. Nonspecific inflammations may be caused by rheumatism, which is perhaps an allergic reaction to bacterial allergy, to other infections such

as tuberculosis, and reaction to focal infection in teeth, tonsils, prostate, female sex organs, paranasal sinus, appendix, etc. In such cases, through invasion of bacteria themselves, pyogenic metastatic scleritis with formation of abscesses may arise. Furthermore, gout is a frequent etiologic factor; syphilis may be an offender.

The episcleritis is seen as episcleritis nodularis and periodica fugax, but no histologic examinations have been done.

The scleritis is seen (a) as anterior scleritis, (b) as progressive sclero-perikeratitis, (c) brawny scleritis, (d) posterior scleritis, but all these forms are related to each other.

Anterior scleritis shows dense lymphocytic infiltration of the anterior sclera with few blood vessels. The infiltration may surround the cornea in a ringlike formation (annular scleritis). If sclerosing keratitis sets in, the cornea becomes very thin, the lamellae are irregular and disintegrated, and edema appears between them. The interlamellar spaces are filled with lymphocytes, monocytes, proliferating fibroblasts and contain vessels with thin walls.

A number of bacteria may locate themselves in the sclera from the conjunctiva or the blood circulation as already mentioned and occasionally may produce circumscribed necrosis. The bacillus of the plague may destroy the trabeculae, Schlemm's canal and the adjacent cornea and sclera.

In progressive sclero-perikeratitis (malignant scleritis), the sclera and cornea are affected at the same time and later the anterior uvea. Finally the cornea, sclera, episclera, chamber angle, iris root, and ciliary body are affected. The episclera and conjunctiva are very thick, blood vessels are dilated and there are nodules consisting of lymphocytes and plasma cells with epithelioid cells in the center. The sclera shows rows of cells consisting of lymphocytes, plasma cells and few eosinophils. Bowman's membrane is displaced from the limbus and folded and surrounded by infiltration. The parenchyma of the cornea contains rows of cells similar to those of the sclera. Vessels of the limbus are sometimes thrombosed, vessels of the episclera, the posterior eye and the orbit have thickened walls with proliferation of the endothelium and perivascular infiltration with

lymphocytes. Necrosis occurs and occasionally Langhans' giant cells appear. The anterior uvea shows infiltration with lymphocytes, plasma cells and epithelioid cells. Lymphocytic infiltrates may finally appear in the extrinsic eye muscles and in the lacrimal gland. Tuberculosis is thought to be the cause but bacilli have never been found and inoculation of animals has always been negative. It is probably a rheumatic disease.

FIG. 22.—BRAWNY SCLERITIS. i, infiltration with lymphocytes; l, scleral lamellae; v, vessel surrounded by infiltration. 65×.

In brawny scleritis (gelatinous scleritis), the sclera appears tremendously thickened due to swelling of the lamellae and degeneration of the fibers and dense infiltration with lymphocytes and plasma cells. The choroid is mostly infiltrated with lymphocytes.

In posterior scleritis (sclero-tenonitis), adhesions are formed between Tenon's capsule and sclera and inflammation of the choroid and retina sets in. Bacteria may enter the posterior sclera by way of the blood circulation and produce there circumscribed abscesses.

The specific inflammations of the sclera are tuberculosis, syphilis and leprosy.

Tuberculosis is diagnosed if typical tubercles are found in the episclera and in the middle and deeper layers of the sclera. They contain bacilli. Most frequently they are situated at the limbus and close to the optic nerve, in areas where ciliary vessels pass through the scleral channels. They originate endogenously by way of the blood circulation. Tuberculosis may extend into the uvea and also into the cornea.

Syphilis is seen in the form of gummata, representing the typical structure of marginal infiltration with lymphocytes, plasma cells and occasional giant cells and central necrosis. Small arteries show proliferation of the intima and infiltration of the walls with round cells.

In leprosy, the episclera shows infiltration with lymphocytes, plasma cells, large lepra cells and many newly formed vessels. Between the scleral lamellae are found lymphocytes and spindle cells. Bacilli may be found easily in great numbers. The infection occurs endogenously.

7. Fungus Diseases

Aspergillosis rarely affects the sclera, which contains a granulation tissue consisting of lymphocytes, plasma cells, epithelioid and foreign body giant cells. Mycelia are found. Aspergillus fumigatus is carried into the sclera mostly by injury through a twig.

8. Neoplasms

Primary tumors of the sclera are extremely rare. The tumors described as fibromata are probably keloid-like connective tissue hyperplasia which originate from injuries or inflammations and which show coarse connective tissue bundles and spindle-shaped connective tissue cells. Neurofibromata occur, originating from ciliary nerves. They show typical whirl-like tracts of fibers and fibroblasts. The episclera may be the seat of dermoids showing hair follicles, sebaceous and sweat glands, and of teratomata which have in addition to glands, also cartilage and bone.

Secondary tumors extend from the surface and from the intrinsic eye and are squamous cell carcinoma and adenocarcinoma, sarcoma, melanosarcoma (malignant melanoma) and retinoblastoma.

READING OF SOURCE MATERIAL

Casanovas reports on atypical scleral ruptures.

Redaelli describes choroiditis with sclerectasia.

Axenfeld found his "intrascleral ciliary nerve loop," consisting of swollen nerve. It is a malformation or variation of unknown cause.

Intrascleral loops of ciliary nerves are described by Fischer. They are found in the anterior segment of the eye in the region between pars ciliata and pars plana of the ciliary body. They are due to congenital abnormal growth of the nerves.

Custodis, Usher report on congenital cysts of the sclera.

Bergmeister's case of microphthalmos with coloboma of the papilla showed numerous pseudocysts of the sclera lined by glial tissue.

Traumatic scleral cysts are reported by Michail, Salzmann, Velhagen, Weymann; further, scleral cysts are histologically examined by Goulden and Whiting.

Leser believes that necrosis of the sclera is caused by vascular disturbances.

Klien-Moncreiff, Lewi described calcareous deposits in necrotic parts of the sclera, mainly anterior to the insertion of the lateral rectus.

Katz describes a localized area of calcareous degeneration in the sclera with calcium carbonate and phosphate in and between the lamellae.

Roper describes senile hyaline scleral plaques with atrophy lying over the episclera and conjunctiva.

Kyrieleis reports scleromalacia in adults, showing thickening and calcification of the sclera.

Urrets Zavalia, Maldonado Allende and Obregon Oliva observed a case of scleromalacia in the course of chronic porphyrinuria, showing fine, yellow droplets in the cornea and sclera.

Verhoeff and King describe scleromalacia perforans showing sequesters of necrotic scleral tissue surrounded by abscesses which finally perforate. As the inflammatory nodule of the sclera resembles gouty nodules, they assume a metabolic disturbance with deposition of chemical substances as cause.

Wood finds histologically in episcleritis and scleritis in gout, crystalline deposits in the infiltrated tissue.

v. Hippel describes a case of malignant scleritis forming a ring infiltration around the cornea and infiltration of the choroid, consisting of lymphocytes, plasma cells, epithelioid and giant cells with the sclera atrophic.

Smoleroff finds in the inflamed sclera in rheumatoid arthritis, circumscribed necrosis, abscesses containing sequestra of sclera, infiltration with lymphocytes, plasma and epithelioid cells, edema and perivascular infiltrates. He proposes the name necroscleritis nodosa (excavans, if perforated).

Eggers found intrascleral abscess with perforation in the eye of a 37 year old woman with chronic arthritis.

Viswalingham finds in scleritis similar histologic changes as well in cornea as in the sclera, showing intense infiltration with lymphocytes,

scarce vascularization, some necrosis and fibrous replacement. Sclerosing keratitis appears histologically similar to tuberculosis (v. Szily).

Thiel reports cases of circumscribed episcleritic abscesses caused by staphylococcus pyogenes aureus ("episcleritis metastatica furunculiformis"); Kuchner describes a case of circumscribed suppuration of the sclera with numerous necroses ("scleritis metastatica furunculiformis").

In severe nonspecific scleritis there are found extensive lymphocytic infiltration, epithelioid and giant cells and numerous necroses (Botteri, Hesse, Zinsser).

The histology of sclera-perikeratitis progressiva of v. Szily is reported by Bossalino, v. Hippel, Ishikawa, Landegger, v. Planta, Suganuma, v. Szily.

Trachomatous affection of the episclera in the form of follicles and perivascular infiltrates is described by Pascheff.

Samuels describes the enormous accumulation of lymphocytes and epithelioid cells in the emissaries and stroma of the sclera in sympathetic ophthalmia as sympathetic scleritis.

Bruckner believes that tubercle bacilli are carried by phagocytes from the conjunctiva through the sclera.

Suganuma finds tuberculous infiltration of the sclera mostly in the area of the most anterior sclera where anterior and posterior ciliary vessels anastomose.

Pellegrini reports the case of an 18 year old boy with deep ulcer of the sclera containing typical tuberculous granulation tissue.

Solitary tubercles of the sclera are reported by Colomb, Fazakas, Pollak, Sun.

Kronenberg found multiple tubercular nodules of the episclera in a 64 year old man with active tuberculosis of the lungs; Chon describes a case of metastatic tuberculous nodules in sclera, iris, ciliary body and suprachoroid.

Fresh and caseous tubercles were found in the sclera of a blind eye by Poyales.

Gallemaerts reports on the histology of the gumma of the sclera.

Gyotoku finds in leprous scleritis granulation tissue consisting of fibroblasts, plasma cells, and epithelioid cells in the anterior episclera; lepra bacilli are easily detectable.

Favaloro found aspergillus fumigatus, Federici a fungus of the species sporomiella in the sclera.

Fibromata of the sclera are reported by Bucur, Redslob, Schmidt, Serra.

A keloid of the sclera is reported by Raverdino.

Kyrieleis, Szabo and Cseh describe neurinomata of the limbus, probably originating from intrascleral loops of ciliary nerves.

Mamoli reports neurofibroma of the sclera in the case of Recklinghausen's disease in a 22 year old man.

Dalsgaard-Nielsen describes a tumor of the sclera as angiofibroma.

Bywater describes myxofibroma of the sclera.

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Chapter VII
PATHOLOGY OF THE UVEA

1. Inflammation of the Uvea (Uveitis)

General considerations: The inflammations are acute or chronic; the latter are nonspecific or specific. They are exudative, infiltrative and proliferative, depending on whether there is exudation onto the surface of the uvea and infiltration with cells of different types, or whether proliferation in its tissue or beyond its border prevails. Often all these changes are combined in the same case, but one of these is prominent. The acute inflammations are mostly exudative, the chronic ones infiltrative and proliferative. If organisms or irritants enter the vitreous body directly from the chambers or from the inflamed uvea, exudate is poured into the vitreous from the ciliary body and the surrounding retina, thus forming hyalitis (Straub) or endophthalmitis (Fuchs). If organisms and irritants enter the uvea directly, then exudation and infiltration take place in the uvea itself (uveitis). If, in the course of an acute inflammation, proliferations appear, the end result may be the same as in a chronic one. The etiology is manifold and cannot always be made certain from the histologic examination, usually only in its specific forms. Frequently, the clinical examination of the entire individual allows us only to guess the cause. In the majority of cases, uveitis is caused by infection, which may appear from an exogenous source after perforation of the eye due to injury, operation or ulcer, or which is carried into the eye from an endogenous source. The inflammation may be caused by chemicals or toxins, or it may continue secondarily from an inflammation of the surrounding tissues, i.e., from the cornea, sclera or retina.

Acute Inflammation

This condition attacks the iris, ciliary body or choroid. It is suppurative, in rare cases purely fibrinous, mostly fibrinous-

suppurative. The iris shows deposits of polymorphonuclears and fibrin on its anterior surface. The anterior chamber is filled with them, forming a hypopyon. The iris tissue is edematous and is filled with polymorphonuclears which sometimes appear also in the form of nodules. There may be present large monocytes, lymphocytes, mast cells, and eosinophils in varying proportions. Blood vessels are dilated and filled with polymorphonuclears and fibrin. Their walls are infiltrated. The adventitia is hydropic and infiltrated with cells. Thrombosis, bacterial emboli and hemorrhages occur. Chromatophores clump together and pigment granules are dispersed in the tissue. Stroma cells become mobile and pigment epithelial cells start to migrate and both may eventually become phagocytes. Pigment epithelium may disintegrate and may be filled with exudate. The obstruction of the vessels along with toxins of the bacteria may produce necrosis of uveal tissue, in which case structure becomes indistinct and nuclei lose their staining quality. Generally, acute iridocyclitis is present; the iris as well as the ciliary body are affected at the same time, but usually to different degrees. The part of the ciliary body bordering the chamber angle is filled with polymorphonuclears which are poured from here into the chamber angle. The ciliary processes are dilated, filled with polymorphonuclears and fibrin and the vessels may show the already mentioned changes. The crests of the ciliary processes show the heaviest accumulation of cells. The epithelium is disintegrated and sometimes both epithelial layers are separated by fluid. The cells of the pigment epithelium break up and the pigment escapes. Exudation is poured throughout the ciliary body and into the anterior and posterior chambers. From the ciliary processes and the pars plana polymorphonuclears and fibrin enter the posterior chamber and from the pars plana also the vitreous body. In rare cases, necrosis of the ciliary processes may set in. The ciliary muscle is frequently free of inflammation. Pus in the vitreous body is produced not only from the uvea but also from the retina and is deposited along the inner surface of the retina (endophthalmitis). The choroid and suprachoroid show hyperemia and edema and are filled with lymphocytes, mononuclears, plasma cells, mast cells and eosino-

phils. Endothelial cells and stroma cells proliferate. In suppurative choroiditis, accumulations of polymorphonuclears, mononuclears and lymphocytes are found, Bruch's membrane is attacked by toxins, holes form in it and pus cells enter the subretinal space. The pigment epithelium disintegrates and the pigment becomes free and finally is taken up by macrophages.

The inflammation may become subacute and finally chronic, and the different stages may exist at the same time. Depending

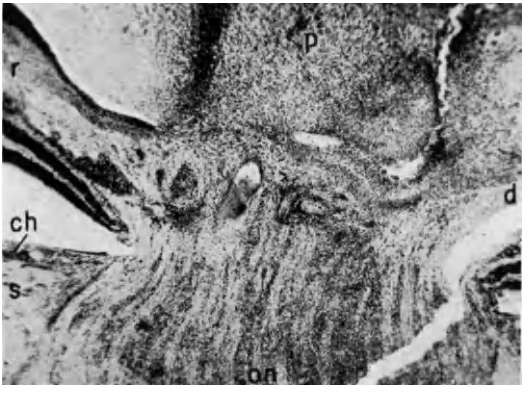

FIG. 23.—ENDOPHTHALMITIS. ch, choroid; d, disc showing infiltration; on, optic nerve; p, pus in vitreous; r, retina covered with pus cells; s, sclera. 50×.

on the intensity of the causative agents, severe and mild forms may appear. The same agent which produces a severe acute inflammation in its immediate vicinity may be so attenuated at a distance that it produces merely the reaction of chronic inflammatory changes. Thus, in a case of suppurative retinitis, the choroid may show only chronic infiltration and in vitreous abscess the ciliary body may be infiltrated with lymphocytes.

The sequelae of the acute inflammation are manifold, depending upon the seat and severity of the inflammation and upon whether the inflammatory irritation persists and the exudate is not reabsorbed. The acute inflammation may continue on to subacute and chronic stages. If the ciliary body produces much pus, there forms in the vitreous body an abscess which may be organized from the choroid and more especially from the pars

plana by granulation tissue. Pus may enter from the choroid into the retina, into the sclera and optic nerve and toxins may affect the cornea from the anterior chamber and produce necrosis and a ring abscess. If all the tissues of the eye are filled with pus cells, a panophthalmitis is present which ends with destruction of all the tissues except the sclera in phthisis bulbi. But if the tissues are not destroyed by pus and organization sets in, the globe starts to shrink and atrophia bulbi is present. Exudate on the iris, in the pupil and around the lens may be replaced by connective tissue, forming membranes. If the posterior surface of the iris is perforated, organizing tissue may produce synechiae between iris and lens and organizing exudate in the pupil may produce seclusion and occlusion of the pupil. Organizing tissue of the posterior chamber may shrink and detach the ciliary body from the sclera. In choroiditis, exudate consisting of serum- and fibrin-containing fluid, polymorphonuclears, lymphocytes and swollen pigment epithelium may detach the retina. Clumps of cells containing lipoids and cholesterol may appear in the subretinal space. Exudate behind the lens in the vitreous or in the subretinal space and its organizing tissue give the appearance clinically of pseudoglioma, in which the pupil of the inflamed eye gives a yellow reflex. The choroid may become fibrous and sclerosed and the fibrous granulation tissue may proliferate through the retina into the vitreous (choroiditis hyperplastica, Schoebl), and the perichoroidal lamellae may thicken to obliterate the perichoroidal spaces (suprachoroiditis). The organizing connective tissue may show degenerative changes of fatty infiltration, deposition of cholesterol, formation of cartilage in rare cases, but more frequently deposition of calcium and formation of bone.

The acute inflammation is either of exogenous origin, such as a perforating wound, or secondary to suppurative inflammation of other ocular tissues, or of endogenous origin, although a metastatic ophthalmia is more prone to attack the retina or to metastasize. The metastasis occurs more frequently through the central artery of the retina than through the ciliary vessels. Some assume that toxins circulating in the blood are not able

to produce a metastatic suppurative inflammation of the eye. Organisms causing a suppurative exogenous or metastatic inflammation of the uvea are streptococci, staphylococci, pneumococci, gonococci, meningococci, bacillus typhosus, influenza bacillus, bacillus coli and actinomyces. As already mentioned, the exogenous suppurative uveitis is produced by organisms or poisons which are brought into the eye through wounds after a perforating injury or intra-ocular operation or through perforating

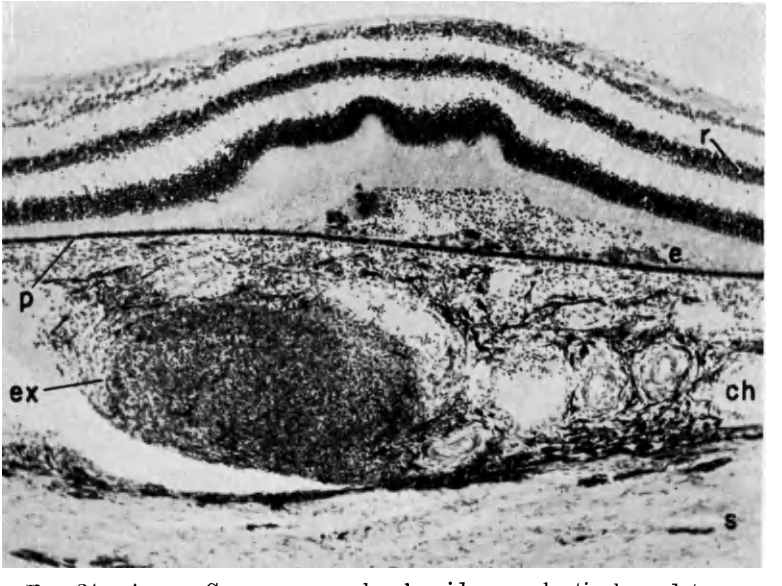

FIG. 24.—ACUTE CHOROIDITIS. ch, choroid; e, subretinal exudate consisting of polymorphonuclears and fibrin; ex, choroidal exudate consisting of polymorphonuclears; p, pigment epithelium; r, retina; s, sclera. 65×.

ulcers and through chemicals which penetrate the outer layers of the eye. It may be caused secondarily without perforation through a suppurative inflammation of the cornea and sclera, the retina and the optic nerve or the orbit, due to a diffusion of toxins. Metastatic acute uveitis is found in pyemia of various origins, especially in puerperal sepsis, in complicated otitis media, pneumonia, meningitis, in cases of influenza, in apical abscesses of the teeth, in tonsilitis, prostatitis; acute exanthemata

of childhood may be the cause, such as scarlet fever and measles. Rheumatism and gonorrhea may also produce acute uveitis.

Chronic Nonspecific Inflammation

The chronic nonspecific uveitis is a continuation of an acute one if the inflammatory stimulus continues, but decreases steadily in intensity without disappearing entirely. The inflammation thus becomes subacute and finally chronic. It may recur in frequent attacks, but it may appear from the beginning as a chronic form. It may be caused exogenously or as a metastatic form secondary to chronic inflammations of other tissues of the eye (endogenous). The types of the inflammation are infiltrative, proliferative and exudative. Sometimes one form prevails alone, but usually all forms are combined. The infiltrating cells are primarily lymphocytes and mononuclears, which may appear diffuse or in nodules. The formation of lymph follicles is rare. Other cells which are found are plasma cells and mast cells. It is probable that the degeneration of plasma cells yields homogeneous, round intensively acidophilic stained rounded corpuscles (Russell's bodies). Exudation of lymphocytes and monocytes and fibrin onto the surface of eye tissues takes place. The exudate appears mainly as a precipitate. The proliferation affects first the pigment epithelium, but uveal tissue and granulation tissue proliferate inside the border of the uvea and beyond it into the surrounding tissues.

The iris shows infiltration with lymphocytes, mononuclears and few plasma cells. The cells are more numerous around the vessels and most dense around the sphincter which is rich in capillaries and here they may also form nodules. Blood vessels are dilated and may show changes in all parts of the wall. The endothelial cells proliferate, the media appears hyalinized and the adventitia thickened. Some vessels obliterate. The stroma of the iris proliferates and the iris is then transformed into fibrous tissue or atrophies. In some instances, an exudation of fibrin and cells onto the surface of the iris takes place, and the endothelial cells and anterior border layer cells proliferate. Fibrin is poured into the pupil and also contains cells. This cov-

ers the anterior lens capsule as a pupillary membrane (occlusio pupillae). The stimulus of the membrane and of the inflammation-producing agents bring about a proliferation of iris tissue at the pupillary margin where the mesodermal iris stroma touches the ectodermal pigment epithelium which extends somewhat into the pupil as a physiologic ectropion. At this meeting point, a potential gap or a locus of lower resistance exists and granulation tissue extends from it into the pupillary membrane. Then desquamated or proliferating cells of the pigment epithelium and free pigment of disintegrated cells enter the membrane. The tissue organizes and forms a tight attachment of the pupillary margin to the lens capsule. These posterior synechiae may become annular and shut off the anterior from the posterior chamber. The aqueous humor continuously secreted from the ciliary body is now unable to enter through the pupil into the anterior chamber and therefore pushes the iris anteriorly and finally attaching it to the posterior wall of the cornea, forming a sharp curve to the adhesion on the lens. This formation, known as iris bombé, is a precursor of secondary glaucoma. If the pigment epithelium disintegrates and tissue proliferates from the iris into the space between iris and lens, both become attached along their entire extent (total posterior synechia). In this case, the center of the anterior chamber is shallower than its periphery, with the result that secondary glaucoma sets in.

The exudate on the iris anterior surface organizes through granulation tissue arising from the iris and a fibrous membrane of various thickness is formed which often becomes lamellar and appears similar to corneal tissue. The fibrous tissue by shrinkage exerts traction on the pigment epithelium of the pupil and pulls it onto the anterior surface of the iris (ectropion of the pigment layer). The organizing tissue may block the chamber angle and produce secondary glaucoma. Proliferating fibrous tissue sometimes fills much of the anterior chamber and undergoes hyaline and lipoid degeneration containing finally cholesterol in crystals. The endothelium of the cornea is able to proliferate onto the tissue covering the anterior surface of the iris and deposit there a newly formed Descemet's membrane. Exudation and proliferation occasionally give rise to circumscribed nodules on

the pupillary margin. These consist of epithelioid cells and lymphocytes and are situated at the ectodermal layer of the pigment epithelium (nodules of Koeppe) or on the anterior mesodermal layer of the iris (floccules of Busacca). They are deposited here from the aqueous humor or may proliferate from the tissue itself. Such nodules are also seen attached to the anterior lens surface and to threads of a congenital pupillary membrane.

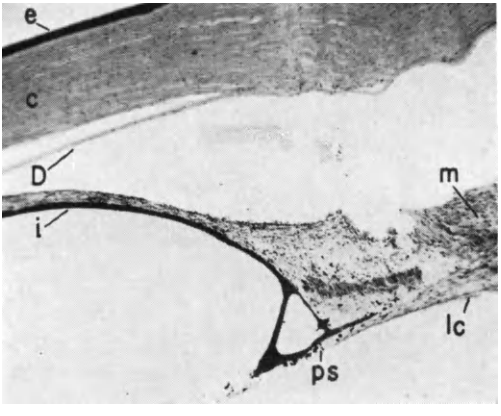

FIG. 25.—IRIS BOMBÉE. e, cornea; D, Descemet's membrane artificially detached; e, epithelium; i, atrophic iris bulging forward; lc, lens capsule; m, occlusion membrane; ps, posterior synechia. 60×.

The pigment epithelium, as already mentioned, degenerates and proliferates, the epithelial cells show edematous swelling and the pigment clumps together and the cells break up and pigment becomes free. Occasionally pigment cells enter the exudate, and after having changed their form to a flat oval shape, may become phagocytes. Epithelial cells proliferate into the tissue, into the chambers and onto the lens surface. The pigment epithelium proliferates actively due to its own growth stimulus, and if the iris stroma atrophies, it extends abundantly over the surface of the iris, forming the ectropion. Proliferation of pigment epithelium and formation of folds on the posterior surface of the iris through traction of strands and shrinking tissue can give rise to cysts. The iris and ciliary body are

affected in the majority of the cases at the same time, although often in different degree, at which time chronic iridocyclitis is present. But if the ciliary body is affected alone and the iris not at all or only to a small degree, cyclitis exists. It forms either a cellular exudate which takes the form of precipitates and appears as a "serous iritis" (serous cyclitis), or it produces more fibrin and proliferation of tissue and appears as plastic cyclitis. The precipitates are seen mostly as keratic precipitates, and as deposits on the iris, lens capsule and in some cases they float in the vitreous body and are deposited on the retina as circumscribed round nodules. Lymphocytes and monocytes enter from the edematous and infiltrated ciliary body through the epithelium into the posterior chamber. Sometimes the monocytes become fibroblast-like cells.

The inflammatory cells and desquamated epithelial cells are clumped together by fibrin and a mucous gluelike substance which is secreted from the inflammatory cells. The cells clump about the zonule fibers, enter the vitreous body, adhere to the lens capsule or move through the pupil into the anterior chamber if they do not adhere to the pupillary margin. They are carried up in the anterior chamber along the iris by the slow circulation of the aqueous, and if they do not adhere to the anterior surface of the iris, they sink down along the posterior surface of the cornea. Here they adhere to the endothelium which has already become edematous and is desquamated, forming the keratic precipitates. If the stimulus of the irritant is stronger, exudation of cells along with proliferation of epithelial cells sets in in the region of the base of the vitreous, where normally some exchange of fluid between choroid and vitreous takes place. The epithelial cells proliferate in the form of plates, strands, nets and tubules. The nonpigmented as well as the pigmented epithelium proliferates into the spaces of the posterior chamber and into the vitreous as in a tissue culture ("free epithelial proliferation") or it proliferates into the connective tissue strands which arise from the organization of the exudate, containing fibroblasts, coarse connective tissue bundles and blood vessels. The proliferating epithelium may appear glandular-like and may simulate adenoma. The epithelium sometimes

secretes homogeneous and fibrinous substance. On the other hand, the epithelium also proliferates into the ciliary body toward the muscle.

The proliferation of the epithelium and connective tissue represents the cyclitic membrane. The shrinkage of the membrane exerts traction on the retina and pulls it toward the center of the bulb, producing in this fashion a total detachment of the retina which finally lies folded and adherent to the cyclitic membrane behind the lens in the shape of a funnel and extends axially through the eye toward the papilla. The vitreous is compressed into a minimal space behind the posterior pole of the lens. The cyclitic membrane shows often degenerative changes with deposition of hyaline, fat, bone, and very seldom cartilage. The cyclitic membrane, which in the beginning is rich in cells and poor in fibers, changes in the course of time to tissue with few cells and many fiber bundles. The coarse fiber bundles shrink more and more and by concentric traction toward the center of the eye causes not only detachment of the retina, but also separation of the entire ciliary body up to the insertion of the ciliary muscle at the scleral spur and diminution in size of the entire globe (atrophia bulbi).

The choroid shows a diffuse infiltration with lymphocytes and mononuclears and frequently the choriocapillaris and inner layers are found to be affected mainly, but there may also be localizations of nodular infiltration. Some stroma cells clump together and many chromatophores become round and disintegrate and the pigment becomes free; some chromatophores and pigment are displaced toward the margin of the nodular infiltration.

Further, vascular changes may appear with swelling of the endothelial cells. Bruch's membrane may be perforated by the infiltrate and round cells along with desquamated pigmented epithelial cells may fill the subretinal space, producing a detachment of the retina. Circumscribed nodules consisting of lymphocytes, mononuclears, epithelial cells and fibrin may adhere as precipitates on the external surface of the detached retina or on the inner surface of the choroid. Fluid and cells may pass through the retina into the vitreous. The pigment

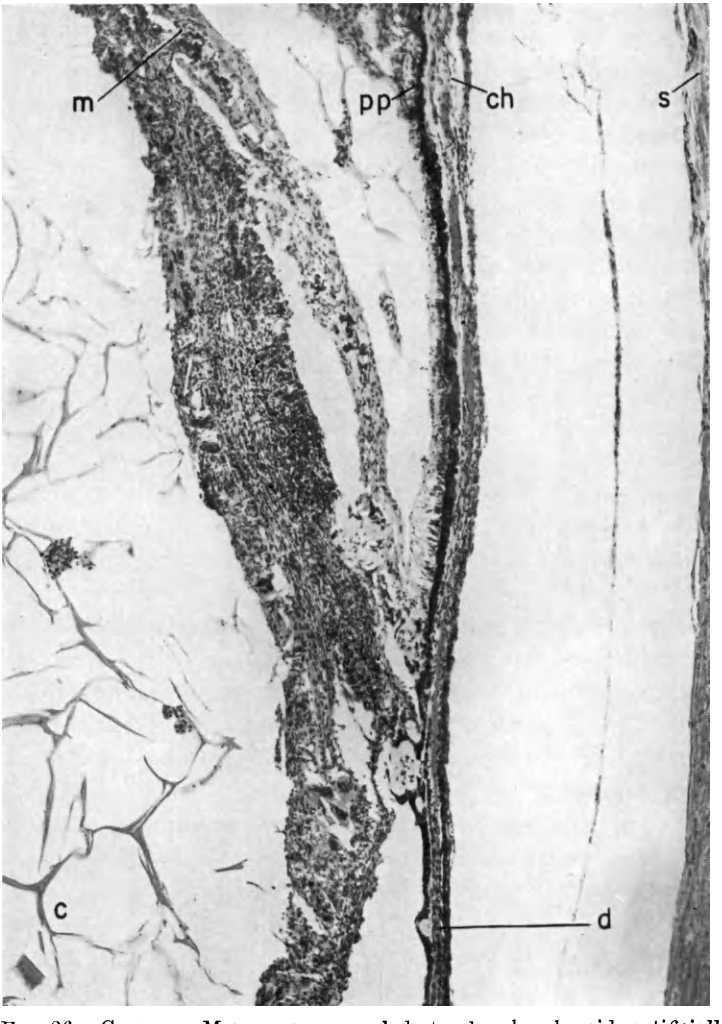

FIG. 26.—CYCLITIC MEMBRANE. c, cholesterol; ch, choroid artificially detached; d, drusen; m, cyclitic membrane; pp, pars plana of the ciliary body; s, sclera. 45×.

epithelium disintegrates over the choroiditic foci, some epithelial cells swell and rupture and their pigment becomes free while other pigmented epithelial cells proliferate in strands and tubules and may secrete a cuticular substance similar to drusen. They grow into the exudate and into the organizing blood clumps or break loose, become round and lie free in the fluid of the subretinal space, where they may show an active ameboid movement.

Some pigment epithelial cells also proliferate through defects of Bruch's membrane into the choroid, while others proliferate into the adherent retina toward the vessels, and the extracellular pigment is carried into the retina, taken up by the tissue current and transported into the perivascular spaces. Infiltrates can disappear again, but leave depigmentation and some scar tissue; few lymphocytes, monocytes and mast cells sometimes remain. Frequently, granulation tissue is formed, producing fibrosis by organization. If Bruch's membrane is perforated, connective tissue from the choroid and glia from the retina proliferate through the gap in addition to the pigment epithelium. Glia may be found in deposits on and in the choroid itself. In this way, the largely disintegrated retina is united with the choroid permanently (chorioretinitis adhesiva). If the formation of fibrous tissue is excessive, it may even proliferate into the vitreous (choroiditis hyperplastica, Schoebl). On the other hand, the connective tissue may remain thin and shrink, and the choroid may represent a fine fibrous membrane with few vessels and few cells. Sometimes the suprachoroid takes part in the proliferation, the chromatophores clump together and disintegrate and the endothelial cells proliferate and form considerable fibrous tissue which may become very thick (suprachoroiditis). Disintegrating pigment epithelium and hemorrhages cause formation of lipoids and cholesterol which can be surrounded by granulation tissue and foreign body giant cells. Calcium is deposited, which also is frequently seen in drusen. The fibrous scar tissue often undergoes hyaline degeneration and is transformed by metaplasia into bone marrow which usually is fat marrow, rarely fibrous or blood marrow, forming rows of osteoblasts. They produce lamellar osteoid substance and

finally bone by absorption of calcium. The bone is mostly formed in the inner layers of the choroid. Very rarely metaplasia with formation of cartilage is found.

FIG. 27.—BONE FORMATION IN CHOROID. m, blood marrow; r, degenerated retina; t, bony trabeculae. 65×.

In otherwise normal eyes, small nodules of lymphocytes with histiocytes which are probably caused by abnormal substances circulating in the blood may be found in the choroid. Such infiltrates probably appear in areas where the eye muscles pull. In inflamed eyes, toxins diffuse throughout the eye and produce similar small foci. They appear in eyes with corneal ulcers, injury, tubercles and sarcoma. Such foci are seen in chronically inflamed eyes and in areas where shrinking scar tissue pulls.

Exogenous causes for chronic uveitis are injury and operation. While in many cases an infecting organism cannot be found, under certain circumstances bacteria which produce an acute suppurative inflammation may produce a chronic uveitis. Some eyes appear sensitive to lens substance, and after an extracapsular extraction an inflammation may appear which is called endophthalmitis phaco-anaphylactica. Other eyes assume the characteristics of a chronic uveitis in an allergic reaction to uveal pigment. If much pigment is destroyed and absorbed—mostly in an injured eye—often in the fellow eye a hypersensitivity is produced so that continuous absorption of pigment excites an allergic reaction. Endogenous chronic uveitis develops secondarily to chronic inflammation of the cornea and sclera and to dissemination of toxic-acting products within the eye, as in necrotic intra-ocular tumors (especially in malignant melanoma of the uvea), and in such conditions as intra-ocular hemorrhage, external retinitis and retinal detachment. Endogenous metastatic chronic uveitis appears in cases of endocarditis, septicemia and focal infections, caused by the lodgment of metastatic foci of streptococci, staphylococci, pneumococci, and gonococci. Toxins of bacteria may produce chronic nonspecific uveitis; even those of bacteria which produce specific granulomata, such as tuberculosis and lues, may be culpable. From infected teeth, tonsils, paranasal sinuses, intestinal and genito-urinary tract, chronic uveitis may be produced. In gout, an inflammation may set in which probably is caused by chemical irritants.

Endogenous chronic uveitis appears in many forms, not only in accordance with the organism but also with the intensity of the stimulus. If the irritation is mild, then only a low grade infiltration, exudation and epithelial proliferation sets in. On the other hand, metastasis causes also the formation of membranes, and under certain circumstances, heavy infiltration and proliferation sets in with occasional giant cells and necrosis (Fuchs).

In heterochromic cyclitis, chromatophores are absent, vessel walls are thickened, the iris and ciliary body are infiltrated with plasma cells and lymphocytes with occasional eosinophils and mast cells and precipitates appear on the cornea.

Chronic Specific Uveitis

Specific infiltration and proliferation are found in (a) lues, (b) tuberculosis, (c) sarcoid of Boeck, (d) leprosy, (e) sympathetic ophthalmia.

Lues is characterized by diffuse and circumscribed nodular infiltrations, consisting mostly of plasma cells and lymphocytes, and vascular changes. The vessels show a proliferation of the endothelial cells up to endovasculitis obliterans, with a normal media and a perivascular infiltration with lymphocytes. Sometimes only the media has undergone hyaline degeneration. Often the extrabulbar vascular changes are more typical than the endobulbar. These are changes of secondary lues. However, the tertiary lues is also represented by the gumma, which contains lymphocytes, and epithelioid cells besides few giant cells and centrally extensive necrosis in which nuclear particles are still found. The gumma and its surrounding tissue, which shows connective tissue proliferation, is rich in vessels; these vessels are normal or show endo- and perivascular changes which may cause hemorrhages. The nodular infiltration may accumulate to form larger granulomatous masses which are perivascular and have many newly formed capillaries. They also contain epithelioid cells which, by confluence, become giant cells. These papules frequently form finally the gummatous proliferations, in which there is usually extensive central necrosis. Papules are located frequently on the sphincter and the root of the iris. Gummata infiltrate and frequently destroy the surrounding tissues. They are situated most frequently in the ciliary body and extend into the iris, cornea and sclera and eventually perforate. After elimination of the necrotic masses, shrinking scar tissue is formed, resulting in atrophia bulbi. The iris, ciliary body and choroid may be affected singly, or frequently the iris and ciliary body together, and sometimes all three simultaneously. Acquired and congenital lues produce the same pathologic changes. Spirochetes are never found in the uveal tissue in acquired, rarely in congenital, lues. Frequently, the inflammation of the uvea in syphilis is nonspecific and diffuse, and a nodular infiltration with lymphocytes and

plasma cells without vascular changes appears in the choroid, with later on eosinophils and mast cells being added. The choriocapillaris and the inner layers are especially affected and the infiltrate may perforate Bruch's membrane. Then the retina becomes affected, its external layers degenerate or disappear, lymphocytic infiltration appears, and through connective tissue and glial proliferation, atrophic retina and choroid are united. The pigment epithelium shows disintegration or proliferates, producing tubules and fibrillated tissue on the intact Bruch's membrane. The pepper-and-salt fundus of congenital syphilis is produced by disintegration of the pigment epithelium on an intact choroid; the retinitis pigmentosa type of congenital syphilis is produced by migration of pigment to the vessels of the retina.

Tuberculosis appears in the uvea as an acute miliary form or as chronic lesions. The latter appear as disseminated circumscribed tuberculomatous foci or as a solitary conglomerate tubercle which has the form of a tumor. However, tuberculosis frequently produces specific and nonspecific diffuse proliferation and nonspecific diffuse acute or chronic exudation. The miliary tubercle consists of a single tubercle which is usually found in the choriocapillaris and the middle layers of the choroid. This oval-shaped nodule has a shell of lymphocytes which surround epithelioid cells. Between these are occasional giant cells of Langhans type and the center of larger tubercles may show a beginning caseation. The vessels enclosed in the tubercle undergo hyaline degeneration. The choroid between the miliary tubercles is normal or is infiltrated with lymphocytes which are attracted by toxins. The pigment epithelium adjacent to the tubercle disintegrates and the neighboring external retinal layers become edematous. Tubercle bacilli may be seen in different numbers in the tubercle, in the vessel walls and their lumina by special staining.

In the chronic form, single tubercles flow together or new tubercles are formed by apposition. Tuberculous granulomata in circumscribed form are produced in the iris, ciliary body or choroid, or are disseminated and affect either a part of the uvea or the entire uvea. The form of the tubercle in this granuloma

can often be clearly distinguished; the peripheral zone of lymphocytes surrounding epithelioid and giant cells can be seen and it can be ascertained whether or not the zone is entirely closed and whether or not the center is caseous. The granulomata have a tendency to proliferate, to replace the normal tissue and to perforate the eye, but they may also regress with the formation of fibrous tissue scars. Disseminated foci may per-

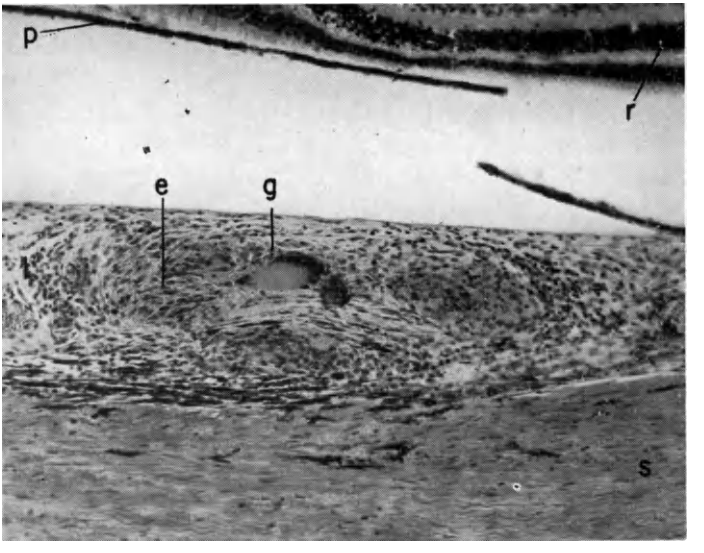

FIG. 28.—MILIARY TUBERCLE, CHOROID. e, epithelioid cells; g, giant cell; l, lymphocytes; p, pigment epithelium; r, retina artificially detached; s, sclera. 55×.

forate the choroid and form granulated tissue on the surface of the choroid into which pigment epithelial cells extend. The adjacent retina is edematous and its veins thrombosed. In such retinochoroiditic plaques, choroid and retina unite when pigment epithelium and glia finally proliferate through the perforated Bruch's membrane into the choroid with the retina showing disintegration of the external layers.

Numerous small disseminated tuberculous granulomata are called chronic miliary tuberculomata. The conglomerate tubercle represents a tumor-like circumscribed granuloma which appar-

ently is formed by proliferating tubercles. Many caseous centers are present, around which epithelioid and giant cells are situated surrounded by accumulations of lymphocytes. The conglomerate tubercle grows into the chambers or perforates the globe, especially in the region of the limbus. Most frequently it begins in the outer layers of the choroid and suprachoroid, but is also found in the iris. In the diffuse proliferative type, the uvea is often infiltrated widely and entirely. The intensive infiltration consists of lymphocytes, epithelioid and giant cells with caseation present, but no typical tubercle formation can be seen. In all these lesions, bacilli may be found more or less frequently in the tissue. The exudative uveitis is acute or chronic and shows a nonspecific infiltration and exudation, but occasionally some epithelioid cell nests or tubercles are found in it. The infection of the uvea takes place by way of the blood circulation from a focus elsewhere in the body, mostly lung or lymph node. Bacilli enter into the eye and settle here accidentally or in an already sensitized tissue. The deposition of the bacilli in the uvea leads to formation of tubercles in their various forms. However, through the effect of tuberculotoxin, an allergic reaction in the uvea may set in, represented by exudation. In general, it is assumed that bacilli with only a small amount of toxin usually cause proliferation, those with considerable toxin, exudation. The bacilli which enter the eye may form tubercles and then spread throughout the eye in various ways. If a tubercle perforates into the chamber from the ciliary body or the iris, cell clumps are carried away, some with giant cells and bacilli. The cells may adhere to the lens capsule or posterior surface of the cornea and proliferate there. Through diffusion of the toxin into the vitreous, or migration of bacilli along the perivascular spaces of the retinal vessels, periphlebitis retinalis and papillitis are produced. In other cases, tuberculous granulation proliferates along the canals of the sclera into the surrounding tissue, into the conjunctiva and orbit, and probably also produces sclerosing keratitis. Large masses of granulations can also invade the ciliary body and finally fill the entire inner eye with necrotic tissue. Such a pseudoglioma (amaurotic cat's-eye) may lead to panophthalmitis.

Tubercle-like formations are found in the uveoparotitis (uveoparotid fever, Heerfordt's disease), in which—besides uveitis—bilateral chronic parotitis, paresis of cranial nerves and general symptoms appear. Epithelioid and giant cells but no caseation are found in the uvea.

From the true tuberculosis, the tubercle-like pseudotuberculous uveitis must be distinguished (ophthalmia nodosa). Nodules are found consisting of lymphocytes, epithelioid cells and giant cells, which are atypical foreign body giant cells and are mostly attached to caterpillar- or plant hairs, plant cells or wood splinters, which enter the inner eye, causing the disease. The nodules show connective tissue capsules with many polymorphonuclears appearing inside and outside of the nodules which may exude into the anterior chamber or vitreous body.

Sarcoid of Boeck shows in the thickened uvea an infiltration with lymphocytes containing nests of epithelioid cells and occasional giant cells. It is assumed to be of a tuberculous nature. There is no caseation present and bacilli cannot be found.

In *leprosy,* there is an infiltration with lymphocytes and monocytes along with proliferation of fixed cells and so-called lepra cells, which are vacuolated and usually harbor a great number of bacilli. Between them are sometimes multinucleated giant cells formed by aggregation of lepra cells. Most frequently, the ciliary body is affected, but the infiltration may extend into the iris and less frequently into the choroid. In the iris, miliary leprotic spots appear, and in the ciliary body lepromata are present which grow into the chamber angle and produce interstitial keratitis. But also a nonspecific, diffuse, plastic iridocyclitis is found. The bacilli enter the uvea via the blood circulation but may also enter from the cornea and episclera. Bacilli are numerous, lying around vessels and in small nerves as well as in the lepra cells.

Sympathetic uveitis (sympathetic ophthalmia, sympathetic ophthalmitis) is characterized histologically by a diffuse dense infiltration of the entire uvea with lymphocytes, in which there are present islands of epithelioid cells in few or in great numbers. The wide blue-stained band of nuclei of lymphocytes shows distinctly the pink spots of the epithelioid cell groups. In the study

of the histologic picture which is so typical in fully developed cases, a great number of changes are found which make the histologic diagnosis definite, such as the following:

1. Sympathetic ophthalmia is essentially a chronic infiltrative inflammation. The massive infiltration of the entire uvea with lymphocytes widens it immensely (tumefaction). The choroid is usually more affected than the iris and ciliary body.

2. The epithelioid cells are closely attached to one another without any intervening intercellular tissue. They are polygonal or spindle-shaped and have oval or round nuclei with little chromatin.

3. Giant cells are found, but not in all cases. They are rarely of the Langhans type; they have irregularly situated nuclei.

4. Necrosis is rare in the infiltrating tissue and appears as a liquefaction of the tissue with karyorrhexis and karyolysis.

5. Sympathetic ophthalmia is to a lesser degree also a chronic proliferating inflammation. The pigment epithelium of the iris is perforated early in many places and later on, also Bruch's membrane and the epithelium of the ciliary body are perforated. A granulation tissue consisting of lymphocytes, fibroblasts, epithelioid cells and vessels proliferates from the iris onto the lens capsule and into the posterior chamber.

6. Cell nodules (Dalén-Fuchs), consisting of pigment-containing epithelial-like cells, spindle cells and, later, lymphocytes, are attached to the apparently intact Bruch's membrane of the choroid and of the ciliary body. They probably originate entirely from the pigment epithelial cells which swell and proliferate, or from migratory epithelioid cells and lymphocytes.

7. Infiltration of lymphocytes sometimes mixed with epithelioid cells is found along the perforating scleral channels, especially the emissary veins.

8. In nearly all cases, a microscopic or larger perforation of the eye is found, frequently filled with typical granulation tissue of lymphocytes and epithelioid cells.

9. The veins of the retina are surrounded by mantles of lymphocytes in different densities and sometimes contain in addition to lymphocytes some epithelioid cells (sympathetic perivasculitis). Of infrequent occurrence is a lymphocytic infiltra-

tion of the retina with lymphocytes extending through the inner limiting membrane into the vitreous body.

10. The optic nerve contains subpial nodules of lymphocytes in a number of cases.

11. Besides the infiltrating lymphocytes, there are occasionally found plasma cells, eosinophils, polymorphonuclears and mast cells in small numbers.

12. In severe cases, granulation tissue proliferates from the choroid into the retina, sclera and the sheaths of the optic nerve.

The histologic picture is the same in the exciting eye (sympathized eye) and in the excited (sympathizing) eye. In the rare event that a sympathizing eye is brought to histologic examination, the disease is found in pure forms to be infiltrating at first and later on to be proliferating without exudation. In the sympathized eye, exudation of cells and fibrin frequently takes place into the anterior chamber and subretinal space because of a mixed infection, in addition to the characteristic infiltrating and proliferating process.

In the beginning, the sympathetic ophthalmia shows a nodular infiltration which soon progresses into a continuous diffuse one. The nodules are located in the iris, especially in the posterior layer and in the choroid in the layer of the middle and large vessels, while the choriocapillaris remains free for a long time. In the course of the disease when diffuse infiltration sets in, the tissue of the uvea is destroyed, vessels disappear and chromatophores disintegrate. The vessels display a swelling of the adventitia and a loss of the endothelium if they have not actually disappeared. Bruch's membrane may be partly destroyed. The suprachoroid is also finally affected by the inflammation; it is infiltrated and shows a proliferation of cells, especially in spindle form. In some cases of sympathetic ophthalmia, a diffuse infiltration of lymphocytes without epithelial cells is present, but even then the diagnosis can be made inasmuch as usually lymphocytic mantles are seen around the tissue in the scleral channels and the pigment epithelium in the iris and ciliary body disintegrates and is perforated.

In rare cases, sympathetic ophthalmia may heal spontaneously with disappearance of the infiltration, but as a rule, proliferation

of a cyclitic membrane and organization of the granulation tissue of the uvea sets in, leading finally to atrophy of the bulb.

The etiology of the sympathetic ophthalmia is uncertain. It was found that if pus-forming organisms are present in the suprachoroid and their toxins affect the choroid, the choroid shows a lymphocytic infiltration with nests of epithelioid cells. Until now, no organisms have been found which can be proven

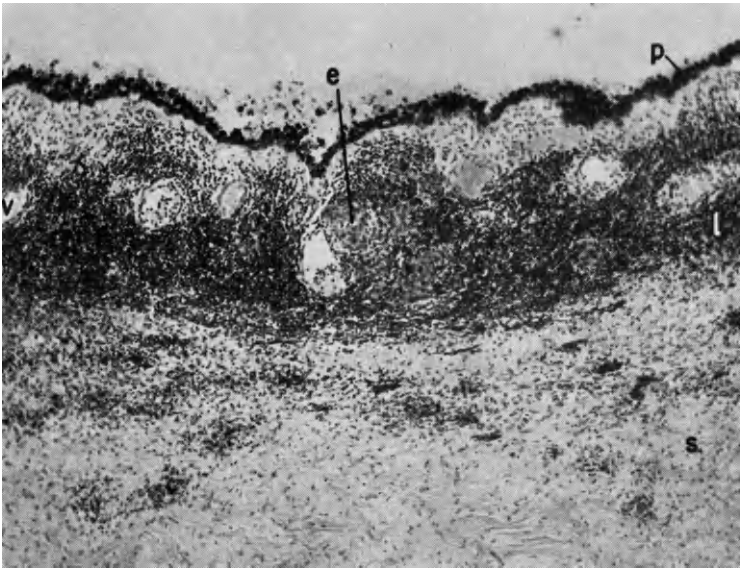

FIG. 29.—SYMPATHETIC OPHTHALMIA. e, epitheloid cells, l, lymphocytes; p, pigmentary epithelium; s, sclera infiltrated; v, blood vessels of choroid. 65×.

to produce sympathetic ophthalmia, but the theory that an infection exists is well established. It is assumed that an unknown organism or its toxin causes the inflammation. The resemblance of the granulation tissue in sympathetic ophthalmia to tuberculosis has led some investigators to assume that sympathetic ophthalmia is a form of tuberculosis. It is assumed that the tubercle bacillus enters the eye directly through the wound or by way of the blood circulation in tubercle bacillemia or that the tuberculotoxin is responsible for the inflammation. How-

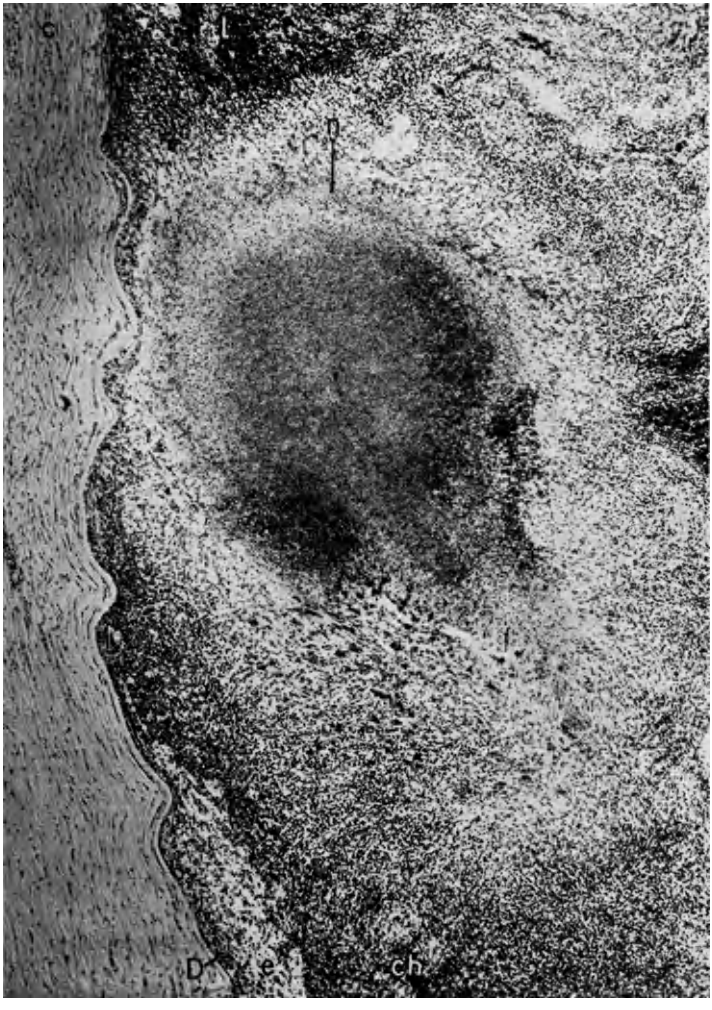

FIG. 30.—SYMPATHETIC OPHTHALMIA. c, cornea; ch, chromatophores of iris; D, folded Descemet's membrane; e, epithelioid cells; l, lymphocytes; n, necrotic area. 45×.

ever, the assumption of tuberculous infection is rejected by many, since the bacillus is found very infrequently and there are differences in the histologic picture of sympathetic ophthalmia and tuberculosis of the uvea. In sympathetic ophthalmia, the lymphocytes appear in the form of a bandlike infiltration in which nests of epithelioid cells are found and giant cells are rare and atypical, but in tuberculosis, the infiltration shows the form of tubercles with lymphocytes peripherally and epithelioid and giant cells in the center with typical caseation, a feature that is never found in sympathetic ophthalmia. Some think that a filterable virus is responsible for the infection.

On the other hand, it has been assumed by other investigators that the sympathetic ophthalmia is produced by anaphylaxis to uveal pigment (Elschnig). Uveal pigment can act as an antigen. According to this theory, there is developed an allergy to uveal pigment which is liberated in large amount by destruction of chromatophores and is absorbed and disseminated. As soon as the uveal tissue of the second eye is sensitized, an allergic inflammation is said to arise. Against this argument is the fact that one can see liberation of uveal pigment in large amounts in a number of different pathologic conditions without the appearance of sympathetic ophthalmia. Furthermore, many cases of sympathetic ophthalmia start as neuritis optica and the optic nerve does not contain any pigment. The histologic picture is rather that of an infection without any resemblance to an allergic condition in which eosinophils, necrosis of vessel walls and periarterial infiltration prevail. How the infection of sympathetic ophthalmia spreads from one eye to the other is still a matter of discussion. Some assume that the transmission takes place by way of the circulation. The hypothetic organism which enters the eye (exogenous) through the perforation, or which has already been circulating in the blood before the perforation (endogenous), is said to affect first the injured eye and later affects the second eye by selective affinity or allergic sensitization.

Some assume that the bacterial transmission takes place by way of the optic nerve, through the chiasm onto the other optic

nerve, and from here into the other eye. Thus, the virus is said to have a special affinity for the nervous tissue in order to spread by way of the optic nerve.

To sum up, it can be said that in the majority of cases, sympathetic ophthalmia follows a perforating injury of one eye especially if the iris, ciliary body or the lens capsule is incarcerated in the wound and if chronic inflammation of the uvea sets in. If suppuration of the eye appears (endophthalmitis, panophthalmitis), sympathetic ophthalmia is almost never seen. However, after operation, especially after a cataract operation, less frequently after iridectomy, sclerectomy, iridencleisis, needling, etc., sympathetic ophthalmia is seen. Subconjunctival rupture of sclera, perforation of a corneal ulcer, necrotic malignant melanoma of the uvea, contusion without rupture are causes.

2. Mycoses and Parasites

Actinomyces, blastomyces and aspergillus fumigatus are known to have produced metastatic mycotic uveitis. More frequently, mycotic uveitis sets in if the organism enters the eye through a perforation of a mycotic corneal ulcer or through a perforating injury. A suppurative iridocyclitis with necrosis and vitreous abscess is formed. Occasionally, a more specific granulation tissue appears, in which case polymorphonuclears surround the accumulation of fungi while monocytes and lymphocytes are found in the peripheral portion.

Regarding parasites, toxoplasma, filaria, cysticercus cellulosae, echinococcus and larvae of the arthropoda can locate in the uvea.

Toxoplasma, the classification of which is still uncertain and which seems to be closest to the Plasmodium malariae, may produce the toxoplasmic retinochoroiditis. The organisms called cysts and pseudocysts can be seen as clusters or aggregates in the tissue showing perivascular and diffuse infiltration with lymphocytes, plasma cells, eosinophils and phagocytes.

The other above-mentioned parasites may appear in the iris and choroid and produce a more or less severe inflammation. They extend from the iris into the anterior chamber and from the choroid into the subretinal space.

3. Degenerations, Atrophies and Senile Changes

Often degenerations and atrophies are caused by aging, but they may also appear spontaneously without recognizable cause or through inflammatory processes. It is possible that an hereditary factor is present in some changes. The senile and spontaneous degenerations are called primary, the postinflammatory degenerations and atrophies secondary. Degenerations may per se cause secondary atrophies and vice versa, and degenerations may lead to further degenerations. Some of these changes are part of a general systemic change; however, a large part is found in the eye exclusively. Many of these changes are known only clinically, but the majority has been investigated by a study of sections along with the clinical aspect; in rare cases through the study of sections alone. In this group belong processes which are different histologically and also in their origin; e.g., (a) angiosclerosis, (b) primary choroidal sclerosis, (c) primary and secondary atrophies of the uvea, (d) degenerations and necrosis of the uvea, (e) drusen of Bruch's membrane, (f) senile changes.

In *angiosclerosis*, arteries, veins, and capillaries are all affected. The arteries show changes of the intima such as atherosclerosis, and changes of the media such as arteriosclerosis. Lipoids, chiefly cholesterol, are deposited in the intima, where connective tissue and elastic fibers with endothelial cells proliferate and hyaline plaques are formed. Hyaline originates from disintegrating tissue and cells of the intima, or perhaps from entering albuminous fluid and erythrocytes. Disintegrating cells also form fat detritus and finally cholesterol. Macrophages may also appear, which contain lipoids and lie between the proliferating intima and elastica. The macrophages may resemble xanthoma cells, having vacuolated cytoplasm with a small, round nucleus. The media shows a proliferation of connective tissue and hyaline degeneration as the changes of the vessel wall often gradually extend from the intima to the media and adventitia, which finally may thicken and undergo hyaline degeneration. Veins show the sclerotic changes less markedly, but their endo-

thelium may proliferate and their media may be thickened and hyalinized. The walls of the sclerotic capillaries are thickened, their nuclei disappear and they are transformed into hyaline nodular strands. Finally they disappear in places. The pigment epithelium in their neighborhood proliferates or disappears.

Angiosclerosis may be primary or secondary. It is most marked in the choroid, less prominent but still discernible in the ciliary body and the least marked in the iris. The posterior ciliary arteries more frequently, and the anterior ciliary arteries less frequently, show sclerosis in their extra- and intrascleral course. The sclerosis may be part of a general sclerosis and is found in various degrees as a senile change. It is most pronounced in chronic nephritis and in albuminuric retinopathy. Severe changes of the ciliary arteries are found in hemorrhagic glaucoma. Secondary sclerosis is found after inflammatory and degenerative changes of the uvea of whatever etiology.

Primary choroidal sclerosis is characterized by sclerotic and degenerative changes of the stroma with proliferation of chromatophores. Not only the arteries but also the veins have a fibrous media with loss of cell nuclei and intact intima. The pigment epithelium becomes depigmented and the pigment proliferates into the retina toward the perivascular spaces. Further, degenerative changes of the retina may take place. The primary choroidal sclerosis is circumscribed or diffuse. It appears in old age but it is often connected with circulatory disturbances.

Primary and secondary atrophies. Primary atrophy is found: (1) as essential (progressive) atrophy of the iris; (2) as essential (gyrate) atrophy of the choroid. Secondary atrophy appears: (1) after inflammation; (2) after trauma; (3) due to ischemia; (4) in glaucoma.

In essential atrophy of the iris, the iris tissue disappears simultaneously with a proliferation of cellular tissue in the root of the iris which is attached to the posterior wall of the cornea in the histologically examined cases. The etiology is unknown; perhaps the atrophy is caused by traction of shrinking newformed tissue in the chamber angle. Finally, absolute glaucoma develops.

Essential atrophy of the choroid is known only clinically.

Secondary atrophy shows a loss of stroma cells, hyalinization of the connective tissue, sclerosis of vessels, thinning of the muscles and disintegration of the pigment epithelium. Ectropion uveae (ectropion of the pigment layer) is seen in the iris and the atrophic choroid and a degenerated retina can be united to an atrophic membrane. The atrophy is circumscribed or diffuse.

Degenerations and necrosis. Fat in fatty degeneration is found free in the tissue, in degenerated cells or inside of histiocytes which finally gather in the perivascular spaces. Fat droplets may appear in the muscles and the epithelium, in the connective tissue and in chromatophores, besides the already mentioned fat depots in the vessels. Cytoplasm may be decomposed to fat in degenerated and necrotic cells and tissue on the one hand (fatty degeneration), and on the other hand fat may be brought into the tissue by metabolism (fatty infiltration). The iris, ciliary body and choroid are affected. Fat appears in eyes with metastatic ophthalmia and vitreous abscess, atrophia bulbi and in necrotic intra-ocular tumors. If severe hemorrhages into the tissue and the chambers appear, cholesterol is formed by disintegration of erythrocytes and the cholesterol crystals are soon surrounded by organizing granulation tissue which may contain foreign body giant cells.

Ossification is found mostly in eyes with chronic uveitis, rarely in noninflammatory conditions as angioma or hypdrophthalmos. Bone is formed by metaplasia of fibrous tissue which originates in the organization of inflammatory products. Occasionally, deposits of calcium into the degenerated tissue precede the bone formation. Fibrous tissue is transformed into bone marrow with the formation of osteoblasts which secrete an osteoid substance and is finally transformed into bone by the intake of calcium. The bone mostly forms trabeculae which are composed of lamellae and contain typical bone corpuscles. The marrow spaces are filled chiefly with fat marrow and fibrous marrow, and in rare cases blood marrow. The bone originates nearly always in the innermost layer of the choroid in the region of the choriocapillaris. The disseminated bone pieces may grow out by apposition to a cuplike cancellous bone formation which extends through the entire choroid and finally becomes more compact. Bone is

frequently formed in cyclitic membranes and occasionally appears in the ciliary body. In excessive cases, compact bone fills the largest part of the shrunken eye. True Haversian systems in which bone lamellae are arranged concentrically around the central thin-walled vessels are rarely found in these new bone formations.

In necrosis, the nuclei disappear entirely or are recognizable only as unstained shadows. Connective tissue fibrils swell and break up, chromatophores disintegrate and clump together, the cells of the pigment epithelium separate, break up and their pigment is dispersed, or they clump into large masses or migrate especially into the anterior chamber. Cells of the nonpigmented epithelium and blood vessels disappear, being less resistant than the pigment layer. Most frequently, the iris is affected, more rarely the ciliary body and choroid. Interruption of the blood circulation by emboli or thrombosis or by trauma, acute glaucoma, toxins from severe inflammation or necrotic tumors are causes of necrosis.

Drusen (colloid bodies) of Bruch's membrane appear as warty or irregularly formed swellings in the cuticular layer of Bruch's membrane. They may originate by degeneration in the membrane itself or from the cells of the pigment epithelium as product of secretion and degeneration of the cells. In degeneration of the membrane itself, the cuticular layer is thickened retinawards and the elastic layer is unchanged. The epithelium is somewhat elevated over small drusen but otherwise unchanged, thinned or absent entirely over larger ones and is clumped on their margin. In general, these drusen appear as half spheres, homogeneous, intensively stained formations. Neighboring drusen may flow together as they grow and become, through apposition, irregular lamellated nodules. When drusen form as product of secretion and degeneration of cells of the pigment epithelium, large amounts of cuticular substance or hyaline droplets are given off from the pigment epithelium onto Bruch's membrane and become nodular masses through apposition. Or the epithelial cells themselves undergo hyaline degeneration after loss of their nuclei and pigment and are transformed into drusen; if new epithelial cells desquamate and degenerate and

are deposited on them, they become lamellated formations. Drusen may be granular in the beginning and later become homogeneous. They may accept an irregular form and may also appear mushroom-like. Sometimes the pigment epithelium proliferates or is folded and surrounds the drusen entirely. Displaced pigment epithelial cells sometimes secrete an homogeneous drusen-like substance, as, for instance, when the cells are displaced into the retina. Sometimes Bruch's membrane is perforated and connective tissue proliferates into the drusen, with consequent organization; they may calcify and even ossify. Drusen may be primary, representing a senile degeneration of Bruch's membrane itself or a degeneration of the pigment epithelium in the condition of primary familial colloidal degeneration (Doyne's honeycomb choroiditis), or secondary to other pathologic changes of the choroid. In senile degeneration and primary familial colloidal degeneration, retina and choroid may otherwise appear intact, show other minor or more severe senile changes or changes unrelated to the drusen formation. Pathologic changes of the choroid and retina which are accompanied frequently by drusen formation are chiefly inflammatory, rarely vascular or neoplastic. Drusen are commonly found in shrinking eyes and in chronic uveitis.

Senile changes are seen in the stroma and epithelium. The collagenous connective tissue is increased throughout the uvea, and in places undergoes hyaline degeneration, frequently in the region of the pupillary margin of the iris, between the bundles of the sphincter, between the bundles of the radial fibers of the ciliary muscle and in the ciliary processes, which become wider and longer, narrowing the circumlental space and pushing the iris root toward the cornea. Elastic fibers are increased in the stroma, especially in the pars plana and anterior to the ciliary muscle, in the tissue neighboring the recessus of the chamber angle where occasionally it forms an elastic ring. On the other hand, circumscribed atrophy of tissue sets in, especially in the iris, in which the crypts disappear more and more.

Sclerosis of the blood vessels is a salient feature, being marked in the ciliary body and choroid with the formation of atheroma-

tous plaques in the intima, thickening and hyalinization of the media and adventitia and hyalinization of the choriocapillaris, but it is difficult to recognize in the iris vessels, which normally consist of a fine intima and media and a wide ring of a more homogeneous adventitia with few fibers. The intima and media proliferate in the sclerotic iris vessels; the adventitia becomes hyalinized and is difficult to separate from the surrounding degenerated hyaline tissue.

The sphincter shows few changes, but the ciliary muscle atrophies as the cells become smaller and many nuclei and cells disappear. The changes affect especially the radial and circular fiber bundles, less the meridional. Chromatophores clump and disintegrate and pigment is spread throughout the tissue. Fat droplets and calcium granules are deposited especially into the tissue of the ciliary body. The epithelium participates in the process of senile changes in its pigmented and nonpigmented layers. Regressive and hyperplastic changes appear.

Depigmentation is seen with clumping and dissemination of pigment granules in the tissue and through the aqueous humor into the meshwork of the trabeculae of the chamber angle. Depigmentation is marked in the region of the pupillary margin, ciliary body and choroid. The atrophy of the pigment epithelium around the papilla, with simultaneous sclerosis of the capillaries and the larger vessels and of the stroma, is seen as a senile halo (senile circumpapillary choroidal atrophy). Fat droplets may appear in the depigmented and pigmented epithelial cells. Cell nuclei disappear and finally the cells disintegrate.

Hyperplasia of the pigmentary epithelium sets in in certain areas; on the posterior surface of the iris, a circumscribed proliferation may appear as a spherical protuberance; in the region of the ciliary body, the layer of the pigmented epithelium may be widened diffusely and the same may occur in the choroid.

A condition known as senile hyperplasia of the nonpigmented layer of the ciliary epithelium makes its appearance in middle age, but without symptoms. The nonpigmented epithelium of the pars plana throughout life shows proliferation of cells which are laid down in groups on the one layer of epithelial

cells or are deposited between the zonule fibers. But in the ciliary processes, the nonpigmented epithelial cells proliferate in flat excrescences or pedunculated or in sessile buds and papillomatous outgrowths. The inner cells of this outgrowth may degenerate to form seromucous fluid, thus giving rise to the formation of cysts. Sometimes the epithelium proliferates to form glandular or tubular, adenoma-like formations.

4. Changes of the Uvea in Diseases of Other Organs and in Systemic Diseases

In this group belong different pathologic changes, such as degenerations, changes of an inflammatory nature and infiltration. We find in this group uveal changes (a) in vascular diseases, (b) blood dyscrasias, (c) gout, (d) diabetes, (e) nephritis, and (f) liver cirrhosis.

Vascular diseases. In general arteriosclerosis, sometimes sclerosis of the choroidal vessels is found. In periarteritis nodosa, which is perhaps the expression of a hypersensitivity, nodular or diffuse infiltration of the adventitia and media of arteries with polymorphonuclears is formed in the choroid as in other organs. Along with the infiltration with polymorphonuclears, lymphocytes and plasma cells and proliferation of the intima are found simultaneously with necrosis of the vessel wall. In this usually fatal disease which most seriously affects the heart and kidney and also the lungs, brain and skin, an inflammation of the entire arterial wall exists and it would be better, therefore, to speak of panarteritis.

Blood diseases, in which the choroid participates, include chiefly leukemia and polycythemia. In leukemia, chiefly the choroid is affected. There is found either (1) dense white blood corpuscle infiltration of the tissue without reaction of the tissue and without changes of the wall of the vessels, which are sometimes dilated and filled with white blood corpuscles; or (2) formation of lymphoma; or (3) stasis of the blood vessels.

In dense infiltration of the tissue, the cells lie compressed close to each other and are usually distorted in form. Cells of the type of the large round cells, and also those with lobulated and indented nuclei are found.

In the case of the formation of lymphoma, circumscribed or diffuse tumor-like infiltration of the tissue appears, which sometimes surrounds the optic disc. The infiltrating cells are lymphocytes and in between giant cells may be found but rarely. Hemorrhages may appear and the cells disintegrate. The infiltration usually spares the choriocapillaris and the veins are often compressed by the enormous cell masses. Sometimes a lymphoma exists at the same time in the retina without a direct connection with the lymphoma of the choroid, Bruch's membrane remaining intact; it may be seen further in the conjunctiva, episclera, and in the orbit.

In blood stasis, the vessels are stretched, dilated and packed with white blood corpuscles; their walls are thinned and may be infiltrated with cells. The compressed interstitial tissue contains only a few infiltrating cells. Although the posterior segment of the uvea is chiefly affected, occasionally changes in the iris may appear, which also may be infiltrated and from which cells may enter into an exudate of the anterior chamber to form a hypopyon. Occasionally the ciliary body is infiltrated.

The etiology of leukemia is unknown. It is caused perhaps by infection or is of neoplastic origin. It may appear as a myelogenous leukemia, lymphoid leukemia or aleukemic leukemia. It is distinguished according to the blood picture. In myelogenous leukemia, especially myeloblasts and myelocytes are found; in lymphatic leukemia, lymphocytes and lymphoblasts in great numbers; and in aleukemic leukemia, the blood picture is normal but a dense leukemic infiltration of organs is found. It seems that in myelogenous leukemia the vessels are dilated and packed with cells, and in lymphatic leukemia the tissue is infiltrated.

In polycythemia rubra vera (Vasquez's disease), there is an enormous increase in the erythrocytes and a marked dilatation of uveal vessels, particularly of the veins.

In *gout*, the uvea is densely infiltrated with lymphocytes without other changes of the stroma. The retina may be detached by a serous exudate containing lymphocytes, macrophages and pigmented cells. The cause is probably a chemical irritation, although urates cannot be proved in crystalline deposits in the

tissue of the inflamed uvea. The diagnosis can be made only from the general clinical examination.

Diabetes can be accompanied by (1) hydropic degeneration of the pigmentary epithelium of the iris; (2) glycogen deposits in the pigment epithelium; (3) rubeosis iridis; (4) lipemia.

In hydropic degeneration, both epithelial layers of the iris are swollen and vacuolated, and pigment is dissolved and

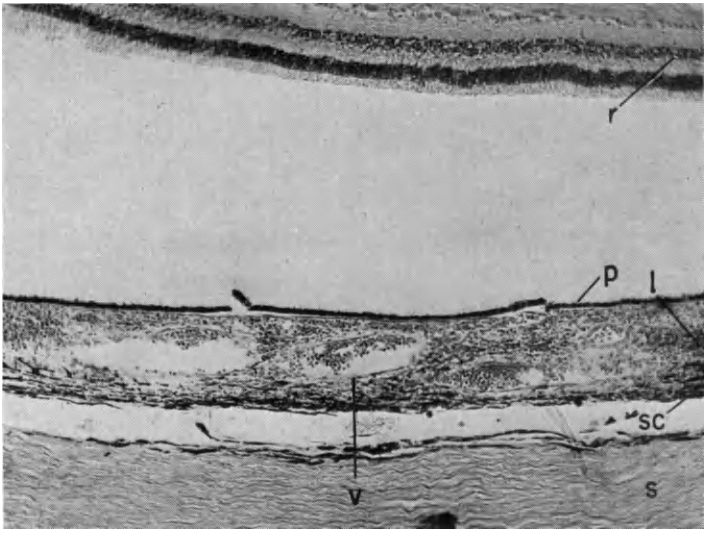

FIG. 31.—LEUKEMIA OF CHOROID. l, leukemic infiltration of choroid; p, pigment epithelium; r, retina artificially detached; s, sclera; sc, suprachoroid; v, vein filled with leukocytes. 70×.

liberated as cells burst and nuclei degenerate. This degeneration rarely extends onto the epithelium of the ciliary body. The rest of the iris usually remains normal but may be edematous. Connective tissue is either increased or atrophies.

Glycogen is deposited in the degenerated epithelium, but may also be found in the area of the sphincter, in the dilator, in the nerves of the eye, in the corneal epithelium and in the retina.

In rubeosis iridis, dilated and anastomosing newly formed blood vessels are found in the pupillary portion and in the root of the iris, and choroidal vessels are dilated enormously. Many

hemorrhages in the tissue may be present. Finally, severe glaucomatous changes appear. Simultaneously, retinopathy may be seen.

In lipemia, the blood vessels of the choroid are filled with fat droplets. This can be confirmed by special staining methods (sudan III or osmic acid).

Nephritis with simultaneous albuminuria most frequently shows sclerosis of the choroidal arteries and capillaries. They contain hyaline and sometimes also amyloid. Occasionally, isolated areas of choroidal sclerosis exists without sclerosis of vessels of the eye or the rest of the body being manifest. There may also be present albuminuric choroiditis with edema, lymphocytic infiltration, hemorrhages and fibrinous exudation in addition to the sclerosis of the choroidal vessels and perivascular infiltration. The pigment epithelium may contain fat and may disappear in some areas and proliferate in others, especially over sclerotic capillaries. Homogeneous fluid is poured into the subretinal space and the choroid may also be detached by serofibrinous fluid. The subretinal space may also contain cells, especially lipoid-containing cells of the pigmentary epithelium. Frequently, retinopathy exists at the same time.

Liver cirrhosis leads essentially to degeneration in the pigmentary epithelium. Its cells become lower, contain less pigment and show, in the basal part, large irregular fat granules. Endothelial cells and connective tissue may proliferate and a round cell infiltration appear.

5. Changes in Myopia

Changes of the choroid in myopia include atrophy and foci similar to sequelae of inflammation. Occasionally, accumulations of lymphocytes are found. The choroid disappears or shows an increase of connective tissue in the foci. Choroid and retina fuse, since the outer nuclear layer, rods and cones, pigmentary epithelium, Bruch's membrane and capillaries in the foci are missing. Tears of Bruch's membrane are frequent, perhaps due to the axial growth of the eye, and through these holes retinal elements, especially glia, but also pigment and pigment epithelium, proliferate into the choroid. The black spot of the

macula is perhaps also caused by pigment proliferation. Hemorrhages are found in the choroidal tissue.

6. Detachment of the Choroid

In detachment, the choroid is separated from the sclera. The retina remains in contact with the choroid, or, sometimes, is separated from it. The suprachoroid is separated, together with the choroid, from the sclera, or frequently the lamellae of the suprachoroid are separated from each other and the potential spaces between them are then transformed into large spaces. These large spaces appear to be filled with serous fluid which is homogeneous or granular in the stained section, containing fibrin plus inflammatory cells such as lymphocytes, monocytes and polymorphonuclear cells. In the enucleated eye, the choroid frequently appears detached but this must not always be considered pathologic. The suprachoroid adheres loosely to the sclera and separates as the inner portion of the bulb shrinks in the fixation fluid. The ciliary body and the anterior choroid separate easily from the sclera, but the space remains empty. In pathologic detachments, stained substance is always seen.

Detachment of the choroid is caused by (a) intra-ocular surgery, (b) traction of a cyclitic membrane, (c) hemorrhage, (d) inflammatory exudate, and is (e) spontaneous.

Surgery. Choroidal detachment may appear during an intra-ocular operation, a few days afterward or may be delayed months after the operation. Most frequently, glaucoma operations such as iridectomy (also Elliot's, Lagrange's operation) but, in addition, cataract extraction, incline to it. Tears in the chamber angle are said to give the aqueous humor entrance to the peri-choroidal space behind the ciliary body and choroid. Such tears cannot always be seen in anatomically examined eyes with detachment of the choroid. It is therefore assumed that the outflow of the aqueous humor during the operation or leakage through the open wound days or months after the operation permits the lens and the vitreous to move anteriorly. Fluid is then moved from the vitreous into the anterior chamber and the intra-ocular tension sinks and fluid transudes from the anterior ciliary vessels

or from the choroidal vessels into the perichoroidal space. The detachment starts in the ciliary body and reaches to the area of the exit of the vortex veins. The fluid beneath the detachment is usually serous, but may contain also fibrin and erythrocytes. The detachment is reversible. If a detachment of the choroid persists for a long time before it disappears, a ridgelike thickening and hyperplasia of the pigment epithelium may be formed on the margin of the detachment.

Cyclitic membrane traction. Cyclitic membranes are inclined to shrinkage and pull on the ciliary body and ora serrata, causing the ciliary body to separate from the sclera and the retina to detach; often at the same time the suprachoroidal lamellae separate from each other, with the result that the interspaces usually become filled with the transuding serous fluid. In this case, if the process is not reversible, tissue may proliferate. Cells of the suprachoroid multiply and form fine fibrillary tissue which seems to originate from the suprachoroid accompanying the perforating channels of the sclera. It may be said then that shrinkage of the vitreous from any cause can be accompanied by detachment of the choroid due to decrease of the intra-ocular tension.

Hemorrhage. In trauma and rupture of diseased vessels of the choroid, extensive hemorrhages into the suprachoroid may appear. The suprachoroidal spaces are filled with masses of erythrocytes. Small hemorrhages are reabsorbed; large hemorrhages give rise to organization. Connective tissue, which in the beginning is cellular, proliferates. The fibroblasts form fibrillary substance which becomes more and more dense, and the fibroblasts change into fibrocytes and decrease in number. The hemorrhages may become enclosed in capsules formed from connective tissue.

Inflammatory exudate. In the presence of a scleritis or a suppurative choroiditis, polymorphonuclear cells accumulate in large numbers in the suprachoroidal spaces and detach the choroid.

The so-called *spontaneous detachment* of the choroid shows serofibrinous fluid and inflammatory cells in the suprachoroidal

space. The etiology frequently cannot be found. The detachment may start in the anterior or posterior part of the eye.

It may be mentioned that edema and retinitis albuminurica may not only cause detachment of the retina but also detachment of the choroid.

7. Primary Neoplasms

Neoplasms of the uvea are primary or secondary. The primary are epithelial or mesodermal, both of which are divided into benign and malignant. Related to the tumors are the cysts. The secondary tumors are extra-ocular tumors which have extended into the inner portion of the eye and metastatic tumors.

The benign epithelial tumors arise from the pigmented and nonpigmented epithelium of the iris and ciliary body. They are (a) melanoma of the posterior surface of the iris (simple melanoma of the pigment layer of the iris) and (b) the epithelial hyperplasia of the ciliary body (benign epithelioma, pseudoadenoma).

The melanoma of the posterior surface of the iris represents a proliferation of the pigmentary epithelium of the iris, and its cells are mostly cylindrical and densely filled with pigment. The epithelial cells proliferate into the stroma of the iris. Such a melanoma may appear clinically as a nevus of the iris.

The epithelial hyperplasia which is perhaps of inflammatory origin may also appear without definite cause or noticeable inflammation. The epithelium proliferates presumably by irritation. The epithelial tumor is situated mostly on the crest of a ciliary process and represents an active proliferation of the nonpigmented epithelium which is followed passively by the pigmented epithelium. The epithelium shows strands, folds and bands, and epithelial tubules frequently appear which are gland-like but consist only of folded epithelium. The cells sometimes hyalinize. Homogeneous substance is secreted between the epithelial tubules and folds. The tumor grows, displacing toward the inner part of the ciliary process.

Malignant epithelial tumors are the (a) diktyoma and (b) malignant epithelioma of the ciliary body.

The diktyoma consists of epithelial strands, which represent mostly glandular tubular formations, and of accumulations of small cells. Besides bands and tubules, rosette formations are found. The strands usually consist of one cell layer, but they may have several layers. The epithelial cells have indistinct cell borders and are cuboidal to cylindric with round or oval nuclei. A limiting membrane is sometimes formed. Mitoses appear.

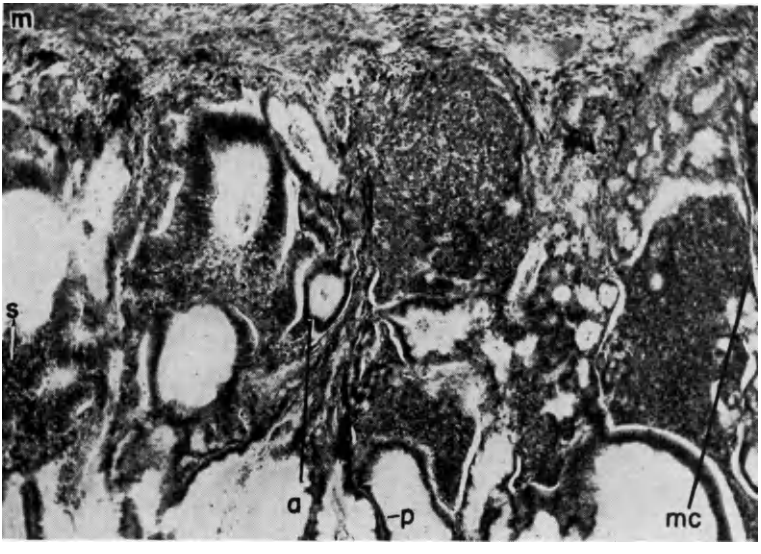

FIG. 32.—DIKTYOMA. a, adenomatous formations; m, ciliary muscle; mc, mass of small cells; p, ciliary processes; s, strands of epithelial cells. 65×.

Stroma is not present. Occasionally, true glial tissue develops. Further, there may be found irregular accumulations of small cells with round nuclei and dense chromatin and little cytoplasm. Necrosis may be found and occasionally hemorrhages. The diktyoma which originates from the nonpigmented layer of the ciliary epithelium represents embryonic retinal proliferation and is similar in its structure to the retinoblastoma. It usually occurs in young children.

The malignant epithelioma of the ciliary body consists of proliferating epithelium in the form of epithelial tubules and strands

of cuboidal and cylindric epithelial cells. The cells more often represent deeply pigmented membranes but may contain only a little pigment. Usually one layer of cells is present, occasionally two layers. The tumor grows into the ciliary body, the iris and the anterior chamber in the form of nodules. The tumor originates apparently from the pigmentary epithelium of the ciliary body and perhaps of the adjacent choroid, rarely from both layers of the ciliary epithelium. It seems to originate on top of chronic inflammatory changes.

It is questionable if malignant epitheliomata originate from the pigment epithelium of the iris. They occur in adults in contradistinction to diktyoma.

The benign mesodermal tumors are: (1) myoma, (2) angioma, (3) melanoma, (4) neurofibroma.

The myoma consists of spindle cells with oval nuclei, arranged in palisades. The tumor is difficult to differentiate from sarcoma. In some cases, a sarcoma may include smooth muscle tissue. Specific staining methods (Mallory's phosphotungstic hematoxylin and gold impregnation) are said to permit the differentiation; when the myoglial fibers which connect the cells are demonstrable, myoma is to be diagnosed. Myoma may be found in the iris, and in this case would be rather of epithelial origin as the sphincter is derived from the epithelium, although the histologic appearance is similar to mesodermal smooth muscle. Myomata may also be found in the ciliary body.

The angioma consists of large endothelium lined blood spaces with little fibrous interstitial tissue and represents a cavernous angioma. It is found nearly exclusively in the choroid and rarely in the iris or ciliary body. Fibrous tissue often proliferates on the inner side of the tumor, occasionally containing bone and the pigmentary epithelium. The retina and the choroid may fuse or detachment of the retina may occur. Frequently, iritis and glaucoma set in. They are said to originate from toxic substances produced by the tumor. The tumor is congenital. It frequently appears simultaneously with nevus flammeus of the face which often may be associated with hydrophthalmos. The nevus vasculosus of the iris contains numerous small and large vessels.

The melanoma consists mostly of densely pigmented cells which are either spindle-shaped and lie closely together with little reticulum between them or have branching processes similar to the chromatophores. Occasionally, the cells contain little pigment and are rich in cytoplasm. Although the melanoma consists of a circumscribed accumulation of chromatophors and has no nevus cells, atypical nevus in tumor-like accumulation are described also in the uvea. Melanomata may appear as nevi in the iris, ciliary body and choroid, and are congenital. A diffuse increase of the chromatophores is found in melanosis bulbi.

The neurofibroma represents cellular fibrous tissue containing many spindle cells of fibroblast type. The cells are arranged in palisades and the bundles of the cells course frequently in whorls. Nerve bundles and nerve fibers may be included in the tissue. Occasionally laminated, sometimes hyalinized bodies arranged in whorls are found, similar to Meissnerian corpuscles. The ciliary body and choroid may be affected. In diffuse neurofibromatosis (von Recklinghausen's disease), the uvea is thickened and simultaneously the orbit, the optic nerve and the face, especially the lids, are affected. Hydrophthalmos may exist at the same time. In a discrete neurofibroma without v. Recklinghausen's disease a circumscribed encapsulated tumor exists in connection with a ciliary nerve. It is assumed that the neurofibroma originates from the sheaths of the nerve, from the perineurium, or endoneurium, but there is another theory that the origin is in the Schwann cell and thus the neurofibroma is of neuro-ectodermal origin.

The malignant mesodermal tumor is the melanosarcoma (malignant melanoma). It is characterized by the great variety of cells which are seen in different tumors and in different parts of the same tumor. They are differentiated by the shape of their nuclei and their cells.

The most common are the spindle cells which are similar to young fibroblasts. They show large oval nuclei with more or less distinct nucleoli and a fine or coarse chromatin network in the form of granules and threads. The cytoplasm of the oval cells is distinct but the cell borders are indistinct. Frequently,

they have branching processes and may contain pigment granules. They lie packed close together in rows and whorls. Less frequent are round cells with rounded nuclei, more or less distinct nucleoli and dense chromatin. They are oval or round and their cell borders appear more or less distinct. They are arranged palisade-like and radiate in fascicles from a central vessel. Sometimes the cells are like epithelioid with rounded or oval nuclei and differently arranged chromatin. They are more round or polygonal, rather distinctly outlined and separated from each other by a reticulum. Infrequently, giant cells with marginal round nuclei appear. Rarely are tumors entirely nonpigmented (leukosarcoma). The pigmented cells are disseminated and in groups in the tumor, or the tumor may consist entirely of densely pigmented cells. The cells resemble chromatophores with branching processes, or frequently other forms appear which are considered as transitional forms of chromatophores. The pigmented cells appear large, polygonal or rounded, have irregularly angulated, sometimes shrunken nuclei and contain fine granular melanin. Normal chromatophores, stroma cells and blood vessels of the uvea may be enclosed in the tumor, so that entirely nonpigmented tumors show pigmented islands. Furthermore, migratory cells appear, containing pigment granules which originate from broken-up chromatophores or hemorrhages into the tumor. Infrequently, pigment cells proliferate from the pigmentary epithelium and are recognizable by their more or less coarse, rodlike pigment. But in the iris, alveolar formed pigmented and also pigment-free tumors grow, consisting of epithelial cells originating from the pigmentary epithelium. The tumor cells and their nuclei in general vary considerably in form and size; their nuclei are frequently hyperchromatic and mitoses are found.

Depending on the arrangement of the cells and the majority of the type of cells present in the tumor, the sarcoma of the uvea is classified differently and considered of different origin. The tumor may arise from the chromatophores (melanosarcoma), from the nonpigmented stroma cells and nerve sheaths (spindle cell sarcoma, leukosarcoma), from structures of blood vessels (angiosarcoma). If many vessels are present, consisting only

of numerous endothelial tubes of sometimes cavernous arrangement, and if their narrow interspaces are filled with alveolar arranged tumor cells, the tumor is called angiosarcoma. But it is questionable if an angioma of the uvea will undergo at any time sarcomatous degeneration. If rounded or oval cells are arranged in wide columns and fasciculi which radiate in the form of palisades from a centrally located vessel, the tumor is called perithelioma, in which case its origin is from the adventitia. It resembles the so-called endothelioma in which more epithelioid-like cells are arranged irregularly or in strands in a distinct reticulum and in which also endothelial lined spaces appear. The stroma of the tumor is quite scarce and the tumor often consists only of cells with very dilated blood vessels enclosed between them, these vessels composed only of endothelium or having also a thin media. But also blood filled spaces are found which have no distinguishable endothelial lining and which are surrounded by tumor cells. Furthermore, tumor particles may penetrate into the vessels. On the other hand, tumors are found with different amounts of collagenous fibers which in areas may become rather dense. By special staining methods, argyrophil fibrils are recognizable as reticulum. Frequently, there is bleeding into a tumor caused by the fragility of the vessel wall, erosion of the walls by tumor cells, finally, by the entire absence of vessel walls. There is bleeding also into the surrounding area of the tumor, into the vitreous body and into the chambers. These hemorrhages cause glaucoma.

Tumors frequently show degeneration and necrosis. Cells and vessels may undergo hyaline degeneration and fatty and glycogen degeneration of the cells may be found. Necrosis is more frequent than degeneration. Parts of the tumor, or the largest part of the tumor, becomes necrotic, nuclei disintegrate and finally disappear entirely, the cells appear as shadows and eventually only granular detritus is present, in which shadows of vessels and disintegrating pigment are still visible. Hemorrhages, interruption of circulation by compression of vessels and insufficient growth of vessels in relation to the growing tumor, endogenous infection acting on susceptible tissue, diffusing cytotoxins are assumed as cause of necrosis. Patchy

necrosis often remains without sequelae, but massive necrosis of the tumor causes, by formation of toxic-acting substances, severe uveitis and necrosis of other tissues in the eye, especially of the iris and ciliary body, also of the cornea and retina. By chemotaxis, polymorphonuclears and fibrin are poured out. The polymorphonuclears are seen in a ring abscess of the cornea or in a scleral abscess and in the anterior chamber. The cataractous lens may be covered in the pupil with polymorphonuclears and fibrin. The polymorphonuclears may dissolve both cornea and sclera, producing perforation of the eye. Endophthalmitis and panophthalmitis follow. The eye shrinks and in rare cases local spontaneous healing of the tumor may result. Inflammation without suppuration is often accompanied by severe glaucoma. However, the acute inflammatory process may subside and fibrosis may set in. Sympathetic ophthalmia is observed occasionally. Glaucoma is a frequently accompanying symptom of the tumor and probably has, in addition to inflammation, still other causes. It may be caused by stasis in the veins which go from the ciliary body into the choroid, by blocking of the exits of the intra-ocular fluid, by deposition of cells or of pigment onto the trabeculae of the chamber angle, by infiltration of the chamber angle by tumor cells and by repeated hemorrhages. In the initial stage of the tumor and in a later stage when the ciliary processes are destroyed or atrophied, hypotony is found.

The malignant melanoma appears either circumscribed or as a diffusely infiltrating tumor. Most frequently the choroid is affected, more rarely the ciliary body and most rarely the iris. The tumor starts in the external layers of the choroid and in the suprachoroid, mostly in the posterior segment of the eye and expands first as a flat growth. Stasis in the choroidal veins often causes an early transudation into the subretinal space and with it a detachment of the retina which occasionally may start quite a distance away from the tumor in the periphery of the retina. Bruch's membrane greatly resists to the growth of the tumor, but finally it is perforated and the tumor grows faster into the subretinal space and appears mushroom-like. The inward-bent ends of the perforated Bruch's membrane surround

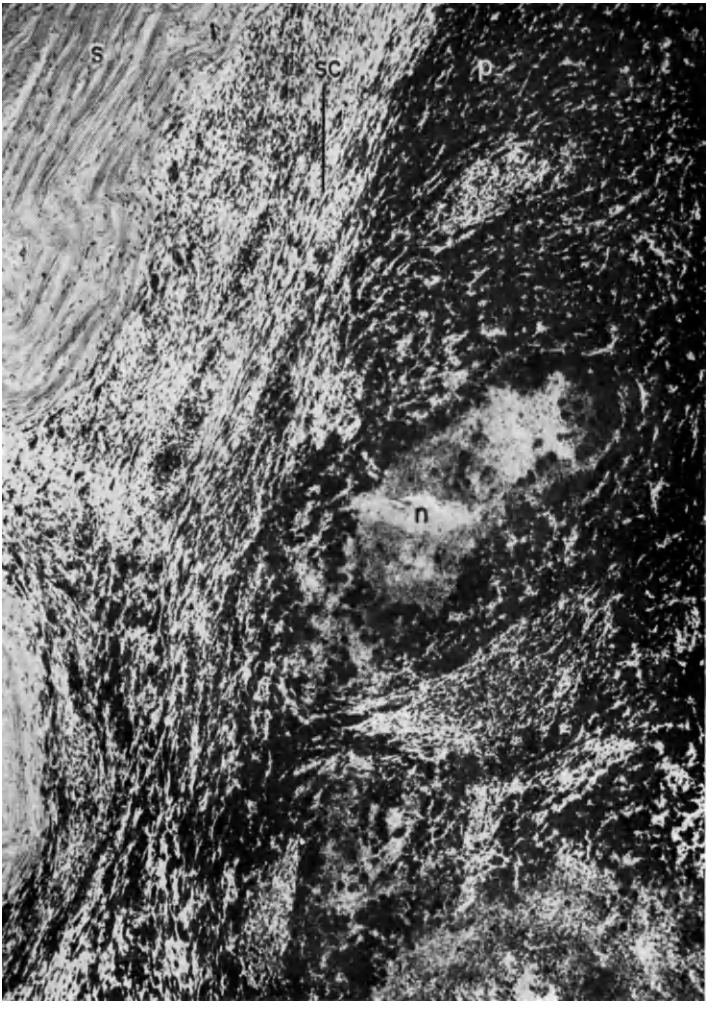

FIG. 33.—MALIGNANT MELANOMA OF THE CHOROID. n, necrotic areas; p, pigmented cells; s, eroded sclera; sc, rows of spindle cells. 45×.

the narrowest part of the tumor. The retina is often attached to the tumor in a small area. The pigment epithelium disintegrates and the adjacent retinal structure becomes irregular. Sometimes a cellular membrane is formed at the attachment. Infrequently the tumor perforates the retina into the vitreous body where, unresisted, it grows rapidly and fills the entire inner eye. If perforation occurs, the retina is first split in the outer plexiform layer by cystoid degeneration. In the further course, the outer retinal layers are folded over the tumor; the inner layers still covering the tumor are finally eroded and the resisting inner limiting membrane perforated. Occasionally, the choriocapillaris and Bruch's membrane remain intact and the tumor widens the choroid universally. Diffuse tumors, especially, but also circumscribed tumors, infiltrate directly into the sclera or extend along the scleral canals into the sclera and finally in both cases into the surrounding orbital tissue. Tumors close to the papilla grow around it, or less frequently infiltrate it or the sheaths of the optic nerve or the optic nerve itself along the lamina cribrosa.

Malignant melanomata originating in the ciliary body are similar to those of the choroid. They are mostly circumscribed tumors which grow toward the lens, deforming and displacing it, producing cataractous changes and bulging toward the vitreous body and the posterior chamber. The ciliary muscle is destroyed by the tumor, which grows into iris and choroid, infiltrates the structure of the chamber angle, Schlemm's canal and trabeculae and extends through the sclera and the anterior perforating scleral canals into the episclera and conjunctiva. The diffusely infiltrating type of malignant melanoma in the ciliary body grows as a flat sarcoma, ringlike (ring sarcoma), and affects also the iris and extends into the anterior choroid. The tumor consists mostly of spindle and round cells and contains sometimes large polygonal, pigment-free cells. Its origin is hypothetically derived from the endothelial structure of the chamber angle. It grows circularly around the structures of the chamber angle and infiltrates the cornea, frequently in front of and behind Descemet's membrane. The tumor finally occupies the entire ciliary body, usually leaving only its epithelium

intact, and grows into the anterior layers of the iris first and later fills its entire width. It soon produces glaucoma.

The malignant melanomata of the iris are manifold in origin and appearance. They are frequently pigmented and rarely nonpigmented. They are, in the beginning, circumscribed and nodular and expand slowly and diffusely. Flat sarcoma is rare; it appears in the iris root and grows chiefly out of the ciliary

FIG. 34.—SARCOMA OF IRIS. c, cornea; i, iris root; p, pigment epithelium; s, sarcoma. 55×.

body, but occasionally takes the reverse course. Pure spindle-celled sarcomata are found, but more frequently polygonal, short spindle-shaped and rounded cell types are seen. Pigmented cells similar to the cells of the anterior border layer of the iris and cells similar to chromatophores with branching processes are found. Tumors containing alveolar-arranged epithelial-like cells are found, apparently originating from the pigment epithelium. Iris tumors grow into the chamber angle, ciliary body and cornea, and perforate the eye toward the conjunctiva through the sclera or anterior perforating scleral channels.

Four stages are distinguished generally in the growth of malignant melanomata: (1) the period of growth restricted to the area of origin, (2) infiltration of the surrounding tissues, (3) perforation of the globe, and (4) metastasis. In the second and third stages, there is often increased intra-ocular tension. The infiltration of the surrounding tissue and perforation of the eye have been described. Not all stages may be gone through in this sequence; stages may be omitted or the sequence may be changed. Metastasis may occur before or without perforation of the eye and may occur in the eye itself or in distant organs. Particles of a choroidal tumor are deposited on the posterior surface of the cornea, on the anterior surface of the iris, in the chamber angle, and tumor cells singly or in groups in the stroma of iris and ciliary body. The metastases follow the course of the intra-ocular fluid. Metastases may grow in the subretinal space at the inner surface of the choroid, on the outer surface of the retina and in the retina itself. The tumor does not spread outside the eye in lymph channels and to regional lymph nodes, but is always carried by the blood circulation to other organs. Metastases are found mostly in the liver, in the vertebrae and ribs, central nervous system, lungs, intestines, spleen, and lymph nodes. The primary tumor and metastasis are not always the same in their finer histologic structure and their pigment content may vary. Malignant melanomata of the uvea originate frequently from so-called nevi which themselves are of various origins and structure. But they may also occur in the absence of a nevus. Their origin is thought to be in the chromatophores, endothelium of the vessels and suprachoroid, in nonpigmented stroma cells, in the ectodermal cells of the pigment epithelium, in the sheaths of the ciliary nerves and in the neuro-ectodermal Schwann's cells of the ciliary nerve. Occasionally, two or more discrete primary melanosarcomata of the uvea are seen, but even in such cases there may be doubt whether or not one tumor is the primary and the other a metastatic one.

8. Cysts

Cysts are found in the anterior segment only, the majority in the iris and rarely in the ciliary body. They are: (1) spon-

taneous (idiopathic, congenital); (2) traumatic (implantation); (3) exudative (retention) and degenerative; (4) parasitic.

The *spontaneous cysts*, in which there is no preceding damage like trauma, inflammation or glaucoma, develop (a) in iris stroma; or (b) in the pigment epithelium.

Spontaneous cysts of the iris stroma are situated closer to the anterior than the posterior surface of the iris. They represent a uniform space or have outpouchings. They are lined by epithelium of one or several layers, the cells of which are composed of small flat cuboidal, occasionally small cylindric elements, but which may also be columnar epithelium with several layers or stratified squamous epithelium. Goblet cells may be found. The content of the space is serous fluid with desquamated epithelium, polymorphonuclears, round cells and debris. If one row of flat cells lines the wall, it is spoken of as endothelium by some. The cysts are probably sequelae of a developmental disorder. The surface epithelium may be included during the development of the eye as an abnormal outpouching into the iris. Under certain circumstances, the epithelium of the lens vesicle is displaced into the iris mesoderm; in other cases, there is, during the development, epithelium displaced from the anterior layer of the pigment epithelium (from which probably the sphincter muscle and clump cells normally originate) into the stroma of the iris where it may proliferate. Others consider the cysts formed through occlusion of crypts or lymph spaces and lined by endothelium.

Spontaneous cysts of the epithelial layer are located at the pupillary margin, the posterior surface of the iris and in the ciliary body. They are uni- or multilocular and are lined by epithelium containing also pigment granules. The epithelium proliferates and the cysts enlarge by proliferation and secretion from the cells into the lumen of the cyst. The cysts originate congenitally by incomplete closure of the space between both epithelial layers of the primary cup. They ultimately lead to secondary glaucoma.

Intraepithelial cysts of the ciliary processes occur as a senile degeneration.

Traumatic cysts are serous or atheromatous (pearl cyst, cholesteatoma, epidermoid). The serous cysts are lined with irregular epithelium, which sometimes contains many goblet cells, and are filled with serous fluid. The pearl cysts are lined by stratified squamous epithelium, whose inner layer continuously degenerates as the cells lose their nuclei, and show fat droplets and cholesterol crystals. Concentric laminated layers consisting of horn debris, fat, and cholesterol fill the space. The epithelium also undergoes cystic degeneration. The traumatic cysts are caused by injury through instruments, glass, other perforating foreign bodies or surgery. Particles of the skin, the corneal and conjunctival epithelium or hair follicles are displaced onto the surface or into the substance of the iris (implantation), or epithelium proliferates along the perforating wound, especially if it stays open (ingrowth). The latter frequently produces chamber-iris cysts, as the epithelium covers the wall of the anterior chamber and the surface of the iris. But it may immigrate into the iris also by way of the crypts. A cyst may press the iris toward the posterior surface of the cornea and extend onto the surface of the lens or through an opening of the lens capsule into the lens substance. A cyst sometimes rather expands in the posterior chamber or extends onto the ciliary body. If corneal or conjunctival epithelium is displaced, serous cysts originate; if skin or hair follicles are displaced, pearl cysts originate. Iridocyclitis and glaucoma are frequent complications.

Exudative cysts are sequelae of inflammation. It happens sometimes in chronic iridocyclitis that the posterior epithelial layer of the pigment epithelium of the iris is adherent through fibrous tissue to the lens capsule and the anterior layer is pushed forward with the iris. Cysts are also formed between both epithelial layers of the ciliary body. Fluid gathers between the two epithelial layers through inflammatory processes, occlusion of vessels or increased permeability of the vessels. It is possible that the dilator pulls off the anterior epithelial layer by its traction and the posterior layer remains adherent to the lens. But epithelium also proliferates through the irritation of the inflammation. Frequently, multiple cysts are formed.

They may extend beyond the pupillary margin into the pupil. Cysts are formed without inflammation in glaucoma and neoplasms by the pressure onto the iris root, obstructing circulation, and in decreased intra-ocular tension when the bulb is opened. Degenerative cysts are formed in the ciliary epithelium as senile changes.

Parasitic cysts are seen in cysticercus cellulosae, the larva of Taenia solium. The cyst develops on the iris or in the choroid, from which it extends into the subretinal space and eventually through the retina into the vitreous body. The capsule consists of coarse connective tissue, surrounded by such infiltrating cells as lymphocytes, monocytes and giant cells. Inside the fluid-filled vesicle is the parasite, consisting in cross section of integument, loose connective tissue and intestinal loops with outpouchings. The cyst frequently causes uveitis.

9. Secondary Neoplasms

Secondary neoplasms grow from outside into the uvea through the cornea and sclera. They are (a) carcinoma of the limbus which reaches the iris and ciliary body through the perivascular lymph spaces or by perforating the tissue itself, and (b) epibulbar sarcoma and malignant melanoma which can infiltrate the iris, ciliary body and choroid. Secondary metastatic tumors are carcinomata of various types. They are (a) medullary carcinoma, consisting of accumulations of polygonal epithelial cells with pleoform large nuclei and a small amount of connective tissue between the cell groups; (b) scirrhus carcinoma, consisting of small columns of epithelial cells and much coarse connective tissue; (c) adenocarcinoma, which is sometimes papillary and consists of cylindric or cuboidal cells surrounding a lumen. They usually grow flat in the choroid and rarely perforate Bruch's membrane. Now and then parts of the metastatic tumor become necrotic, especially if the vessels are compressed or eroded by the growing tumor. They are located more frequently in the choroid than in the ciliary body or iris since they are carried as vascular emboli into the posterior ciliary arteries and less frequently into the anterior ciliary vessels. The primary

tumor is most frequently in the breast, less frequently in the lungs, gastrointestinal tract, liver, thyroid and prostate. Metastatic hypernephroma is found in the iris, ciliary body and choroid and is characterized by large, clear epithelial cells with relatively small irregular nuclei. The occurrence of a metastatic sarcoma and malignant melanoma in the uvea is questionable, as the uveal tumor might be the primary tumor or multiple primary tumors might be present. Lymphosarcoma and spindle cell sarcoma of the uvea are seen with similar tumors in lymph nodes, breast and ovaries. Also, a chorionepithelioma may metastasize to the uvea, showing polygonal cells and syncytial masses with nuclei of various sizes.

READING OF SOURCE MATERIAL

Redslob, who once assumed that the choroidal pigment has its origin in the retinal pigment, could prove with the help of the staining method of Masson (staining with ammoniated silver nitrate which stains the prepigment of the melanin), that the chromatophores of the choroid produce the melanin.

According to Wolfrum, there is no endothelium at the anterior surface of the iris.

Gilbert and Plaut, Wolf are of the opinion that the exudative cells originate not only from the blood, but also from the tissue, from the stroma cells of the uvea and even from the endothelium of the cornea.

Suganuma finds Bruch's membranes rather resistant to suppurative inflammations, but little resistant to tuberculous and syphilitic processes. The pigment epithelium shows only secondary proliferation and regressive changes when its nutrition is cut off.

Cocci may enter by way of the anterior ciliary vessels into the inner eye and produce metastatic ophthalmia (Lindner).

Mylius saw cases of metastatic abscesses in the iris and ciliary body.

Horner and Cordes found metastatic abscesses of the iris and ciliary body in a case of an abscess beneath the lower jaw, containing staphylococci.

Dollfus describes a choroidal abscess caused by staphylococcus aureus.

A metastatic focus in the choroid in a case of furuncles of the nose and lid is described by Hanke.

Higuchi observed cases of metastatic choroidal abscesses with large furuncles.

Exogenous infection of the uvea can be caused by bacillus pyocyaneus, according to Schneider, Garretson and Cosgrove, Safar, Shearer, by bacillus coli according to Morax and Coppez, by bacillus subtilis according to Flieringa, Gifford and Hunt, Hoffmann, by bacillus fluorescens according to Horvath, xerosis bacillus according to Lindner, Scheffels.

Braun, Luttringer found in metastatic uveitis streptococci; Bussola, Hetinonen, Hulka, Lawson pneumococci; Jeandelize, Laval meningococci; Laval staphylococci; Velhagen gonococci; François bacillus coli.

Hulka reports a case of metastatic pneumococcic uveoscleritis following pneumonia and showing organizing abscesses and infiltration of the episclera, sclera and ciliary body.

Ring infiltration of the cornea due to bacterial toxins and suppurative iridocyclitis is described by Flieringa, Gifford and Hunt.

Nakayama found in recurrent hypopyon uveitis round cell infiltration in iris and ciliary body, infiltration of the anterior part of the choroid and the retina filled with polymorphonuclears. The polymorphonuclears probably come along the zonule fibers through the pupil into the anterior chamber.

Von Hippel found in an eye with recurrent hypopyon uveitis, iridocyclitis and proliferation of connective issue. He considers the disease as a metastatic suppurative process involving the eye by way of the central retinal artery and the long ciliary nerves.

Cases of recurrent iridocyclitis with hypopyon which mostly are of septicemic origin, are histologically examined by Blobner, Gilbert, Weve. They find fresh infiltrations with polymorphonuclears and erythrocytes and old infiltrations with lymphocytes and plasma cells distributed over the entire uvea with advanced atrophy and dispersion of the pigment. Finally, retina and choroid lie folded behind the calcareous and ossified lens and the intra-ocular tissue disintegrates.

Gas gangrene panophthalmitis after perforating injury with a thin, dark secretion, formation of gas bubbles in the anterior chamber and presence of bacillus Welchii is reported by Berry, Capus, Hamilton, Heath, Ridley, Walker.

Marchesani believes that the uvea is sensitized in rheumatism by toxins, leading to a reaction if the individual is newly infected.

Acute and chronic inflammation of the uvea can exist simultaneously. Lamb describes dense accumulation of polymorphonuclears in the inner layers of the choroid and ciliary body and dense accumulation of monocytes in the outer layers.

Seguini finds in metastatic ophthalmia accumulations of polymorphonuclears, lymphocytes or plasma cells and endarteritis obliterans in the choroid and retina, which latter frequently represents the port of entrance; very frequently there are inflammations in the entire uvea and posterior chamber.

Archangelsky found that the non-pigmented ciliary epithelium participates in many intro-ocular diseases with pathologic changes.

The proliferation of the ciliary epithelium in chronic uveitis is studied by Fuchs. He calls the epithelial proliferation without fibrous membranes "free epithelial proliferations." The proliferating epithelium may grow also over a detached retina.

Fuchs finds that the epithelium of the iris and the ciliary body forms a barrier against toxins attacking from the chamber side and that the pars ciliata and pars plana of the ciliary body are inflamed to a various degree depending if the inflammation progresses from forward backward or attacks from the vitreous body.

Pupillary nodules develop in the ectodermal layer of the iris and penetrate into the mesodermal tissue. Floccules originate in the mesodermal tissue from exudate of the iris and can also float in the humor aqueous (Busacca).

Fuchs finds in flocculi iridis multiple excrescences of the pigment epithelium at the pupillary margin. Large pigmentary epithelial cells show an abundant growth at the free margin.

Speciale-Picciche describes a vesicle freely floating in the anterior chamber consisting of pigmented connective tissue and degenerated pigment epithelial cells. It represents probably a free flocculus of the pupillary margin.

Nodules of the pupillary border and anterior surface of the iris consisting of accumulation of mononuclear cells can be symptom of a chorioretinitis with the iris and ciliary body unaffected, according to Friedenwald and Friedenwald.

Nodules at the pupillary margin in chronic uveitis may consist of lymphocytes and epithelioid cells (Derby, Vogt).

Meesmann describes nodular deposits on the remnants of the pupillary membrane in chronic uveitis.

Spicer found nodular deposits on the lens in chronic uveitis.

Fuchs finds that the lymphocytes and plasma cells may melt together in chronic iritis, forming a homogeneous cover. Lymphocytes can change into fibroblasts. Sometimes there are two layers of an exudative covering, an anterior cellular and a posterior homogeneous layer. The endothelium sometimes proliferates and forms a new layer of endothelial covering.

Ginsberg states that large mononuclear cells develop from histiocytes under the influence of stimuli in the choroid. These cells may form, when they are packed closely, epithelioid cells. The large mononuclears are macrophages and are formed especially in the perichoroidal space.

Foci consisting of lymphocytes, histiocytes and monocytes with finest eosinophil granules can appear in healed uveitis, but also in normal eyes, according to Fuchs. He considers them caused by abnormal substances circulating in the blood or formed in the eye itself as in coexisting tubercles, sarcoma, corneal ulcers or injuries.

Ginsberg describes true lymph follicles in the ciliary body and iris in a chronic uveitis of unknown origin, and Albrich describes them in the choroid.

Marx describes highly refractile globules in chronic iridocyclitis resembling Russell's bodies.

Verrey found reticulo-endothelial cells in the aqueous humor in infections of various genesis and studied their phagocytosis of bacteria (staphylococci, pneumococci, pseudo diphtheria and diplobacilli).

Fuchs sees in chronic infiltrative iritis of traumatic and endogenous origin lymphocytes mainly originating from the cells of the adventitia, plasmacells originating from lymphocytes and plasmacytoid cells originating from plasmacells.

Lamb believes that macrophages pass through the ciliary epithelium and are transformed in fibroblasts with long processes and form fibrous tissue.

Meller finds in disseminated chorioiditis circumscribed destruction of the pigmentary epithelium, connective tissue scars enclosing epithelioid cells and lymphocytic infiltration.

Pressburger studied eyes in which a few peripheral old chloroiditic foci could be found in which choroid and retina were united. They cause vitreous opacities and are found especially in eyes with glaucoma and sympathetic ophthalmia.

Zimmerman finds in atrophic eyes of various etiology infiltration of the uvea with lymphocytes and plasma cells where the uvea is exposed to tension, as in the area of the insertion of the extrinsic eye muscles and in scars in the choroid, in the region of the sphincter and the root of the iris, and very frequently at the ora serrata.

Meller finds frequent spontaneous hemorrhages in atrophic foci of the eye. Vessels may be torn by membranes or thrombose when they are bent, and the bleeding occurs from congested vessels.

Kreibig describes unusual foci of proliferating glia in the choroid of a case of uveitis.

Spaeth considers uveitis, cataract and detachment of the retina as a disease unity caused by an endogenous infection. He describes metastatic endogenous uveitis in surgical cases without complications and with clean conjunctival sacs.

Gilbert sees in chronic metastatic uveitis (opththalmia lenta) with participation of the vitreous body mainly foci of infiltration in the area of the ora serrata; he finds swelling of the spleen, affections of the joints, otitis media, sinusitis and furunculosis in the general examination.

Friedenwald and Rones describe foci in the choroid consisting of large lymphocytes and mononuclears in septicemia (septic choroiditis).

Fuchs finds even in cases of so-called iritis serosa (chronic cyclitis), in which the iris appears normal clinically, the iris densely infiltrated and the ciliary body hardly affected.

Lister, Samuels describe in posttraumatic uveitis exudative deposits in the form of fine precipitates or large accumulations on the retina and some infiltration of lymphocytes and plasma cells in the inner layers of the retina (retinitis serosa).

Meller describes changes in the wall of the circulus arteriosis iridis major in spontaneous chronic, posttraumatic and sympathetic uveitis. The endothelium proliferates with obliteration of the lumen, the media is thickened and infiltrated with lymphocytes and epithelioid cells.

Bacteria could be found histologically in the uvea in endogenous uveitis and could be cultivated from ocular tissue by Braun, Levine, Sedan.

If there is a systemic infection, hypersensitivity of the ocular tissues may develop. Should products of the bacteria enter these eyes again at a later date an allergic reaction sets in. Sometimes there is present bacteremia from a focus which otherwise does not cause symptoms, but if the ocular tissues are sensitized against these bacteria, inflammation sets in. Such a mechanism is assumed for the tubercle bacillus by Meller, Urbanek. Also nonpathogenic bacteria can produce such an allergic reaction as, e.g., the xerosis bacillus according to Marchesani, v. Szily.

Not only toxins or other bacterial products can produce sensitivity, but also the germs themselves can be deposited in the uvea and cause inflammation, although they are present in such small numbers and so infirm that they cannot produce a generalized reaction. Wood observed the same streptococcus in an apical abscess and in the anterior chamber. Trout found streptococci in the blood in chronic iridocyclitis. Urbanek and

Meller found tubercle bacilli in the blood in chronic iridocyclitis. Transitory trauma and elective localization of the bacteria favors their appearance in the eye.

Lens substance represents a good culture medium even for otherwise nonpathogenic bacteria and surface parasites like staphylococcus of the skin or xerosis bacillus, according to Lindner, Orloff.

An inflammatory reaction appearing after liberation of lens substance in the eye is assumed as allergic by Burky, Burky and Woods, Courtney, Goodman, Lemoine and McDonald.

Verhoeff and Lemoine brought forward the theory that an anaphylactic inflammatory reaction to lenticular tissue can appear in sensitive persons and that they present a positive skin reaction if examined for lenticular protein.

Braun, Ellis explained the inflammation due to lens substance as toxic without allergy, especially as animal experiments were negative.

Burky showed in animal experiments that after repeated injection of lens protein and staphylococcus toxin a severe inflammation appeared in the eye following needling of the lens, and he believes that the sensitivity in man is produced by an additional appearance of toxin, from a focus in the body.

Archangelsky believes that the ciliary nerves are stretched and irritated by adherence of the iris in a wound and displacement of the ciliary body and take part in producing inflammatory changes in the uvea by vasomotor reflexes.

Zamenhof describes as a desquamative form of the cyclitis an inflammation in which large, rounded cells are present in the anterior chamber and the chamber angle, on the anterior surface and posterior surface of the iris, and the ciliary epithelium is defective. The cells obliterating the chamber angle may cause secondary glaucoma.

D'Amico observed in several cases of severe uveitis with exudation and organization a lens shaped formation in the anterior chamber and calls it "pseudoluxation of the lens".

Gilbert, Meller describe respectively uveitis in herpes simplex and herpes zoster and find round cell infiltration around ciliary nerves and ciliary vessels with consecutive complete necrosis causing hemorrhages. Meller considers the violence of the inflammation as reaction to the necrosis and the infectious agents.

Gardilčic finds in a case of herpes zoster ophthalmicus with perforation of a corneal ulcer infiltration of lymphocytes and plasma cells around the ciliary nerve and vessels and infiltration in the choroid and suprachoroid.

Revin's case of a 3 year old girl showed metastatic uveitis with atrophia bulbi following measles.

Givner found in bilateral uveitis, poliosis and retinal detachment histologically in the iris infiltration with lymphocytes, plasma cells and eosinophils.

Scullica finds three types of vascularization of the anterior surface of the iris: (1) terminal branches without formation of networks in the ciliary zone in absolute glaucoma (2) formations of tortuous anastomosis from the periphery to the pupil in iridocyclitis and (3) small vessels forming a network in rubeosis iridis.

Reese finds entropion uveae as (1) spastic, (2) due to shrinkage of a membrane extending from the anterior surface of the iris to the lens capsule, (3) due to posterior synechiae with iris bombé.

Redslob saw in an hydrophthalmos, entropion of the iris with a strand reaching from the pupillary border to the ciliary processes.

Rasmussen finds acquired ectropion uveae in the presence of peripheral anterior synechia with simultaneous membranes of the anterior surface of the iris, atrophy of the iris and proliferation of the pigmentary epithelium. The iris is shortened due to the peripheral synechiae and the contracting sphincter rolls the posterior surface of the iris over the anterior surface. The presence of posterior synechiae prevents the appearance of an ectropion.

Hanssen finds formation of a membrane on the anterior surface of the iris in chronic inflammations and glaucoma. The membrane may, due to homogenizing of the intercellular substance, take the character of a glass membrane.

Herbert finds that the pigment epithelium can produce glass membranes and such are deposited in chronic uveitis accompanied by proliferations of the pigmented epithelial cells in the chamber angle and on the ciliary body.

Rauh describes new formation of glass membranes on the anterior surface of the iris in secondary glaucoma.

Jeandelise reports a pseudoglioma in a 4 month old child showing the cyclitic membrane behind the lens.

Heine reports a familial congenital pseudoglioma with severe inflammation of the entire uvea and detachment of the retina.

Xanthomatosis bulbi originates as infiltrative fatty deposits in the iris when its cells are damaged by glaucoma or chronic inflammation (Engelking).

Santonastoso finds in xanthomatosis in the anterior chamber and the iris cholesterol, neutral fats, saponified fatty acids and pigmented lipoids, and Stock saw cholesterol crystals in the anterior chamber of an eye with chronic iridocyclitis.

Heath, Williamson-Noble describe intra-ocular cholesterol deposits in the form of crystals surrounded by proliferating cells.

Walichan finds frequently in endophthalmitis hyaline degeneration, hemorrhages, serous exudate and newly-formed connective tissue in the suprachoroid.

Borello describes ossification of the choroid which appears ringlike around the papilla or ora serrata, disseminated or diffuse. The bony trabeculae are lined by connective tissue which produces the osteoblasts.

Herrenschwand reports on metaplastic bone formation in the eye. The bone develops chiefly in adhesions where the tissue is continuously exposed to changing tension.

Schilling found now and then blood marrow in the bone inside the eyeball.

Ossification of the choroid is reported by Bresgen, Crowley, Detroy and Morel, Dunn, Huber and Picena, Kassner, Shapira.

Guyton and Woods find characteristic granulomatous changes of the uvea in tuberculosis, syphilis, sarcoid, brucellosis and lymphogranuloma venereum.

Luetic iritis is examined histologically by Schwenker, Tomé y Bona. There are nodules consisting of lymphocytes and plasma cells at the pupillary margin and the root of the iris.

Rumbaur finds in congenital lues with a severe iritis, infiltration of lymphocytes and plasma cells, further new capillaries, proliferating fibroblasts and atrophic changes.

Vali-Chan found in a case of congenital lues the ciliary body and the nerve fiber layer of the retina infiltrated with lymphocytes and epithelioid cells, destruction of the outer layers of the retina and the retina attached to the infiltrated choroid.

Spicer describes nodules consisting of lymphocytes and plasma cells in the choroid in cases of lues.

Kunze found in an eye with interstitial keratitis healed chorioretinitic foci and still active foci in the choroid, consisting of lymphocytes, epithelioid and few giant cells.

v. Hippel, Li describe syphilomata of the iris and the ciliary body.

Fuchs describes cases of neuritis papulosa with nodular infiltrations in the iris, lymphocytic infiltration along retinal vessels, especially also around arteries, the lumina of which are obliterated by proliferating endothelium. In the retina and on its inner surface there is much fibrinous exudate transformed into fibrous tissue producing retinitis proliferans.

A tumor-like syphilitic granuloma close to the papilla, affecting also the optic nerve, is described by Jacoby.

Finnoff distinguishes four types of uveal tuberculosis: diffuse, miliary, confluent and mixed.

Meller was able to cultivate tubercle bacilli from the tissue of an eye with uveitis.

Katznelson, Koyanagi find numerous tubercle bacilli in the discharge of the tuberculous panophthalmitis.

Soria Escudero and Casanovas Carnicer report various cases of intra-ocular tuberculosis.

v. Szily describes in intra-ocular tuberculosis migratory tubercles originating from the ciliary body; they are deposited on Descemet's membrane and the anterior lens capsule.

According to Cattaneo, polymorphonuclears and lymphocytes precede the formation of a miliary tubercle in the uvea which is the expression of absence of tissue immunity or of anergy.

Penman and Wolff found tubercle bacilli frequently in miliary tuberculosis of the choroid, especially in the caseated part of the tubercle.

Bollack, Hillemand and Laperte report a case of miliary tubercles of the choroid in a 15 year old girl with tuberculous meningitis. Cases of miliary tuberculosis of the choroid are reported further by Lee, Tooke.

Kyrieleis found small tubercles in the iris of a 2 year old child.

Histologic findings of nodular and disseminated tuberculous uveitis are reported by Igersheimer, Kaegi, Meller, Stock.

Circumscribed exudative tuberculous uveitis is described by Bonnet and Colrat, Woods.

Asbury, Lestage and Soulommiac, Thomas describe cases of uveal tuberculosis.

Li describes an extensive tuberculosis of the uvea in an infant, and also Poyales reports cases of tuberculosis in eyes of infants.

Knapp describes cases of intra-ocular tuberculosis affecting the outer and vascular layers of the eye.

Histologic findings of the small nodules at the pupillary margin and on the anterior lens capsule in cases of chronic tuberculous iridocyclitis which partly proliferate from the stroma, partly are formed in the aqueous humor by an aggregation of cells, are reported by Derby, Vogt.

Landman saw a case of iridocyclitis with tuberculous nodules in the uvea and fatty degeneration in the cornea, iris, anterior chamber, ciliary body, choroid and sclera.

Verhoeff describes small, fresh, tuberculous foci in the iris of an eye which has been blind for 20 years due to iridocyclitis.

Vogt believes that tuberculoids of the iris do exist and that they consist histologically of lymphocytes, epithelioid and giant cells.

v. Hippel reports cases of tuberculosis of the choroid.

Bergmeister saw a case of tuberculosis of the choroid with necrosis in a 42 year old woman. The optic nerve had tubercles in vessel walls.

Verhoeff describes histologically a localized tuberculous chorio-retinitis.

Lagrange found in a case of disseminated tuberculous chorioditis the choriocapillaris partly obliterated and the pigmentary epithelium, rods and cones and outer nuclear layer missing.

Verhoeff reports a case of choroidal tuberculosis and tuberculous periphlebitis.

Meller states that tuberculosis spreads from the uvea into the ora serrata and is carried from here through the perivascular spaces of the veins into the optic nerve.

Frank describes tuberculous periphlebitis retinalis originating from direct extension from conglomerate tuberculosis of the ciliary body into the retina.

A conglomerate tubercle of the choroid was found in a 15 year old girl by Dowling and Brown.

A tuberculoma of the eye which destroyed its greater part is reported by Dodds in a 12 year old boy.

Brusselmans, Gronwall, Saggesse and Castane Decoud report cases of conglomerate tuberculosis of the choroid.

Montalti reports conglomerate tuberculosis of the iris and ciliary body.

Kaganowa reports a tuberculoma of the iris.

Derkač reports a case of solitary tuberculoma of the choroid with spread over the entire eye in a 6 year old girl. Panico, Petrović describe solitary tuberculomata of the choroid.

Byers reports a case of severe uveitis with proliferating granulation tissue which he interprets as tuberculous.

Rønne found elementary tubercles in an iris nodule in a case of febris uveo-parotidea.

Bahr describes in uveo-parotitis nodular infiltration with giant cells in the uvea.

Schultz found in a case of uveo-parotitis and dacryo-adenitis Boeck's sarcoid in the tear gland.

Appelmans and v. Horenbeeck consider Heerfordt's syndrome as Boeck's sarcoid.

Woods and Guyton describe sarcoidosis of the uvea showing small nodules with epithelioid and giant cells and diffuse lymphocytic infiltration, but they could not find "Schaumann bodies." They find lymphoid nodules in the iris in brucellosis.

Rochat reports cases of iridocyclitis in the disease of Besnier-Boeck with nodular masses, consisting of masses of epithelioid cells with a few giant cells without caseation.

Goldberg and Newell report iridocyclitis due to Boeck's sarcoid.

Rasmussen describes Boeck's sarcoid of the ciliary body showing connective tissue with round-cell infiltration interspersed with conglomerates of epithelioid cells.

Mylius and Schuermann, Walsh find nodules consisting of lymphocytes and epithelioid cells distributed over the uvea in sarcoid of Boeck.

Around caterpillar hairs are formed nodules consisting of lymphocytes and giant cells in the iris (iridocyclitis pseudo tuberculosis), according to Dejean and Harant, Villard and Dejean.

Pendergast describes the pathology of the uvea in leprosy with infiltration with mononuclears and large multinuclear lepra cells.

Morax found in leprotic iritis diffuse infiltration with lymphocytes and bacteria.

According to Woods, tuberculosis can be distinguished from sympathetic ophthalmia as in the latter (1) infiltrates appear early around perforating veins of the sclera, (2) the uvea is uniformly infiltrated, (3) the posterior layers of the iris are affected, (4) the surrounding tissues of the uvea are not destroyed, and (5) there is an early phagocytosis of pigment granules in epithelioid and giant cells.

Fuchs finds as early symptoms of sympathetic ophthalmia, lymphocytic infiltration around the veins of the choroid.

Kuemmel states that eyes enucleated before the onset of the sympathetic ophthalmia in the fellow eye, or years after the onset, may show only slight changes.

Meller found in cases of sympathetic ophthalmia in the fellow eye occasionally fleeting inflammations.

Eleonskaja finds in sympathetic ophthalmia small and large lymphocytes, plasma cells, mononuclear eosinophiles, polymorphonuclears, epithelioid cells, giant cells and macrophages. The cavities of the eye contain erythrocytes, endothelial cells of the cornea, stroma cells of the iris, pigmented and nonpigmented epithelial cells of the ciliary body, connective tissue cells of the ciliary body, pigment epithelium of the retina, large mononuclears, macrophages, free chromatophors and fibroblasts. The vitreous body shows large mononuclears in an early stage of the disease.

Seregin finds in sympathetic ophthalmia frequently perineuritis of the optic nerve in continuation of the choroidal infiltration.

Lamb finds proliferative exudative elements in some cases of sympathetic ophthalmia as well in the sympathized as in the sympathizing eye.

Trowbridge describes in sympathetic ophthalmia that pigment is phagocytosed in epithelioid cells and that a portion of the infiltration consists of eosinophils and plasmacytoids.

Rønne describes a case of sympathetic ophthalmia with tuberculosis-like granulations restricted almost exclusively to the iris and ciliary body.

Marchesani reports as important findings in sympathetic ophthalmia irregularities of the pigmentary epithelium, drusen in Bruch's membrane, a dense accumulation of cells at the limbus and foci of epithelioid cells in the episcleral tissue.

Pantassatos reports necroses in the granulation tissue of the sympathetic ophthalmia and specific periphlebitis.

Meller decribes periphlebitis in sympathetic ophthalmia as sympathetic perivasculitis; further, Echeverria. The vitreous body can be heavily invaded from it (Wood).

Fuchs found in 71 eyes with sympathetic ophthalmia inflammatory changes in the optic nerve fifty-four times, in 24 cases a specific infiltration of the nerve and its sheaths in which the infiltration is in continuation of infiltrations of the choroid along ciliary vessels.

Schreiber describes as changes of the retina in the sympathized eye degeneration of the ganglion cells, complete absence of the rods and cones, periphlebitis and periarteritis and infiltration of the uvea with lymphocytes.

The pathology of eyes with sympathetic ophthalmia is described by Andersson, Dvorak-Theobald, Jaeger, Redslob, Samuels, Schreiber, Wood. Jaeger, Wood could examine the sympathizing eye.

Pfeiffer reports a case of sympathetic ophthalmia following indirect scleral rupture caused by the blow of a cow's horn.

Lamb reports sympathetic ophthalmia in a 6 year old child with contusion of the eye showing a nonperforating trauma.

In Andersson's case, a 3 year old boy suffered an eye injury with minor hemorrhage, without a clinically visible perforation. He developed sympathetic ophthalmia. The enucleated eye showed first on serial sections a very small perforation through sclera, choroid and retina.

Perera reports a case of subconjunctival rupture with incarceration of the lens and uveal tissue, followed by sympathetic ophthalmia.

De Veer believes that endophthalmitis phako-anaphylactica is often followed by sympathetic ophthalmia due to simultaneous hypersensitivity to uveal pigment and lens substance. He finds around remnants of the lens polymorphonuclears, epithelioid cells, proliferation of capillaries and fibroblasts.

Herbert describes a case of sympathetic ophthalmia following a trephine operation after seven years.

Veltishtshev reports sympathetic ophthalmia following evisceration of an eye which has been burned with sulphuric acid.

Haldimann reports cases of sympathetic ophthalmia following herpetic keratitis without perforation and typical histologic findings.

Sommer reports cases of sympathetic ophthalmia following herpes zoster ophthalmicus.

Sympathetic ophthalmia due to intra-ocular malignant melanoma is reported by Butler and Evans, Daniels, Joy, Melanowski, Riwehun and de Coursey, Schwartz.

Cohen reports a melanosarcoma in a 35 year old man with plastic iridocyclitis, secondary glaucoma and shrinkage of the globe without showing

infiltration typical for sympathetic ophthalmia. The fellow eye also had a plastic iridocyclitis with precipitates.

Samuels, Woods, find sympathetic ophthalmia in rare instances following post-traumatic panophthalmitis.

A primary lesion (inoculation chancre, Redslob) is said to be the portal of entry in the perforating wound (Felsenthal, Redslob, Samuels).

Fliri opposes Redslob's conception of a primary lesion in sympathetic ophthalmia. He finds beginning lesions at the posterior ciliary vessels indicating an endogenous origin of the disease.

Hentschel, v. Hippel, Meller, Peters, Riehm, Urbanek, believe that the tubercle bacillus causes sympathetic ophthalmia; Guillery believes that sympathetic ophthalmia is caused by tuberculotoxin.

Guillery explains the sympathetic ophthalmia as caused by toxins, which are produced by tissue destruction in the injured eye. They act by way of the blood circulation on the fellow eye.

Sallmann found the blood culture positive for tubercle bacilli in a case of sympathetic ophthalmia.

Purtscher reports positive cultures of tubercle bacilli from the blood and the tissues of the sympathizing eye of an 8 year old boy with a perforating injury.

Addario la Ferla calls the sympathetic ophthalmia uveitis anaphylactica tuberculosa.

Marchesani could present B. subtilitis in an eye with injury and sympathetic ophthalmia.

Gifford and Lucie, Meesmann and Volmer, v. Szily, Undelt believe that sympathetic ophthalmia is caused by virus.

v. Szily could produce experimentally sympathetic ophthalmia by implantation of herpes virus into a prepared pocket of the ciliary body.

Woods, Woods and Little, are of the opinion that sympathetic ophthalmia is of allergic origin.

Gill considers the disintegration of the uveal pigment as responsible for sympathetic ophthalmia.

Henton finds that uveal pigment can act as antigen and that active phagocytosis of the pigment can take place.

Woods finds in the serum of normal persons substances which fix the uveal pigment acting as antigen and complement and in persons with chronic iridocyclitis these substances missing. If uveal pigment is injected in such persons intradermally, a positive skin reaction appears. In sympathetic ophthalmia the antibodies are missing in the blood, but cellular hypersensitivity to uveal pigment is present. In a positive intracutaneous reaction, the pigment is absorbed by numerous phagocytes.

Also, Friedenwald advocates an intradermal reaction which appears as an inflammatory reaction to inoculated pigment in cases of sympathetic ophthalmia.

Fridman believes that sympathetic ophthalmia is accompanied by a serous meningitis of the chiasmal cistern.

Beauvieux and Bessiere report a lymphocytosis of the liquor in sympathetic ophthalmia; Corcelle finds the liquor in sympathetic ophthalmia

indicating a lymphocytic meningitis and calls the sympathetic ophthalmia lymphocytic uveomeningitis.

Verhoeff describes a case of metastatic mycosis of the choroid perforating into the subretinal space and into the retina, showing polymorphonuclears, phagocytes, and actinomycosis-like corpuscles.

Schwartz finds the iris partly necrotic and infiltrated with polymorphonuclears and giant cells in blastomycosis.

Cassady found blastomyces histologically in the uvea which was infiltrated with lymphocytes, plasma cells, epithelioid and giant cells.

Kreibig found in a case of severe sepsis intra-ocular nodules of polymorphonuclears and destruction of walls of blood vessels, mainly in the ciliary processes. Blastomyces could be found in special staining.

Herrenschwand describes a metastatic fungus infection in an aphakic eye caused by trichomycetes.

Rohner and Huber found in an eye with metastatic aspergillosis a vitreous abscess and infiltration of polymorphonuclears in the necrotic iris and ciliary body.

A severe uveitis was caused by aspergillus fumigatus in a 42 year old man, according to Archangelsky.

Castroviejo and Muñoz Urra describe aspergillosis of the uvea following perforation of a mycotic corneal ulcer.

Weiss and Shevsky found in a case of iridocyclitis in the culture torula histolytica (cryptococcus hominis), a yeast-like organism.

Verhoeff found in a mycosis of the choroid, abscesses in various stages of necrosis containing fungoid corpuscles surrounded by epithelioid and giant cells. The disease developed in a 30 year old man bilaterally after extraction of a congenital cataract in one eye and appeared clinically as sympathetic ophthalmia.

Albrich found a case of metastatic ophthalmia due to fungus.

Neame found in iridocyclitis caused by trypanosomiasis the organism, in the aqueous humor.

Heath and Zuelzer report on toxoplasmosis.

Heidelman reports on evaluation of toxoplasma neutralization tests in cases of chorioretinitis and found in a positive case macular chorioretinitis with toxoplasma in the lesion.

Rones describes the histology of sclerosis of choroidal vessels in senile eyes.

Crigler found in a case diagnosed as sarcoma of the choroid, hyaline degeneration of the choroidal vessels and a large hemorrhage in the subretinal space.

Cohen describes the histology of primary choroidal sclerosis.

Ruby found in a case of essential atrophy of the iris microscopically pannus and scars of the cornea, only the peripheral portion of the iris preserved, with loss of stroma, cystoid degeneration of the pigmentary epithelium of the iris and the ciliary body and cystic degeneration of the retina.

Rones describes in essential atrophy of the iris, anterior peripheral synechia, displacement and distortion of the pupil, holes in the iris, sclerosis of the vessels and cystic degeneration of the cornea.

Ellet believes that a newly formed tissue in the chamber angle produces by shrinkage essential atrophy of the iris and secondary glaucoma.

Rochat and Mulden observed a case of progressive atrophy of the iris, showing peripheral anterior synechia, formation of holes in the iris and glaucomatous excavation.

The histologic examination of essential atrophy of the iris is reported further by Liesko.

Peris finds histologically in choroideremia complete absence of the choroid in an otherwise normally developed eye.

Levinson brings the depigmentation of the iris and the ciliary body in connection with glaucoma, insofar as the pigment is deposited between trabeculae of the chamber angle.

Fuchs describes edema and cysts of the posterior part of the nonpigmented epithelium of the pars plana of the ciliary body arising when the density of the vitreous body prevents the outflow of the fluid produced by the epithelium.

Guist describes the histology of a pigmented ring-line of the iris which follows an injury and is parallel with the limbus. It represents a depression of the iris with overhanging margin on which the anterior border layer is condensed.

Fuchs describes histopathology of inversion and recession of the iris. He finds in luxation of the lens the ciliary processes turned posteriorly, as a result of the backward sliding of the lens.

Verhoeff finds in angioid streaks excessive fibrosis in hemorrhages with folds of the pigmentary epithelium, Hagedorn thickening of Bruch's membrane with fine tears, Law folding of the retina with accumulated pigmentary debris and degenerated cells.

Busacca reports about fatty infiltration of the nonpigmented epithelium of the ciliary body for which a cause cannot always be elicited.

Fuchs finds in normal and pathologic eyes vacuolated masses in the choroid, representing probably confluent endothelial cells enlarged by intake of lipoid or fat.

Jaensch describes fatty degeneration of the uvea. He finds it especially in the neighborhood of malignant tumors, also extra-cellular fat beneath the ciliary epithelium in senility.

Jaensch, Meesmann find fatty degeneration of the uvea in secondary glaucoma after injury of the eye.

Villani describes fatty degeneration of the ciliary muscle.

Samuels reports necrosis of the iris due to trauma, circulatory disturbances and glaucoma.

D'Oswaldo reports cases of traumatic necrosis of iris and ciliary body. If the lens epithelium becomes necrotic also, cataract develops.

Edeskuty describes iris necrosis in a 61 year old man with fibrinous-purulent exudate into the anterior chamber. He classifies the case as zoster necrosis.

Gruber describes in Fahr's nephrosclerosis circumscribed necrosis, and thickening of the intima and media of the arteries of the choroid.

Nitsch describes drusen of the choroid resembling central choroiditis.

The senile iris shows hyalinization of the pupillary margin and sclerosis of its vessels (Rones). He also describes senile changes of the ciliary body

in the form of proliferation of the epithelium with formation of cysts and hyalinization of the processes. Hanssen described fatty degeneration of the ciliary processes, Kadletz their calcareous degeneration. Herbert finds hyaline degeneration of the interstitial tissue of the ciliary muscle with deposition of fatty and calcareous granules. Rones reports large, flat excrescences in a festoon-like arrangement of pedunculated or sessile knobs in the ciliary processes. Vervey describes senile changes of the choroidal vessel.

The pigment epithelium of the iris is vacuolized and depigmented in senile eyes, but this is still exaggerated in eyes with cataract, according to Cucchia.

Whiting describes hyperplasia of the nonpigmented ciliary epithelium in senility.

Stewart reports a case in which detachment of the retina was caused by enormous hyperplasia of the ciliary epithelium.

Loewenstein and Foster describe histologically iridoschisis in a glaucomatous eye of a 75 year old man. The iris is separated in an anterior and posterior layer and the anterior one floats in the aqueous humor as a thin membrane resembling fine lace; some threads separated from the iris contain blood vessels with a thick, glassy endothelium. Senile processes aggravated by proteolytic enzymes of the aqueous leading to atrophy of the anterior layers of the iris play a role.

Paul describes a senile disciform degeneration of the macula with a large hemorrhage between the pigmentary epithelium and Bruch's membrane which passed through a hole in the latter from the ruptured choriocapillaris. The hemorrhage organized with formation of hyaline degeneration, and the formation of cartilage and bone.

The pathology of senile macular degeneration is described by Friedenwald, Rones.

Duynstee, Junius and Kuhnt, Ormond accuse the retinal vessels as cause of the senile disciform degeneration of the macula.

Coppez and Danis, Paul believe that inflammatory changes of the choroid cause the senile disciform degeneration of the macula; Cords, Holloway and Verhoeff, Pallarès, Soudakoff that sclerotic changes of the choriocapillaris are the cause.

Goldstein and Wexler describe periarteritis nodosa of the choroid with circumscribed nodes of neutrophils, eosinophils, lymphocytes, plasma cells and epithelioid cells.

Goldsmith reports a case of periarteritis nodosa of the choroid with fibrinoid necrosis, endothelial proliferation and infiltration with lymphocytes, polymorphonuclears, eosinophils and plasma cells.

Boeck reports a case of periarteritis nodosa with changes in the ciliary vessels of the eye. Periarteritis nodosa of the choroid is found further by Christeller, Helpern and Trubek.

Fileti finds besides infiltration of choroid and retina in leukemia also infiltration of conjunctiva, sclera and cornea.

Pathologic findings of the uvea in leukemia are reported by Bal, Weve.

Goldstein and Wexler believe that in leukemia the vessel walls are infiltrated with leukocytes which pave the way for the passage of the monocytes.

Borgeson and Wagener believe that the infiltration of the uvea in leukemia originates from the orbital vessels and enters the bulb along the perivascular spaces of the posterior ciliary vessels.

Wood describes diffuse lymphocytic infiltration in gouty uveitis.

Corrado describes hemorrhage in the choroid appearing like a tumor.

Garcia reports on hemorrhages from the ciliary body in injury.

Fuchs rarely finds hemorrhages in the choroid without injury in myopic eyes in which Bruch's membrane and choriocapillaris rupture due to stretching, further in retinitis albuminurica, luetic vascular diseases and leukemia.

Meller found that in cases of injury the ciliary epithelium may be important for a phagocytosis of the blood pigment.

Clapp describes the hydropic degeneration of the pigment epithelium in diabetes as diabetic iridopathy. The freed pigment is ingested by phagocytes.

Kurz found in rubeosis iridis diabetica histologically the iris covered with erythrocytes and fibrin and enormous proliferation of blood vessels in the region of the sphincter.

Fehrmann found in rubeosis iridis diabetica numerous newly formed blood vessels of the type of capillaries in the pupillary part of the iris and also preretinal vessels and degenerative changes of the retina.

Rubeosis iridis is caused by circulatory disturbances and shows newly formed blood vessels in a layer of connective tissue in the anterior border layer.

Fuchs finds in albuminuric choroiditis exudation, vascular changes and migration of pigment.

Koyanagi found in a case of icterus and xerosis of the conjunctiva in a 10 year old girl the pigment epithelium filled with lipoid and pigment accumulated between the rods and cones.

Gilbert finds foci of lymphocytes in myopic choroiditis and occasionally also the retina invaginated into the choroid.

O'Brien finds in otherwise normal eyes sometimes a minimal serous detachment of the choroid.

Spaeth and Long report detachments of the choroid of various origin.

Verhoeff and Waite describe a spontaneous detachment of the choroid in a 54 year old man with chronic diarrhea leading to increase of the salt content of the blood, decrease of the intra-ocular pressure, hyperemia and transudation from the choroidal vessels.

Arjona found in expulsive hemorrhage lymphocytic infiltration around choroidal vessels.

Manschot found in one case of expulsive hemorrhage after cataract extraction an angioma racemosum around the vortex vein, in another extensive necrosis of the walls of a few ciliary arteries with thrombosis.

According to Meller, subchoroidal hemorrhage can be caused by degeneration of vessel walls and can produce spontaneous rupture of the bulb if the sclera is already thinned.

Seefelder saw an extensive suprachoroidal hemorrhage originating from a granuloma of the equatorial region which probably was the sequela of an injury.

Hagen considers the fluid in postoperative detachment of the choroid as a transudate from the choroidal vessels. The aqueous humor is substituted

by fluid from the vitreous. The less voluminous vitreous loses its pressure on the retina and choroid. The latter separates from the sclera and fluid transudes from the vessels into the vacuum.

Lindner believes that in a leaking eye the aqueous humor is substituted first by vitreous body which itself starts to leak, causing detachment of the choroid.

Verhoeff finds the pigmented streaks caused by separation of the choroid microscopically as furrow-like creases of the surface of the choroid and ridgelike thickenings of the pigment epithelium.

Koliopoulos finds that chiefly tumors of the anterior segment of the bulb are liable to produce glaucoma.

Simple melanomata of the pigmentary epithelium of the iris are described by Gilbert, Klien, Schmidt.

Seefelder reports on melanoma of the iris with gliosis of the epithelial layer.

Alexander found a benign melanoma of the ciliary body consisting of cells of the pigmentary epithelium.

Givner saw a benign melanoma of the pars plana of the ciliary body in a 63 year old woman.

Levy-Wolff reports on benign epithelial proliferation of the ciliary body.

Collins observed an enormous proliferation of the pigment cells into the stroma in a case of injury with partial iridodialysis.

Cattaneo describes hyperplasia and new formation of the nonpigmented ciliary epithelium as hamartoblastoma.

Weekers described pigmented tumors originating from the pigment epithelium of the ciliary body.

Nordmann, Offret describe the tumors of the ciliary epithelium.

Wunderlich reports three cases of benign epitheliomata of the ciliary body.

Szabo found in a 42 year old man a benign epithelioma of the ciliary body originating from the nonpigmented epithelium and growing into the ciliary body in trabecular rows with homogeneous interstices showing glandular tubes of adenoma type.

Zentmayer describes an adenoma of the ciliary processes in a 56 year old woman.

Stough reports a case of benign adenoma of the ciliary body with a simultaneous hypophysial adenoma.

Boeck reports a case of diktyoma in a 16 year old girl containing glial fibers and islands of cartilage.

Histologic examinations of diktyomata are reported further by Czukrasz, Satanowsky, Soudakoff.

Cucchia describes a neoplasm of the ciliary body in a 4 year old child consisting of rosettes and round cells as neuroepithelioma.

Mawas describes a nevo-carcinoma of the base of the iris.

Pascheff reports a primary neuroblastoma of the iris originating from the retinal elements of the iris.

Malignant epitheliomata of the ciliary body are found by Hine, Merkel.

Fleischer and Wissmann describe a primary melanocarcinoma of the ciliary body.

Barrow and Stallard describe a pigmented epithelial neoplasm of the ciliary body infiltrating chamber angle and Schlemm's canal in a 61 year old man.

A malignant epithelial tumor of the ciliary body containing pigmented and nonpigmented epithelium with metastases in the optic nerve and in the brain is described by Maertens.

Custodis found a malignant melanotic tumor of the iris in a 53 year old man originating from ectodermal and mesodermal elements.

Bietti describes melanosarcoma of the ciliary body originating in the pigmentary epithelium.

Asbury describes as medullo-epitheliomata tumors of the angle between the iris and ciliary body which infiltrate and destroy locally. They originate from the pigment epithelium and appear as medullary growth.

Leiomyoma of the iris consists of meshwork of spindle cells containing myoglia fibrils (Frost).

Davis, Sheppard and Romejko describe leiomyoma of the iris as a tumor consisting of interlacing fascicles of nonpigmented spindleshaped cells with long, fibrillar processes and oval nuclei.

Van Heuven reports a leiomyoblastoma of the iris originating from the sphincter in a 54 year old man.

Kahler, Wallace, Irvine and Irvine report a leiomyoma of the iris in a 46 year old woman. Velhagen reports a leiomyoma of the ciliary body in a 47 year old woman. Ellett, Verhoeff describe myomata of the iris.

Rodin describes an angioma of the iris of the type of a vascular nevus.

Daily found a hemangioma of the ciliary body in a 5 month old child replacing the ciliary body and projecting into the chamber angle as a necrotic and bleeding capillary hemangioma.

Heine reports hemangiomata of the ciliary body.

Brons, Kern, Lent and Lyon, Mulock-Houwer, Zamenhof and Arkin describe hemangiomata of the choroid. v. Hippel, Marlow report hemangiomata of the choroid.

Evans, Evans and Evans, Jaensch, Jahnke, de Haas describe angiomata of the choroid with simultaneous glaucoma.

Wood describes small protrusions of the anterior surface of the iris consisting of small cells and containing pigment intra- and extracellularly as melanosis of the iris.

Cattaneo calls the melanoma of the choroid a circumscribed melanosis. It consists of a dense accumulation of chromatophors leaving free only the choriocapillaris.

v. Szily finds the melanoma of the uvea consisting of closely packed chromatophors without participation of the pigment epithelium. Also Knapp finds the melanomata of the choroid consisting of accumulation of chromatophors. Rones reports choroidal melanomas.

Pseudomelanomas of the iris may consist of pigment phagocytosing, proliferating endothelial cells and cells of the anterior border layer, according to Klien.

Nevi of the uvea are examined histologically by Gilbert, Goldstein and Wexler, Johnston, Mulock, Houwer, Usher.

Wheeler describes plexiform neurofibromatosis of the lids, the ciliary body and the choroid, consisting of nonmedullated nerve fibers, ganglion

cells and laminated structures with laterally arranged nuclei (Meissnerian tactile corpuscles) and neurofibromatosis of the optic nerve in a 6½ year old girl.

Trevor-Roper describes a neurofibroma of the choroid probably originating from the intrascleral portion of a ciliary nerve in a 3½ year old girl.

Robson, Blackwood and Cookson saw an 18 year old patient with neurofibromatosis of the lids and neurofibromata of the short ciliary nerves and "ovoid and round bodies" in the choroid.

Callender and Thigpen described neurofibromata of iris, ciliary body and of the choroid close to the optic disc in the same eye.

A neurofibroma of the choroid in a 56 year old man with no other tumor formations in the body is reported by Freeman.

Knight reports a plexiform neuroma in the choroid of an hydrophthalmos.

Circumscribed neurofibromata of the uvea are reported by Davis, Fuchs, Kyrieleis, Moorhouse.

The pathology of the malignant melanoma of the uvea is described by Annen, Bruner, Bushard, Callender and Wilder, de Castano Decoud, Chalamis, Dejean, Freeman, Goulden and Stallard, Heinsius, Li, Lijo Pavia, McCoy, Marmoiton, Meyer and Kubik, Merrill, Neame, Nelson, Norman, Patterson, Prevec, Reese, Rønne, Rosenbaum, Samuels, Terry and Johns, Waetzold, Zentmayer.

Callender distinguishes several cell types in the malignant melanoma of the eye: (1) Spindle-cell type; subtype A, cells arranged in sheets and whorls with fiber-like cytoplasm around oval nuclei; subtype B, showing less intercellular substance and darker staining nuclei with distinct nucleoli; (2) a fascicular type with columns of fasciculi, the long axis of cells being arranged at right angles to a central capillary blood vessel; (3) an epithelioid cell type; (4) a mixed cell type, composed of two or more of the mentioned cells, the most frequent form.

Endotheliomata of the uvea consisting of flat, polygonal cells occasionally arranged in palisades are described by Butler and Assinder, Giannini.

Salzmann reports histologic findings of sarcomata of the choroid and compares them with the ophthalmoscopic picture.

Fuchs finds a circumscribed retinal detachment at the ora serrata in beginning sarcomata of the choroid, and Klien a relatively frequent detachment of the pars ciliaris retinae in malignant intra-ocular tumors.

Archangelsky finds the retina over sarcomata of the choroid entirely degenerated and only pigment cells present.

Bergstrand finds that the pigment gathers in the melanoblastomata in the peripheral vascularized parts of the tumor.

Greeves reports a slightly pigmented spindle-cell sarcoma of the choroid in the macular region.

Halbertsma and Pieck, Williamson-Noble report circumpapillary sarcomata of the choroid.

Samuels found necrotic areas in every examined choroidal sarcoma.

Jaensch and Zeidler found fine fatty droplets in the cytoplasm of the cells of choroidal sarcomata. They state that the lipoid storage is the function of the living tumor cells as the lipoid seems to be a prestage of the pigment. In necrotic areas of the tumor large fat droplets are deposited.

Laval found an extended hemorrhage in a sarcoma of the choroid which had perforated blood vessels of the choroid.

McGregor and Hill find in studying the reticulin content in malignant melanomata of the uvea that for the determination of its malignancy the cell types are of importance in the first line and the reticulin content is a subsidiary factor.

Magnasco, Margotta found melanosarcomata of the choroid in atrophic bulbi.

Nitsch describes a case of a sarcoma of the choroid which started to grow after an injury to the eye, and Stieren a sarcoma of the uvea appearing several years after the injury of the eye. Further, Chance reports a sarcoma of the choroid encapsulated by fibrous tissue in a shrunken globe of a 50 year old woman. The patient was injured by a blow to her head three years previously.

Rønne describes a choroidal sarcoma which grew through the retina into the vitreous and showed cavernous spaces and hemorrhages in the vitreous.

Jaensch, Lo Russo describe extension of malignant melanomata into the optic nerve through the lamina cribrosa.

Zeeman describes a flat sarcoma of the choroid spreading along a ciliary nerve.

Kreibig reports intra-ocular sarcoma metastases; he believes that the tumor originally starts in the suprachoroid and if a small melanosarcoma starts in another place it has to be considered as metastatic.

Paradoxov saw a diffuse pigmented sarcoma in the uvea with small metastases in the same eye.

Tooke describes a melanotic sarcoma of the choroid with metastases in the optic nerve sheaths and in the orbit.

Cornil, Heckenroth, Mosinger and Silvan found nonmelanotic metastases in the liver appearing three years after enucleation for ocular melanoma.

Velhagen examines the subretinal fluid in detachment of the retina, especially when a sarcoma is suspected with the melanin reaction of Cibis (a droplet of the subretinal fluid is absorbed on a filter paper, is saturated with ferric chloride and becomes brown in presence of melanin) and after centrifuging in smears and paraffine sections and eventually fibrinous networks and large, irregular cells can be found singly and in clumps.

Cibis examined the subretinal fluid in cases of melanosarcoma of the choroid and found it by examination with ferric chloride positive for melanin.

Seefelder finds perforations of sarcomata of the choroid into the orbit to exist frequently.

Samuels describes the histologic details of perforations of the bulb in malignant melanomata of the choroid.

Poos, Puglisi Duranti report small melanosarcomata of the choroid spreading chiefly extrabulbar.

In Beery's case of a melanosarcoma of the choroid, spindle and polyhedral cells grew into the orbit and conjunctiva.

Smith describes a black melanosarcoma extending throughout the entire choroid, perforating the sclera along the channels and forming metastases in the iris and limbus.

Tirelli saw a melanosarcoma of the choroid with extension into the bulbar conjunctiva and skin of the face.

Melanosarcoma extending through the wound after cataract operation of five years' existence is reported by Beaujon.

Lukens reports a recurrent melanosarcoma of the orbit after enucleation of an eye with melanosarcoma of the choroid.

Dvorak-Theobald brings forward proof that the choroidal sarcoma develops from the Schwann cells of the posterior ciliary nerves. Nevi can be detected along these nerves in the scleral channels.

Picena and Paez Allende saw an achromatic melanoma of the choroid in an 80 year old woman in which intracellular melanin granules could be stained. They consider the melanocytes derived from the nerve sheaths of Schwann.

Schubert reports a small cell spindle-cell sarcoma of the choroid originating from a neurinoma.

Berger and Vaillancourt could find sensory corpuscles in a malignant melanoma of the choroid and consider it as a ganglio-neuroma.

Asbury and Vail saw a primary malignant melanoma of the choroid and later a primary glioblastoma multiforme in the same patient. They argue that both tumors were ectodermal and the malignant melanoma were a neuroectodermal tumor.

Knight believes that the melanotic tumors of the choroid originate from the pigment epithelium and he calls them melano-epitheliomata. Further, Mier and Rivas consider the melanoma of the choroid as melanoepithelioma and Mawas believes that the melanotic tumors of the choroid are melanotic epitheliomata as derivates of the pigmentary epithelium. Waetzold and Gyotoku consider the malignant melanoma as of ectodermal origin, but as they observed that the smallest choroidal sarcomata are not pigmented, they are opposed to the assumption of an epithelial origin as the pigment epithelium never perforates Bruch's membrane in cases of tumors.

Jaensch describes a very pigmented melanosarcoma of the iris and describes it as a true chromatophoroma.

Mawas describes a sarcoma of the choroid in which he could stain numerous threads of fungi and he calls it a "mycetoma."

Treacher Collins believes that the malignant melanomata of the choroid originate from endothelial cells (endotheliomata) and adventitia (peritheliomata).

Barlow reports a mixed cell sarcoma of the choroid.

Gourfein-Welt, Lacroix and Pesme, Peterfi, Terrien report cases of leukosarcomata of the choroid.

Leopoldsberger describes cases of small nonpigmented tumors consisting of spindle-cells originating from the ciliary nerves in the choroid.

Lacroix and Pesme describe leukosarcoma of the choroid consisting of elongated fusiform cells with large nuclei. They consider the tumors of neuroepithelial origin as the cells appear epithelioid.

Leser reports a flat leukosarcoma of the choroid extending through a cyclodialysis wound underneath the conjunctiva.

Pressburger describes an infiltration of the choroid with cells of myelogenous and epithelioid types in a case of Paltauf-Sternberg leukosarcoma (a disease, showing leukemic tumors without a leukemic blood picture).

Parker and Stokes report round cell sarcomata in children originating from the choroid and from the retina.

Cosmettatos describes a round cell sarcoma of the choroid of a 55 year old woman. The cells are arranged concentrically around blood vessels which makes him think that they originate from the perivascular sheaths.

Friedman reports a perithelioma of the choroid in a 64 year old woman.

A sarcoma of the choroid of endothelial structure is reported by Balacco.

Cardell, Jona describe cases of angiosarcomata of the choroid.

Heine found benign nevi and a malignant melanoma in the same eye.

Velhagen saw a melanoma and a very small sarcoma of the choroid in the same eyeball in an 86 year old woman.

Rochat describes two equal flat spindle-cell sarcomata of the choroid of one eye. There is a question as to whether the second tumor is a metastasis or represents an independent new-growth. Klein, v. Kurz, Pressburger, Velhagen saw two sarcomata of the choroid in one eye.

Seefelder found a squamous cell carcinoma of the cornea and a small sarcoma of the choroid, which had infiltrated the optic nerve, in the same eye.

Williamson-Noble found in a case of detachment of the retina operated on with diathermy a completely necrotic melanoma of the choroid into which capillaries and fibroblasts had proliferated.

Goldsmith found as effect of diathermy on a malignant melanoma new capillary loops and fibroblasts proliferating into the necrotic tumor.

Hartmann, Kaminsky, Leser describe melanosarcomata of the ciliary body.

Pieck found a myosarcoma of the ciliary body in a 62 year old woman.

Lewizkaja found a leukosarcoma of the ciliary body.

Lewizkaja describes an endothelioma of the ciliary body of a 20 year old woman.

Boje reports ring sarcoma of the iris and ciliary body in the eye of a 6 month old boy.

Adams, Dejean, Klein, Murray, Szymanski report ring sarcomata of the iris and the ciliary body.

Terrien describes primary and secondary tumors of the iris.

Scullica observed in ring sarcomata a ringlike infiltration of the chamber angle with tumor cells, pigment and plasma.

Truc and Dejean report a pigmented ring sarcoma of the iris in a 35 year old woman containing endothelial-like cells.

Kaganowa, Pincus report cases of sarcomata of the iris.

Berberov reports primary sarcomata of the iris originating in pigmented nevi.

Mayou found that a sarcoma of the iris originating from a pigmented nevus consisted of large spindle cells.

Chance reports a mixed cell sarcoma of the iris in a 42 year old man.

Terrien describes cases of leukosarcoma, further epithelial and inflammatory tumors of the iris.

Heine reports a leukosarcoma of the iris with rapid spread after iridectomy.

Duke-Elder and Stallard, Zentmayer report leukosarcoma of the iris consisting of spindle cells.

Papolczy saw a spindle-cell sarcoma of the iris appearing after a traumatic uveitis and disseminating in the anterior chamber.

Narog describes a perivascular perithelial sarcoma of the iris with atrophy of the bulb in a 2 year old child.

Knapp describes a sarcoma of the iris consisting of three layers: (1) a compact layer of spindle cells with varying pigment content, (2) a layer of loosely pigmented cells and (3) a layer of little pigmented cells with large nuclei.

Ehlers found two melanosarcomata and one leiomyosarcoma of the iris.

Black found pigmented spindle-cell sarcoma in the iris of a 64 year old woman.

Remonda and Ferraris saw a fusiform melanosarcoma of the iris in a 13 year old boy.

Wildi reports a melanosarcoma of the iris partly of alveolar and partly of strandlike structure in a 62 year old man. Doherty, Laignier report melanosarcomata of the iris.

Pressburger reports a case of sarcoma of the iris in which the tumor showed dissemination in the aqueous humor.

Schappert, Kinuyser and Mulock Houwer found in an eye with sarcoma of the iris a so-called "smallest" sarcoma of the choroid which they declare as melanoma.

Kurz reports a symmetrical iris tumor consisting of nonpigmented spindle-shaped cells which he considers as endothelioma.

Eleonskaja reports angiosarcoma of the iris.

Spontaneous cysts of the pigmentary epithelium of the iris and the ciliary body are described by Anargyros, Bliedung, Braunstein, Elschnig, Fischer, Granstroem, Remky, Town.

Gowland and Gallino report spontaneous serous cysts of the iris arising from the anterior layers of the iris.

Laval found a spontaneous cyst of the iris lined with a membrane of endothelium.

Fillippow reports spontaneous serous cysts of the iris.

A congenital cyst of the ciliary body lined by the two layers of the ciliary epithelium is described by Elschnig. It is formed by congenital adhesions of ciliary processes.

Cary reports cyst of the ciliary body.

Caramazza reports histologic findings in traumatic and spontaneous epithelial cysts of the iris.

Roth and Geiger saw a multilocular cyst lined with squamous epithelium between iris, ciliary body and lens following a perforating injury.

Brownlie describes an eye enucleated on account of a cyst produced by a stitch in operation for squint.

A cyst of the iris stroma is described by Hudelo as endothelial cyst due to retention after trauma.

Lundberg, Magni and Menestrina, Rumbaur report traumatic cysts of the iris.

Schoepfer reports a case of traumatic implantation cyst of the ciliary body produced by shreds of epithelium freely implanted between the ciliary body and the sclera.

Elschnig considers some cysts of the ciliary body as senile changes.

Barsan saw cysticercus in the anterior chamber where it probably came from the ciliary body.

Epitheliomata of the limbus may perforate through the sclera into the uvea (Beauvieux and Pesme, Michail, Sattler).

Cushing and Eisenhardt describe meningiomata extending from the optic nerve into the uvea.

Klein reports a choroidal sarcoma originating from diffuse sarcomatosis of the white matter of the brain and meninges extending into the orbit and eyeball.

Gilbert describes metastatic neoplasms of the choroid.

Metastatic carcinomata of the uvea are reported by Behr, Bollack, Bertillon and Roques, Cohen, Davis, Dimissianos, Giri, Hudson, Lemoine and McLeod, de Long, McDannald and Payne, Sanders, Siegrist and Cramer, Smoleroff and Agatston, Usher.

Kreibig found in a metastatic carcinoma of the eye and orbit numerous tumor emboli in choroidal capillaries and in lymph vessels of the orbit (lymphangiitis carcinomatosa orbitae.)

Archangelsky saw in choroidal veins and in the choriocapillaris and also in anterior ciliary veins carcinoma emboli. It was a metastatic breast carcinoma in a 32 year old woman, showed alveolar type and was mostly necrotic.

Brendel finds that a metastatic carcinoma of the uvea perforates the sclera along the posterior ciliary nerves, a sarcoma along the ciliary vessels.

A metastatic medullary carcinoma from the breast in a 36 year old woman is described by Clapp, and Potechina saw a case of medullary carcinoma of the choroid with primary tumor in a bronchus.

De Logu's case of a 41 year old woman had metastatic scirrhus carcinoma of the choroid and optic nerve with primary tumor in the breast.

Knapp reports a metastatic adenocarcinoma with the primary tumor in the breast.

Stallard saw a metastatic adenocarcinoma of the iris with the primary tumor in the bronchus.

Zamenhof and Pluskier, report an adenocarcinoma of the choroid with the primary tumor in the stomach.

A metastatic adenocarcinoma of the choroid with the primary tumor in the sigmoid is reported by Dixon and Benedict and a gelatinous carcinoma of the choroid with the primary tumor in the rectum by Sallmann.

Orr and Johnstone report a thyroid carcinoma metastasizing into the ciliary body.

Venco reports a choroidal metastasis of an adenocarcinoma of the thyroid consisting of alveoli with colloidal content in a 59 year old man and Cords and Eigel report the metastasis of colloid goitre in the choroid of a 34 year old woman.

Goldstein and Wexler report a metastasis in the choroid from an adenocarcinoma of the testis in a 4 year old boy.

Cordes found metastatic adenocarcinomata in the choroid of both eyes in a 30 year old woman with a scirrhus carcinoma of the breast.

A bilateral metastatic adenocarcinoma of the choroid was found by Bedell in a 49 year old woman whose breast had been amputated 4 years previously.

Isaak reports the metastasis of adenocarcinoma in the choroid of both eyes in a disease of the stomach.

A metastatic carcinoma of the choroid of a 51 year old woman with a primary tumor in the breast was of a papilliferous, alveolar type (Finkelman and Mayer), and Michail found a papilliform glandular tumor of the choroid in a 63 year old man, probably a metastasis from a primary intestinal tumor.

Morax and Valiére-Vialeix found a metastatic intra-ocular tumor in a 61 year old woman with an epithelial structure, as in an ovarian tumor or Wolffian body.

Goodsitt reports a metastatic carcinoma of the choroid with a primary squamous cell carcinoma of the lid, and Larsen found a metastatic carcinoma of the iris in a case of basal cell carcinoma of the esophagus.

Stallard describes cases of metastatic carcinomata of the choroid with the primary tumors in the breast, lungs and prostate.

Schinz describes metastases in the eye from carcinomata of the breast.

Goldsmith reports extensive carcinoma metastases of the uvea extending into the anterior chamber with the primary tumor in the breast.

Asbury and Vail saw metastatic carcinoma of the iris from a breast tumor in a 49 year old woman, and Tooker reports a metastatic carcinoma of the iris and choroid with the primary tumor in the breast in a 46 year old woman.

Giri, Johnston, Vetter describe cases of metastatic carcinomata of the choroid with the primary tumor in the breast.

Valhoun, Nelson, Orth, Papolczy report metastatic carcinomata of the choroid and of the optic nerve with the primary tumors in the breast.

Kreibig reports carcinoma metastases in the iris and ciliary body with the primary carcinoma in the bronchus.

Ask saw histologically the metastasis of a bronchus carcinoma in the choroid in a 69 year old man.

Fileti's case of a 74 year old man with a metastatic carcinoma of the choroid extending into retina and optic nerve died of carcinoma of the lungs.

Thomas and Sladden describe a metastatic carcinoma of the choroid with the primary tumor in the mediastinum.

A metastatic carcinoma of the ciliary body with the primary tumor in the stomach in a 68 year old man is reported by Adda.

Hypernephroma can metastasize into the uvea (Fledelius, Hird, Hudson and Lister, Shcheglova, Stock).

Kreibig describes a metastatic hypernephroma of the eye growing along the posterior ciliary nerves in the sclera.

Casanovas reports a case of metastatic uveal sarcoma with primary tumor in the kidney.

Cordes and Horner found metastatic melanomata of both eyes in iris, ciliary body and optic nerve, following the removal of melanosarcoma of the left scapular region.

Lisa and Givner found in a 68 year old man with malignant melanoma of the axilla, metastases in the uvea and the orbit; Corrado a metastatic melanosarcoma of the ciliary body in a 26 year old man with a nevus of the leg. A sarcoma of the choroid metastatic from a nevus is further reported by Fry, and Elschnig reports metastatic spindle cell sarcoma of the uvea with its primary seat in the ovary.

v. Hippel reports a round cell sarcoma of the lacrimal gland of a 10 year old child metastasizing into the iris and the ciliary body of the eye of the other side.

Lees describes metastatic osteosarcoma forming in the choroid osteoid tissue and showing cells with rounded and oval nuclei. The primary tumor appeared in the knee after an injury.

Metastatic retothelial sarcoma of the choroid with the primary tumor in the small intestine is reported by Buschke.

McDonald found a choroidal chorionepithelioma secondary to a teratoma of the testicle.

Metastatic chorionepitheliomata of the choroid are further reported by Godtfredsen, Reichling.

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Chapter VIII

PATHOLOGY OF THE RETINA

1. General Considerations

The pathologic changes here are determined by the fact that the retina is composed largely of ectodermal elements forming the nervous substance and the supporting tissue (glia), and in smaller part of mesodermal elements of the blood vessels, and further, that only the inner retina is supplied by these vessels, while the outer retina is nourished from the uvea. The nervous elements never hypertrophy. They react to pathologic irritation with degeneration. The ganglion- and bipolar cells and nerve fibers degenerate in disturbances of the blood circulation in the retinal vessels, in inflammatory processes of the vitreous and in intoxication. The chromatin of the nuclei disintegrates, the cell structure becomes indistinct and may contain lipoid substance and finally the cell disappears. The nerve fibers swell and disintegrate. Rods and cones and their cells suffer in diseases of the uvea. The former are transformed into clumps, the nuclei migrate into the subretinal space and the cells disintegrate. If the supply of oxygen and the nutrition are impaired, autolysis sets in; under the influence of toxins, heterolysis of the protein with decomposition sets in. Often fat appears free, in the tissue in the form of droplets and clumps and in glia, pigment epithelium and in vessel walls as fat droplets and as droplets in phagocytes which originate from elements of the pigment epithelium and the glia.

The glia, which is composed of cells which are of varied structure and of fibers, forms especially a dense glia mantle around the adventitia of the vessels (limitans perivascularis) and cellular accumulations around larger ganglion cells. This separates nervous tissue from mesoderm and protects the nervous substance by letting through only certain nutritional elements. Defects of the glia are soon replaced by glial proliferation

and defects of the nervous substance are substituted chiefly by gliosis. Proliferating glial cells frequently take manifold forms, becoming similar to epithelial cells or ganglion cells; they form cells similar to fibroblasts and may surround connective tissue and mix with it, proliferating into the vitreous and even more frequently into the choroid. Occasionally, compensating glial hypertrophy sets in if the glial tissue substituting for the destroyed nervous elements continues to grow excessively. In this condition—called gliosis of the retina—the retina in this area is thickened and consists of spindle-shaped cells and fine and coarse fibers. The pigmentary epithelium frequently participates in the pathologic process. The pigmentary epithelium is primarily affected or participates in diseases of the retina and uvea. The cells become separated, clump and lose their granular pigment. The cells can remain as ghost cells in the subretinal space and such ghost cells accumulate occasionally to form large masses, often containing fatty granules, or the epithelial cell migrates pigmented into the retina or choroid. Isolated cells of the pigment epithelium may become macrophages. The degenerating cell participates in the formation of drusen. Pigment epithelium can also proliferate continually. Malnutrition and senile changes of the tissue lead to necrobiotic processes in which cysts are formed by edema, calcium is deposited and corpora amylacea appear.

2. Vascular Diseases of the Retina

Alterations due to different causes showing similar histologic pictures are grouped together, such as senile, metabolic and toxic changes, on the one hand, and circulatory disturbances which can be observed only functionally but not histologically, on the other. In this group belong: (1) vascular sclerosis, (2) retinal hemorrhages, (3) circulatory disturbances of the central retinal vessels (especially their obstruction), and (4) inflammatory changes of the walls of the veins and arteries.

Vascular sclerosis shows similar histologic changes if it is caused by senile degeneration or is of metabolic or toxic nature or the sequela of increased pressure on the vessels from outside the vessel wall. The arteries are more frequently affected than

the veins but not to the same extent; in many cases, all layers of the vessel walls are involved and the changes are patchy or diffuse.

(a) The subendothelial tissue proliferates and hyaline plaques appear; endothelial cells also proliferate. Circumscribed atheromatous plaques of the intima are found patchy in their distribution, with fatty and even calcareous deposits in the retinal arteries only infrequently.

(b) The muscular media becomes fibrous and thicker, elastic tissue is newly formed and the entire media also undergoes hyaline degeneration.

(c) The adventitial tissue becomes fibrous and enlarges and may also undergo hyaline degeneration.

It should be noted here that appearance of sclerosis of the retinal vessels is often more distinct ophthalmoscopically than in microscopic section. It is frequently difficult to find in the microscope those changes which have been detected with the ophthalmoscope. Sclerotic vessels are found localized inside the eye without further vascular pathology outside of the eye due to increased local tissue pressure, or locally often due to chronic specific and nonspecific inflammation. Sclerotic vessels are found in glaucomatous eyes even in children, in shrunken eyes, and in detachment of the retina. Sclerotic changes are sometimes part of a retinopathy or its cause. In this case, the muscularis of the media is usually hyaline degenerated and thickened. On the other hand, the hyaline degeneration of the media may also be part of the general hyaline degeneration of the affected tissue. Furthermore, the sclerotic changes are part of a generalized vascular disease, especially of cerebral vessels, but also of the vessels of the entire body. Diffuse senile arteriosclerosis, which brings about a hyaline degeneration of the media as part of the wear and tear of life and often occurs without an increase of the blood pressure, brings about similar changes of the media of the retinal vessels. Extensive sclerotic changes can be present without a disturbance of the circulation. The retina may stay normal otherwise or show senile changes. The hyaline degeneration and thickening of the media corresponds to the ophthalmoscopic picture of the copper-wire arteries. If the hyaline degen-

erated wall becomes very thick and the lumen narrow, the ophthalmoscopic picture of the silver-wire arteries originates. The central retinal vein scleroses mostly where it passes through the lamina cribrosa. In senile arteriosclerosis with increased blood pressure (involutionary arteriosclerosis with hypertension), there are also changes of the media and proliferations of the endothelium, which are concentric, eccentric or appear in the form of folds. In all of these cases, the lumen is narrowed or even occluded; also when the folds of the intima grow together. The attenuation of the retinal arteries is the result. Subendothelial hyaline and fatty degeneration with increase of the connective tissue can appear as sheathing in the ophthalmoscopic picture. In some cases, the entire wall may be infiltrated with round cells and the separation of the layers of the vessel walls become indistinct. The adventitia becomes fibrosed and thickened, also resulting in sheathing. The constriction of the veins in their different forms (concealment, tapering, compression), described by Gunn, and the deflection (described by Salus) are apparently caused by thickening of the adventitia of the artery and vein at their crossing.

Essential hypertension represents a hyperirritability of the vasomotor center in the brain, the cause of which may be heredity, endocrine disturbances, toxemia, infection, or of psychologic nature. A reactive contraction of the smaller vessels develops, which first exists without pathologic changes and disappears after cessation of the hypertension, or is followed when the hypertension lasts longer by hypertrophy of the muscularis and thickening of the intima, therefore by sclerotic changes. Frequently, renal damage is found in the latter case, which in itself keeps the blood pressure high.

Transitory hypertension is caused by acute and subacute glomerulonephritis, toxemia of pregnancy and hyperthyroidism. Small arteries become spastic. But this, as in essential hypertension, is equally unrecognized histologically except that hypertrophy of the media has already set in.

Benign arteriolosclerosis is a reaction to increased strain in long-lasting hypertension and affects diffusely the arterioles of the body and especially those of the kidney. It produces here

alterations in glomeruli and parenchyma, causing irreversible hypertension. In the smaller retinal arteries, the intima is affected, in which subendothelial hyaline and fatty degeneration sets in and proliferation of the endothelium appears with narrowing or closure of the lumen. The otherwise thin media of the arterioles is frequently thickened. The thickened arterioles are more easily visible than the normal vessels in the normal fundus and have a corkscrew appearance.

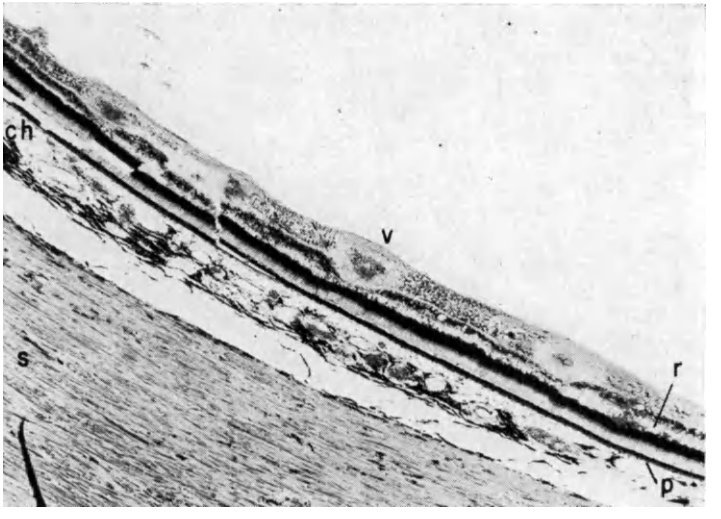

FIG. 35.—SCLEROSIS OF RETINAL VESSELS. ch, choroid; p, pigment epithelium; r, retina; s, sclera; v, sclerotic vessel showing hyalinization of the adventitia and proliferation of the media and intima. 70×.

Malignant arteriolosclerosis is rare in the eye. It forms a circumscribed necrosis of the walls of the arteriole.

It can be concluded from the above description that hypertension is usually the primary change and the vascular changes follow secondarily, but it is possible that vascular changes may be primary and produce secondary hypertension.

Retinal hemorrhage. The appearance of retinal hemorrhages depends on the intensity and type of sclerosis of the retinal vessels as well as the locality of the hemorrhage. They are the result of diapedesis from the capillaries when the blood circula-

tion is slowed in the veins or when the walls of larger vessels become fragile by sclerotic changes. Thrombosis sets in, usually in sclerotic veins, less frequently in sclerotic arteries. This happens in veins especially where they cross the arteries and is usually due to obstruction by the sclerotic artery. Venous thrombosis leads to extensive hemorrhages. The retinal hemorrhages appear in the nerve fiber layer where the blood spreads along the course of the nerve fibers (flame-shaped in the ophthalmoscopic picture) and in the inner plexiform and nuclear layers where they are round or more irregular.

The circulatory disturbances in the distribution of the central vessels of the retina (especially their obstruction). Passive hyperemia appears in the veins of the retina under different conditions, especially if the large veins in the skull or in the chest are congested. It is found, therefore, in heart failure, emphysema, thrombosis of the venous sinus of the brain, inflammations and neoplasms of the orbit, thrombosis of the central vein in the optic nerve. The hyperemia is of high degree in cyanosis of the retina, which usually is associated with polycythemia rubra or congenital stenosis of the pulmonary artery. The retinal vessels are enormously dilated and filled with blood. If the passive hyperemia appears in cases of endovascular changes with thrombosis, massive hemorrhages appear in the retina.

Retinal ischemia (anemia) is chiefly seen in obstruction or rupture of the central artery, in lasting spasm of the retinal arteries and in their obstruction by concentric thickening of the wall, but also in general anemia (especially after profuse loss of blood), in arterial hypotony (as in decompensation of heart failure). The pathologic changes are retinal edema in the layer of the nerve fibers and ganglion cells and degeneration of ganglion cells and nerve fibers and finally complete atrophy of the optic nerve.

Obstruction of the central retinal vein (endophlebitis, thrombosis of vein) affects the main stem in the optic nerve or its distribution in the retina. Usually depending on the stage or etiology, are found: (1) blood coagulum in the lumen, (2) organization of the thrombus, (3) wall changes (meso- and endo-

phlebitis, with and without formation of thrombus), (4) hemorrhages in the retina, (5) edema, cysts, fibrin and homogeneous coagulates in the retina. Intravital thrombus and postmortem blood coagulation in the vessels are often difficult to distinguish from each other. If fibrin is formed then a thrombus is present. If a thrombus exists for only a short duration secondary changes appear, endothelial cells, fibroblasts and fibers grow into the thrombus, the erythrocytes break up and are dissolved or blood pigment is formed. Causes of thrombus formation are slowing of circulation, abnormal composition of blood, but frequently there is an alteration of the vessel wall, usually of an arteriosclerotic nature. The media is thickened and the endothelium proliferates. The vessel wall is infiltrated and finally becomes indistinct, if the wall degenerates and fuses with the organized thrombus. Pigment gathers sometimes in the vessel wall and around the vessels. Stasis in the veins distal to a thrombus or another obstruction of the lumen causes an exuding of blood from the dilated capillaries in great quantities and then the nerve fiber layer is filled with hemorrhages appearing flame-shaped clinically, which sometimes are subhyaloid. Hemorrhages into the vitreous occur only in profuse hemorrhages which mechanically break the internal limiting membrane, or in venous thrombosis due to inflammatory processes in the walls of the veins, or in the retina which erode the membrane. The inner retinal layers become edematous and cystic, but in more severe cases cysts appear also in the outer layers; albumen and fibrin are deposited, and finally the inner layers atrophy. Cystic changes and accumulation of pigment occur also in the macular region. New anastomosing vessels are formed, which connect the distal parts of the thrombosed veins with free branches or the main stem of the central vein. Vessels and tissue grow into the vitreous body, if vitreous hemorrhages are present, and organize them.

Thrombosis has many causes and frequently several act together. The curvatures of the veins are predisposed to thrombosis. Slowing of the blood flow can produce thrombosis without primary changes in the walls. The blood flows slower in the veins for various reasons, as when the arteries are

narrowed for any reason, when the blood pressure is very low as in marasmic states, or when the veins themselves are narrowed in circumscribed areas by a thickening of the wall or compression from the ouside. The last-mentioned condition occurs especially in the region of the lamina cribrosa if the vessel is sclerosed, or if the neighboring artery shows sclerotic thickening of its wall, or if the connective tissue which envelops both vessels proliferates. At a crossing of an artery and vein where both possess a common adventitia, the sclerotic artery compresses the vein. A pathologic composition of blood may cause thrombosis. Meso- and endophlebitis narrows the lumen and at the roughened areas of the endothelium which are mostly of a sclerotic nature the blood coagulates. In the majority of cases, sclerotic changes are the cause of the venous obstruction, but in rare cases endophlebitis caused by toxin is said to be responsible for the thrombosis. Severe infection with various organisms, with bacteremia and toxemia is held as cause. Toxin diffusing from iridocyclitis through the vitreous body is said to cause thrombosis. Thromboangiitis obliterans may be the cause. If the main stem of the central vein thromboses, very often secondary glaucoma sets in, the cause of which is not quite known. Inflammation of the chamber angle caused by toxin from the deteriorating retina ending in obstruction of the angle is considered to be the cause of this glaucoma.

Obstruction of the retinal arteries causes edema and degeneration of the nerve fiber and ganglion cell layer of the affected retina due to cessation of the blood flow. The nerve fibers first manifest a varicose and fatty degeneration, albuminous coagulation follows and later the inner retinal layers atrophy completely. Hemorrhages are rare and are caused probably by a back flow of blood in the veins. The obstruction is caused by (a) angiospasm, (b) embolism, (c) endarteritis, and (d) thrombosis. Angiospasm happens in persons with vasomotor disturbances of a functional nature due to toxemia and poisoning (alcohol, tobacco, quinine, lead) and in persons with arteriosclerotic and syphilitic vessel changes complicated by hypertension. An embolus may occlude the stem or a branch of the central artery without the vessel wall itself being diseased. An

embolus may occlude the lumen completely or partly; however, a mural embolus may also lead by apposition to a thrombus completely occluding the lumen. Endothelium and fibroblasts may proliferate from the vessel walls into the embolus and thrombus respectively, so that they become organized. A large embolus nearly always stops in the artery where it passes through the lamina cribrosa and where its lumen is narrowed, while smaller emboli reach a branch in the retina and often stop at a bifurcation. Emboli break off from mural thrombi and vegetations of the valves of the heart, but are also blood coagulates, septic material, particles of malignant tumors, fat and air. Frequently, the lumen of the central artery is occluded in the lamina cribrosa or in the retina by proliferation of the intima, to which thrombosis may be added. Thromboangiitis obliterans is said to be associated with occlusion of retinal arteries.

Retinal hemorrhages, as already mentioned, usually originate from the capillaries. Blood exudes from them in stasis of the circulation, further in hypertension, in malnutrition, in toxic and inflammatory changes of the endothelia and in a sudden decrease of the intra-ocular pressure. Hemorrhages more rarely have their origin from arteries or veins, if their walls are brittle in sclerotic processes and in infective processes. The hemorrhages are in the nerve fiber-ganglion cell layer or reach through the inner nuclear layer into the outer plexiform layer. They seldom disappear without leaving sequelae. They leave degeneration and atrophy of the affected part of the retina with proliferation of glia in their wake, but there may be lipoid and cholesterol, hyaline-like material and cystic spaces remaining to indicate preceding hemorrhages; hemosiderotic pigment is deposited and occasionally phagocytes appear. Retinal hemorrhages are caused by trauma in retinopathy and blood diseases, occlusion of retinal veins or stasis of the venous outflow due to thrombosis of the cavernous sinus or papilledema, by inflammation, intoxication or arteriosclerosis. Similar causes may produce a subhyaloid (preretinal) hemorrhage which seems to take a special position, since it frequently, but not always, disappears without sequelae. It is situated between the inner limiting membrane and nerve fiber layers and rarely between

detached vitreous and inner limiting membrane. Cases are rare in which the hemorrhage apparently is situated between two membranes which seem to be formed by splitting of the inner limiting membrane.

Vasculitis, especially perivasculitis. Inflammatory processes which are, in the majority of cases, nonspecific, more rarely tuberculous and syphilitic, appear more frequently in the veins

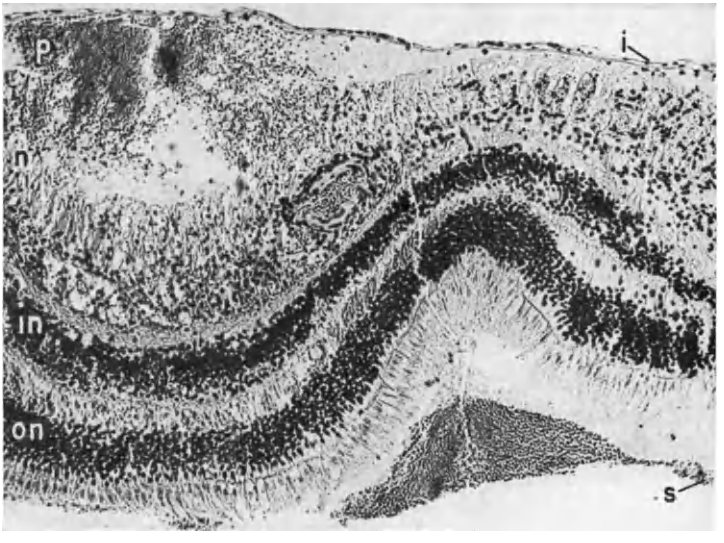

FIG. 36.—PRERETINAL (SUBHYALOID) HEMORRHAGE. i, internal limiting membrane; in, inner nuclear layer; n, layer of nerve fibers; on, outer nuclear layer; p, preretinal hemorrhage; s, subretinal hemorrhage.

than in the arteries. Most frequent is periphlebitis. It may be primary, in which case it is produced by an agent which is carried into the eye by the central artery and stops in the capillaries and small veins, from where it extends along the vessel sheaths into the larger veins; or it may be secondary to an inflammation of the uvea, which extends from the anterior choroid into the retina and affects here the sheaths of the smaller vessels or diffuses toxins into the vitreous body which affect the veins through the internal limiting membrane. The sheaths of the veins are filled with lymphocytes, plasma cells, monocytes and

epithelioids. The lymphocytic mantle increases in intensity and finally fills the entire adventitia. Cells can be seen to pass through the loose structure of the vessel walls, often only on one side, often circularly. They may cover the entire vessel wall and narrow the lumen without altering the endothelium. Probably the infiltrating cells of the vessel sheath originate directly from the adventitia. It seems that in the presence of organisms or in long-lasting metabolic disturbances, the vessel wall itself finally suffers and takes part in the inflammation and degeneration. The vessel wall splits up, becomes hyalinized or is intensely filled with inflammatory cells. Finally the endothelium participates in the process; it swells, proliferates and disintegrates. As a sequel of the vascular disease, thrombosis sets in (thrombophlebitis), and with this, hemorrhages appear. They can be very massive since frequently the capillaries are also diseased and break. By the amount of the blood itself or the internal limiting membrane being affected by the inflammatory changes in the surrounding tissue of the periphlebitis, the blood pours into the vitreous body. Thrombosed vessels finally show organization. Connective tissue proliferates and fills the infiltrated vascular tissue and the thrombi and finally a fibrous node remains which may contain round cells and into which glial tissue proliferates.

In chronic iridocyclitis, not only toxins, but also lymphocytes and fibrin, exude through the base of the vitreous and into it, and are then carried into the posterior segment of the eye. The cells clump and are deposited on the inner limiting membrane as retinal precipitates. Such a condition may also originate if the cells enter the vitreous from the lymphocytic mantles of the vein through the inner limiting membrane. Frequently, precipitates are situated over periphlebitic veins. The toxins themselves, as already mentioned, diffuse through the limiting membrane and cause the appearance of lymphocytes in the sheaths of the veins, a reaction of chemotaxis. If the stimulus is strong, the retina becomes edematous, especially in the macula, with formation of small cysts and even a circumscribed detachment of the retina; there is diffuse infiltration of the nerve fiber ganglion-cell layer with lymphocytes and few plasma cells

(retinitis secondary to iridocyclitis). Or inflammation of the anterior choroid extends into the ora serrata and the vascular sheaths of small veins become secondarily affected. From here, the process expands into the larger veins, in this way again producing periphlebitis. Perhaps, more likely, toxins diffuse from an iridocyclitis into the vitreous and produce periphlebitis by chemotaxis. Though these cases usually do not lead to severe changes in the retina and vitreous, such changes appear immediately when the vessel wall is affected and thromboses are formed. Then, as already mentioned, it starts to bleed into the vitreous, the condition being seen in juveniles as recurrent intraocular hemorrhages (Eales' disease, angiopathia retinalis juvenilis), and also appearing in older individuals as single or recurrent hemorrhage.

Tuberculosis is considered a principal cause of the vascular changes in juveniles which can be primary or secondary, producing typical tuberculous tissue in the walls of the retinal veins. Furthermore, the vessel changes appear as manifestation of allergic conditions and sometimes caused by toxins of various origins. They are sequelae of repeated disseminations of bacteria due to mild septicemia. Some cases seem to be caused by thromboangiitis obliterans (Buerger's disease) which affects arteries and veins and is accompanied by an infiltration of the adventitia and media with polymorphonuclears and lymphocytes and thrombosis with organization and closure of the lumen; it is said to be caused by nonhemolytic streptococci and to be an allergy to tobacco. Tuberculosis must also be considered in the etiology of periphlebitis in old individuals; syphilis, diabetes, and arteriosclerosis are to be mentioned, too, not only as processes of inflammatory but also of degenerative nature.

Retinitis proliferans (Manz) appears as a sequela of the vitreous hemorrhages with new vessel formation in the vitreous which help to absorb the hemorrhages or organize them, and also provide a collateral circulation for the obliterated veins. The latter rarely happens in thrombosis of retinal veins without hemorrhages into the vitreous, in which case a collateral vessel connects a vein of the retina with one in the disc. Strands and membranes consisting of fibroblasts and connective tissue fibers

grow in retinitis proliferans from the surrounding tissue of the large retinal vessels through the internal limiting membrane, as well as from the physiologic cup of the papilla into the vitreous. The tissue is sometimes a fine membrane consisting of large, flat endothelial-like cells with oval nuclei (endothelial membrane). Sometimes the tissue is coarse, sometimes there are numerous vessels with thin walls, and sometimes there is a paucity of vessels. The quantity of the fibrous tissue is often in reciprocal relation to the number of vessels—the more fibrous tissue, the less vessels and vice versa. Apparently also the glial tissue of the inner retinal layers participates in the proliferation into the vitreous. The proliferating tissue contains few cells of inflammatory nature such as lymphocytes and monocytes. The contraction of the proliferating tissue may produce a detachment of the retina. The newly formed vessels of the vitreous have thin walls and consist of an endothelial tube with a thin media which occasionally becomes thicker. The vessels are often accompanied by a homogeneous tissue which contains few spindle-shaped cells and fibers. The endings of the vessels in the vitreous often form coil-like convolutions and brushlike capillaries, from which vessels return to the retina. The vessels originate either entirely from the retina and their circulation closes in it, or they come from the papilla and return to the retina, in this way being distinguished from vascular loops which enter the vitreous from the central vessels of the papilla and return to the papilla. The vessels sometimes form an extensive suspended network in front of the papilla and retina (rete mirabile). The vessels can show regressive changes also and disappear again after absorption of the hemorrhages. The tuberculous periphlebitis which originates either hematogenously through the deposition of tubercle bacilli in the venous walls, or through transport of tuberculous material from the ciliary body (tubercle bacilli and wander tubercles in form of epithelioids and giant cells) through the vitreous or through the ora serrata directly into the vascular sheath of the veins in the retina, is characterized by an accumulation of lymphocytes, epithelioids and giant cells in the vascular sheaths of the veins. Usually the media and intima of the vein also become inflamed, throm-

bosis sets in with recurrent hemorrhages in retina and vitreous and finally retinitis proliferans results. Frequently in tuberculosis of the anterior uvea there may appear nonspecific periphlebitis with its sequelae. In syphilis, specific and nonspecific inflammatory deposits in the vascular sheaths of the veins with their sequelae probably appear if spirochetes are deposited in them. In general, the periphlebitis is considered to appear first

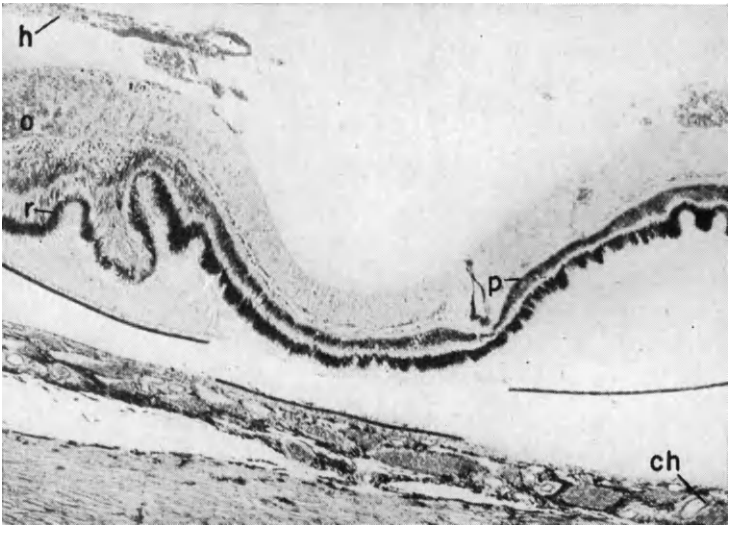

FIG. 37.—PERIPHLEBITIS RETINALIS, VITREOUS HEMORRHAGES. ch, choroid,; h, vitreous hemorrhages; o, occluded retinal vein; p, periphlebitis; r, folded detached retina.

and from it the inflammation of the other layers of the walls results with the formation of thrombosis. The accumulation of cells in the vascular sheath is the response to irritants, which act from without on the vessel, and is a defense mechanism leading finally to their arrest and elimination. On the other hand, in some instances the vessel wall is affected first when the inflammatory agent is in the circulation and is deposited in the walls, and the periphlebitis is secondary to the inflammation of the wall and is the attempt to hinder the progress of these agents to proceed from the vessel wall into the surrounding nervous tissue.

Periarteritis is seen less frequently than periphlebitis. The thick arterial wall certainly resists the transmigration of cells very strongly. The accumulation of lymphocytes in the perivascular sheath of the arteries is, in the majority of cases, continuous from the sheath of the veins in the region of the arterio-venous crossing. The accumulation of cells in the periarterial sheath can also continue into the media. A special form develops, the periarteritis nodosa, in which inflammatory nodules appear in great numbers on small arteries. The adventitia more than the media are filled with polymorphonuclears, lymphocytes and plasma cells, the media is split into fibers, connective tissue proliferates and the intima thickens. The wall becomes necrotic in circumscribed areas. Thromboses and eventually aneurisms are formed if the wall gives way. The cause of this generalized vascular disease which mainly attacks the gastrointestinal tract, the kidneys and heart, is unknown. It is thought to be an infection, especially with streptococci and staphylococci; some nodules may be mycotic aneurisms, but perhaps it is an allergic manifestation.

3. Retinopathies and Retinitides

Retinopathies

Degenerative and exudative processes appear in the diseased retina for various reasons, mostly as sequelae of general diseases and as sequelae of diseases of the retinal vessels, which themselves may be caused by general disease. There are: (1) vascular retinopathies, (2) renal retinopathy, (3) retinopathy in pregnancy, (4) diabetic retinopathy and (5) retinopathies due to toxin. Common to them are hemorrhages in different layers of the retina, deposition of various substances in the layers of the retina which appear histologically as fibrin, hyaline, colloid, lipoid, and fat and which represent the retinitic patches, and more or less definite vascular changes.

In *vascular retinopathy* the sclerotic changes of the vessels are prominent and changes in the kidneys are absent or minimal. It is seen (a) as an arteriosclerotic retinopathy and (b) as a malignant hypertensive retinopathy.

Arteriosclerotic retinopathy appears in long-lasting sclerotic changes of the retinal vessels and hypertension. The retina is free of edema and the papilla is normal. Rounded hyaline masses are deposited in the external plexiform layer and small hemorrhages appear in the nerve fiber and in the plexiform layers.

Malignant hypertensive retinopathy, on the other hand, shows an especially severe edema of the papilla and of the peripapillary retina. In the area of the edema, the veins are congested and surrounded by lymphocytes, severe hemorrhages appear in the plexiform layers and there is exudation of hyaline substance and of serous fluid in small quantities into the subretinal space. The pigment epithelium may degenerate and proliferate. Arterioles show necrosis of their walls, vessels of the choroid are very sclerotic and some are obliterated.

In both cases, the vascular damage is the primary condition, and, due to the constriction of the vessels, the retina does not get enough blood, resulting in anoxemia and malnutrition. Slowing of the blood circulation, dilatation of the capillaries with transudation of fluid and especially toxemia seem to produce the severe changes of the malignant retinopathy which may exist without renal disturbances.

Renal retinopathy is characterized by changes in all layers of the retina; marked edema is present in the inner retinal layers. The nerve fiber layer shows varicose swellings of nerve fibers (ganglioform degeneration, cytoid bodies). They appear as large, cell-like formations with darker staining nuclear-like bodies in the center, with acidophil-staining qualities like the rest of the formation. They are interpreted as swollen, degenerated nerve fibers in cross section or as degenerated phagocytes. Fatty granules are found when the nerve fibers and ganglion cells disintegrate. Old and fresh hemorrhages are present in the nerve fiber and inner plexiform layers. The nuclei of the inner nuclear layer are separated. The outer plexiform layer (including the fibers of Henle) shows the most changes. It contains networks of fibrin in apposition with fat lying basket-like in cystic spaces which are surrounded by Mueller's fibers. Exudate also appears as homogeneous albuminous and hyaline masses in the same layer. In addition, there are cystic spaces filled with

phagocytes which appear as large, rounded bodies with small, compressed eccentric nuclei, the cytoplasm of which contains many lipoid droplets appearing as small vacuoles, due to the solution of the lipoid in the fixation fluid (bladder cells). Homogeneous particles in connection with the supporting tissue of the retina are scattered diffusely in the tissue. Netlike formations appear also as products of degeneration of the nervous elements. Rods and cones are disintegrated. All the pathologic processes may be seen ophthalmoscopically as white patches: edema, fibrin, varicose swollen nerve fibers, fatty deposits and hyaline masses. The radial arrangement of Mueller's fibers in the macula produces the star-figure of the whitish patches. Serous fluid and fibrin can be poured out into the subretinal space, producing detachment of the retina. The retinal vessels are sclerotic and only infrequently normal. Degenerative changes and proliferation of pigment epithelium are infrequent. Sometimes migration of pigment epithelial cells in the form of bladder cells can be seen which appear as rounded large cellular bodies with pyknotic nuclei containing little pigment. If the pathologic material is removed from the retina, some restitution can be expected, but usually a shrunken, disorganized membrane remains in which glia and connective tissue elements proliferate. Edema of the papilla with hemorrhages and exudation frequently exists. Renal retinopathy is seen in renal damage leading to toxemia and hypertension with sclerosis, and is seen in chronic glomerulonephritis and benign and malignant nephrosclerosis. The chronic glomerulonephritis (chronic interstitial nephritis, granular contracted kidney) caused by repeated infections or intoxications produces fibrosis of the intima of the arteries with narrowing of their lumen. This leads to renal ischemia which produces or increases hypertension. Essential (benign) hypertension may produce in time renal insufficiency when benign nephrosclerosis appears, in which hyaline degeneration of the arterioles results with narrowing of the lumen followed by fibrosis of glomeruli and degeneration of some tubules, and which takes a chronic course. If circumscribed arteriolar necrosis with endothelial proliferation is caused by toxemia, malignant nephrosclerosis follows, in which glomeruli swell, degenerate and become

necrotic and tubules undergo fatty and hyaline degeneration, and which takes a more acute course. The cause of the retinopathy is said to be the damage of the tissue by the vascular changes. The lumina of the arteries and arterioles are narrowed in hypertension, causing ischemia and degeneration of the tissues by malnutrition and anoxemia of the capillaries with endothelial damage, diapedesis of blood and transudation of fibrin and plasma into the tissue. Accumulation of nitrogenous metabolites

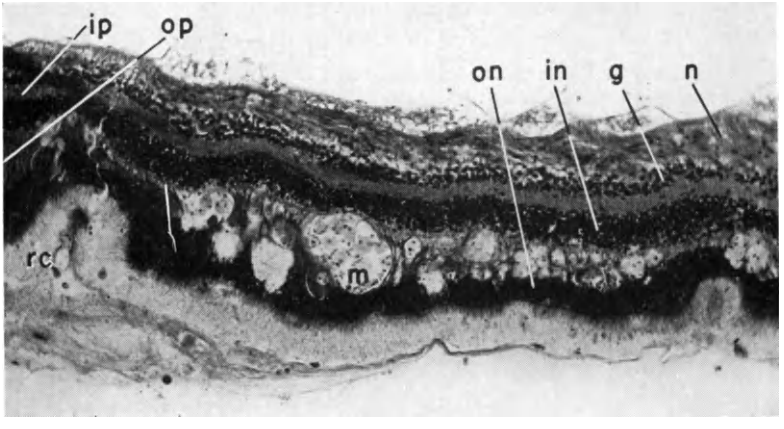

FIG. 38.—ALBUMINURIC RETINOPATHY. g, ganglion cell layer; in, inner nuclear layer; ip, inner plexiform layer; m, macrophages; n, layer of nerve fibers; on, outer nuclear layer; op, outer plexiform layer; rc, layer of rods and cones. 75×.

in the blood due to renal insufficiency (azotemic retinitis) or increase in toxic polypeptides, are said to damage the retina. Another assumption is that toxins of unknown nature are necessary for the onset of the retinopathy.

Retinopathy in pregnancy is accompanied by nephrosis characterized by tubular degeneration and hypertension. The toxemia in pregnancy and also the changes of the eye are mostly transitory and therefore the eyes are rarely examined histologically. The retina shows changes similar to those in renal retinopathy and retinal detachment may appear due to a subretinal exudate. The cause is toxemia of unknown origin.

Diabetic retinopathy shows small hemorrhages and albuminous masses in the outer plexiform layer with many cystic spaces containing fatty deposits. Vessels generally are sclerotic and the endothelium proliferates. The pigment epithelium contains glycogen. Hypertension, vascular changes and probably also renal disturbances are responsible for the appearance of the

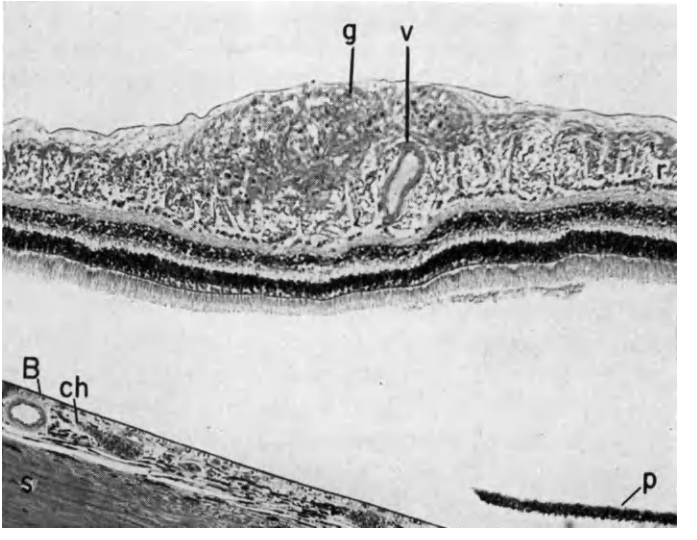

FIG. 39.—GANGLIOFORM DEGENERATION OF NERVE FIBERS OF THE RETINA. B, Bruch's membrane; ch, choroid; g, ganglioform degeneration; p, pigment epithelium artificially broken; r, retina artificially detached; s, sclera; v, sclerotic blood vessel. 70×.

retinopathy. Acetone is said to be toxic and to damage the retina.

Retinopathies due to toxin form a group of clinically different diseases of the retina, which show degeneration and exudation. Also, retinopathies caused by vascular disease, as already mentioned, are often explained by a hypothetic toxic factor. In some retinopathies, only toxic influences can be found to explain the pathologic changes. The toxins which directly damage the nerve substance and the endothelium of the vessels originate in infections (measles, influenza or focal infections) and in

advanced anemias, especially in carcinomatous patients. In the former case, retinitis pseudonephritica stellata is seen showing edema and exudates resembling a star in the macula, with edema of the papilla and the peripapillary retina; in the latter case, retinitis cacheticorum appears in which nerve fibers atrophy and the retina contains much lipoid. Dermatomyositis, which is characterized by edema, dermatitis and multiple muscular inflammations, usually ending fatally and probably possessing a toxic etiology, can produce extensive edematous changes, varicose swelling of nerve fibers, hemorrhages and albuminous deposits in the retina.

Blood diseases produce manifold changes of the retina, especially leukemia; polycythemia, anemias and lipemia may produce retinal diseases.

In leukemic retinitis, the retinal vessels are widely dilated and filled with nucleated blood cells, the nuclei of which appear rounded and indented and of various sizes. The perivascular spaces are massed with the same cells and are very dilated. Besides, extensive hemorrhages arise, which also contain many nucleated blood cells, and albuminous and fibrous deposits in the retina. The nerve fiber layer contains ampullar and spheroid-like varicosities and the outer plexiform layer, cystic spaces. The subretinal space may contain blood and serofibrinous fluid which detach the retina. The papilla is swollen and its vessels and the surrounding tissue show large amounts of white blood cells and hemorrhages. Mainly the choroid is markedly infiltrated with white blood cells in the vessels and in the tissue. The retinal disease occurs in acute and chronic myeloid leukemia, and in lymphoid leukemia.

In polycythemia (erythremia) which appears either as congenital polycythemia rubra vera (Vaquez-Osler's disease) or secondary in congenital heart failure, pulmonary stenosis and emphysema, the veins are immensely dilated and congested and the retina and papilla are edematous.

Of all anemias, pernicious anemia is most often accompanied with changes in the retina in the form of hemorrhages, the center of which has degenerated leukocytes and varicose nerve fibers. Secondary anemias, especially if they are severe, as

already mentioned, lead to changes in the retina, to dilatation of veins and exudation of albuminous and lipoid substance. Probably toxic factors damaging the endothelium of the capillaries with subsequent hemorrhages and transudation of plasma are responsible for some of these changes aside from the damage that anoxemia and malnutrition have already produced in the nervous substance of the retina directly. Posthemorrhagic anemias less frequently cause retinal changes and these mainly by ischemia of the retina, showing edema and degeneration of nerve fibers and ganglion cells.

Lipemia produces changes of the retina (lipemia retinalis) nearly exclusively in diabetes with acidosis and sometimes after fractures of bones, although lipemia of other origin such as alcoholism, asphyxia or phosphorus poisoning, do not produce retinal changes. The vessels are filled with fat droplets, which can be demonstrated by staining with osmic acid or sudan III and fat is found in the perivascular spaces.

External exudative retinitis of Coats (external hemorrhagic retinitis of Coats, Coats' disease, sero-fibrinous degenerative chorioretinitis of Leber) is characterized by an accumulation of blood, exudate and organizing tissue in the subretinal space. The retina itself may contain albuminous and edematous fluid, retinal vessels show perivascular lymphocytic infiltration and sclerotic changes. The walls are hyalinized, the endothelium proliferates, occluding the lumen, and thrombi may be present. The retina may disintegrate and rods and cones degenerate. The subretinal spaces fill in different cases with sero-fibrinous fluid, albuminous masses, hemorrhages, and the retina is detached. The pigmentary epithelium proliferates and sometimes in the subretinal space and in the retina numerous large bladder-like cells appear which are considered as swollen and disintegrated white blood cells, or which are derived from the pigment epithelium and appear as ghost cells, or which are explained as degenerative products of the rods and cones or as histiocytes. The subretinal pathologic formations which usually degenerate to debris are organized by proliferation of connective tissue and glia. In the organizing, hyaline degenerating tissue into which also retinal vessels proliferate, debris is enclosed in the form of

granules and particles and cholesterol crystals, proliferating pigment epithelium, calcium and giant cells. The retina, studded with hemorrhages, finally degenerates itself. The etiology of this disease is unknown and might have a different cause in each case. Some assume degenerative changes, some mild inflammatory processes. The first changes are said to arise in the vessels of the retina, causing hemorrhages and transudation in the subretinal space and the changes are said to be of a degenerative nature or toxic in origin. Multiple miliary aneurisms in the retinal vessels may sometimes be the result of this hypothetic etiology (retinal degeneration with multiple miliary aneurisms of Leber). Also, congenital anomalies of the smaller retinal vessels are postulated. Inflammatory changes of the vessels probably caused by metastatic emboli in infections of different genesis are held by some to be the cause. Birth trauma may cause subretinal hemorrhages if the small vessels of the inner nuclear layer and outer plexiform layer burst. While vascular disturbances are put in the foreground by some, others explain them as sequelae of the retinal disease itself.

Retinitides

Although the retinopathies represent a group of retinal diseases which originate without inflammatory processes and take a noninflammatory course, it is difficult to decide if the external exudative retinitis belongs to this same group, inasmuch as perhaps it is only degenerative and exudative, but in addition a doubt remains as to whether or not inflammatory changes are the main cause. In the case of the retinitides, a definite inflammatory and often infectious etiology is found. The retinitides are of acute and chronic nature; the latter are often caused by a chronic, specific inflammation and sometimes show specific changes in the retina. Although in the retinopathies the degenerative processes are in the foreground and the exudation is secondary, in the retinitides the inflammatory changes are in the foreground, leading to exudation and producing as sequelae proliferative and degenerative processes. The vessel walls swell and polymorphonuclears are poured out in acute, and lymphocytes in chronic inflammations; edema, exudation of

fibrin and hemorrhages then follow. The polymorphonuclears of the acute inflammation often soon dissolve the nervous elements of the retina by enzymes. Chronic inflammation on the other hand produces proliferative and degenerative processes. Glia and connective tissue elements proliferate in the retina itself, finally substituting all nervous elements. The proliferation of the glia is sometimes excessive and hyperplastic and thickens the membrane (gliosis). Sometimes tumor-like massive gliosis is formed. The tissue contains groups of fine fibers and coarse fiber bundles with branching cells with rounded and oval nuclei. The proliferating tissue can extend through gaps of the internal limiting membrane into the vitreous, endothelial membranes forming in front of the retina, and through Bruch's membrane into the choroid. The tissue proliferating into the subretinal space can elevate the retina in folds when shrinking. The lost tissue is not always replaced by proliferating tissue and degenerative changes are distinctly visible affecting nerve fibers and ganglion cells, which swell first and later shrink and disintegrate. Fatty droplets originate from the disintegrating cytoplasm. Later, also elements of the nuclear layer and rods and cones degenerate. Cystic spaces are produced and if the supporting elements themselves undergo fatty degeneration the membrane collapses and shrinks. Blood vessels exhibit hyaline degeneration. Pigment epithelium degenerates and disintegrates and pigment is liberated. It is carried off by phagocytes and enters the retina with the fluid current and is carried into the perivascular lymph spaces. The pigment-free cells swell, their nuclei become pyknotic and they lose their staining quality (ghost cells, bladder cells) or eventually become phagocytic themselves. Occasionally, they are heaped upon each other in many layers in the subretinal space. They also proliferate into the retina. Cystic spaces in the retina are filled with hyaline masses, fatty and granulated masses, desquamated cells, phagocytes, but usually containing only serous, often only lightly stained fluid. Cholesterol crystals and calcium are deposited in the degenerated tissue.

The infectious retinitides are acute and chronic. The acute retinitides appear to be endogenous as (a) retinitis septica of

Roth, and (b) metastatic endophthalmitis and panophthalmitis, or exogenous as (c) purulent retinitis.

In *retinitis septica,* emboli of bacteria fill retinal arteries, the surrounding tissue of the vessels is studded with polymorphonuclears and degenerates, edema and hemorrhages appear and eventually subretinal exudation. The endothelium of the capillaries swells and shows hyaline change. Nerve fibers exhibit varicose degeneration and granular disintegration. Ulcerous endocarditis and puerperal sepsis are the chief causes and the bacteria are streptococci, staphylococci and pneumococci. They

FIG. 40.—RETINOCHOROIDITIS. ch, disintegrating choroid; p, disintegrating and proliferating pigment epithelium; r, disintegrating retina; s, sclera; v, sclerotic blood vessel. 40×.

are assumed to be of low virulence. But sometimes no emboli are found and toxins alone are responsible for the disease affecting the endothelium of the small arteries and capillaries.

In *metastatic endophthalmitis* and panophthalmitis, the retinal vessels are surrounded by polymorphonuclears and show disintegration of their walls, the retina is necrotic and filled with polymorphonuclears. They are poured through the disintegrating internal limiting membrane into the vitreous. The suppuration continues rapidly into the uvea and finally affects also the cornea and sclera and reaches the conjunctiva and orbit through a perforation or along outgoing vessels. The infection spreads from bacterial emboli in the retinal vessels as in this instance the bacteria are virulent. It starts as an acute metastatic

retinitis, fast progressing beyond the borders of the retina in contrast to retinitis septica. Occasionally also metastatic retinitis remains localized and forms an abscess which can be encapsulated in fibrous tissue.

Exogenous purulent retinitis is part of an exogenous endophthalmitis and panophthalmitis. If virulent organisms enter the interior of the eye through a perforating wound or perforating suppurative corneal ulcer and proliferate in the ocular chambers, purulent iridocyclitis and abscess in the vitreous are formed (endophthalmitis). Toxins destroy the retina and polymorphonuclears are poured out from the retinal vessels and into the retina and the vitreous. The retina is dissolved and the process continues on to suppurative panophthalmitis.

Chronic infectious retinitides appear as nonspecific even if they are caused by acute infectious diseases, and also if they are produced by chronic specific infectious diseases. Many of these retinitides are observed only clinically and show venous thrombosis, hemorrhages, edema and white patches in the retina in various arrangements and of varied appearance. Often the retinal changes are not inflammatory in nature, but degenerative.

Retinitis in typhus fever is characterized by a proliferation of endothelium in the retinal vessels with obliteration of the lumen; excessive thrombi appear in the retinal veins with the formation of cellular and granular deposits. The vessel walls are densely infiltrated and retinal hemorrhages set in.

In actinomycosis, circumscribed accumulations of mononuclears and epithelioid cells appear in the retina; however, the foci do not contain the fungus itself.

In malaria, parasites may be found in great numbers in the retinal vessels and cause an exudation into the retina, thrombosis and hemorrhages. Even retinitis proliferans is seen.

Infantile toxoplasmosis, caused by the parasite toxoplasma, is associated with encephalomyelitis and chorioretinitis. The infecting organisms are found as cysts or pseudocysts in the inflamed retina which shows necrosis, perivascular and diffuse infiltration with lymphocytes, plasma cells, few neutrophils and lipoid containing phagocytes. Glial tissue proliferates and pigment migrates into the inner layers of the retina.

Other diseases, such as influenza, typhoid fever, measles and gonorrhea can produce alterations in the retina.

Chronic specific infections frequently causing specific retinitides are (a) syphilis, (b) tuberculosis, and (c) leprosy.

Syphilitic retinitis (respectively syphilitic chorioretinitis or syphilitic neuroretinitis) is essentially a disease of congenital lues but appears also in acquired lues. The spirocheta pallida enters the eye of the fetus or the adult through the blood circulation, settles first in the vessel wall and produces here an inflammation and secondary destruction of the retinal tissue or enters from the vessels into the retina or choroid and produces an inflammation there. The syphilitic granulation tissue is characterized by a tendency of lymphocytes and especially plasma cells to aggregate in nodules, although they may be spread diffusely and perivascular infiltration with lymphocytes and plasma cells and a proliferation of the endothelium and elastica leading to endarteritis obliterans. Finally fibrosis appears and atrophy results. The expansion of the lesion and the secondary changes result in variations of the clinical picture in congenital lues, with very minute foci appearing more in the anterior segment of the eye as in the salt and pepper fundus and the peripheral small fleck form or with large disseminated foci or with marked pigmentary migration as in the retinitis pigmentosa type. The pigment epithelium undergoes patchy disintegration in the salt and pepper fundus and neuroepithelium degenerates; in places all layers of the retina degenerate and glia proliferates. The choriocapillaris is often absent. In other cases, the inner retinal layers are more affected where lymphocytes and plasma cells are deposited and nervous elements degenerate. In other cases again, pigment migrates from the pigmentary epithelium into the retina and is deposited along blood vessels. The optic nerve is sometimes edematous and swollen and infiltrated with lymphocytes which also fill the optic nerve sheaths. This inflammation can be followed by atrophy and formation of new connective tissue on the papilla. Frequently, the choroid is also infiltrated. If Bruch's membrane is perforated, retina and choroid unite and after disappearance of the inflammatory elements and with proliferation of glia and

connective tissue a scar is formed and the end result is the same as in chorioretinitis of any etiology.

Acquired syphilis shows a great number of variations, depending on the dissemination of the lesion, and the retinitis is seen as (a) diffuse syphilitic neuroretinitis, (b) disseminated syphilitic chorioretinitis, (c) secondary retinitis pigmentosa, (d) syphilitic perivasculitis (syphilitic retinal angiopathy) and (e) neuritis papulosa which is associated with periphlebitis and chorioretinitis. The inner retinal layers show edema, lymphocytes and plasma cells, albuminous exudate; nerve fibers and ganglion cells degenerate; arteries show endothelial and elastic proliferation; and finally vessels are transformed in narrow connective tissue strands. Veins show perivascular infiltration of lymphocytes and thickened walls and may thrombose, followed by hemorrhages in retina and vitreous, causing new vessel formation. In addition, the optic nerve can be infiltrated with round cells and its vessels are affected. In the case of neuritis papulosa, retinitis proliferans is produced if the exudate situated on the papilla organizes and thick membranes with vessels proliferate from here into the vitreous, extending to lesions of the peripheral retina. The choroid is often diffusely infiltrated with lymphocytes, including the choriocapillaris. Gummatous lesions of the retina are rare and are secondary to gummata of the ciliary body or the choroid, or originate from gummata extending from the region of the lamina cribrosa through the papilla.

Tuberculosis retinae is rare and is seen as conglomerate tuberculosis or as miliary tubercles. In the first case, the retina is substituted for by tuberculous granulomata in which the confluent tubercles are still recognizable with lymphocytes surrounding epithelioid and giant cells and central caseation. It is always secondary to specific inflammations of the uvea and extends from the choroid through the perforated Bruch's membrane and the pigment epithelium, or from the ciliary body directly into the retina; in this case, usually the choroid is diffusely infiltrated nonspecifically by lymphocytes. The papilla is often included into the process, but tuberculosis of the optic nerve can also be the origin of retinal tuberculosis. Miliary

tubercles which are common in the choroid, are rarely found in the retina. They are isolated small tubercles consisting of lymphocytes, surrounding epithelioid cells and beginning caseation. The tissue between the miliary tubercles remains unaffected. Tubercle bacilli can be found in the tissue in these cases. They are found sometimes also in foci which take the form of nodules, consisting of lymphocytes and epithelioid cells,

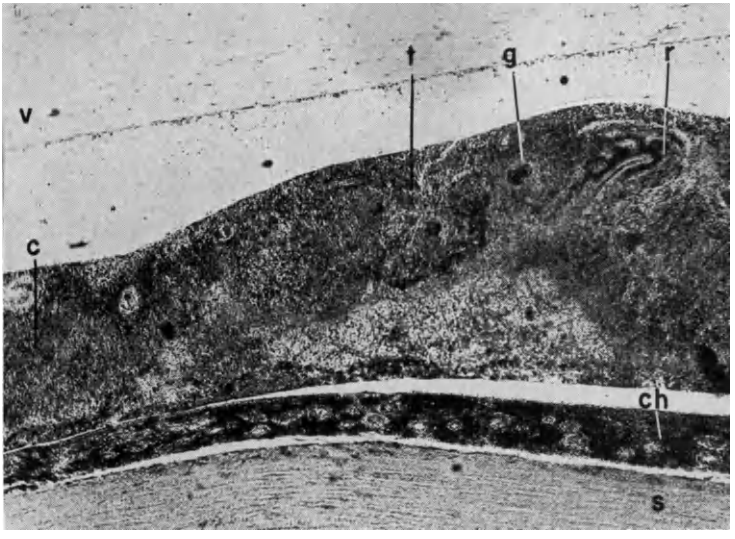

FIG. 41.—TUBERCULOSIS OF THE RETINA. c, caseation; ch, choroid infiltrated with lymphocytes; g, giant cell; r, folded disintegrated retina; s, sclera; t, tubercle; v, vitreous containing round cells. 30×.

in tuberculous periphlebitis which is more common than the other above mentioned tuberculous lesions of the retina. Clinically, an exudative tuberculous retinitis is observed in which veins are congested, hemorrhages are present and the retina is covered with retinitic patches and which is said to be produced by tuberculotoxin.

Leprosy produces changes in the retina secondary to infiltration of the choroid. Small nodules are found in the anterior retina (anterior leprotic retinitis) or larger chorioretinitic foci. Lymphocytic infiltration is found with large lepra cells containing bacilli.

4. Degenerations and Atrophies of the Retina

Degenerations and atrophies of the retina are primary and secondary. To the primary belong (a) retinitis pigmentosa and related diseases, (b) familial colloid degeneration, (c) heredomacular degeneration, (d) the various forms of the familial lipoid degeneration; to the secondary belong (a) cystic degeneration of the retina, (b) circinate degeneration of the retina. Of course, degeneration and atrophy also appear as senile changes.

Retinitis pigmentosa (primary pigmentary degeneration of the retina) is essentially a progressive degeneration of the neuroepithelium, especially of the rods, and in the further course the entire retina atrophies with proliferation of glia and migration of pigment. Besides the disintegration and disappearance of the rods, there is degeneration of the cones, which are preserved the longest in the macula and between macula and papilla, and the outer nuclear layer disintegrates. The destroyed neuroepithelium is substituted for by glia and the progressive gliosis produces fibers, coursing parallel to Bruch's membrane and curving around into Mueller's fibers from which the newly formed fibers also partially originate. In places where the neuroepithelium atrophies, the external limiting membrane disappears, but the inner nuclear layer, ganglion cells, nerve fibers remain long intact and disappear slowly in advanced cases. The walls of the retinal vessels are thickened and hyalinized and the adventitia and intima proliferate, their lumen is narrowed and the peripheral vessels are frequently transformed into hyaline connective tissue strands with lumen. The pigment epithelium disappears in areas entirely or the cells become nonpigmented; in others, it proliferates and becomes many layers thick. It proliferates further into the retina, especially into spaces arising by the loss of nervous elements. The freed pigment is taken in by glial cells or carried into vessel sheaths, and masses of pigment granules cover the vessel walls. The pigment epithelium contains lipoid in great amounts. This circumstance is said to be responsible for night blindness. The optic nerve atrophies and glia proliferates in the papilla. The papilla may also contain drusen. The choroid is normal

or shows severe damage. The choriocapillaris disappears, the choroidal vessels become sclerotic and the vascular sclerosis is sometimes patchy, corresponding to the patchy changes in the retina. Bruch's membrane contains drusen which sometimes are calcified. Complicated posterior cortical and polar cataract appears through malnutrition. The etiology of this retinal degeneration is not known. It is assumed that the neuroepithelium is first affected and the rest of the changes follows its degeneration.

This degeneration according to various theories is caused by (1) vascular changes in the retina or choroid, (2) disease of the pigmentary epithelium, (3) abiotrophy, (4) influence of light, (5) disturbances of inner secretion, (6) disease of the liver, (7) avitaminosis, and (8) toxins. The disappearance of the choriocapillaris and sclerosis of choroidal vessels are said to disturb the nutrition of the neuroepithelium, leading to its atrophy. But even in advanced cases the choroid can be entirely normal. It is assumed that the sclerosis of the retinal vessels produces the degeneration of the retina, but the sclerosis of the retinal vessels is rather the sequela of the retinal degeneration and not its cause; in addition, the appearances in occlusion of the central artery and in angiospasm with subsequent ischemia of the retina are different from retinitis pigmentosa. The neuroepithelium apparently depends on a normal pigmentary epithelium, and in pigmentary degeneration much lipoid fills the pigment cells. But the degeneration of the retinal elements observed in retinitis pigmentosa is different from changes of the retina otherwise observed in disintegration of the pigmentary epithelium. Therefore, the cause is primarily put on the neuroepithelium itself, but the modus of the damage is explained by various factors. Degeneration is said to be of the nature of abiotrophy, in which premature senility of the organ or organ parts appears. It is assumed that the neuroepithelium here is less resistant to light and that light directly damages the rods. Endocrine disturbances, especially hypofunction of the hypophysis, are made responsible for the pigmentary degeneration by some. The coincidence of the retinitis with inner secretory disturbances in the Laurence-Moon-Biedl syndrome, in

which besides pigmentary retinal degeneration there is obesity, polydactyly, hypogenitalism and mental retardation, is mentioned as an example. But also the influence of sex hormones is thought to be of importance for the origin and course of the disease, as it starts in puberty and is more frequent and more severe in the male. Liver damage brings about a deficiency of the regeneration of the visual purple with consequent night blindness. Also, in cases of retinitis pigmentosa, night blindness is said to be caused by a dysfunction of the liver. Vitamin A is important for light adaptation and its deficiency brings about night blindness. Therefore, pigmentary degeneration is explained as a deficiency disease. A hypothetic toxin is assumed to be the cause of the degeneration of the neuroepithelium, as toxins in the blood or in the vitreous may be able to act in this way. It is seen that now and then in diseases producing toxins, retinitis pigmentosa-like changes appear in the retina.

Pigmentary degeneration is a definite hereditary disease of dominant inheritance, sometimes even sex-linked, transmitted by females to males only. Marriage of relatives increases the incidence. The degeneration of the retina is accompanied by other degenerations, such as deaf-mutism and mental disturbances. Related diseases which also are associated with night blindness and appear congenital and hereditary are retinitis pigmentosa sine pigmento, in which the papilla has a waxy appearance and the vessels are thin but no pigmentary migration is visible, retinitis punctata albescens in which the fundus is covered with small white patches, or Oguchi's disease; however, not all of them have been examined histologically. It seems that in all of them the night blindness is caused by a deposition of lipoid granules in the pigment epithelium, damaging the formation of the visual purple. In Oguchi's disease (which is hereditary in Japan and is characterized by the fact that in the light adapted eye the eye ground is grey and the macula appears dark, though in the dark adapted eye the distribution of the choroidal vessels appears—Mizuos phenomenon), the cones of the macula extend further temporally than normal, many nuclei of the extramacular cone cells are displaced into the layer of the inner segments of the cones, and between the pigmentary

epithelium and neuroepithelium there is an abnormal layer consisting of protoplasm and pigment granules. The pigment in the pigment epithelium moves toward the retinal side and the base is free of pigment and contains much lipoid substance.

Familial colloid degeneration (honeycomb choroiditis of Doyne), in which large yellow patches appear in the center of the eyeground and which is hereditary familial, shows these patches as numerous drusen of Bruch's membrane exerting pressure onto the retina.

Heredomacular degeneration (heredodegeneration of the macula), which is seen as infantile, juvenile, adolescent, adult, presenile and senile type and is of hereditary familial nature, shows in the macular region grey spots mixed with pigment spots. Probably the retina is primarily diseased, but the choroid participates also. It has usually been observed only clinically, but not studied pathologically in all its forms.

Familial lipoid degeneration is understood as the various forms of the amaurotic family idiocy and essential lipoid histiocytosis.

Amaurotic family idiocy appears hereditary familial and shows mainly lipoid degeneration of the ganglion cells of the retina. In the infantile form (Tay-Sachs disease) the ganglion cells, if they are not destroyed, are swollen and rounded, especially in the macular region; their fibrils and Nissl bodies disintegrate and the cytoplasm appears foamy and vacuolated as it is studded with lipoid granules which are dissolved in the usual fixation. In fat stain, the lipoid-loaded ganglion cells are very distinct. Their nuclei are pyknotic and lie eccentrically. The nerve fibers disappear and the optic nerve is atrophic. The nuclei of the inner nuclear layer are usually separated by coagulated albumen. The immense swelling of the lipoid-filled ganglion cells produces clouding of the macula in the ophthalmoscopic picture; the central cherry-red spot corresponds in contrast to it with the ganglion cell free fovea which has become so thin that the choroid becomes visible, or a hole appears. In the juvenile form (Batten-Mayou disease, familial maculocerebral degeneration of Oatman), the lipoid degeneration of the ganglion cells is accompanied by degeneration and atrophy of the neuroepithelium. It is substituted by proliferating glia.

Pigment migrates into the retina. In the late infantile form (Jansky-Bielschowsky disease), either only lipoid degeneration of the ganglion cells is present or this is combined with degeneration of the neuroepithelium and migration of pigment. The infantile form of amaurotic idiocy, which is progressive and fatal, is restricted to the Jewish race, though the juvenile and late infantile type appear also in others. The ganglion cells of the cerebrum, cerebellum and spinal cord and their dendrites swell and are filled with lipoid granules. There is essentially an abnormal lipoid storage in the ganglion cells, the cause of which is obscure.

In the essential lipoid histiocytosis (Niemann-Pick disease, lipoid hepatosplenomegaly), not only the ganglion cells of the retina undergo lipoid degeneration, but also the cells of the nuclear layer show a foamy appearance and the plexiform layer and especially Henle's fiber layer are edematous. The glial cells of the optic nerve and all the cells of the septa and of the sheaths are filled with lipoids. Lipoid-loaded cells are found in the choroid and they are situated especially around vessels, but they are also found in the sclera and episclera. In this disease, which is a hereditary familial condition and occurs nearly always only in Jewish infants, there is a lipoid storage of unknown etiology in the reticulo-endothelial cells and histiocytes, especially in the spleen and liver, with enormous enlargement of these organs. However, many other organs of the body may be affected.

Secondary degeneration in the retina is more frequent than the primary and is to be seen in many forms of retinopathy and retinitis in which it follows vascular disturbance or inflammation and probably also degenerative changes of the choroid. There appear the extensive destruction of nervous elements already described, proliferation of glia, deposition of fat, lipoid and hyaline masses. Sometimes the migration of pigment is in the foreground and changes are seen which simulate retinitis pigmentosa (secondary pigmentary degeneration). The pigment epithelium often degenerates together with Bruch's membrane, and drusen (colloid bodies) are formed as a result of senile degeneration, but may also be due to diseases of the retina and

frequently of the choroid. Some authors describe the drusen as rather belonging to the diseases of the choroid. Especially studied is the frequent cystic degeneration of the retina which represents the sole change under certain circumstances, but mostly is secondary to other pathologic processes of the retina and other parts of the eye.

Cystic degeneration of the retina originates by disintegration of the nervous elements of the retina when their defect is not replaced. In this way, holes are formed in the tissue which are filled with debris or less frequently with clear, albuminous fluid. The small cysts often represent the spaces between Mueller's fibers. Large spaces are formed by confluence when the supporting tissue, and especially Mueller's fibers, break down. There is a gradual transition from the cystic degeneration to cysts of the retina. In the beginning, the cystic degeneration attacks the nuclear layers in which the fibers of the glial supporting apparatus are the weakest. All elements inside the retina between the inner and outer limiting membranes disappear in the process of the cystic degeneration. If finally these membranes also break down, a retinal hole is formed. Cystic degeneration at the ora serrata (Blessig spaces, Iwanoff's edema) is physiologic, but some believe that it actually represents a pathologic degeneration. It is found also in the eyes of young persons and in myopes. Degeneration and loss of small vessels and capillaries, occlusion of larger vessels and the associated malnutrition or inflammatory and degenerative processes in the retina and choroid cause cystic degeneration. Senile degeneration increases the cystic degeneration of the peripheral retina but also causes the same to occur in the center. If toxins enter the vitreous body in iridocyclitis, cystic degeneration appears, especially of the macula. Trauma is a cause of retinal edema (commotio retinae, retinal clouding of Berlin), a histologic examination of which is not known. It is probably caused by paralysis of vasomotor nerves, with dilatation of the vessels and transudation of fluid or is brought about by small ruptures of the inner limiting membrane which allow vitreous to enter into the retina. The edema may disappear or, if the damage is severe enough, degeneration follows and small cysts stay in

the retina. Papilledema spreads into the adjacent retina and the edematous retina becomes cystic by an accumulation of fluid in large quantities. Glaucoma sometimes at first shows a cystic degeneration of the inner layers of the central retina which

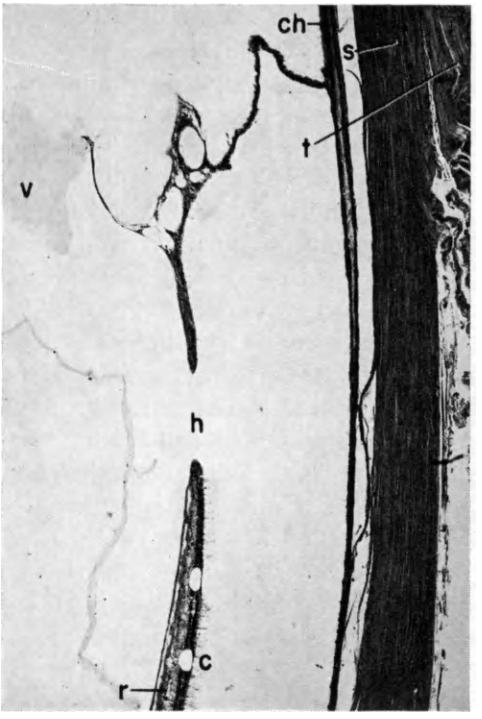

FIG. 42.– HOLE IN CYSTIC RETINA. c, cyst; ch, choroid; h, hole; r, detached retina; s, sclera; t, tendon of extrinsic eye muscle; v, vitreous. 30×.

continues into the outer layer. The retina covering a melanosarcoma of the choroid undergoes cystic degeneration. The detached retina often shows cystic degeneration which, on the other hand, is held responsible for the cause of the detachment.

Circinate degeneration (retinitis circinata) is also considered a secondary degeneration of the retina. This infrequent retinal disease is very seldom examined histologically and only in very advanced cases. The outer plexiform layer is primarily affected

and the region of the foci, seen with the ophthalmoscope, reveals a girdle of white spots surrounding the macula, with granular fatty cells. Besides this, there are found hyaline masses and the pigmentary epithelium shows disintegration; fatty degeneration and fibrous tissue proliferates between the pigmentary epithelium and retina. Rods and cones are degenerated and the outer nuclear layer disintegrates. Vessels show sclerotic changes. The choroid is infiltrated with round cells corresponding to the foci of the retina. The etiology of this disease of old people is in dispute. It is considered to be a sequel of disintegrating retinal hemorrhages due to arteriosclerosis or toxic factors, but often a sequel of primary damage in the choroid.

Senile changes are diffuse arteriosclerosis, and, as sequelae, disappearance of nervous elements and their substitution by glia. The choriocapillaris is partly missing. The cystic degeneration of the periphery increases and eventually also cystic degeneration of the macula is evident. The pigment epithelium becomes irregular and its pigment is irregularly distributed. Some cells undergo fatty degeneration and become vacuolated, their pigment being liberated and scattered. Some areas show proliferation of the cells. In connection with these changes, drusen in Bruch's membrane (colloid bodies) are formed.

Medullated nerve fibers are seen in the retina as congenital variation. The myelin sheaths can be noted in special staining. They are usually found close to the papilla but at times extend into the neighborhood of the macula. The myelin sheaths develop normally in the optic nerve which is the last of the cranial nerves to become medullated, descend from the brain to the lamina cribrosa and end here. The myelin sheaths never continue through the lamina cribrosa. If medullated nerve fibers appear in the retina itself, they are always to be considered as abnormal anlage in the retina itself.

Angioid streaks which appear as dark brown vessel-like branching subretinal stripes and are not a very common condition, have, until now, not been satisfactorily explained pathologically. The opinion in regard to their etiology differs considerably. They are said to represent numerous small ruptures of Bruch's membrane or its absence altogether with thickening in other

parts, and an irregularity of the pigment epithelium and widening of the walls of choroidal arteries with the disappearance of their elastic fibers. In the opinion of others, the pigmentary epithelium is missing in the area of the streaks, folds of the outer retinal layers are present and beneath them degenerated cells and pigment are accumulated. Degeneration of the elastic portion of Bruch's membrane is especially mentioned as angiod streaks are frequently associated with pseudoxanthoma elasticum, in which the elastic fibers of the skin degenerate. Others consider the streaks as sequelae of hemorrhages, as supernumerous new vessels or folds of the pigment epithelium.

Pathology of the Macula

Of special interest are the easily understandable pathologic changes in the center of the retina (fovea, macula and their close surroundings). Often, as already mentioned, secondary changes arise which are caused by other diseases of the eye as well as primary diseases of the center or at least those conditions for which no other changes in the eye can be found as causes. Although the clinical examination shows manifold ophthalmoscopic pictures like edema, hemorrhages, hole, disciform degeneration (Junius-Kuhnt), heredodegeneration or Fuchs' spot in myopia, the pathologic findings are rather uniform and show a formation of cysts, hemorrhages and abnormalities of the pigment epithelium. Furthermore, the pathologic findings are often difficult to interpret, as the very sensitive macula and fovea are easily altered by fixation, and hence, artifacts are numerous.

Secondary diseases of the macula appear in acute and chronic iridocyclitis, in central choroiditis, in primary and secondary glaucoma, in high myopia, in detachment of the retina and in trauma. Even in the short course of a severe acute iridocyclitis, toxins can enter the vitreous and produce a degeneration of nervous elements in the macula. However, more frequent are macular changes caused by a diffusion of toxins in the vitreous in long-lasting iridocyclitis due to chronic specific and nonspecific infection. The macula becomes edematous followed by

cystic degeneration and large cysts are formed by confluence of smaller ones, and a complete hole appears when such large cysts break through the limiting membranes and fluid extends into the subretinal space. Edema of the retina and disintegration of the pigmentary epithelium and finally proliferation of glia and connective tissue are caused by the common central choroiditides of various origins which frequently appear isolated because the macular region has a relatively self-contained circulation. The macula shows cystic degeneration and is detached in primary, and more frequently in secondary, glaucoma by massive subretinal exudation, containing albumin, fibrin, and desquamated cells. The black spot of Fuchs in the macula of high myopia consists of proliferated pigmentary epithelium with a cellular exudate in the subretinal space and unification of the retina with the pigment epithelium. Edema of the macula, hemorrhage and eventually severing of the nervous elements occur in contusion of the eye, in intra-ocular foreign body or are caused by strong electrical current. The changes of the retina in these cases are mostly secondary to changes of the choroid; less frequently they are caused primarily by the physical irritant directly.

Primary diseases of the macula, and those for which the eye itself apparently does not show any etiology, are heredodegeneration of the macula (heredo-macular degeneration), disciform degeneration of the macula (Junius-Kuhnt), cystic macular degeneration (honeycomb macula), central serous retinopathy and senile macular degeneration (Haab). These macular affections have rarely been studied pathologically and are almost exclusively observed clinically. The heredo-macular degeneration, which is seen as congenital, juvenile, adult, presenile and senile forms, probably represents a degeneration of the neuro-epithelium with glial proliferation and migration of the pigment into the degenerated tissue. There is also found cystoid degeneration of the macula and simple atrophy of the nervous elements without glial proliferation and without changes of the pigmentary epithelium. The disciform degeneration of the macula appears as senile and juvenile form. In the senile form, there are extensive hemorrhages between Bruch's membrane and

the pigment epithelium, arising from rupture of the choriocapillaris and being organized by fibrillar connective tissue. Pigmentary epithelium proliferates. Blood vessels of the choroid proliferate into this tissue through holes in Bruch's membrane and occasionally also small vessels from the retina. In addition, elastic fibers seem to enter the newly formed tissue from the elastic portion of Bruch's membrane. There are often tumor-like accumulations of newly-formed tissue between the retina and choroid, finally consisting of masses of fine fibrillary, vascular connective tissue. Hyaline degeneration, formation of cartilage and bone appear in this tissue and the retina shows degeneration and atrophy of nervous elements and slight edema. The rest of the choroid, except for sclerotic changes of vessels, is free of pathology. The juvenile form may show similar alterations beginning with hemorrhages between retina and choroid. The origin of the affection is sought in the choroid by some, who assume it to be a primary sclerosis of the choriocapillaris, and by others in the retina having sclerotic vessels. The origin of the proliferating organizing tissue is sought in the choroid as well as in the retina. Cystic macular degeneration (honeycomb macula), eventually leading to macular holes, is characterized by a formation of holes in Henle's fiber layer filled with clear fluid. If fluid also extends to the subretinal space, a flat detachment of the macula follows. A hole is formed in the macula in progressing degeneration. When the macula is damaged by a severe blow of the eye by contrecoup, edema (vesicular macular edema, Nuel), cysts and holes are extremely likely to appear. Central serous retinopathy (central angiospastic retinopathy, idiopathic flat detachment of the macula) probably represents an edema of the center of the retina due to vascular spasm caused by toxins or an allergy; it has not been studied histologically. Senile macular degeneration of Haab (senile macular chorioretinal degeneration), which seems to be closely related to the disciform degeneration of the macula, is accompanied by disorganization and atrophy of the external nuclear layer, and rods and cones with the inner nuclear layer and ganglion cells vanishing partly. The cells of the pigmentary epithelium atrophy in areas and proliferate in others and pigment may also migrate into the

diseased retina. Exudate appears between the pigmentary epithelium and Bruch's membrane, which shows many drusen. The choriocapillaris disappears in its greater part and the vessels of the hyaline degenerated choroid are sclerotic. The origin of the disease is said to be in the choroid, due to senile arteriosclerosis.

5. Detachment of the Retina

The detachment of the retina is easy to diagnose histologically. The potential space between the layer of the rods and cones and the pigment epithelium is enlarged and the rods and cones are no longer in contact with the processes of the pigment epithelium. The space is filled with fluid which contains more or less protein and is therefore stained. The fluid appears in section as a homogeneous mass, sometimes granulated or containing fibrils. It may contain only a few, but sometimes more cellular elements. They are chiefly cells of the pigment epithelium and neuroepithelium, cells of the pigment epithelium without pigment (ghost cells), macrophages, lymphocytes, polymorphonuclear cells, and erythrocytes. In old cases, sometimes cholesterol is found in the subretinal fluid. Proliferation of pigment epithelium and of abnormal tissue may occur from the retina and choroid into the subretinal space. This space is called subretinal, and fluid, exudate and abnormal tissue is called also subretinal, in spite of the fact that developmentally the space is really inter-retinal. In many eye sections, separation of the retina from the pigment epithelium is found through shrinkage or cadaverous changes. In the case of an artifact, the subretinal space appears empty and nonstained. Detachment is circumscribed or affects the entire retina and reaches then from the ora serrata to the papilla. In this case, the retina is displaced funnel-shaped toward the center of the eye.

Cysts of various extension, and holes and tears which are considered as result of the cystic degeneration are found in the detached retina. The majority of the cysts appear empty, but some may be filled with debris and serous fluid. Holes and tears appear easier when the retina is reduced to the inner and outer

limiting membrane. The cysts may extend far into the subretinal space. Holes are single or multiple. At the margin of the holes, the retina tapers and the margins are frequently turned toward the vitreous. A part of the margin may become adherent eventually with the choroid, while the rest is detached. Sometimes the hole is covered by an operculum of the retina. The retina may be torn off at the ora serrata from the pars orbicularis, very rarely from the papilla and then only in severe trauma. One speaks of these changes as dialysis of the retina. The detached retina appears stretched or as folded. Changes appear in the retina, depending on the cause and course of the disease. The folds may be united by newly formed connective tissue and glia. The neuroepithelium degenerates as it is separated from the source of nourishment, i.e., the choriocapillaris. As long as the circulation of the retinal vessels is intact, the inner retinal layers remain sound. As soon as disturbances appear in their circulation, the nervous elements degenerate, cysts are formed or glia proliferates. The retina may degenerate to a very fine membrane or may disappear partly or entirely according to the underlying pathologic process.

Detachment of the retina is differentiated as (a) spontaneous or ideopathic, and (b) secondary. When spontaneous, it is the main phenomenon and other pathologic changes in the eye are minimal and frequently not easily detected; when secondary, other pathologic conditions are more important, are the cause of the detachment, and determine the fate of the eye. In many cases, it is evident from the pathologic examination of the eye whether or not secondary detachment exists, as, for instance, in choroidal tumor or in severe iridocyclitis. In other cases, the detachment is the evident finding and other pathologic changes are minor; the question then arises whether they are causes or sequelae of the detachment. Minimal inflammatory changes of the uvea are able to produce much serous fluid which may fill the potential space between retina and pigment epithelium; on the other hand, products of disintegration in the subretinal fluid act in a toxic manner and can cause uveal inflammation of various degrees. In this way, the question

arises if the detachment of the retina is altogether a disease in itself or is only the symptom of another disease of the intrinsic eye.

Retinal detachment is found in inflammation of the choroid with exudation or in retinal diseases with edema and hemorrhages beneath the retina. Furthermore, inflammation of the sclera, episclera and even of the orbit may be the cause. As already mentioned, pathologic changes are found in the surrounding tissue of the detached retina. Hyaline degeneration of the choriocapillaris, sclerosis of choroidal vessels and disintegration of the pigment epithelium are seen. Also, circumscribed inflammatory foci exist in the choroid. They are fresh and contain lymphocytes or are old and show atrophy and new formation of connective tissue. They may correspond with holes in the retina. Such changes are already in existence in some early cases of detachment of the retina. Changes in the vitreous are rarely found histologically. Membranes in front of the retina, which are sometimes seen, are often caused by iridocyclitis, as in cases of long-lasting detachment. Also, in early cases, fine membranes consisting of cells and fibers can be noted adherent to the retina. Proliferation of the nonpigmented, but also of the pigmented ciliary epithelium takes place even in early cases. It is often difficult to judge because of the possible physiologic variations.

Eyes with spontaneous serous detachment of the retina and formation of holes are treated today by surgical coagulation with diathermy. In the histologic examination of such eyes after surgery, there is found hyaline degeneration of the sclera with swelling of the lamellae which become homogeneous, and in stronger reaction show necrosis of the sclera in the area of the coagulation. In the latter case, the swollen lamellae do not stain and the nuclei disappear. Hemorrhages and accumulations of lymphocytes and fibrin are found in the choroid, and, depending on the severity of the reaction, also circumscribed destruction of Bruch's membrane and of the pigment epithelium. Then inflammatory cells and fibroblasts proliferate beneath the retina. By organization of this inflammatory tissue, the choroid and retina become adherent. The latter also either show signs of inflammation or remains unaffected entirely.

The etiology of the so-called spontaneous detachment of the retina is not entirely understood. Several theories are forwarded. The question arises as to whether the retina is separated by traction from within on the inner limiting membrane or by pressure from without on rods and cones. The first modus (a) is known as traction or retraction, the latter (b) as secretion or exudation. Furthermore, the main role is attributed to the

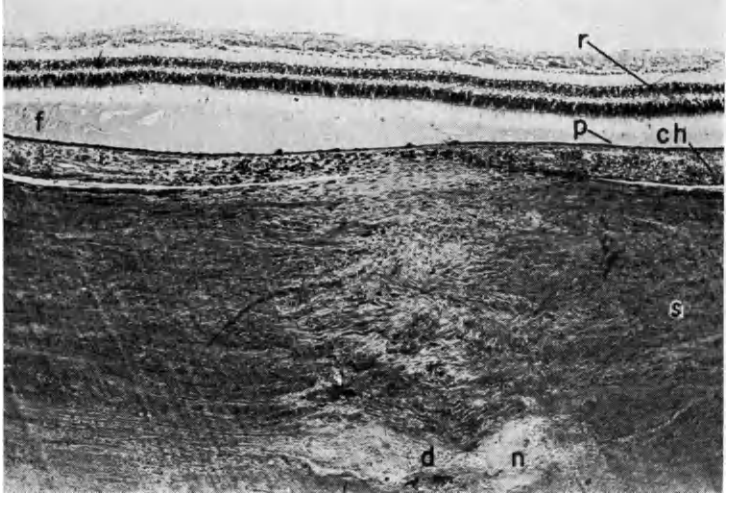

FIG. 43.—DETACHMENT OF RETINA, SURGICAL DIATHERMY. ch, choroid; d, diathermy puncture showing scar in choroid and sclera; f, subretinal fluid; n, necrosis; p, pigment epithelium; r, detached retina; s, sclera. 45×.

decrease of pressure in the vitreous (c) and finally (d) the formation of holes in the retina.

The retina is said to be pulled inwardly by retraction of the vitreous. A primary degeneration of the vitreous is assumed with the formation of membranes which retract the retina inwardly, producing at the same time tears in it. Fluid can enter into the subretinal space through those holes. Also, shrinkage of the vitreous can produce the same result. In this case, fluid accumulates first between retina and vitreous in its posterior part. The anterior shrinking vitreous still adherent

to the retina pulls and tears the retina so that finally fluid enters the subretinal space through the tear. As in these two cases, the primary change causing traction has been looked for in the vitreous from the findings of several histologically examined eyes with recent detachment of the retina; the result has been the formulation of the theory that the primary cause is the proliferation of the epithelium of the ciliary body. This is said to lead to preretinitis with new formation of a membrane on the inner surface of the retina formed by cuticular secretion from the epithelium; shrinkage of this preretinal membrane adherent to the retina may cause tears in the retina, through which fluid flows into the subretinal space.

The external layers of the retina are nourished from the choroid and a current of fluid is supposed to go from the choroid to the retina. The fluid is said to penetrate finally through the retina into the vitreous body. Changes in the vitreous can lead to stasis; the fluid then becomes enriched in protein and is not able to pass through the retina, but remains beneath it. The pressure of this fluid may also tear a cystic degenerated retina and may turn the margin of the hole inward. In other cases, pathologic changes of the choriocapillaris lead to exudation beneath the retina.

The tension in the vitreous is said to decrease if, by the appearance of a slight uveitis, degenerative changes appear in the vitreous body with consequent shrinkage of the vitreous, and sinking backwards of the lens-iris diaphragm. As the tension is lower in front of the retina, fluid may transude beneath the retina from the uveal vessels already injured by the uveitis. According to Baurmann, the retina remains adherent to the choroid because of the difference in the pressure in the capillaries of the ciliary body and the choroid. If the pressure is lower in the former, fluid transudes from the choroid, as the osmotic hydrostatic equilibrium is disturbed.

The important factor is said to be the cystic degeneration. Formation of holes in the retina and the changes in the choroid and vitreous are said to be secondary, being merely the occasional cause in the tearing of the cystic retina which allows the entrance of fluid into the subretinal space. It is also assumed

that the traction of the vitreous, by its inertia in fast movements of the eye, tears the inner wall of the cyst, thus producing the hole. But, on the other hand, it is brought forward that the hole in the retina can be produced also by pressure of fluid entering the subretinal space at the time of the occurrence of the detachment. It must be noted that one finds also detachments without holes and holes without detachment histologically.

In a number of pathologic changes of the eye, detachment of the retina appears secondarily, and in these cases the mechanism of its appearance is easily understandable. In perforating injuries by sharp instruments and foreign bodies, the retina may be cut and torn, and fluid or blood enters the subretinal space. Contusion of the eye sometimes produces tears and hemorrhages and the retina can be torn on the ora serrata or on the papilla. Vitreous hemorrhages, spontaneous or by injury, often organize, and the fibrous strands frequently pull on the retina and separate it. The same can occur in inflammation and injuries of the ciliary body by formation of a cyclitic membrane. Detachment sometimes occurs, after cataract extraction, less frequently after other intra-ocular operations. Holes in the retina now and then appear over a small focus of inflammation or degeneration of the choroid. This is perhaps the cause of the frequent detachment in myopia. The retina is pushed ahead by tumors which grow from the choroid or retina into the subretinal space, or by parasites which develop in the subretinal space, as, for instance, by cysticercus. The retina can be separated by inflammatory exudate in the choroid, sclera or orbit (different types of retinitis and retinopathy, choroiditis, scleritis, tenonitis, orbital abscess or tumors).

Striae retinae are formed when a separated retina is replaced again. They consist histologically of fibrous tissue which appears between retina and choroid. They are formed probably by organizations of subretinal exudate.

6. Cysts of the Retina

Cysts of the retina in general are rare, although cystic degeneration may uncommonly be physiologic in the anterior retina. Cysts of the retina sometimes have their origin in cystic degen-

eration. Fluid-filled spaces are formed in the inner nuclear layer and increase steadily to be outlined ultimately only by the inner and outer limiting membrane. Sometimes in the beginning, the inner nuclear layer is split to a large extent and if fluid increases in this slit a large cyst is formed which can detach the retina. On the other hand, large cysts extending into the subretinal space are formed in a detached retina. Pseudocysts are formed when retinal folds in detachment of the retina grow together. Retinal cysts are congenital in microphthalmos and also in normal sized eyes, or are the end result of a cystic degeneration or they may be caused by traction of shrinking fibrous bands of the vitreous. Parasitic cysts (cysticercus cellulosae and echinococcus) are situated subretinally or are preretinal and attached to the retina.

7. Neoplasms

Neoplasms of the retina are primary or secondary. The primary tumors are neuroblastoma, angiomatosis retinae, tumors in tuberous sclerosis and neurofibromatosis. The latter three types are also called associated tumors, as they are associated with other symptoms in the body. The secondary tumors are malignant melanoma of the choroid extending into the retina, and metastatic carcinoma and sarcoma.

Neuroblastoma retinae (glioma retinae, neuroglioma) consists of primitive retinal cells which are often nondifferentiated, the classification of which is uncertain. Only infrequently does the tumor consist of differentiated cells, the classification of which is relatively easy. It is assumed that the embryonic cells lining the epithelial neural tube are either primitive neuroblasts which further develop into neurons, primitive spongioblasts which later form the supporting substance and the ependyma lining of the ventricle in the brain or medulloblasts which probably develop into glia and nervous cells. Depending on the histogenic origin from primitive cells, the neuroblastoma is divided into (a) retinoblastoma originating from primitive retinoblasts, (b) neuroepithelioma which originates from the primitive neuroepithelial cells, respectively primitive spongioblasts. The rare forms are (c) neurocytoma and (d) astrocytoma, which represent a higher

degree of differentiation, the former of retina formation, the latter of true glial tissue and both of which are relatively benign.

The retinoblastoma type is most frequent. Its cells are relatively small, the nuclei vary in size but are in general small and rich in chromatin with scanty cytoplasm; the cells are rounded or polygonal and have fine processes. The cells are packed closely together with hardly any intercellular substance. Scarce glial cells are found in special stains between these primitive tumor cells; these supporting cells are of normal quality and form mantles around vessels which consist almost exclusively of endothelia. Mitotic figures are numerous. The cells are arranged radially around blood vessels and form cylindric masses which are called cellular mantles or pseudo-rosettes. Only around vessels are seen living, well-stained tumor cells, which, as nondifferentiated fast-growing cells, need rich nourishment. At some distance from the vessels, the cells are degenerated, their nuclei become pyknotic and shrink and still further away they become necrotic and lose their stain, being visible only as shadows. Lipoid degeneration and even calcareous deposits appear in the degenerated and necrotic parts. Also, metastases show similar degeneration. The tumor grows rapidly into the choroid and optic nerve. It causes deposits on the posterior wall of the cornea and on the iris. It can perforate through the cornea or into the orbit through the sclera. It grows into the brain along the optic nerve and rarely forms distant metastases. The tumor growing outside the eye shows larger fusiform cells and no longer the characteristic arrangement around vessels. This transformation is said to be caused by the different blood supply of the tumor inside and outside the eye. Inside the eye it has small end arteries of the retina at its disposal, but outside the eye it has the networks of the vessels with their many collaterals. The origin of the fast-growing tumor in the early embryonal life is from primitive nondifferentiated retinoblasts of the type of the medulloblasts. The tumor cells develop from the inner nuclear layer.

Neuroepithelioma is also often found, characterized by the appearance of rosettes. The rosette consists of columnar cells arranged circularly around a central cavity. Their cell borders

are rather distinct and toward the lumen they are lined by a distinct cell membrane. Cilium-like processes reach from the cells through the membrane into the lumen which is filled with coagulated hyaline-like material. The nuclei of these epithelial-like cells, reminding one very much of sensory epithelium, are situated in the center of the cell and are rounded or oval, of various form and size and rich in chromatin. The rosettes are often extremely numerous and the tumor seems to consist exclusively of them, often, too, being surrounded by smaller cells with little cytoplasm which are similar to those of the retinoblastoma and which surround the rosettes but without distinct cell borders. Often the rosettes are scarce and the nondifferentiated small cells are more numerous, forming mantles around blood vessels. In addition, this tumor contains well-developed and ripe supporting cells in the form of astroblasts, astrocytes, oligodendroglia and spongioblasts. Areas of the tumor are degenerated and necrotic. The rosettes are described as spherical, closed-off formations but they may be cylindrical and their lumen is open at one or both ends.

Rosettes are found exclusively in the tumor inside the eye, but never outside the eye when the tumor perforates or metastasizes. The tumor growth outside the eye shows large fusiform cells similar to the retinoblastoma. The rosettes are often explained as neuroepithelium, the distinct membrane enclosing the lumen as a derivative of the external limiting membrane, the cilium-like processes as rudimentary rods and cones and the columnar cells as primitive rod and cone cells, the nuclei of which correspond to the outer nuclear layer. Several other explanations are offered which are less plausible. The rosettes are said to result from tumor cells being arranged around processes of astrocytes and their cell membrane is said to correspond to the contour of the unstained astrocytes. Some believe the rosette to be simply the sequela of the rapidly following cell division. Still others feel that the rosette simply represents the cross section of glial cells which proliferate in the form of chains.

Rosette-like formations are seen in congenitally deformed eyes and in eyes which are exposed during the fetal development to

x-ray. However, they are distinguished from the true rosettes as they are the result of a folding of the outer limiting membrane and are always continuous with it, although the true rosettes of the retinal tumor never show any connection with the limiting membrane. Furthermore, the lumen in the former always opens into the subretinal space, therefore is always in continuity with the space of the primary optic vesicle. The

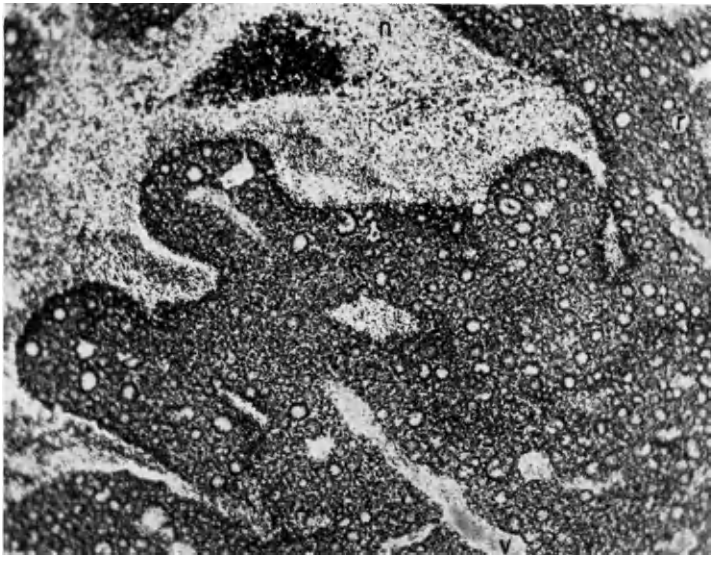

FIG. 44.—RETINOBLASTOMA. n, necrotic area; r, rosette; v, blood vessel.

neuroepithelioma originates as already mentioned from the primitive spongioblast which also forms the primary neuroepithelium. These congenital malignant tumors which often appear to be hereditary in families and sometimes bilateral grow first intra-ocularly. For a time, they expand inside the retina, causing it to widen (glioma planum). They originate from the outer nuclear layer and grow into the subretinal space and detach the retina (glioma exophytum) or they originate from the inner nuclear layer and invade the vitreous, leaving the retina in its place (glioma endophytum). They soon cause

secondary glaucoma. During their intra-ocular growth, they spread by direct extension into the various tissues of the eye or through local metastasis when particles of the tumor are separated and are carried off by the fluid current. They are deposited on the iris, on the posterior surface of the cornea and are suspended in the posterior and anterior chamber in clusters.

The eye sometimes appears to be fetal in its structure, showing congenital deformities, but a degeneration of its tissue always sets in. The retina, optic nerve, choroid, ciliary body and iris become atrophic. The lens is displaced, deformed and cataractous. In its further course, the tumor extends extra-ocularly, as it perforates the sclera, growing along the ciliary vessels outward, breaks into the orbit through the optic nerve or enters the brain along the fibers or sheaths of the optic nerve. The tumor metastasizes by way of lymph and blood vessels, mostly to regional lymph nodes, rarely to distant organs like bone and liver. Spontaneous regression is rare when the tumor undergoes complete necrosis. Then the eye has a normal form and some function left, but in the main it becomes atrophic.

Retinal tumors are rare in which retinal structure is distinct and which mostly appear at a later age. The neurocytoma reminds one of a folded retina with a resemblance to nuclear layers mixed with nondifferentiated proliferating cells, part of which are small and have rounded nuclei with much chromatin, part larger and having more oval nuclei with less chromatin. The astrocytoma develops intraretinally without affecting the limiting membranes and consists of spindle-shaped cells with oval nuclei and fine processes and fibrillar tissue. In addition, there are also larger cells with larger branching processes and rounded nuclei.

Angiomatosis retinae (von Hippel-Lindau disease) shows a varying picture, depending on the extension of the lesion and secondary changes. The retina is detached and folded, containing numerous convoluted vessels and cystic spaces. Many capillary spaces with endothelial lining and solid endothelial proliferation are found besides glial cells and fibroblasts and a dense interlacing network of fibers. This newly formed tissue occupies parts of the retina. Blood is found inside the vessels, but also

in the tissue where it degenerates and is transformed into cholesterol crystals. The subretinal space is filled with exudate and blood with various degrees of degeneration and proliferating fibrous tissue. Apparently, the primary is a mesodermal tumor, a hemangioblastoma, which is intercalated as a network between dilated retinal arteries and veins, the gliosis and exudation being secondary, but sometimes predominant. Therefore, some authors consider the tumor as primarily ectodermal and as a gliosis which is vascularized secondarily. This gives rise to the introduction of various terms, such as angiogliomatosis retinae (Ginsberg-Spiro), gliosis retinae diffusa (Guzmann), angiogliosis retinae (Heine). The angiomatosis is considered as a congenital anomaly.

Tumors of the retina in tuberous sclerosis (Bourneville's disease) are mostly flat, more rarely papillary tumors of the nerve fiber and ganglion cell layers occasionally occupying the entire width of the retina, sometimes extending onto the papilla. The cells are flat, large, of varying size and shape, sometimes round, angulated, having processes and large rounded or fusiform nuclei with chromatin in granules and a distinct nucleolus. The cells are vacuolated and form syncytia occasionally. A great amount of fibers exists and large spaces are filled with blood and serum. Deposition of calcium and other incrustations appear. The cells are explained as nondifferentiated glial cells.

Tumors of the retina in neurofibromatosis (von Recklinghausen's disease) mostly including the papilla, consist of palisade-like arranged spindle-shaped cells coursing in whorls. Fibrillar bundles with hyaline degeneration and many cystic spaces are found between the cells.

Those three tumor formations of the retina appearing to be congenital and multiple, hereditary familial are grouped together as phakomatoses (van der Hoeve). They are associated tumors, especially associated with symptoms and pathologic alterations of the central nervous system. Angiomatosis retinae is associated with angiomatous cysts of the cerebellum, the medulla and the spinal cord, and with polycystic and angiomatous tumors in pancreas, liver, kidney and adrenals. Tuberous sclerosis has scattered gliomatous tumors of the cortex consisting mainly of

astrocytes and has as an outstanding feature the association with adenoma sebaceum of the face (Pringle), and also sometimes with other types of tumors in various organs of the body. In neurofibromatosis, there are multiple neurinomata of the cranial nerves, and also of peripheral nerves. The Sturge-Weber syndrome is a fourth disease to be added to this group in which no tumor is formed, but hydrophthalmos and new vascular formations in the cortex cerebri.

Secondary neoplasms of the retina are rare. A malignant melanoma of the choroid may infiltrate the retina. An adenocarcinoma metastasizes rarely to the retina, where it grows in the nerve fiber and ganglion cell layers from an embolus in a retinal vessel and expands through all the layers of the retina. A sarcoma rarely metastasizes to the retina, but usually develops first in the papilla and grows from here into the retina.

READING OF SOURCE MATERIAL

According to Scheerer the thickness of the walls of the retinal vessels does not change markedly during the entire life as far as healthy eyes are concerned.

Scheerer describes the normal appearance of the central vessels in their passage through the lamina cribosa where they have a common connective tissue ring. The wall of the vein is very thin and lies directly on the adventitia of the artery. But there are many variations in the shape of the vessels, relative width of the lumen, and thickness of the connective tissue ring. This fibrous ring becomes wider with increasing sclerosis of the vessels and an increasing connective tissue septum between artery and vein. This leads to uncomplicated obstruction of the central vein. In additional sclerosis of the arterial wall, the vein can be compressed by the rigid artery to a slit. The lumen of the vein can further be occluded by degeneration and proliferation of the intima. If the nutritive vessels of the lamina cribrosa become sclerotic, the lamina itself and the central vein become sclerotic also.

Loewenstein finds that retinal arteries and veins have vasa vasorum in their walls. As they do not exist in young healthy men they have to be considered as an attempt of healing of diseased vessels.

Arruga, Lister, Vogt find in holes of the retina only degeneration of the retinal tissue, but no proliferation.

Proliferation is rare in wounds of the retina and represents only an abortive attempt (Weil and Mayer).

Sugita believes that the phagocytes appearing in the retina originate from the pigment epithelium.

Damel, Adrogué and Malbran Lamb, Perez Llorca are of the opinion that proliferating pigmentary epithelial cells can phagocytose and be transformed by metamorphosis into fibroblasts.

Soudakoff describes a staphyloma of the cornea with hemorrhages into the nerve fiber layer of the retina leading to gliosis.

Jaensch describes fatty degeneration and disintegration of processes of the glial cells in gliosis of the retina.

Massive gliosis of the retina is reported by Friedenwald.

Involutionary arteriosclerosis of the retina in high blood pressure is studied histologically by Bailliart, Ballantyne, Michaelson and Heggie, Cohen, Friedenwald and Friedenwald, Keith, Wagener and Kernohan, Koyanagi, Kyrieleis, Sallmann, Vervey.

Friedenwald describes arteriosclerosis of the retina as hyaline thickening of the media; Ballantyne, Michaelson and Heggie as thickening of the subendothelial tissue; Sallmann as marked increase of the adventitia.

Koyanagi finds that the retinal arteries and veins have at their crossing a common intervening wall and that the vein is easily compressed by the sclerotic artery and thrombosis follows.

Sallmann, who describes histologically the arterio-venous crossing in eyes of various age levels, finds that the artery always remains in its place and that the vein is displaced; in old people the adventitia of the vein is thickened and can grow around the artery, so that artery and vein become united, e.g., in essential hypertension.

Friedenwald describes circumscribed atheroma in arteriols of the retina which took the fat stain.

Koyanagi examined eyes histologically which showed during life the phenomenon of Salus, and found the vessels normal. Occasionally the tissue surrounding the vessels was increased.

Sallmann observed histologically the displacement of the vein at the crossing by the artery, producing Salus' sign, but Cohen describes arterioles of retina and choroid with hyaline degeneration and intima proliferation and occasional necrosis of the vessel wall in malignant hypertension.

Kyrieleis found in a case of nephritis and arteriosclerosis with negative ophthalmoscopic findings histologically sclerosis of the vessels of the retina and diffuse fatty infiltration of the retina.

Gibson and Smith find in retinal phlebosclerosis proliferation of the endothelial cells and hyaline degeneration of the media.

Agatston described hyaline degeneration in retinal arteries and veins of both eyes of a 64 year old man without hypertension. The sclerotic changes lead to venous thrombosis and hemorrhages in nerve fiber, ganglion cell and plexiform layers.

Ballantyne describes micro-aneurysms of the retinal capillaries in diabetes. First small fatty granules appear in the vascular endothelium and there is also phlebosclerosis with an intra- and preretinal network of large thin-walled vessels and hemorrhages.

Retinal micro-aneurysms in the inner nuclear layer of the macular region of diabetics as result of nodular vascular ectasia were described by Ballantyne and Loewenstein. Punctate hemorrhages occur due to diapedesis and rhexis; thrombosis and fibrosis can be found.

Kronfeld found histologically in cyanosis retinae the vessels of the choroid and retina very dilated and hyperemic, hemorrhages and papilledema.

Goerlitz found in anemia of the retina histologically edema and degeneration of the ganglion cells.

Scheerer finds in cadaver eyes frequently blood clots in the lumina of the central retinal vessels near the lamina cribrosa; he believes that the clots described as emboli are frequently post mortal and that the detachment of the endothelium may be caused by a shrinking clot.

Klien distinguishes four types of primary occlusion of the central retinal vein: (1) occlusion by compression from outward by sclerosis of surrounding tissue or tumors; (2) occlusion due to thrombosis in phlebitis; (3) occlusion by primary thrombus in blood dyscrasia and (4) occlusion by stagnation thrombosis.

Ballantyne reports pathology of thrombosis of the central retinal vein.

Incze finds, like Scheerer, that the so-called "thrombosis of the central vein" is caused by occlusion of the vein by thickening of its wall due to hyaline degeneration, increase of cells, infiltration with polymorphonuclears, plasma cells and eosinophils and proliferation of the endothelium or its compression by the sclerotic artery.

Seidel found a thrombosis of the central retinal vein caused by spasm of the central artery by which the blood circulation was slowed down, the vein collapsed and finally formed a thrombus.

v. Hippel and Kiel find that the central retinal vein might be occluded in the presence of a normal wall or a normal artery and its course is often obscure.

Koyanagi finds the compression of a retinal vein by a thickened sclerotic artery at their crossings as the cause for thrombosis of the branches of the central retinal vein.

Metz-Klok observed in cerebro-spinal meningitis thrombosis of the central retinal vein, papilledema and exudation into the retina and vitreous body.

Manschot found in subarachnoidal hemorrhage extensive hemorrhages of the retina caused by complete occlusion of the central retinal vein in the subarachnoidal space.

Histologic findings of secondary glaucoma due to thrombosis of the central retinal vein are described by Krause, Salzmann, Samuels. Fisher considers it as caused by perivascular sclerosis, Wood by turgescence of the vitreous body due to absorption products of the hemorrhages.

Recent occlusions of the central retinal artery without disease of the vessel wall caused by a clot in the lumen are described by Engelbrecht, Karbe, Meinshausen.

Opin saw in embolism of the central retinal artery an homogeneous mass obstructing the lumen, the endothelium proliferating and the ganglion cells of the retina and the nerve fibers degenerated.

The retinal vessels in the eye of a 78 year old man with embolism of the central retinal artery showed hyaline degeneration and the retina had oval vacuols (Berger).

Degeneration and atrophy of the ganglion cells and nerve fiber layer of the retina is found histologically in occlusion of the central retinal

artery, due to emboly, thrombosis and endarteritis by Mohr and Boehm, Schall.

Embolism of the central retinal and ciliary arteries occurred in a 12 year old boy with chronic lipoid nephrosis with arteriosclerotic changes and beginning organizations of the plaques (Goldstein and Wexler.)

Villard and Dejean describe a complete occlusion of the central retinal artery due to sclerotic wall changes and an organized thrombus accompanied by glaucoma.

Schall saw an emboly in a macular artery with intact walls in a case of endocarditis. The inner retinal layers showed pyknosis and karyorrhexis and vacuolization of the nerve fibers.

Cordes and Aiken found in disseminated lupus erythematodes thrombi in the arterioles without changes of their walls and in sclerotic arteries, hemorrhages and hyaline in the retina accompanied by hypertension and renal changes.

Kyrieleis believes that retinal hemorrhages in purpura and septic diseases are caused by toxins.

Kyrieleis describes in a 29 year old man with lymphogranulomatosis histologically a large hemorrhage in the nerve fiber layer of the retina, probably the result of anemia.

Drews and Minckler report massive preretinal hemorrhages associated with subarachnoidal hemorrhage of the brain and of the optic nerve caused by rupture of an aneurysm in the anterior communicating artery of the brain.

Meves found hemorrhages in the retina in subarachnoidal hemorrhages of the brain without pathologic changes of the retinal vessels and without hematoma in the sheaths of the optic nerve. He considers the passive congestion of the retinal vein due to suddenly increased intracranial pressure as cause of the hemorrhages.

Axenfeld, Moscardi describe histologically preretinal hemorrhage.

Goldstein and Wexler found acute tuberculous periphlebitis in retina and optic nerve secondary to anterior uveitis. Eppenstein describes tuberculous periphlebitis of the retina.

Gilbert could stain tubercle bacilli close to the retinal veins in periphlebitis with recurrent vitreous hemorrhages.

Lluesma, Mayrhofer, Radnot consider tuberculosis as cause of the periphlebitis.

Verhoeff and Simpson describe a tubercle in the central retinal vein at the lamina cribrosa with thrombosis in a 31 year old man.

Suganuma describes primary specific infiltration around arteries and veins of the retina consisting of round, epithelioid and giant cells without changes in the uvea and believes that tubercle bacilli are deposited in the capillaries and extend into the perivascular lymph spaces.

Birnbaum, Prinzmetal and Connor, Marchesani find in periphlebitis changes similar to those of Burger's disease.

Scheerer found in a case of a brain abscess caused by diplococci, periphlebitis retinae without thrombosis.

Lister believes that the periphlebitis secondary to iridocyclitis starts in a similar way as the hematogenous periphlebitis, that lymphocytes appear

first around the vessels, that they enter the walls later and produce finally thrombosis.

Spanlang describes as end stages of the periphlebitis retinalis in cases of postoperative and spontaneous iridocyclitis nodular organization of the infiltrate mainly by glia and less by connective tissue, obliteration of the vessels and eventually new formation of vessels in the nodules to which the pigment migrates.

v. Hippel found in recurrent hemorrhages into the vitreous, tuberculous periphlebitis.

Safar saw in a case of juvenile vitreous hemorrhages, tuberculosis of the sclera, the optic nerve, periphlebitis with lymphocytes, epithelioid and giant cells and hemorrhages in retina, subretinal space and vitreous. He considers the disease as a "direct hematogenous dissemination" into the veins of the retina.

Histologic findings in retinitis proliferans are noted by Gallenga.

Klien finds two types of retinitis proliferans: (1) that consisting of numerous connective tissue bundles which can appear in the center and periphery of the bulb and (2) that consisting of numerous vessels with thin walls and delicate connective tissue between the vessels which appears at the optic disc and its surroundings.

Redslob believes that gliosis sets in first in retinitis proliferans, followed by secondary ingrowth of fibrous tissue. Glaucoma sets in in these cases due to vascular changes, stasis, abnormal transudation of fluid and swelling of the vitreous body.

Marchesani describes cases of retinal hemorrhages and retinitis proliferans in cases of thromboangiitis obliterans (Burger's disease).

Wolf finds that the retina in juvenile angiopathy is detached by serofibrinous exudate, producing an external proliferating retinitis. The choroid remains intact. Tubercle bacilli could not be found in spite of clinical evidence of tuberculosis.

Periarteritis nodosa of the retina is described by Boeck, Goldstein and Wechsler, King.

Herrenschwand found in a 35 year old man with sepsis periarteritis nodosa in the long ciliary and central retinal arteries.

Sampson describes periarteritis nodosa of retinal, choroidal and orbital vessels.

Gaynon and Asbury describe edema, detachment and fibrinous and hyaline deposits of the retina and choroid and thickened walls of the arteries in a 38 year old man with syphilis and periarteritis nodosa.

Hippel describes as primary syphilitic changes of the retinal vessels an increase of the connective tissue of the intima and adventitia, disintegration of the elastica and perivascular lymphocytic infiltration.

Fuchs finds that the first neuron of the retina is mostly affected in degenerative familial diseases, the second and third neuron in acquired diseases.

Igersheimer observed that in incresaed intra-ocular pressure an extravasation into the retinal and papillary tissues (hemorrhages, retinitic spots and papilledema) does not appear.

Wagener finds in malignant hypertension edema of the papilla and the adjacent retina, increase of glial cells, hemorrhages, fibrinous and hyaline

exudation, phagocytes with lipoid content, sclerosis of the arterioles and arteries and advanced sclerosis of the choroidal arteries. The disease is caused by constriction of the arteries with following ischemia.

Hanssen and Knack conclude from histologic examinations that the renal retinopathy is mainly a toxic inflammation which produces in the choroid a granuloma and proliferation of fibrous tissue along the vessel.

Lo Cascio finds nephritic neuro-retinitis in diffuse glomerulonephritis and arteriosclerotic kidney. He finds a basophilic substance produced by exudation from choroidal and retinal vessels deposited between pigmentary epithelium and rods and cones, further proliferation of the supporting substance and deposition of hyaline, granular and reticular-appearing clumps in the outer plexiform and inner nuclear layer. He considers the disease "as retinitis azotemica-like."

Raadt finds a strong concentration of ammonium, which acts strongly toxic, in blood and tissue fluid in chronic kidney diseases and considers this responsible for the appearance of the albuminuric retinitis as it has a special affinity to the nervous system which is rich in lipoids.

Schieck considers the high blood pressure as responsible for the appearance of renal retinopathy. Changes of the retinal vessels cannot be important as the alterations of the retina appear also with normal blood vessels. A typical renal retinopathy can develop in central essential hypertension with perfect renal function. The responsible angiospasm accompanies the hypertension which cannot be proved if the heart fails and which produces arteriosclerosis in long duration.

Volhard considers angiospasm leading to hypertension as necessary for the origin of the retinitis albuminurica which, in his opinion, is caused by arterial ischemia with damage of the retina due to insufficient oxygen supply. He proposes the name retinitis angiospastica. Also Gasteiger believes that retinopathia albuminurica is caused by angiospasm (retinitis angiospastica).

Koyanagi finds in cases of retinitis nephritica sclerosis of the choroidal vessels showing endothelial proliferation, hyaline degeneration of the wall, deposition of lipoid, formation of thrombi and hemorrhages, sclerotic changes of the choriocapillaris with deposition of fat, hyaline degeneration and obliteration, and degeneration of the pigment epithelium. He considers the changes caused by severe damage in the short posterior ciliary arteries. He also considers the subretinal fluid in detachments of the retina arising in nephritic retinitis as hyaline produced by a hyalin hypersecretion of the pigmented epithelial cells.

Dejean believes that the increase of peptides in the blood (polypeptidemia) acts toxically and produces renal retinopathy. Also Villard, Dejean and Cazals believe that toxic polypeptides are responsible for the origin of renal retinopathy, Chabanier, Gaudissard, that hypercholesterinemia is responsible.

de la Fontaine Vervey finds the cause of retinitis albuminurica in a diffuse lipoid degeneration of the walls of arteriols.

Woelfflin finds in retinitis albuminurica also the anterior segment of the eye changed due to increased arterial pressure which he considers responsible for the retinal disease; edema and thickenings of the vessel walls are the sequelae.

Mylius finds in eclampsia no vascular changes, but fatty degeneration of the glia, the rods and cones, and fat infiltration of the tissue. He believes that vascular spasms cause ischemia and are followed by edema, hemorrhages and exudation.

Kinukawa found in eclampsia with retinitis histologically hydropic swelling of the pigmentary epithelium and subretinal fluid.

Koyanagi finds albuminous exudate in the toxic retinopathy of pregnancy.

The changes in the retina are alike in diabetic and renal retinopathy, but the vessels are markedly affected in the former (Beauvieux and Pesme). But in the examined cases simultaneous nephritis existed.

Cohen found in diabetic retinopathy histologically arteriosclerotic changes.

Lo Russo finds in diabetic retinitis hemorrhages and cystoid degeneration, depositions of fibrin and endothelial proliferation and hyaline degeneration of the vessels.

Ballantyne and Loewenstein find in diabetic retinopathy fatty droplets in groups in the retina, which shows degeneration, and pre-retinal vessels embedded in a primitive connective tissue. Phlebosclerosis is seen as nonsymmetrical fibrillary thickenings of the wall of the vein with normal lumen and intensive thickenings with complete hyalinization and narrowing of the veins.

Raadt believes that the perivascular edema in diabetic retinitis contains ammonium which is responsible for the spasm and histologic changes of the vessel walls.

Calhoun, Thomas, Cordier and Rohr find degeneration of ganglion cells of the retina in methyl alcohol poisoning.

McGregor found in acute methyl alcohol poisoning fatty droplets in the ganglion cells of the retina but which correspond to the normal changes in the same age group.

The star figure of the macula containing cells loaded with fat is caused by loss of blood vessels in the choroid, according to Koyanagi.

Magitot finds stellate retinopathy accompanying nephritis, hypertension, papilledema and anemia, caused by vascular disturbances, changes of the tissue fluid, changes in the hydro-mechanic pressure of the blood and the radial arrangement of the structures in the macula.

Puscaria and Nitzulescu report pathologic findings in retinitis cachecticorum and find atrophy of the nerve fibers and lipoid degeneration of the retina and consider them caused by toxic factors and anemia.

Bruce describes retinitis in dermatomyositis and finds edema of the inner layers of the retina with varicose nerve fibers and hemorrhages and albuminous deposits in the external layers.

Pathologic findings of the retina in leukemia are reported by Archangelsky, Bab, Gibson, Goldstein and Wexler, Kreibig.

Seergeeva finds as eye changes in leukemia hemorrhages and exudation of cells in the retina and diffuse lymphoid infiltration of the choroid.

The retina in pernicious anemia shows hemorrhages mainly in the nerve fiber layer with homogeneous glassy centers surrounded by well-formed red cells, ganglioform degeneration of nerve fibers, dehiscences in vessel walls and thromboses (Fileti).

Pathologic findings in lipemia of the retina are reported by Hardy, Muskat.

Heine finds that a clinically diagnosed retinitis exudativa Coats can be caused by glioma, pseudoglioma, metastatic ophthalmia, circumscribed chorioditis, chorioretinitis, apoplectic retinitis and primary shrinkage of the vitreous.

Pathologic examinations of external exudative retinitis are reported by Damel, Adrogué and Malbran, Gourfein-Welt, Koyanagi, Lamb, Laval, Marshall and Michaelson, Meller, Perez Llorca, Rados, Zinsser.

Coats' disease is primarily caused by subretinal hemorrhages, according to Crigler, Demaria, Gourfein-Welt, respectively primarily by exudation, according to Davis, Marshall and Michaelson, Meller, Lamb.

Woelfflin finds in external exudative retinitis the retina disintegrating and containing fresh and old hemorrhages and sero-fibrinous exudate, connective tissue masses between the choroid and retina and the choroid intact. He assumes that the primary is a transudate of fluid from the choroid.

Hanssen finds in external retinitis only inflammatory changes with formation of granulation tissue between retina and choroid and proliferation of the pigmentary epithelium.

Sattler sees in external exudative retinitis necrotic foci in the retina with deposition of fibrin and circumscribed hemorrhages, proliferation of the pigment epithelium and new formation of connective tissue from the choroid. The process is of toxic embolic nature with secondary hemorrhages.

Elwyn finds in Coats' disease teleangiectasiae causing local circulatory disturbances. He finds: (1) dilatation and stasis of vessels; (2) thrombosis; (3) hyaline degeneration of vessel walls; (4) hemorrhages; (5) exudation in the retina; (6) necrosis of retinal elements with deposition of fibrin and lipoid; (7) phagocytes in the retina and (8) organization of hemorrhages and exudates.

ten Doesschate finds in external exudative retinitis, fibrous tissue subretinal and as cause vascular changes.

Mayou finds in the juvenile form of Coats' disease no vascular changes, but chronically dilated choroidal vessels and formation of exudation in the choroid and the subretinal space. Also, Kalt describes exudative retinitis without vascular changes probably caused by toxins.

Marshall and Michaelson consider the proliferating subretinal cells in Coats' disease as histiocytes, Meller as epithelioid cells.

Koyanagi believes that the subretinal fluid in exudative retinitis is produced by secretion of the pigmentary epithelium.

Halbertsma describes histologically an extensive subretinal hemorrhage appearing clinically as tumor.

Rados describes in an external exudative retinitis, folds of the retina with formation of rosettes and proliferation of glia and a cellular and vascular tissue between the retina and choroid. He believes that vascular disturbances primarily produced malnutrition, and inflammation followed.

Krueckmann believes that there is no difference between metastatic embolic suppurative retinitis and simple septic retinitis (Roth). The latter is formed by single cocci or emboli of smallest numbers of bacteria.

Doherty and Drubek find in bacterial endocarditis hemorrhages in the inner layers of the retina, and call the infection endocarditic retinitis.

Carnegie Dickson, Pritchard, Savin and Sorsby report histologic findings of emboli of retinal arteries without arteriosclerotic changes or thrombosis in subacute endocarditis causing round cell infiltration of the retina, optic nerve and choroid.

Retinitis septica is examined pathologically also by Gilbert.

Scrub typhus, caused by Rickettsia orientalis and transmitted by mites, is accompanied by extensive congestion of retinal vessels and some perivascular round cell infiltration (Donegan).

Grant describes histologically hemorrhages of the retina in patients who died of malaria. The hemorrhages are caused by multiple embolic and thrombotic occlusions of small vessels and plasmodia were found in the blood vessels of the retina, the choroid, and optic nerve. Saba sees frequently in anemia following malaria retinal hemorrhages in all layers close to saclike enlarged veins.

Archangelsky found a conglomerate of aspergillus fumigatus subretinal in a 42 year old man.

Clapp, MacDonald, Velter and Blum report retinal tuberculosis.

In Lagrange's case there was caseous tuberculosis of ciliary body, lymphocytic nodules in the retina and conglomerate tubercle in the papilla.

MacDonald found histologically several masses of miliary sarcoids scattered throughout the retina in the eye of a 60 year old woman with recurrent iritis.

Prendergast describes extensive inflammation of the retina with a great amount of bacilli in leprosy.

Wolf and Paige describe toxoplasmic chorioretinitis in cases of fetal encephalomyelitis. The organisms which are called cysts or pseudocysts can be seen in the tissue in clusters or aggregates. The retina shows perivascular and diffuse infiltration with lymphocytes, plasma cells and occasional neutrophils, eosinophils and lipoid containing phagocytes, necroses, proliferation of glial tissue which extends also into the vitreous, hyperplasia of the endothelium of the capillaries and immigration of pigment into the inner layer. The choroid shows similar infiltration.

Hartmann and Braun-Vallon finds in toxoplasmic chorioretinitis perivascular infiltration with lymphocytes, epithelioid cells and some eosinophils, toxoplasma intra- and extracellularly or in isolated pits similar to pseudo cysts; granulation tissue may proliferate into the vitreous.

Verhoeff finds in retinitis pigmentosa histologically degeneration of the neuroepithelium, enormous thickening of the adventitia of the vessels, gliosis of the papilla and posterior cortical cataract.

Koyanagi finds in pigment degeneration of the retina sclerosis of the choroidal arteries, absence of the choriocapillaris and atrophy of the neuroepithelium.

Primary pigmentary degeneration of the retina is histologically examined by Ascher.

In a case of retinitis pigmentosa, lipoid accumulations were found in the pigmentary epithelium by Asayama and Takagi, Sugita.

Stock describes a rapidly progressive form of pigmentary degeneration of the retina with dementia. The retina was attached by exudate and contained a hole, the pigmentary epithelium extended into the retina and the ganglion cells were degenerated.

As etiology of the primary pigmentary degeneration of the retina are considered sclerosis of the retinal vessels by Agatston, abiotrophy by Collins, pituitary and diencephalic disturbances by Pletevna, Viallefont, Zondek and Koehler, influence of sexual hormones by Lorenz, Wibout, disturbances of the liver by Takahashi and vitamin A-1 defect by Levine.

Friedenwald and Chan believe that melanin granules destroy the neurons of the retina and cause proliferation of Mueller's fibers in retinitis pigmentosa; they also find that Mueller's fibers become actively phagocytic.

Ehlers finds as cause of retinitis pigmentosa an abnormal course of the long ciliary arteries which show a long episcleral and short choroidal course, causing malnutrition of the postequatorial zone.

The cones extend far temporally from the macula, nuclei are displaced into the layer of the cones far out in the fundus periphery and there is an abnormal layer between the outer segment of the rods and cones and the pigmentary epithelium in the form of a protoplasmatic band filled with pigment granules in Oguchi's disease (Oguchi).

Yamanaka found that in Oguchi's disease the pigment granules move in the pigment epithelium inwardly as in a light-adapted eye and that its basement parts contained much lipoid.

Uyama found in an eye with luxation of the lens into the anterior chamber and myopia, vacuoles in the cones which were numerously temporal and showed nuclei, therefore revealing some similarity to Oguchi's disease.

McMillan describes in Tay Sachs disease lipoid depositions in the ganglion cells of the macula and in some bipolar cells. The papilla contains many astrocytes and microglia and the connective tissue is increased in the optic nerve.

Grinker describes in infantile amaurotic idiocy depositions of lipoids in the ganglion cells of the retina consisting of cholesterol-phosphatides and cerebrosides. Further, Bielschowsky, Heath describe lipoid degeneration of ganglion cells of the retina in infantile amaurotic idiocy.

Szymanski saw in Tay-Sachs disease hydropic swelling, loss of Nissl's granules, formation of vacuoles, pyknosis, karyorrhexis and karolysis of the ganglion cells and edema of the plexiform layers.

Greear found in infantile amaurotic idiocy complete absence of the nerve fiber layer of the retina and necrobiotic changes of its ganglion cells.

Greenfield and Levin find in the late infantile form of the amaurotic family idiocy lipoid degeneration of the ganglion cells of the retina; Bielschowsky additionally such in the outer retinal layer.

Givner and Roigin find in juvenile amaurotic familial idiocy disintegration of the internuclear layers of the retina and of the rods and cones, and irregularity of the pigmentary epithelium.

Bielschowsky, Dide, Guiraud and Michel, Holmes and Paton, Torrance find the outer retinal layers substituted by proliferating glia and pigmentary epithelium in the juvenile form of amaurotic family idiocy.

Goldstein and Wexler found in Niemann-Pick's disease histologically degeneration of the ganglion cells, vacuolization of the nuclear layers and histocytes around vessels of the sclera and episclera.

Samuels finds cystic degeneration of the retina in its various layers in detachment, occlusion of the central vein, renal retinopathy, Coats' and Hippel's disease, and in papilledema. Cystic degeneration of the macula is found in glaucoma, iridocyclitis and endophthalmitis.

Archangelsky, Casanovas describe cystoid degeneration of the retina.

Roscin finds anatomically in "commotio retinae" edema which he considers caused by retinal tears and dilation of vessels.

Seefelder finds in retinitis circinata cystoid degeneration of the retina, accumulations of macrophages and loss of the external nuclear layer. A connective tissue membrane with young connective tissue cells filled with fat granules lies between pigmentary epithelium and choroid. The choroid shows a few foci of lymphocytes.

Morax found in circinate retinopathy sclerotic changes of the vessels and deposition of hyalin and fibrin in cystic spaces of the outer plexiform and inner nuclear layers.

Woelfflin finds in retinitis circinata the diseased area of the retina filled with fibrin and hyalin.

Loewenstein and Garrow find in circinate retinopathy extensive fatty infiltration in the form of sheathing of vessels and fatty droplets in round patches throughout the entire width of the retina and a nonfatty substance in the outer plexiform layer.

Medullated nerve fibers in the retina are the expression of an abnormal anlage (Borrello).

Loewenstein describes cases in which the optic nerve fibers are at the papilla displaced between the retina and the pigmentary epithelium by maldevelopment or mechanically.

Klien finds in angioid streaks a diffuse degeneration of Bruch's membrane leading to ruptures. The earliest rupture takes place in the elastic portion of the membrane which is defective and calcified. Secondary changes are production of a cuticular substance from the epithelium, serous exudation from the choriocapillaris and proliferation of glia and vascular fibrous tissue.

Boeck finds in angioid streaks of the retina ruptures of Bruch's membrane and of the elastic tissue of choroidal arteries. Hagedoorn, too, finds the angioid streaks as ruptures of Bruch's membrane.

Holm found proliferation of the pigment epithelium in the macula in retinitis circinata, angiomatosis retinae, exudative juvenile macular retinitis and chronic, central retinochorioditis. He describes the destruction of the retina and choroid in the macular region in a case of buphthalmos and myopia. He found hemorrhages in the macula in glaucoma and myopia and detachment of the retina in tumors of the choroid.

Heine describes the anatomy of the macula lutea in various inflammations of the eye and finds a detachment of the macula relatively frequent, but he also finds the macula very often intact in eyes with myopia and secondary glaucoma.

Cystic degeneration, disintegration of the neuroepithelium and subretinal transudation may appear in the macula in iridocyclitis (Zeeman).

Wolff believes that edema appears in iridocyclitis easily in the macula, as Henle's fiber layer absorbs fluid greedily.

Casanovas is of the opinion that the neuroepithelium in the macula is exposed unprotected to the toxins of the vitreous body and therefore is easily affected.

Cystic degeneration of the macula is examined pathologically by Williamson.

Fuchs describes the formation of retinal folds when the eye is getting smaller. They occur most frequently in the fovea and sometimes the retina is displaced on the choroid.

Behr subdivides the "heredodegeneration" of the macula in congenital, juvenile, virile, presenile and senile forms. In the senile form, the pigmentary epithelium is anatomically normal and the macula shows cystoid degeneration with disintegration of the neuroepithelial layer.

Disciform degeneration of the macula shows microscopically: (1) arteriosclerotic changes of the choroid, (2) damage of Bruch's membrane, (3) ruptures of this membrane, (4) small subretinal hemorrhages from the choroid, (5) proliferation of connective tissue through the rupture, (6) fixation of the pigment epithelium to this tissue, (7) connective tissue proliferation between the retina and the pigmentary epithelium, (8) degenerative changes of the retina, (9) proliferation from the choroid between pigmentary epithelium and Bruch's membrane, (10) extensive vascularization of the connective tissue and (11) extensive hemorrhages in the neighborhood of the scar tissue (Braun.)

Junius and Kuhnt find in disciform degeneration of the macula atrophy of the retina and a tumor-like proliferation of glial and vascular fibrous tissue between retina and choroid.

Magitot finds in disciform macular degeneration conglomerations of pigment epithelial cells, degenerated nervous elements of the retina and glial tissue. He considers it as a primary pathologic process in the pigmentary epithelium.

Seefelder finds in disciform degeneration of the macula tumor-like connective tissue new formation in the subretinal space. The choroidal vessels are here sclerotic, the retina is cystic degenerated, pigment epithelial cells extend in heaps, tubules and palisades through the connective tissue, and vessels grow from the retina into the choroid. The altered choroidal vessels produce exudates which become organized.

Holloway and Verhoeff find in disklike degeneration of the macula a tissue between the retina and choroid containing spindle-shaped nonpigmented cells originating from the pigment epithelium and blood vessels growing in from the choroid through Bruch's membrane.

Behr believes that proliferative processes follow the transudation between the pigmentary epithelium and Bruch's membrane in cases of disciform degeneration of the macula. Elastic and fibrous tissues and the pigmentary epithelium proliferate and blood vessels grow in from the choriocapillaris.

Woelfflin considers the disciform degeneration of the macula as senile external exudative retinitis and believes that the primary cause is in the choroid. Exudate is poured out through holes of Bruch's membrane into the subretinal space which irritates the retina. The disciform new tissue consists of hyaline degenerated connective tissue, fine fibrillar connective tissue and enclosed pigment epithelium in the form of strands

and tubules. The pigment epithelium and neuroepithelium are missing in places. The connective tissue can contain bone.

The retroretinal tissue in Kuhnt-Junius' degeneration of the macula proliferates, according to Brown, from the choroid through numerous ruptures of Bruch's membrane.

v. Walbeck reports disciform degeneration of the macula and accuses as its cause an inflammation of the chorioeapillaris.

Hanssen, Verhoeff and Grossman describe histologically the disciform degeneration of the macula.

Lucie describes histologically a case of juvenile disciform degeneration of the macula.

Histologic examinations of early cases of detachment of the retina are reported by Bartels, Fuchs, Gonin, Kronfeld, Redslob, Sourdille, Vogt.

Kuemmell describes a case of four days old detachment of the retina showing two tears of the retina. The uveal vessels were congested, but no inflammation was present.

Kuemmell describes the detachment of the retina of seven weeks' duration with marked hypotony, very deep chamber with the iris reflected posteriorly and a very reduced vitreous. The aqueous humor, subretinal fluid and preretinal fluid in front of the retinal tear showed the same staining qualities. He assumes that the subretinal fluid perforated the retina as the margins of the tear were turned anteriorly. He believes that the subretinal fluid is produced by chronic uveitis and that the pressure in the subretinal space surpasses the pressure in the vitreous. In this way, the retina is pressed forward by the fluid and is aspirated by the vitreous.

Retinal tears can be found in a recent detachment of the retina histologically as precedent of the detachment (Kuemmell).

Kuemmell finds in retinal detachment early tissue proliferation in front of the retina which eventually may be the cause of the detachment.

Martin reports cases of anterior and posterior dialysis of the retina.

Lister describes separation of the retina from the optic disk in detachment.

Samuels describes changes of the vitreous body and retina in retinal detachment.

Shoemaker reports a case of detachment of the retina with gelatinous masses in the subretinal space and severe lymphocytic infiltration of the uvea.

Harlowe reports a tuberculoma of the choroid causing retinal detachment.

Lachman, Pesme describe detachment of the retina in newborns, due to subretinal hemorrhages.

Fuchs describes folding of the retina in softening of the eyeball due to disproportion between the area of choroid and retina. When the tension rises again, the folds smooth out, but the neuroepithelium atrophies here.

The subretinal fluid in retinal detachment is examined by Arruga, Baurmann, Jasinsky, Magitot and Lenoir, who found various amounts of albumin, depending on whether the detachment were serous or of inflammatory origin, some blood and cells of inflammatory and desquamative nature.

Longhena finds in analyzing the subretinal fluid in retinal detachment that it represents an exudate and is different from the vitreous, and considers the detachment of the retina of inflammatory origin.

The subretinal fluid in detachment can produce inflammation (Fuchs). Therefore, uveitis soon follows the detachment and can cause secondary glaucoma.

Weve found in ablatio falciformis congenita, connective tissue containing blood pigment in the anterior vitreous, fixed to the lens and retina which shows proliferation in the area of the fixation. There are no inflammatory changes visible. Probably hemorrhages into the tunica vasculosis lentis and the vitreous play a role in the origin of the malformation.

Heine considers the detachment of the retina not as a disease in itself but only as a symptom of various ocular diseases.

Dor, Fuchs, Gilbert, Lauber, find histologic evidence that the presence of many adhesions between the degenerated retina and the atrophic choroid in myopia decreases the incidence of detachment of the retina.

Gonin believes that the retinal tear plays the main role in the origin of detachment of the retina. The fluid collected preretinally pressed out from the scaffold of the vitreous, finds its way through the tear beneath the retina and separates it as a subretinal fluid from the choroid. He found in detachment of the retina holes of the retina to which rests of the retina correspond remaining on the retracted vitreous. He explains the retinal tear as sequela of the attachment of the vitreous body to the periphery of the retina. In eye movements the retina can be torn off by the pull of the attachment. He thinks that chorioretinitis anterior of the equator produces adhesion between retina and vitreous body and that the retraction of the vitreous body can cause retinal tear.

According to Baurmann, the retina stays in position by the difference in the pre- and retroretinal pressure. If the preretinal pressure becomes lower than the retroretinal, the result is detachment of the retina. Then albuminous fluid is exuded by the choroidal vessels into the subretinal space. Tears of the retina are secondary. In accordance with him, Deutschmann, Stein are of the opinion that with a decrease of the pressure in the posterior chamber due to changes in the blood circulation of the vitreous body the pressure in the subretinal space has a great preponderance and separates the retina.

Kuemmell states the opinion that the decrease of tension in the vitreous space produces retinal detachment as the decrease of the tension in the center of the eye sucks in the retina, iris, lens and choroid. The congested choroid produces an albuminous fluid by transudation. The retinal tear is of no importance.

Pascheff resumes findings and states that although the majority of the examiners consider a retinal tear a frequent cause of the detachment, the detachment can also take place without hole.

Hanssen finds as cause of detachment of the retina cystic degeneration of the retina and liquefaction of the vitreous body.

Sourdille believes that pathologic changes in the pigmentary epithelium cause detachment of the retina with loss of the physiologic contact between rods and cones and pigmented processes of the epithelium. Giannini, Marquez, Rollet represent the same opinion.

Redslob believes that the choroid is primarily affected in retinal detachment and that the subretinal exudate detaches the retina and that retinal tears appear in the further course with the formation of cysts.

Chronic inflammation of the anterior segment of the choroid is cause of the detachment of the retina, according to Loewenstein. The inflammation is brought about by stasis in the circulation due to obliteration of the choriocapillaris between the equator and the ora serrata.

The chronic uveitis responsible for detachment of the retina is caused by a tuberculosis infection, according to Schall.

Hanssen, Vogt believe that an inflammatory irritation of the uvea can produce a subretinal transudation and an inflammation can be caused by toxic irritation of the fluid.

Fuchs believes that stretching of sclera and choroid is the cause of the detachment of the retina.

Hypotony as cause of retinal detachment is credited by Kuemmell, Redslob.

Kurz reports histologic examinations after Gonin's operation, and finds scars surrounding the cauterized area and numerous connective tissue strands extending into the vitreous.

Pathologic findings in eyes subjected to diathermy operations for detachment of the retina are reported by Amsler, Coppez, Fischer, Lefkoeva, Safar.

Terry found after sclero-cautery puncture for separation of the retina the latter adherent in the area of the cauterization.

Weekers finds that in an operation for detachment of the retina fibrous tissue penetrated through the scleral perforation and adhered to the underlying choroid and retina and that these adhesive episcleral reactions supported the operative result and preclude recurrences.

Striae retinae after reattachment of a previously detached retina consist, according to v. Hippel, of a partly pigmented homogeneous substance. The striae retinae represent folds of the retina with degeneration and glia proliferation (Hagedoorn).

Borello distinguishes true and pseudocysts of the retina. The latter are often folds of the retina. The true cysts are caused by trauma, malnutrition, inflammation, degeneration. Cysts of the retina are examined histologically by Fuchs, Kronfeld, Neame.

In Derkač's case of a 30 year old woman, a cysticercus was situated in a fold of the retina and the entire uvea, cornea and sclera were infiltrated due to toxic irritation.

Cenisowa found a cysticercus in the subretinal space surrounded by proliferating glial and connective tissue in a 43 year old man. Menestrina, Orlowa-Kurasowa saw subretinal cysticercus.

Archangelsky and Braunstein found a diptera larva subretinal in a 4 year old girl. A diptera larva located subretinally caused uveitis with many eosinophils in a 2 year old boy (Ennema). Zeeman saw a diptera larva in the subretinal space of a 6 year old boy, reaching it along the ciliary vessels. Larvae of flies were found subretinally in an enucleated eye by Behr.

McCrea classifies the neoplasms of the retina as (1) retinoblastoma, (2) neuroepithelioma, (3) medulloepithelioma originating from the ciliary epithelium, (4) neurocytoma and (5) astrocytoma.

Grinker distinguishes the gliomas of the retina as (1) medulloepitheliomas arising from the primitive epithelium of the retina and ciliary body

(2) retinoblastoma and retinocytoma arising from a hypothetic bipotential undifferentiated retinoblast and (3) neuroepithelioma arising from primitive spongioblasts or the neuroepithelium. He finds in a neuroepithelioma of the retina spongioblasts, astroblasts and astrocytes.

Susman distinguishes: (1) neuroepithelioma consisting of primitive epithelium; (2) spongioblastoma consisting of primitive retinoblasts and, (3) neuroblastoma with already developed retinal structure.

Favaloro believes that the glioma retinae has normal and anaplastic glia cells. It shows epithelial cells, uni- and multipolar spongioblasts, astrocytes, sometimes also fibrillar forms. He distinguishes glioma and neuroblastoma. He subdivides the glioma in: (1) anaplastic afibrillar glioblastoma; (2) spongioblastoma of the astrocyte series; (3) spongioblastoma of the ependymal series forming rosettes; (4) glioblastoma with fibrillar cells.

Dejean distinguishes: (1) neuroepithelioma originating from the cells of the primitive neural tube; (2) neurospongioma originating from the spongioblasts and (3) retinocytoma already showing differentiation.

Muñoz Urra employed glia staining in the study of retinoblastomas. He believes that the retinoblastoma is formed by glial cells which grow without intercellular substance as floating cell masses in the vitreous and deposits on membranes and in the tissue. The gliocytes extend long and small processes to capillaries and arrange themselves in mantles around vessels. The gliocytes can develop to astrocytes which form glial fibrils. Tumor cells can also arrange themselves radially between the processes of the astrocytes, in this way forming rosettes. The apparent lumen of the rosette is filled in reality by an astrocyte.

Ascunce stained gliomas of the retina after the methods of Golgi-Cajal, Weigert, Rio-Hortega and Achucarro and found only elements of the neuroglia.

Redslob describes the cells of the tumors of the retina as polymorphous and considers them as very young cells of the central nervous system which form, as first differentiation, ependyma cells. He calls the retinal tumor "retinocytoma." Mawas, too, calls the tumors of the retina "retinocytoma."

Goldstein and Wexler found in the retina of a 6½ month old irradiated human embryo rosettes due to scattering of cells from the nuclear layer.

Jaensch describes formations of folds and rosettes in the retina of a 9 month old child which he considers as the earliest form of the glioma of the retina.

Zeiss considers the formation of rosettes in retinoblastoma as expression of the fast-continuing cell division. The proliferating cells are arranged in chains and heaps which can form loops. In sectioning of such chains the appearance of rosettes can be produced.

Wolff finds in phosphotungstic acid-hematoxlin staining the columnar cells of the rosettes identical with those of the neuroepithelium. He believes that the tumor cells of the retinoblastoma originate from the primitive layer which forms the inner nuclear layer.

Caramazza thinks that rosettes are formed in retinoblastoma by proliferation of tumor elements around lumina.

Dejean believes that in cystic formation of the iris, ciliary body and retina, in detachment of the retina, in tubular formations of the ciliary

body, in chronic inflammation, in retinal tumors of the child and the adult there is always seen a return to the primitive ependymal cavity of the early embryonal development.

Parkhill and Benedict find that the glioma of the retina mainly originates from the inner nuclear layer.

Ch'in describes intraretinal glioma arising from the inner nuclear layer.

Fuchs finds in beginning glioma, retina cells rich in cytoplasm apparently originating in the inner nuclear layer.

Wolff states that the glioma retinae originates from elements of the primitive nuclear zone and that the rosettes are formed from fetal rod and cone cells.

Stock found in a 1 year old child multiple gliomata of the retina starting in the bipolar cells and at the posterior surface of the lens at the insertion of the hyaloid artery.

Scheerer saw a glioma of the retina in an eye with persistent hyaloid artery, in the sheath of which glioma nests appeared independently from the retinal tumor.

Rutherford finds that in glioma of the retina the endothelial cells of the vessels are displaced by tumor cells and destroyed.

Von der Hoeve, Holland and Rutherford, Teulieres report cases of gliomata of the retina.

Velhagen could find glioma cells in great amount in the anterior chamber, in which they appear very easily when the zonule lamellae are perforated.

Zentmayer and Schoenig report glioma with infiltration of the chamber angle, formation of nodules on the anterior surface of the iris, accumulation between the zonule fibers and the ciliary processes and infiltration of the optic nerve.

Vogt describes motile globular precipitates in glioma.

Zeiss describes a glioma perforating the eyeball anteriorly and showing much proliferation of connective tissue dividing the glioma tissue in numerous nests.

Knapp reports bilateral glioma retinae with gliomatous involvement of iris and ciliary body and perforation of the corneae.

Guyton reports a case of bilateral glioma retinae with an acute inflammation in one eye, probably due to toxins of the tumor.

Stuebel observed a bilateral retinal glioma with necrosis and calcification in a 1½ year old boy. Rogers observed bilateral glioma retinae with spread to the orbit.

Gerard and Morel report one glioma retinae in an 11 year old child and another one in a 35 year old man. Gerard and Detroy report glioma retinae in a 66 year old woman.

Rados found gliomata of the retina and of the brain in cousins and both tumors showed the same histologic type.

The metastases of gliomas outside the eye often vary considerably in their structure from the intra-ocular tumor. Collins relates to the difference in the blood supply. There are numerous anastomosing blood vessels extra-ocular in contrast to the scarce end arteries of the retina.

Cattaneo considers retinoblastoma of epithelial origin originating from embryonal retinal cells and proposes the name "retinoma."

Castelli found a malignant retinoma in a 3½ year old child with extension into the optic nerve.

Unilateral retinoblastoma shows small nuclei, scarce cytoplasm and no rosettes, in bilateral retinoblastoma the cells have more cytoplasm and there are sometimes found rosettes (Cummings and Sorsby).

Cohen, Cutino and Lloyd report on retinoblastoma. Addario la Ferla describes retinoblastoma in a fourteen month old girl. Rasmussen found a retinoblastoma in a 40 year old man.

Cairns and Russell, Rand report retinoblastoma which perforated into the sheaths of the optic nerve and proliferated in the subarachnoidal space towards the brain.

Reese describes a retinoblastoma invading the optic nerve behind the lamina cribrosa.

Collins finds that a retinoblastoma invading the choroid produces new formation of fibrous tissue and that it proliferates along lymphatic spaces.

Lemoine reports retinoblastoma in a 3½ year old boy extending into the orbit and intracranial cavity.

Denti describes a case of retinoblastoma with formation of an hypopyon.

Complete retrogression of retinoblastoma is reported by Hine, v. Hippel, Siegrist.

Metastases in distant organs are described in retinoblastoma by Irvine, Jaffe, Verhoeff.

Hu reports a neuroepithelioma of the retina with extensive metastases in the skull, the bones, muscles, lymph nodes, meninges and central nervous system.

Patwardhan reports a neuroepithelioma of the retina which appeared six months after an eye injury.

Jeandelize and Cornil report a neuroepithelioma of the retina with metastasis in the preauricular lymph node. Neurocytomata are described also by Dejean, Susman.

Pieck saw a neurocytoma of the retina showing epithelioid cells and ganglion cell-like tumor cells in a 75 year old woman.

Scheeler observed a neuroblastoma of the retina.

Astrocytomata of the retina are described by Dejean, McLean.

Huggert and Hulthquist report a true glioma of the retina consisting of polymorphous cells with honeycomb vacuolated cytoplasm and short processes. The tumor is probably an oligodendroglioma.

Cristin found in a 28 month old child a retinal tumor extending along the optic nerve and the vortex veins and consisting of anaplastic spongioblasts and astroblasts (spongioblastoma retinale).

Carr and Stallard describe a retinal tumor consisting of endothelial cells and glia containing few cystic spaces.

Schuster describes a tumor apparently originating from the pigmentary epithelium of the retina as retinoepithelioma malignum pigmentosum.

Histologic findings of angiomatosis retinae are reported by Czukrasz, McDonald, Marchesani, Mawas, Miyashita and Nisyake, Niccol and Moore, Paton, Sladden, Williamson-Noble and Greenfield.

v. Hippel describes cases of angiomatosis retinae and external exudative retinitis of Coats.

Lindau finds cerebellar cysts with angiomata in their walls together with angiomatosis retinae. Both the angioma of the cerebellum and of the retina have only one afferent artery and one efferent vein. The tumor consists of proliferating capillaries with swollen endothelial cells. He considers the gliosis as secondary. He describes capillary angiomata and small cysts of the retina and proliferation of the glia in a 37 year old man.

Rochat finds in familial angiomatosis retinae, nodes consisting of glial proliferation and compressed capillaries and simultaneous cerebellar cysts with capillary tumors in their walls.

v. Hippel describes in angiomatosis retinae, tumors containing dilated vessels and newly formed capillaries and glycogen droplets.

Gourfein-Welt found angioma of the retina together with extensive exudation into the subretinal space.

Cross found angioma of the retina consisting of endothelial-lined channels varying from capillaries to large vessels.

The tumors in angiomatosis retinae are endotheliomata, according to Brandt, in which mucus, fibrin, fat, and glycogen can be deposited.

Berblinger considers the tumor in angiomatosis retinae as primary proliferation of capillaries and the glia proliferation as secondary.

Heine describes in angiomatosis retinae gliosis, cysts of the retina, small angiomatous nodules, proliferation of pigment epithelia, and bone formation in the choroid. He considers proliferation of the glia and of the pigmentary epithelium as the primary, and vascular changes as the secondary. He speaks of angiogliosis.

Meller and Marburg find in v. Hippel's disease mostly proliferation of glia and less proliferation of vessels. They call it glioblastoma retinae teleangiectodes.

van der Hoeve describes tumors of retina and papilla in tuberous sclerosis. The tumors consist of cells and fibers corresponding to embryonic retinal elements; they have spaces filled with serum and erythrocytes and are situated in the nerve fiber layer.

Messinger and Clarke describe retinal tumors in tuberous sclerosis with oval cells with thick processes, multinuclear cells, calcareous concretions and ossification.

Schob describes in tuberous sclerosis small retinal tumors restricted to the nerve fiber layers consisting of glial cells and fibers.

Pathologic examinations of retinal changes in tuberous sclerosis are reported further by Feriz, Fleischer.

Loewenstein and Steel find in tuberous sclerosis multiple tumors in the nerve fiber layers of the retina containing nerve fibers, small cysts and rounded tumor cells, angiomatous growth in the retina and angioma of the choroid.

Zbinden saw in a 23 year old man with adenoma sebaceum and multiple fibromata, retinal tumors consisting of proliferating glia.

Stallard describes a tumor of the papilla consisting of neurocytes and neurofibrils in Recklinghausen's disease.

Simoleroff and Agatston report a metastatic alveolar adenocarcinoma of the retina with the primary tumor in the stomach.

Moore and Stallard describe metastatic carcinoma of the choroid with the primary neoplasm in the lung.

Uhler describes a case of metastatic malignant melanoma of the retina in a 26 year old man with diffuse melanotic sarcomatosis.

Boente describes a metastatic melanoblastoma of the retina besides melanoblastoma of the choroid in a 45 year old woman with universal melanosarcomatosis.

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Chapter IX

PATHOLOGY OF THE OPTIC NERVE

1. General Considerations

The optic nerve, which originates in the ganglion cells of the retina, courses through the orbit and extends to the primary optic centers in the brain and is, in reality, a tract of the central nervous system whose nerve fibers are myelinated in the greater part of its course, but have no sheaths of Schwann. The nerve is surrounded by meninges. Therefore, the optic nerve takes part in diseases of the intrinsic eye, the orbit and generalized diseases of the body, and especially in diseases of the central nervous system.

Only infrequently is the optic nerve primarily affected. The nerve fibers respond to injury by swelling of the axon cylinders and of the myelin sheaths and, if the process is not reversible, by degeneration and atrophy. This can be the case in physical and chemical injuries, inflammation and malnutrition. The changes are distinguished only insofar as they take a more acute or chronic course. If the fibers are acutely interrupted by tear or cut, wallerian degeneration sets in in both directions simultaneously, toward the retina distally (retrograde degeneration, which eventually also includes the ganglion cells), as well as toward the central nervous system proximally. In the area of the injury, the fibers can become necrotic. The axon cylinder and the myelin sheath disintegrate to detritus and fragments; polymorphonuclears enter first and later phagocytes proliferate, both of which remove necrotic material, and connective tissue proliferates from the septa and glia. In chronic cases, nerve fibers degenerate, the medullated sheaths are broken up into fatty droplets and particles, the axon cylinder disintegrates and the products of disintegration are slowly removed by phagocytes. Only rarely and to small extent do optic nerve fibers regenerate. They may grow out to form small balls, but never

do interrupted nerve fibers reunite. The glial tissue reacts, as already mentioned, to the pathologic stimulus of trauma, inflammation and degeneration. The supporting tissue of the glia is composed of cells and fibrils. The cells are micro-glial cells, astrocytes and oligodendrocytes. The former are considered by some as of mesodermal origin and both the latter as ectodermal neuro-glial. The micro-glial cells are oval with fine processes and become phagocytes under pathologic stimuli. The cells become larger and retract their processes. They proliferate and ingest into their cell body the substance of the myeline sheaths, disintegrating into fatty droplets and larger particles. The cells appear vesicular and vacuolated and their nuclei eccentric and pyknotic (compound granular corpuscles). They are situated in the meshwork of the glial fibers, septa, perivascular lymph spaces and in the intervaginal spaces. The decomposed material can be transported by the phagocytes directly into the perivascular lymph spaces of the vessels. If they have given up their material and reformed, they become similar to lymphocytes and may imitate perivascular infiltrates. The faster the tissue disintegrates, the more cells appear. The astrocytes are large cells with many processes and fibrils and everywhere they separate the nervous tissue from the mesodermal tissue. The oligodendrocytes are small cells with rounded nuclei and few small cellular processes. The cells swell under pathologic conditions. Their processes become thickened, the fibrils increase and they also replace disintegrated nervous tissue by their proliferation (gliosis). But the glia can also undergo regressive changes and can degenerate along with the nervous tissue. The nuclei become pyknotic, the processes fragmented, the cell body dissolves and in this way caverns are formed. The connective tissue of the optic nerve takes part in the inflammatory processes and it becomes infiltrated and proliferates. In degenerative processes, it remains unchanged or condenses and scleroses like the vessels coursing in the septa.

The study of the histopathologic changes is made more difficult inasmuch as the nervous tissue easily undergoes cadaverous changes, and by fixation artifacts are easily produced. Furthermore, complicated special staining methods are often necessary

to make the complex tissues accessible. An apparent degeneration of the myeline sheath may be simulated by precipitation of fat; by shrinkage, holes may be formed, imitating edema. Sometimes round holes are formed in the optic nerve by fixation.

2. Pathology of the Nerve Sheaths

Pathological changes of the nerve sheaths and of the nerve itself are distinguished. In the latter are included diseases of the papilla and of the nerve stem.

The nerve sheaths show (1) abnormal dilation with accumulation of fluid, (2) hematoma, and (3) inflammation.

The nerve sheaths are enormously dilated and sometimes ampullar, especially in cases of increased intracranial pressure (hydrops of the nerve sheaths). Abnormally wide sheaths are found in hydrophthalmos where the pia runs nearly parallel to the sclera, although the dura keeps its normal course perpendicular to the sclera; in optic atrophy where there is a decrease of the volume of the nerve; and on the side opposite a conus where the dura inserts abnormally distant into the sclera.

Hemorrhages into the optic sheaths take place into the subdural or into the subarachnoidal spaces, sometimes into both at the same time. Subdural hemorrhages are nearly always caused by trauma, rarely by extensive spontaneous cerebral hemorrhages. In intracranial trauma with accumulation of blood in the subdural space, in fracture of the optic canal, after rupture of the dura, or from the ruptured ophthalmic artery, blood can appear in the subdural space. Subarachnoidal hemorrhage may be spontaneous or traumatic. Spontaneous hemorrhage is usually caused by rupture of congenital basal aneurisms, spontaneous cerebral hemorrhages and hemorrhages from meningeal vessels in blood diseases, diabetes or chronic nephritis. Traumatic hemorrhage is caused by rupture of meningeal vessels in basal fracture. With subarachnoidal hemorrhages, papilledema and retinal hemorrhages may occur.

Inflammation of the nerve sheaths (perineuritis, peripheral interstitial optic neuritis) is a meningitis, and appears as (a) exudative and (b) suppurative perineuritis.

In exudative and adhesive perineuritis, the subdural space is filled with fibrin, lymphocytes, polymorphonuclears, and desquamated endothelial elements. Vessels of the dura show perivascular infiltrates, connective tissue cells are increased and endothelium proliferates. The pia is diffusely and circumscribedly infiltrated with polymorphonuclears and lymphocytes and its vessels show perivascular infiltration. The septa of the optic nerve in its peripheral circumference can also be infiltrated with lymphocytes and polymorphonuclears. The exudate can be resorbed, connective tissue and endothelium proliferate, and finally the intervaginal spaces are obliterated.

In suppurative perineuritis, the sheaths of the optic nerve are filled with polymorphonuclears, and small abscesses appear in the peripheral optic nerve bundles.

3. Inflammatory Processes (Optic Neuritis)

In the optic nerve itself are distinguished (a) inflammatory processes (optic neuritis) in which the nerve is primarily affected, but the sheaths can also be affected by acute or chronic inflammations, the latter being nonspecific and specific, (b) degeneration and atrophy, (c) combination of inflammatory and degenerative processes, (d) papilledema, (e) deposition of abnormal and degenerated substances in the nerve and its sheaths.

Optic neuritis is either restricted to the papilla (papillitis) or to the nerve stem (retrobulbar neuritis) or both are affected at the same time. If the retina is also inflamed, neuroretinitis exists and the inflammation extends from the optic nerve to the retina or from the retina to the optic nerve or both are inflamed at the same time. The inflammation is primary when bacteria or toxins attack the optic nerve by way of the blood circulation, or is secondary to inflammation of the globe and of the tissue surrounding the optic nerve in the orbit and paranasal sinuses and of the central nervous system. The etiology is still often quite uncertain, since most cases are observed only clinically and the relation of the inflammation in the optic nerve to other diseases of the body cannot always be established. Often, spontaneous cures happen. Furthermore,

it can not always be decided with certainty whether primary inflammatory processes or degenerations prevail and if both began simultaneously.

Acute suppurative optic neuritis is seen with edematous swelling of the papilla, polymorphonuclears along the vessels and in the vascular funnel, new formations of vessels and swelling of the endothelium, small hemorrhages, infiltration of the edematous septa with polymorphonuclears and lymphocytes, swelling and disintegration of nerve fibers and appearance of scavenger cells. The vessel walls may become necrotic under some circumstances. With the disappearance of the nervous substance, glial and connective tissue proliferate. The infiltration is scattered diffusely over the optic nerve or circumscribed heaps of polymorphonuclears exist simultaneously with emboli in arteries and thrombophlebitic processes. Circumscribed necrosis and abscesses appear. The inflammation in the nerve stem is restricted more to the central axial connective tissue with its central vessels (axial retrobulbar neuritis) or affects the entire nerve stem (total transverse neuritis). Primary metastatic acute inflammation of the optic nerve is rare, occurs in endocarditis, meningitis, furunculosis, pyemia and acute infectious diseases and is produced by bacteria or by toxins. Acute inflammation of the optic nerve is usually secondary to endophthalmitis and panophthalmitis, suppurative perineuritis following meningitis, abscesses and necrosis of the orbit, suppuration of the posterior ethmoids and sphenoid. Erosion of the bone, thrombophlebitis of veins connecting the paranasal sinuses and the orbit and inflammation of the marrow spaces of the cancellous bone bordering paranasal sinuses and orbit sometimes transmit the infection.

Chronic optic neuritis is infrequently observed and occurs in its pure form rarely as interstitial neuritis. There is perivascular infiltration of lymphocytes, the septa contain lymphocytes and plasma cells, connective tissue and glia proliferate and destroyed nervous tissue is slowly removed by macroglia. It is usually seen secondary to lesions in the eye in chronic nonspecific and specific uveitis, especially in sympathetic ophthalmia, perhaps now and then also following retinitis and chronic inflammations of the posterior paranasal sinus. Inflam-

matory and degenerative processes usually are mixed from the beginning.

Neuritic atrophy arises as the end stage of acute and chronic optic neuritis. The large and small septa are thickened and sometimes connected by a newly formed tissue. The nerve tissue is substituted by glia and especially in an early stage there are

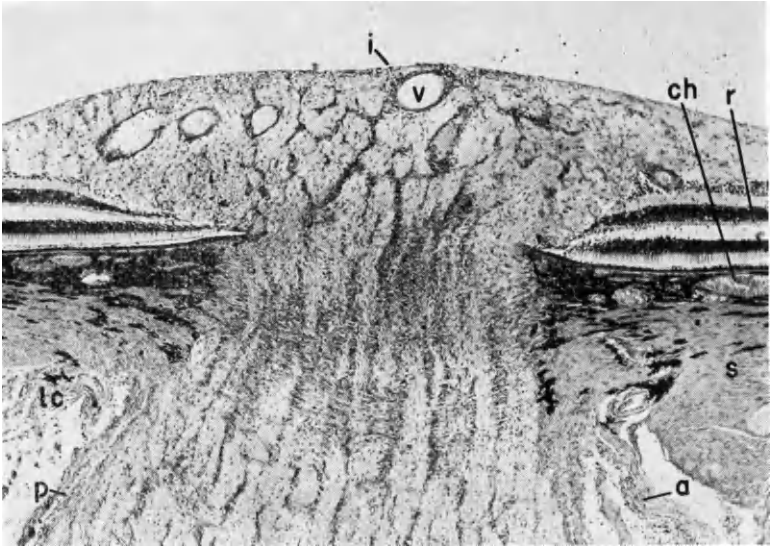

FIG. 44-a.—OPTIC NEURITIS. a, arachnoid; ch, choroid; i, infiltration in the papilla; lc, lamina cribrosa; p, pia; r, retina; s, sclera; v, blood vessel with perivascular infiltration. 45×.

numerous nuclei present, although in a later stage shrinkage and loss of cells is seen.

Chronic specific inflammations of the optic nerve are due to tuberculosis and syphilis, and the nerve and its sheaths are affected.

The tuberculosis of the optic nerve appears as (a) miliary tubercles and (b) tuberculous granulomata, frequently in the form of a solitary tubercle. Miliary tubercles, consisting of epithelioid cells and few giant cells surrounded by lymphocytes, lie in the stem of the optic nerve, in the vascular sheath, attack vessel walls themselves, or are situated in the sheaths of the

optic nerve and are accompanied by infiltration of the papilla, the septa and the vaginal spaces with lymphocytes, and connective tissue proliferates. The tuberculous granuloma is seen in the optic nerve as a conglomerate tuberculosis with typical confluent tubercles, and as tumor-like solitary tubercle consisting of many epithelioid and giant cells and caseation substituting the tissue. The papilla usually is affected and severe iridocyclitis,

FIG. 45.—NEUROMYELITIS. d, dura; e, edematous infiltrated nerve bundles; h, hemorrhage and disintegration of nerve bundles; p, infiltrated pia; s, thickened septa; v, vessel surrounded by infiltration. 30×.

detachment of the retina, venous thrombosis, and hemorrhages follow. The wall of the central retinal vein is infiltrated with round cells and contains giant cells. Tuberculous granulation tissue often extends widely in the optic nerve and perforates through the sheaths into the orbit. Tubercles of the dura can heal by fibrosis, calcifications, and ossifications. Tuberculosis enters the optic nerve by way of the blood circulation or from the surrounding tissue. The spread of a miliary tuberculosis goes by way of the blood circulation. Tuberculosis can spread

in the eye itself from the uvea (especially tuberculosis of the choroid) and retina directly into the sheaths and the nerve, but can also spread along the perivascular lymph spaces of the retina; tuberculous lesions of the orbit can perforate into the optic nerve and tuberculosis can continue from tuberculous basal meningitis or tuberculous formations in the chiasm directly into the sheaths of the optic nerve and into the nerve itself.

Syphilis of the optic nerve is found as (a) interstitial neuritis and perineuritis and as (b) gumma. The pia and arachnoid are studded with lymphocytes and plasma cells and the infiltration extends from here into the nerve tissue. Furthermore, there are perivascular infiltrations with lymphocytes, and the intima of the vessels proliferates. With destruction of the nervous tissue, the connective tissue of the septa and the glia proliferates. Gummatous processes affect both the sheaths and the nervous substance. Lymphocytes are seen to surround small rows of epithelioids and few giant cells and proliferating blood vessels, as the largest part represents necrotic tissue. The gummatous tissue may substitute the larger part of the nerve. The papilla can also be affected by gumma, but often it is restricted to the retrobulbar part of the optic nerve and the inflammation extends to the chiasm. Spirochetes are sometimes found. The affection of the optic nerve frequently continues from the meninges, especially from a syphilitic basal meningitis or gummatous meningitis, which is often established in the chiasm, but the optic nerve can be affected primarily. The disease of the optic nerve sometimes extends into the inner eye. Syphilitic changes of the optic nerve are found in acquired syphilis as well as in congenital lues.

4. Degeneration and Atrophy

Degeneration and atrophy are characterized in the beginning by disintegration of the myelin sheaths into droplets (Marchi disintegration). The nerve fibers swell and show irregular thickening and interruption of their continuity. The axon cylinders show fine granules and break up in particles. The products of the disintegration disappear, as they are dissolved or removed by macrophages. The direction of the degeneration

does not follow certain rules; it extends, as already mentioned, either from the retina, ascending into the nerve up to the primary centers where it stops if the anterior neuron (retina-primary optic center) is affected, or it appears as retrograde degeneration toward the ganglion cells. In diseases of the posterior neuron (primary optic center—visual cortex), the degeneration sometimes extends beyond the primary centers into the optic tract and the optic nerve. If nerve fibers have disappeared, a circumscribed or diffuse optic atrophy is present, and then only connective tissue septa and glia remain which frequently proliferate. The atrophy is (1) simple atrophy, if nervous tissue is destroyed without antecedent inflammation; it is (2) neuritic (postneuritic) atrophy if inflammation precedes and destroys the nervous tissue, and (3) cavernous atrophy, when large spaces filled with fluid form in the nervous tissue as are found especially in glaucoma, but also in myopia, and, occasionally, in rupture of nerve fibers. Very small holes are seen rarely in various atrophies when no reparatory glial proliferation takes place. The nervous tissue of the papilla can disappear entirely in noninflammatory degeneration, and atrophic excavation be formed which is flat dishlike. In simple atrophy, the septa are thickened and isolated, the small septa disappear and the nervous tissue is substituted by glial fibers with few cells. Simple degeneration and atrophy is of varying etiology. Exogenous and endogenous poisons are the usual causes; it is frequent in tabes and progressive paresis. It is found in hereditary optic atrophy (Leber's disease); the nerve also degenerates due to trauma, due to pressure of adjacent vessels, due to circulatory disturbance and due to pressure of tumors and exostoses and pull of adhesions.

Exogenous poisons affecting the optic nerve are methyl alcohol, ethyl alcohol, tobacco, optochin, and arsenic.

Poisoning has been studied in numerous animal experiments on higher and lower mammals, and often the results of these conform to anatomic findings in man. Often optic nerve poisoning is observed only clinically, and studied in animal experiment without histologic confirmation in the human. In these cases of poisoning, it is not always certain how much of a role inflam-

matory changes play. Such poisonings are produced by carbon disulphide (which is used in vulcanizing of rubber), iodine (especially iodoform), thallium (which is applied as thallium acetate in ointments), filix mas (aspidium), salicylates, ergot, anilin, dinitrobenzol, and inorganic arsenicals.

Methyl alcohol (wood alcohol) affects ganglion cells of the retina and the optic nerve simultaneously. Some assume that the affection of the optic nerve is secondary to the affection of the retina and others postulate the simultaneous attack on retina and optic nerve. The ganglion cells of the retina are swollen, their nuclei become pyknotic and disintegrate. Cells disappear and debris is deposited beneath the inner limiting membrane. Single myeline sheaths of the optic nerve stem break up into fine fat granules, the axon cylinders swell, detritus accumulates around blood vessels, and cells appear, loaded heavily with fat granules. It is generally assumed that the incomplete oxidation of the methyl alcohol leads to acidosis due to the formation of formic acid, and the oxidative processes of the retina and the optic nerve are therefore disturbed.

Ethyl alcohol brings about a Marchi degeneration of the papillomacular bundle in which intact fibers always remain. The atrophy extends through the geniculate body in a continuous or patchy fashion. Connective tissue septa and glia hypertrophy in the area of the atrophic nerve bundles and new vessels are formed in the proliferating tissue. Their walls may become sclerotic and the endothelium proliferate, leading eventually to endarteritis obliterans. Ganglion cells between the papilla and fovea show chromatolysis of their Nissl bodies and pyknotic nuclei and partly disappear. Sometimes, also, lymphocytes appear secondarily around degenerated nerve fibers. It is assumed that malnutrition from alcoholic gastroenteritis due to lack of absorption of vitamin B is the cause.

In general, tobacco causes the same alterations as ethyl alcohol. Some assume that neither ethyl alcohol nor tobacco alone produce changes, but always in combination, although others have observed cases in which one of these poisons alone produced the same disease as both together. Inflammatory changes, if present, are secondary; therefore, in general, the theory that the poison-

ing is primarily inflammatory is refuted. It is assumed that either the nerve tissue itself is primarily directly poisoned, the nerve fibers in the optic nerve first and the ganglion cells of the retina later and both independent of each other, or that primarily the small vessels are spasmodically narrowed with secondary damage to the nerve fibers.

Optochin (quinine) produces irregularly distributed degeneration of myeline sheaths, in the optic nerve with appearance of myeline particles, disintegration of glial cells, and appearance of compound granular corpuscles. The optic nerve atrophies and glia proliferates. The nerve fiber layer of the retina shows edema, the ganglion cells become vacuolated, outer nuclear cells and rods and cones degenerate, and finally the ganglion cells disappear. The retina and optic nerve are damaged by the poison at the same time and it attacks the nervous substance itself directly and primarily; also, the nerve fibers innervating the vessels are damaged, and in this way vascular spasm, which is so marked in quinine poisoning, is produced. The vascular spasm continues, fibrillar thickening of the adventitia and media occurs, and both of these increase the tissue damage secondarily by ischemia. More eyes have been examined histologically after optochin poisoning than after quinine, because optochin has so often been used in cases of pneumococcus pneumonia.

Organic arsenic compounds (especially atoxyl, arsazetin, but also others, such as acetylarsan and tryparsamide) cause deterioration of the myeline sheaths and axon cylinders with proliferation of glia in the optic nerve, further disappearance of nerve fibers and ganglion cells in the retina and shrinkage of the inner nuclear layer. Inflammatory changes are absent. Occasionally observed inflammatory reactions such as excessive accumulations of lymphocytes and plasma cells around vessels and in the septa are generally thought to be primarily caused by the underlying and treated disease, especially lues.

To the group of atrophies and degenerations caused by endogenous poisons belong especially those of diabetes, histologic findings of which exist in human eyes. Diseases of the optic nerve appearing in anemia, malignant neoplasms, pregnancy and lactation, excessive burns and avitaminosis (A and B) which are con-

sidered as toxic disturbances are observed only clinically. It is uncertain whether they are degenerative or of inflammatory nature.

Diabetes mellitus produces slowly progressive degeneration of the fibers of the optic nerve, usually more marked in the papillomacular bundle, and leads finally to diffuse discontinuous atrophies with swelling of glial cells, increase of the glia and thickening of the septa. Secondarily, perivascular infiltration of lymphocytes, plasma cells and vacuolated histiocytes sometimes appears. The acidosis of diabetes may be the cause, or perhaps the accompanying severe arteriosclerosis.

Simple (primary) optic atrophy is often observed in tabes, dementia paralytica and taboparesis (meta-luetic or parasyphilitic manifestations). At first, varicosities of the myeline sheaths appear, which later break up into clumps. At the same time, the axon cylinders swell, show beading and finally disintegrate. The products of disintegration are taken up in the form of droplets and small particles by scavenger cells. The cells of the adventitia and intima of the vessels may be filled with a fatty substance. The degenerated nerve tissue is replaced by glial cells which produce numerous fibers. With the increase of fibers, the glial cells decrease. Finally, after all nervous substance has disappeared, the spaces between the septa are entirely filled with glial fibers. The finer septa atrophy and shrink and the spaces normally filled with nervous tissue coalesce. The larger septa become thicker by homogeneous sclerosis and the vessels also sclerose. The pia thickens, the arachnoid shrinks and the dura, due to decrease of volume of the nerve, is folded. Nerve fibers of the papilla disappear and glia proliferates, replacing the nervous substance. Occasionally, also, accumulations of lymphocytes and plasma cells are found in the pia and septa, often with proliferation of the intima of vessels, mainly in the chiasm, and particularly in cases of general paresis rather than tabes. Nerve fibers and ganglion cells of the retina may disappear secondarily, corresponding to degeneration in the optic nerve. This degeneration is interpreted as one going from the nerve to the ganglion cells. The degeneration of the optic fibers and their atrophy, uniform or patchy, starts either in the chiasm

or close to the globe, but also in sections in between, more centrally in the nerve or closer to the pia. Spirochetes are found, but only in the mesodermal tissue and not in the nervous substance itself. Regarding the pathogenesis of the optic atrophy, opinion is divided. Toxic degeneration of the nerve substance is assumed to be produced by endotoxins, liberated from the dying spirochete, causing a change of the immunity condition

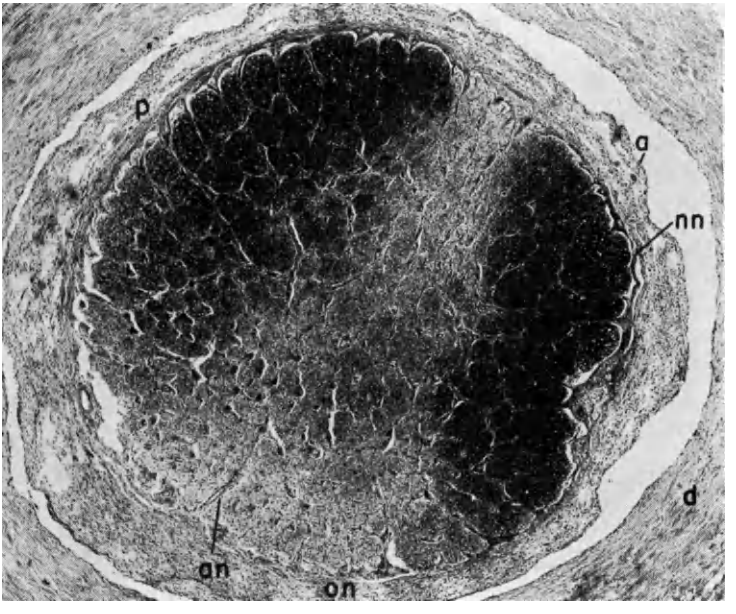

FIG. 46.—ATROPHIA NERVI OPTICI (WEIGERT STAIN). a, arachnoid infiltrated; an, atrophic nerve; d, dura; nn, normal nerve; on, optic nerve; p, pia. 30×.

of the glial border membrane, finally leading to sclerosis of the glia. Nutritional substances are brought to the nervous system with difficulty and the elimination of metabolic products is restricted; in this way, the nervous substance deteriorates and is replaced by glia. On the other hand, a primary inflammatory reaction in the pia and in the septa is postulated, which may lead to perivascular infiltration and secondarily to degeneration of the nerve fibers and proliferation of the glia.

In hereditary Leber's disease, the papillomacular bundle atrophies and the adjacent optic nerve bundles and glia proliferate. Ganglion cells and nerve fibers of the retina atrophy. The cause is said usually to be abiotrophy, which implies the premature aging of the living substance.

Sclerotic vessels and aneurisms may press on the optic nerve and produce atrophy. A sclerotic and frequently calcified internal carotid presses on the chiasm itself or presses the optic nerve at its entrance into the optic canal against the canal wall. The optic nerve can be compressed between the sclerotic internal carotid and anterior cerebral artery, or a sclerotic ophthalmic artery may compress the nerve in the canal and it may be flat or sometimes separated in two parts. The nerve fiber bundles atrophy and connective tissue increases. Sclerotic and nonsclerotic vessels can be pressed into the optic nerve also by a tumor, especially of the hypophysis. Sclerosis of the central vessels of the retina, and particularly of the smaller arteries which supply the optic nerve itself, is frequent in senile degeneration and leads to circulatory disturbance and subsequent ischemia of the nerve. As in the brain, multiple softening of the entire course of the nerve up to its entrance into the midbrain may occur, the nerve fibers degenerate and compound granular corpuscles appear. Also, peripherally situated atrophic foci of the optic nerve appear with thickening of the septa due to sclerotic changes of the vessels entering from the pia into the septa. The ischemic degeneration of the optic nerve, owing to progressive sclerosis of the vessels, is followed by complete atrophy of the nerve fibers of the papilla, which in this case appears as simple atrophy. Since glia does not proliferate, the resulting excavation is usually shallow and dishlike and its margins appear (in cases with conical scleral canal) slightly overhanging. If, also, the retrobulbar nerve fibers atrophy, and, perhaps, the lamina cribrosa is congenitally weak, or weakened by malnutrition, its recession is possible, and, in this case, a glaucoma-like excavation originates (pseudoglaucoma).

Atrophy of the optic nerve due to pressure and traction is also caused by vascular changes, by pressure of pathologic bone on the optic nerve, by exostosis in the optic canal after fracture,

by narrowing of the canal in osteitis deformans (Paget) and oxycephaly, by pressure of tumors of the sheaths of the optic nerve or of the orbit, of the optic canal or the region of the sella turcica and by adhesions in basal arachnoiditis.

Atrophy of the optic nerve may be caused by injury, as in basal skull fracture, injury of the optic nerve in the orbit by sharp instruments, or damage by electric current.

As already mentioned, inflammatory and degenerative processes frequently run parallel, and the question arises as to the sequence of these factors or their simultaneous existence. In many cases, this is uncertain. There are cases in which certainly, or very probably, the inflammation is primary and the degeneration is caused by the inflammation; in other instances, the degeneration is first and the inflammation follows. But for some diseases we must assume that the causative factors simultaneously produce inflammation and degeneration of the optic nerve. In these cases, simultaneous parenchymatous degeneration and interstitial inflammation exists. This is found in some acute and chronic diseases of the central nervous system in which the optic nerve participates. These may be of infectious nature or not. Examples are the chronic diseases of disseminated sclerosis and epidemic encephalitis (encephalitis lethargica), the acute diseases of acute disseminated encephalomyelitis, neuromyelitis optica (Devic) and diffuse periaxial encephalitis (Schilder). All these forms are similar in their pathologic picture and produce disseminated foci of spotty demyelinization, varying in location and course. They may be produced by a neurotropic virus or a toxin. Especially are the nerve stem and the chiasm affected, rarely the papilla which has only nonmyelinated nerve fibers. The disintegration of the myelin sheaths is marked and the myelin particles are removed by phagocytes, appearing as fatty granular cells ("gitter cells") and rod cells. The axon cylinder may remain intact, show varicosities or break up into fibrils. Simultaneously, perivascular infiltrates of lymphocytes and mononuclears of varying intensity appear, vessels are dilated and pia and septa are infiltrated with lymphocytes, mononuclears, plasma cells and mast cells. Rarely, small holes appear in the nervous tissue of the type seen in cavernous atrophy;

usually the glia proliferates secondarily. The pathologic process is, if not too far advanced, reversible, or it results in neuritic atrophy of the optic nerve.

5. Papilledema

In papilledema, the papilla is elevated toward the vitreous body and is wider. The physiologic excavation is flattened. Edema appears between the nerve fibers which are separated by fluid in the interfascicular spaces, and in intrafascicular spaces, i.e., between the single fibers. The retina is displaced laterally by the increased volume of the papilla and folded. The pigmentary epithelium, and in connection with it, Bruch's membrane, remain in place and the rods and cones are pushed away from them to some extent. The nerve fibers bulge as they pass from the retina to the lamina cribrosa. They appear S-shaped and take this curved course from the nerve fiber layer of the retina underneath the displaced and folded retina, are sometimes squeezed in between the outer and inner nuclear layers and course along the pigmentary epithelium, bending around the margin of Bruch's membrane toward the lamina cribrosa. Under certain circumstances, also, the nerve fibers themselves become edematous, swell and appear varicose. The edema continues for some distance on to the nerve fiber layer of the retina, and the internal limiting membrane is sometimes detached in small vesicles. It also continues beyond the lamina cribrosa into the nerve stem to the point where the central retinal vessels enter or leave the optic nerve. The veins and capillaries of the papilla are dilated and the arteries compressed. Frequently, small blood extravasates are found, and also exudates of albumen and fibrin. Perivascular infiltrations of lymphocytes are infrequent. The choroidal part of the lamina cribrosa presents an anterior convex bulge, there is subpial edema and the perivascular spaces of the central vessels are dilated. The subarachnoidal space may be enlarged; also the dura may be edematous and contain small hemorrhages. The central vein crossing the intervaginal space is often compressed at this point. As long as only edema is present, the process is reversible. If the cause of the papilledema is eliminated, it disappears and the papilla becomes normal again. But if the cause persists, degeneration of the edematous

nerve fibers sets in, the varicose nerve fibers split into fibrils and exhibit fatty and lipoid degeneration. The varicose enlargements of the nerve fibers appear as ovoid bodies (cytoid bodies) especially if separated from the rest of the fiber. If nerve fibers break up, phagocytes appear which belong especially to the microglia. Together with the removal of the destroyed nervous substance, glia proliferates in its place and also between the displaced retina and the pigmentary epithelium. The shrinking

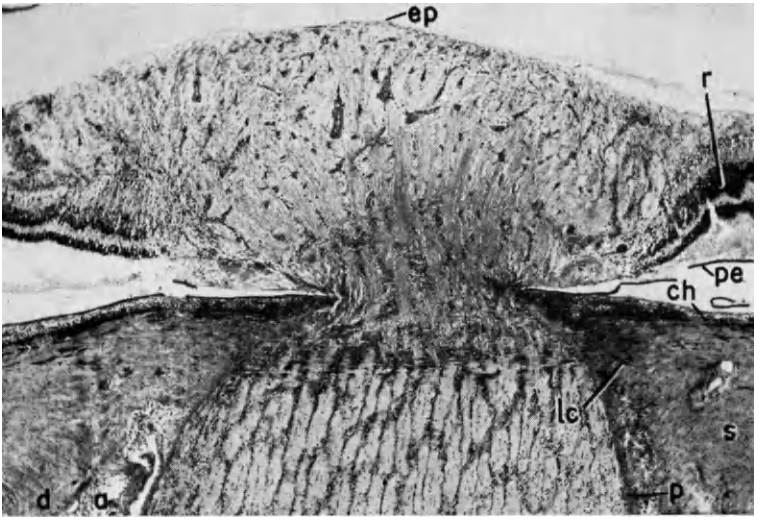

FIG. 47.—PAPILLEDEMA. a, arachnoidea; ch, choroid; d, dura; ep, edematous papilla; lc, lamina cribrosa; p, pia; pe, pigmentary epithelium; r, displaced retina; s, sclera. 25×.

glia may pull the retina back over the papilla. The cup is filled with proliferating glia. The vessel walls are thickened and small vessels obliterated. Degeneration may progress toward the ganglion cells, showing chromatolysis, and proceed into the chiasm and the tractus opticus. As atrophy sets in, more inflammatory cells sometimes appear. Finally, neuritic atrophy of the optic nerve results.

Papilledema has different causes: (1) intracranial, (2) general diseases, (3) ocular causes, (4) orbital causes. Papilledema appears most frequently in rise of the intracranial pressure of

different origins, due to intracranial neoplasms, but also in edema of the brain, meningitis, intracranial hemorrhage. Of the generalized diseases, nephritis and hypertension are the chief causes. Papilledema appears with sudden and intense decrease of the intra-ocular tension (soft eye), especially after injury or operation if a fistula is established. Pressure of tumors, but also of inflammatory tissue, on the optic nerve in the orbit causes papilledema.

The pathogenesis is not entirely understood and several theories try to explain the origin of papilledema. Best founded are the mechanical theories. The origin of papilledema is explained: (1) as stagnation of the outflow of the liquor from the sheaths of the optic nerve into the cerebro-spinal spaces of the brain, as back pressure or as backward stagnation of the liquor; (2) stagnation of the lymph current from the eye along the axial strand of the optic nerve, or backward stagnation of the lymph in these spaces by increased pressure in the sheaths of the optic nerve; (3) compression of the central retinal vein in its crossing through the intervaginal space of the optic nerve. In the transport theory (Schmidt-Rimpler-Manz), it is assumed that due to increased pressure in the subarachnoidal spaces of the central nervous system, the liquor is pressed back from here into the sheaths of the optic nerve, and in this way a serous exudation into the nerve head is produced. This theory is simplified in the assumption that the liquor cannot leave the optic nerve because of overpressure in the subarachnoidal spaces of the brain (Knies). In other theories, the origin of the mechanism causing papilledema is placed in the axial strands of the optic nerve in which are found the large vessels, connective tissue and perivascular lymph spaces. Liquor is said to be pressed into them from the sheaths of the optic nerve, and in this way edema originates here and continues into the papilla (Schieck). Another opinion is that there is a continuous lymph current from the vitreous through the physiologic cup into the lymph spaces of the central retinal vessels, and it is obstructed when the pressure is raised in the sheaths of the optic nerve. In this way, stasis occurs in the lymph spaces and finally edema of the papilla appears (Behr). Older theories postulate that there is stasis

in the ophthalmic vein due to compression of the cavernous sinus or the lateral sinus, thus producing papilledema. But it must be remembered that the venous outflow of the orbit has collaterals to the pterygomaxillary plexus. Newer theories try to prove that the central vein is compressed by increased pressure in the sheaths of the optic nerve. In this manner, the pressure in the central vein increases, although the pressure of the noncompressed artery remains normal, since its stronger wall resists the overpressure. Stasis follows, and as the raised venous pressure extends to the capillaries, fluid exudes into the papilla and the nerve stem. For every one of these theories, some evidence is brought up in the histologic examination of respective cases, in experiments on cadaver eyes and in living patients whose eyes have had to be removed. There are other theories, however, which lack proof: (1) the inflammation theory (Leber, Deutschmann) that hypothetic toxins produce inflammatory edema; (2) the vasomotor theory (Benedikt, Adamkiewicz) that sympathetic nerve fibers controlling the nutrition and circulation of the papilla are affected; (3) the theory that papilledema is part of a generalized edema of the brain (Parinaud, Sourdille).

6. Depositions of Abnormal Substances

Abnormal and degenerative substances are occasionally deposited in the optic nerve, but more frequently in its sheaths. They are corpora amylacea, corpora arenacea, hyaline bodies (drusen), glycogen and amyloid.

Corpora amylacea appear as homogeneous rounded bodies of different sizes which show concentric lamination in the unstained specimen. They are stained yellowish by iodine and bluish by adding sulphuric acid or hydrochloric acid. They may show some sort of a capsule. They are found infrequently in the papilla and orbital nerve stem, but frequently in the intracranial nerve stem and chiasm. They are usually senile, but are also found in degenerated atrophic nerves. Their origin is questionable. They are considered to be degenerated glial cells, as they are mostly found in connection with the glia, but also as deposition from axon cylinders, from myelin sheaths, as

precipitation from the tissue fluid combined with myeline or as products of degeneration of ganglion cells.

Corpora arenacea appear as concentric laminated bodies of various sizes, sometimes extremely large, in which calcium is frequently deposited. They never give a reaction with iodine and sulphuric acid. Spindle-shaped cells may surround them. They are mostly found in the arachnoid, but also in the inner

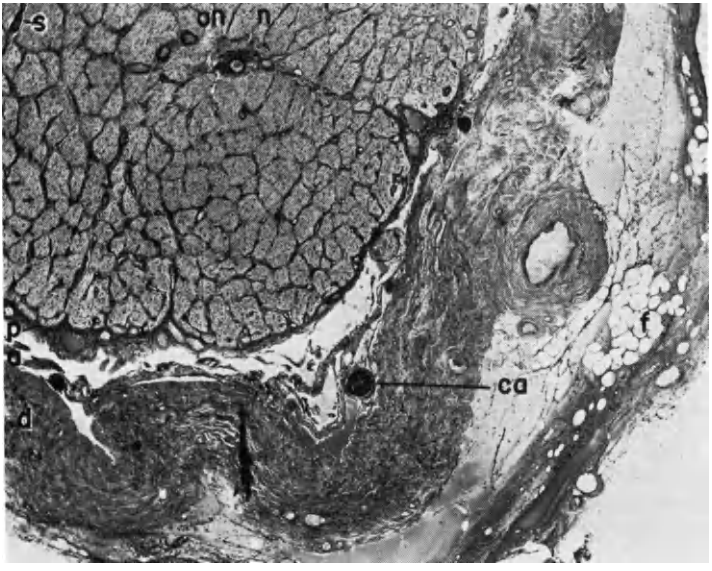

FIG. 48.—CORPORA ARENACEA. a, arachnoid; ca, corpora arenacea; d, dura; f, fat; n, nerve bundle; on, optic nerve; p, pia; s, septa. 30×.

layers of the dura and in the pia. They originate from onion-shaped layers of endothelial cells of the sheaths. They are found frequently in otherwise normal but also in pathologic optic nerves, and are especially numerous in meningioma (psammoma) forming here the psammoma bodies.

Hyaline bodies (hyaline concretions, drusen) appear in the papilla as irregular homogeneous, often calcified formations with concentric laminations of various sizes. They may surround the central vessels between separated nerve fiber bundles and sometimes extend with them into the surrounding retina and may

affect the outer nuclear layer. They stain intensely with eosine, are hyaline-like, are stained yellowish with iodine and are resistant to acids and alkalis. They accompany atrophy of the optic nerve or may cause atrophy by pressure; they are found in connection with retinitis pigmentosa, retinopathies, chorioretinitis, glaucoma and injury. Their origin is explained in various ways: they are depositions of insoluble substances in metabolism; they are degenerated pigmentary cells which are displaced into the papilla, or they are degenerated neuroglia.

Glycogen may be deposited into the tissue of the optic nerve. It is especially increased in diabetics and appears together with neuritis.

Amyloid material may be found infrequently in the dura, which is enormously thickened and appears homogeneous. The amyloid degeneration of the dura is part of a generalized amyloid degeneration of the adnexa of the eye.

7. Neoplasms of the Optic Nerve and Its Sheaths

They are primary or secondary. The primary are glioma, endothelioma, fibroma (meningioma) and malignant melanoma. The secondary are tumors extending from the surrounding tissues of the eye into the optic nerve, and metastatic ones. The former are retinoblastoma and sarcoma of the choroid and malignant tumors of the orbit, the latter carcinoma and sarcoma.

Glioma consists of proliferating, long spindle-shaped cells with oval nuclei and straight or tortuous cell processes. The cells, often closely packed, often farther apart, are separated by intercellular substance, consisting of a fine and coarse fibrillar meshwork and a glassy homogeneous mass of varying quantity. By specific stain, the cells of the tumor are recognized as glial cells; they show different types, and pathologic variations of otherwise normal appearing types are preponderant in the optic nerve. There are astrocytes, in the processes of which the fibrils have disappeared, or the processes may be split up; the cells are eventually very enlarged (giant astrocytes). There are also small oligodendrocytes with few, sometimes thickened processes and spindle-shaped and oval nuclei. Cells with sickle-shaped

nuclei may appear. The cell processes show vacuolization, representing hyaline masses. The connective tissue septa of the optic nerve are usually separated by the accumulation of glial cells, replacing the degenerated, demyelinized and broken-up nerve fibers. The septa can be thinned and often the septa are thickened by reactive proliferation of the connective tissue and by invasion of glial tissue. The diameter of the nerve increases enormously and the entire tumor appears oval-shaped. The pia is invaded by the tumor and cells and fibers of the tumor fill the intervaginal spaces. The dura also contains neoplastic material and is thinned but never perforated. Accumulation of a mucinous substance filling cystic spaces in the tumor makes it myxomatous. Calcareous concretions may be deposited in the tumor tissue. Small hemorrhages occasionally appear in the tumor. Numerous vessels are present, frequently show hyaline degeneration and partial thrombosis, and their walls can calcify. In general, the tumor appears sarcoma-like with the usual staining, and has been not infrequently misdiagnosed as fibrosarcoma or myxosarcoma. The neoplasm is especially a disease of youth and almost exclusively affects the intraorbital nerve stem. It may extend from here into the papilla but rarely originates in the papilla itself. Also, the intracranial optic nerve is infrequently affected.

Endothelioma (meningeal fibroblastoma) originating from the sheaths of the optic nerve shows flat cells with smaller rounded, or larger oval nuclei which often appear in concentric whirls, and also in irregular lobules and columns. Fibrillar collagenous connective tissue lies between the cells and also forms dense trabeculae between the alveolar arranged cell groups. Also, endothelial-lined spaces and blood-containing endothelial tubes appear. The concentrically arranged endothelial cells undergo hyaline degeneration and form the psammoma bodies which frequently calcify and are on their outer surface surrounded by layers of nucleated endothelial cells. After perforation of the dura, the tumor, probably arising intraorbitally, invades the surrounding orbital tissue and even the paranasal sinuses and, less frequently, after perforation of the pia, the optic nerve itself. The nerve

is usually compressed and atrophied. Rarely it affects the papilla and the sclera itself in the neighborhood of the papilla and of the posterior pole, but extends through the optic canal into the intracranial part of the nerve; however, it may also arise primarily in this part. The tumor originates from the endothelial lining of the sheaths, mostly from that of the dura, but also from the endothelial lining of the arachnoid. It is chiefly a tumor of adults.

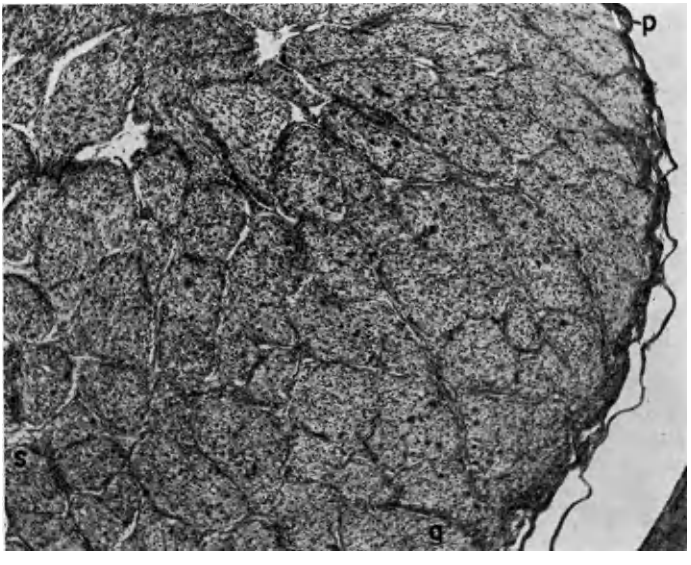

FIG. 49.—GLIOMA OF THE OPTIC NERVE. g, nerve bundles filled with glial cells; p, pia; s, septa. 45×.

Fibroma (neurofibroma) represents a diffuse, fibrous hyperplasia with dense collagenous fibrous bundles, exceeding the cells in quantity. On its margin, round cell and plasma cell infiltration sometimes appears, surrounding vessels also showing proliferating endothelium. The spread continues into the sclera and orbit. The optic nerve is compressed by the tumor. It originates from the sheaths of the optic nerve stem, from the pia, arachnoid cell nests, and dura. This rare tumor is a disease of youth. Discrete neurinomata of the dura are also found.

Diffuse neurofibromatosis (von Recklinghausen's disease) may be combined with all these forms of optic nerve tumors. Perhaps even combinations of these tumors may exist (as endothelioma and gliomatous proliferations) in this disease in which multiple neurofibromata, especially in the skin, appear as soft nodules (molluscum fibrosum) or diffuse hyperplasia (elephantiasis neuromatodes). The cranial nerves, other than the optic nerve, especially the acoustic, but also others may be affected, and intracranial meningiomata may occur.

Malignant melanoma rarely originates primarily in the papilla, and when it does it develops probably from displaced uveal elements (nevus, simple melanoma) which often are situated in the lamina cribrosa. It develops as a more or less intensely pigmented tumor, replacing the tissue of the papilla and bulging into the vitreous and growing through the lamina cribrosa into the optic nerve stem.

Secondary tumors sometimes grow from the surrounding tissues into the optic nerve. Especially does retinoblastoma usually continue along the nerve fiber layer of the retina into the papilla and the nerve stem and in this way finally reach the brain. Behind the lamina cribrosa, the nuclei of this tumor often appear elongated and sickle-shaped and a dense meshwork of fine fibrils appears. This might be a reaction of the glial tissue of the optic nerve which starts to proliferate. Less frequently, sarcoma of the choroid extends into the optic nerve and occasionally grows in a ring shape around the disc, but there is considerable resistance in the circumpapillary tissue against extension of the tumor into the nerve. However, the tumor may extend along the ciliary nerves and vessels into the dura and further into the optic nerve. Occasionally, a carcinoma metastasizing in the choroid proliferates into the papilla. Sarcoma of the orbit, such as lymphosarcoma, may proliferate into the sheaths of the optic nerve, but the nerve is usually compressed so that pressure atrophy results and the nerve itself is entered late. Metastatic carcinoma of the orbit may grow into the optic nerve.

Carcinoma metastasizes infrequently into the optic nerve or its sheaths. Usually the carcinoma establishes itself in the

sheaths, first compresses the nerve and finally enters the nerve itself. But the tumor may also metastasize to the nerve or even to the papilla directly and proliferate from here. Usually it is an adenocarcinoma. Carcinoma of the breast, the stomach, the lungs, or the genitalia may be the primary tumor.

Sarcoma metastasizes very rarely into the optic nerve and the papilla even in extensive sarcomatosis of the body.

READING OF SOURCE MATERIAL

Scheerer describes pigmented cells from the type of chromatophores in a glaucomatous disc.

Schieck believes that there are open connections between the sheaths and the septal system of the optic nerve, into which fluid is pressed from the former. He concludes this from an experiment in which he injected india ink into the intervaginal spaces in an enucleated eye; the ink was pressed into the septa and along the central vessels.

Fuchs found, in glioma retinae, the blood vessels of the optic nerve frequently very dilated and considers this as a distant influence of the tumor in the form of a growth stimulus.

Degeneration and regeneration of the nerve fibers after injury of the optic nerve are described by Cajal.

Cone finds that in regeneration after injury of the optic nerve the mesodermal microglia acts phagocytic and removes detritus, and that the ectodermal neuroglia replaces the destroyed nervous tissue.

Seissiger observed in a case of glioma in the lentiform nucleus of the brain in a 49 year old man, widening of the septa and phagocytes in the optic nerve.

Glia and connective tissue proliferate irregularly after severance of the optic nerve (Bachstez).

Schnaudigel finds caverns of the optic nerve (1) in the form of holes as in other areas of the central nervous system, (2) as lacunar degeneration, and (3) as complete skeletonizing of the glia. The pathologic changes take their origin from the destruction of the ganglion cells of the retina.

Loewenstein finds cavernous degeneration of the optic nerve associated with advanced vascular damage and malnutrition of the tissue, but not caused by increased intra-ocular pressure.

McDonald reports the histologic findings of a subdural hemorrhage in a massive cerebral hemorrhage due to vascular disease.

Subarachnoidal hemorrhage of the optic nerve is histologically examined by Cairns and Goulden.

Subretinal hemorrhage follows subarachnoidal hemorrhage of the optic nerve, due to obstruction of the central vein as it passes through the intervaginal space (Paton).

Riddoch and Goulden find, in subarachnoidal hemorrhages caused by aneurysm of the internal carotid artery, the optic nerve sheaths filled with

blood, papilledema and retinal hemorrhages due to compression of the central retinal vein in the intervaginal space.

Barletta found, in a 16 year old girl with extensive hematoma of the cerebral ventricles, hemorrhages in the dilated and edematous sheaths of the optic nerve, papilledema and the central retinal vessels bloodless due to compression.

Grimminger describes a case of a traumatic hemorrhage in the subdural and subarachnoidal spaces of the optic nerve. He believes that the hemorrhage extended from the orbit along the ciliary nerves and by the way of the passage of the central retinal vessels into the intervaginal spaces.

Cohen found, in a 36 year old woman with torula histolytica in the liquor, infiltration of pia and arachnoid of the optic nerve.

Reese describes abscesses of the optic nerve produced by toxins and infectious emboli.

Cheney found, in a case of orbital abscess due to staphylococcus aureus, infiltration of sclera and choroid, detachment of the retina and edema of the papilla. The optic nerve contained necrotic areas, due to septic thromboses extending from the orbit.

Kyrieleis reports about minute abscesses in both optic nerves in a case of sepsis caused by hemolytic streptococci.

Direct continuation of inflammations of the paranasal sinuses into the optic nerve is proved anatomically by ten Doeschate, Herzog, van der Hoeve, Pickworth, Worms.

Dieffenbach, Lamb report cases of tuberculous papillitis.

Mauksch described caseous tuberculosis of the optic nerve originating from periphlebitis.

In tuberculosis of the optic nerve, periphlebitic nodules containing tubercle bacilli were observed by Bergmeister, besides conglomerate tubercles in the subdural and subarachnoidal space.

Manolescu reports a case of tuberculosis of the optic nerve in a 14 year old child with tuberculous meningitis and another following tuberculous osteoperiostitis of the sphenoid.

Igersheimer finds in tuberculous meningitis infiltration and tubercle bacilli in the retrobulbar optic nerve and regularly macrophages in the optic nerve sheaths.

Szabo describes a case of basal meningitis following tuberculosis of the optic nerve.

Goldstein and Wexler report miliary tubercles in the optic nerve.

Schoepfer saw a case of tuberculous metastatic ophthalmia affecting the papilla and retina.

Satanovsky found in neuritis papulosa (Fuchs) lymphocytic infiltrates around arteries and veins, hemorrhages in the retina and papilla, proliferation of the endothelial cells of arteries, fibrin on the retina, the lamina cribrosa infiltrated and pushed backwards and exudate and connective tissue on the papilla.

The central retinal artery shows lymphocytic infiltration of the adventitia and proliferation of the endothelium in syphilis of the optic nerve (Bridgett).

The optic nerve is histologically examined in methyl-alcohol amblyopia by Eleonskaja, McDonald.

Optic atrophy in alcohol-tobacco amblyopia is histologically examined by Behr. Spasms of small vessels is seen as cause by Farnarier, Raverdino, de Rosa, Scalinci. Traquair considers as cause primary intoxication of the neuron.

The optic nerve is histologically examined in quinine-optochin intoxication by Giannini, Velhagen, who find degenerative changes in ganglion cells and nerve fibers.

Thomsen describes histological findings of optic neuritis in diabetes.

Abelsdorff describes atrophy of the optic nerve in diabetes with arteriosclerosis but which he does not consider as the cause of the atrophy.

Behr, Ingvar, Richter, Spielmeyer support the theory that the primary optic atrophy in the tabetic is interstitial neuritis followed by secondary degeneration of the nerve fibers. Richter believes that exudation of lymphocytes and plasma cells introduce the process, Behr believes that sclerotic changes of the glia produce malnutrition of the nervous tissue, but Paton considers simultaneous degeneration of the interstitial and nervous tissue as important in the pathology of the atrophy.

Behr finds in optic atrophy in tabes the myelin sheaths swollen and disintegrated in granular masses. The disintegrated nerve fibers are replaced by glia. The small septa atrophy and the large become thicker and sclerotic. He believes that the spirochetes are located in the connective tissue septa and not in the nervous substance. The endotoxin of the dying spirochetes produces the degeneration of the glia and fine septa with disturbance of the nutrition of the nerve fibers with secondary degeneration of the latter.

Myelin sheaths and axon cylinders degenerate in tabetic optic atrophy at the same time, according to Igersheimer who could find spirochetes in the thickened sheaths and septa, with inflammatory changes but none or minimal inflammatory changes otherwise. He believes that the atrophy starts retrobulbarly. Schindler also finds atrophic changes in the optic nerve more pronounced closer to the eye than further distant.

Biffis, too, found spirochetes in the optic nerve in tabes and general paresis.

Fudjiwara finds in optic atrophy in tabes cellular infiltration in glia and septa.

Rehsteiner finds in Leber's atrophy histologically atrophy of the optic nerve, chiefly of the papillo-macular bundle and of the ganglion cells of the retina.

Saphir describes compression of the optic nerves by an arteriosclerotic internal carotid. Occasionally there are perivascular lymphocytic infiltration, increase of glia and connective tissue and corpora arenacea.

Alpers and Wolman found in a 44 year old woman both optic nerves compressed by the internal carotid, further sclerotic vessels inside the optic nerves which showed foci of lymphocytes, fibroblasts and macrophages.

Foster Moore describes a case in which an aneurysm of the ophthalmic artery tore the optic nerve.

Optic nerve atrophy can appear in occlusion of the central retinal artery due to arteriosclerosis (Abelsdorff).

Fuchs finds degeneration in the optic nerve in old age, caused by vascular sclerosis of the septa, more frequently in the peripheral than in the central parts of the nerve.

Igersheimer found anomalous blood vessels, branching off from the central retinal artery behind the lamina cribrosa and contributing to the nourishment of the nerve. These vessels and the vessels of the retina can be affected in arteriosclerosis, causing atrophy of the optic nerve.

Rintelen finds in arteriosclerotic optic atrophy glial and connective tissue scars, cysts and hemorrhagic infarcts due to partial and total obliteration of blood vessels and marked sclerotic changes of small vessels behind the lamina cribrosa.

Stief describes sclerosis of the arteries and arterioles of the optic nerve causing atrophy.

Bridgett finds sclerosis of central retinal artery more frequent outside of the nerve than inside, with mainly the intima affected.

Bridgett reports periarteritis of the central retinal artery.

Loewenstein finds that optic nerve fibers can rupture in the papilla at Bruch's membrane and that arclike hemorrhages appear in this place. This may happen (1) in trauma, (2) in expulsive hemorrhage and (3) in hemorrhagic glaucoma.

Marburg observed in retrobulbar neuritis in disseminated sclerosis, sclerosis of blood vessels, new formation of vessels and few hemorrhages.

Lisch found in multiple sclerosis in the chiasm and optic tract degeneration of the myelin sheaths, increase of glia and thickening of vessel walls.

Herrmann found in syringomyelia circumscribed round-cell infiltration in the walls of small vessels of the atrophied optic nerve.

Kohut and Richter found in neuro-optic myelitis destruction of nerve fibers, increase of astrocytes and microglia and appearance of gitter-cells. The pia, adventitia and septa showed marked perivascular round-cell infiltrates and a newly formed reticulum appeared in the form of a network of fiber bundles.

Bouchut and Dechanne found in a case of acute neuromyelitis optica destruction of myelinated nerve fibers, appearance of compound granular corpuscles, shrinkage of ganglion cells, small hemorrhages and perivascular lymphocytic infiltrates.

Noran and Polan describe in Devic's disease atrophy of the optic nerve due to necrosis and replacement of microglia, fatty granules and newly-formed vessels.

Papilledema is caused by subdural hemorrhage (Cairns and Goulden), meningitis of various etiology (Drake, Tanasescu and Lazarescu, Terrien), blood diseases like anemia and leukemia (Jaensch, Rolleston).

Papilledema in subarachnoidal hemorrhage of the optic nerve is caused by compression of the central retinal vessels in the sheaths of the nerve and their stretching in the distended intervaginal space (Riddoch and Goulden, McDonald).

Papilledema due to local disease is found in eyes with fistulae (Scardapane, Schieck), in soft eyes after ignipuncture for detachment of retina (Knapp), after trephining (Smith), after rapid decrease of the intraocular tension due to miotics in glaucoma (Carle), concussion injury (Polányi), due to pressure of orbital tumors on the optic nerve (v. Heuss, van der Hoeve, Rumjantzewa, Tahano), in aneurysm of the ophthalmic artery (Pfingst), in echinococcus cysts of the orbit (Teulieres).

Papilledema is examined histologically by Kyrieleis, Samuels.

Schieck finds in microscopic examination of papilledema always edema of the axial connective tissue strand and of the perivascular lymph sheaths of the central vessels in the optic nerve and considers it as the cause.

Behr finds that in papilledema the sheaths of the central retinal vessels are blocked by dense connective tissue. Stasis of the tissue fluid in the optic nerve occurs as this fluid cannot flow normally along the glia into the perivascular spaces. Normally the pressure decreases from the papilla toward the chiasm, but the current is reversed when the intra-ocular pressure becomes very low or the pressure in the third ventricle very high. He further believes that a duplication of the dura is pressed into the optic canal in case of increased intracranial pressure and that there is found beneath the duplication an indentation of the optic nerve. Chronic stasis is caused, producing endothelial proliferation in the intervaginal spaces.

Fry finds in papilledema marked compression of the central retinal vein in the subarachnoidal space of the optic nerve, and considers the compression as the initial cause of the papilledema. The venous stasis causes consequent transudation of lymph into the tissue of the papilla. A second cause is a forward pressure of fluid inside the optic nerve as cerebrospinal fluid is pressed under increased pressure into the perivascular lymph spaces.

Behr, Behrens, Fischer, Levinsohn, Liebrecht, Smith and Cornwall, consider the stasis of the outflow of the tissue fluid from the eye through the tissue spaces of the optic nerve as cause of the papilledema.

Schieck believes that fluid is pressed into the perivascular lymph spaces of the axial connective tissue of the optic nerve, causing papilledema.

Marchesani believes that papilledema represents edema by stasis as an expression of a generalized cerebral edema.

Lauber, Sobanski express the opinion that papilledema appears when the pressure relation of the central retinal vein to the central retinal artery becomes 1:1.5.

Igersheimer found degenerative changes in the optic nerve and papilledema in a case of malignant nephrosclerosis.

Behr could produce experimentally papilledema in an eye which had to be enucleated together with a carcinoma of the orbit. He ligated the optic nerve 2 mm. behind the eyeball and found after 90 minutes histologically typical papilledema. He believes that retention of the tissue fluid in the optic nerve produces the edema.

Fuchs believes that nerve fibers can be affected by the pressure of corpora amylacea.

Lauber believes that drusen of the papilla represent pathologic products secreted by degenerated pigment epithelial cells displaced into the optic nerve. Drusen can displace nerve fibers and cause their atrophy.

Goldstein and Givner, Samuels describe drusen of the papilla and believe that they represent hyaline secreted from the glial cells. Also, Cibis assumes that the drusen consist of hyaline material, but that they are the sequela of an exudative vascular process and Tobler considers the drusen as hyaline-like material, as split product of protein.

Gomez, de Long, Oberling and Nordmann discuss tumors of the optic nerve.

Rio del Hortego distinguishes, according to the structure of the cells in special staining methods, the tumors of the optic nerve as an astrocytic

series in the form of glioblastoma, astroblastoma and astrocytoma and as an oligodendrocytic series with oblong cells as oligodendrocytoma which has the same origin, but a different histologic structure as the lemmocytoma of Recklinghausen's disease (neurinoma and Schwannoma).

Odincov found great variations of the structure of gliomata of the optic nerves and distinguishes: (1) ripe blastomata, (a) glioma which developed from glia cells and fibers and (b) gliomatous neuroepithelioma with cells similar to the embryonic epithelium; (2) unripe blastomata with atypical unripe glial cells; (3) congenital hyperplasia of the glial tissue.

Gibson found a glioma as a primary tumor of the papilla.

Gliomata of the optic nerve are histologically examined by Fleischer and Scheerer, Foerster and Gagel, Grinker, Hidano, Irvine and Reeves, Kiehle, Kiel, Leonardi, Lindberg, Martin and Cushing, Mawas and d'Autrevaux, Mannheimer, Mehney, Musial, Rand, Reuling, Vancea, Verhoeff, Wyllie.

Goldmann and Gruenthal describe a gliomatous tumor of the optic nerve and its sheaths in von Recklinghausen's disease.

Favaloro finds that the cells of the glioma of the optic nerve resemble in glial stain embryonic and fetal neuroglia, the so-called "spongioblasts."

Wilson and Farmer describe gliomata of the optic nerve belonging to the group of the spongioblastomata.

Blagovechensky and Morgenstern report gliomata of the optic nerve which develop from abnormal embryonic vesicles.

Goldstein and Wexler found a spongioneuroblastoma of the optic nerve in neurofibromatosis Recklinghausen.

Braendstrup, Santoni, Schreck report cases of oligodendrogliomata of the optic nerve.

Miller describes a neuromyxoma of the optic nerve.

Weeks reports a fibroglioma of the optic nerve in a 26 year old woman.

Wagner describes a glioma of the optic nerve as extension into the subretinal space in a 5 year old girl.

Siegrist finds that glioma cells can reach the other eye by way of the optic nerve sheaths and the meninges over the chiasm.

Monbrun, Offret and Guillaume found in cases of glioma of the optic nerve characteristic tumor cells only in the sheaths of the nerve as the tumors inside the nerve were degenerated.

Sidler Huguenin reports a case of an endothelioma of the papilla proliferating from rests of the hyaloid artery, and Argaud and Couadau describe a psammoma of the optic nerve as primary tumor of the papilla.

Archangelsky, Azny el Kattan, Bussola, Casori, Cohen and McNeal, Coston, Dandy, Goar, Dejean and Harant, Goulding, Hope-Robertson, Li, Love, Love and Rucker, di Marzio, Mathewson, Neame, Neame and Wolff, Offret, Regoli, Satanowsky and Adrogué, Scullica, Stallard, Stimson, Thompson, Twelmeyer, Verzella, Villard report endotheliomata, resp. meningoblastomata of the optic nerve.

Neurofibromata of the optic nerve are described by Gilchrist, Harvey, Hilgartner, Hilgartner and Watt.

Neurinomata of the optic nerve arising from the nerve sheaths are examined by Jessel, Mueller, Reverdin and Grumbach.

Stough saw in a 21 year old man a tumor attached to the inside of the sclera with spindle cells in palisades, whirls and folds, and interprets it as perineural fibroma.

Babel and Mario Valerio found an amputation neuroma accompanied by chronic inflammation on the stump of the optic nerve after enucleation which originated in a ciliary nerve, and Rottino and Kelly saw a neuroma of the optic nerve in a 59 year old man whose eye was removed after an explosion injury.

Davis describes a case with autopsy showing plexiform neurofibromatosis of the right orbit and uvea and glioma of the optic nerve, further gliomatosis of the left optic nerve and of the brain.

Koyanagi found in an 8 month old child with glioma retinae independent of it, probably congenital angiomatous caverns in the septa of the optic nerve.

van der Hoeve describes tumors of the papilla in tuberous sclerosis consisting of cells forming syncytia, fine glial fibers, small cysts and hemorrhages. The tumor cells are considered to be nondifferentiated cells of the retina anlage.

White and Loewenstein describe in a 9 year old boy a tumor of the papilla containing large, foamy cells which infiltrate the surrounding retina. They consider it as a nonpigmented phakoma arising from the neuroectodermal cells of the optic stalk.

Safar reports a congenital cyst of the orbit containing retinal elements, pigment epithelium, glial proliferation and a rudiment of the optic nerve. He believes that the retina had grown into the optic stalk which remained open.

Bucalossi, Speciale-Cirincione report sarcomata of the papilla.

Malignant melanomata of the optic disk are reported by Laval, Oguchi, Paulo Filho.

Tanner and Herzog describe a fibrosarcoma of the optic nerve, and Schwarz describes a sarcomatous new-growth of the optic nerve with cells resembling endothelial cells and fibroblasts.

Graf and Reis found a case of angio-sarcoma of the sheaths of the optic nerve.

Ginzburg reports an endothelial cyst originating from the sheaths of the optic nerve, which was closed off by an inflammation and a round- and spindle cell sarcoma of the optic nerve extending from the choroid.

Metastatic carcinomata of the optic nerve are reported by Behr, Cords, Ginsberg, Goldstein and Wexler, McDannald and Payne, Terry.

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Chapter X

PATHOLOGY OF THE LENS

1. General Considerations

The lens as an avascular tissue reacts to injury not with inflammatory reaction but with degeneration of its tissue and eventually with proliferation of the capsule epithelium. As a result, the transparency of the lens is changed by circumscribed or diffuse opacities, called cataract. Only when the lens capsule is open and the tissue surrounding the lens is acutely or chronically inflamed, are inflammatory changes established secondarily in the lens. Polymorphonuclears of the anterior and posterior chamber or of the vitreous body enter through the opened capsule into the lens, or chronic inflammatory tissue, especially that of a cyclitic membrane, perforates the capsule and proliferates inside the lens.

Rupture of the lens capsule and entrance of aqueous humor always produces cataractous degeneration of the lens fibers which usually prolapse through the wound, are dissolved by lytic enzymes and allow further access of the humor. Only infrequently and in small wounds does the capsule close and the degeneration remain circumscribed.

In general, the formation of cataractous changes follows alteration of the physiochemical processes inside the lens. The lens fiber responds with swelling which may be reversible, or with coagulation of the protein which is irreversible, becoming denaturalized and flocculant. The proteins which are present in the lens as soluble and insoluble change in old age and in the cataractous lens so that active soluble proteins disappear more and more and inactive solubles increase. Furthermore, protein is decomposed and the alkaline reaction changes into an acid one in which proteolytic enzymes become active and the soluble protein is transformed into an insoluble one. Lipoids and calcium increase in cataract. The water content is larger

in cataract and water becomes chemically free from the protein and gathers beneath the capsule and in the sutures. Hydration is finally succeeded by dehydration. The metabolism of the lens which is necessary for its transparency decreases in cataract. The oxidation lessens and the permeability of the lens capsule is diminished.

In the formation of cataract, the capsule, the epithelium and the lens substance can be affected. The capsule shows exfoliation as fine strands of superficial lamellae peel off from the normal or thickened capsule. The homogeneous capsule consists of a fine pericapsular membrane, a zonule lamella which is especially distinguishable in the periphery of the lens, and the capsule proper, which again may be split up into lamellae. The capsule splits into these parts and the parts again separate from them, by various causes such as trauma, by influence of toxins, by heat and in old age. Circumscribed thickening of the inner layers of the capsule appear as degenerative alterations in the form of drusen (colloid bodies) which are deposited perhaps from the epithelial cells. The capsule epithelium proliferates under certain circumstances. This occurs mostly at the anterior pole of the lens, due to the influence of mechanical and toxic conditions, especially after a central perforating ulcer, but it also appears as congenital. The cuboidal cells of the capsule epithelium become elongated and polygonal, develop long processes and finally appear as long cells with oval nuclei and become in this way similar to connective tissue cells. The increasing cells bulge the capsule and may take the form of a pyramid (pyramidal cataract). The form of a pyramid can also be caused when the anterior pole of the lens, after perforation of a corneal ulcer in a young eye, remains adherent to the cornea. The adhesion is pulled as the chamber deepens to the form of a pyramid. The anterior polar cataract sometimes degenerates to a structureless hyaline mass; or fat, lipoid and cholesterol crystals (dystrophia epithelialis lentis adiposa) and calcium are deposited. The capsule epithelium proliferates in some cases onto the posterior surface of the cataract or its cells become vesicular. The proliferating cells are able to secrete a homogeneous membrane which finally separates them from the lens.

The lens fibers themselves, as long as they are not sclerosed in the nucleus, in case of cataract disintegrate, are autolyzed and become necrotic. The sclerosed nucleus may become very dense and nontransparent. The lens fiber swells, becomes granular and disintegrates in irregular fragments, the fluid collects in clefts between the fibers and around the fragments of the fibers. The fluid may contain dissolved albuminous substances. The substance of the broken-up fiber appears as an albuminous coagulum, homogeneous and in granular pieces, as irregular detritus, or frequently as round, homogeneous, slightly stained formations of different sizes in the fluid (Morgagnian globules). Fat droplets, lipoid and crystals of organic and inorganic nature, as cholesterol, leucin and tyrosin, calcium phosphate and carbonate, eventually appear in the fluid besides the protein substances.

The mechanism of cataract formation is obscure in its ultimate cause. Apparently there are many causes, but it is not known how they induce cataractous changes. Senile changes of the ciliary epithelium and of the blood vessels in the ciliary body, with alteration of the metabolism in the chamber and in the lens and loss of oxidizing substances (glutathion and vitamin C and B_2), decreased permeability of the lens capsule, accumulation of metabolites in the lens are mentioned as causes. Irregular sclerosing of the lens is said to loosen the fibers surrounding the nucleus and to cause their disintegration by traction. The development of cataract may be predetermined genetically; the lens protoplasm may possess congenital structural changes which should make them more accessible to degenerative processes. Immunologic factors have been mentioned as far as lens protein or certain fractions of it should be organ-specific. They can produce specific antibodies which would dissolve lens protein when the body becomes sensitized to it. It is assumed that the lens fibers suffer due to the strain of accommodation changing their form continuously; when they grow older, they gradually lose their softness and adaptability. Local and general disturbances of metabolism have been accused as causes of cataract. The former play a role especially in complicated cataract, when the surrounding tissue undergoes pathologic

changes or new tissue proliferates and produces more or less extensive membranes around the lens capsule and toxic substances enter the lens and metabolites are not eliminated. Disturbances of the metabolism as in severe general diseases (diabetes, kidney insufficiency), presence of poison (naphthalene, thallium, dinitrophenol) and of toxins in the blood and inner secretory disturbances as in tetany due to decreased function of the parathyroid and in idiocy due to thyroid insufficiency may cause cataract.

Experimental cataract is often used to explain the causes of cataract in man and the mechanism of its origin. Cataract can be produced in different animals in different ways, but the mechanism is still quite obscure. Cataract can be produced by mechanical trauma, asphyxia, by obstruction of the blood circulation, by radiational energy of any kind, electricity, poisons, osmotic changes, decrease of the permeability of the lens capsule and removal of parathyroid. Concussion and massaging of the lens produces damage of the epithelium and displacement of cells and coagulation of the protein of the lens fibers. Pigment is deposited on the anterior lens capsule. It is obvious that incision of the lens capsule leads to disintegration of lens fibers by access of aqueous humor. Fibrin may be deposited onto the wound of the anterior capsule, cells may proliferate from the iris onto it and the lens epithelium start to proliferate. A wound of the posterior capsule may be closed by proliferation of cells at the equator. Prolonged and repeated asphyxia is said to produce acidosis and transformation of soluble lens protein into insoluble lens protein. Ligation of the ciliary arteries or vortex veins with resulting malnutrition and acidosis with subsequent necrosis produces cataract. Osmotic disturbances appear in the lens after injection of concentrated solution in the body or into the eye. If the lens capsule is covered with nonpoisonous substances which block the entrance of nutritional substances and the elimination of products of metabolism and cause acidosis, cataractous changes appear. Infra-red rays and heat waves, thermal rays, x-rays and radium are able to damage the lens. The capsule epithelium disintegrates and proliferates. Fluid appears between the cells and the lens fibers, lens fibers at the posterior lens pole break up,

granular masses appear and lens fibers of the equator swell immensely. It is not certain how far the lens substance itself is damaged directly or how far it is affected indirectly by injury to the iris and ciliary body affecting the lens metabolism. The rays denaturalize the lens protein, transforming it into labile composition in which it can be coagulated by any small injury. The rays perhaps affect the metabolism of the lens as they influence its oxidation-reduction system by loss of glutathion and lactoflavin. Electrical discharge and shock cause the disappearance of capsule epithelium and appearance of irregular masses beneath the epithelium. The epithelium flows together into formless masses and proliferates. On the other hand, lens fibers swell and disintegrate. Many poisonous substances formed in the eye itself or entering it by way of the circulation may produce cataractous changes. If iron enters the eye, it is deposited in the lens capsule and lens substance; copper if brought into the vitreous accumulates in the lens capsule. Feeding of naphthalene causes accumulation of fluid beneath the capsule, appearance of vacuoles in the fibers, and their disintegration. Further alterations in the ciliary body, retina and choroid appear in the form of swelling, albuminous exudate and crystalline deposition. The mechanism of all these changes is not known. Thallium seems to produce cataract by way of endocrine disturbances with changes in the adrenals, loss of hair and nephritis. Vacuoles are formed in the epithelium, the cortex disintegrates and liquefies. Feeding of lactose and galactose rapidly produces cataract with vacuoles in the cortex, disintegration of fibers and liquefaction of the cortex. The cause is unknown. Bee or wasp sting into the anterior chamber without direct injury of the lens may produce disintegration of the lens epithelium. Similarly, injection of tetanus and diphtheria toxins into the anterior chamber and adrenalin into the vitreous body can cause cataract. Removal of parathyroid is accompanied by degeneration of the epithelium and disintegration of lens fibers with formation of vacuoles and deposition of fat droplets and cell detritus. Irregular particles are seen at the posterior capsule inside the lens. It seems that decrease of the serum calcium causes cataract.

Different types of cataracts are found: (a) noncomplicated cataract, (b) complicated cataract, (c) cataract caused by inner secretory disturbances, and (d) cataract caused by physical and chemical trauma.

2. Noncomplicated Cataracts

The noncomplicated cataracts are: (1) the senile cataract, (2) cataracta nigra, (3) nuclear cataract, (4) hypermature cataract, (5) Morgagnian cataract, (6) punctate cataract, (7) disc-shaped cataract, (8) perinuclear cataract, (9) dystrophia epithelialis lentis adiposa, (10) lenticonus, and (11) secondary cataract.

The *senile cataract* shows changes of the capsule, the capsule epithelium, the lens fibers and the nucleus. The capsule may show senile exfoliation. The capsule either remains normally thick and the superficial layers peel off in flakes and fine strands, or it is first circumscribed or diffusely thickened with split up lamellae, or it separates in the form of continuous lamellae. The capsule may finally become very thin. It is thought that the iris moving across the capsule, causes peeling of the capsule. The capsule epithelium shows manifold changes. The cells which normally shrink in old age show in senile cataract an irregularity of form, size and boundaries. Some nuclei are large and clear, others pyknotic. Nuclei may disintegrate and disappear in areas. Cell boundaries may be blurred and intercellular spaces appear. Large, clear hydropic cells may appear (vesicular cells). Capsule and epithelium can separate. Not only degeneration but also proliferation can be seen. Then epithelial cells lie in several layers and some of these cells grow out to a spindle form which somewhat resemble fibroblasts beneath the capsule. The cells also secrete a cuticular substance. Sometimes calcium, cholesterol, and amorphous masses are deposited in the proliferating masses. The posterior capsule occasionally shows epithelium originating from the equator cells. The lens whorl of the equator is disturbed by the appearance of vesicular cells and transformation of recent lens fibers. The lens fibers separate and swell. Clefts appear between the fibers filled with clear fluid,

with fine granular content, large round masses (Morgagnian globules) and fine droplets (myeline droplets). The lens fibers break up and show irregular ends. As the cataract increases, more and more particles of fibers, protein coagula, Morgagnian globules, myeline droplets and crystaline depositions appear. Finally, all the fibers disintegrate and, from the cortex, only granular detritus, albuminous fluid and fat globules remain. In the stage of intumescence, the lens is enlarged and the lens

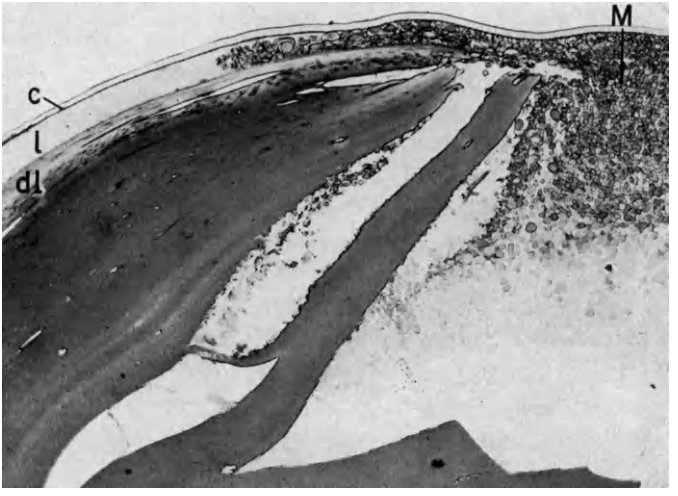

FIG. 50.—CATARACT. c, capsule of lens; dl, disintegrating lamellae; l, liquefaction; M, Morgagnian globules. 35×.

fibers are swollen, splintered and disintegrated and beneath the lens capsule they are abnormally curved and folded. Intumescent cataract may be complicated with secondary glaucoma. The lens nucleus stays normal for a long time, but it can also be broken up, clefts and holes appear or the nucleus becomes homogeneously sclerotic.

Black cataract (cataracta brunescens sive nigra) is a rare type of senile cataract. The entire lens becomes homogeneously sclerotic, less frequently granular, with concentric lamellations without holes and without fluid-filled spaces. The region of the equator shows few cell nuclei. Occasionally, a deposition of fat

droplets, irregular masses, crystals and pigment granules are found. The origin of the brown to black color of the lens is not entirely known. Some observers believe the discoloration is caused by a nonpigmented precursor of melanin such as tyrosine or some other substance, transformed by ferments into melanin. Others believe the dark color may be caused by lipofuscin. Other theories that the stain is blood or bile pigment have not been proven. The color is also thought to be brought about by a physical phenomenon, by an increased index of refraction of the sclerosing lens.

Nuclear cataract. The black cataract is considered a special form of the nuclear cataract, which frequently appears as senile cataract, although congenital nuclear or central cataract has been found. In the senile form, the nucleus becomes hard and homogeneous and concentric lamination appears. Slowly progressing, the lens fibers of the cortex sclerose and are compressed, and only few interfibrillary empty clefts are present. In the congenital stationary form, the nucleus is displaced posteriorly, and between it and the cortex are clefts filled with granular masses. The irregular nucleus contains slits, droplets and granular masses. The congenital nuclear cataract is probably produced during the embryonal development by strands of the tunica vasculosa lentis pulling on the lens capsule and breaking it.

The *hypermature cataract* develops in the one form from the ripe senile cataract; in another form it may also appear congenital and juvenile. In the senile form, the cortex is filled with fiber particles and Morgagnian globules, is partly liquefied with homogeneous clumps lying beneath the capsule. At the equator are large spaces filled with fluid and vesicular cells. The nucleus often is displaced and broken up and shows Morgagnian globules in clefts. The lens shrinks by dehydration through the capsule. Secondary glaucoma may be produced in hypermature cataract by resorption of toxic substances from the lens, sometimes after rupture of the capsule, but it may also be caused by obstruction of the chamber angle by lens particles or due to neurovascular reflexes. The hypermature cataract

causes rupture of the zonule by shrinkage, and luxates partly or entirely, producing inflammation of the anterior and posterior uvea with and without glaucoma. In the congenital and juvenile form, the capsule epithelium is usually normal, but the cortex is liquefied to a variable extent and eventually beneath the capsule large, homogeneous masses form. At the equator are few unchanged lens fibers, or fluid accumulates and vesicular cells are seen. The nucleus shows concentric lamellation and is sometimes very small, rounded and displaced. Not infrequently in this form the capsule ruptures spontaneously and lens fibers proliferate occasionally in several areas. The rupture of the capsule is caused by an increased internal tension due to an increase of volume and is closed by a new formation of the capsule at the area involved.

Morgagnian cataract. The hypermature cataract may gradually change into a Morgagnian cataract, in which the nucleus is resorbed and finally disappears. This development may occur in senile and in juvenile cataract also. The epithelium is first thickened and vesicular cells are seen to be present under the posterior capsule which reveals an epithelial-like formation; later, however, the epithelium separates from the capsule and may be entirely absent. The cortex is liquefied, contains much protein and coagulated homogeneous and granular masses. At the equator, eventually numerous vesicular cells are found. The nucleus in the beginning is compact and is displaced in the fluid-containing sac, but later it breaks up, crystals appear and finally it becomes smaller and may disappear entirely. The capsule may rupture. As in hypermature cataract, displacement and secondary glaucoma can arise.

Punctate cataract (coronary cataract, cataracta coerulea et viridis) is characterized by opacities arranged wreathlike in a peripheral zone in the deepest cortical layers and on the surface of the nucleus. It appears as a congenital or juvenile and presenile form. The opacities are small, elliptic and fusiform slits between the fibers, filled with homogeneous and fine granular masses. Otherwise, the lens fibers and the nucleus may be normal.

The *disc-shaped cataract* (ring cataract) is characterized by the disappearance of the nucleus and the central lens substance with more or less cataractous changes of the remaining lenticular parts. The remaining lens rest resembles a closed ring like a life-saver. The lens capsule is folded and shrunken at the anterior and posterior poles, the capsule epithelium proliferates and centrally no lens fibers are to be found. The ring shows disintegrated fibers, Morgagnian globules, droplets and granules in holes of the lens substance. These are primary changes of the lens in congenital aplasia of the nucleus or frequently secondary changes after perforation of the eye, mostly in corneal ulcer.

Perinuclear (zonular, lamellar) cataract is most frequently congenital but is also found as perinuclear punctate cataract as a transitional senile form. A circumscribed lamella or zone of the lens is affected. In the congenital form, the nucleus is normal, but it can also be shrunken and sclerotic and displaced, but in the senile form the nucleus is always sclerotic. The boundary between cortex and nucleus is distinct and is formed by a thin concentric layer of granular substance. Close to the nucleus, the cortex has concentric fissures of various sizes between the lens fibers, round and oval vacuoles with coagulated hyaline and granular content and larger spaces with irregular outlines and intensely stained granular substance. They appear clinically as riders. Sometimes calcareous deposits are seen in these coagulations.

Dystrophia epithelialis lentis adiposa consists, as already mentioned, of a proliferation of the capsule epithelium at the anterior pole into which fat is deposited in the form of droplets and masses inside and between degenerated cells. Numerous cholesterol crystals are seen. The proliferation of the epithelium is primary and the distintegration of the epithelial cells with abnormal fatty degeneration or perhaps fatty infiltration is secondary.

Lenticonus represents a protrusion of the anterior or posterior lens pole. There has been no anatomic investigation concerning anterior lenticonus which develops when the anterior capsule is weak. In posterior lenticonus the capsule is thin or torn and frequently a persistent hyaloid artery is found with much fibrous tissue in the vitreous.

Secondary cataract remains after extracapsular extraction of a cataract or after traumatic opening of the lens capsule. If, after formation of a traumatic cataract, the greater part of the lens and especially the still soft nucleus is absorbed, the opened anterior capsule rolls in and retracts and adheres to the posterior capsule. The remainder of the lens cortex and equator, closed off in the capsule, show alterations. The lens fibers for the most part degenerate and few remain intact. There are found swollen lens fibers, Morgagnian globules, colloid masses and fluid, bearing larger globules which contain parts of lens fibers and also calcium granules. Some of the fibers appear hydropic and form large, rounded or irregular giant cell-like formations (so-called lens globules) containing many nuclei. The cells of the equator proliferate by mitosis and may grow out to form lens fibers which may be considered as an attempt at regeneration. The capsule epithelium proliferates and may even grow around the ruptured capsule anteriorly. Irregular hyaline membrane-like masses can be deposited from the proliferating epithelium. The proliferating epithelial cells sometimes grow out to large vacuolated forms (globular or bladder cells of Elschnig) which are considered as rudimentary new lens fibers. Sometimes cystlike epithelial formations are seen. When there is bleeding into the capsule sac, spindle-shaped cells and fibers proliferate which appear like connective tissue and are considered as iris elements, but which probably also originate from the capsule epithelium. The capsule may be covered with numerous fine pigment-granules which are dispersed from the injured pigment epithelium. Sometimes the cells of the pigment epithelium proliferate and mix with the proliferating cells of the lens and with the lens material. If inflammatory changes appear, polymorphonuclears enter the secondary cataract. If a cyclitic membrane is formed, it often enters the secondary cataract and unites with it. The anterior and posterior capsule often close off, the equator part of the lens remaining intact and appearing ringlike (Soemmering's ring or cushion), enclosing cells and lens fibers which may proliferate inside the ring. The zonule fibers insert at the equator and often are stretched. The ring may luxate into the anterior chamber or the vitreous body if the stretched zonule fibers rupture.

3. Complicated Cataract

Complicated cataract appears as a sequela of intra-ocular disease. The capsule epithelium and the lens substance show pathologic changes which sometimes appear very similar to those of noncomplicated forms clinically as well as histologically. Often the changes of the lens substance are clinically and also histologically different from the noncomplicated forms, in that clinically they appear mostly in the posterior cortex and posterior pole where they manifest a star or rosette form and show a polychromatic luster. They are often intensely calcified. Nonspecific and specific uveitis are the most frequent causes; heterochromia, diseases of the retina such as retinitis pigmentosa and detachment of the retina, myopia, glaucoma, suppurative keratitis and intra-ocular tumors may be precursors of cataracta complicata. The lens capsule may show membranous deposits and deposits of varying nature and may be folded. The epithelium proliferates markedly to line the posterior capsule and penetrate into the cortex with vesicular arrangement of the cells (Wedl's vesicle cells). The lens may be substituted by fibrous tissue and bone. It is assumed that toxins diffuse from the aqueous humor into the lens, especially through holes of the posterior capsule and produce changes or that the disease process opens the lens capsule, producing cataract in this way or substitutes for the resorbed lens substance.

The posterior cortical cataract shows numerous clefts filled with protein masses and detritus close to the posterior capsule. Lens fibers disintegrate, the capsule epithelium proliferates and at the equator the epithelium proliferates posteriorly and the lens fibers become irregular. However, in time the degenerative changes spread over the entire lens, liquefaction takes place, cholesterol is deposited, and calcification appears. The capsule thickens and the epithelium proliferates, frequently to form several layers containing vesicular cells. The changes take place especially when the lens is surrounded by a cyclitic membrane. Different degenerative diseases of retina and choroid are frequent causes.

Membranes and amorphous deposits on the anterior lens surface are found in the form of floccules and mushroom-like formations which also may be situated on the pigment epithelium of the iris and the epithelium of the ciliary body. They are interpreted often as incrustations from the aqueous humor. They are found in chronic glaucoma.

The anterior lens capsule can be covered with various tissues, especially due to inflammation of the uvea and intraocular tumors. Often pigment is found free in clumps or inside of phagocytes, but also large pigmented cells with processes similar to the chromatophors are seen, but which also should be identified with congenital pupillary membrane. Precipitates consisting of lymphocytes and monocytes, newly-formed vessels, connective tissue membrane and particles of neoplasm can be found.

The lens capsule and the subcapsulary epithelium are affected by various causes. The changes can be caused by degenerative and inflammatory processes. Pupillary membrane, and especially cyclitic membrane play a role as well as contusion and perforation. Similar changes can appear as flat formations congenitally or are found with juvenile, senile, or hypermature and also with other complicated cataracts. There may be circumscribed thickening of the capsule, corresponding with posterior synechiae. There are folds of the capsule and epithelial cataract especially at the anterior pole with transition to pyramidal cataract. The capsule is often folded several times and usually the epithelial cells beneath proliferate to form spindle-shaped cells parallel to the surface; the intercellular substance is transformed to fibers (pseudometaplasia). They are separated from the cortex by a layer of cuboidal cells, which continue from the epithelium of the capsule. The cell nuclei degenerate often and the entire epithelial structure may become hyalinized and form drusen in the capsule, and calcium and cholesterol are deposited. The lens fibers beneath the epithelium are often degenerated. Anterior polar cataract is usually formed when the lens capsule is exposed in perforation of the cornea or when it is attached to the posterior surface of the cornea. The corneal endothelium

may unite with the anterior lens surface and may be separated from the cornea when the anterior chamber is restituted. In such cases, the lens may show on its capsule an endothelium, forming a homogeneous cuticular membrane in front of it.

Posterior polar cataract is often connected with persistent hyaloid artery and a posterior tunica vasculosa lentis. It is also connected with pathologic depositions from the vitreous on the posterior lens surface. The lens capsule may be invaginated and this space filled with detritus. If the lens capsule ruptures, fibrous tissue penetrates into the lens from the embryonal vascular membrane. On the other hand, the posterior pole can protrude conically by traction of the persistent hyaloid artery. If blood collects on the posterior surface of the lens, connective tissue proliferates on the posterior pole and along the entire posterior surface of the lens, and the adjacent cortex often degenerates. One sequel of ingrowing fibrous masses is a shrunken fibrous tissue cataract. Pigment arising from degenerated uvea is sometimes deposited on the posterior lens surface.

Pseudoaphakia fibrosa (membranous cataract) is the substitution of the lens by fibrous tissue and blood vessels surrounded by rests of the capsule. Inflammation during the intra-uterine life or in early childhood produces a cyclitic membrane which opens the capsule and produces total cataract. The degenerated lens masses are reabsorbed and substituted for by connective tissue.

Dystrophic depositions into the lens are of a different nature. They are fibrin, blood and its derivatives, amyloid, lipoid, fatty and albuminous crystals, but frequently calcium (cataracta calcarea) and sometimes bone (cataracta ossea). In most of these cases, the lens capsule is opened. Some of these are end products produced by decomposition of necrobiotic lens substance, some are introduced into the lens from the surrounding aqueous humor and by a penetrating tissue. Fatty impregnation occurs in lipemia. Complete fatty degeneration of the lens or of lenticular rests originating from fatty infiltration and fatty degeneration of the lens substance or ingrowing connective tissue is

called xanthomatosis lentis. Lipoid may be deposited in the form of crystals, especially as cholesterol crystals. Apparently, however, albuminous crystals exist, most likely tyrosin. Calcium is found very frequently in complicated cataracts in the form of rounded crystals, but more often in dustlike and irregular amorphous masses. If the lens is calcified in its greater part, cataracta calcarea exists. Tissue from cyclitic membrane ingrow-

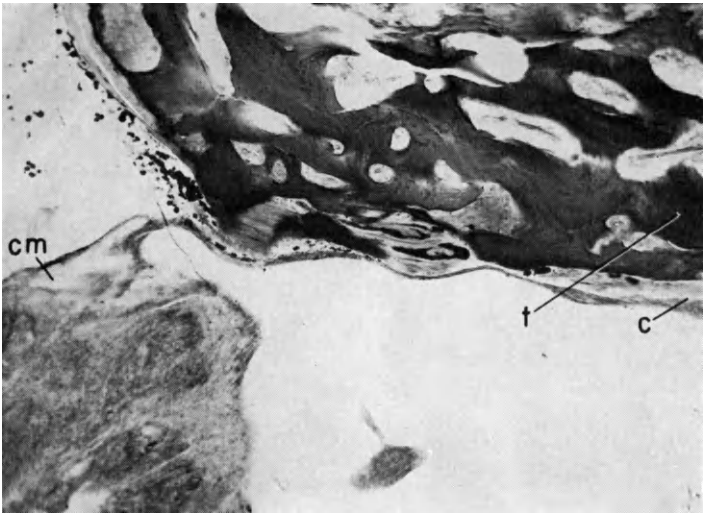

FIG. 51.—CATARACTA OSSEA. c, lens capsule; cm, cyclitic membrane; t, bony trabeculae. 35×.

ing into the lens through multiple ruptures of the capsule can form a marrow substance which, by a formation of osteoblasts, produces at first an osteoid substance and later regular calcified bone. This cataracta ossea then consists of vascular connective tissue, fibrous marrow and cancellous or in places even compact bone which may show Haversian systems.

In intra-ocular tumors the shape of the lens is often altered, lens fibers degenerating, and the capsule is eventually rupturing. A neoplasm protruding into the vitreous body, arising

from the retina or uvea, especially from the ciliary body, compresses the lens and indents it at the equator or displaces it; but it also opens the lens capsule and produces a type of traumatic cataract. Circumscribed disintegration of lens fibers is caused apparently by toxins produced by the disintegrating tumor. Finally total cataract results.

4. Cataract Caused by Endocrine Disturbances

Cataracts caused by inner secretory disturbances are (a) diabetic cataract, (b) cataract in tetany ,(c) in myotonic dystrophy, (d) in cretinism and idiocy, and (e) in certain skin diseases. But it must be admitted that other causes can be assumed for these cataracts, as especially for the diabetic cataract.

The *diabetic cataract* shows liquefaction of the anterior and posterior cortex; in the early stage, the subcapsular parts of the cortex are liquefied first. The lens epithelium is hydropic with vesicular cells, and proliferates in places. The lens capsule may be detached by fluid accumulation. The lens fibers of the deep layers of cortex are split up and the same occurs in the nucleus. The pigment epithelium of the iris is often hydropic. The diabetic cataract which develops very rapidly, especially in young individuals, starts clinically with subcapsular opacities in the form of fine dots and flakes and vacuoles, but in older individuals suffering from diabetes usually senile cataract is formed, although diabetic cataract may be observed, too. The diabetes mellitus is probably of an endocrine origin, caused by an insufficiency of insulin which is produced by the islets of Langerhans in the pancreas and which is essential for the normal carbohydrate metabolism. Endocrine failure has been mentioned as direct cause of the cataract, but often the cataract is assumed to be secondary to changes produced elsewhere in the eye of the diabetic. The ciliary epithelium is assumed to become edematous and to degenerate and to influence the metabolism of the lens. Toxic products of the metabolism in diabetes as well as the acidosis which activates proteolytic ferments and a greater inflow of water into the lens due to decrease of the osmotic pressure are mentioned as causal factors.

Cataract in tetany (cataracta aparathyroidea) shows very fine droplets in the cortex, smaller and larger clefts at the equator with granular masses and punctuate detritus. Rounded or oval homogeneous or granulated corpuscles are present. A completely homogeneous zone lies between cortex and nucleus. The nucleus shows numerous droplets and a disintegration of fibers. Clinically, the opacities appear subcapsular in the posterior cortex. The cataract may appear in postoperative tetany (tetania strumipriva) and in idiopathic and latent tetany, therefore, in the presence or absence of muscular convulsions or spasms. The blood calcium is decreased and potassium and phosphorus increased. The mechanism of the origin is unknown. It is assumed that the deficiency of calcium caused by the missing hormone of the parathyroid produces chemical changes in the lens or that the hormone deficiency liberates toxins.

Cataract in myotonic dystrophy shows similar changes in the cortex close to the posterior lens capsule in the form of clefts with granular masses and detritus, with the opacities sharply localized in a thin zone of cortex beneath the anterior and posterior capsule. In this apparently congenital muscular disturbance, with excessive contractility of numerous striated muscles of the body, the muscle fibers are atrophic and show circular fibrils beneath the sarcolemma. Glands with inner secretion show atrophic changes. However, it is unknown how the lens opacities are produced.

Cretinism and idiocy; skin diseases. Similar cataractous changes appear in various diseases apparently caused by endocrine disturbances, but which have been examined clinically only: cataract in Mongolian idiocy, cretinism, in skin diseases, e.g., neurodermatitis, sclerodermia, Darier's disease, poikiloderma atrophicans vasculare. In the latter, the cataract is called cataracta syndermatotica (dermatogenous).

5. Cataracts Caused by Physical and Chemical Trauma

Lenticular changes can be caused by physical injury, such as contusion, perforating injuries, foreign bodies and by chemical injuries.

Cataract in contusion and its special form, the ring opacity of Vossius, have been examined only clinically and experimentally.

The lens can be dislocated by trauma directly (contusion, rupture, perforation, foreign body) or in a later stage by shrinking connective tissue as sequela of an injury. The lens may be subluxated or luxated: (a) into the anterior chamber, (b) into the vitreous body, (c) beneath the sclera, (d) beneath the conjunctiva, (e) beneath Tenon's capsule. Zonule fibers break and rests of the zonule lie mixed with blood on the lens capsule. If the rupture takes place only on one side, the lens remains dislocated in the pupil (subluxated). The lens luxated into the anterior chamber undergoes different cataractous changes in the course of time and the posterior corneal lamellae swell because of the pressure. The iris is pressed onto the posterior lens surface. The capsular epithelium degenerates and eventually disappears. The lens fibers split up and disintegrate, amorphous masses collect between capsule and cortex, the nucleus becomes eroded and calcium may be deposited. The lens can shrink in toto. If the capsule is opened, it rolls up and the exposed lenticular substance becomes embedded in granulation tissue with giant cells and at the same time severe iridocyclitis sets in. Luxation of the lens into the anterior chamber produces secondary glaucoma. The lens displaced into the vitreous body is sometimes only slightly changed if the capsule remains intact, but if the capsule is separated, the lens shrinks, calcifies and is surrounded by granulation and scar tissue. Usually, retinochoroiditis appears, or even sympathetic ophthalmia. The lens luxated into the vitreous floats in the liquefied vitreous (lens natans) or is fixed usually on to the retina (lens fixata). Rarely the lens is displaced beneath the torn retina or between detached ciliary body and sclera (subscleral luxation). The lens can be incarcerated into a perforation of the cornea caused by ulceration or trauma (phacocele) or in a rupture of the sclera. But it can also completely pass through the ruptured sclera and rest beneath the elevated conjunctiva, intact in its capsule and surrounded mostly by blood, or luxate into Tenon's capsule. The

lens fibers eventually disintegrate and the lens is absorbed partly or entirely. If the conjunctiva ruptures, the lens is displaced entirely out of the body.

However, without a sign of external force a lens can be found subluxated or luxated, the luxation then being congenital or spontaneous (consecutive). The congenital displacement of the lens is ectopia lentis, caused by a defect of the zonule, the origin of which is not always certain. It is caused by intra-uterine inflammation, malformation, underdevelopment of the ciliary body or persistence of the perilenticular vascular membrane. The ectopia lentis also appears hereditary or familial and is associated with other defects of the eye and of the body, arachnoidactyly, for example. Liquefaction of the vitreous body, detachment of the retina and secondary glaucoma sometimes appear as complications. The zonule may rupture in diseased eyes spontaneously and give rise to displacement of the lens as in cases of hydrophthalmos, glaucoma, shrinking cataracts, so that in cases in which the lens is small in relation to the size of the eye, the zonule is under increased tension. If the capsule of the luxated lens is opened, iridocyclitis nearly always results and lymphocytes, polymorphonuclears and foreign body giant cells surround the lens. The lens fibers of the luxated lens are distorted irregularly and the nuclei of the epithelium and of the equator are shrunken. Also, in spontaneous or congenital luxation, the lens may enter the anterior chamber, float in the vitreous body or may be fixated at the ciliary body or retina; retinochoroiditis, iridocyclitis, detachment of the retina and glaucoma may set in just the same.

Perforating injuries of the eye are often associated with injuries of the lens; either they remain aseptic or become infected. In aseptic cases, the lens fibers swell, prolapse through the capsule wound and are absorbed and the entering aqueous humor causes in the course of time a total cataract. The cataract is absorbed in juveniles. The partly absorbed and diminished lens shows folds of the capsule with proliferating epithelium. If the capsule wound is covered by fibrin and the

iris, it is closed in this way and cataractous changes may still progress, or halt entirely. Malformed lens fibers occasionally proliferate through the wound of the capsule. Blood can enter the lens through the wound of the capsule. The torn capsule sometimes remains incarcerated in the perforating wound of the cornea or sclera. This sometimes happens in cataract operations. The capsule at times bursts at the equator during glaucoma operation due to sudden decrease of the high tension. The lens can be luxated into the perforation as already mentioned and stay incarcerated in the wound (phacocele). If bacteria enter the disintegrating lens, they find here a good medium. Polymorphonuclears surround the prolapsing lens masses and enter through the capsule wound and form a lens abscess. But polymorphonuclears also erode the unopened capsule from an abscess in the vitreous body. The inflammation causes attachment of the iris to the lens capsule and closes it in this way. In some instances, the cortex is entirely absorbed and the nucleus surrounded by polymorphonuclears, lymphocytes and giant cells, if granulation tissue proliferates into the lens. If the anterior chamber is gone, Descemet's membrane and lens capsule can unite and the inner surface of the capsule sac can be lined by proliferating endothelium.

Foreign bodies, especially iron, less frequently copper, occasionally wooden splinters, even the body's own epithelium and cilia can be carried into the lens in the event of a traumatic perforation of the globe. Metals produce chemical reaction. Iron is deposited in the lens capsule, in the epithelium, in the sutures and in the lens fibers of the cortex. Proliferating capsular epithelium is filled with fine iron granules. Iron also appears in Morgagnian globules. Finally the lens shrinks. Copper is found in thin layers between the epithelium and the capsule and in the epithelial cells as well as between the lens fiber. It is precipitated perhaps as basic copper carbonate.

If inorganic acids burn the cornea and enter the chamber, the capsule epithelium degenerates, vacuoles appear at the equator and the lens fibers of the cortex disintegrate. Ammo-

nium hydroxide enters swiftly through the cornea and causes necrosis of the iris and rapidly appearing total cataract. The lens capsule is folded, the epithelium flat, endothelial-like, and grows along the capsule, and the lens fibers change into amorphous masses.

Radiational energy and electricity are able to produce cataract. Infra-red rays, x-rays, radium, and electrical current can produce cataract in the human eye. In numerous experiments, the effect of these rays and ultra-violet rays on animal lenses have been studied. The infra-red rays are apparently responsible for the appearance of the glass-blower's cataract. Heat conducted from the iris appears to produce lenticular changes. A lamella splitting off from the capsule to half of its thickness, and also having curled up margins, may freely float in the chamber fluid. The lens epithelium becomes irregular, nuclei move further apart, cells become spindle-shaped and disappear in areas. The lens fibers beneath the epithelium disintegrate and vacuoles appear. At the posterior pole and posterior cortex, fibrils may disintegrate. Under the influence of x-ray and radium, epithelial cells degenerate and proliferate. Vesicular cells appear, lens fibers of the equator swell, granular masses lie beneath the anterior and posterior capsule, highly refractile globules and homogeneous albuminous coagulant are seen and lens fibers also proliferate. Electricity passing through the eye, by producing ultraviolet rays and heat waves or electrochemically may cause slitlike holes in the lens capsule and degeneration of epithelial cells. The subcapsular cortical layers show granular disintegration. In the course of time, a total cataract may form.

Poisons rarely affect the human lens. Most frequently dinitrophenol cataract is observed and total cataract develops rapidly. There have been clinically observed cases of cataract due to ergot poisoning, causing "cataracta raphanica," and a type of cataract in severe diseases due to exhausting infections or other exhausting diseases, sometimes with severe loss of blood, known as "cataracta cachectica." Extensive examina-

tions of different poisons, vitamin deficiencies and nutritional disturbances have been done in animals in which naphthalene, thallium, lactose, galactose and vitamin deficiency, especially of vitamin C, produced lenticular opacities.

READING OF SOURCE MATERIAL

Fischer reports on development of the lens in early embryonic stages.

The development and regression of the tunica vasculosa lentis is described by Versari.

The lens capsule shows lamellar structure, according to Boehm.

Busacca believes that a thin, pericapsular membrane surrounds the lens capsule proper all around.

The zonule lamella originates, according to Busacca, from the fringing of the zonular bundles which partly insert in the capsular membrane and perforate it partly. The zonule lamella can separate from the pericapsular membrane, probably due to degeneration on the end of the zonule bundles.

Beauvieux distinguishes layering of the lens capsule by staining.

Tonofibrils are present in the lens epithelium, according to Busacca.

Cholesterol- and tyrosin crystals can be found in the lens (D'Alajmo).

Morax finds bacillus subtilis in abscesses of the lens.

Seefelder reports histologic findings of rupture of the lens capsule in a 4 month old child with congenital total cataract with liquefaction of the lens material.

Szekely describes proliferation of lens substance after rupture of the lens capsule for the purpose of closing the wound.

Sanna finds that wounds of the lens close by proliferation of the epithelium.

Tuberculous granulation tissue can enter the lens and produce complicated cataract (Schall).

Histologic findings of separation of the zonule lamella are reported by Busacca, Vogt.

Clapp examined seventy immature cataracts, extracted by the intracapsular method, and found the epithelial cells atrophic, some of them proliferating, and migration of the nuclei of the epithelium into the depth.

Samuels studied the proliferation of the epithelial and germinative cells of the lens. He finds that the epithelium extends posteriorly if the germinal zone is destroyed. The germinative cells are often vesicular and epithelial cells may float freely in the liquefied cortex.

Spontaneous absorption of juvenile and senile cataract without opening of the lens capsule is reported by Ballantyne, Butler, Ferrer, Holloway and Cowan, Paterson, Vancea.

The histology of pyramidal cataract is described by Maucione, Nista.

With progressing age the protein content of the lens increases (Jess, Shoji), the soluble protein decreases and the insoluble one increases (Krause).

Adams, Calhana, Goldschmidt, Salit and O'Brien, Parhon and Werner find increase of lipoids in the aging lens and Boente deposits of calcium carbonate.

Glutathione which forms a reversible oxidation-reduction system with the proteins of the lens, is decreased in the aging lens and disappears in cataract (Farmer and Bellows, Gifford, Jess, Rosner, Tassmann and Karr), and vitamin C, which forms an irreversible oxidation-reduction system with the lens proteins, is decreased in the lens in old age and disappears in cataract (Bellows, Bietti, Mueller, Nakamura).

Kirby, Kranz, Mackay, Stewart and Robertson find increased calcium content in cataractous lenses.

Krause's finding is that acid reaction appears in the aging lens activating proteolytic enzymes. Protein constituents are coagulated and are broken up into amino-acids which diffuse away.

Labbe and Lavagna, Sauermann find the reaction of the senile cataract acid, although the normal lens reacts alkaline.

Bourdon-Cooper finds crystalin deposits of tyrosin in cataract.

Friedenwald finds that the lens capsule is less permeable in old age than in cataractous lenses in general.

Bellows, Yudkin consider vitamin deficiency as etiologic factor in the origin of cataract.

Langdon, O'Brien consider disturbance of the carbohydrate metabolism as cause of the cataract.

Burdon-Cooper considers the decrease of the molecular concentration and the increase of the surface tension of the aqueous humor as cause of cataract.

Hektoen and Schulhof, Woods and Burky believe that cataract is an immunologic phenomenon.

Elschnig, Groenholm, Loewenstein, Siegrist assume disturbances in the function of endocrine glands as etiologic factor in the origin of cataract.

Kirby finds that small decrease of calcium content in tissue culture acts toxically on lens epithelium.

Bakker, Kirby, Kirby, Estey and Tabor observe the outgrowth of epithelial cells to formations similar to fibroblasts in tissue culture.

Diet deficient in tryptophane (amino-acid) produces cataract in experimental animals (Curtis, Hauge and Kraybill), further, lack of vitamin B_2 (Day, Langston and O'Brien).

Toxic cataract can be produced in experimental animals (a) by naphthalene (Michail and Vancea, Panico), (b) by lactose and galactose (Mitchell and Dodge, Yudkin and Arnold), (c) thallium (Buschke).

Osmotic cataract can be produced experimentally in animals by subconjunctival and intra-ocular injection of hypertonic solution (Panico); further, cataract develops in asphyxia (Biozzi).

Radiational cataract can be produced experimentally by infra-red rays (Buecklers, Duke-Elders, Mueller), by ultra-violet rays (Jess and Koschella, Truempy), by x-ray and radium (Peter, v. Szily).

Cataract can be produced in animals by removal of the parathyroid (Campos, Goldmann, Hiroishi, Lo Cascio, Luckhardt and Blumenstock, Pellathy, Siegrist).

Cataract was produced experimentally by massaging the lens in man and animal by Busacca, Cavara who finds the epithelium of the anterior capsule hydropic with nuclei pyknotic and irregular cell proliferation and lens fibers disintegrated to detritus.

Riehm, Roetth deny sensitivity to lens protein, as their animal experiments were negative.

Histopathologic findings in senile cataract are reported by v. Szily.

Wiederkehr finds histologically in senile exfoliation of the lens capsule (1) foil-like separation of the superficial lamellae, (2) exfoliation with thinning of the capsule, and (3) leaflike dissociation of the capsule lamellae.

Pathologic examinations of senile exfoliation of the lens capsule are reported by Busacca, Caramazza, Vogt.

Depigmentation of the pupillary margin, exposure of the sphincter, formation of hyaline deposits, deposition of granular material on the posterior surface of the iris, the surface of the ciliary body and on the zonule fibers are found in exfoliation of the lens capsule (Sobhy Bey).

Hoerven finds in "exfoliatio superficialis capsulae anterioris (Vogt)" the zonule fibers covered with scurflike particles similar to those at the pupillary margin.

Bunge finds increase of cholesterol with the progress of a senile cataract. He stained cholesterol with the help of scarlet red and nile blue sulfate, further with acetic acid-sulfuric acid (according to Schultze) which results in colored oxycholesterol. Also, Magnasco, Metzger found increased content of cholesterol in cataract.

Deposits of calcium in crystals are found in senile cataract by Wessely.

Black cataract is thought to be caused (a) by increased refractive index (Busacca, Magnasco, Rollet and Bussy), (b) blood pigment, (c) bile pigment, (d) lipoid substances, (e) melanin or its nonpigmented precursor (Bourdon-Cooper, Krause, Michail and Vancea).

Busacca finds in black cataract accumulations of droplets and granules in the lens fibers and highly refractile droplets between the fibers. They can be stained with sudan III as fat droplets. The color is caused by a special structure of the cytoplasm of the lens fiber.

Cataracta nigra shows histologically densely packed lens fibers, but no pigment, according to Corrado. The color is probably caused by amino acids.

Shoji finds in black cataract pigmented granules, probably melanin in the relatively small lens.

Takeishi could decolorize black cataracts with chlor, potassium permanganate and oxalic acid. He believes that a substance related to melanin produces the color of the black cataract.

Carmi, Slusenkov could not find melanin in black cataract.

Cholesterol crystals situated in vacuoles were found in black cataract by Neuschueler.

Strebel found that an extraction of cataracts becomes dark brown in a diluted solution of adrenalin. He gets a black staining of the lens with chrom-formalin which also stains the granules of the adrenalin-producing cells of the adrenals black. He assumes chemical and photocatalytic relations between the metabolism of the lens, ascorbic acid and the adrenals.

Gifford and Puntenney can find neither tyrosin nor tyrosinase in normal or cataractous lenses, but they could get reactions with dopa in brown cataract and nuclear sclerosis and believe that there is a ferment present in these lenses and that products of the metabolism of the lens produce the color in black cataract.

Gabrielides finds in hypermature cataracts histologically branching formations, round discs and dustlike granules in a liquefied cortical substance.

Gabrielides found in the Morganian cataract of a 73 year old woman finest granules throughout the lens and coagulated masses in the liquefied cortex. He believes that the granules can pass the lens capsule and clog the chamber angle causing glaucoma. Further, Osterberg reports on Morgagnian's cataract.

In Morgagnian and brownish nuclear cataract, calcium phosphate is deposited radially to a central organic mass (Boente).

Double reflectile lipoids were found in cataracta coronaria by Metzger.

Hannsen found in cataracta pulverulenta histologically numerous multiform spaces with granular contents and the peripheral lens fibers hazily defined.

Haro finds in disc-shaped (ring) cataract histologically the center of the lens consisting of anterior lens capsule, epithelium and posterior lens capsule surrounded by a ring of cortex with cataractous changes and complete absence of the nucleus.

Congenital aplasia of the lens nucleus is reported by v. Szily.

Sommering's ring was found by Marchesani in the case of a staphyloma of the cornea. The cornea and the intact lens capsule were connected by a strand.

Smallest irregular clefts with granular and fibrillar contents are found in zonular cataract by Hanssen.

Dystrophia epithelialis lentis adiposa is reported by v. Szily, Handmann, Sagher.

Cowan and Fry observed the proliferation of lens epithelium onto the anterior surface of the anterior lens capsule in secondary cataract; some cells became very swollen and vacuolated.

Especially in secondary cataract after diabetic cataract pigment epithelium proliferates, intermingling with the rest of the lens (Mans, Sgrosso).

Riedl found multiple, free lentoid structures in the secondary cataract, after needling of a hereditary perinuclear cataract and considers them as regenerative lens fibers.

Custodis reports a case of ingrowth of epithelium after cataract operation in which the epithelium grew across a secondary cataract.

Fatty degeneration of an after-cataract is described by Sala.

Luxation of the secondary cataract into the anterior chamber is described by Jacoby and Wolpaw, Schneider, Tooke, Vannas.

Pathologic findings of complicated cataract are reported by Schall, v. Szily.

Fatty substances were found in complicated cataract by Jess.

Folds of the capsule due to shrinkage of the lens are reported by Buecklers, Bedell, Harms.

Samuels finds that the complicated cataracts associated with spontaneous detachment of the retina show vesicular cells in the posterior segment of the lens as the epithelium proliferates backwards.

Samuels describes various forms of cataract, especially membranous and calcified cataracts, after perforation of corneal ulcers. Spontaneous expulsion of a calcified lens may occur. The capsule may be separated from the lens substance. The lenses are shrunken, the capsule folded and the epithelium proliferated. A Morgagnian cataract can form. If the epithelium is absent entirely, one speaks of a dead lens. In nontraumatic iritis the lens capsule shows ruffling and folding. The epithelium proliferates and lens fibers disintegrate. In glaucoma the lenses show circumscribed necrosis of the epithelium and proliferation. Lens fibers disintegrate and liquefy and frequently show vacuolation. There is a peculiar form of fragmentation of the fibers.

Anterior polar cataract is described histologically by Beauvieux and Germain, Lamb.

Deposition of fat in anterior polar cataract is described by v. Szily, and homogeneous, intensely stained masses in van Gieson stain were found by Peters. He believes that fluid enters the lens capsule and coagulates beneath the capsule.

Depositions of connective tissue at the posterior pole of the lens are reported by Heine, Jacoby, Pollock. Heine believes that they are the result of organization of hemorrhages from the hyaloid artery.

Findley reports a congenital membranous cataract in a 2 month old infant with defective lens capsule and shrunken lens fibers.

Busacca describes coagulation of granular substances of indefinite nature in the aqueous humor. They can deposit on the iris, ciliary processes and anterior surface of the lens.

Loewenstein, Riedl find pigment also beneath the lens capsule.

Pesme believes that congenital starlike deposits of the anterior lens capsule are remnants of the pupillary membrane.

Persistent capsulo-pupillary vessels are responsible for the formation of congenital cataract, according to Lauber, Loewenstein, Mann, Riedl. Loewenstein believes that the tissue of the pupillary membrane can proliferate actively and intrude the lens capsule.

Grimminger reports blood staining of the anterior lens capsule following cyclodialysis with a severe hemorrhage into the anterior chamber.

Xanthomatosis lentis is described by Sala, v. Szily.

Michail describes bone formation in the lens of a shrunken eye with a dense cyclitic hull which surrounded the anterior and posterior surface of the lens and from which small blood vessels perforated the lens capsule.

Pitsch reports ossification of the lens preceded by calcification and ingrowth of vascular connective tissue.

Betsch found bone formation in the lens frequently. In all cases the lens capsule is opened, due to injury or ulcer, metastatic vitreous abscess or tuberculous iritis. Fibrous cyclitic membranes invade the calcareous lens and form here bone by metaplasia. Bone marrow is not present, but Haversian canals.

Merrill, Nordmann, describe complicated cataract caused by rupture of the lens capsule due to malignant intra-ocular tumors.

Samuels finds in cataracts associated with intra-ocular tumor folds of the capsule, proliferation, but also necrosis of the subcapsular epithelium, vesicular cells at the equator, pressure atrophy where the lens is in direct contact with the tumor, dislocation of the lens, liquefaction and calcification.

Loewenstein describes endocrine cataracts and assumes as cause vitamin B_2 deficiency, producing toxic destruction of the lens epithelium.

Bellows finds in diabetes cortical cataract with swelling and disintegration of the peripheral lens fibers.

The histology of cataract in myotonia is described by Gil and Garcia Querol, Vogt.

A lens opacity observed by Jess in pseudosclerosis did not show any pathologic change in section.

Maggiore finds in luxation of the lens the zonule fibers torn, mostly at their insertion at the lens and pigment of the ciliary epithelium migrating into the nonpigmented epithelial cells and along zonule fibers into vitreous.

Subconjunctival luxation of the lens is described by D'Amico, cases of incomplete subconjunctival luxation by Cantonnet.

Fuchs, Waardenburg emphasize the relative small size of displaced lenses.

Zeeman found in congenital ectopia of the lens the pupillary part of the iris inverted and fixed by zonule fibers. The lens capsule was very folded and consisted of granular masses. He considers the persistence and transformation of the primary vitreous fibrils as the cause of the ectopia.

Capsule epithelium extends posterior, the nuclei of the lens fibers are irregular, the lens fibers are malformed, there is a fissure at the posterior pole in the luxated cataract in patients with arachnodactyly, according to Bakker.

D'Oswaldo believes that necrosis of iris, ciliary body and lens epithelium in severe blunt injury of the eye is responsible for the formation of cataract.

Szekely saw in cases of rupture of the lens capsule new formation of so-called "deformed lens fibers" close to the posterior equatorial zone. The proliferation is influenced by the aqueous humor.

Morax and Chiazzaro found in perforating injuries of the eye with injury to the lens, organisms forming spores in the latter.

Folds of the lens capsule after perforating injury are described by Hedinger and Vogt.

Attachment of the lens to the cornea with ingrowth of newly formed blood vessel after perforating injury is reported by Moretti.

Formation of cataract due to sting of wasp and bee are described by Herrenschwand, Panico.

Siderosis lentis is reported by D'Amico, Hertel, Narόg, chalcosis lentis by Jess, Vogt.

Exfoliation of the anterior lens capsule due to infra-red rays is described histologically by Goldschmidt, Riedl, Vogt.

According to Vogt, the "fire lamella" of the glass-blower cataract shows intensive striation and separation in a thick layer.

According to Goldschmidt, the "fire lamella" is histologically a pellicle consisting of the entire capsule and epithelium.

The zonular lamella, appearing microscopically as a structureless membrane, is separated from the lens capsule by influence of heat or by pull of exudate, according to Elschnig.

Krueckmann found histologically in Roentgen-cataract an epithelial-like layer at the posterior pole, destruction of the cells at the equator and lens fibers swollen and vacuolated.

Grzedzielski describes x-ray cataract in a 31 year old man. The anterior subcapsullary cortex is disintegrated and globular and vesicular formations are found beneath the posterior capsule.

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Chapter XI

PATHOLOGY OF THE VITREOUS BODY

The vitreous body has a composition similar to the intra-ocular fluid, except that the vitreous gel contains larger quantities of protein than the chambers. These proteins are albumin and globulin, and, further, muco-protein (hyaluronic acid) and residual protein, which are found also in blood and intra-ocular fluid. The vitreous body has a very high viscosity and is somewhat more alkaline than the intra-ocular fluid. It is assumed that the vitreous body is of ectodermal origin and that its protein constituents are produced mainly by the retina. These protein constituents give the base for the vitreous gel, into which fluid dialyzes from the capillaries of the uvea. There exists little circulation of fluid in the vitreous, from which fluid is eliminated through the optic nerve.

The vitreous body represents a reversible elastic gel, i.e., it can give off and take in water and show turgescence and deturgescence. As the eye is surrounded by the slightly distensible sclera, a change of the volume of the gel of the vitreous body produces some changes of the intra-ocular pressure. The vitreous body is normally in a state of maximal turgescence. Changes of the reaction of the vitreous body cause marked changes of the volume of the gel but the swelling pressure of the gel is very small. The consistency of the vitreous body is unstable; fluid can be separated from the gel, especially by use of pressure and if the metabolism is disturbed and the gel transformed into the sol state.

The vitreous body is not substituted for after loss of a part or all of its protein substances but only intra-ocular fluid fills the defect. This can occur in injury, during or after intra-ocular operation, but also in inflammatory processes of the eye. It happens in myopia as the eye elongates.

The reaction of the vitreous body is not changed in glaucoma and an eventually existing swelling of the vitreous body seems to have no influence on the increase of pressure.

In degeneration of the retina, tears and detachment may set in if the proteins of the vitreous body originating from the retina adhere to the internal limiting membrane and shrinking forces act in the vitreous body, which have greater effect perpendicular than parallel to the retina (anisotropism).

If fluid separates from the gel of the vitreous body, the latter remains in a shrunken state and fine fibers and strands and large membranes representing the residual protein float in it.

If the vitreous body reacts acid, its proteins are disintegrated by enzymes, and autolysis of the protein sets in (proteolysis). It is followed by deturgescence of the gel, liquefaction of the vitreous and formation of floating deposits. If exogenous enzymes of bacteria and of polymorphonuclears act in infection, the protein is also decomposed and the reaction becomes acid (heterolysis).

The proteins of the vitreous body are increased in inflammatory changes of the eye with increased permeability of the vessels.

1. General Considerations

Many changes of the vitreous body are more easily diagnosed with the ophthalmoscope and by slit-lamp biomicroscopy than by histiologic examination. Furthermore, the vitreous consists nearly entirely of water, with little organic substance, and is very difficult to fix. The vitreous is entirely inert, as it hardly has metabolism, does not contain vessels, has no cells of its own and the normally few cells found in it immigrate from the retina. The vitreous normally appears to be composed of very small fibrils, appearing optically in irregular strands and membrane-like formation. The vitreous plays a passive role and changes in the vitreous are caused by changes in the surrounding tissue. If pathologic changes appear in the eye, the vitreous responds, if altogether, passively with degeneration of various kinds; in case of an inflammation, inflammatory elements enter from the surrounding parts. The vitreous body

is a good medium for bacteria, even for those otherwise only slightly pathogenic.

2. Congenital Changes

Congenital changes found are (1) persistent hyaloid artery and (2) coloboma of the vitreous body. The persistent artery frequently is found in otherwise malformed eyes, as in congenital microphthalmos, congenital coloboma of the iris and lens, persistent tunica vasculosa lentis, associated with medullated nerve fibers of the retina or lenticonus posterior. It represents a strand of connective tissue and glia, extending from the excavation of the papilla in the central canal of the vitreous body, can be followed onto the posterior surface of the lens, and contains the obliterated but sometimes patent artery. As frequently during the growth of the eye the central strand does not continue to grow, it often breaks up in its continuity. Sometimes strands imitating a persistent artery originate from hemorrhages into the central canal and later organize. The vitreous body may be indented coloboma-like by a congenital retinal fold.

3. Acquired Changes

The vitreous body may be condensed, shrink, liquefy, the content of its fluid may change, it may be resorbed, tear, prolapse, detach, and hemorrhages and inflammatory products may appear in it. It can contain foreign bodies, cysts and parasites. Many of the pathologic changes appear clinically subjectively and objectively as vitreous opacities which are either fixed or float freely.

The normally fine fibrils which are visible in the fixed vitreous body and are assumed by some to be coagulation artifacts can be condensed under pathologic conditions. They appear in bundles which run parallel to the retina and posterior surface of the lens or perpendicular to them and membranes are visible. They contribute, if they shrink, to detachment of the retina. Some do not speak of shrinkage of the vitreous, since they assume that all processes in the vitreous as entirely passive, but rather of compression of the vitreous by collection of fluid.

The spaces between the fibrillar bundles and membranes often appear filled with fluid, with free pigment, or with cells having one or two nuclei, and pigment granules. The vitreous liquefies, probably by separation of the water from the colloidal gel due to nutritional disturbances. The liquefaction may be lacunar (partial liquefaction) or may occupy a large part of the space of the vitreous body, especially the posterior part. Senile degeneration, myopia, chronic uveitis, contusion, contribute to these changes.

The vitreous fluid shows changes in its composition under pathologic conditions, especially if the epithelium of the ciliary body is affected, and elements of the blood may enter the aqueous humor, which normally are retained. The fluid usually becomes richer in albumen. If fibrin exudes into the vitreous body it may coagulate here. Coagulation products of the fluid are found in the form of long threads and mucoid membranes, between which erythrocytes in small and large numbers can appear. Pigment and cellular elements at the same time may enter the vitreous body. Pigment from the pigment epithelium and after hemorrhages is found in the form of granules, threads and crystals, or it is contained in desquamated pigment epithelial cells or in macrophages, and is found after trauma and inflammations, in glaucoma and senile degeneration. Furthermore, granular cells and vesicular fat-containing cells (histiocytes, reticulo-endothelial cells) are met besides cells with fine anastomosing processes, which originate from glia or mesodermal elements.

Crystalline formations are deposited in the altered vitreous fluid as (1) asteroid bodies and (2) as synchisis scintillans. The former (scintillatio corporis vitrei, scintillatio albescens or nivea, asteriod hyalitis or Benson's disease) appear as fixed small rounded disseminated bodies in a nonliquefied vitreous and are calcium soaps (compounds of palmitic and stearic acid) and calcium phosphate and chloride. They are of unknown origin and are found in different localized diseases of the eye. Perhaps arteriosclerotic vessel changes play a role in their development if at the same time the vitreous fluid is changed pathologically. The latter appear as floating irregular forma-

tions in a liquefied vitreous. They are mainly deposition of cholesterol, but also fatty acids, calcium phosphate and carbonate are detected. They are probably brought in from the blood circulation when the nutritional cells surrounding the vitreous body are damaged.

The vitreous body may be compressed and resorbed, as in detachment of the retina and in tumors which eventually cause total disappearance of the vitreous body. It is questionable if tumor cells metastasize and proliferate in the vitreous body. Tumors grow in the vitreous space always in connection with their seat in the surrounding tissue, but tumor cells sometimes float in the vitreous and are carried through it. As the vitreous body has no cellular elements, it cannot regenerate when there is loss of a part or the whole. It can only be substituted by aqueous humor or not at all.

The substance of the vitreous body is ruptured by a penetrating wound, foreign body, or by massive exudate. Holes of the vitreous are formed and cells migrate to their margins, but no new fibrillar substance is formed and the separated fibrils are not united. The holes are filled with clear fluid or products of inflammation. If the vitreous membrane is perforated, herniation of the vitreous sets in if the vitreous enters another cavity in which it is normally not present and vitreous prolapse if the vitreous body reaches the outside of the globe. The vitreous hernia is seen in the anterior chamber chiefly after cataract extraction, or when the lens is luxated into the vitreous, or appears between iris and subluxated lens. After intracapsular extraction of a cataract, after discission of a secondary cataract or after luxation of the lens, the vitreous may, in general or sacculated, bulge into the anterior chamber and a condensed marginal layer, membrane-like, may separate it from the aqueous humor; this may also occur if the anterior vitreous membrane tears. However, sometimes holes exist in the membrane or in the membrane-like condensation and liquid vitreous flows into the aqueous humor. The vitreous in the anterior chamber may adhere to the iris or posterior surface of the cornea. Cells and pigment may be contained in the herniated vitreous body. The vitreous can prolapse through a wound of the cornea

or sclera in front of the eye and may be covered in the latter case by conjunctiva. The prolapsed vitreous tissue often condensates with the help of elements entering from the surrounding parts and can be covered by granulation tissue. Secondary glaucoma frequently develops in these cases.

The vitreous body can be detached somewhere in its entire circumference to various degrees, most frequently posteriorly, less frequently above and anteriorly. It appears then chiefly condensated and especially its outer layer appears denser, membrane-like. Between the surrounding tissue, mostly retina, and the condensed outer layer of the vitreous, there is serous fluid. In this way, there is usually a distinct border between vitreous body itself and the newly-formed pathologic fluid-filled space. The condensed outer layer may show holes (hyaloid holes). In a specially fixed eye in which shrinkage of the vitreous is avoided, the detachment can easily be seen, but it can also be observed in the living eye with the help of slit lamp, contact lens and biomicroscope. Some consider the detachment of the vitreous found in pathologic specimen as artifact, produced by shrinkage of the vitreous in the fixation fluid, and separation of fluid from it into the surrounding parts. The detached vitreous is funnel-shaped with its tip at the papilla and base at the ora serrata. But it can be torn from the papilla and appear of oval shape, and finally it may be compressed into a small body. Under certain circumstances, the vitreous separates from the base at the ora serrata itself and infrequently from the zonular membrane. The detached vitreous is little changed or contains degenerated dense bundles, strands, pigment cells and organizing tissue proliferating from the surrounding retina or ciliary body. Trauma, inflammation and degeneration of the eye are causes of the detachment which is found relatively frequently in senile and myopic eyes, eyes with retinochoroiditic foci due to trauma, degeneration or chronic inflammation and eyes with detachment of the retina. The detachment is brought about by degeneration and shrinkage of the vitreous due to malnutrition, further as detachment e vacuo by elongation of the eye, leaving a space between vitreous and retina.

Hemorrhages detach the vitreous body and lie on its outside (hemorrhagic vitreous detachment), but frequently they enter the vitreous and fill more or less wide spaces. The hemorrhagic vitreous detachment is caused by hemorrhages (a) into the postlenticular space; (b) the orbicular space, and (c) by hemorrhages from the posterior retina. If blood comes off the ciliary body, it may spread between the lens and vitreous body and push the latter backward or fill the posterior chamber and the space between the zonule and anterior hyaloid membrane and displaces the vitreous sideway. Pre-retinal hemorrhages detach the vitreous forward. The blood often penetrates the internal limiting membrane and suffuses into the vitreous body. The erythrocytes often lie beadlike in rows between the fibrils of the scaffold of the vitreous, the rows sometimes spreading fanshaped. Occasionally the hemorrhage is limited to (a) the canalis hyaloideus, (b) spaces produced by lacunar liquefaction, and (c) a wound channel produced by a cut or foreign body. If, in case of perforation of the globe, the hemorrhage is profuse, it may push the vitreous together with the lens out of the eye. Blood stays liquid for some time in the vitreous and cannot be resorbed. Erythrocytes disintegrate and blood pigment deposits or hemolysis takes place and cell shadows remain. Fluid current carries blood pigment away, migratory cells phagocytose and remove it, but also newly formed vessels and an organizing tissue of a retinitis proliferans enter the vitreous to dispose of the blood.

If inflammation-producing material is brought into the vitreous body, acute inflammation takes place (hyalitis, vitreous abscess), characterized by accumulation of polymorphonuclears which apparently emigrate from the vessels of the ciliary body, choroid, retina and optic nerve; albuminous and fibrinous fluid is exuded. In the further course, they are mixed with lymphocytes and plasma cells and substituted; also pigmentary cells enter the vitreous. Other cells of the exudate found in the vitreous in acute, subacute and chronic inflammation are monocytes, eosinophiles, phagocytes, giant cells, fibroblasts, endothelial and glial elements. Micro-organisms of different types can enter the vitreous, producing inflammation, in injury, ulcers

of the cornea, along a leukoma adherens or by the blood circulation, as in cases of meningitis, sepsis and infectious exanthemata. They find a good medium in the vitreous which has no immune bodies and cannot be inflamed itself, but receives the exudate only passively. Such micro-organisms are (1) bacteria, (2) fungi, and (3) yeast. Bacteria are staphylococci, streptococci, pneumococci, subtilis, coli, pseudodiphtheria and tetanus; fungi are aspergillus fumigatus, streptothrix and leptothrix. As in chronic inflammation micro-organisms are rarely detected, its etiology is often uncertain. Degeneration of the vitreous, besides exudative cells, is found in sympathetic ophthalmia and heterochromic cyclitis.

Organization tissue is formed in the vitreous body as sequela of an inflammation as well as of a hemorrhage. In case of chronic inflammation, the retina is detached by shrinkage of the vitreous and traction of newly formed membranes. Vessels, cells and fibrillar tissue proliferate from the ciliary body, choroid, retina and papilla. This tissue, substituting the vitreous partly or entirely, may undergo degeneration or metaplasia. It may be formed by (1) calcification, (2) cartilage, (3) bone, and (4) fatty tissue. The hyaline degenerated and necrobiotic tissue can absorb calcium in the form of granules which coalesce to masses (petrification). Hyaline cartilage may be deposited, which also is formed in microphthalmic eyes without inflammation, by atypical growth of the embryonal vitreous body. Fat marrow can appear, and from its osteoblasts osteoid tissue originates, which becomes typical bone by deposition of calcium. Fatty tissue can develop from connective tissue and often is fat marrow, but it can also develop abnormally without any inflammation from the embryonal vitreous tissue.

Perforating inorganic and organic foreign bodies frequently remain in the vitreous where they are sometimes tolerated, but usually go into solution, damage the surrounding tissue or stimulate formation of granulation tissue. Aluminum, glass and stone particles are tolerated; iron, copper, lead, zinc have damaging influence. Eye lashes especially produce heavy granulation tissue.

Cysts of the vitreous body are extremely rare and have been described chiefly only clinically; their anatomic structure and

etiology is questionable. Some are considered congenital anomalies derived from rests of the hyaloid artery and Bergmeister's papilla, or are cysts of the ciliary epithelium; some are traced to inflammation and hemorrhage, and some are considered as degenerated retina. Parasitic cysts of the vitreous are encountered occasionally which are also examined histologically. In

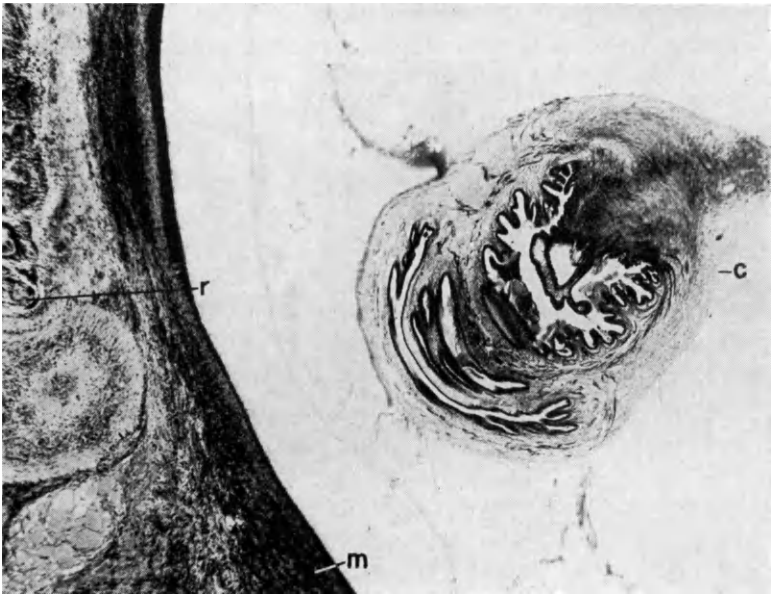

FIG. 52.—CYSTICERCUS IN VITREOUS. c, cysticercus; m, membrane of the parasite; r, folded retina. 25×.

addition, however, parasites appear in the vitreous body, which are not cystic and encapsulated.

Parasites appearing in the vitreous body are grouped as (a) the platyhelminthes, (b) nemathelminthes and (c) arthropoda. To the first group belong the Taenia solium, forming the cysticercus cellulosae, and the Taenia echinococcus. The cysticercus, representing the larva of the taenia, enters into the blood circulation after perforation of the wall of the stomach in which it is produced as embryo from the ovum, and can be carried to all parts of the body. It is deposited often between choroid and retina and can appear after perforating the retina in the

vitreous body. But it can also directly enter the vitreous from the vessels of the retina. It forms a vesicle consisting of a pyogenic membrane to which the scolex (head) is attached. The larva is characterized by its tortuous epithelial ducts from which the epithelium continues onto its surface. The membrane may calcify and be surrounded by giant cells; generally, inflammatory changes affect the eye, leading to cyclitic membrane. The echinococcus representing the larva of the Taenia echinococcus forms the hydatid cyst. The embryo enters the circulation from the intestine and is carried to various organs, forming cysts, as it does also in the subretinal space and occasionally in the vitreous body. The cyst is characteristic as it contains a parenchymatous inner layer with muscle fibers and vessels; it is surrounded by a hyaline laminated ectocyst and the scolex is attached to the membrane. The cyst develops filial cysts. To the group of the nemathelminthes belong the filariæ. Filariæ circulate in the larva stage in the blood and appear as small, rounded worms. They are noted also in the vitreous body. As already mentioned, also arthropoda produce diseases of the vitreous. Larvæ of flies, especially of hypoderma bovis and Wohlphartia magnifica, may perforate the outer layer of the eye and enter the subretinal space and the vitreous itself, where the larva is surrounded by inflammatory tissue.

READING OF SOURCE MATERIAL

Kronfeld finds that physico-chemical processes play the main role in the regeneration of the aqueous humor, but they do not conform entirely either with dialysis or with filtration.

Lehmann and Meesmann find that the fluid in the intra-ocular spaces coincides with the liquor and the endolymph of the inner ear. It has little protein and much salt in contrast to the blood serum.

Magitot considers the aqueous humor as a dialysate through the semi-permeable membrane of the capillaries. The pressure in the capillaries surpasses the intra-ocular pressure with an amount which equals the difference between the osmotic pressure of the blood and that of the aqueous humor. The aqueous humor is produced from the capillaries of the uvea and the retina and the production regulates the excretion.

Baurmann found in measuring the volume of the vitreous body when mixing it with fluids of various pH that the vitreous gel shows maximal turgescence.

Friedenwald and Stiehler find the viscosity of the vitreous body twice of that of the water, and Meyer and Palmer ascribe the high viscosity of the vitreous body to the presence of hyaluronic acid.

The vitreous is compared to a sponge filled with liquor-like fluid (Magitot and Mestrezat).

Duke-Elder reports extensive studies of the chemistry of the intra-ocular fluid, which is studied further by Gebb, Jess.

Ionized diffusible substances pass from the blood into the intra-ocular fluid as far as they are anions such as acid dyes, organic anions (drugs), inorganic anions (chlorides, iodides) (Ascher, Gaedertz and Wittgenstein).

Nonionized, diffusible substances divide equally between blood and intra-ocular fluid, like sugar (Duke-Elder), as it was found also in diabetes (Dieter).

Meyer and Palmer isolated a polysaccharid from the vitreous body which they called hyaluronic acid and which they identified with the muco-protein.

Krause called the residual protein of the vitreous body vitrein.

Diastasis-ferment is present in the intra-ocular fluid according to Boeck and Popper, Ikebata; proteolytic ferments according to Ikebata, Magitot.

The existence of antibodies in the intra-ocular fluids was proved by Blatt, Cronstedt, Franceschetti, Gala and Fabian, Gilbert, Kodama.

The vitreous is an excellent culture medium for bacillus subtilis, pyocyneus and anthrax. The normal vitreous contains bacteriolytic substances which can be activated by small ineffective quantities of serum, agglutinating bacteria (Cronstedt).

Woods could sensitize the vitreous by repeated injection of protein substances.

The morphology of the vitreous body is described by Fracassi.

Hiesch describes a fibrillar network in the vitreous in ultra-microscopic examination.

Contino considers the vitreous body as a living cellular tissue. He could demonstrate spider-shaped and star-like cells in the vitreous by fixation in a one per cent mercury chloride solution.

Samuels finds the opacities of the vitreous pathologically as cells of exudates, erythrocytes, pigmented epithelial cells, blood vessels, connective tissue strands, glial spheres, tissue spheres with pigment or without pigment.

Bachstez distinguishes between synchisis scintillans and scintillatio corporis vitrei. In the former the vitreous body is liquid and the freely movable particles are cholesterol; in the latter the particles are fixed, round and consist of fat acid calcium.

Manschot finds synchysis scintillans microchemically as calcium soaps.

Asteroid bodies of the vitreous are examined chemically and histologically by Bachstez, Clapp, Gallenga, Holloway and Fry, Verhoeff, and are found to be calcium soaps.

Hannsen found in four cases of opacities of the vitreous body histologically and microchemically calcium phosphate as the constituent of the tiny spherules.

Janson finds in a perforated eye numerous phagocytes and cholesterol crystals in the vitreous from the type of the synchysis nivea.

Prolapse of the vitreous body into the anterior chamber is described by Bassin.

Sallmann brings microscopic findings of posterior detachment of the vitreous body showing an albuminous fluid between the detached vitreous and the retina. The border of the vitreous can be made distinct as the hyaloid membrane can be specifically stained by Redslob's pyridic method.

Maeschlin-Sandoz found as histologic structure of the vitreous ring (Vogt) spindle-shaped splitting of the posterior hyaloid membrane with proliferation of glial cells.

The proteins of the vitreous body are increased in inflammation, according to Gebb, Guggenheim and Franceschetti.

The intra-ocular fluid contains much protein in inflammations of the iris and the ciliary body, due to increased permeability of the capillaries. (Gilbert, Hagen, Loewenstein, Magitot and D'Antrevaux, Roemer, Yudkin). The intra-ocular fluid is plasmoid after paracentesis as far as the capillaries dilate and become permeable (Mueller and Pflimlin, Wessely).

Metz-Klok reports an abscess of the vitreous in a case of epidemic meningitis.

Fuchs found plasma cells, Rados eosinophiles in inflammation in the vitreous.

Histiocytes filled with fat are found occasionally in the vitreous body (Heath).

Lopez Enriquez describes mesodermal phagocytes originating from the retina in the vitreous body.

Exudative cells are occasionally restricted exclusively onto Cloquet's canal (Butler).

Dejean found ossification in the connective tissue which had proliferated into the vitreous, and Schilling fat marrow in the calcified necrotic tissue of the vitreous body producing bone.

Alumen is well-tolerated in the vitreous (Jess, Fricke).

Morax describes a case of fungus infection of the vitreous.

Cockburn, Kress, Longhena report histologic findings in cysticercus of the vitreous.

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Chapter XII

PATHOLOGY OF THE CONJUNCTIVA

Examination of the living eye with the slit lamp and corneal microscope shows many changes which cannot be found in the histologic picture and are more typical than the histologic section. Changes of the blood vessels of a sclerotic nature, disappearance of the marginal loops of the cornea in old age, anemia and hyperemia belong in this group.

1. Circulatory Disturbances and Noninflammatory Vascular Changes

Circulatory disturbances and noninflammatory vascular changes of the conjunctiva may be classed under four headings.

(a) *Edema:* The loose submucosa can easily take up fluid. Histologically, fluid with small amounts of protein fills the meshes of the tissue. Besides, few polymorphonuclear cells and lymphocytes are present. The epithelium is loosened and epithelial cells have vacuoles.

(b) *Lymphangiectases:* They appear histologically as dilated tubes with thin walls and incomplete endothelial lining.

(c) *Hemorrhages* which appear after trauma or spontaneously, through intra-ocular disturbances, arteriosclerosis, diabetes, renal diseases, venereal infections, scurvy, hemophilia, intoxication, coughing, sneezing, constipation, vomiting, etc., show diapedesis of red cells into the tissue meshes of the conjunctiva.

(d) *Sclerotic changes* of the intima and media of the vessels, hemangioma-like convolutions of vessels, thrombi with following hyaline and calcareous degeneration may be seen.

2. Inflammations of the Conjunctiva (Conjunctivitis)

General Considerations

Often inflammatory hyperemia sets in; the capillaries beneath the epithelium and the vessels of the episclera are very dilated

and filled with many polymophonuclear cells. Exudate is poured into the tissue. Fibrin, fluid rich in protein and cells of different origin are found. In acute inflammations, polymophonuclear cells form dense perivascular mantles, infiltrate the tissue and migrate into the epithelium. Lymphocytes follow or are present from the beginning in chronic inflammation, and are perivascular, in lymph vessels and in the tissue. Plasma cells appear and are seen especially in trachoma and vernal catarrh. Sometimes eosinophiles are present in great numbers, as in vernal catarrh, pemphigus, allergic conjunctivitis. Histiocytes (macrophages) and fibroblasts often proliferate.

Erythrocytes leave the vessels in passive hyperemia and damage of the vascular endothelium through diapedesis. Emboli in vessels are seen especially in metastatic conjunctivitis.

Infiltration is circumscribed and diffuse. Circumscribed infiltrates of lymphocytes appear as phlyctenules in eczematous conjunctivitis. Circumscribed dissolution of tissue by polymorphonuclear cells surrounded by a capsule is a true abscess of the conjunctiva, is rare and appears mostly in metastatic conjunctivitis. If the epithelium is filled with polymorphonuclear cells and finally desquamated, an ulcer is formed which can form a contact ulcer, from the tarsal conjunctiva onto the bulbar conjunctiva and vice versa.

Exudation can appear on the surface. It is of a serous or mucous nature. It contains fibrin which helps form a pseudomembrane in necrosis of the surface. Between the fine fibrils, erythrocytes, polymorphonuclear cells, lymphocytes, epithelial cells, bacteria, necrotic debris may be entangled. The secretion of the conjunctiva can contain neutrophil polymorphonuclears, eosinophils, lymphocytes, monocytes and plasma cells.

Proliferation of cells and tissue sometimes sets in. Then fibrocytes in the tissue multiply, with an increase in endothelial and adventitial cells and lymphocytes.

In some conjunctivitides, mostly in chronic types, lymph follicles are formed, as in conjunctival folliculosis, follicular conjunctivitis, trachoma, atropin and eserine catarrh. There is still the question as to whether follicles are physiologically preformed. Follicles often are seen without inflammation, as

in children with lymphatic hypertrophy. The follicle represents a sphere with lymphocytes peripheral and toward the center larger clear cells with less stained nuclei (germinal center); also histiocytes are present which phagocytose.

Some conjunctivitides are accompanied by papillary hypertrophy, sometimes simultaneously with the formation of follicles. Papillary hypertrophy is formed by enlargement of the papillary connective tissue and the furrows deepen. The present papillae widen and new ones are formed where they were not present before.

The epithelium participates in the inflammation primarily or secondarily. Bacteria and virus enter the epithelium and multiply here damaging it primarily (active participation of the epithelium in the inflammation). Exudate is poured into the epithelium and through it into the conjunctival sac, damaging it during the passage (passive participation). The epithelium, which is nourished from the propria, suffers through the inflammatory damage of the latter and through the toxins of the inflammation. Epithelial cells become edematous and show vacuoles. The superficial epithelial layers often become necrotic and are desquamated. Pyknosis and karyolysis appear. The epithelium is filled with migratory cells in different densities especially with polymorphonuclears and lymphocytes.

Various pathologic changes of the epithelium are possible in chronic inflammation: (a) increase of mucus producing goblet cells; (b) proliferation of the epithelium in the form of buds into the depth; and (c) fatty degeneration and hornification. Goblet cells are increased singly and in groups. They contribute mucus to the conjunctival secretion. The epithelium invaginates or existing furrows become deeper and show mostly a lining with two rows of cylindrical cells, the epithelium growing actively into the depth in the form of solid buds and strands, which may be canalized by disintegration of the central cells. These formations can appear tubular, especially on cross section, glandular-like, mostly with an epithelium of two layers. By occlusion of these tubular formations through secretion and disintegrating cells or closure of the entrance by the epithelial cells themselves, cysts can be formed as the goblet cells con-

tinue to secrete. Their content is mucus, fibrin, serum and cell debris and sometimes it calcifies and forms concretions. The conjunctiva in the case of ectropion, in xerosis or trachoma may show transformation of the columnar epithelium into stratified squamous epithelium with hornification.

Special Forms

Special forms of conjunctivitis are not always histologically differentiated from each other. Usually the intensity of the damage gives the resulting histologic picture. They are subdivided into (1) abacterial and (2) bacterial affections.

The causes of abacterial are (a) mechanical, (b) thermic, (c) chemical, (d) electrical, and (e) rays.

Mechanical irritation causing chronic inflammatory alterations of the conjunctiva can be dust, smoke, wind, concretions of the conjunctiva, ingrowing cilia, secretion of inflamed Meibomian glands; the goblet cells are increased and the subepithelial tissue is infiltrated with lymphocytes.

Thermic dangers are mostly burns, rarely intensive cold. They are mostly caused by hot water, hot fat, but also intensive heat rays. The epithelium is necrotic and the propria shows intensive hyperemia. If the necrosis reaches deeply, it may include the sclera and the bulb may be perforated. Scars are formed, mostly secondarily after formation of granulations which organize.

Chemical irritants which damage the conjunctiva are numerous. In many cases only the clinical, but no histologic examination has been done, or only sections of conjunctiva in animal experiments are examined histologically. Chemical lesions of the conjunctiva are seen occupationally, by accidents, through drugs, poison gas, toxins, from caterpillar and plant hairs or by self infliction. The number of substances which produce occupational and industrial chemical inflammations of the conjunctiva is large. Many of them act at the same time as chemical and mechanical irritants. One of the most frequent damages is the lime burn. Acids and alkalis cause damage of various intensities. They produce more or less extensive and deep-reaching necrosis, the acids coagulate the protein and do not

enter deeply, the alkalis form rather a soluble compound with the protein and enter more deeply. Inorganic and organic compounds are found as causes. Lead, copper, quicksilver, silver, arsenic, are such inorganic compounds. Organic compounds are tar, oil, trinitrophenol, trichloracetic acid, basic aniline dyes (the acid and neutrals are indifferent), the methyl violet of the indelible pencils, and dyes used in dying the eye lashes are frequent causes. A great number of drugs which are used in the treatment of the eye itself may damage the conjunctiva, such as silver nitrate, quicksilver in various compounds (calomel, yellow mercuric oxide), zinc, bismuth, arsenic, atropine, eserine, cocaine, butyn, chrysarobin, croton oil and cantharides. Some of these substances are damaging only in hypersensitive individuals or when the conjunctiva has been treated a long time with the drug and becomes sensitized, an allergic reaction of the conjunctiva appearing suddenly. By long-lasting treatment with ointments, the conjunctival tissue can be filled with fat droplets and finally bone can be formed. Poisonous gases affecting the conjunctiva are lacrimatory gases such as chlorine, phosgen, and dichlorethylsulphid. Of the caterpillars, the hairs of which produce inflammation, there are mostly found bombyx, cnethocampa and liparida; among plants, the hairs come from hop, the hip of the hawthorne, from helichrysum or the down of the thistle. Stings, bites and juices of many insects or worms can produce conjunctivitis of different intensities. Malingerers of all kinds, prisoners, psychopaths (especially hysterical women) use different types of substances to inflict severe conjunctivitis upon themselves. Indelible pencil, lime, lye, tobacco, pepper, salt or ashes are used as offensive agents.

Lime burn of the conjunctiva is characterized histologically by: (1) superficial necrosis; (2) appearance of eosinophils, besides polymorphonuclears and lymphocytes; (3) scar tissue; (4) calcareous incrustations. One can see on the surface necrotic changes and exudate rich in fibrin. Many polymorphonuclears and many eosinophils appear which are also found in the conjunctival secretion. The deeper conjunctival layers are infiltrated and show proliferation of connective tissue. Granulations may be formed which grow through the epithelium free

tissue into the conjunctival sac and form polyps. If areas of the bulbar and tarsal conjunctiva denuded of the epithelium adhere through fibrin, they unite through organization of the fibrin and granulation (symblepharon). Lime is deposited, under certain circumstances, in the tissue of the conjunctiva in great quantities, as carbonate, phosphate or sulfate. Plaques of such calcium compounds may be surrounded by lymphocytes, many eosinophils, foreign body giant cells, newly formed vessels and much connective tissue. The resulting inflammation is called conjunctivitis petrificans which is especially seen in self infliction.

Acid burn of the conjunctiva leads to: (1) coagulation necrosis, and (2) infiltration with polymorphonuclears. The alkali burn leads to: (1) colliquation necrosis, and (2) infiltration with polymorphonuclears. In acid burns, the tissue appears fixed and hard, the nuclei disappear, but the outlines of the cells and the tissue are preserved, although in alkali burn the outlines of the tissue are indistinct.

Aniline burn causes deep necrosis besides intensive staining of the tissue. Polymorphonuclears infiltrate the tissue.

Silver nitrate produces: (1) exfoliation of the epithelium as a necrotic membrane and (2) fibrin and polymorphonuclears leaving the dilated vessels of the propria.

Atropin forms follicles in the subepithelial tissue which are well defined above and below and continue on the sides in a more or less diffuse infiltration of polymorphonuclear cells. The center of the follicles is not always distinct as germinative center. Such a center shows large clear cells and capillaries with swollen endothelium. The epithelium, which otherwise shows little change above the follicles, contains polymorphonuclears in small number.

If plant or animal hairs enter the conjunctiva, conjunctivitis nodosa appears as a result of the effect of toxin and foreign body. The hairs are embedded in foreign body tubercles which are situated subepithelially and have marginal lymphocytes, epithelioid cells toward the center, and foreign body giant cells around the hairs. They may be surrounded by a thick, fibrous capsule.

Substances producing irritation of the conjunctiva often affect more or less severely the cornea, and also the sclera and the skin

of the lids. Lesions of the epithelium and infiltration of the cornea, and also severe suppuration with formation of ulcers and intra-ocular complications may be seen.

Ophthalmia electrica is produced mostly by strong electric current or high tension electric spark, but also by ultraviolet rays which accompany the electric spark (ophthalmia photo-electrica, photophthalmia electrica). The conjunctiva shows burns with epithelial blisters and defects of the epithelium. The conjunctivitis is often only part of more extensive damage of the eye.

Rays. Visible rays and infra-red and ultraviolet rays, x-rays and radium rays can damage the conjunctiva.

The visible and the infra-red rays, if they affect the eye in great intensity, produce thermal damage. Ultraviolet rays have a different effect (abiotic or chemical) which usually appears after a latent period (photophthalmia of various causes, e.g., snowblindness or ophthalmia nivea). The rays are absorbed into the protein molecule and produce photochemical changes with degeneration of the cell. Microscopically, after a single, not too intensive, exposure to rays, there appears: (1) infiltration of the subepithelial tissue with lymphocytes, plasma cells and polymorphonuclears; (2) capillaries are dilated and surrounded by cell infiltration. In a single intensive exposure or repeated exposure there appear: (1) severe degeneration of the epithelium with karyolysis and desquamation of epithelial cells; (2) pigmentation of basal cells; (3) proliferation of epithelium into the depth; (4) deposition of hyaline into the subepithelial tissue; (5) infiltration with lymphocytes, eosinophils, plasma cells and mast cells; (6) hyaline degeneration of vessel walls.

Similar changes are produced by x-ray or radium. Degeneration of the epithelium sets in with dissolution of cell nuclei, hydropic swelling of cells and appearance of vacuoles, infiltration of the subepithelial tissue with lymphocytes, eosinophils and plasma cells and vacuolizing degeneration of the intima.

Conjunctivitis vernalis (aestival conjunctivitis, spring catarrh) is a seasonally recurrent inflammation of the conjunctiva of uncertain etiology, but it is, perhaps, produced by the action of light, especially of ultraviolet rays in persons who are constitutionally sensitive. Other theories concerning the cause of this disease have been brought forth. It is considered to be

an expression of an allergy, or perhaps a disturbance of inner secretory function. It is said to appear in persons of a lymphatic type, who show vasomotor lability, tachycardia, and hypoadrenalism (Angelucci's syndrome). However, other endogenous causes are mentioned, such as general lymphatic adenopathy and arthritis. The disease is characterized histologically: (1) by plump, large papillae, elevated above the surface and covered with columnar epithelium; (2) the connective tissue is poor in cells and shows hyperplasia which is considered the primary feature and produces the papillary hypertrophy and secondary proliferation of the epithelium; (3) the connective tissue and vessels undergo hyaline degeneration and a hyaline layer lies directly beneath the epithelium which, together with the thickening of the epithelium, probably causes the milky appearance of the conjunctiva; and (4) the infiltrating cells are plasma cells and numerous eosinophils which accumulate sometimes to form nodules, while the vessels are dilated. In areas, a stratified squamous epithelium is formed. Epithelial cells may show edematous degeneration and the epithelium is permeated by lymphocytes, eosinophils and mast cells. The epithelium sends numerous ingrowths into the depth as solid strands and as glandular tubuli with eosinophils in the lumen. Goblet cells are found in the buds, and cysts may appear. Sometimes the tissue shows fatty and calcareous degeneration. The changes at the limbus and in the plica semilunaris are similar, except that on the limbus the epithelial proliferation is stronger than the proliferation of the fibrous tissue, and high papillae and deep reaching epithelial strands appear.

Conjunctivitides Caused by Micro-organisms or Their Toxins

The number of micro-organisms which may produce slight or severe inflammation is large. The most pathogenic bacteria are epithelial parasites and are less frequently found in the secretion. They grow on living epithelium, but the saprophytes like xerosis bacillus develop on degenerated epithelium. Not all bacteria found in the secretion are responsible for the conjunctivitis present. Sometimes conjunctival inflammation is produced by toxins of bacteria which are located in a distant area of the

body (endogenous conjunctivitis). Bacteria show predilection for the place of their location, e.g., staphylococci which proliferate mostly on the lid margins and diplobacilli in the lid angle.

The bacterial causes of conjunctivitides can be subdivided according to the organism or according to the pathologic and clinical picture which is produced by a number of organisms. In many infectious conjunctivitides, the cornea participates.

Acute catarrhal (muco-purulent) conjunctivitis shows: (1) the epithelium to be permeated by polymorphonuclears and pyknosis and vacuolization of epithelial cells, (2) subepithelial accumulation of polymorphonuclears and lymphocytes, besides dilated vessels and hemorrhages; and (3) the infecting organism (Koch-Weeks' bacillus, pneumococcus, influenza bacillus) are situated in and on epithelial cells and are sometimes found also subepithelially between the polymorphonuclears. This conjunctivitis sometimes accompanies general infections such as influenza. This form can also be produced endogenously or metastasizing by a gonococcus, meningococcus or dysentery bacillus, in which case the infiltration is mostly submucous and episcleral, e.g., in endogenous gonococcal conjunctivitis (subconjunctivitis epibulbaris gonorrheica).

In exanthems, acute conjunctivitis appears, especially in measles and scarlet fever. In measles, the conjunctivitis shows histologically as desquamation of the superficial epithelial layers, pyknosis and vacuolization of the deeper epithelial layers and subepithelial infiltration with polymorphonuclears, eosinophils and lymphocytes. Frequently a mixed infection of the conjunctiva is found with streptococci, staphylococci, pneumococci and influenza bacilli.

Subacute catarrhal conjunctivitis (diplobacillary blepharoconjunctivitis, angular conjunctivitis) is characterized by: (1) proliferation of the epithelium with ingrowth into the depth and increase of goblet cells, the formation of numerous papillae being effected by an increase of cells in the mucosa and submucosa; (2) subepithelial infiltration, mostly with plasma cells with dilation of the blood and lymph vessels, and (3) eczematous alteration of the skin of the canthi which is thinned and shows

edema, formation of vesicles and parakeratosis of the epithelium, which is filled with migratory cells. The diplobacillus is found in fibrin, excreted in the angle and inside and between epithelial cells of the canthus, from which site the infection of the conjunctiva takes its origin.

Membranous conjunctivitis (conjunctivitis membranacea, conjunctivitis diphtheritica) is either a fibrinous or diphtheritic inflammation, depending on the intensity of the agent, and can be caused by various bacteria. If the virulence is mild, fibrin is exuded onto the surface of the epithelium. If the virulence is more intensive, the surface becomes necrotic and fibrin is exuded onto the surface and into the substance of the necrotic tissue.

The fibrinous form is also caused by chemical irritants as already mentioned. In the fibrinous type, fibrin covers the epithelium, containing many polymorphonuclears and desquamated epithelial cells. The epithelium is studded with polymorphonuclears, which also fill the subepithelial tissue. It appears as acute and chronic or recurrent type, sometimes with dense infiltration (ligneous conjunctivitis). Mainly, the diphtheria bacillus, but also streptococcus, pneumococcus, meningococcus, gonococcus and others are found, and sometimes the causing bacterium cannot be discovered.

In the diphtheritic form, the epithelium and sometimes the subepithelial tissue is necrotic, the connective tissue fibrils of the mucosa swell, vessels are thrombosed and Meibomian glands degenerate. Fibrin is found on the surface and in the necrotic tissue. Polymorphonuclears, in addition to the monocytes, are in the fibrin and infiltrated tissue. Granulations form beneath the necrotic tissue, which finally is eliminated, and considerable scar formation sets in, leading to symblepharon and entropion. The causative factor is the diphtheria bacillus which proliferates in the epithelial cells and produces an exotoxin.

Purulent conjunctivitis (blennorrhoea) is caused by the gonococcus and shows: (1) degeneration of the superficial epithelial cells with loss of nuclei, appearance of vacuoles and disappearance of the cell borders; the degenerated layers are desquamated; (2) edema, intensive hyperemia and hemorrhages in the subepithelial tissue; (3) appearance of numerous polymorpho-

nuclears which infiltrate the mucosa and migrate through the epithelium; (4) gonococci are found on, in and between epithelial cells and also appear later in the subepithelial tissue; and (5) in later stages, lymphocytes, plasma cells, mast cells, and some giant cells appear in the mucosa, the epithelium has mitoses and proliferates into the depth, and fibroblasts and endothelium of smaller vessels proliferate. The gonococci are phagocytosed by polymorphonuclears and epithelial cells. They appear in the secretion extra- and intracellularly with epithelial cells, polymorphonuclears, lymphocytes, plasma cells and mast cells. Occasionally, follicular formations appear in the subconjunctiva, which consist of lymphocytes and have polymorphonuclears and plasma cells peripherally. The infection occurs mostly exogenously, as in the newborn (ophthalmia neonatorum), children and adults, less frequently endogenously, either metastatic or through toxins, in which case the bacteria themselves cannot be found in the tissue of the conjunctiva.

Trachoma is a chronic conjunctivitis, probably caused by infection which affects all the tissues of the conjunctiva and also the tarsus. It is characterized by a combination of (1) epithelial changes with papillary hypertrophy, (2) subepithelial formation of follicles and (3) proliferation of connective tissue, forming scar tissue. The epithelium shows degenerative changes, exfoliation, proliferation and change of its type. The cell nucleus degenerates and the cell flattens. Cells are desquamated on the surface and the epithelium thins out. It starts to proliferate into the depth and forms papillae and long solid and tubular strands. Some consider this proliferation as active (epitheliosis Axenfeld) due to primary epithelial infection. On the other hand, more rarely the epithelium can also proliferate on the surface and form stratified squamous epithelium with hornification. In early stages, inclusion bodies are found in the flat epithelial cells. The long, solid epithelial downgrowths can be transformed through central degeneration into tubular formations and these folds and furrows of the epithelium or tubuli which proliferate from the beginning as such can be obstructed by infiltration and form cysts. Cysts can also originate as retention cysts by obliteration of the ducts through desquamated

epithelial and migratory cells, and secretion of the increased goblet cells of the downward proliferating epithelium. The epithelium contains migratory cells in different numbers. The subepithelial tissue is increased, edematous and forms papillae with dilated blood vessels and lymph vessels. The proliferation and papillary hypertrophy is considered by some to be secondary to the primary epithelial proliferation and the infiltration of the subepithelial tissue as secondary infection from the epithelium. The propria is densely infiltrated, mainly with lymphocytes lying in a small connective tissue reticulum; polymorphonuclears, eosinophils and mast cells are rare. In a later stage, plasma cells appear. The lymphocytes may aggregate to form follicles. They are spherical bodies consisting of a marginal zone of lymphocytes surrounding a clearer center consisting of epithelioid cells (germinative center). Transitory forms are seen from the epithelioid cells to the lymphocytes. The follicles contain large phagocytosing histiocytes ("trachoma corpuscles," "Koernchenzellen of Leber") which have large nuclei and numerous inclusions, such as brown pigment, erythrocytes, nuclear particles, of which some are sickle-shaped. They are cells of the connective tissue scaffold of the follicle, belong to the reticulo-endothelial system and are found occasionally in normal lymph follicles. They may, rarely, penetrate the epithelium and empty themselves, or are frequently reabsorbed. The follicles develop in the deeper layers, perhaps in lymph spaces which are filled densely with lymphocytes, and are pushed toward the surface. Also giant cells with three to ten nuclei may be present. The follicles are surrounded secondarily by blood vessels from which newly formed capillaries enter the follicle. The follicle has a fine reticulum. The submucuous layers have, besides lymphocytes, plasma cells and eosinophils "half-moon cells" (Leber), characterized by marginal sickle-shaped nuclei. Also, there are polymorphonuclears in small groups. Connective tissue elements proliferate which more and more form fibrous tissue which finally shrinks. Connective tissue also enters into the follicles and condensates around these, forming a type of capsule. The shrinking connective tissue obliterates blood vessels and causes degeneration and necrosis of the tissue with substitution by fibrous tissue.

Hyaline, amyloid, fatty and calcareous substances may appear in the fibrous tissue.

The tarsus is edematous and more or less densely infiltrated with lymphocytes and mast cells. In the tarsus, too, scar tissue is formed which by shrinkage curves the tarsus abnormally. It also undergoes hyaline and fatty degeneration. Glandular ducts can be obliterated by dense infiltration and connective tissue and dilate to become cystic.

The bulbar conjunctiva and episclera also show infiltration with lymphocytes and plasma cells and sometimes have follicles. The inflammation, which may even start primarily in the bulbar conjunctiva, extends into the cornea, taking the shape of the trachomatous pannus. The epithelium of the pannus shows nuclear degeneration and later proliferation or formation of papillae. Beneath Bowman's membrane, which finally is destroyed, is cellular infiltration. The pannus shows lymphocytes, polymorphonuclears and numerous plasma cells, fibroblasts proliferate, capillaries grow in and follicles appear.

The tear gland shows infiltration and later scar formation, with obliteration of ducts. The tear sac may be inflamed and have follicles.

Trachoma is endemic in many countries. It is considered a contagious disease. Numerous bacteria have been accused as etiologic factors, different diplococci, bacilli and fungi. But it is very probable that trachoma belongs in the group of the virus infections. Frequently, inclusion bodies are found in the epithelium of the conjunctiva of trachoma victims, especially in fresh cases. These intracellular inclusion bodies are called "trachoma bodies" or "chlamydozoa"; but other inclusion bodies are found, too, which belong in the group of the Rickettsia bodies.

Follicular conjunctivitis is produced by bacteria and virus, but also dusty air, different chemicals, drugs such as atropine and eserine. Follicles appear in the conjunctiva and inflammatory changes are more or less marked. The course is acute or chronic, the latter apparently more frequent. The appearance of follicles is sometimes an expression of a lymphatic constitution and is seen more frequently in children than in adults. In chil-

dren, the formation of discrete follicles in the lower fornix without other inflammatory changes is a constitutional disorder (conjunctival folliculosis; follicular catarrh). Malnutrition, local irritation, hypertrophy of the adenoid tissue in general are mentioned as predisposing factors. Characteristic features are: (1) the epithelium is normal or shows only minor changes such as thickening and more numerous goblet cells and formation of flat papillae; (2) follicles are formed, which consist nearly exclusively of lymphocytes and few plasma cells and which show little if any indistinct germinative center; (3) there is little or no infiltration between the follicles; and (4) the submucous layers are free of infiltration. The follicles are finally reabsorbed and no scar tissue is formed.

A special form is the acute, mostly infectious, follicular conjunctivitis of Béal, which can appear epidemically. It shows, histologically, formation of papillae and downgrowth of the epithelium in the form of glandular-like strands. Follicular-like formations are found subepithelially and infiltration with lymphocytes, few polymorphonuclears and monocytes are seen. It is perhaps a virus infection.

The *epidemic keratoconjunctivitis* which also is considered to be a virus infection shows follicles and swollen preauricular lymph nodes. The epithelium is flattened or shows papillary hypertrophy and the edematous subepithelial tissue is infiltrated with lymphocytes and monocytes.

Inclusion conjunctivitis comprises inclusion blennorrhea of the newborn, swimming bath conjunctivitis and epitheliosis desquamativa conjunctivae. Intracellular inclusion bodies are found in the epithelial cells which represent either the virus itself or are connected intimately with it. The pathologic findings in all of them are very similar. In blennorrhea of the newborn and in similar nontrachomatous inclusion blennorrhea of the adult, and in swimming bath conjunctivitis, the epithelium is missing in large areas on the surface and proliferates into the depth in the form of epithelial rods; subepithelially, the tissue is diffusely infiltrated to a greater degree with plasma cells and lymphocytes and to a lesser degree with lymphoblasts and polymorphonuclears, while endothelial cells and histiocytes prolif-

erate. In epitheliosis desquamativa conjunctivae, the epithelium is atrophied and subepithelially there are found many plasma cells and some mast cells, also hemorrhages due to diapedesis from dilated vessels and follicles similar to those in trachoma.

Other rare virus infections of the conjunctiva are found in variola and vaccinia. Ulcers may form which are surrounded by degenerated epithelium and the subepithelial tissue is filled with phagocytes.

Chronic Specific Inflammations

Leprosy of the conjunctiva is histologically characterized by typical leproma which contains round cell infiltration, fibroblasts, many new-formed vessels and large vacuolated lepra cells in which the acid-fast lepra bacillus is found.

Tuberculosis of the conjunctiva is manifest in various pathologic types: (1) The typical miliary tubercle in the mucosa and submucosa shows central caseation, contains numerous bacilli and is surrounded by cellular granulation tissue and follicles (nodular type). (2) The conjunctival tuberculoma consists of epithelioid and giant cell tubercles with little caseation, few bacilli and has few lymphocytes in the surrounding tissue. The epithelium remains intact. (3) Small celled granulation tissue proliferates, containing also large polygonal cells (hypertrophic papillary type). (4) Ulcerations are formed by destruction of tubercles containing tubercle bacilli (ulcerative type). (5) A papilloma-shaped tumor is found; it is pedunculated and shows histologically dense connective tissue with lymphocytic infiltration and occasional giant cells (polypoid type). (6) Lupus of the conjunctiva shows nodules and superficial ulceration with scanty caseation. It spreads flatly and inclines to formation of scars. The infection of the conjunctiva may be primary of exogenous origin, in which case it spreads the infection through the regional lymph nodes. However, the infection may be exogenous and secondary if pulmonary tuberculosis is present and the patient infects himself with his own contaminated fingers. But usually the infection is endogenous, as the tuberculosis is transmitted either by the blood circulation or from surrounding tissues, as in lupus from the skin of the face or

from the bulb or from the orbit by direct extension onto the conjunctiva.

Tuberculides of the conjunctiva are fleeting nodules which consist of epithelioid and giant cells and show the structure of the miliary tubercle, as in the lichen scrofulosorum. They contain bacilli only infrequently. They are considered the expression of allergic sensitization in the presence of the tubercle bacillus in the body.

Phlyctenular keratoconjunctivitis (scrofulous, eczematous, lymphatic conjunctivitis) is also an allergic response to endogenous toxins or some protein. In the majority of cases, sensitization to tuberculoprotein produces the reaction. Nutritional defects and unsanitary environment may hasten the beginning of the disease. The conjunctival phlyctenule appears as a spherical subepithelial accumulation of lymphocytes which penetrate the epithelium. They are mixed with polymorphonuclears and in the center some epithelioid-like cells are found. Also, giant cells may be present. The blood vessels of the surrounding tissue are dilated and show proliferation of the endothelium. Bacilli cannot be found. The phlyctenule sometimes exulcerates and edema and thrombosis of the surroundings result.

Multiple sarcoid of Boeck is rare as conjunctival lesion, mostly accompanied by iritis and histologically shows confluent nodules consisting of lymphocytes and epithelioid cells without necrosis. Bacilli cannot be found. However, as the disease is often seen in tuberculous individuals, it may perhaps have some relation to tuberculosis.

Parinaud's conjunctivitis (Parinaud's oculo-glandular syndrome) is a syndrome which may be produced by different infectious agents, among which tuberculosis has been considered. The conjunctiva shows follicles, hypertrophy and ulceration; the regional lymph nodes and parotid gland are swollen. Histologically, tubercle-like formations with epithelioid and giant cells are found. Sometimes numerous plasma cells are present. Often parts of the tissue are necrotic. Rarely tubercle bacilli can be found and sometimes animal experiments are positive for tuberculosis. In some cases, pseudotubercle bacilli have been seen.

The syndrome can appear also in syphilis and tularemia; in addition, leptothrix and sporotrichosis may produce it and the necrotic infectious conjunctivitis also belongs clinically in this group.

Syphilis of the conjunctiva is seen as a primary chancre, secondary syphilis and tertiary gumma. The primary chancre, which may be transmitted by infection through a soiled handkerchief, infected tongue, by contact with the nasal secretion of a syphilitic child or during surgery shows histologically: (1) dense infiltration with plasma cells besides lymphocytes and monocytes; (2) new formation of blood vessels, many of them ensheathed with lymphocytes and with proliferation of the endothelium in four to five layers; and (3) proliferation of the connective tissue with formation of many young connective tissue cells. Preauricular and submaxillary lymph nodes are swollen on the side of the infection. The secondary stage is clinically manifold and shows also histologic variations, but in all forms there is an infiltration with plasma cells and lymphocytes. The lymph vessels are ensheathed with round cells and especially the arteries show end-arteritic processes with endothelial proliferation. In the secondary stage are found: (1) the diffuse conjunctivitis which shows characteristically a severe edema and hydropic degeneration of connective tissue cells and endothelial proliferation in lymph vessels; (2) syphilitic sclerokeratoconjunctivitis, which shows many new vessels with end-arteritic changes and connective tissue proliferation besides massive round cell infiltration; (3) conjunctivitis granulosa syphilitica (granular syphilitic conjunctivitis, conjunctivitis papulosa) which shows formation of numerous hypertrophic papillae and infiltration with lymphocytes; large cells with pale oval nuclei, plasma cells and giant cells of Langhans type, mantles of lymphocytes and plasma cells around many new-formed blood vessels; (4) syphilitic papules which consist of infiltration with plasma cells and lymphocytes around dilated vessels. Gumma, which is also seen in congenital syphilis, is rare. It consists of: (1) a large central necrotic area with chromatin in finest granules and diffusely dissolved; (2) the zone of necrosis is

surrounded by proliferation of connective tissue; and (3) outside of it are plasma cells, lymphocytes and occasionally giant cells.

Tularemia (conjunctivitis tularensis) is caused by the bacterium tularense, which is transmitted to man by an insect bite or from infected rodents. It produces either an ulceroglandular type or typhoid type. The first type, in which a necrosing ulcer on the side of the entrance of the infection and regional lymphadenitis appears, contains the ocular-glandular form in which the ulcer appears on the eye. Histologically, a granuloma is present consisting of lymphocytes, plasma cells, epithelioid cells, surrounded by a dense infiltration of plasma cells, epithelioid, mast cells and vessels with endothelial proliferation. The thickened epithelium is filled with polymorphonuclears. The bacterium can be found in the tissue.

Conjunctivitis necroticans infectiosa (Pascheff) (necrotic infectious conjunctivitis) is characterized by a small nodular subepithelial infiltration. It consists: (1) of dense accumulation of polymorphonuclears; (2) central necrosis; (3) peripheral zone of lymphocytes; and (4) proliferation of granulation tissue. The covering epithelium is perforated and an ulcer is formed. It is caused by a gram-negative, nonmotile bacterium called microbacillus polymorphicus necroticans.

In *leptothricosis conjunctivae* (Verhoeff), histologically there is found: (1) necrotic areas beneath the epithelium; (2) large number of macrophages which contain nuclear fragments and leptotriches in clumps; (3) dilated lymph vessels with proliferating endothelium; (4) granulation tissue beneath necrotic areas forming nodules; and (5) edema, dilated blood vessels and plasma cell infiltration. The mode of the infection is unknown. The infecting organism, leptothrix, can be found in sections by Verhoeff's modified Gram staining and in cultures. The clinical picture is that of Parinaud's ocular-glandular syndrome.

There is some discussion as to whether this genus exists altogether. It shows great variations and grows sometimes in coils and spirals and mostly in bacillary form. It is grouped among the bacteria, also among the pathogenic fungi.

3. Mycoses of the Conjunctiva

Mycoses of the conjunctiva are rare and are caused by higher fungi.

Streptothricosis of the conjunctiva is histologically easily recognizable if heaps of streptothrix are seen in the form of mycelial threads. The streptothrix belongs to that group of actinomyces which causes actinomycosis. The mycelial threads are surrounded by polymorphonuclears and further away there is granulomatous tissue consisting of lymphocytes, epithelioids, fibroblasts, and giant cells. The filaments of the anaerobic growing streptothrix are gram-positive.

Rhinosporidiosis conjunctivae shows a very characteristic histologic picture, as the tissues contain many large parasitic cysts which contain numerous nuclei forming spores. The tissue is fibro-cellular, filled with lymphocytes and giant cells. The epithelium proliferates into the depth. This fungus (rhinosporidium Seberi) which is closely related to coccidioides forms polypous formations in the mucosa, most frequently in the nose, rarely in the conjunctiva. The single organism grows by mitosis to a large cyst (sporangium) which has a double contoured chitinous membrane and finally contains thousands of spores, which are discharged through a germinal pore in the membrane.

Blastomycosis of the conjunctiva forms a chronic granuloma which consists of large monocytes, few lymphocytes, and giant cells. The yeastlike organism, blastomyces, is inside the monocytes and giant cells and is characterized (1) by a clear double contour and (2) by budding. The organism can easily be found in the discharge by adding a few drops of sodium hydroxide.

Sporotrichosis conjunctivae forms a granuloma consisting of lymphocytes and histiocytes, which inclines to pus formation. The yeastlike organism, sporotricum, can be seen in the histologic section.

Trichophyton causes a dense infiltration with plasma cells and can be found in the epithelial cells in the secretion. It belongs to the group of the tinea (ringworm) and shows many types which usually grow around and on hairs.

4. Parasites of the Conjunctiva

Leishmania tropica, a parasite which belongs in the group of the unicellular protozoa, can infect the skin of the face and from here, secondarily, the conjunctiva. It produces an infiltration consisting of lymphocytes, plasma cells, large monocytes and between these large cells there may be present some which contain many parasites. The epithelium proliferates, forms papillae and invades into the depth. Necrosis may result.

Filariae (thread worms) belong to the group of the nematodes (round worms). They appear in and beneath the conjunctiva where they are frequently seen moving. There are many kinds of filariae and many are removed from the conjunctiva without histologic examination of the enclosing tissue. The same can be said of the group of the flat worms, which invade the conjunctiva. Filariae are in lymph vessels and eventually in pterygia, which consist of hyaline tissue. They may also contain cysts filled with fat.

Filaria oculi (filaria loa, microfilaria diurna) scarcely makes any inflammatory changes in the conjunctiva.

Other parasites of this group found in the conjunctiva are: filaria inermis (filaria palpebralis or conjunctivae), filaria lacrimalis (filaria circumocularis) and filaria medinensis (dracunculus medinensis, Guinea worm).

In *habronemic conjunctivitis,* the conjunctiva is densely infiltrated with endothelial and migratory cells which contain yellowish pigmentation. Small circumscribed granulomata contain the thread worm habronema.

The *schistosoma haemotobium* (Bilaharzia haemotobia) belongs to the group of the flukes, which are flat worms, and forms in the conjunctiva granulomata consisting of lymphocytes, plasma cells, eosinophils and giant cells which surround the ova of the parasite.

Cysticercus cellulosae is the larva of Taenia solium which belongs to the group of the cestodes (tape worms), which are also flat worms. The parasite consists of the head (scolex) and a highly tortuous body canal; it lies in a toxic fluid surrounded

by a connective tissue capsule which contains lymphocytes, eosinophils and giant cells.

Ocular myiasis exists if larvae (maggots) of certain flies invade the conjunctival sac and lie on the mucosa, sometimes producing an inflammation there or forming spaces lined by endothelium and connective tissue. Sometimes they penetrate deeper and can appear intra-ocularly. The larvae belong to the group of the muscidae, oestridae, sarcophidae and anthomyidae.

5. Conjunctivitides Associated with Skin Diseases

In some of these, infection is present, but as a rule the etiology is obscure. Clinical observations are made in many cases, but not histologic examinations in all of them.

Acne rosacea produces follicular accumulations of lymphocytes with monocytes in the center, mostly in the bulbar conjunctiva. The etiology of this disease is unknown but intestinal disorders, exposure to weather, and riboflavin deficiency have been accused as the cause.

Pemphigus is characterized by vesicular detachment of the epithelium, edema of the epithelium with intra-epithelial vesicles. The epithelium and vesicles are filled with migratory cells. The epithelial cells degenerate and are desquamated, papillae are formed and the epithelium can also proliferate atypically into the depth. Fibrin and serum are secreted between epithelium and substantia propria. Mucosa and submucosa are densely infiltrated, the infiltration being diffuse and nodular. Lymphocytes, plasma cells, eosinophils and histiocytes are found. Blood vessels as well as lymph vessels are numerous and dilated. Characteristic is the proliferation of vascular connective tissue which grows around and through the nodules. In later stages, vessels disappear, the connective tissue shrinks and the conjunctival sac is narrowed (essential shrinkage of conjunctiva). The chronic form is more frequent; the acute form rare. The disease affects skin and mucosa of different organs. The etiology is unknown. Staphylococci and pneumococci have been found in the vesicles, but they seem to be secondary infections. It is assumed that pemphigus results from toxins or is a neurotrophic disease.

Erythema exudativum multiforme affects the skin and mucous membranes. There is a serous and fibrinous exudation on the surface and into the tissue of the mucosa and hyaline is formed. Vessels are congested and hemorrhages appear through diapedesis. The epithelium may necrotize and form, with the fibrin, a pseudomembrane. The disease is probably caused by an infection of unknown etiology or is the result of toxin.

In *epidermolysis bullosa,* serous fluid is accumulated between the epithelium and the substantia propria. The disintegrating epithelium represents many degenerative changes. The propria shows a loss of elastic fibers and scattered infiltration with lymphocytes and monocytes. In this congenital disease, vesicles in the skin are caused by slight trauma.

In *hydroa vacciniformis,* the epithelium proliferates in the form of buds into the depth through the infiltrated tissue and forms cysts lined by epithelium of several layers. It is a skin disease due to light sensitization, with papule formation on the places of the skin which are exposed to light. The sensitizing substance seems to be hematoporphyrin, which is excreted in urine.

Acanthosis nigricans is characterized by pigment granules appearing near the nuclei of the epithelial cells. The epithelium is thickened, proliferates and shows papillary hypertrophy. There is a subepithelial infiltration of lymphocytes, plasma cells, eosinophils and oval pigmented cells. Pigmented warts appear in this disease of unknown etiology.

6. Degenerations of the Conjunctiva

In *pinguecula,* the important findings are: (1) swelling of elastic fibers which increase in length and thickness, are transformed to wavy, knotty strands, split brushlike and undergo granular disintegration; (2) an increase of collagenous connective tissue fibers of the conjunctiva and episclera which undergo hyaline degeneration; (3) deposition of free hyaline in the form of homogeneous clumps in the tissue; (4) formation of concretions; and (5) the epithelium is irregular, partly thickened, partly thinned, and has goblet and cylindrical cells in the superficial layers.

In *xerosis of the conjunctiva,* the epithelium of the conjunctiva becomes epidermis-like. It is thicker and shows the structure of stratified squamous epithelium with typical hornification. The epithelial cells contain fatty globules and degenerative changes appear as pyknosis and formation of vacuoles. Especially, Bitot's spots show vesicular formation and irregular epithelium. Hornified lamellae desquamate on the epithelium surface, containing numerous xerosis bacilli, which are also found in the deeper

FIG. 53.—PINGUECULA. e, conjunctival epithelium; es, episclera; f, degenerating fibers; p, pinguecula; s, sclera. 55×.

layers intra- and extracellularly. Depending on the etiology, conjunctival glands and medullated nerve fibers degenerate. Xerosis is the expression either of a local severe degenerative process of the conjunctiva or of a general nutritional disturbance. In the first case, the condition is called xerosis parenchymatosa, and follows trachoma, pemphigus, diphtheria, burns resulting usually in extensive conjunctival scars. In the latter case, the condition is called xerosis epithelialis, a vitamin A deficiency is present and general nutritional disturbance caused by preceding severe diseases as dysentery, cholera, typhus, malaria, or general malnutrition and starvation. The disorder apparently affects the nerves first and secondarily the epithelium as a neurotrophic disturbance.

In *hornification of the conjunctiva* (tyloma), the epithelium is circumscribed enormously, thickened and elevated as an epithelial plaque. The surface is hornified, flat papillae are formed, the subepithelial tissue shows hyaline and amyloid degeneration of the connective tissue, granular disintegration of elastic fibers and concretions. The etiology is unknown. Although in xerosis the entire conjunctiva is affected, in tyloma the process of metaplasia and hornification of the epithelium is circumscribed. In some cases, tyloma appears similar to the tumor formation of a papilloma. Epithelial plaques also appear congenital and are considered to be rudimentary dermoids.

The origin of *hyaline and amyloid degeneration of the conjunctiva* is uncertain. Disintegration of cells is considered responsible for their appearance. However, connective tissue fibers may become hyaline or amyloid or coagulating masses are secreted into the spaces of the connective tissue. Amyloid is said to originate from blood cells also. Hyaline and amyloid degeneration are rarely part of a generalized disease, being mostly a local condition. In some cases of amyloidosis, one eye alone is affected.

Conjunctiva of the lid, of the bulb and the semilunar fold may be affected. There are cases in which only amyloid or only hyaline substance is found; others, in which both are present at the same time. There are cases in which biopsy reveals at first only hyaline and later only amyloid substance. Local diseases often precede, e.g., chiefly trachoma or vernal catarrh, or the degeneration affects formerly unchanged tissue. There is either a meshwork of homogeneous strands or large homogeneous masses present in the conjunctiva. The stratified squamous epithelium is for the most part thin, and the epithelial cells contain vacuoles. Dense infiltration of lymphocytes, plasma cells, polymorphonuclears and mast cells are between the homogeneous masses. Plasma cell mantles may accompany the blood vessels. Homogeneous particles are often surrounded by giant cells. Also, blood vessels show hyaline degeneration and the lumen may be obliterated. However, vessels are also compressed from the outside by hyaline and amyloid masses and only a little elastic tissue and endothelium remain or the lumen disappears

entirely. Vessels of the surrounding tissue in this region may undergo a compensatory dilatation. Blood extravasations may appear. Muscles and glands may participate in the degeneration. Sometimes specific staining gives positive results, but often the staining is indistinct. Hyaline and amyloid now and then calcify, or cartilage and bone is deposited.

Plasmoma of the conjunctiva (plasmocytoma) represents tumor-like circumscribed dense accumulation of plasma cells with few lymphocytes and mast cells. Plasma cells also accompany the blood vessels in mantles. Hyaline and amyloid degeneration is frequently found. Hyaline is seen also in the form of Russell bodies. Plasmoma is considered either as a benign tumor or chronic inflammation of an unknown etiology. Sometimes trachoma precedes the plasmoma. In some cases, it is uncertain whether the plasma cell infiltration is primary and hyaline and amyloid degeneration is secondary.

7. Concretions and Pigmentations of the Conjunctiva

These are found in tubuli with two layers of flat epithelial cells, surrounded by a lymphocytic infiltration. Their lumen contains the concretions consisting of homogeneous or laminated masses of hyaline, mucus, degenerated epithelial cells and migratory cells. The concretions enlarge by apposition. They are usually preceded by chronic inflammatory changes of the conjunctiva.

In the majority of cases of abnormal pigmentation of the conjunctiva clinical examinations only have been made, while histologic examinations have rarely been performed.

Depositions of hematogenous pigment can be found after hemorrhages in the conjunctiva, especially after injuries. Uveal chromatophors can appear in the conjunctiva in the presence of perforating injuries, or when they proliferate along the perforating vessels.

Deposits of melanin in the deeper epithelial cells are found histologically in cases of keratomalacia, and in vitiligo with infiltration of the conjunctiva with lymphocytes and plasma cells.

Pigmentation by foreign substances most frequently occurs in silver deposits (argyrosis), which can produce a generalized

argyrosis after prolonged internal medication and a local argyrosis in prolonged local medication of the conjunctiva. Silver is deposited free in the conjunctiva apparently as silver albuminate in granules, beneath the epithelium and in deeper layers. The granules have a special affinity for elastic fibers, but they also lie free between connective tissue fibers and cells and are deposited in the cement substance between the muscle fibers and endothelial cells of the vessels.

8. Cysts of the Conjunctiva

Cysts of the conjunctiva are manifold and are: (1) epithelial cysts, (2) traumatic cysts, (3) lymph cysts, (4) parasitic cysts, and (5) congenital cysts.

Epithelial cysts are seen as (a) retention cysts, (b) cysts formed by conjunctival folds, and (c) cysts formed in epithelial buds.

The retention cysts have an epithelium of two layers which partly is atrophic, partly hypertrophic; they contain mucus and serum and cell debris. They are formed mostly in the Krause glands in the fornix. Their origin is initiated by closure of the duct through scars, especially in trachoma, by a dense infiltration with swelling of the surrounding tissue, or by incomplete canalization during development.

Cysts are also formed as the severely inflamed conjunctiva is lifted in folds and such folds unite by apposition. The enclosed epithelium continues to secrete mucous and serous fluid.

Cysts also form from solid epithelial buds which proliferate into the depth, especially in severe conjunctivitis. Through mucoid degeneration and central disintegration of cells lumina are formed which are lined by stratified squamous or columnar epithelium and enlarge to form cystic spaces.

Traumatic cysts appear through displacement of superficial epithelium through injury or operation, most often being implantation cysts. Sometimes a foreign body, such as a piece of wood or cotton, or cilia enter the conjunctiva and carry epithelium with it. The epithelium displaced into the depth continues to grow and degenerates centrally, forming the cyst.

Lymphatic cysts appear as spaces lined by endothelium in the mucosa, the covering epithelium of which is usually thin.

Parasitic cysts are mostly cysticercus vesicles or are formed more rarely around filaria larvae and are really pseudocysts, as they represent spaces filled with fluid but have no epithelial or endothelial lining.

Congenital cysts are cysts of the lower fornix associated with microphthalmos.

9. Neoplasms of the Conjunctiva

Neoplasms of the conjunctiva are (1) mesoblastic, (2) epithelial, and (3) congenital.

The mesodermal tumors are very manifold, especially the benign ones. The benign are granuloma, fibroma, lipoma, angioma, and lymphoma. The malignant are sarcoma and endothelioma.

A *granuloma* is in reality an inflammatory hyperplasia and consists of young connective tissue with many lymphocytes and new-formed vessels. In addition, few polymorphonuclears and monocytes are found. Most of the surface is denuded of epithelium. It is caused by injuries, forms around foreign bodies, appears after surgery (enucleation, squint operation) or is formed from an outgrowing chalazion. Often the cause is unknown.

A *fibroma* consists of fibroblasts and fibrillar connective tissue. It is distinguished as a soft or a hard fibroma, depending on whether there are more cells and less fibers or more fibrous tissue and less cells present. Hyaline degeneration can set in. A neurofibroma is rare and appears on the lids and bulbar conjunctiva. It can grow along the course of the nerves as part of von Recklinghausen's disease. If a fibroma contains edematous myxomatous tissue, it is a myxofibroma or myxoma.

A true *lipoma,* consisting of young, unripe fat cells, is rare and frequently is merely a part of a congenital tumor (dermolipoma).

The *angioma* is frequently an angiofibroma and is therefore a fibroma which contains many blood vessels. Vascular tumors in which the blood vessels alone form the tumor are hemangioma,

as far as it originates from blood vessels, and lymphangioma, as far as it originates from lymph vessels. The hemangiomata are the capillary angioma (angioma simplex) and cavernous angioma, representing new growth and proliferation of blood vessels and their tissue elements, and related to them are the dilatations and tortuosities of the otherwise unchanged blood vessels of the plexiform angioma and venous aneurism. The lymphangiomata are dilatations of lymph vessels (lymphangiectases) and new formations of lymph vessels which usually appear cavernous.

The *hemangioma* is a congenital new growth. The cavernous hemangioma consists of spaces lined by endothelium with thin walls. Its walls are incomplete and the lumina communicate with each other. Thrombi may be present, along with hyaline masses as well as calcification (phlebolith). The capillary angioma consists of an accumulation of capillaries with a paucity of tissue in between and closed endothelial tracts. A plexiform angioma (cirsoid aneurism) consists of tortuous, partly dilated vessels of a normal structure (teleangiectases). A venous aneurism is composed of very dilated venous vessels.

A *lymphomatous tumor* is either true neoplasm or part of a constitutional disease. Sometimes it is the expression of a local, inflammatory or degenerative disease. There are lymphomata, leukemic and pseudoleukemic tumors, tumors in lymphogranulomatosis and plasmomata.

The *lymphoma* (lymphoblastoma) appears as true neoplasm and consists of a dense accumulation of lymphocytes beneath the epithelium, with scarce connective tissue and vessels, and the covering epithelium is thinned.

A lymphomatous infiltration appears as part of a lymphatic leukemia, together with multiple nodules on other places in the body and hyperplasia of the lymph nodes; it is also seen in cases of pseudoleukemia and lymphogranulomatosis (Hodgkins). The primary location is frequently in the orbit and the lymphomatous infiltration extends into the conjunctiva.

The *plasmoma* is considered by some as a tumor formation, as frequently a tumor-like circumscribed accumulation of plasma cells exists with some sort of capsule; however, it belongs, in

the opinion of others, among inflammatory and degenerative changes as it is seen frequently together with amyloidosis of the conjunctiva.

Sarcoma consists of a mixture of spindle-shaped, round and polygonal cells of various sizes with relatively large nuclei, which are oval or round and show hyperchromatic staining. Also, multinucleated cells are present. Mitoses may be seen. The stroma between the cells is usually scarce. The spindle cells especially show arrangement in whirls and spirals; otherwise the cells are irregularly arranged. If more connective tissue is present, then the cells may be grouped and an alveolar arrangement appears in which the cells are imbedded in the spaces between the connective tissue septa (alveolar sarcoma). Sarcomata are mostly pigmented (melanosarcoma), but can also be pigment-free (leukosarcoma). The pigment is melanin, rarely blood pigment, and may be intracellular in the tumor cells and in the cells of the connective tissue; it may also be extracellular. A sarcoma of the limbus penetrates between the epithelium and Bowman's membrane and eventually destroys Bowman's membrane and the superficial lamellae. Sarcomata most frequently originate primarily from pigmentations of the limbus, more rarely from other places such as the plica semilunaris, caruncle, tarsal conjunctiva and fornix. It may appear secondarily from a uveal sarcoma after penetration of the sclera but rarely penetrates from conjunctiva into the interior of the eye. Trauma or severe inflammation are occasionally the causes of its growing. A sarcoma recurs frequently, and soon after surgical removal. Sarcomata can appear multiple also.

Malignant melanoma consists histologically mostly of spindle-shaped cells with and without pigment in an alveolar arrangement. Also, pigment-free tumors frequently contain potential melanoblasts, which can be made visible by special reaction ("Dopa"). On the other hand, histologic variations are possible in which the cells may appear either more of an epithelial or endothelial type. The origin is mostly a pigmented area of the limbus which consists of pigmented stroma or typical pigmented nevus cells. As nevus, as already mentioned, is considered by some as epithelial, by others as neuro-ectodermal, by still

others as mesodermal, the malignant neoplasms originating from pigmented areas are named differently according to the different theories and the formal histogenesis; e.g., melanocarcinoma, epithelioma, endothelioma or nevo-carcinoma. However, many prefer the indifferent name, malignant melanoma.

Some mesodermal tumors show transitional forms from the benign ones to the malignant, such as fibrosarcoma, angiosarcoma or lymphosarcoma.

Fibrosarcoma starts as fibroma: the soft cellular type can undergo malignant degeneration and the cells show hyperchromasy and polymorphism and infiltrate the surrounding tissue.

Lymphosarcoma is histologically a lymphoma in which, besides the numerous lymphocytes, larger round cells appear. The nuclei are irregular and the reticulum cells proliferate. The cells perforate an existing capsule and infiltrate the surrounding tissue.

Angiosarcoma is a capillary angioma with strands of endothelial cells which assume sarcomatous character and replace surrounding tissue.

Endothelioma and *perithelioma* are related. The endothelioma consists of clear cells with oval or round, small nuclei which lie close together without any fibrillar intermediary substance, have an alveolar arrangement and grow in cords and cylinders which sometimes have a lumen. The perithelioma shows cells arranged in whirls around blood vessels.

Epithelial tumors are papilloma and adenoma as benign, and carcinoma as malignant forms.

In a *papilloma*, the papillae are increased in size and numbers. Papillary hypertrophy is present when the papillae are higher and wider, and the stratified squamous epithelium, containing goblet cells and showing hornification, is widened with an even surface. These are the primary papillae which are enlarged. In this case, the tumor is sessile and flat. However, if the epithelium grows outward and the newly formed tissue is elevated, folded leaflike or treelike branch formations appear, which are called secondary papillae. In this case, the tumor is usually pedunculated and lobulated. The connective tissue in papillary hyper-

trophy is often reduced and contains thin-walled vessels and in a lobulated papilloma it is often enlarged and forms a central core of connective tissue with blood vessels from which the secondary papillae branch off. Some consider this form of the papilloma as connective tissue tumor, in which the connective tissue proliferates primarily and the epithelium secondarily. A papilloma may appear in the bulbar conjunctiva and in the conjunctiva of the lids and is frequently also situated in the limbus, but has no tendency to infiltrate the cornea.

Adenoma appears manifold in its histologic structure depending on the glandular type from which it originates. Adenomata originating from the serous Krause's glands, or the sweat glands of the caruncle, consist of tubules lined by cylindrical epithelium of one layer. The tubules are sometimes cystically dilated (cystic adenoma) and may show also papillomatous proliferation of the epithelium into the lumen. Between the glandular elements is fibrous tissue. There is sometimes lymphocytic infiltration of various densities. Sometimes only a fine strand of fibrous tissue is present which has cylindrical cells on both sides, lining the lumen filled with secretion and debris. If sebaceous glands hypertrophy and new ones are formed, a sebaceous adenoma appears in which the typical structure of the sebaceous glands is saved.

Carcinoma appears mostly as squamous cell carcinoma and is easily recognizable as such. It consists of a proliferation of prickle cells in groups and columns which have hyperchromatic nuclei and show differences in shape and size. They show hornification and formation of epithelial pearls. In between, there are often single, smaller and larger anaplastic epithelial cells in the tissue. Epithelial strands growing into the depth are surrounded by round cell infiltration. Basal cell carcinoma is less common. In this case, more uniform appearing strands proliferate into the depth, consisting of cylindrical and spindle-shaped cells. Conjunctival carcinoma may be a continuation of carcinoma of the lid or caruncle or is situated most frequently at the limbus where it grows sometimes ring-shaped around the cornea. It may originate from a pterygium or limbus papilloma. Carcinoma cells infiltrate and replace the surrounding tissue,

the tarsus, episclera, Tenon's capsule and the epithelium of the cornea. Bowman's membrane resists its expansion, but as soon as it is perforated the propria is destroyed. They grow along the perivascular spaces and along the nerves into the intrinsic eye, into Schlemm's canal, into the corneo-scleral meshwork and may grow into the suprachoroid, choroid, chamber angle, iris and ciliary body. They may also form intra-ocular metastatic foci. Metastases in lymph nodes can appear, but are rare in distant portions of the body.

Congenital tumors are dermoid, lipodermoid (subconjunctival lipoma), teratoma, osteoma and nevus.

The *dermoid* consists of hornifying squamous epithelium with the formation of papillae covering coarse connective tissue plates mixed with elastic tissue, in which hair follicles, sebaceous glands, sweat glands and fat tissue are embedded. Acinous glands of the type of the tear gland, smooth muscle fibers and nerves rarely appear. This would show a transition to teratoma. If invaginated epithelium is separated from the surface epithelium, or the glandular ducts dilate, dermoid cysts are formed. The dermoid is situated chiefly at the limbus but is seen also in other places in the conjunctiva and especially in the caruncle. It is assumed from an etiologic standpoint that the lids do not unite during the fetal development and that the surface of the bulb remains exposed with a transformation of the exposed area in skin-like tissue or that the dermoid is present as remnant of an amniotic band.

In the *lipodermoid,* the fat tissue is prominent, but there are also strands of fibrous tissue with hair follicles and sebaceous glands, acinous glands, muscle fibers and stratified epithelium with degeneration of the surface. Sometimes large fat masses are present in the subconjunctival tissue (subconjunctival lipoma). These tumors are multiple on the eye. They are frequently between the superior and external recti muscles, like the teratoma and osteoma.

The *teratoma* consists of elements of the ectoderm and mesoderm. Besides hair follicles, sebaceous glands and sweat glands, there are also acinous glands of the tear gland type present, fat tissue, smooth and striated muscle fibers, cartilage and bone.

The *osteoma* shows periosteum with a layer of osteoblasts and consists of pieces of cancellous bone with small Haversian canals and concentrically arranged bone lamellae. It contains fibrous tissue and blood marrow.

The *nevus* consists of groups of nevus cells. They are arranged in round or oval nests, wide bands or small, long cell tracts and between them there is fibrillar connective tissue with blood vessels. The nevus cell has little cytoplasm, a large nucleus, is round or polygonal and is pigment free or contains pigment in brown granules. There is no intercellular tissue between the closely packed cells. Pigment is also found in epithelial cells, free in the tissue and in connective tissue cells. Nevus cells as well as also epithelial cells may give "Dopa" reaction. Between nevus cell nests and the epithelium there is an interspace, or nevus cells are present in the epithelium and the epithelium continues into the depth, into the accumulation of nevus cells. Nevus cells may disappear through mucoid degeneration and lumina may appear in the nevus (nevus cysticus), lined by nevus cells. Nevi show pigmentation of various degrees and are sometimes entirely nonpigmented. Nevi are found mainly in the limbus, but also in other areas of the connective tissue, in the plica and in the caruncle. As already mentioned, the nevus cell has been recently shown to originate from the terminal neuro-apparatus and is considered as neuro-ectodermal (Masson). Nevi frequently undergo malignant degeneration. In melanosis conjunctivae, flat pigmentation without circumscribed tumor formation and appearance of nevus cells may be present.

10. Diseases of the Lacrimal Caruncle

The caruncle contains elements of the skin and mucosa and shows, therefore, manifold pathologic changes. The epithelium may hornify and the goblet cells may disappear. In a furuncle small abscesses appear in hair follicles and sebaceous glands. Sebaceous glands may obliterate and form atheroma and concretions.

Epithelial and connective tissue tumors can be seen. The epithelial tumors are papilloma, adenoma (especially adenoma of the sebaceous glands), cyst-adenoma (if glands are cystically

dilated) and carcinoma, which may arise from the surface epithelium as well as from the glands. Connective tissue tumors are fibroma, and rarely angioma. As already mentioned, the congenital nevus can be present and from it the malignant melanoma may arise.

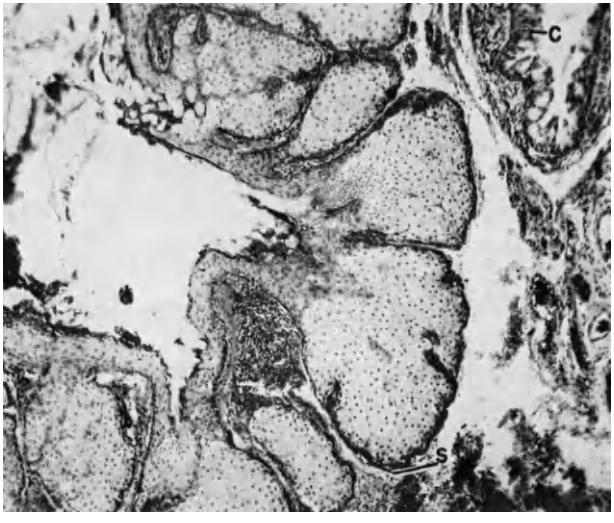

FIG. 54.—SEBACEOUS ADENOMA OF THE LACRIMAL CARUNCLE. c, conjunctiva; s, sebaceous glands. 55×.

READING OF SOURCE MATERIAL

Redslob finds most of the pigment at the limbus, from here decreasing into the periphery of the conjunctiva and increasing again in the fornix.

Oettinger describes small hemorrhages in the conjunctiva in cases of endocarditis as expression of an inflammatory embolic process in the small vessels which are surrounded by infiltrating cells.

Abkina and Normark found relatively frequently pink spots in the conjunctiva in typhus consisting of stasis hemorrhages and proliferative perivasculitis.

Kraus, Colombo, Oguchi and Majima find in the conjunctival secretion neutrophil polymorphonuclears in acute inflammations, lymphocytes and plasma cells in chronic inflammation and eosinophils in allergic conditions.

Thygeson finds in conjunctival scrapings, exudates and follicular expressions, lymphocytes and mononuclears in virus diseases, eosinophils in allergic diseases, polymorphonuclears in acute bacterial infections, keratinization of epithelial cells in vitamin-A deficiency, and many goblet cells in keratoconjunctivitis sicca.

Cange and Duboucher report on a 27 year old woman with dense infiltration of the subconjunctiva and tarsus with lymphocytes and plasma cells.

Igersheimer describes a symmetrical tumor of the conjunctiva consisting of epithelioid cell nodes surrounded by lymphocytes.

Pascheff believes that there are four different forms of diffuse lymphomatous hyperplasia of the conjunctiva: (1) diffuse infiltration with lymphocytes, usually in lymphatic leukemia, (2) diffuse proliferation of lymphocytes in the conjunctiva from the orbit, (3) small metastatic lymphomata of the conjunctiva usually in leukopenia and (4) diffuse primary lymphomatous conjunctivitis without any other disease.

Pascheff considers the conjunctival follicle as tissue reaction to an irritation.

Morax does not find any difference in the histology of the follicles in atropine catarrh, folliculosis or trachoma.

Lijo Pavia describes the formation of follicles in the conjunctiva in tuberculous persons as consisting exclusively of lymphocytes and covered by a thin epithelium.

Oguchi and Majima find transition of the epithelioid cells of the follicles to histiocytes.

Peters could show in scrapings of the conjunctiva rounded, oval and rod-like formations, in connection with a widely branching fiber system, which are increased in chronic conjunctivitis.

Pellathy and Nemeth describe conjunctivitis with glandular-like proliferation of the epithelium containing detritus of epithelial cells and mucous secretion and infiltration with lymphocytes, plasma cells and few polymorphonuclears.

Weill describes nodules of the conjunctiva containing caterpillar hairs surrounded by giant cells.

Plant hairs are surrounded by foreign body tubercles in conjunctivitis nodosa (Karbe, Knapp, Marcotty).

Jakolewna describes nodules of the conjunctiva caused by hairs of a plant; the hairs lie in diverticula of the epithelium surrounded by infiltration of leukocytes.

Schneider observed in a 63 year old woman who had been treated for years with ointment a nodular conjunctivitis in which histologically epithelium proliferated into the depth and cavities filled with fat were between the papillae.

Bonazzi describes a very large conjunctival granuloma caused by a foreign body.

Birch-Hirschfeld reports proliferation of conjunctival epithelium under the influence of x-rays. A wide stratified squamous epithelium may also hornify and buds containing goblet cells can extend into the subepithelial tissue which becomes hyalinized and infiltrated with lymphocytes, plasma cells and occasionally mast cells.

Hoffman finds as characteristic features of vernal catarrh hyalinization of the subepithelial tissue, infiltration with plasma cells and eosinophils. The papillary hypertrophy is the result of the infiltration and the connective tissue finally undergoes fatty degeneration.

D'Amico examined serial sections of the limbus swelling in vernal catarrh. The epithelium sends strands into the deeper layers. They con-

tain spaces lined by cuboidal epithelium which are formed by mucoid degeneration. The submucous connective tissue is infiltrated with lymphocytes, eosinophils, plasma and mast cells.

Pascheff finds in vernal catarrh nodules showing papillary hypertrophy and necrotic areas surrounded by epithelioid and giant cells resembling tubercles.

The pathology of vernal catarrh is described by El-Tobgy, Lehrfeld, Lindemann.

Rizzo and Motta describe spherical granules in the connective tissue cells of the nodules of the vernal catarrh, which are rich in cytoplasm, probably representing a kind of cytoplasmatic degeneration.

Uhthoff found occasionally calcareous degeneration in vernal catarrh.

Occasionally intracellular inclusion bodies were found in vernal catarrh by Howard, Torres and Torres.

Pillat states that bacteria found free in the secretion are saprophytes and that pathogen bacteria live parasitically in living cells, e.g., staphylococcus albus proliferates on degenerated epithelium of the conjunctiva and lid margin as a saprophyte.

Histologic findings in various stages of gonococcic conjunctivitis are reported by Howard, Lindner, McKee. Lindner describes the immigration of gonococci into the epithelium of the conjunctiva which acts phagocytically. Their toxins produce the suppuration of the mucosa.

Odegaards found primary conjunctivitis caused by meningococcus.

Hayes and Chamberlain found in a meningococcal conjunctivitis, meningococcus type 1. The conjunctivitis was followed by suppurative meningitis.

Kahaner and Lanow found in an exogenous meningococcic conjunctivitis, meningococcos type 2.

Reese describes a severe conjunctivitis caused by meningococcus, followed by meningitis.

Lindner finds that the Koch-Weeks bacilli grow on the superficial epithelial cells.

Miller and Blower report cases of primary diphtheria of the conjunctiva in young children.

Michail describes a hematogenous conjunctivitis caused by staphylococci due to a tousillitis histologically; the epithelium was filled with polymorphonuclears and the subepithelial tissue contained mononuclears and newly-formed vessels and many small abscesses.

According to Vancea, the pseudomembranous conjunctivitis caused by streptococci consists of vascular granulation tissue with thrombi containing numerous polymorphonuclears and epithelial proliferation.

The bacteria of Vincent's angina (spirochete Vincenti and fusiform bacillus) cause occasionally a suppurative conjunctivitis, according to Dunnington and Khorazo, Herrenschwand. Also, Dejean and Temple report a conjunctivitis in a 68 year old woman caused by Vincent's angina showing degenerated epithelium and fibrinoid masses.

Bacterium coli can produce conjunctivitis, according to Sanyal.

Drosdova and Petrova found dysentery bacillus in severe conjunctivitis.

Bacillus fecalis alkaligenes produces occasionally an epidemic of conjunctivitis (Barrow).

Stella found two months following a Koch-Week's conjunctivitis a heavy fold of the fornix containing enormously vascularized connective tissue and infiltration with polymorphonuclears.

Taborisky also considers the epitarsus as a result of a severe conjunctivitis.

Paul describes histologic changes of the conjunctiva in measles with desquamation of the superficial cells, vacuolization and pyknosis in the deep cells.

Diplobacillus Morax-Axenfeld grows mainly on hornifying epithelial cells (Lindner).

Schuster finds in conjunctivitis membranacea histologically networks of fibrin with polymorphonuclears, lymphocytes, destroyed epithelial cells, connective tissue cells and blood vessels.

Valli describes in membranous conjunctivitis a granulation tissue with numerous vessels, infiltration of lymphocytes, plasma cells and a few polymorphonuclears.

Knapp and Roessle describe a recurrent membranous conjunctivitis in which the membrane represented a hyalinizing fibrinous product with a few polymorphonuclears.

Hogan finds that membranous conjunctivitis may be caused by a great variety of bacteria; furthermore, by virus and fungi and that it may be also of allergic, traumatic, chemical and toxic nature (vernal catarrh, pemphigus and erythema multiforme).

Hamburger describes conjunctivitis with membrane formations caused by micrococcus catarrhalis.

Castroviejo found in ligneous conjunctivitis pseudomembranes and dense inflammatory infiltration.

vom Hofe describes connective tissue hyperplasia of conjunctiva and subconjunctival tissue in cases of pseudomembranous conjunctivitis.

Morax finds in pseudomembranous conjunctivitis histologically hyalin masses separated by blood vessels and leukocytes. The surface of the conjunctiva is covered with fibrinous masses.

Elschnig is of the opinion that all follicular affections of the conjunctiva are similar and are mild and severe forms of trachoma.

Sgrosso finds histologically differences between follicular conjunctivitis and trachoma. In the former the epithelium is intact and the follicles exist without reaction in their surroundings. In the latter the epithelium is filled with mesenchymal elements and shows decrease in nuclei, formation of vacuoles, papillae and pseudoglands; the subepithelial tissue between the follicles is infiltrated and connective tissue is newly formed.

The pathology of the trachoma is reported by Addaria, Birch-Hirschfeld, Dejean and Temple, Lopes de Andrade, Morax and Petit, Oguchi and Majima, Pascheff, Taborisky, Wilson.

Wilson finds histologically in trachoma in the beginning congestion of the subepithelial tissue with lymphocytic infiltration which is followed by infiltration with plasma, epithelioid and mononuclear cells. Down-growth of the epithelium and follicles appear in a later stage.

Oguchi and Majima find large mononuclears and plasma cells in the conjunctival secretion in trachoma; they consider the epithelioid cells and Leber's granular cells in trachoma as histiocytes. The latter contain lymphocytes, disintegrated erythrocytes, melanin and fatty substances.

Taborisky describes changes of the epithelium in trachoma examined in scrapings and sections. There is degeneration, exfoliation and proliferation of the epithelium with formation of papillae.

Peters describes lattice fibers representing a system of reticular fibers around the follicles and beneath the epithelium in trachoma and contributing to scar formation.

Lo Vecchio finds in trachoma of the bulbar conjunctiva proliferation of the epithelium and subepithelial cellular connective tissue and lymphocytes.

Heilmann considers the follicles in trachoma as secondary follicles with germinative centers, formed by proliferating reticulo-endothelial elements.

Deeply penetrating epithelial downgrowth with formation of pseudoglands are described in trachoma by Lamb. Follicles are formed in trachoma from the diffuse lymphocytic infiltration, according to McCallan.

Herschendoerfer finds pigment in and around connective tissue cells of the subepithelial tissue and the tarsus in trachoma.

Lumbroso finds in the stage of scar formation in trachoma that fibroblasts substitute the tissue and that further perivascular infiltration is present consisting of polyblastic histiocytes and plasma cells with few lymphocytes, esinophils and basophils.

Saba saw cases of trachoma with heavy plasmacellular infiltration, hyaline degeneration of blood vessels and deposits of amyloid.

Kubik found in a case of trachoma a combination of plasmacellular infiltration and hyalin and amyloid.

Birch-Hirschfeld believes that the plasma cells in trachoma originate from adventitial cells.

Kacso finds in trachoma infiltration mainly between the mucosa and tarsus and very little in the tarsus itself.

Saba describes an atypical unilateral trachoma with wartlike formations consisting of fibroblasts, fine fibrils, lymphocytes, plasmacells and large monocytes.

Tarsi show in trachoma, according to Birch-Hirschfeld, infiltration with lymphocytes and plasmacells, degeneration of Meibomian glands, newly formed connective tissue arising from the adventitia of blood vessels, fat cells, hyaline degeneration and necrosis.

Spassky finds in the tarsus in trachoma dilated and newly formed blood vessels, infiltration with lymphocytes, plasma cells, polymorphonuclears, eosinophils, mast cells, giant cells and fibroblasts and loss of glands.

Aubaret, Rouslacroix and Herrmann describe trachomatous pannus.

Typical follicles are found in trachomatous pannus by Busacca, Thygeson, Tschirkovsky and Dymschitz.

Busacca describes the connective tissue meshwork of trachomatous pannus.

Dusseldorp believes that the pannus in trachoma grows first between epithelium and Bowman's membrane, but Morax, who finds in the pannus mononuclears and histiocytes between Bowman's membrane and the lamellae of the cornea, states that the trachomatous pannus starts beneath Bowman's membrane.

Kreiker finds in the clinically normal bulbar conjunctiva, in cases of pannus, infiltration with plasma cells, perivascular infiltration and even follicles. He considers the pannus as a direct continuation of the pathologic changes of the conjunctiva.

Pokrovskij finds that the bulbar conjunctiva shows in trachoma a similar histological appearance as the pannus; Miyake found a continuation of the subconjunctival and episcleral infiltration to the pannus.

El-Tobgy reports deposition of fatty globules on the cornea in trachoma.

Michail reports changes of infiltrative and regressive nature in the tear gland in trachoma.

Caramazza and Silvagni find in the nasal mucosa of trachomatous patients microscopically metaplasia of the epithelium and infiltration with lymphocytes and plasma cells in the subepithelial stroma.

Pascheff finds that follicles are formed again and again in trachoma even after extirpation of the mucosa and even in buccal mucosa transplanted into the conjunctiva (Denig's operation). Also, Friedman, Towbin find the transplanted mucosa in trachoma (Denig's operation) histologically affected similar to the surrounding conjunctiva.

Pascheff describes a conjunctivitis hyperplastica lymphadenoides diffusa with proliferation of connective tissue, diffuse lymphocytic infiltration and numerous blood vessels rather resembling trachoma.

Michail and Vancea could infect blind eyes with trachomatous material after scraping and massaging of the conjunctival epithelium.

Aust, Hamburger, Nagy, Roetth, Rohrschneider, Taborisky report inclusion bodies in trachoma.

Wolchonsky finds in nearly all cases of trachoma Prowazek's bodies in the follicles.

Busacca, Cuenod and Nataf describe Rickettsia-like bodies in trachoma.

Busacca assumes that the virus in trachoma attacks the corneal epithelium first and that secondarily as defense reaction pannus is formed.

Pascheff calls trachoma an ophthalmia follicularis confluens or folliculomatosa and considers it as endogenous constitutional lymphadenoid vegetation of the conjunctiva.

Lindner could never find inclusion bodies in conjunctival folliculosis.

Taborisky finds histologically in conjunctival folliculosis small and large follicles and scant cellular infiltration between them.

Dejean describes lymphoid hypertrophy in conjunctival folliculosis.

Van Duyse describes chronic folliculosis of the conjunctiva.

Loewenstein finds the appearance of inclusion bodies different in scrapings and sections. In the former they are polymorphous, and individual elementary bodies and initial bodies may be found in the cells. In the latter, encapsulated inclusion bodies are visible in the superficial epithelial layers and reticulum cells filled with granules and granules free in the tissue are found in the subepithelial layers and in the tarsus.

Comberg, Morax, Sgrosso find in bathing conjunctivitis histologically follicles with early hyaline degeneration and disintegration of the epithelium.

Lindner calls the inclusion blenorrhea of the newborn and bathing conjunctivitis as paratrachoma. He considers them identical, in accordance with Aust, Morax.

Feigenbaum, Michaelson and Kornblueth find in epidemic kerato-conjunctivitis histologically the epithelium flattened, capillary dilated and edema in the subepithelial tissue, besides infiltration with lymphocytes and monocytes and papillary hypertrophy.

Luiggi describes intracellular bodies of the rickettsia type in epidemic nummular keratoconjunctivitis.

Typical epithelial changes in the conjunctiva in molluscum contagiosum mostly continuing from the skin of the lid, are described by Bardelli, Cavara, Gifford and Gifford, Michelatti.

Lepromata of the conjunctiva consisting of lymphocytic infiltration with fibroblasts, many newly-formed vessels, large lepra cells with lepra bacilli are described by Neame, Riad, Santonastaso.

Blegvad, Browning, Musial, Tita, Weskamp and Vila Ortiz describe tuberculosis of the conjunctiva.

Bruce and Locatcher-Khorazo describe primary tuberculosis of the conjunctiva. The scrapings showed acid-fast bacilli and animal inoculation had a positive result. Further, Goldfarb and Seltzer, Gonzalez Lelong and Dusseldorp, Sitchesvska and Sedam report cases of primary tuberculosis of the conjunctiva.

Boshoff and Grasset report a tuberculoma of the conjunctiva following laceration; further, Jordan, Junius describe tuberculomata of the conjunctiva.

Katsnelson saw cases of tuberculous granulomata of the bulbar conjunctiva.

Lundsgaard, Neame, are of the opinion that conjunctival tuberculosis originates endogenously by way of the blood circulation.

Kalt describes a conjunctivitis showing numerous lymphocytes, epithelioid and giant cells and sporelike formations; he questions whether tuberculosis or sporotrichosis is present.

Bacillus pseudotuberculosis can be found in granulations of conjunctivitis pseudotuberculosa (Cavara, Galeazzi, Pflimlin and Rintelen).

Weekers finds in the beginning of the phlyctenule dilation of vessels, diapedesis of polymorphonuclears and serous imbibition of the connective tissue. Mononuclears follow soon and finally epithelioid and giant cells appear. Phlyctenules originate due to a reaction to tuberculo-toxin which acts by way of the tears on a hypersensitive conjunctiva.

Stargardt finds the phlyctenules histologically containing lymphocytes, epithelioid and giant cells.

Keratoconjunctivitis phlyctenulosa is characterized by circumscribed nodules of lymphocytes, surrounded by edema (Piesbergen).

Engelking finds in fleeting tubercles of the conjunctiva lymphocytes surrounding epithelioid and giant cells with central necrosis.

The fleeting tubercles of the conjunctiva (Lichen scrofulosorum) are histologically miliary tubercles, according to Friede.

Accompanying parenchymatous keratitis there are found papulo-necrotic tuberculids of the bulbar conjunctiva which are histologically tubercles, according to Seefelder, Wiegmann.

Blegvad, Kissmeyer, Seefelder, find in multiple sarcoid of Boeck in the conjunctiva, granulation tissue histologically of the type of tuberculosis but without caseation.

Ochapovskaya, Schnierer report cases of exogenous conjunctival tuberculosis taking the form of Parinaud's syndrome.

v. Szily found in a case of Parinaud's disease the conjunctiva infiltrated with lymphocytes, the blood vessels thickened, showing areas of necrosis; he considers tuberculosis as cause.

According to Gifford, the follicles of Parinaud's conjunctivitis show in an early stage edematous connective tissue infiltrated with small and large mononuclears and epithelioid cells and in a late stage necrotic foci and numerous micro-organisms (leptothrix), lymphocytes, polymorphonuclears, eosinophils and epithelioid cells.

Szymanski found in a case of Parinaud's disease diffuse infiltration with lymphocytes, epithelioids and plasma cells.

Arganaraz and Lijo Pavia found in Parinaud's conjunctivitis mostly infiltration with plasma cells.

Nida describes in follicular conjunctivitis with preauricular lymph nodes diffuse lymphocytic infiltration of the thickened conjunctiva.

The gram-positive pseudotubercle bacillus was found in Parinaud's conjunctivitis by Pereyra.

Spanic reports a case of primary lesion in syphilis of the conjunctiva showing many spirochetes, vacuolized epithelium and infiltration of the subepithelial tissue with lymphocytes, plasma cells, polymorphonuclears, eosinophils, mast cells, and fibroblasts and many blood vessels with swollen endothelium.

T'ang and Hu found a primary lesion of the retro-tarsal fold with treponema pallida in the serum.

Papolczy describes as secondary syphilis of the conjunctiva round-cell infiltration, increase of blood vessels, phlebitis and closure of arteries with resulting circumscribed necrosis.

Francois reports a lymphomatous syphilitic infiltration of the lower fornix of the conjunctiva.

Syphilitic lymphomatosis shows dense lymphocytic infiltration in the conjunctiva with proliferation of connective tissue (Orloff).

Schweig saw a case of gummata of the conjunctiva.

Weiss finds spirochetes in the conjunctival secretion of infants with congenital lues. Infiltrations of plasma cells and lymphocytes appear in the tissue and around vessels, in the tarsus, the fornices and the tear sac.

Dvorak-Theobald found in ocular glandular tularemia nodules in the conjunctiva containing lymphocytes, plasma cells and centrally epithelioid cells, besides diffuse infiltration of lymphocytes, plasma cells, epithelioid cells and mast cells.

Pascheff describes a conjunctivitis necroticans infectiosa with dense subconjunctival infiltration of polymorphonuclears, surrounded by a mass of lymphocytes, circumscribed necroses and ulcers and finds a microbacillus polymorphus necroticans causing the diffuse end nodular infiltration.

Lemoine, Verhoeff, Verhoeff and King could find lepothrix in histologically examined cases of Parinaud's syndrome and could also cultivate these organisms.

Gifford and Dillon, Harner found leptothrix in cases of nodular conjunctivitis with regional lymph-adenitis, and Gifford and Day in necrotic follices of the conjunctiva histologically and in culture medium.

Chronic nodular conjunctivitis is occasionally produced by leptothrix (Bakly, Dunphy, Rasheed Bey and Khairat).

Barushaw and Read saw a case of rhinosporidiosis of the conjunctiva. The granulation tissue consists of lymphocytes, plasma cells and foreign body giant cells. The organism (sporangium) contains spores, is spherical and has many nuclei; it lies free in the tissue.

Arnold and Whildin found in a polypous mass of the conjunctiva of an 8 year old boy chronic inflammation with areas of acute inflammation and sporangia filled with endospores belonging to rhinosporidium.

Duggan reports a papillomatous tumor of the conjunctiva representing a granulation tissue of rhinosporidium.

Rhinosporidium seeberi was found further by Denti, Elles, Kaye, Kurup, Narayano Rao, Orlandi, Wright.

Wilson, Ferguson describe granulomata of the conjunctiva with large mononuclear and multinuclear cells containing cryptococci (blastomyces) in large numbers.

Gordon found in an ulcer of the conjunctiva, sporotrichum schenckii, Gifford in a granuloma of the conjunctiva.

Deuchler found in herpes tonsurans of the lid, trichophyton cerebriforme in the conjunctival secretion and plasmacellular infiltration of the conjunctiva.

Motais reports sparganosis of the conjunctiva.

Scalzitti saw in the conjunctivitis polymorphonuclear cells, lymphocytes, fibroblasts, giant cells, vascularization and threads of fungi.

Theodore found yeastlike organisms in a case of Parinaud's syndrome in the secretion and histologically.

Scalzitti found mycelial filaments of a nondifferentiated species in the conjunctiva of an 11 year old boy.

Pascheff describes granulomatous hyperplasia of the conjunctiva in granuloma fungoides. Histologically, there are numerous blood vessels present with perivascular infiltration consisting of lymphocytes, plasma cells and fibroblasts.

Belgeri and Dusseldorp report Leishmania infection of the conjunctiva.

Filaria loa is found in the conjunctiva by Begle, Pacalin, Volmer, filaria inermis by Villard.

Howard, Hsu-Hsi-Fan report papillomatous tumors of the conjunctiva of the lower lid containing filaria lacrimalis.

Adams observed in an excised piece of the bulbar conjunctiva of a 34 year old miner, microfilaria (Onchocerca volvula).

Small tumors of granulation tissue with areas of granular disintegration surrounded by endothelial cells and giant cells are described as habronemic conjunctivitis by Bull.

Sobhy Bey, Wilson, describe nodules of the conjunctiva consisting of their endothelial cells surrounded by lymphocytes, plasma cells, eosinophils with centers filled with Bilharzia ova surrounded by giant cells.

Badir discovered in a granuloma of the conjunctiva and caruncle a great amount of terminal-spined Bilharzia eggs and male and female Bilharzia worms in a 12 year old boy with trachoma cicatriceum. The nodular infiltration consisted of lymphocytes, epithelioid cells, plasma cells and numerous eosinophils. Giant cells and fibrosis were noticeable around degenerated ova.

Cysticercus of the conjunctiva is described by Contino, Guaraldi, Hare, Joaques and Reinflet, Laignier-Terasse.

Larvae of the hypoderma bovis and of other flies were found in the conjunctiva and anterior chamber by Bietti, Hartmann, Kuriks.

v. Szily finds in the keratoconjunctivitis of acne rosacea in the conjunctiva lymphocytes and epithelioid cells and dilated vessels in the early stage, nodules consisting of granulation tissue, obliteration of vessels in a late stage and in the cornea perforation of Bowman's membrane by granulation tissue with accumulations of lymphocytes and fibroblasts.

Velter finds in acne rosacea of the cornea and conjunctiva histologically desquamation and partial vacuolization of the corneal epithelium, complete destruction of Bowman's membrane and subepithelial nodules consisting of lymphocytes, plasma cells, epithelioid and giant cells, fibroblasts, polymorphonuclears, eosinophils, blood vessels and fibrillar tissue.

Histologic examinations of phemphigus of the conjunctiva are reported by Smith, Myers and Lamb.

De Castañé Decoud finds in the pemphigus of the conjunctiva edema of the subepithelial tissue, myxoid appearances, angiohyperplastic granuloma, infiltration with plasma cells and lymphocytes, conspicuous sclerosis, cystic degeneration of the Meibomian gland and lipophagic granuloma.

Schoenfelder finds in pemphigus of the conjunctiva the epithelium separated in vesicles from the edematous subepithelial tissue which shows numerous round cells and dilated vessels.

Kapuscinski finds in pemphigus granular degeneration of corneal lamellae and degenerative vacuolization of the conjunctival epithelium and infiltration with round cells.

D'Amico could examine the entire eye and its adnexa of a 70 year old woman with pemphigus and found the epithelium of the conjunctiva epidermis-like with some blebs, chronic inflammation and shrinkage due to scar formation.

Accardi found in the infiltration of the conjunctiva in pemphigus eosinophils and severe alterations in cell nuclei. The epithelium was detached in vesicles in the area of inflammation. Streptococci were present.

Sommer and Hollander report a case of pemphigus mucosae showing diffuse and nodular infiltration and proliferation of connective tissue in the conjunctiva.

Alajmo found in erythema exsudativum multiforme in a 28 year old woman, the epithelium of the conjunctiva normal and subepithelial numerous lymphocytes, some edema, hemorrhages and dilated blood vessels. In the deeper layers were larger spaces lined by polymorph cells and connective tissue proliferated into the spaces.

Pascheff describes in conjunctivitis of erythema exudativum multiforme infiltration and edema of the subepithelial layers, formation of papilla necrosis of the epithelium with formation of pseudomembranes and scars.

Cohen and Sulzberger describe in epidermolysis bullosa histologically decrease of elastic fibers and separation of the epithelium from the conjunctiva by fluid in places.

Friede finds histologically in the conjunctiva in hydroa vacciniforme proliferation of the epithelium into the depth with formation of cysts and also ulceration.

Weiss finds microscopically accumulations of dustlike darkish pigment in the epithelial and connective tissue cells and infiltrations with lympho-

cytes, eosinophils and plasma cells in the conjunctiva in acanthosis nigricans.

Stella finds in the true pterygium mucous degeneration of the epithelium with the formation of buds and mucous glands, hyaline degeneration of the connective tissue and splitting of the elastic fibers, sclerotic vessels and infiltration with plasma cells; in pseudopterygium formation of papillae, edematous swelling, dilated vessels, few elastic fibers and infiltration are found.

Claus describes a pterygium which developed directly from a nevus.

Sie-Boen-Liang finds in Bitot's spots the fat content of the epithelium increased and kerato-hyalin bodies in the superficial layers of the stratified squamous epithelium.

Kreiker finds the spots of Bitot consisting of an epidermis-like epithelium representing the prexerosis. In a later stage hornification sets in, forming xerosis of the conjunctiva.

Histologic examinations of Bitot's spots are reported by El-Tobgy and Wilson.

Marinosci describes the epithelial xerosis of the conjunctiva as a partial cuticularization of the epithelium, the parenchymatous xerosis as complete cuticularization.

Favaloro found in the tarsal conjunctiva of old trachoma circumscribed xerosis with hyaline and granular degenerated epithelial cells and typical hornification.

Mori finds in xerosis epithelialis conjunctivae brownish pigment in the basal cells representing melanin.

Jacqueau and Bujadoux describe keratosis of the conjunctival epithelium in a 70-year old woman.

Nicholls saw epithelial plaques of the conjunctiva and cornea in a 14 year old boy in the form of an epithelial hyperplasia.

Hertgberg, Jervey report epithelial plaques of the conjunctiva.

Stock describes horn of the conjunctiva consisting of high layer of hornified epithelium covering mass of undifferentiated degenerated tissue.

Tyloma of the conjunctiva with hyaline and amyloid degeneration of the sub-epithelial tissue is described by Stock, Koyanagi.

Lutman and Favata saw in Sjoegren's syndrome in the lacrimal gland infiltration of numerous lymphocytes, condensation of connective tissue and deposition of a thick, hyalin-like substance, and in the conjunctiva stratified squamous cell epithelium and subepithelial infiltration consisting chiefly of plasma cells. They consider chronic ariboflavinosis as cause.

Keratoconjunctivitis sicca shows microscopically corneal epithelium thinned, degenerative panuus, Bowman's membrane destroyed, hydropic swelling of the conjunctival epithelium, loss of elastic fibers, atrophy and infiltration of tear gland (Bruce).

Senile changes of the conjunctiva produce thickening of the epithelium with some keratinization, hyalinization of the connective tissue, and disappearance of elastic fibers, according to Wilmer.

Kubik, Njadtisch report hyaline and amyloid degeneration of the conjunctiva as simultaneous with plasma cell infiltration. They are often mixed

in the conjunctival tissue which gives chemical and staining reaction of both (Slavick).

Hyaline and amyloid appear avascular due to occlusion of small vessels; compensatory vessels in the neighborhood can be dilated and even racemous aneurysms may appear.

Ernyei describes tumor-like hyalin and amyloid degeneration of the conjunctiva in trachoma.

Fileti reports on hyaline degeneration of the conjunctiva.

Pascheff describes a conjunctivitis hyperplastica hyaliniformis with proliferating and very thickened collagenous fibers.

Wallgren and Vannas find in amyloidosis of the conjunctiva amyloid localized in the perivascular tissue and in the vessel walls and containing well-preserved connective tissue fibers. Amyloid is also found in regional lymph nodes.

Lundsgaard describes amyloidosis of the conjunctiva in which the connective tissue forms bars and a network of fibers.

Elles considers amyloidosis of the conjunctiva as vitamin deficiency. Reticulo-endothelial cells of the adventitia of small arteries are primarily affected.

Bryan-Brown, Echanekim-Slykova, Eleonskaia, Wright describe amyloid degeneration of the conjunctiva.

Pollock describes amyloid-like tumor of the cornea in trachoma.

Gejlikman found in primary familial degeneration of the cornea homogeneous masses beneath the epithelium, blood vessels partly thickened and partly obliterated, the epithelium atrophic and Bowman's membrane disintegrated. He considers it an amyloid degeneration.

Hoffman describes cases of plasmoma of the conjunctiva containing plsama cells, polymorphonuclears and mast cells. They originate from chronic inflammation, especially trachoma, but also from vernal catarrh.

Kreibig considers the plasmocytoma of the conjunctiva as an inflammatory tumor, chiefly appearing in trachoma, and proposes the name plasmocellular granuloma.

Plasmoma consists of plasma cells embedded in fine network of connective tissue and is to be considered as chronic inflammation (Chojnacki).

Schwarzkopf finds in old plasmoma always hyaline degeneration, changing later into amyloid.

Baurmann finds plasmoma of the conjunctiva cause of hyalinized connective tissue septa.

Derkac finds in plasmoma hyperplasia of plasma cells, lymphocytes, cells of reticulo-endothelial origin and simple fibrocytes. Also Botteri and Španić, Cattaneo, Guglianetti, Papolczy, report plasmomata of the conjunctiva in trachoma. Halbertsma denies that hyaline or amyloid degeneration appears in the plasma cell. Cortes, Donati, Dusseldorp and Gonzales Lelong, Hoen and Halbertsma, James, Michail, Pascheff, Patwardhan, Puscariu, Raverdino, Rollin, Sondakoff also report plasmocytomata of the conjunctiva.

Botteri and Španić find in conjunctivitis plasmacellularis the conjunctiva infiltrated with plasma cells which are arranged in rows by connective tissue

septa. They believe it is distinguished from plasmoma only quantitatively. Also Biffis, Hoen and Halbertsma describe conjunctivitis plasmacellularis with granular thickenings which contain plasma cells and fibroblasts.

Mazzola reports calcareous degeneration of the conjunctiva in the form of deposition of calcium salts.

Loehlein, Zimmerman report melanosis of the conjunctiva. They consider the pigmented cells as similar to nevus cells.

Reese describes as precancerous melanosis an acquired flat pigmentation of the conjunctiva of granular appearance. The basal cells undergo hydropic changes, cells proliferate intraepithelially and invade the underlying tissue which shows lymphocytic infiltration. As a result, malignant melanomata (cancerous melanosis) appear.

Vitiligo of the conjunctiva is described by Hanssen. The thin epithelium contains yellowish pigment, the subepithelial tissue is infiltrated with lymphocytes and plasma cells.

Pillat finds in the conjunctiva in vitamin A deficiency, dendritic cells in the deep layers of the epithelium and numerous droplet-like formations as precursors of the increased pigment.

Vail finds in argyrosis of the tarsal conjunctiva, superficial granulation tissue containing pigment granules and chronic inflammatory reaction of the deeper tissue.

The elastic fibers of the conjunctiva are impregnated with dark granules in argyrosis (Blind).

McKee found in severe argyrosis of the conjunctiva dustlike depositions along collagenous bundles, phagocytes filled with silver and silver deposited in the perivascular spaces and beneath the endothelium of the blood vessels.

Reese observed a pigmentation of the conjunctiva resulting from mascara with plasma cell infiltration and black pigment in and around stroma cells.

Tarducci describes conjunctival cysts of various origins.

Werner finds a subconjunctival epithelial cyst in trachoma originating by stasis of the secretion in blocked Krause's glands.

Cysts of the conjunctiva containing communicating spaces are described by Hugel and Worms.

Wolff describes a large implantation cyst of the conjunctiva.

A cyst lined by cylindric epithelium was found in a pterygium by Bistis.

Inflammatory proliferations of the epithelium are the cause of conjunctival cysts, according to Duverger and Redslob. Mucous degeneration of the central cells of the epithelial buds give rise to formations of cysts.

Shoda describes subconjunctival implantation cysts consisting of several spaces lined with stratified epithelium appearing after injury, respectively unilocular cysts lined with cuboidal, partly pigmented epithelium after surgery.

Corrado, Kurz report inclusion cysts of the limbus after trauma.

Mulock-Houwer describes cysts of the fornix and epitarsus which he considers as epithelial remnants of duplicated conjunctival folds.

Congenitally displaced epithelium can give cause to conjunctival cysts (van der Straeten and van Duyse).

Mylius reports inflammation of the conjunctiva with budding of the epithelium which, by softening and liquefation, formed cysts (cystic conjunctivitis).

Samuels describes the various tumors of the conjunctiva.

Solares and Orosco report cases of carcinoma, sarcoma, and malignant melanoma of the conjunctiva.

Santonastoso describes a case of epibulbar giant cell leukosarcoma, one case of vascular, pigmented spindle-cell sarcoma and one case of lymphangioma.

Roselli reports an epibulbar round cell sarcoma and fibroepithelioma.

Morelli describes a tumor in an 84 year old man consisting of large cells with vesicular nuclei, fine connective tissue, lymphocytes and eosinophils. It is questionable whether the tumor is epithelial or endothelial.

Granulomata of the conjunctiva containing foreign bodies are described by Barrie, Carboni, Smith, granulomata without foreign body by McRae, Redsdlob.

Montanelli describes granuloma of the inferior fornix of the conjunctiva after injury.

Freeman describes a granulation tumor of the conjunctiva with glandular proliferation of the epithelium in a 30 year old man.

Hurst found in a case of conjunctival granuloma with adenopathy histologically only necrotic tissue.

Kiewe reports a granuloma telangiectaticum of the conjunctiva following squint operation; Wollenberg saw a connective tissue mass originating from a granuloma following squint operation.

Fibroma of the limbus is described by Wright.

Accardi found a well-vascularized fibroma of the bulbar conjunctiva of a 12 year old boy.

Neurofibromata of the conjunctiva are described by Allende, Guist.

Scala reports a keloid of the conjunctiva, probably originating from a hemorrhage.

Carboni's case of a 14 year old girl had a lipoma of the conjunctiva.

Moscardi describes cases of subconjunctival lipomata.

A subconjunctival chondroma in a 19 year old boy is reported by Ajo.

Byrn, Colombo, Motto, Redslob, Villard and Dejean describe cases of hemangiomata of the bulbar conjunctiva.

White found in a 40 year old woman with bloody tears a capillary angioma of the tarsal conjunctiva, the reticulum of which was filled with lymphocytes.

Redslob saw a cirsoid aneurysm of the bulbar conjunctiva consisting of densely arranged partially obliterated blood vessels and originating from a congenital angioma by proliferation of all parts of the vessel walls.

Lymphangiomata of the conjunctiva are described by Franke, Ray, Schoepfer.

Lymphomata of the conjunctiva are described by Bedell, Ennema, Jensen, Leinfelder and O'Brien, Speciale-Picciche, Tiscornia, Wright.

Boehm describes lymphocytoma of the conjunctiva covering also the cornea partly.

A bilateral lymphoma of the fornix is reported by Meyer, and Saradarian describes a bilateral lymphoma of the conjunctiva due to leukemia, in which lymphocytes, but also myelocytes, plasma cells and nondifferentiated juvenile forms were found.

Staehli reports bilateral recurrent lymphomata of the bulbar conjunctiva.

Shannon and McAndrews describe lymphomata of the conjunctiva and consider them as extensive hyperplasia of the lymphoid tissue.

Siemund reports a lymphomatosis of the conjunctiva.

Reese and Guy saw in leukemia exophthalmos and solid masses of lymphocytes in the bulbar conjunctiva.

Kreibig describes round cell infiltration of the conjunctiva in leukemia.

Reinsberg and Kadlicky describe in a case of lymphogranulomatosis nodules in the subconjunctival and episcleral tissue containing plasma cells, endothelial, epithelioid and additionally mono- and multinuclear polygonal cells.

Scalzitti describes pigmented and nonpigmented sarcomata of the conjunctiva and lacrimal caruncle.

Sarcomata of the conjunctiva are described by Alexiades, Bistis, Rifat, Roemer.

A partly pedunculated sarcoma of the conjunctiva is described by Morton.

Fernando reports the spread of sarcoma of the conjunctiva after removal of a pedunculated sarcoma.

Sarcomata of the conjunctiva and cornea are reported by v. Berger, Besso, Gastev and Werpoukhovsky.

Bistis, Kissin report round cell sarcomata of the conjunctiva extending into the orbit.

Smith describes a polymorphous sarcoma of the conjunctiva.

Malignant melanomata of the conjunctiva are reported by Dawson, Lane, Liesko, Morelli, Posey, Rossi, Steyn, v. Szily, Tomkin, Triossi, Waetzold.

Rizzo reports an epibulbar melanosarcoma of alveolar structure following a cystic nevus in the inner canthus.

Morton found an atypically situated melanotic sarcoma of the conjunctiva with irregular alveolar arrangement of closely packed cells.

Melanosarcoma following melanosis of the conjunctiva is seen by Musial.

Scalzitti found pigmented spindle-cell sarcomata of the conjunctiva and the caruncle.

A lymphosarcoma of the bulbar conjunctiva with atypical cell forms and mitosis was seen by Barrière and Malet, and Goldenburg, too, reports a malignant lymphoma of the conjunctival sac.

Rados describes a reticulum cell sarcoma of the conjunctiva (Retothel sarcoma of Roulet), a form of the lymphosarcoma. Its cells are larger than in the latter and have much acidophil cytoplasm and are embedded in reticular substance. Also, Jona, v. Walbeck describe reticulum cell sarcomata of the conjunctiva and plica semilunaris.

Posey saw an angiosarcoma of the palpebral conjunctiva with metastases in the lungs and brain.

De Rosa, Stojalowsky and Stasinska report endotheliomata of the conjunctiva.

Drak, Sentoro report cases of endotheliomata of the plica semilunaris.

Sgrosso describes bilateral melanotic lymphangio-endotheliomata of the conjunctiva in a 10 year old boy.

Boulans, Morelli, Rizzo report peritheliomata of the conjunctiva.

Musial describes lymphogranuloma malignum of the semilunar folds.

Mura reports epitheliomata of the lid conjunctiva.

Grossgebauer found in a case of multiple epithelial tumors of the eye and in its adnexa, papillomata of the conjunctiva and limbus and basal cell carcinomata of the fornix and of the lid margin.

Doherty, Fieandt, Walker saw papillomata of the conjunctiva.

Menestrina reports papillomata of the conjunctiva and lacrimal caruncle.

Redslob saw a papillary cystic epithelioma of the palpebral conjunctiva.

Gonzales Vaurell describes an adenopapilloma of the semilunar fold.

Drak describes a cystic adenoma of the limbus in a 19 year old boy with tubules lined with cylindric epithelium and papillomatous proliferation and infiltration with lymphocytes and plasma cells. He considers the tumor as displaced part of the caruncle or of the glands of Manz.

Cystic adenomata of the bulbar conjunctiva arising from displaced glandular elements were also found by Duclos, Marshall.

Gérard and Morel report an adenoma of the Meibomian glands.

Khanolkar found Bowen's disease of the conjunctiva.

Papolczy reports flat epibulbar squamous cell carcinomata which show a thickened polymorphous epithelium and subepithelial round-cell infiltration and usually perforate through the scleral canals.

Carcinomata of the conjunctiva are reported by Aubaret and Sèdan, Camison and Feingold, Gjessing, Veasey.

Feingold reports a carcinoma of the conjunctiva, appearing after injury.

Chevallereau and Offret describe a carcinoma of the limbus in a case of xeroderma pigmentosum.

Squamous cell carcinomata of the palpebral or bulbar conjunctiva, are reported by Bachstez, Beauvieux and Pesme, Law, Mazzi, Menachè, Michail, Wolf.

Titsche saw a case of epidermoid carcinoma of the bulbar conjunctiva of papillary type.

Basal cell carcinomata of the palpebral or bulbar conjunctiva are reported by Blatt, Liekso, Maucione, Seno.

Coover describes basal cell carcinoma appearing after removal of pterygium.

Key describes an epibulbar basal cell carcinoma in a 62 year old man with penetration of the globe and extension into the orbit.

Bachstez saw a carcinoma of the tarsal conjunctiva in a 36 year old woman. It showed microscopically areas of basal cell carcinoma and others of hornifying squamous cell carcinoma.

Valude and d'Autrevaux, Veil, Waetzold, Weismann-Netter and Blum report nevo-carcinomata of the conjunctiva.

Redslob found adenocarcinoma of the conjunctiva.

Narog reports a case of epibulbar dermoids of both eyes.

De Logu describes a nevus tumor in a 13 year old boy of the type of a dermo-epithelioma of Parinaud, showing strands of epithelium-like cells and cystic spaces lined with cells in the stage of mucous and vascular degeneration and filled with cell debris. Also, Carmi describes polycystic epithelial tumor of the conjunctiva as dermo-epithelioma.

Gros and Schecter consider Parinaud's dermoepithelioma as naevus cysticus.

Baquis found a lipodermoid of the plica semilunaris in an 18 year old girl.

Kranz saw a bilateral pterygium-like symmetical lipodermoid consisting of fat, glands, cartilage and smooth muscles.

Puscaria describes an epibulbar dermo-lipo-chondro-adenoma in a 6 week old girl.

Scoccianti saw in a new-born, bilateral teratomata of the fornices and bulbar conjunctiva containing fat, vessels, nerve fibers, sweat, Krause's, lacrimal and sebaceous glands, cartilage and bone. Also, Carmi reports two cases of teratomata of the conjunctiva.

Arcuri, Bozzoli, Rodin and Hall, Valude describe the histology of conjunctival nevi.

Nonpigmented nevi of the conjunctiva are reported by Clerici, Lumbroso.

Nevus tumors are described by Duclos and Mawas, Monthus.

Lijó Pavía and Dusseldorp describe a cystic nonpigmented nevus of the conjunctiva with epithelial budding.

Schneider describes a congenital vascular nevus of the conjunctiva consisting of dilated veins.

Carrère, Mawas and Prosper Veil, Tallei consider the nevi of the conjunctiva of epithelial origin.

Pohissov considers the nevi of the lid and conjunctiva of mesodermal origin, originating from the cells of the lymph vessels which become pigmented.

Oberhoff's theory is that the mother tissue of the nevi is in a chyme tissue which is morphologically bound to the walls of the smallest blood vessel.

Feigenbaum, Groenvall describe cases of supernumerary caruncles.

Peters finds hornification of the epithelium of the caruncle as cause of epiphora.

Nicoletti describes the various tumors of the lacrimal caruncle and semilunar fold.

Serra reports cases of papilloma and fibro-angioma of the caruncle.

Menestrina reports nevus tumor and endothelioma of the lacrimal caruncle.

Satanowsky, Adrogué and Senna describe epithelioma and lymphoma of the caruncle.

Radnot describes an oncholytic cyst and a giant cell sarcoma resembling a perithelioma of the caruncle.

Baquis found epithelial cyst in the caruncle of a 57 year old woman.

Cyst adenoma of the caruncle is reported by Green.

Baquis found sebaceous gland adenoma in the caruncle of a 58 year old man.

Antonibon describes papilloma of the caruncle in a 14 year old girl and 72 year old woman.

Scheerer describes vascular granulomata of the caruncle and the tear sac (granuloma teleangiektodes).

Menestrina found soft fibromata of the lacrimal caruncle.

Walravens describes a fibro-adeno-chondroma of the caruncle.

Bardanzellu reports a large angioma of lid, caruncle and semilunar fold.

Sciotto describes a case of melanoma of the lacrimal caruncle.

Lamb, Shumway describe pigmented nevi of the caruncle.

Wetzel reports a malignant melanoma of the caruncle in a 76 year old man.

Melanosarcoma of the caruncle is reported by Dorsey and Gillett.

Terrien and Veil report a nevocarcinoma of the caruncle.

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Chapter XIII

PATHOLOGY OF THE EYELIDS

The skin of the eyelids may be involved in many of the skin diseases of the rest of the body. The pathologic changes are sometimes restricted to the skin of the lids or they exist together with alterations of the skin of the face and skin of other parts of the body. The changes found on the lid are similar to those found otherwise in the skin.

1. Atrophy

In atrophy of the skin, the papillae are flattened and the elastic fibers disappear. Horn substance accumulates in hair follicles and sebaceous glands. It occurs especially in old age.

2. Scleroderma

In scleroderma, the cells are increased in the cutis and blood vessels are dilated. Connective tissue fibers are thickened and elastic fibers are torn and broken up. Finally the first enlarged connective tissue layer disappears. The etiology is unknown, but it might be a trophoneurosis due to changes in the central nervous system.

3. Changes in Pigmentation

Changes in the pigmentation of the skin appear if the skin is exposed to ultraviolet light or sun rays, the pigment is increased in the basement layer of the epithelium and appears also in its higher layers. In ephelides, the basal cells of the epithelium are strongly pigmented in circumscribed areas. In vitiligo and leukoderma, the basal cells contain circumscribed pigment, do not diffuse it, and have lost the ability to form pigment. Therefore, the dopa reaction is negative in these areas of the skin.

In *xeroderma pigmentosum,* excessive accumulation of pigment sets in in basal and prickle cells and pigment also lies free

between the cells and in the papillae; the epithelium extends budlike into the depth. Vessels of the cutis are dilated and surrounded by lymphocytes; collagenous fibers degenerate and elastic fibers clump and disappear. In the further course, carcinoma and sarcoma are formed. This disease appears hereditary-familial. Inferiority of the skin, which reacts pathologically to light stimuli, is accused as cause.

4. Eczema

In eczema, fluid collects between the cells of the rete, and by confluence of fluid spaces intra-epithelial cavities originate. These cavities are filled with serofibrinous fluid and the cells themselves contain fluid droplets. Epithelial vesicles burst and serofibrinous fluid pours onto the surface where the fibrin coagulates. Polymorphonuclears migrate through the epithelium, prickle cells multiply by mitosis and parakeratosis, and acanthosis may be present. Parakeratosis is a disturbance of the hornification; the keratohyaline layer is missing and a wide horn layer is formed in which cell contours and nuclei remain. Acanthosis is a disturbance of the prickle cell layer which shows many mitoses and proliferates to elongated and newly-formed interpapillary epithelial processes. The cutis becomes edematous, lymph and blood vessels are dilated and show sheathing, lymphocytes and plasma cells appear in the tissue, fibroblasts proliferate and elastic fibers may be destroyed. If blood and lymph vessels remain dilated permanently and the tissue stays edematous, induration sets in (sclerosing edema). The acute or chronic appearing eczematous inflammations of the skin have extrinsic and intrinsic causes among which are mentioned mechanical, thermal, chemical irritants and toxins.

5. Psoriasis

Psoriasis is a relatively frequent skin disease, characterized by parakeratosis and acanthosis. The subepithelial layers are edematous, have small circumscribed accumulations of polymorphonuclears and dilated vessels and periphlebitis. It is questionable whether the parakeratosis or the cutaneous inflam-

mation is primary as the latter is said to produce the former by nutritional disturbance.

6. Ichthyosis

Ichthyosis is characterized by hyperkeratosis. The stratum granulosum and lucidum is missing and a wide horn layer without nuclei lies on top of the epithelium. The horn masses extend into the hair follicles and efferent ducts of the sweat glands; sebaceous glands disappear. The lid skin is thin, showing connective tissue proliferation around vessels and minimal infiltration of lymphocytes and monocytes with some mast cells. It is probably a congenital anomaly.

7. Acanthosis Nigricans

In acanthosis nigricans, the horn layer is widened and the stratum lucidum is missing. The prickle cells are irregular, show mitoses and are increased and the interpapillary buds are lengthened and widened. The basal layer is highly pigmented, and the central layers and even the horn layer may contain pigment. It can affect the lid margin in old age.

8. Lupus Erythematosus

In lupus erythematosus, the hornification is heavy and horn substance covers the entrance of the follicles also. The cutis shows infiltration with lymphocytes which gather especially around dilated blood and lymph vessels. Elastic fibers swell and disintegrate. Its cause is uncertain.

9. Urticaria

Urticaria represents a circumscribed edema with intraepithelial vesicles and widened intercellular spaces and hydropic subepithelial connective tissue. It is brought about by idiosyncrasy, allergic manifestation or is a sequela of intestinal diseases.

10. Pemphigus Vulgaris

In pemphigus vulgaris, the epithelium is separated from the papillary body in the form of vesicles, and vesicles may also be

present intra-epidermally. Their content is sero-fibrinous fluid which may contain polymorphonuclears, eosinophils, epithelium and erythrocytes. The subepithelial layers are edematous and contain numerous lymphocytes, polymorphonuclears and eosinophils, dilated blood and lymph vessels and hemorrhages. The cause is uncertain but toxins and infection are assumed as cause.

11. Impetigo Contagiosa

In impetigo contagiosa, intra-epithelial vesicles are formed, containing polymorphonuclears and staphylococci. Polymorphonuclears migrate through the dilated intercellular spaces of the epithelium and the vessels of the papillary body are surrounded by polymorphonuclears, plasma and mast cells.

12. Changes of the Lid Skin in Generalized and Local Infections

In *typhoid fever* caused by the typhus bacillus, blood vessels are dilated and the derma shows edema, increase of fixed cells and very small necroses.

In *typhus fever* caused by Rickettsial bodies, capillaries are engorged and small vessels thrombosed. Arterioles show necrosis of the intima with swelling of the surrounding vessel wall.

In *measles,* which probably is a virus disease, the prickle cell layer is edematous and shows vesicles. Epithelial cells are expelled toward the corium and round cells are accumulated around vessels and hair follicles.

In *scarlet fever,* which probably is caused by streptococci, the cutis is edematous and fibrin and polymorphonuclears fill the superficial layers of the cutis and the epidermis.

In *variola* (small pox) and vaccinia, which are caused by filtrable elementary bodies (discovered by Paschen) which mature in the cell and produce as reaction of the cytoplasm darkly staining formations, so-called Guarneri's bodies, the papillae are edematous, and polymorphonuclears which frequently disintegrate under the influence of toxin surround vessels. Degenerative changes and necrosis affect the epithelium. Basal cells undergo coagulation necrosis and are finally changed

into homogeneous round bodies. The epithelium undergoes vacuolization and epithelial cells in the deep layers show balloon degeneration. Vesicles in the epithelium are covered by horn layer and have a base of degenerated cells, and are filled with fibrin, polymorphonuclears and cell debris. The epithelium proliferates in the vicinity of the vesicles, covering the defect after the burst.

Chickenpox (varicella) also shows epithelial vesicles with serous content, in later stages filled with polymorphonuclears. Basal and prickle cells show balloon degeneration and basal cells form giant cells by amitosis. Vessels of the papillae are sheathed by cells.

In *herpes,* many nuclei of the epithelial cells become homogeneous acidophil bodies (Lipschuetz bodies), and the cells finally become spheres with granular content. The basal cells show coagulation necrosis. Vesicles are formed when edematous epithelial cells disintegrate. Polymorphonuclears migrate through the epithelium and fibrin and erythrocytes are deposited in the tissue. Vessels of the papillae dilate, their endothelium proliferates and thromboses appear. They are surrounded by lymphocytes and polymorphonuclears.

In *erysipelas,* the tissue is edematous, filled with polymorphonuclears, and veins and capillaries are dilated. The epidermis is separated from the papillary body and the interspaces are filled with fibrinous fluid into which polymorphonuclears immigrate later.

In *anthrax,* blood vessels are very dilated, the tissue is edematous, lymph vessels and veins are occluded and hemorrhages appear. Heavy infiltration with polymorphonuclears sets in, the destruction of tissue leads to multilocular spaces, tissue is finally destroyed onto the subcutaneous layer and granulations are formed.

Specific granulomata are: (1) syphilis; (2) tuberculosis; (3) leprosy; and (4) ulcus molle.

Syphilis is seen as (a) primary, (b) secondary, (c) tertiary lesion and (d) as tarsitis syphilitica.

The primary lesion is characterized by accumulations of lymphocytes and plasma cells, especially around many newly formed

blood vessels with swollen and proliferating endothelial cells. Elastic tissue, fibroblasts and collagenous fibrils are present in large amount. The epithelium above the lesion disintegrates and an ulcer is formed.

In secondary lesions, infiltration with lymphocytes and especially with plasma cells is seen; the connective tissue is edematous, its cells are increased and giant cells may appear. Blood vessels are dilated and endothelial cells are swollen and proliferating. The epithelium extends buds into the subepithelial layer and epithelial cells are separated by fluid; parakeratosis sets in and horn layers are removed.

Tertiary syphilis is characterized by the formation of a gumma which is situated in the subcutaneous tissue but soon forms a deep ulcer. The gumma has outside lymphocytes, plasma cells, epithelioid and occasional giant cells; many newly-formed vessels are present, their walls swell and are filled with cells, the elastica is split, elastic fibers are increased, endothelial cells proliferate and finally occlude the lumen (endovasculitis obliterans). The center of the gumma is necrotic and contains liquefied tissue besides nuclear debris and diffusely dissolved chromatin, but elastic fibers persist. The necrotic tissue finally perforates, forming an ulcer. Finally, granulation tissue appears and a scar is formed.

Circumscribed gummatous changes in the tarsus are called tarsitis syphilitica. The nodules consist of lymphocytes and plasma cells besides large, faintly stained cells of epithelioid character. Elastic tissue is present in great number and vessels show endovasculitis.

Tuberculosis is characterized by accumulation of tubercles of typical structure with lymphocytes surrounding epithelioid and giant cells and caseation in the center. Diffuse lymphocytic infiltration is present between the tubercles. The epithelium proliferates budlike into the depth. Tuberculous tissue may stay enclosed in the subcutaneous tissue, but granulations also perforate the epithelium to form ulcers. The tarsus and lid glands may be affected. Meibomian glands disintegrate on one place and may proliferate in other areas. The granulations

may organize and form scar tissue and even calcification. Frequently, lupus vulgaris of the face continues onto the lid, but also tuberculosis of the conjunctiva extends into the lid. Tubercules of the periosteum frequently break through the lid skin forming fistula (scrofuloderma). The lid may also be affected metastatically.

In *leprosy,* the lid is infiltrated with lymphocytes; plasma cells and connective tissue cells proliferate in the form of epithelioid cells. Characteristic is the leprosy cell, which appears vesicular and vacuolated, has a small marginal nucleus and is studded with lepra bacilli which may also occlude lymph spaces and fill in a great number of blood vessels. Vessels are surrounded by lymphocytes, plasma cells and epithelioids. Nerves show similar sheathing and nerve fibers disintegrate in granular masses.

In *ulcus molle* (soft chancre), polymorphonuclears and lymphocytes fill the connective tissue which rapidly disintegrates and coagulates. Peripheral to it are plasma cells which also surround the deep vessels. Epithelium swiftly disintegrates and an ulcer is formed which is surrounded by proliferating prickle cells. The streptobacillus Unna-Ducrey is present in dense rows.

13. Diseases of the Lid Glands

Diseases of the lid glands are: (1) comedo, (2) acne rosacea, (3) hordeolum, (4) furuncle, (5) chalazion.

Comedo and acne vulgaris affect the efferent ducts of the sebaceous glands and the hair follicles which are covered with a horn layer, finally occluding the widening and ducts appearing cystic. If bacteria, mostly staphylococci, enter, the walls become infiltrated; the epithelium is filled with polymorphonuclears, and the surrounding connective tissue with lymphocytes, plasma cells and mast cells; vessels show perivascular infiltrates. The hair is expelled and foreign body granuloma forms around the suppurating sebaceous gland containing phagocytes and foreign body giant cells. Finally this tissue is organized.

In *acne rosacea,* vessels are very dilated and surrounded by infiltration with lymphocytes, polymorphonuclears and plasma cells, connective tissue proliferates and the tissue becomes edematous. Infiltrates gather around hair follicles and sebaceous glands which are entered by polymorphonuclears and surrounded by foreign body granuloma.

In *hordeolum,* the follicles of the cilia and their glands show suppurative inflammation as bacteria enter them. Polymorphonuclears fill sweat and sebaceous glands. The septa between the lobules of the latter disintegrate and a large abscess cavity is formed. Polymorphonuclears may enter the tarsus from here and perforate toward the conjunctiva. Polymorphonuclears disappear in the healing stage from the cavity, which becomes filled with granulation tissue.

Furuncle represents a suppurative inflammation of the hair follicles, the sebaceous and sweat glands and their vicinity, reaching into the subcutaneous tissue and forming necrosis.

Chalazion is caused by obliteration of the efferent duct of the meibomian glands. The secretion is retained and the glands disintegrate, the fat is decomposed and acts as foreign body or gives rise to anaphylactic reaction. Perhaps bacteria enter and produce inflammation of the glands. First fibrin mixed with polymorphonuclears is exuded into the glandular lobule and the tarsal tissue. The glandular epithelium is dissolved and the surrounding connective tissue fibers disintegrate. In the further course, lymphocytes appear, connective tissue starts to proliferate and finally a granulation tissue forms, consisting of lymphocytes, plasma cells and few polymorphonuclears, besides numerous fibroblasts and epithelioids. A capsule of connective tissue is formed, all around which may show mucous degeneration. Histiocytes and foreign body giant cells in the granulation tissue may show intensive fat phagocytosis. Further, spaces appear with coagulated fine masses, probably the result of necrosis of tissue. The glands disappear entirely in the area of the granulation tissue or broken up rests are present. The glands in the vicinity are normal or are pushed aside by granulation tissue and may be degenerated. The covering conjunctiva is thickened, infiltrated with round cells and folded.

14. Diseases of the Lid Margin and Cilia

Diseases of the lid margin and the cilia are: (1) blepharitis and (2) poliosis.

Blepharitis is seen as: (a) blepharitis squamosa and (b) blepharitis ulcerosa.

The former is characterized by parakeratosis, acanthosis and scales filled with fat lying on the epithelium. The prickle cells of the epithelium are separated by fluid and serous intraepithelial vesicles appear, the cover of which is formed by horn layer. The subepithelial tissue is infiltrated with lymphocytes. Hair follicles show parakeratosis and acanthosis and are filled with lymphocytes which can also be found in sebaceous glands. In the latter, the changes are more severe, frequently due to secondary infection by staphylococci. The epidermis and the hair follicles show parakeratosis, acanthosis and serous imbibition of the epithelium with formation of vesicles and immigration of polymorphonuclears, lymphocytes and plasma cells. Polymorphonuclears also fill the hair follicles and infiltrate the sebaceous and sweat glands and the surrounding connective tissue from which again the deep parts of the hair follicles are affected. The papillae show dilated vessels and dense infiltration with lymphocytes, plasma cells and polymorphonuclears. Cilia can pass through serous and suppurative vesicles of the epidermis. When hair follicles and their glands become suppurative, hairs are expelled and granulation tissue appears, which later is organized into scars.

In *poliosis,* the cilia become grey by loss of pigment and air bubbles appear in small slits surrounding the medulla of the hair. The cause is unknown.

15. Degenerative Changes

Degenerative changes are (1) hyaline and (2) amyloid degeneration.

Hyaline degeneration is noted as thickening and homogenization of the connective tissue bundles in the skin and tarsus, deposition of homogeneous substance into the tissue spaces of the connective tissue and transformation of the intercellular

substance and of the vessel walls into an homogeneous structure. It is seen in old age and in old inflammatory proliferations.

Amyloid degeneration affects the connective tissue and vessel wall. Rounded or cylindric, thick homogeneous masses appear in the tissue, showing starchlike reaction, staining red with iodine. They are surrounded by inflammatory tissue which also contains giant cells. Amyloid, which is not a uniform substance, originates from the protein of the tissue or is deposited into the tissue. It is derived from plasma cell masses or from hemorrhages, or it is considered as product of the protein metabolism produced by cells and enzymes which are able to decompose protein freed from endothelial cells and disintegrating polymorphonuclears. Amyloidosis of the lid is usually secondary to amyloidosis of the conjunctiva. It is part of a general amyloidosis in which usually the blood vessels also are affected, or of a local amyloidosis in which the blood vessels usually are free. Amyloidosis is found in trachoma, tuberculosis and sarcoma.

Hypertrophy and atrophy. Hypertrophy is represented by elephantiasis, and atrophy by blepherochalasis.

Elephantiasis is found (1) as elephantiasis teleangiectatica and (2) elephantiasis mollis (lymphangiectatica). The papillae are flattened and the derma is thickened by enormous connective tissue proliferation. The subcutaneous tissue is also increased and the connective tissue bundles are sclerosed, but edema, too, can prevail in the connective tissue and muscles. Lymphocytes and accumulations of plasma cells can be seen. Lymph vessels are increased and dilated and filled with a serum-like fluid and blood vessels also are dilated. Elephantiasis is congenital or acquired due to occlusion of the lymph- and blood circulation. Erysipelas is the most frequent cause. However, there are also cases of traumatic and neoplastic origin.

In *blepherochalasis,* the papillae are flattened, the connective tissue is loosened and the elastic fibers disappear. Blood and lymph vessels are dilated. It is a congenital malformation or acquired due to endocrine disturbances, transitory low-grade inflammation and angio-neurotic edema.

Positional changes. Positional changes of the lids are known as (a) ectropion and (b) entropion.

In *ectropion,* the exposed conjunctival epithelium is edematous and the goblet cells disappear. The epithelium shows long projections, and round cells infiltrate the subepithelial tissue in which the elastic fibers disappear. The efferent ducts of the meibomian glands are dilated and the glands of the skin increase adenoma-like. Ectropion is usually found as senile change.

In *entropion,* glands of the tarsus and the lid margin diminish. Connective tissue scars appear in the tarsus and in the conjunctiva and hair follicles are displaced. Trachoma is its frequent cause.

16. Neoplasms

Neoplasms are: (1) Epithelial of benign and malignant nature; (2) congenital, consisting of epithelial and mesodermal structure; (3) mixed tumors; (4) neuro-ectodermal tumors and (5) mesodermal tumors of benign and malignant nature.

Epithelial Tumors

Epithelial tumors of benign nature are (a) warts, (b) papillomata, (c) cornu cutaneum, (d) molluscum contagiosum, (e) cysts of the adnexa of the skin and (f) adenoma.

The *warts* are divided into verrucae juveniles, verruca vulgaris and verrucae seniorium. In the verrucae juveniles, the epithelium is thickened, shows some acanthosis and immense hyperkeratosis. In the verruca vulgaris, the horn layer is much increased and the epithelium sends projections into the underlying tissue. It becomes by enlargement, elongation and branching of the papillae a papillomatous wart. The subepithelial tissue shows infiltration with lymphocytes and plasma cells. In the verrucae seniorium, the surface is irregular and the epithelium is thickened with projection into the depth forming an epithelial network. The basal cells are deeply pigmented. The horn layer is somewhat thickened and forms in some areas horn masses which are embedded in a cuplike depression.

The *papilloma* is characterized by branchlike ramification of the papillae and widening of the epithelium with prickle cells

undergoing mitosis. The epithelium proliferating beyond the surface elevates the papillae and proliferates also in projection into the papillary body and divides it in this way into branch-like, mostly thin fibrillar strands which are occasionally densely infiltrated with lymphocytes and plasma cells. The horn layer of the epithelium is minimal. The relation in the amount of epithelium and connective tissue varies.

In *cornu cutaneum,* the papillae are very elongated and contain large blood vessels. The horn layer is widened and appears high and conical as there is no desquamation. The hornification is normal but also parakeratosis is present to a great extent.

The *molluscum contagiosum* is characteristic as the epithelium contains typical molluscum cells. Circumscribed, nodular enlargements of the epithelium are formed in which the basal cells are unchanged. Vacuoles appear in the prickle cells, containing granular and fine fibrillar masses. The nuclei are flat and displaced to the cell margin and the cytoplasm becomes slowly more hyaline. The stratum granulosum contains masses of keratohyaline-like substance, the cell nucleus disintegrates and the cell periphery hornifies. Here the molluscum cells develop, occupy in great number the center of the node and contain a relatively large homogeneous mass which may be expelled after rupture of the cell. Very small spherical particles have been shown to be a filtrable virus, forming, by confluence, the inclusion bodies in the cells (Strongyloplasma hominis, Lipschuetz).

Cysts of the skin and its adnexa are: (a) atheroma and (b) cysts of the glands of the lid.

Atheroma (sebaceous cyst) which establishes itself on the eyebrow, rarely on the upper lid and nasal root, is lined by degenerating stratified squamous epithelium surrounded by a fibrous capsule; its content consists of desquamated epithelial cells, cell debris, horn masses, fat, cholesterol and hair particles. When the tissue becomes necrotic, calcium is deposited. It originates from skin epithelium displaced into the depth (embryonic remnants), from hair follicles or occluded sebaceous glands as retention cysts.

Closely related to the atheroma is the milium which is considered as a tiny sebaceous cyst, but it is also explained as horn cyst of the hair follicle. In the middle part of the hair follicle, especially in a lanugo hair, dilatation may occur with deposition of lamellated horn masses, which are surrounded by stratified squamous epithelium. A true cyst is formed or the epithelial sac is open towards the surface of the skin.

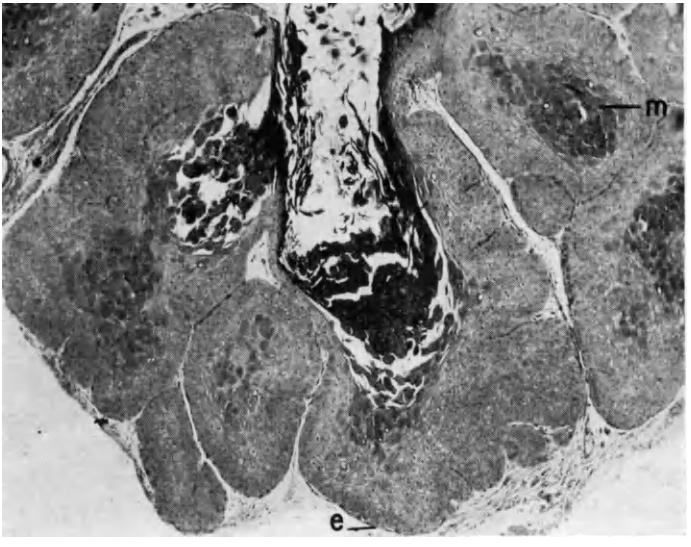

FIG. 55.—MOLLUSCUM CONTAGIOSUM OF THE LID. e, stratified squamous epithelium; m, molluscum bodies. 70×.

Cysts of the lid glands are: (1) Cysts of the sweat glands, (2) cysts of the accessory tear glands, (3) cysts of the sebaceous glands and (4) cysts of the meibomian glands.

Cysts of the sweat glands (hydrocystoma) are cysts of the sweat glands of the cilia (Moll's glands) and sweat glands of the lid surface. The lining is a flat or cuboidal epithelium and the content consists of serous or colloidal masses and sometimes of fat crystals. The cysts are situated in the subcutis and cutis and reach up to the epidermis which covers them externally. The blocked efferent duct of the gland is dilated and the dilation extends into the secretory part of the gland.

Cysts of the accessory tear glands (Krause's glands) represent spaces lined by a cuboidal epithelium. They originate from occluded ducts, often due to scars, as in trachoma.

Cysts of the sebaceous glands (Zeiss glands) are small sebaceous cysts on the cilia. They are formed through occlusion of the hair follicle and dilation of the sebaceous glands.

Cysts of the meibomian glands are mostly dilated ducts and are formed through hyperkeratosis in the latter with closure of the ostium. The cells of the duct are flattened.

Adenomata are: (1) adenoma of the sweat glands, (2) cyst-adenoma, (3) adenoma of the accessory tear glands, (4) adenoma of the sebaceous glands and (5) adenoma of the meibomian glands.

Although in cysts, the lumen is dilated by closure, in adenoma the glandular tissue proliferates and again can form cystic spaces.

The adenoma of the sweat glands (syringo-cyst-adenoma) which is rare grows from the Moll's glands and shows tubular formations with two layers of epithelium, pseudo solid strands and small cysts. The epithelium is accompanied by a basement membrane. Sometimes, also, the interstitial connective tissue proliferates intensively and may also become hydropic. A special form of the adenoma of the sweat glands is the epithelioma hydroadenoides cysticum, in which rows of flat epithelial cells appear, showing many branching netlike proliferations and budding.

In cyst-adenoma, the glandular tissue proliferates, forming large cysts. Into their lumen the epithelium is projected papillomatously. Its origin is mostly to be found in sweat glands.

Adenoma of the accessory tear glands is situated on the orbital margin of the tarsus and consists of tubules with an epithelium of two layers which eventually also form projections into the lumen.

The adenoma of the sebaceous glands (adenoma sebaceum) consists of hypertrophic sebaceous glands with proliferating lobules which usually show an irregular sebaceous formation. The lobules frequently show a great number of cells of the cuboidal basal cell type. Also, epithelial strands and small

cysts are formed. Closely related is the epithelioma adenoides cysticum, which shows bulblike cysts and netlike and budlike branching of the epithelium in connection with the epidermis into which small cysts are enclosed. The adenoma of the meibomian glands shows increase of normally appearing lobules and solid strands of epithelium in the tarsus.

Carcinoma is seen: (a) as basal cell carcinoma, (b) as squamous carcinoma, and (c) as adeno-carcinoma.

(a) Basal cell carcinoma (ulcus rodens, rodent ulcer) is characterized by solid, irregularly outlined epithelial projections. Their connection with the basal cells of the epidermis can often be proved. Cylindric cells with hyperchromatic nuclei are situated at the periphery of the epithelial projection and toward the center there are epithelial cells of different shape and size, elongated cells, balloon-like cells and polygonal cells, showing hyperchromatic nuclei and degeneration. Mitoses and amitoses are found. Langhans' cells move peripherally in the epithelium and their cell processes become fine. The surrounding connective tissue is of varying density and participates actively in the growth of the tumor. The cylindric basal cells perforate the basement membrane if and where such is present and infiltrate the connective tissue. This is filled more or less densely with lymphocytes, plasma cells and eosinophils. The surface epithelium is often eroded and an ulcer is formed which frequently is surrounded by polymorphonuclears. A pigmented basal cell carcinoma contains pigmented cells in the epithelium and stroma.

(b) Squamous carcinoma shows proliferation of prickle cells of different sizes and shapes which infiltrate the deeper tissue in rootlike branching. Epithelial fibration (latice-fibers) can be demonstrated by silver stain. The center of these epithelial strands undergo hornification and horn pearls appear showing parakeratosis. The epithelial masses are often surrounded by lymphocytes and plasma cells.

A basal-squamous cell carcinoma contains both formations: mostly epithelial strands similar to those of the basal cell carcinoma which have in their interior the structure of a squamous carcinoma.

(c) Adeno-carcinoma develops from the glands of the lid, from the glands of Moll, Zeiss and Meibom and sometimes represents a malignant degeneration of an adenoma. Occasionally, cystic degenerations are seen in a basal cell carcinoma which in this way becomes similar to an adenocarcinoma. This shows adenoma-like formations with irregular proliferating cell layers and degeneration of the cells. The epithelial proliferation extends into muscles and tarsus.

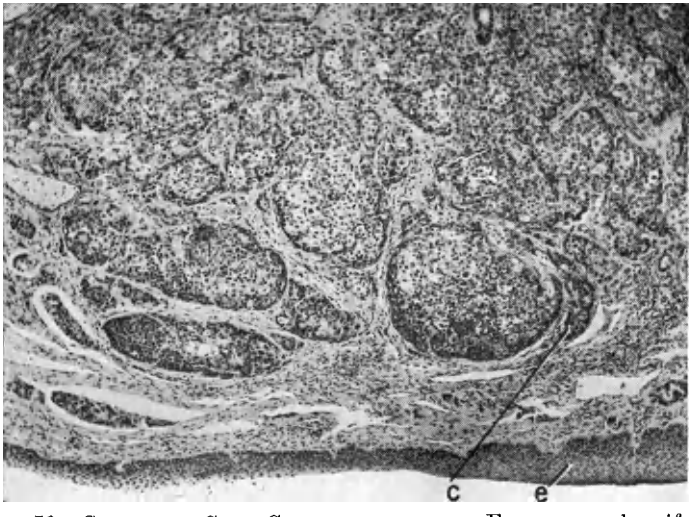

FIG. 56.—SQUAMOUS CELL CARCINOMA OF THE EYELID. c, hornifying squamous cell carcinoma; e, surface epithelium. 70×.

Dermoid tumor (dermoid cyst) consists of a stratified squamous cell epithelium with or without hornification, hair follicles, sebaceous and sweat glands, striated muscles and coarse connective tissue bundles, often a cystic lumen filled with oily masses. Calcification may set in. This congenital tumor is formed when epithelium is cut off from the surface in embryonic clefts and above bone sutures. Therefore, it is located between the root of the nose, eyebrow and inner canthus. It shows connection with the periosteum and extends into the orbit.

The *teratoma* contains, besides elements of the skin and fat, striated and smooth muscles and intestines with glands.

Mixed Tumors

Mixed tumors are called rare tumors, the classification of which is difficult, since elements of different origin are enclosed in them, epithelial as well as mesodermal tissue. They may be similar to the mixed tumors of the tear gland and salivary glands, showing adenoma-like formations and proliferation of connective tissue. Tumors are found containing adenomatous, sarcomatous and fibrous elements or epithelial, cartilaginous and fibrous elements (fibro-adeno-sarcoma, fibro-chondro-epithelioma).

Neuro-ectodermal Tumors

Neuro-ectodermal tumors are the nevus and the malignancy originating from it, and the rare benign ganglioneuroma.

The *nevus* is characterized by the nevus cell nests. Beneath the otherwise normal epithelium, in connection with it or without connection, nests of closely packed epithelial-like cells with rounded nuclei and distinct chromatin granules are found. The nests are round, oblong, small or large. They are close together or separated by a large amount of connective tissue, which also often sends fine fibrils between the cells of the nests. The cells may show different degrees of pigmentation and pigment may also be deposited between the cells and in the connective tissue. The nevus cells are now assumed to be derived from the sensory end organs of the papillae but formerly were believed to derive from the basal cells of the epithelium or from the Langerhans' cells which are situated in the epithelium, but are said to be of mesodermal origin. Nevus cells give the dopa reaction.

Malignant melanoma may originate from a nevus and it contains groups of spindle-shaped cells of different size, and different densities of pigmentation surrounded by small connective tissue septa; it also contains various cells of rounded or polygonal shape and giant cells. It is similar sometimes to carcinoma (nevus carcinoma), more frequently to sarcoma (melanosarcoma).

The *ganglioneuroma* consists of a meshwork of medullated and nonmedullated nerve fibers with deposition of clump-shaped ganglion cells with foamy cytoplasm and degenerated nuclei.

Closely related is the neurinoma (Schwannoma) which proliferates from the Schwann cells of the medullated nerves and contains, besides nerve fibers and connective tissue strands, numerous fibroblast-like cells.

Mesodermal Tumors (Benign)

Connective tissue or mesodermal tumors of benign nature are: (a) fibroma, (b) neurofibroma, (c) lipoma, (d) xanthoma (xanthelasma), (e) chondroma and osteoma, (f) angioma and (g) myoma.

The *fibroma* consists of proliferating fibroblasts of equal shape in different densities and is encapsulated. The fibroblasts are numerous and lie close together with a small amount of intercellular fibrillar substance (soft fibroma), or they are present in relatively small numbers but the fibrillar substance is abundant (hard fibroma). A hard fibroma often develops in scars (keloid).

A *neurofibroma* is characterized by whirl-like arrangement of fibroblasts and connective tissue bundles in which rests of medullated nerve fibers can be demonstrated easily by special staining methods. Apparently they originate from the fibrous nerve sheaths (endo- and perineurium), but a similar tumor may also originate from the ectodermal sheath cells of the nerve, the Schwann cells (neurinoma). Neurofibromata are mostly multiple and pedunculated and part of a generalized neurofibromatosis (von Recklinghausen). It represents a congenital degeneration and is associated also with hydrophthalmos. Elephantiasis nervorum (mollis, molluscum) is a diffuse connective tissue proliferation of a certain region, as of the lid, the face, the tongue (hemilateral facial hypertrophy), originating from the nerve sheaths of the subcutaneous, resp. submucous tissue. The neuroma racemosum forms strands of a dense network of degenerated nerves surrounded by proliferations of the endoneurium.

The *lipoma* represents an increase of mature fat cells surrounded by a connective tissue capsule. It is multiple and congenital or appears in advanced age. In ptosis adiposa, orbital fat extends through holes of the orbital fascia into the lid.

The *xanthoma (xanthelasma)* has, beneath the epithelium, accumulations of xanthoma cells which appear as large polygonal vacuolated cells with small nuclei rich in chromatin. The cystoplasm contains lipoid droplets which are dissolved from the cells in the usual fixation methods and therefore the cells appear honeycomb-like. The droplets may be stained with sudan III. Giant cells may be found. Fat droplets are further seen in and between basal cells of the epidermis, and in the cells of the vessel walls. The tumor probably arises from adventitia cells which accumulate lipoid due to a disturbed fat metabolism.

The *chondroma* and *osteoma* originate by displacement of embryonic elements of the maxilla as congenital tumors, but they may also appear in later age by metaplasia. The chondroma shows a homogeneous ground substance with large, clear cells in groups of two and three. The osteoma shows the lamellar structure of the bone, occasionally with the lamellae arranged circularly around Haversian vessels, and rows of osteoblasts and occasional osteoclasts in the marrow. Abnormally, the tarsus may contain cartilage. Cartilage may be present first and may be dissolved by ingrowing vessels and transformed into bone. Bone may develop in a fibroma and sarcoma, but it may also be formed in inflammatory tissue when granulations organize.

The *angioma* is: (a) lymphangioma or (b) hemangioma.

The lymphangioma may be seen (1) as lymphangiectasis (lymphangioma simplex) and (2) as lymphangioma proper (lymphangioma cavernosum and cysticum). The latter can be very extensive and affect the lids, conjunctiva and orbit. Histologically, a connective tissue network is found, with large spaces lined only with endothelium and containing a coagulated granular content. The septa between the spaces are thin and in places incomplete. Few lymphocytes are found inside or outside the lymph spaces.

The hemangioma can be found (1) as telangiectasia and (2) as hemangioma proper, which again, respectively, is angioma simplex and cavernosum. The former consists of thin walled small vessels and capillaries with more or less well-developed septa between them and proliferation of endothelial cells without

lumen. The latter shows large blood-filled spaces with thin walls, which often are incomplete so that lumina communicate with each other. A hemangioma often produces atrophy of the surrounding tissue.

Myoma is: (a) leio- and (b) rhabdomyoma.

The leiomyoma shows proliferation of smooth muscle fibers. They are numerous and uniform spindle-shaped cells, with oval nuclei lying closely together.

The rhabdomyoma consists of large cells with large, rounded nuclei without striation or striation in a small cell process. Stages to well-formed striated muscle fibers can be seen. Amyloid degeneration and ossification may set in.

Mesodermal Tumors (Malignant)

Mesodermal tumors of malignant nature are: (1) sarcoma, (2) melanosarcoma, (3) lymphosarcoma, (4) endothelioma and perithelioma, and (5) rhabdomyosarcoma.

Sarcomata are seen as round, spindle cell and epithelioid cell sarcoma; further, mixed cell sarcoma is found, containing also polygonal and giant cells. Sarcomata rapidly infiltrate the connective tissue, globe and orbit. If a sarcoma extends through the epithelium to the surface, it may ulcerate. A sarcoma of higher tissue maturity is the fibrosarcoma, which shows in areas distinctly the arrangement of the fibroma with uniform fibroblasts, and in some areas the malignant degeneration with spindle-shaped cells of different sizes and types of nucleus.

The *melanosarcoma* is multiform, containing round and spindle cells, large pigmented and nonpigmented cells. It may also originate from areas in which pigmented nevi are not preformed.

The *lymphosarcoma* consists of small and large lymphocytes and has a tendency to infiltrate the surrounding tissues. It is not always easily distinguished from lymphoma appearing in leukemia and aleukemic leukemia.

The *endothelioma*, originating from the endothelia of lymph- and blood vessels, shows cells with various nuclei which are partly rounded, partly oval or spindle-shaped in epithelial-like arrangement, often showing concentric arrangement. Sometimes it shows alveolar structure with a rather well developed connective

tissue capsule; however, infiltrating proliferation can be found also, and sometimes it undergoes hyaline degeneration. Occasionally the cells proliferate in cylindric shaped strands. As the accompanying tissue degenerates, occasionally mucoid, the cell rows are separated by apparent spaces in the tissue (cylindroma). Vessels may be enclosed in the tumor. The *perithelioma,* which originates from the adventitia cells of the vessels, show rounded and cylindric cells arranged epithelial-like as mantles around vessels. The cells are arranged fascicularly and radiate perpendicular to the axis of the vessel.

The *rhabdomyosarcoma* develops from a rhabdomyoma and frequently shows the transition from the benign to the malignant form. The cells become very large and have large round or oval nuclei and a small process with faint striation.

READING OF SOURCE MATERIAL

De Cristofaro found atrophy of the skin of the upper lid resulting in marked transparency.

Gallenga found the elastic tissue of the tarsus affected in generalized argyrosis.

Stenbeck describes scleroderma of the lid and orbit with increase of the collagenous connective tissue in subcutis, around muscles and vessels and deposits of fibrin.

Puscariu and Lazarescu report cases of xeroderma pigmentosum with multiple epibulbar epitheliomata.

Fibroma and sarcoma develop in xeroderma pigmentosum, according to Junès.

Guyton and McLean describe an isolated rheumatic nodule of the upper lid showing a necrotic center surrounded by fibroblasts, macrophages and newly-formed capillaries.

Khalil finds in tarsitis syphilitica infiltration of lymphocytes, numerous dilated blood vessels with thickening of the adventitia. Sabbadini describes necrosis in tarsitis syphilitica. Ryss-Zalkind, Vejdovsky observed gummata of the lids.

Bencini, Lijo Pavia, Salvati report on tuberculosis of the lids.

Muzaffer describes a case of fibrous tuberculosis of the lids.

Gallenga reports nodular tuberculosis of the lid.

Bencini saw a subcutaneous tuberculous nodule in the skin of the lid arising after a blow with a fist.

Wilmer reports bilateral tubercle-like nodules of the lids and episclera, and Pascheff bilateral tuberculomata of the lids and the orbit.

Kreiker describes endogenous tuberculosis of the tarsus.

Ernsting, Holm describe Boeck's sarcoid of the lids.

Fernandez and Soto report tubercle-like leprotic lesion of the eyelid.

According to Adamjuk, the tarsus in trachoma shows some infiltration with plasma cells, lymphocytes, polymorphonuclears, eosinophils and hyaline degeneration.

Ciaceri describes chronic edema and diffuse lymphocytic infiltration in lid skin and sclera in leontiasis ossea.

Krueckmann calls the inflammation of the meibomian glands accompanying seborrhea "comedo of the meibomian glands" as the efferent duct may be occluded by dark horn masses.

Schall describes the pathologic changes of the chalazion which originate, in his opinion, by stasis of the secretion in the meibomian gland without infection.

Histologic findings of chalazion are further published by Kuemmel, Schubert.

Franklin and Cordes describe an ossified chalazion containing fat marrow.

Kalt describes inflammation of all four tarsi with accumulations of epithelioid and giant cells in the meibomian glands and polymorphonuclears and giant cells in the subconjunctival tissue and calls the pathologic changes "diffuse chalazion."

Wirth reports chronic inflammation of the meibomian gland.

Cowper, Gifford report on the pathology of the meibomian glands in cases of blepharitis.

Cosenza finds cystic dilation of the tubuli of the meibomian glands and infiltration with lymphocytes, monocytes, plasma cells and polymorphonuclears (perimeibomitis).

Schreiber reports that the life cycle of the eyelashes is about 120 to 150 days and that they grow out to full length in 8 to 10 weeks. They grow faster in diseases of the lid margin.

If the eyelashes become gray, the granular pigment disappears first (Jacobi).

According to Antinobon, the hair follicles are flattened after electrolysis of the cilia; the bulbus of the hair is destroyed and granulation tissue substitutes the follicle.

Thygeson finds very frequently a budding yeast form—pityrosporum ovale—and pathogenic staphylococci in the scrapings from the lid margin in chronic squamous and ulcerous blepharitis.

According to Carletti, elephantiasis of the lids is caused by filaria or recurring erysipelas and shows histologically edema, increase of connective tissue, lymphocytic infiltration, dilation of vessels and degeneration of muscles and elastic tissue.

Fage finds in elephantiasis of the lids inflammatory changes of the lymph vessels, very dilated blood vessels, extensive hypertrophy of the submuscular tissue with many young connective tissue cells and much fat tissue.

Mienicki describes a case of acquired elephantiasis of the lids in a 14 year old girl after recurrent erysipelas, showing perivascular round cell infiltration, proliferation of fibrocytes and connective tissue bundles and dilation of lymph spaces and vessels.

Candian found in elephantiasis of the lid histologically numerous inspissated and tortuous nerve fibers embedded in cellular connective tissue.

Rintelen reports a case of elephantiasis of the lid due to primary hypertrophy of the connective tissue in the tarsus and conjunctiva as symptom

of the osteo-dermopathic syndrome of Tourraine-Solente-Golè which consists in enlargement of hands and feet and thickening of the skin.

Towbin and Adamyk describe as histologic changes in blepharochalasis irregularity of the epithelium, accumulation of adventitial cells around capillaries and veins, showing their endothelium thickened, hyalinization of the connective tissue and club-shaped thickenings of elastic fibers, the majority of which have disappeared.

The skin in blepharochalasis of a 21 year old girl showed the epidermis reduced, the subcutaneous tissue highly atrophic, the elastic fibers irregular, degenerated and broken up and brown and yellow intra- and extracellular pigment (Accardi).

Verhoeff and Friedenwald, Stein find in blepharochalasis the epithelium thinned with vacuoles in the basal and prickle cells, the papillae flattened, the connective tissue fibers small and the subcutaneous tissue diminished. Friedenwald finds also decrease of the elastic fibers.

Folding of the conjunctiva in cases of blepharochalasis is found by Schreiber.

Ascher reports cases of blepharochalasis associated by mucosa folds of the upper lip and goiter. Similar reports come from Eigel, Wirths. Edema and perivascular infiltrates of lymphocytes and polymorphonuclears are seen.

Amyloidosis of the lids is reported by Gabrielides, Hoffman, Satanowski and Sena, Wallgren and Vannas, Wright. Gabrièlidés describes an amyloid degeneration of the lid with calcareous and osseous deposits and considers it as a product of a luetic infection. Wallgren and Vannas believe that the amyloid does not originate from cells, but is deposited in the tissue and transported by the lymph vessel.

Aubaret, Rouslacroix and Hermann describe the histology of the ectropion of the lid.

Weiner, Gaynor and Oshewitz describe granuloma inguinale of the eyelid containing monocytes with Donovan's corpuscles.

Feigenbaum found in leishmaniasis of the lid diffuse infiltration with epithelioid cells, plasma cells, lymphocytes and occasional giant cells.

Calderaro describes skin leishmaniasis of the lids with Leishman-Donovan bodies inside of large mononuclears, and granulation tissue consisting of lymphocytes, epithelioid and plasma cells. Kamel, too, saw cases of leishmaniasis of the lids.

Forsberg and Stern saw blastomycosis of the eyelids.

Tisseraud saw botryomycosis of the eyebrow in a 10 year old child, Schmeltzer a vascular granuloma of the lids produced by botryomycosis.

Esteban, Gifford and Konne removed filaria loa from the lids.

Saba saw a filaria inermis of the eyebrow encapsulated in connective tissue surrounded by polymorphonuclears and giant cells.

Harley found in a chalazion of the lid a larva of dermatobia hominis.

v. Hippel found the insect demodex folliculorum in cystic meibomian glands.

Rifat reports cases of granulomata of the lid, consisting of lymphocytes, plasma cells and large cells with clear cytoplasm.

Aldridge and Kirk described as mycetoma of the lid of a 4 year old girl a tumor which showed nonspecific infiltration with plasma cells, polymorphonuclears, occasional giant cell and hyaline fibrosis.

Mita saw two cases of foreign body tumors of the lid following operations for acute mastoiditis in which the wound was filled with "Granugenol-Knoll." The tumors consisted of proliferating endothelial cells, tough connective tissue and foreign body giant cells.

Schubert describes chalazia which were histologically foreign body tubercles, one around the wing of an insect.

Dejean, Harant and Vernières find a recurring pseudotumor in a 25 year old woman showing plasma cells, giant cells, hyaline degeneration and necrosis of the eyelid; further Bachstez reports inflammatory pseudotumors of the lids.

van der Hoeve reports malignant neoplasms of the lids and orbit, and Hollander and Krugh describe various types of lid cancer.

Feingold reports cases of papilloma, hemangioma and melanosarcoma of the eyelids.

Mawas finds that in simple and precancerous hyperplasia of the epithelium of the skin of the lid the so-called Langerhans cells proliferate and become hyperplastic without changing their form. They can be found also in squamous cell and basal cell carcinoma.

Wieczorek describes a papilloma of the lid margin.

Precario, Redaelli describe cutaneous horns of the lids.

Gualdi describes as lid horn an extensive hyperkeratosis, with parakeratosis, accompanied by infiltration with lymphocytes, plasma cells and disappearance of the elastic tissue.

Cornu cutaneum degenerating to carcinoma is reported by Heine, Muñoz Urra, Redaelli.

Contino describes three phases in the epithelial cells in molluscum contagiosum of the lid: (1) hydrolysis of the cytoplasma, (2) appearance of Lipschuetz bodies, and (3) incomplete keratinization.

Julianelle and James, Offret and Duperrat found molluscum contagiosum affecting the skin of the lid, the tarsal and bulbar conjunctiva and the cornea.

Molluscum contagiosum of the lid is further reported by Castroviejo.

Lijo Pavia and Dusseldorp report a cystic nonpigmented nevus of the conjunctiva with budding of the epithelium (dermoepithelioma of Parinaud).

Cysts of the lid glands are described by Gabrielides, Hagedoorn, Pereyra.

Keckich describes a large retention cyst of the eyelid lined with cuboidal epithelium originating probably from sweat glands.

Greenbaum describes syringocystomata of the eyelid consisting of strands of cylindrical cells and cystic spaces.

Arzt describes tumors in the lid having cystic formations and solid epithelial strands as epithelioma hydroadenoides.

Purtscher and Wendlberger observed a follicular nevus of the lid in a case of Bourneville-Pringle's disease, containing rudimentary sebaceous glands and epithelial cysts.

Adenoma of the sweat gland of the lid is reported by Golay, Greenbaum.

Hagedoorn found an adenoma hydroadenoides of Moll's glands.

Bertoldi, Soetojo report cases of adenoma of the meibomian glands.

Bachstez, Frões, Gifford, Lewitskaja, Maucione, Saba report carcinoma of the lid.

Mawas believes that the carcinomata of the lid originate from the Langerhans cells of the epithelium.

Hagedooru describes a carcinoma of the eyelids in a case of cicatricial trachoma of the type of Paget's disease.

Birge finds the majority of lid cancers to be basal cell carcinomas.

Castroviejo, Levizkaja, Tallei, Vancea report basal cell carcinoma of the lid.

Cochrau and Robinson observed multiple papillomata and epidermoid carcinoma of the lids, the conjunctiva and the limbus in a 20 year old man.

Safar found a squamous cell carcinoma of the lid in a 12 year old boy.

Keyes and Queen report a trichoepithelioma of the eyelid with a hyaline fibrous stroma, palisades of epithelial cells and immature hair follicles.

Fleischanderl describes metastatic carcinoma in the tarsus.

Puscariu observed a large naevo-carcinoma of the area between the brows.

Gallega Fernandez describes a case in which after x-ray treatment for carcinoma of the lid the cornea became necrotic and perforated.

Adenocarcinoma of the glands of Moll in the eyelids is observed by Dusseldorp.

Michail describes a primary epithelioma of the glands of Zeiss.

Carcinomata of the meibomian gland are reported by Cavara, Courtial and Devignes, Dollfus, Joseph, Lazarescu, Lazarescu and Ionescu, Letulle and Lapersonne, Pereyra, Riva, Sie-Boen-Liang.

Dermoid cysts of the lids are reported by Duclos, Gradle and Stein, Wieczorek.

Truc and Dejean describe a dermoid of the lid with malignant degeneration in an 11 year old boy.

Reese saw a recurrent tumor of the eyebrow, probably originating from an incompletely removed dermoid cyst and now showing granulation tissue and necrosis.

Kiewe, Puscariu describe mixed tumor of lids, Gerlach of the eyebrow.

Wick describes a fibrochondroepithelioma of the lid containing fibrous tissue, cartilage-like structure and epithelial-lined spaces.

Callahan reports histologic findings in adjacent nevi of the eyelids.

The histology of lid nevus is studied by Mawas and Veil.

Stough saw malignant melanomata of the lids.

Multiple fibromata of upper lid and forehead are reported by Bakry.

Neurofibromata and plexiform neurinomata are found in the lid, mostly in cases of von Recklinghausen's disease, according to Argaud and Calmettes, Candian, Guist, Ismet and Monzaffer, Juler, Pavisic, Lazarescu and Lazarescu, Mans, Meyer, Pomplun, Redslob, de Rosa, Stella, Vancea, Wagenmann, Wiegmann.

Awguschewitsch, Gala, Heine saw neurofibromatosis and elephantiasis of the lids.

Weaver describes fibrolipoma of the lids, affecting also the skin around the ear.

Vinaver describes the histology of the xanthelasma and accuses hypercholesterinemia as its cause.

Town describes a myxoma of the lid with stellate cells, with scanty cyptoplasm and large nuclei and fibrillar and homogenous intercellular substance.

Wildi saw an osteochondroma of the lid skin of a 10 year old boy.

Stanka found an osteoma of the lid after tarsitis.

Speciale-Pieciche reports a lymphangioma of the lids existing, besides diffuse lymphoma of the face and neck.

Folk reports on angiomata of lid and orbit.

Kirby describes an angioma of the lid of a 30 year old man of the type of a neuro-myo-arterial glomus tumor.

Lewis found an aneurysm in the eyelid of a 19 year old girl with defect of the muscularis of the vessel wall.

Cristini reports a myoblastoma of the lid containing a great variety of cells and structures and some primitive muscle fibers.

Mayer describes rhabdomyoma of the lid surrounded by dense connective tissue, lymphocytes and plasma cells.

Cattaneo, Wassenaar saw leiomyoma of the lid.

Clapp, Fisher, Gabriélidès, Juler, Odisio, Lijo Pavia, Belgeri and Dusseldorp, Odisio, Rifaat, Roy, Satanovsky, Shannon, Terrien and Monthus report primary sarcoma of the lid.

Rizzo describes pigmented sarcomata of the lid.

Tooke found in a 65 year old man a lymphatic tumor of the lid (aleukemic lymphosis) with anemia and considers it as a borderline case of lymphatic leukemia and lymphosarcomatosis.

Goedbloed and Wyers saw a lymphoblastoma follicularis in the lid of a 60 year old man.

Kukan describes a lymphosarcoma of the eyelids in a 65 year old woman who had also a lymphosarcoma of the tonsil. Further, Metivier reports a lymphosarcoma of the eyelid.

De Schweinitz reports on angiosarcoma of the lid.

Rintelen describes an angiosarcoma of the lid which he classifies as hemangiosarcoma endotheliosum.

Langdon describes a hemangiomatous endothelioma of the lid, Fiore of the tarsus.

Luppino found an endothelioma of the lid in a newborn.

De Rosa describes an endothelioma of the lid apparently arising from the conjunctiva.

Battista describes a hemangioma simplex of the upper lid in a 2 year old girl, passing into endothelioma. It showed compact strands of cells, partially of cylindromatous structure, infiltrating muscle and nerve.

Schindler saw a hemangioma of the orbit in an infant whose capillaries showed mantles of cells with little cytoplasm and large vesicular nuclei. He interprets the tumor as hemangio-endothelioma.

Lijo Pavia and Dusseldorp report a cylindroma of the lid.

Charsley found a perithelioma of the lid with metastasis in regional lymph modes and spinal column.

Donnell reports a perithelioma of the upper lid in a 74 year old man.

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Chapter XIV

PATHOLOGY OF THE LACRIMAL ORGANS

The lacrimal organs include the lacrimal gland, puncta and canaliculi, lacrimal sac and nasolacrimal duct.

1. The Lacrimal Gland

In the lacrimal gland are found cysts, concretions in the ducts, fistulae, luxations, acute and chronic inflammations, lymphomatoses and neoplasms.

Cysts. The palpebral lacrimal glands may have uni- and multi-locular cysts lined with cuboidal epithelium of one or two layers, more rarely with cylindrical epithelium, and also may contain goblet cells. The cysts have connective tissue capsules with lymphocytic infiltration. The alveoli of the gland usually have enlarged lumina. The cysts originate when efferent ducts are blocked by detritus, trauma or scarification, as in trachoma and pemphigus, and perhaps also through mucoid degeneration of the glandular tissue itself or through ascending inflammation from the conjunctiva.

Concretions of the ducts consist mostly of calcareous deposits, eventually around inspissated secretion and cell debris.

Fistulae of the lacrimal gland are congenital or acquired after injury, surgery or abscess formation and consist of skin epithelium with hair follicles and sebaceous glands.

The *luxated lacrimal gland* is normal in its histologic structure although it may show evidence of hyperplasia. It descends when atrophy of the upper lid deprives the gland of its support.

Inflammations. The lacrimal gland may be acutely inflamed, but frequently chronic nonspecific and also specific inflammations are found.

In the acute inflammation, the connective tissue septa are densely infiltrated with lymphocytes and polymorphonuclears.

Lymphocytes accumulate around the ducts and also form lymph follicles. The interstitial connective tissue proliferates immensely and the glandular tissue atrophies. Around the vessels are mantles consisting of lymphocytes and polymorphonuclears. Streptococci and pneumococci may be seen in the tissue. The acute inflammation may appear in arthritis, tonsillitis, scarlet fever, measles, influenza, gonorrhea and mumps.

Chronic dacryoadenitis is characterized by intense infiltration with lymphocytes and occasionally lymph follicles in the connective tissue septa. Vessels show sheathing with lymphocytes and plasma cells. The connective tissue proliferates and the glandular tissue is increased. The tubules and alveoli are dilated and their epithelium as well as the epithelium of the ducts undergo fatty degeneration. Chronic dacryoadenitis is secondary to chronic conjunctivitis or trachoma and is an ascending inflammation.

Chronic specific inflammation is seen as tuberculosis and syphilis.

Tuberculosis appears as miliary tuberculosis or as conglomerate tuberculosis. The miliary tubercle consists mostly of epithelioid cells with a small margin of lymphocytes and caseation in the center. The conglomerate tubercle shows a typical structure containing lymphocytes, marginal and epithelioid, and giant cells and caseation centrally. Tubercle bacilli can often be stained in the section. The tuberculosis of the lacrimal gland may be hematogenous or primary locally, but often is secondary to tuberculosis of the lid or the conjunctiva.

Mikulicz's disease appears at times to be a typical tuberculosis, affecting the lacrimal gland and salivary glands, especially the parotid. Often, however, numerous very small nodules are disseminated over the gland, with round cells peripherally and epithelioid and giant cells in the center, but without caseation and without tubercle bacilli. These cases resemble Boeck's sarcoid. Mikulicz's syndrome may also be caused by mumps, lues, leukemia, lymphosarcoma and Hodgkin's disease.

Lues of the lacrimal gland appears either as primary lesion or as gumma. Primary lesion of the conjunctiva may extend into

the lacrimal gland showing dense accumulations of lymphocytes and polymorphonuclears in the tissue besides perivascular infiltrates of plasma cells and swelling and proliferation of the endothelium. A gumma shows a large necrotic center surrounded by a small margin consisting of lymphocytes, giant cells and epithelioid cells, in addition to proliferating fibroblasts and blood vessels showing endo- and perivasculitis.

Lymphomatoses appear as a cellular infiltration and as a benign or malignant lymphoma. In leukemia and aleukemic leukemia, the tissue may be diffusely infiltrated with lymphocytes. Circumscribed, tumor-like accumulations of lymphocytes may exist, surrounded by a connective tissue capsule (lymphoma), and the glandular tissue is mechanically compressed and atrophies or the remaining glandular tissue may appear as giant cells. The lymphocytes may become polymorphic and penetrate the septa and the connective tissue capsule and the tumor may invade the orbit (lymphosarcoma). If this happens in the salivary glands and regional lymph nodes, Mikulicz's syndrome is present.

Neoplasms of the lacrimal gland are almost exclusively mixed tumors and rarely dermoid, teratoma or endothelioma. The mixed tumor consists of epithelial and mesodermal elements. The epithelial proliferations take different forms, proliferating in small, solid strands, and in more glandular-like structures in which the lumina are surrounded by epithelial cells in two or three layers; they have colloidal and hyaline substance as their content. The inner cells are more cylindrical and the outer ones cuboidal and rest sometimes on a basement membrane. Such epithelial formations may be followed in transition from normal glandular tissue; however, they are also endothelioma- and cylindroma-like in connection with the mesodermal tissue, which appears in varying amount between the cellular formations and prevails to a great degree. The mesodermal tissue is fibrillar, undergoes hyaline and myxomatous degeneration and contains hyaline cartilage and bone. Displaced nondifferentiated embryonic tissue has been assumed to be the cause of the mixed tumor and may be differentiated in various ways. The tumor is malignant and infiltrates the surrounding tissue.

Dermoids show the structure of the skin; teratoma in addition fat, muscle tissue and intestines.

The endothelioma consists of flat polygonal, closely-packed cells, but may show the epithelial-like cells arranged mantle-like around a cylindrical, transparent hyaline-like substance.

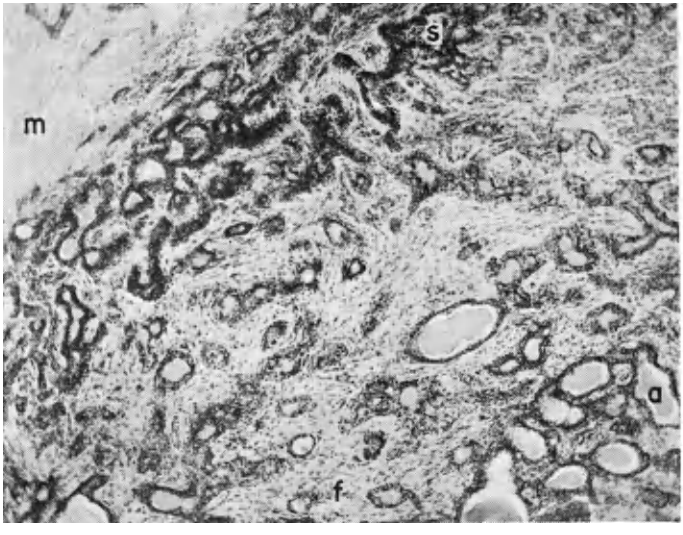

FIG. 57.—MIXED TUMOR OF TEAR GLAND. a, adenomatous formations; f, fibrous tissue; m, myxomatous tissue; s, strands of cells. 70×.

2. THE PUNCTA AND CANALICULI

The puncta show congenital anomalies, eversion and obliteration, the canaliculi atresia and displacement, nonspecific and specific inflammations and neoplasms.

Congenital anomalies. Congenital anomalies of the puncta such as atresia or supernumerary puncta are known clinically. If the structure of the lid relaxes, the puncta turn anteriorly and the surrounding conjunctiva becomes inflamed and its epithelium shows more or less intensive hornification. In blepharitis, the hornifying squamous epithelium of the skin may extend beyond the inner lid margin into the conjunctiva, replace the

columnar epithelium and obliterate the entrance of the canaliculi with horny masses. Horny masses may occlude the puncta without inflammation if the caruncle is covered with hornifying squamous epithelium which extends onto the puncta. The atresia of the canaliculi can be caused also by scars.

Congenital anomalies of the canaliculi such as atresia, supernumerary canaliculi or nipple-shaped elongation are known clinically. Congenital displacement is seen in congenital lacrimal sac fistula. In this case, a duct histologically similar to a normal canaliculus ends in the skin of the inner canthus or in the conjunctiva close to the caruncle. The duct is lined by stratified nonhornifying squamous epithelium and may also develop cilia. The fistula probably develops from an abnormal epithelial bud of the uppermost part of the epithelial crest, representing the first anlage of the lacrimal passages.

Inflammations. Acute inflammation of the canaliculi is known clinically and seems to be caused by cocci and fungi.

The canaliculi are usually inflamed simultaneously with chronic dacryocystitis or chronic conjunctivitis. In dacryocystitis, the common duct of the canaliculi is usually affected. This duct has the same columnar epithelium as the tear sac and represents in reality a tear sac diverticulum. This shows a lymphocytic infiltration of the epithelium and of the subepithelial tissue, occasionally numerous lymph follicles and dilated vessels. The canaliculi proper as a rule remain free of inflammation. In chronic conjunctivitis and blepharitis, the tissue surrounding the canaliculi is infiltrated, granulation tissue is formed and polyps may be produced.

Chronic specific inflammation of the canaliculi include trachoma and tuberculosis.

Trachoma may produce a follicular form or a diffuse form of inflammation. In the follicular form, the same typical lymph follicles are found as in the conjunctiva and inclusion bodies may also be detected in them; they often perforate through the epithelium into the lumen. The follicles are surrounded by a more diffuse infiltration with lymphocytes and plasma cells. The epithelium frequently shows a mucoid degen-

eration. Connective tissue proliferates, replacing the infiltration and obliterating the canaliculus. In the diffuse form, the subepithelial tissue, and to a lesser degree the muscle fibers, are intensely infiltrated with lymphocytes and plasma cells which also fill the degenerating epithelium. The lumen is filled with cell detritus which also contains polymorphonuclears.

Tuberculosis of the canaliculi appears in the form of epithelioid tubercles.

Neoplasms. Neoplasms of the canaliculi are papilloma, fibroma and myxofibroma, which clinically appear as polyps, and endothelioma.

3. The Lacrimal Sac and Nasolacrimal Duct

The tear sac is frequently diseased, mostly chronically. Both nonspecific, and specific chronic inflammation and neoplasms of the tear sac are found.

Chronic dacryocystitis is characterized by changes of the epithelium, the mucosa and submucosa. They are slight in catarrhal conditions of the tear sac and become intensive in blennorrhea. The epithelium may show a proliferation as well as defects. It becomes stratified and more than ten layers of cylindrical and cuboidal cells may appear; there may be mucoid degeneration of the cylindrical cells forming numerous goblet cells. On the other hand, the epithelium may be flattened and disappear in areas with the formation of ulcers. The epithelium is penetrated with round cells and polymorphonuclears. The lumen of the tear sac is filled with cell debris, lymphocytes, polymorphonuclears, epithelia and bacteria. The subepithelial tissue is densely infiltrated with lymphocytes, plasma cells, polymorphonuclears, and sometimes numerous eosinophils are found. Russell bodies lie between the cells. Numerous lymph follicles may occur with a typical germinative center and they perforate occasionally through the epithelium into the lumen with the formation of ulcers. From these, granulation polyps may proliferate, consisting of loose vascular connective tissue with lymphocytes and polymorphonuclears. Vessels are very dilated and new ones

are formed, and the connective tissue and elastic fibers may be increased. The mucosa in its entire width is frequently considerably folded and deep crypts are formed, simulating on cross section a glandular formation. The submucous infiltration may encroach upon the muscle; on the other hand, in the presence of bacteria producing heavy toxins, it may be poor in cells and necrotic. If ulcers are present and bacteria enter through them into the submucosa, frequently a suppurative infiltration sets in, which may extend into the subcutaneous tissue (dacryophlegmon). This may finally perforate through the skin, forming an external tear sac fistula. In case suppuration of the bone sets in, a suppurative sinus may open into the nose, forming an internal tear sac fistula. The hyperplastic wall of the tear sac may shrink with the loss of elastic fibers and when the connective tissue contracts, strictures are formed and folds of the mucosa may grow together. On the other hand, ectasia of chronically inflamed tear sacs is found, the walls of which are atrophic and slightly infiltrated. The inflammatory changes in the nasolacrimal duct, which has the same histologic structure as the tear sac, are similar to those of the tear sac. Chronic dacryocystitis is mostly caused by obstruction of the tear passages due to various pathologic changes. Swelling of the mucosa of the inferior nasal meatus may block the mouth of the nasolacrimal duct, and it can further be blocked by folds and septa. The nasolacrimal duct is closed by stricture and stenosis, by hyperemia of the venous plexus surrounding the duct, by disease of the surrounding bone in lues and tuberculosis and by fracture of the bone. Chronic inflammation of the nasal mucosa may extend into the nasolacrimal duct and sac as in ozena. Furthermore, empyema of anterior ethmoidal cells may affect the nasolacrimal duct and sac as they are surrounded by these cells. Toxins and inflammations may, without perforation of the separating osseus walls and of the tear sac, continue into tear sac by way of marrow spaces from the ethmoid. The ectasia or shrinkage appearing as sequelae of the inflammation is not necessarily dependent upon certain pathologic features of the

nasolacrimal duct. Ectasia may be a sequel of stasis of secretions, the result of stenosis in the beginning of the duct, or occlusion of its ostium in the nose; it may also appear in wide open ducts, probably mechanically by extension through air blown in from the nose. Ectasia and shrinkage may be found alike in open and closed nasolacrimal ducts. When tears do not transport bacteria from the conjunctival sac into the nose, they increase in the tear sac. Most frequently, pneumococci are found, more rarely staphylococci, streptococci, diplobacilli and influenza bacillus. However, in addition, spirochetae and fungi are found, which latter may form concretions of mycelia.

Chronic specific inflammations of the tear sac are caused by trachoma, tuberculosis and syphilis.

In trachoma of the tear sac inclusion bodies may appear in the epithelium and follicles in the subepithelial tissue which perforate through the epithelium into the lumen. Frequently are also found in trachoma nonspecific chronic inflammatory changes.

Tuberculosis of the tear sac is characterized by tubercles of the mucosa showing epithelioid cells and giant cells, and caseation and tuberculous granulation tissue may finally destroy the entire wall of the tear sac, filling the lumen, and may perforate through the skin. Tuberculosis is of hematogenous origin or continues from the conjunctiva, the bone or frequently from lupus of the face and the nasal mucosa.

Syphilis of the surrounding tissue may continue onto the tear sac as well as from a primary lesion from the skin or from a gumma of the nose.

Neoplasms of the tear sac are cysts, papilloma and fibroma as benign tumors, carcinoma and sarcoma as malignant tumors.

Lacrimal sac cysts ("pre-lacrimal tumors"), which lie lateral and anterior to the normal tear sac proper, are histologically similar to the normal tear sac. Sometimes their walls are lined by cuboidal epithelium of two layers. They are assumed to be retention cysts of the hypothetical glands of the wall of the tear sac, or to be diverticula of the tear sac, cut off from the lumen by inflammation, or to be displaced embryonic tissue. In some

cases, a dermoid cyst is found originating from displaced surface epithelium, lined by stratified squamous epithelium and their walls containing hair follicles and sebaceous glands.

Papillomata appear as polyps of the tear sac and consist of branching papillae covered with columnar epithelium or squamous epithelium.

Fibromata appear also as polyps of the tear sac and consist of young fibroblasts in various amounts and connective tissue bundles.

Carcinoma of the tear sac is rarely primary, usually secondary, infiltrating from the paranasal sinus, and may also appear as adenocarcinoma. Very rare are lympho-, spindle cell- and melanosarcomata. Also, plasmoma may be found.

READING OF SOURCE MATERIAL

Large granulated cells found by Schaffer in the human salivary glands were called onkocytes by Hamperl. Boeck found such cells also in human lacrimal glands and considers them as degenerative cell forms.

Gronwall describes argyrosis of the lacrimal gland. He found a case of dacryolith consisting of calcium, silver, magnesium, iron, phosphor, aluminum, copper and perhaps silica.

Wiedersheim finds following occlusion or removal of the efferent ducts of the lacrimal gland, atrophy of the glandular substance frequently, and now and then dilatation of the lumina and formation of cysts.

Krachmalnikov finds extensive round cell infiltration around efferent ducts of the lacrimal gland causing retention and formation of cysts.

Rolett reports cases of cysts of the lacrimal gland lined with stratified squamous epithelium and surrounded by lymphocytes, plasma cells and large mononuclears.

A small periosteal circumscribed suppuration can produce cysts of the tear gland surrounded by infiltrated fibrous tissue, according to di Marzio. He describes a single cyst in the region of the lacrimal glands.

Castello describes multiple cysts of both tear glands with inflammatory infiltration.

Tron, Wiedersheim believe that a slowly progressing incomplete closure of the efferent ducts produces dacryops.

Cases of dacryops are reported by van Duyse and van Lint, Landman, Magnus.

Schornstein found the congenital fistula of the lacrimal gland having the structure of the skin.

Ling describes an anomalous duct of the lacrimal gland lined with squamous cell epithelium and a few hair follicles, sebaceous and mucous glands in its wall.

van Heuven finds the luxated lacrimal glands histologically normal.

Tokareva describes a case of dislocated lacrimal gland showing interstitial inflammation.

Richardson describes acute metastatic gonorrhoic dacryoadenitis with polymorphonuclears and bacteria in the gland.

Gat reports on inflammation of the lacrimal gland in influenza.

Herken found histologically inflammations of the lacrimal glands and lymphomatosis with atrophy of the gland in infections diseases, chiefly in sepsis, tuberculosis and also in carcinoma.

Beigelman found chronic dacryoadenitis in cases of chronic epiphora after tear sac extirpation. There was dense infiltration with lymphocytes, plasma cells and polymorphonuclears, the connective tissue was sclerosed and epithelial cells of the glands were degenerated.

Gangi believes that the lymphocytic infiltration of the tear gland in trachoma is nonspecific but only secondary to inflammatory irritation from the conjunctiva.

Kreiker finds in trachoma infiltration of the tear gland with lymphocytes and plasma cells and considers it nonspecific.

Crawley describes an inflammatory tumor of the lacrimal gland with numerous lymphocytes, plasma cells and atrophic glandular elements.

Beauvieux and Pesme, van Duyse and Weymeersch, Lauber, Moscardi, Motto and Rowen, Skydsgaard, Zeidler report tuberculosis of the tear gland.

Rosenbaum describes Boeck's sarcoid of the lacrimal gland with clusters of epithelioid cells arranged in tubercles and similar findings in lymph nodes; in Sniderman's case it was accompanied by bilateral iridocyclitis.

Barclay, Heine, Marquez and Rodriguez, Owen and Hennessey, Preston and Jeaffreson, Ross and Shepheard-Walwyn, Scales, Schaffer and Jacobsen, Smith and Bump report on Mikulicz's syndrome. The tear gland contains disseminated nodules which show lymphocytes peripherally and in the center epithelioid and giant cells, diffuse round cell infiltration or the tear gland substituted by lymphocytes and connective tissue.

Meyer reports bilateral gummata of the lacrimal gland.

Michail describes symmetrical lymphoma of the lacrimal gland.

Pfingst reports mixed tumors, adenoma and lymphoblastoma of the lacrimal gland.

Perera describes a lymphosarcoma of the lacrimal gland.

Patry, Scardapane, Szabo report cases of cavernous hemangiomata of the lacrimal gland.

Bruner reports a fibro-myxo-lipoma of the lacrimal gland.

Mixed tumors of the tear gland are reported by Battista, Cornalba, Crawley, Davies, Denti, Dentrelle and Heraux, van Duyse, Ehlers and Okkels, Flick, Francis, Lane, Luppino, di Marzio, Pfingst, Shoda, Sykes and Williams, Ten Thije, Tourneaux et Lefebvre, Twelmeyer, Zeidler, Zentmayer.

Rubin reports a case of recurrent mixed tumor of the lacrimal gland which finally represented an adenocarcinoma.

Adenocarcinomata of the lacrimal gland are reported by Benedict and Broder, Denti, Flick, Santori.

Halbertsma found a primary carcinoma of the lacrimal sac with perforation into the paranasal sinuses.

Bruner reports a teratoma of lacrimal gland and Weidler describes a teratoma of the lacrimal gland with myxomatous and cartilaginous transformation of the interstitial connective tissue.

Castello reports cylindromas of the tear gland and Saveljev describes a cylindroma of the lacrimal gland with hyalin and cartilaginous changes.

A spindle cell sarcoma of the lacrimal gland was found by Colley.

The caruncle is occasionally covered by a hornifying squamous cell epithelium which finally obliterates the puncta (Peters).

The development of the canaliculi is described by Ask and van der Hoeve.

Erggelet reports anatomic findings of congenital lacrymal fistulae.

Pneumococcus infections of the canaliculi are reported by Theobald, Wiltschke.

The canaliculi may show in trachoma a diffuse subepithelial infiltration with lymphocytes and plasma cells which partly break into the epithelium (Carboni).

Thies found in a case of dacryocystitis actinomycosis of the lower canaliculus.

Concretions of the canaliculi originating from fungi are described by Avizonis, Carsten, Ginsburg, Stanka.

Serra describes a foreign body granuloma of the canaliculus enclosing a cilium.

Baquis described polyps of the canaliculi being histologically inflammatory granuloma, and papilloma of the canaliculus is described by Nicoletti.

A polyp of the canaliculus found by Aubineau was a fibroma.

Contino reports perithelioma and lymphangioendothelioma of the canaliculi.

Tirelli finds the congenital fistula of the lacrimal sac lined with stratified squamous epithelium and believes that the fistula originates from the lateral epithelium budding from the fetal lacrimo-nasal duct.

Mamoli finds that the wall of the tear sac contains also normally lymphatic tissue.

Serous glands are found in the submucosa of the normal tear sac, according to Accardi. He found in a chronic inflamed tear sac a tubuloacinous gland with an efferent duct, similar to a Krause's gland.

Baquis found 10 of 100 examined tear sacs with chronic inflammation glands. They were: (1) of tubular-acinous type, (2) smaller tubular glands, (3) of simple tubular form. He found irregular spaces lined by epithelium with short efferent ducts filled with mucus, so-called "mucous crypts."

Aliquo-Mazzei, Argaud and Antoine find glandular formations only in chronically inflamed tear sacs.

Serra describes the transformation of the epithelium of the inflamed tear sac into stratified squamous epithelium and the formation of glandular-like epithelial buds and cryptlike diverticles and papilloma- and polyp-like protrusions of the mucosa.

The histology of chronic dacryocystitis is described by MacKee, Muñoz-Urra.

According to Rollet and Bussy, connective tissue proliferates in chronic inflammation in sac and naso-lacrimal duct and the elastic tissue disappears. The shrinking connective tissue produces stenoses.

Schall finds the stenosis in the naso-lacrimal duct in chronic dacryocystitis consisting of inflamed, usually coarse connective tissue.

Changes of the bone are rare, but sinusitis plays an important role in the etiology of chronic dacryocystitis. If the naso-lacrimal duct is dilated, air is pressed into the sac in blowing of the nose, producing ectasia (Wagenmann, Wollenberg).

Guglianetti, Sander find in chronic dacryocystitis hyperplasia of the connective tissue and mainly plasma cells in the infiltration.

Plaut-Vincent infection of the tear sac is reported by Albrich, Cange, streptothricosis by Fava, localized sporotrichosis by Gifford.

Fine and Waring report mycotic obstruction of the naso-lacrimal duct by the yeastlike budding candida albicans.

Cange, McCallen and Sobhy, Papolczy find in trachoma of the lacrimal sac follicles in the infiltrated mucosa.

Ploman describes as inner fistula of the tear sac a tuberculosis of the mucosa of the sac and nose.

James and Colledge report a secondary tuberculosis of the tear sac in lupus.

Peterfi reports cases of tuberculosis of the tear sac, and Roland a tuberculoma adjoining the tear sac and forming an encapsulated abscess cavity lined with tuberculous granulation.

Gumma of the tear sac is described by Augstein, Derby and Cheny, Elschnig.

Prelacrimal cysts are reported by Frieberg, Kubik, Magnasco, Margotta, Marquez, Michail, Tallei.

Cases of papilloma of the tear sac are described by Denti, Eberle, Herrmann, Penman and Wolff.

Pascheff describes an adenoma of the tear sac in a 52 year old man.

Mucocele of the naso-lacrimal duct was found in a 35 year old man by Dusseldorp.

Piesbergen, Rizzo describe granulomata of the tear sac.

Sedan, Astier and Candiere, Weve report lymphoblastomata of the tear sac.

Roselli found a congenital tumor in a 3 month old child of the type of a myxo-fibro-lipoma.

Fenton, Posey, Spratt, Strada and Urrets Zavalia describe carcinomata of the tear sac.

Roberts and Wheeler observed a primary carcinoma of the tear sac originating from the basal cells of the epithelium; a basal cell carcinoma of the naso-lacrimal duct is described by Bakker and Oudenal, of the tear sac region by Desvignes and Offret.

Gandolfi saw a primary papillary epithelioma of the tear sac, Hilden found a malignant papilloma of the tear sac covered partly with columuar and partly stratified squamous epithelium and Dupuy-Dutemps found 24 years after removal of a papillary epithelioma of the tear sac a recurrence in the nose.

Freyberg describes a medullary adenocarcinoma of the lacrimal gland in a 41 year old woman.

Wheeler saw a primary basal cell carcinoma of the tear sac and of the middle turbinate of the nose, the cells of which were similar to oat-cells of a lung carcinoma.

Singer reports an alveolar round-cell sarcoma of the tear sac, Pfingst a spindle-cell sarcoma, Czukrasz, Velhagen fibrosarcomata originating from the periosteum of the lacrimal fossa.

Sarcomata of the tear sac are further reported by Tessier, Zannoni.

Margotta reports primary melanosarcoma of the tear sac.

Argañaraz and Parodi describe a spindle-cell sarcoma of the caruncle as endothelial angiosarcoma.

A myoblastic myoma over the tear sac was found by v. Bahr, containing large spindle cells with large nuclei, granular cytoplasm and fibrils at the ends of the cells.

Witham reports a case of teratoma of the lacrimal gland.

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Chapter XV

PATHOLOGY OF THE ORBIT

1. General Considerations

Many pathologic changes are known only clinically or only their gross pathologic alterations are examined. It is known that the orbit remains shorter and smaller in cases of oxycephaly, hydrocephalus, rickets and retards in growth when the bulb remains smaller. The orbit becomes large when, during growth, the eye becomes large or when a tumor develops in the orbit.

Exophthalmos arises when the orbit becomes smaller or remains small, the orbital walls bulge inward or thicken or the orbital content increases. This may happen when intracranial tumors infiltrate the orbital walls or metastasize into them. Orbital fat increases in acromegaly, but it may also be pressed through a congenital hole of the orbital septum and push the globe forward. The orbital content is increased by lymph stasis and stasis in the veins. Varices may be present on the bony wall and posterior segment of the eye and cause intermittent exophthalmos, which appears by stooping forward, compressing of the jugular vein in the neck, as well as by congenital narrowing of the orbital fissure and of large efferent veins. Pulsating exophthalmos is nearly always produced by a spontaneous or traumatic arteriovenous aneurism of the internal carotid artery in the sinus cavernosus.

Enophthalmos appears when the orbital walls recede or the orbital content decreases. It is frequently traumatic due to depression of the wall of the orbit, especially the inferior wall into the antrum, or due to loss of fat and shrinkage of fibrous tissue which occasionally organizes hemorrhages. Abnormal fibrous bands and congenital substitution of eye muscles by fibrous bands are responsible for congenital enophthalmos. The globe may be dislocated by injury and surgery. It may be

luxated in front of the lids in Graves' disease and in an injury with severe orbital hemorrhages or emphysema or rupture of the eye muscles and optic nerve (avulsio nervi optici). Other injuries of the orbit are fractures of its bony walls, rupture of the nerves of an eye muscle, and the entrance of foreign bodies.

Lesion of the optic nerve may call attention to itself by visible changes of the orbit, by visible changes of the papilla or by changes in the visual field.

Spontaneous hemorrhages of the orbit appear in the septa, in the fat tissue, in the muscles and periorbita, and may be due to various causes. They may be caused by infantile scurvy (Barlow's disease), in which through vitamin C deficiency the bone marrow is damaged, and secondary anemia sets in with subperiosteal hemorrhages and disturbances of the bony growth. Hemophilia, whooping cough, pernicious anemia and arteriosclerosis are other causes of hemorrhages.

2. Inflammations

Inflammations of the orbit are acute and chronic nonspecific and specific. They are either primary in the orbit or are metastatic or are continuations from the surrounding tissue.

Acute inflammation affects Tenon's capsule, the orbital septa, the optic nerve, the extrinsic muscles, periosteum and bone. The acute tenonitis may be serous or suppurative. In the former, serous fluid with few lymphocytes appears in the episclera and Tenon's capsule; in the latter, polymorphonuclears appear along with fibrin. The further course of a suppurative inflammation may lead to organization with development of new fibrous tissue which is infiltrated with lymphocytes and monocytes. The serous tenonitis is mostly rheumatic. The suppurative tenonitis is sometimes primary in infectious diseases, usually secondary, extending from suppurative diseases of the globe and the paranasal sinus. In the orbital septa, polymorphonuclears may accumulate and the edema may spread forming a phlegmon; polymorphonuclears and proliferating fibrous tissues surround the vein with consequent thrombophlebitis as the bacteria circulate in the blood and are deposited here. Necrosis of the tissue, especially of the fat tissue, and abscess may follow, resulting

in fistulae. Suppurative inflammation of the orbital tissue is primary in an injury which becomes infected, and in infectious diseases of different etiologies—even anthrax can be found; however, this is mostly secondary due to suppuration of the globe, as of panophthalmitis, and often is a sequel to suppurative paranasal sinusitis. Acute orbital inflammation originate most frequently from the frontal sinus, less from the ethmoid and antrum and most rarely from the sphenoid. Dehiscences, necrotic areas and thrombophlebitis of the bony walls of the sinus cause the extension of the suppuration from the sinus into the orbit. Dacryophlegmon, thrombophlebitis of the face due to a furuncle or erysipelas, lateral sinus phlebitis and suppurative apical granulomas may cause the suppuration. Pneumococci, streptococci, staphylococci and influenza bacilli, are responsible for it. When the orbital tissue is inflamed, the optic nerve may participate in the inflammation as well as its sheaths and the nervous substance itself. Acute suppurative myositis is part of the acute inflammation of the orbital tissue and is found chiefly as interstitial inflammation with secondary degeneration of striated muscle fibers. The interstitial connective tissue contains polymorphonuclears and lymphocytes and soon shows an increase of fibrous tissue. Suppurative inflammation of the periosteum, subperiosteal abscess and suppuration of the marrow spaces with thrombophlebitis and osteolysis usually start from suppurative inflammation of the paranasal sinuses. The bone becomes necrotic and sequesters are formed. Finally, fistulae lead to the skin surface or toward the brain.

Chronic nonspecific inflammation may affect Tenon's capsule, the orbital septa, the optic nerve, the extrinsic eye muscles, the periosteum and the bone. Tenon's capsule is infiltrated with lymphocytes, plasma cells and polymorphonuclears. Vessels and fibroblasts proliferate and finally the tissue becomes organized. It is always secondary to inflammations of the bulb. Eye muscles are chronically inflamed in local processes and generalized diseases. In Graves' disease, chronic edema and lymphocytic infiltration in the septa may appear, followed by an increase of the connective tissue (induration) due to stasis in the veins which perhaps are compressed in the orbital fissures by an increased tonus of the smooth muscles. In chronic paranasal

sinusitis, chronic infiltration of the orbital tissue, the sheaths of the optic nerve or the optic nerve itself may arise, causing symptoms of retrobulbar neuritis and even papilledema. In rare cases, an apical granuloma of a highly placed canine tooth may penetrate into the orbit and cause here chronic inflammation or proliferate tumor-like as a circumscribed granuloma. Chronic interstitial myositis may appear as infiltration and proliferation of the interstitial fibrous tissue with lymphocytes in addition to edema and degeneration of muscle fibers. Metaplasia of the fibrous tissue, which is especially increased after traumatic hemorrhages and also replaces degenerated muscle fiber, may produce bone. In Graves' disease, edema and chronic infiltration often enlarges the striated eye muscles which are also elongated due to a decrease of their tonus, thus contributing to an exophthalmos. Also, in myasthenia gravis, the etiology of which is unknown, although enlargement of thymus and thyroid sometimes makes an endocrine cause probable, extensive lymphocytic infiltration of the muscles is seen. Chronic paranasal sinusitis may cause pressure atrophy and chronic inflammation of the bone and of the periorbital tissues, leading to their necrosis and a prolapse of the chronically inflamed polyp-forming mucosa into the orbit. A fistula may result.

Chronic specific inflammations include tuberculosis and syphilis. Tuberculous granulation tissue may appear in all parts of the orbit either of hematogenous origin or extending from the surrounding tissue, for example, the conjunctiva, the bulb, the tear gland or the tear sac. Most frequently the periosteum is affected and caries of the bone results, but also eye muscles, the septa and the optic nerve become affected. Fistulae are eventually formed. But the orbita itself in the presence of tuberculosis of the surrounding tissue may show only a nonspecific chronic inflammatory reaction. Syphilis affects the periorbital tissue mainly but may also affect the muscles, and, as already mentioned, frequently the optic nerve.

3. Fungus Diseases

Among the fungus diseases, actinomycosis and sporotrichosis are seen. The former affects more often the muscles and septa,

but also periorbital tissue, while the latter mainly affects the periorbital tissue.

4. "Pseudotumor"

A special form of the chronic inflammation of the orbit is the so-called "inflammatory pseudotumor of the orbit." There are found strands and foci of infiltration with lymphocytes and plasma cells, also follicle-like accumulations of lymphocytes along with eosinophils in large masses of dense fibrillar connective tissue bundles which are partly degenerated hyaline. The orbital tissue itself and also the muscles may be infiltrated densely with lymphocytes. Sometimes the infiltration resembles a lymphoma. Rarely, numerous cells containing lipoid are found which, if they appear exclusively, form xanthoma. The etiology of this which appears clinically to be a tumor is unknown. It is frequently regressive, spontaneously or with treatment.

5. Hypertrophy, Atrophy, Dystrophy and Degeneration

The tissues of the orbit itself, or pathologically formed tissue, may hypertrophy. Fat tissue, connective tissue and smooth muscles may hypertrophy as well as blood vessels which also may be hyperemic. Such hypertrophies are found especially in Graves' disease as sequelae of lymph- and blood stasis. Hypertrophy of the bone appears as exostosis and hyperostosis, the former mostly after trauma due to excessive proliferation of the regenerating bone. Exostosis originates from the periosteum and is circumscribed solid or cancellous in its texture, the bone showing lamellar structure, but usually without Haversian canals. Hyperostosis is diffuse increase of periosteal bone and mostly part of leontiasis which is caused by osteitis deformans. Striated eye muscles may hypertrophy in exophthalmos. Atrophy of fatty tissue and connective tissue of the orbit is observed in cases of traumatic enophthalmos. The atrophy is frequently a sequel to decreased blood circulation due to rupture of blood vessels and fibrosis of the tissue after resorption of hemorrhages. Dystrophy is found in the bone, such as osteitis fibrosa and osteitis deformans (Paget) which rarely affect the orbital wall. In osteitis fibrosa, which appears in hyperplasia of the para-

thyroid, the normal bone disappears and is replaced by fibrous tissue which again forms trabeculae of bone. Osteitis deformans is of obscure etiology; the original bone is replaced by irregular cancellous bone with fibrous marrow. Hyaline and amyloid degeneration especially affects the eye muscles. Hyaline degeneration of septa and blood vessels may be observed.

A special form is "the amyloid tumor of the orbit." It appears symmetrically, arises from the conjunctiva, and forms amyloid masses in both orbits. Blood vessels show amyloid degeneration. The amyloid masses are surrounded by plasma cell infiltration and occasionally also foreign body giant cells.

6. Parasites of the Orbit

Parasites affecting the orbit are echinococcus, cystericercus, filaria and trichina. Echinococcus forms hydatid cysts in the body and in the orbit. They increase by budding. They are located in different parts of the orbital tissue and damage secondarily the optic nerve and the bulb. They are characterized by their clear content, contain scolices and have a laminated wall. Their contents may thicken, undergo suppuration or frequently may show fat, cholesterol and calcium.

Cysticercus cellulosae is characterized by a connective tissue capsule with its inner surface lined with the continuation of the epithelium of the tortuous canal of the body of the larva. The capsule may show calcareous incrustations, infiltration and newly formed blood vessels.

Filaria are sometimes found in the orbital tissue.

Trichinae may be found in the striated eye muscles. The affected muscle fiber degenerates and loses its striation. The encapsulated trichina appears coiled up and shows infiltration with polymorphonuclears, eosinophils, lymphocytes and giant cells. The hyaline capsule may calcify.

7. Neoplasms

Neoplasms of the orbit are mostly mesodermal, less frequently epithelial. They are benign or malignant. Special forms are lymphomatoses and cysts both of which often are of inflammatory origin. Neuro-ectodermal neoplasms are infrequent.

Benign Mesodermal Neoplasms

The benign mesodermal neoplasms are osteoma, chondroma, angioma, fibroma, lipoma, myoma and xanthoma.

The *osteoma* is really a disease of the paranasal sinus, extending into the orbit. It consists mainly of compact bone, but sometimes of a cancellous bone with fibrous marrow, and may contain much fibrous tissue. Mucosa of the paranasal sinus may be enclosed in the tumor and form cysts or may have undergone myxomatous degeneration. The tumor originates from the bone marrow, sutures, periosteum or cartilage which is displaced during the embryonic development.

The *chondroma* originates from displaced cartilagenous islands and consists of hyaline cartilage in which the cells are arranged singly and not in groups as in normal cartilage. The tumor is frequently a fibro-chondroma, as it contains considerable fibrous tissue besides cartilage.

The *angioma* is frequently a hemangioma, more rarely lymphangioma. The hemangioma is either capillary or cavernous. The surrounding tissue contains lymph follicles, lymphocytes, plasma cells, mast cells and rests of blood pigment after hemorrhages. This congenital tumor causes exophthalmos, which will pulsate if arteries are enclosed in the tumor, and damages the optic nerve. If the angioma contains much fat tissue, it is called angio-lipoma; if it contains much fibrous tissue, fibro-angioma. The lymphangioma is connected with the perivascular sheaths of the posterior ciliary vessels and consists of connective tissue septa which surround spaces lined by endothelium. The septa may show elastic tissue and lymphocytic infiltration.

The *fibroma* consists of many wavy connective tissue bundles, often whirl-like in arrangement, and fibroblasts. It is congenital. It originates probably from the nerve sheath and may show hyaline degeneration and calcification. The myxofibroma contains mucoid degenerated tissue. A special form is the neurofibromatosis with tumors which originate most frequently from the endo- and perineurium of the ciliary nerves in the orbit, and in which lids and ciliary body are simultaneously affected and hydrophthalmos may appear due to malformation of the chamber angle. Between the connective tissue bundles are deformed

medullated nerve fibers, fine branching cells and large round cells with fine granular cytoplasm. Some tumors may perhaps originate from the ectodermal sheath cells of the medullated nerve fibers (Schwannoma). Another form is the fibromatous tumor originating from the sheaths of the optic nerve (meningioma, meningeal fibro-blastoma, psammoma). It consists of whirl-like long fibroblasts along with fibrous bundles, and contains numerous psammoma bodies. They are formed by hyaline degeneration of the whirls, show lamellar structure and are frequently calcified. The tumor itself originates from the tissue of the dura, or from the endothelium of the dura or of the arachnoid.

A *lipoma* is rare and appears as encapsulated tumor consisting of fat cells; it is rather often fibro- or angio-lipoma.

The *myoma* may appear as leiomyoma, consisting of smooth muscle fibers. Rhabdomyoma is very rare and consists of large cylindrical cells with longitudinal striations and large, non-striated cells with round nuclei; it is attached to a striated muscle.

The *xanthoma* consists of groups of large polygonal and rounded vacuolated cells with rounded or oval nuclei with more or less dense chromatin, surrounded by fibrous septa filled with lymphocytes and occasionally giant cells. It is due to a disturbance of the lipoid metabolism with an abnormal lipoid accumulation in reticulo-endothelial cells. In Schueller-Christian's disease, xanthomata fill the orbital bone and the orbit, producing exophthalmos, and surround the pituitary gland, causing diabetes insipidus.

Lymphomatoses

Lymphomatosis represents a dense lymphocytic infiltration of the orbit, but there are also larger cells of the type of the myelocytes and myeloblasts. Tenon's capsule may be infiltrated densely, as well as the conjunctiva and tear gland, the lymphoid tissue of which is perhaps the origin of the lymphomatosis; the choroid and retina also may be affected simultaneously. It is seen in lymphatic and myelogenous leukemia and aleukemic leukemia.

Cysts

Cysts are found as: (1) serous cyst, (2) dermoid, (3) teratoma, (4) bulbus cyst in microphthalmos, (5) mucocele, and (6) encephalocele.

A *serous cyst* consists of columnar epithelium and occasionally of ciliated epithelium surrounding a serous content. It is assumed to be a traumatic implantation cyst originating from displaced nasal mucosa.

In a *dermoid,* there is a connective tissue capsule surrounding a flattened, stratified, hornifying squamous epithelium and contains hair follicles, sebaceous and sweat glands and smooth muscle fibers. The content consists of desquamated hairs, epithelial elements and atheromatous masses. The dermoid may erode bone and extend into the paranasal sinuses and the intracranial cavity; the capsule may show inflammatory changes with granulation tissue and giant cells. It is formed by displacement of the surface epithelium during the embryonal development at the time when the facial cleft closes. A related form is cholesteatoma, which shows layers of polygonal epithelial cells and is filled with granules, fatty material and cholesterol crystals and lamellae of horny substance.

The *teratoma* shows an irregular arrangement of skin, muscles, cartilage, bone, nervous elements, rudimentary intestines and glands.

The *bulbus cyst* consists of inverted retina in which nerve fibers and ganglion cells are absent and glia proliferates; its liquid content is connected with the vitreous body. The bulbus itself is rudimentary. This congenital malformation represents an abnormal development of the primary or secondary eye cup.

A *mucocele* shows, in its wall, mucosa of the paranasal sinus and mucoid content. It represents an enlarged paranasal sinus, the efferent duct of which is obliterated by trauma or inflammation of the surrounding tissue. The mucosa continues to secrete and its pressure distends the cavity. The frontal sinus is affected more often than any other paranasal sinus. The protruding paranasal sinus bulges the bone, thins it out and causes its atrophy, and finally perforates the bone and periorbita and

displaces the orbital tissue. The mucocele may undergo suppuration.

Encephalocele consists of a fibrous sac showing on its inner surface a thickened and cystically degenerated arachnoid lined with an ependyma and a thin layer of nervous substance. It is a congenital malformation in which there remains a dehiscence between neighboring bones of the skull through which the brain herniates.

Malignant Mesodermal Neoplasms

The malignant neoplasms are mainly mesodermal, primary or secondary. The malignant epithelial neoplasm and mixed tumor are secondary.

The malignant mesodermal neoplasms are sarcoma, myeloma, and endothelioma.

The sarcomata appear in all possible forms according to their origin as round cell sarcoma, spindle cell sarcoma, fibrosarcoma, liposarcoma, osteosarcoma, chondrosarcoma, myosarcoma and melanosarcoma. Many of these tumors represent malignant degeneration of benign forms, like fibroma, lipoma, chondroma and myoma.

The round cell sarcoma is common and is a lymphosarcoma consisting of typical lymphocytes and lymphocytes with larger nuclei containing much chromatin, lymphoblasts, and cells of embryonic character with vesicular nuclei. It infiltrates and substitutes for the tissue of the orbit and finally of the surrounding tissue, extending into the paranasal sinuses and intracranial cavity and metastasizes to the skull, lungs, and liver like other sarcoma types.

The spindle-cell sarcoma originates from the periorbita and the sheaths of the optic nerve and consists of spindle-shaped cells with fusiform nuclei of various sizes and chromatin content. If it contains much fibrillar tissue it is a fibrosarcoma which may develop by malignant degeneration of a fibroma. If the fibrous matrix undergoes mucoid degeneration, a myxosarcoma is present.

The liposarcoma is difficult to diagnose, as the histologic picture is not always typical. It consists mainly of swollen polygo-

nal granular cells which may contain fat, sometimes demonstrable only with special fat stains and embryonal fat cells and giant cells. In the beginning, the tumor is seen encapsulated in the fat tissue, finally perforates the capsule and infiltrates the surrounding tissue of the orbit.

The osteosarcoma (osteogenic sarcoma) which may affect the orbital wall is distinguished by its pleomorphism. It grows from the osteoblasts and shows small spindle-cells, large polygonal and giant cells and the matrix is fibrous, osteoid, or bone. In contrast to this exceedingly malignant tumor is the relatively benign giant cell tumor which consists of numerous giant cells of the osteoclast type surrounded by spindle and round cells.

The chondrosarcoma is very similar to the chondroma except that it infiltrates and replaces the tissue. It usually shows a myxomatous degeneration and the cells are distinctly pleomorphic.

The myosarcoma is of two forms: the leio- and rhabdomyosarcoma. The leiomyosarcoma (malignant myoma) is similar to the benign myoma, except that the cell nuclei are larger and pleomorphic and many mitotic figures appear. Rhabdomyosarcoma consists of large polygonal cells with large nuclei and small cell processes which show faint cross striation.

The melanosarcoma (malignant melanoma) which is assumed to have a neuro-ectodermal origin is secondary from the conjunctiva, lid, caruncle, and especially from the uvea after having perforated the bulb. It infiltrates the orbital tissue or metastasizes to the eye muscles and the optic nerve.

The *myeloma* is a tumor of the bone marrow (myelocytoma) and shows round or polygonal cells which are closely packed together without any intercellular substance. Numerous plasma cells and lymphocytes are found in the tumor. This tumor, originating from the bone, rapidly infiltrates the orbit. Similar to this multiple-appearing tumor is also the multiple-appearing chloroma. This very rare tumor accompanied by a leukemic blood picture may fill the entire orbit. It consists of large round cells with deeply stained nuclei, myelocytes and myeloblasts which also may penetrate the optic nerve, and lymphocytes which are embedded in the scarce connective tissue stroma. The greenish color of this tumor is said to arise from greenish cell

granules which are assumed to be a lipoid or colloidal iron-sulfur compound.

The *endothelioma* shows mainly an alveolar structure consisting of groups of flat, clear cells with small nuclei arranged like epithelial cells. The fibrillar intercellular tissue may vary in amount. A tubular and network-like cellular arrangement is also seen. If the amount of intercellular tissue is small and undergoes myxomatous degeneration and the cells become more cylindrical, they appear to be arranged around a lumen similar to an adenoma (cylindroma). On the other hand, it also grows sarcoma-like (angioplastic sarcoma), showing transitional forms to hemangio- and lymphangiosarcoma.

Malignant Epithelial Neoplasms

The malignant epithelial tumors are secondary carcinomata which extend from the neighborhood or metastasize into the orbit. They are squamous cell- and rarely basal cell- or adenocarcinomata. They extend from the lids, lacrimal gland, tear sac, caruncle and paranasal sinuses. From the latter, a carcinoma may arise in structure similar to cyst-adenoma, showing large lumina lined by columnar epithelium (cylindroma, cylindric cell carcinoma). Metastatic carcinomata arise from the breast, stomach and uterus and are adeno- and squamous cell carcinoma. Carcinomata invade especially the eye muscles, but also the optic nerve and other parts of the orbit. Metastatic hypernephroma can be found.

Mixed Tumors

The mixed tumors of the lacrimal gland may extend into the orbit. They apparently consist of a mixture of epithelial elements in the form of strands, and cells arranged adenoma-like around the lumina and of dense partly hyaline degenerated connective tissue.

The neuro-ectodermal neoplasms are neuroblastoma, retinoblastoma and glioma.

The neuroblastoma, which appears as a very malignant tumor congenital in the child, metastasizes to the orbit from the primary

tumor in the medulla of the adrenal which originates from primitive sympathetic neuroblasts. The tumor consists of small round cells and fibrils which are arranged in longitudinal bundles or in small rounded masses, and cells with rounded nuclei and dense chromatin are situated around them, giving a structure similar to rosettes.

The retinoblastoma grows after perforation of the bulb into the orbit or extends by way of the optic nerve.

The glioma originates either primarily in the optic nerve or grows from the brain into the orbit; in the latter case, it is often pleomorphic, containing round and oval cells of different sizes and also giant cells.

READING OF SOURCE MATERIAL

Lindenmeyer considers a unilateral congenital narrow jugular vein responsible for intermitting exophthalmos.

Fat herniae are produced by defects of the fibrous capsule of the orbital fat and of the orbital fascia, according to Bourguet, Gerard.

Thomson finds intensive edema of the orbital tissue in exophthalmic goiter.

Clairborne considers intensive hyperemia and hyperplasia of the orbital tissue as cause of the proptosis in Graves' disease.

Kubik believes that weakness of the eye muscle causes the exophthalmos in Graves' disease.

According to Unverricht, the exophthalmos is the result of venous stasis or toxic vasomotor paresis.

Krause believes that the smooth muscles in the depth of the orbit have increased tonus, compressing blood vessels, in Graves' disease.

Mulvany and Glas find as cause of exophthalmos of hyperthyroidism changes in the eye muscles which show loss of striation, fibrillation and granulation of the sarcoplasm, disintegration of muscle fibers and finally fatty replacement. Also their nerves show degeneration and swelling with granulation of the neuroplasm. Round cell infiltration and edema can set in, and edematous, fibrous infiltrative tissue may remain after the muscles have disappeared.

Merrill and Oaks found in hyperthyroidism edema of the muscles with atrophy and new formation of fibrous tissue, uniting nerves, muscles, fat and vessels of the orbit and producing progressive exophthalmos.

Naffziger finds in progressive exophthalmos degeneration, fibrosis and round-cell infiltration of the extra-ocular muscles.

Battaglia, Ehlers, Nakashima, Seyfarth could prove that rupture of the internal carotid in the sinus cavernosus is the cause of pulsating exophthalmos.

A cavernoma of the orbit was found as cause of pulsating exophthalmos by Loehlein, a hypernephroma-like tumor by Pollack.

Jaensch believes that the intra-ocular pressure is increased in pulsating exophthalmos due to thromboses of retinal and choroidal veins.

Exophthalmos due to congenital varicocele is reported by Fromaget and Fromaget.

Friede describes a case of hydroa vacciniforme in which necrosis of the sclera produced inflammation and proliferation of the orbital tissue causing exophthalmos.

Congenital enophthalmos with retraction is caused by a fibrous band substituting the external rectus (Clausen).

Crisp, Genet report suppurative tenonitis.

Benedict and Knight, Lijo Pavia report on tenonitis with infiltration and new formation of connective tissue.

Wick describes inflammations in eye muscles in cases of orbital phlegmone.

Tertsch saw in a case of periarteritis nodosa infiltration of polymorphonuclears around and in the walls of arteries of the extrinsic eye muscles.

Engelking describes thrombophlebitis of the orbit following infection of the conjunctiva by staphylococcus pyogenes aureus. He also found progressive tuberculosis of the orbit originating in old tuberculomas of the conjunctiva.

Orbital inflammations invading from the surrounding tissues and causing edema, hemorrhages and thrombophlebitis are examined anatomically by Maggiore, Magnus, Moscardi, Wick.

Mulock Houwer found in thrombosis of the carotid artery emboli in the arteries of the choroid, retina and orbit and degeneration of the ganglion cells of the retina and hematoma of the optic nerve sheath.

Orlow describes myositis fibrosa of the extrinsic eye muscles with lymphocytic infiltration, thinning of the muscle fibers and obliteration of small vessels.

Magnus found follicles in extrinsic eye muscles in patients with carcinoma of the lid.

Chronic orbital myositis causing exophthalmos of unknown origin is characterized by lymphocytic infiltration, fibrosis and Zenker's waxy degeneration (Dunnington and Berke).

Chronic inflammation with connective tissue proliferation of all extrinsic eye muscles is reported by Kloth, Posey.

Benford and Brunner describe chronic inflammation of the orbit following chronic inflammation of the frontal sinus, in one case polyps extending from the sinus into the orbit.

Tuberculomata of the orbit are reported by Engelking, Manstrangeli, Mulock-Houwer, Pascheff, Sander, Schoepfer, Stajduhar.

Tuberculosis of extrinsic eye muscles is found by Axenfeld, Meisner, Mulock-Houwer.

Michail describes a pseudotumor of the orbit of tuberculous origin showing perineuritis and interstitial orbital myositis with giant cells.

Tuberculous orbital tissue was found by Hinterleitner.

Musial, Rochat report cases of gummata of the orbit; Pascheff cases of symmetric syphilitic tumors of the orbit.

Laricchia reports on very small gummata, and Chon, Kalt found histologically orbital actinomycosis.

Moretti found in a tumor of the orbit fungi resembling aspergillum.

A case of aspergillosis of the orbit is reported by Wright, a case of streptotrichosis by Morax.

Morax and Rousseau discovered in an orbital tumor of an 11 year old girl a mycelial growth which they could not classify.

About pseudotumors of the orbit report Babel, Benedict and Knight, Bollack, Bertillon and Rogues, Elschnig, Franceschetti, Huber, Jakobovits, Krautbauer, Mohr, Mursin, Pines, Przybylska, Sautter, Seka, Schmincke, Williamson-Noble, Stargardt, Williamson-Noble, Wright. They consist at variance of fibrous tissue, lymphocytes, polymorphonuclears, plasma cells, endothelial, giant cells, phagocytes, eosinophils and blood vessels.

Townsend reports symmetrical granulomata of the orbit with exophthalmos in a 21 year old man, and Orlow found symmetrical tumors of the orbit showing lymphogranulomatosis of the type of Gaucher's disease.

Pineus describes primary fat necroses (lipogranulomatosis) of the orbit of an 82 year old woman surrounded by lymphocytes polymorphonuclears, plasma cells, epithelioid and giant cells, containing fat granules.

Pollens found a tumor of the orbit containing amyloid, plasma cells and foreign body giant cells.

Echinococcus of the orbit is reported by Alkin, Arnau Maorad, Awguschewitsch, Ballod, Burlanesco, Charamis, Cuenod and Roger-Nataf, Judin, Kankrov, Magnus, Natale, Poljak, Seale, Speciale-Cirincione, Teulieres, Varnier, Vasquez Barriere, Wood.

Palomar de la Torre reports on cysticercus of the orbit.

Wright found dracunculus medinensis in the orbit.

Herrenschwand, Key report on trichinosis of the extrinsic eye muscles.

Sen and Ghose report ocular gnathostomiasis. Gnathostoma is found in the East in the stomach of wild and domestic animals. In a 26 year old man, the orbit was infected and the iris contained pigmented nodules representing the worm.

Juler found a serous cyst caused by an aniline pencil.

Mylius found after injury with an indelible pencil extensive necrosis and granulations in lid and orbit.

Injury of the orbit with indelible pencil is further described by Iritzer-Braun.

Dobizaniecki and Sowiakowski, Hardy and Hardy, Schreck, Shoda, Zytovska describe the tumors of the orbit of various origins, and Samuels in describing these tumors finds that carcinomata and cylindromata show marked inflammatory reaction.

Osteomata of the orbit are reported by Ballantyne, Casanovas, Mouret and Dejean.

Davis describes an osteoma of the orbit in a 20 year old man originating in the frontal sinus, and Vincent and Mahoudeau describe an osteoma of the ethmoid extending into the orbit, showing Haversian canals; the tumor was surrounded by a thin membrane of one layer of cuboidal epithelium.

Chondroma of the orbit are reported by Bane, Torrigiani.

Hemangiomata of the orbit are reported by Balbuena, Barletta, Braunstein, Brunner, Byers, Castello, Creswell and Briggs, Knapp, Kreiker, Lopes

de Andrade, Di Marzio, Meisner, Meisenbach, Panico, Parodi, v. Romunde, Sobhy, Shapiro, Shoda, Wick, Ten Thye, Truc et Dejean.

Bass, Battista, Cashell, Luppino, Niyazi, Paul, Soloviev, Stallard, Truc and Dejean, Vancea, Villard and Dejean, deVries, White report cases of cavernous hemangiomata of the orbit.

Poos finds the cavernous hemangioma of the orbit containing occasionally lymph nodes.

Ring reports a cavernous hemangioma of the orbit with pulsating exophthalmos.

A mixed capillary and cavernous hemangioma of the orbit of a 30 year old man is reported by Crawford, King and Rogers.

Lymphangiomata of the orbit are described by Franklin and Cordes, Gradle, Michail, Nizetic, Niosi, Radnot, Smith, Wolff.

Angiofibroma of the orbit is reported by Foliano.

Fibroma was removed from the muscle cone of the orbit of a 23 year old woman by Fowler and Terplau. Further, Garcia, Miranda, v. Imre, Kreiker, describe fibromata of the orbit.

Blegvad reports a myxoma of the orbit of a 29 year old woman consisting of muco-fibrillar tissue with small nuclei arranged around small blood vessels.

Bistis reports myxoma of the orbit with origin probably in an embryologic rest in the loose connective tissue of the orbit in a 24 year old man.

Gifford reports a case of multiple myxomata of the orbit, and Lamb, too, saw a myxoma of the orbit.

Accardi, Hine and Wyatt, Lawson and Neame, McMillan and Cone, Mans, Mawas and Veil, Morgan, Motto, de Schweinitz and Baer, Seghieri, Stieren, Sykes, Terrien report neurofibromatosis of the orbit.

Marin Amat reports a plexiform neuroma made up of cords of modified nerve tissue surrounded by connective tissue, and Kiel, too, saw a plexiform neuroma of the orbit.

Cohen, Seghieri, Stieren report neurinomata of the orbit consisting of spindle cells in palisades and possibly originating from the Schwann cells of ciliary nerves.

Papolczy describes a neurinoma which developed intra- and retrobulbar in a posterior ciliary nerve in a shrunken globe.

Kankrov describes an amputation neuroma of a ciliary nerve following enucleation of the eyeball.

Meningiomata (psammomata) of the orbit arising from the dura are described by Benedict, Collevati, Gilchrist, Mathewson, Mayer, Schuster, Twelmeyer, Wiegmann.

van der Hoeve saw an osteofibroma of the orbital wall in a 12 year old girl.

Castillo Ruiz reports a fibro-adenoma of the orbit.

Fibroepithelioma of the orbit forming also cylindroma originates from displaced tissue of the oculo-orbital region (van Duyse).

Van Duyse and Moret describe an orbital tumor as calcified fibro-myo-lipo-epithelioma.

Lipomata of the orbit are described by Duro, Schuster.

Lipoma of the orbit may follow implantation of fat into Tenon's capsule of an enucleated eye, according to Cushman.

Renard and Offret report an angiolipoma of the orbit.

Leiomyomata of the orbit are described by Cattaneo, de Quervain.

Rhabdomyomata of the orbit are described by Bietti, Derer, Redslob, in whose care there was a recurrence in a lymphosarcoma.

Feigenbaum and Sondermann report a spindle cell xanthofibroma of the orbit of a 29 year old man.

Elschnig, Franklin and Cordes describe xanthomata of the orbit.

Behr, Herzan and Pinkus, Jason and Abraham, Wheeler report cases of Schueller-Christian's disease with xanthomata of the orbit containing cells with clear foamy cytoplasm, and eventually also proliferation of connective tissue, hemorrhages, cysts and ossification.

Wheeler describes an eosinophil tumor of the roof of the orbit.

Lymphomata of the orbit are described by Cohen, van Duyse, Goldenberg, Hartshorn, Hine, Igarashi, Kiep, McGavic, McKinney, Mulock Houwer, Rodriguez Villegas and Daniel, Triebenstein.

A lymphomatous tumor of the superior rectus is described by v. Hippel.

Symmetrical lymphoblastomata are found in the orbit by Bormacher, Goedbloed and Wijers, Voelkel.

Holm found an orbital plasmocytoma in a 73 year old woman with numerous mitoses, some giant cells, hemorrhages and circumscribed necroses.

Przybylska saw a plasmoma of the orbit, extending into the ethmoid and sphenoid, containing numerous plasma cells, but also polymorphonuclears, lymphocytes, epithelioid and giant cells.

Golowin reports so-called blood cysts of the orbit and finds them: (1) as encapsulated hemorrhages following trauma or spontaneous, (2) as hemorrhages into already present cysts and (3) as hemorrhagic cavities in true tumors.

Awerbach describes hemorrhagic tumors of the orbit consisting of organizing connective tissue with a central cavity containing blood.

Niyazi found a serous cyst in the sheaths of an external rectus muscle with absence of the muscle itself.

Handmann found a serous cyst of the orbit lined with cylindrical and cuboidal epithelium which he considers originating from a displaced nasal mucosa.

Gradle describes a cyst of the forehead and orbit.

Dermoid cysts of the orbit are described by Axenfeld, Belski, Buchanan, Cange, Cange and Argaud, Cucco, Debenetti, Ellet, Farina, Gradle, Gradle and Stein, Knapp, Moffat, Perwoeg, Stepka, Velhagen, Verebely, Vissich.

Jones reports an oil cyst (dermoid) of the orbit containing squamous cell carcinoma.

Cholesteatomata of the orbit are reported by Basterra, Constans, Michail, Teplowsky.

Spencer reports a case of primary cholesteatoma of the orbit extending into the frontal sinus. Fourteen years later squamous cell carcinoma appeared in the orbit.

Teratomata of the orbit are reported by Cattaneo, Corbett, Kearney, Malkin, Offret, Saradarian, Truszynska.

Orbital cysts arising from the eye are reported by Halbertsma, Safar, Stargardt, Weyman.

Van Duyse reports a bulbous cyst in an apparent anophthalmos which he interprets as an enlarged primary optic vesicle.

Cange, Valliere-Vialeix, Beynes and Thouvenet, Zentner describe origin and growth of the mucocele.

Encephalocele of the orbit is reported by Aulamo, Cohen, Kreiker, Lotin, Schousboé, Stuart, Zeidler.

Belski, Hartmann, van der Hoeve, Magnus, Mann, Schindler, Tirelli report sarcomata of the orbit.

Sarcomata affecting extrinsic eye muscles are reported by Lewitskaja, Sheveleff. Also, Offret reports the primary malignant tumors of the orbital musculature which represent fibrosarcoma, rhabdomyosarcoma, leiomyosarcoma and polymorphosarcoma.

Thies reports a case of sarcoma of the antrum perforating into the orbit and the eye globe.

Eber found all structures of the orbit including the eye destroyed in a leukosarcoma of the orbit. Also, Lopes de Andrade reports a leukosarcoma of the orbit.

Lymphosarcomata of the orbit are described by Bietti, Franklin and Cordes, Hartshorn, McKinney, Rumbaur.

Velter reports a lymphosarcoma of the orbit originating from the paranasal sinuses.

Lopes de Andrade found bilateral small-cell sarcomata of the orbit.

Courtis, Gomez-Marquez, Ridley report round-cell sarcomata of the orbit.

Schlippe considers a retrobulbar spindle-cell sarcoma in a child as originating during the fetal life.

Levkoeva describes histologically a fibrosarcoma of the orbit with numerous psammomatous bodies extending into the paranasal sinuses.

Cunningham removed an encapsullated fibrosarcoma from the orbit of a 17 year old boy.

Buckley reports on myxosarcoma of the orbit.

Giant cell sarcoma of the orbit is described by Accardi.

Nida reports osteosarcoma of the orbit arising from the frontal sinus.

Zentmayer reports a spindle-cell sarcoma of the orbit with ossification (osteosarcoma).

Derer describes a melanotic rhabdomyosarcoma arising from the inferior rectus.

Francois observed a rabdomyosarcoma of the external rectus muscle in a 61 year old woman.

Calhoun and Reese report on rhabdomyosarcoma of the orbit.

Goldstein and Wexler report a tumor of the orbit of the type of osteochondro-fibro-sarcomatosis.

Rottino and Kelly saw a case of primary malignant melanoma of the orbit; further a malignant melanoma is reported by Foster in a 65 year old woman.

Birch-Hirschfeld, Goes, Mulock Houwer report melanosarcoma of the orbit.

Casanovas believes that the orbital melanomata originate from chromatophors of the sclera.

A case of malignant myeloblastoma of the orbit is reported by Sjoegren.

Malkin describes a chloroma of the orbit with polymorphous cells with little cytoplasm and large nuclei and containing greenish lipoid granules.

Blatt, Cohen, Goodman and Iverson, Merkulov report chloromata of the orbit.

Three cases of chloroma of the orbit consisting of dense fibrous stroma with few vessels and mononuclear cells are described by Ashby and Smith. They further describe a chloroma of the orbit in a 9 year old boy in which small round or angular cells with deeply stained nuclei lay in a fine reticulum.

Gamble reports a 7 year old girl with myelogenous leukemia and chloroma of the right orbit. The eye of this side showed detachment and hemorrhages of the retina and a heavy infiltration of the choroid with lymphocytes and myeloblasts.

Derer and Friedmann report chloroma of the orbit of a six year old boy with myologenous leukemia with infiltration of liver, spleen, kidney, dura, stomach and bone marrow. They call the orbital tumor a chloromyelosarcoma.

Pascheff reports cases of chloroma of the orbit containing eosinophil myelocytes.

Gump, Hester and Lohr found a monocytic chloroma in the orbit of the type of a reticuloblastoma in a 55 year old man with leukemia.

Endotheliomata resp. peritheliomata of the orbit are reported by Arnold, Bledsoe, Boulans, Collevati, Contino, Lamb, Lundsgaard, Mayer, Schindler, Sgrosso, Sugita.

Cylindromata of the orbit are described by Baron, Castello, Colrat and Rollet, del Duca, Favoloro, Sijpkens.

Black reports reticulum-cell sarcoma of the external rectus muscle consisting of densely packed cells with spherical or oval nuclei and indistinct cytoplasm.

Buerki describes a retothel sarcoma of the orbit corresponding to Ewing's sarcoma in a case of generalized retothel sarcoma. The sarcoma is probably of reticulo-endothelial origin.

Offret describes a malignant reticulo-endothelioma of the orbit in a 45 year old woman.

Delane and Offret report malignant reticular tumors of the orbit and face which frequently have undifferentiated myeloid and lymphoid cells.

A case of lymphangio-endothelioma of the orbit originating in the lacrimal gland is reported by Caramazza.

Arnold found an angiosarcoma in a 56 year old man. The many vessels were surrounded by cell mantels with many mitoses.

Happe reports a primary retrobulbar squamous cell carcinoma of the orbit.

Suker reports a case of squamous cell carcinoma of the orbit which probably developed from an anlage of ameloblast cells.

Ball found squamous cell carcinoma of the antrum extending into the orbit.

Schousboe describes a basal cell carcinoma of the lid skin extending into the orbit and paranasal sinuses.

van der Hoeve reports a case of basal cell carcinoma of the orbit.

Veasey and Veasey saw a medullary basal cell carcinoma of the orbit.

Davis and Garret found an epithelioma adenoides cysticum in the orbit of a 5 year old child.

Sniderman and Neel found metastatic adenocarcinoma of the orbit situated in the muscles with the primary tumor in the pancreas.

Epithelioma of the orbit arising from an epithelial tumor of the ciliary body is described by Saelhof.

Metastatic carcinomata of the orbit are found by Bonnet and Paufique, Finoff, Green, van der Hoeve, Knapp, Larsen, Meyer, Michail, Rollet and Colrat, Wessely.

Burch, Rollet and Colrat report metastases of hypernephroma to the orbit.

Gerlach, Jaensch, Lane report mixed tumors of the orbit.

Fleischer and Scheerer, Rodriguez Villegas, Damel and Casalins Molinari report extensive gliomata of the orbit.

Coppez, Simon and Claes report metastatic sympathicoblastoma of the orbit in a 5½ year old child with primary tumor in medulla of the adrenal. The tumor contains lymphocytoid elements, sympatholblasts and fibrils.

Hughes and Ambrose found in a 20 year old woman an orbital tumor consisting of cells of the adrenal cortex type with arrangements as in the zona reticulata, and round cells. They consider the tumor as an adrenal rest which is found occasionally in the head region.

Guibor reports an adrenal neuroblastoma with orbital metastasis showing nondifferentiated neuroblasts.

Metastatic sarcoma with the primary tumor in the adrenal in a three year old child was found by Zanetti.

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Chapter XVI

OCULAR DEVELOPMENTAL ABNORMALITIES

1. General Considerations

The causes of these often familial hereditary, but also sporadically appearing abnormalities of the eye are in many cases still unknown. The deformities arising spontaneously in nature are based on germ variations (gene variations) and can be inherited. Inhibitions in the development of the embryonic eye occur in various stages so that the whole or parts of the organ develop abnormally. Malformations, although very different in the completed stage, can often be traced back to the same origin. The investigation of the deformities is often by animal experiment. Animals with deformities of the eye are bred according to plan and the eyes of the embryo are examined at different stages of development. Furthermore, the developing germ plasm is alterable by chemical and physical influences, as by adding or subtracting minerals and salts of sodium, potassium or magnesium, by vitamins and by exposure to x-ray; thus, in these ways also, abnormalities can be produced in the eye. It is understandable that mechanical influences like trauma of any kind disturb development. Amniotic bands are often accused of causing malformations. Faulty implantation of the ovum in the uterus is occasionally responsible for deformities. Congenital abnormalities are often the result of intra-uterine inflammations, either acute or chronic; among the latter, especially lues is to be noted. It is often difficult, in any particular case to decide whether germ variation, mechanical influences or inflammation caused the congenital anomaly.

With the congenital abnormality of the eye are associated congenital defects of the skull (especially of the brain) and of other parts of the body. These are: arrhinencephaly, meningocele, encephalocele, cysts in the central nervous system, defects

of cranial nerves and brain substance, micrencephaly, anencephaly, defects and deformities of bones of the skull, failure of closure of embryonic fissures of the face, otosclerosis, congenital deformities of the heart and blood vessels, congenital deformities of the skeleton (osteogenesis imperfecta, osteopsathyrosis, fragilitas ossium, syndaktylism, hyperdactylia), spina bifida, neurofibromatosis and polycystic inner organs (kidney, liver, pancreas). The more degenerative changes that can be found in other parts of the body, the more likely will the diagnosis of a hereditary familial anomaly be well founded.

Not all deformities of the eye seen in man are examined anatomically.

2. Coloboma

Coloboma is frequent and can affect any part of the eye. It appears most often as a typical coloboma due to prevention of closure of the fetal cleft. Atypical coloboma is the formation of a cleft corresponding to other parts than the fetal cleft. Closely related to this group are the inferior conus and pits of the papilla. These developmental disturbances are often associated with others in the same eye.

Coloboma of the uvea affects the iris, ciliary body and choroid either separately or in combination, and the eye is microphthalmic or shows other abnormalities. Coloboma of the iris represents a circumscribed total defect in the tissue. It may reach to the ciliary border or the defect may be partial, as when a stump is still present in the coloboma in which the sphincter is largely absent, or is still recognizable as deformed muscle tissue. The coloboma is in both cases complete, as every tissue is absent in the coloboma. The pigmentary epithelium usually borders the folded margin of the stump. Mesodermal strands which extend into the chamber angle are sometimes found in the coloboma. The coloboma can be traversed by mesodermal tissue representing remnants of the lamina iridopupillaris (bridge coloboma). The pupillary membrane or part of the fibrovascular capsule of the lens can persist, or the iris can adhere to the cornea. The formation of the chamber angle is often inhibited. Coloboma of the lens may also be present.

Typical and atypical colobomata of the iris are seen, which are of different origin. The typical coloboma apparently arises by prevention of the closure or the abnormal closure of the fetal cleft, and is associated with coloboma of the ciliary body and the choroid. In this case, the elements from which the iris should normally grow are not present on the anterior margin of the open cleft. The primary cause seems to be in the ectoderm of the optic vesicle. The inner retinal layers grow excessively at the margin of the fissure and become everted and doubled and the eversion prevents the closure of the cleft, although the mesoderm remains normal. But, according to other theories, the primary cause is said to be in the mesoderm which grows into the fissure. If it develops in too great an amount and is dense, it persists abnormally and the fissure cannot close. The atypical iris coloboma (iridoschisma, simple coloboma) may originate either when growth of the iris is prevented by persisting strands of the fibrovascular sheath of the lens; or when the origin of the defect lies in the ectoderm, where, normally, deep notches are present at the rim of the optic cup; if the cup does not continue to grow, mesodermal tissue remains in these notches. There are some who advocate theories that the appearance of typical and atypical colobomata can be explained by the same cause. It is assumed that the eye, and with it the fetal cleft, undergoes rotation during development (rotation theory). It is said that atypical subsidiary fissures can be present which normally are found only as deep notches at the rim of the optic cup. All colobomata are also traced to early intra-uterine inflammations which are said not to leave any residua in the sense of newly-formed tissue, but prevent the development of the normal tissues in the inflamed area (inflammatory theory). It is also assumed that in case blood vessels do not develop in areas, the tissues do not develop at all in those places (vascular theory). The theories advanced for the explanation of coloboma of the iris are also applied for typical and atypical coloboma of the ciliary body and choroid.

In coloboma of the ciliary body, there is complete absence of the ciliary body in circumscribed areas of various extent. This coloboma may be an isolated finding or part of a complete

coloboma of the uvea. The ciliary body is interrupted in the involved area by an indention which is lined by hypertrophic ciliary processes. In the area of the coloboma, all the constituent tissues of the ciliary body are absent and are replaced by fibrous vascular tissue in which eventually cartilage can also be present. This tissue may also represent persisting mesodermal tissue of the embryonic vascular system which prevents the formation of the ciliary body in this area. Remnants of the hyaloid artery or of the tunica vasculosa lentis can unite with this tissue. Sometimes the ciliary body is shifted either as a whole or only in its ectodermal parts, anteriorly or posteriorly.

Coloboma of the choroid is characterized by the absence of choroidal tissue in the involved area. The sclera is thinned and its inner layers are missing entirely. The pigmentary epithelium stops at the margin of the coloboma and pigmented cells may accumulate here. The retina is either normal in the area of the coloboma or is reduced to a thin membrane, sometimes with one or two layers of cells; the undifferentiated membrane can contain, besides elements of the retina, also elements of the choroid (intercalary membrane). The retina sometimes shows rosettes, glial proliferation or cystic spaces in the coloboma. It may be folded or reduplicated, so that two rows of rods and cones lie in apposition. The normal papilla may be included in the coloboma of the choroid, or the papilla may participate in its formation.

Colobomata at the optic nerve entrance show great variety. The coloboma may contain (a) choroid and nerve, or (b) only the nerve and its sheaths. In the former case, there is an ectasia at the lower margin of the papilla in which there are rests of the retina, the choroid is absent and the papilla is turned into the ectasia, so that the lamina cribrosa is perpendicular to the sclera. There are either normal central vessels present with the parts of the rotated papilla being normal, or the vessels are abnormally developed and enter the retina as cilio-retinal vessels, or enter the retina only through the sclera at the margin of the ectasia without passing through the optic nerve at all. In the latter case, retina and choroid are normal and the formation of the coloboma affects, to varying extent, only the optic

nerve and its sheaths. Usually, the lower half of the optic nerve is defective, the lamina cribrosa may show circumscribed defects or be missing altogether. Retina can be evaginated into the defect and eventually form a cystic projection which can be situated between choroid and sclera or displaced into the sheaths of the optic nerve. Probably it is brought about by active ingrowth of elements of the secondary optic vesicle into the surrounding tissue. A deep excavation can originate through defects of the sheaths of the optic nerve, in which case the optic nerve fibers are entirely pushed to the opposite side. The coloboma of the optic nerve can be brought about by excessive growth of the ectodermal part of the secondary optic vesicle or by persistence of mesodermal tissue in the fetal cleft.

In a macular coloboma, the choroid is entirely absent or the choriocapillaris and the remainder of the choroid is more or less rudimentary and the pigmentary epithelium is defective. The retina shows various degrees of disintegration. Its origin is explained by defective formation of the choriocapillaris in the macular region. Probably it is the result of intra-uterine inflammation.

3. Heterotypical Conus

Related to the colobomata are the heterotypical conus and pits of the papilla. There are gradual transitions between them.

The heterotypical conus is congenital in contrast to the acquired, temporal conus and is usually inferior conus, rarely the nasal or superior type. The choroid is absent in the region of the conus or is formed rudimentarily. Retina, pigmentary epithelium and Bruch's membrane cease at the margin of the conus and only the latter sometimes reaches somewhat deeper into the conus. The nerve fibers traverse the conus and enter into the papilla. Sometimes they lie on a single row of cells or on an irregular tissue consisting of glia. The sclera is often thin or ectatic in the region of the conus. It goes into the lamina cribrosa and dura on the side of the conus in a flat arc; on the opposite side, the sclera projects spurlike into the papilla together with choroid and pigmentary epithelium. Inferior conus is often accompanied by two completely separated

entrances of the retinal vessel and double physiologic excavation. There is, perhaps, an anomaly in the closure of the fetal cleft with primary malformation of the papilla epithelialis, but the lesion may also be in the mesodermal tissue as the choroid and eventually the sclera are said to be formed hypoplasticly in the area of the conus.

4. Pits in the Optic Disc

Pits in the optic disc (crater-like holes) are usually situated on the temporal side. They are surrounded by pial tissue and they extend through the defective lamina cribrosa toward the sheaths of the nerve. Glia, nerve fibers and rudimentary retina line the pial tissue of the pit. They extend from otherwise normally developed retina and tissue of the papilla. The space of the pit is traversed by a net-work of fibers expanding fan-wise into the vitreous body. Nerve fibers from the retina course around the pit and continue into the normal tissue of the optic nerve but at the outside of the pit there are aberrant nerve fibers which traverse the sheaths and end blindly in the orbital tissue. The pit is considered as a malformation in the development of the fetal papilla, since the posterior part of the cavity of the optic stalk is said to remain open. On the other hand it is explained as the result of an active proliferation of retina into the papilla or into the intermediary tissue. There may be present in the papilla also a metaplasia of the nervous elements into retinal elements.

5. Microphthalmos

Microphthalmos is present only infrequently in pure form (nanophthalmos); in this condition, an otherwise normal eye is congenitally small. Usually the macula is not developed and there are other hereditary deformities. It is an hereditary abnormality and is frequently accompanied by glaucoma due to a small cornea, shallow chamber and relatively large lens. In the majority of cases, microphthalmos is combined with coloboma. Microphthalmos is often secondary to other defects of the eye. The cornea is remarkably small and shows various defects. Bowman's and Descemet's membranes are absent and

the endothelium is defective. The small cornea sometimes contains many vessels. The chamber has fetal structure. There is a more or less complete congenital pupillary membrane which can be attached to the posterior surface of the cornea. At the same time, vascularized tunica lentis can remain into which extend vessels from the pupillary membrane. Iris shows ectropion uveae and posterior synechiae or is absent or developed deficiently. The relatively abnormally large cataractous lens is displaced. By traction of membranes, the lens capsule can be opened and the lens resorbed entirely. The cornea as a whole is sometimes underdeveloped or is absent entirely. With the absence of the cornea, iris and lens can also be absent, so that no anterior or posterior chambers are present and only sclera surrounds the retina. The folded retina displaces the vitreous body and is sometimes not attached from the beginning. If a retinal fold bulges far forward from above and below and both unite, bulbus septatus results. The pigmentary epithelium can form extensive reduplications which eventually project freely from the iris into the interior of the eye. The hyaloid artery and its branches persist and unite with the vessels of the tunica vasculosa lentis. Hyaline cartilage, fat and bone can be formed by metaplasia in the persisting connective tissue. The retina often consists exclusively of glia, sometimes producing tumor-like gliosis. Due to aplasia or atrophy, the optic nerve has only glia with few or no nerve fibers. Microphthalmos often has colobomata of varying extent. In the region of the coloboma, the retina can protrude and form solid tissue or bulge greatly, evaginate and form a cyst (microphthalmos with retinal cyst). The cyst lies inside the muscle cone and is surrounded by a connective tissue capsule. In the majority of cases of microphthalmos, a developmental abnormality is present; only rarely is intra-uterine inflammation found. But as the patient gets older, microphthalmos often undergoes inflammation, resulting in infiltration, membranes, scars and formation of bone.

6. Anophthalmos

Anophthalmos is said to be present if there is no vestige of the bulb. But usually there is, in spite of clinical absence of

the eye, microphthalmos of marked degree deeply hidden beneath conjunctival tissue (cryptophthalmos). The eyelids are underdeveloped and the extrinsic eye muscles, if present, insert into undifferentiated tissue. There are small formations containing ganglion cells, nerve fibers, glial and pigment cells. Sometimes there are minute cystic formations containing some pigment epithelium and retina. The optic nerve is absent or there is only a fine strand. The chiasm, optic tract and primary optic ganglia are absent or are rudimentary. Other abnormalities of the cranial nerves and brain may be found. The optic anlage either does not develop at all or there is only a rudimentary development of mesodermal parts of the eye or rudimentary ectodermal and mesodermal development.

7. Cyclopia

In cyclopia (synophthalmos) both eyes are partly fused in the midline in various degrees. Externally there is one eye seen to be present in the mid-line. In the majority of cases, both eyes are still recognizable inside, since parts of the organ are represented in a pair each of cornea, iris, lens, ciliary body, vitreous body, retina and optic nerve. The sclera of both eyes unites in the region of the fetal cleft. The resulting eye frequently is rudimentary, shows colobomata and aniridia and is eventually associated with orbital cysts. Four lids are developed and fused, with loss of the lacrimal punctae. Extrinsic eye muscles are fused in varying proportions, more often those innervated by the oculomotor nerve than those innervated by the trochlear and abducens nerves. There are many variations and possibilities: (1) Both eyes may be moved close together but each lies in a separate orbit, and there is a very narrow, simple nasal cavity; (2) the globes may be close together and the nose is moved upward in the form of a proboscis (snout); (3) the eyes lie in one common orbit; (4) there is a common sclera for both globes; (5) the optic nerves are moved close to each other, the scleral tissue is thin, but the other parts of the eye are double; (6) the cornea is single and horizontally oval, the other parts are double; (7) the cornea is single, two lenses

are fused in the midline, sclera, uvea, retina and optic nerve are single; (8) the eye is single, the optic nerve is absent and the eye muscles are double; (9) there is one single eye; (10) there are in a single orbit two microphthalmi without lenses as simple cysts. The optic nerves are missing entirely, or if they are present they are developed rudimentarily. The papilla is frequently absent. The optic nerves (sometimes there is only one nerve present) can be replaced by connective tissue strands. There are extensive defects in the central nervous system, especially in the anterior brain. The olfactory nerve and hypophysis are absent. Related is the diophthalmic diprosopia. The opposite faces of twins unite and, with this, the eyes. Two opposite eyes fuse together and are turned toward the shoulder. Depending on the plane in which the faces fuse with each other, there can also be present three or four eyes in this malformation (triophthalmic and tetrophthalmic diprosopia).

It is questionable how cyclopia originates. It may be assumed that two optic anlage are present and that they unite, but there may also be cases in which there is only one optic anlage formed. A mechanical theory exists, with some experimental proof, that amniotic membranes exert pressure in the midline. Furthermore, it is assumed that the middle parts of the face do not develop and that in this way the eyes move closer together. On the other hand, much emphasis is put on chemical theories which hold that toxic influences in a very early stage inhibit the normal development of the optic anlage.

8. Cryptophthalmos

Cryptophthalmos exists, as already mentioned, if no eyeball is visible, but buried in the depths of the orbit; there is a malformed eye or part of an eye. Often only skin, without formation of the tissues of the lid, extends over the rudiment of the globe. In this case, cornea, anterior chamber and iris are absent and rests of the lens and vitreous body can be present and the posterior segment of the bulb be developed. Pressure of the amnion before the development of the lids is mentioned as the cause.

9. Cysts

Orbital cysts appear congenitally in various forms: (1) as cysts of the primary optic vesicle (congenitally cystic eyeball); (2) as cysts with microphthalmos; (3) as serous cysts without connection with the globe. The congenitally cystic eyeball shows lining with a simple layer of epithelial cells in its posterior part which are partly pigmented; anteriorly, there is a tissue in which retinal layers arranged irregularly can be recognized. The retinal layers are arranged in inverted manner, the normal outer layers being turned toward the inside of the cyst. The retinal tissues can swell to tumor-like masses of glial tissue. Anteriorly, a malformed lens invaginates into the cyst; externally the cyst, which is uni- or multiocular, is surrounded by fibrous, sclera-like tissue into which underdeveloped eye muscles insert. The optic nerve occasionally enters the glial masses. A rudimentary uvea may be present. If, besides the malformed lens, a defective cornea, iris and ciliary body develop, the deformity gradually passes to that which is called congenital nonattachment of the retina. The space of the cyst represents the primary optic cup in which invagination did not take place or has only begun without becoming complete. A cystic eyeball may remain small and can be hidden in the tissue, resembling anophthalmos. The cysts which exist together with microphthalmos, originate in reality from colobomata of microphthalmic eyes. The cysts remain small in relation to the globe, but can exceed the eye rudiment many times in size. There are various degrees between the extreme cases, producing a number of varieties. The microphthalmic bulb may have a colobomatous opening through which the retina is evaginated, forming small cysts. But often there is a large cyst surrounded by connective tissue bulging into the lower lid. Also, choroid can partly extend into the wall of the cyst which is lined entirely by retina. The retina itself undergoes manifold changes. The outer lining is formed by the pigment epithelium which undergoes changes; part is nonpigmented, part proliferates to form several layers and also encloses retinal elements. The retina itself is changed: some layers can be recognized but they are rarified and disintegrated

and contain cystic spaces; the glia proliferates and rosettes are formed. The folded retina sometimes alternates with an accumulation of glia and connective tissue and even glial tumors can develop. At times in the same layer pigmented and nonpigmented epithelium, glia and imperfectly differentiated retina alternate with each other. The rudimentary retina turns its normally inner layer to the inside of the cyst or it is inverted and its normally external layer, in which rods and cones are absent, turns toward the inside of the cyst. This is usually the case at the margin of the coloboma where the retina is reduplicated. The cystic space is filled with protein-rich fluid or is more or less narrowed by proliferation of glia and connective tissue. The rudimentary bulb shows defects of the cornea with missing Bowman's and Descemet's membranes, the iris is often missing, the lens is displaced and cataractous and shows defects or is missing altogether, and the vitreous body is filled secondarily with vascularized connective tissue which eventually contains cartilage and bone. The cyst can be surrounded by lymphocytes. The lumen of the cyst opens by a pedicle or by direct wide communication, either into the vitreous body, or through the neck of a connecting channel with the subretinal space (primary optic vesicle). This extended subretinal space can open secondarily into the vitreous body following atrophic changes and rupturing of the retina. The orbital cysts correspond, in the majority of the cases, with the position of the fetal cleft and therefore bulge the lower lid, but such cysts also appear beneath the upper lid (atypical orbital cyst). Several possibilities can be mentioned for the origin of the cyst. It is possible that the pigmentary epithelium stops at the margin of the unclosed cleft and the retina grows into the orbit through the cleft. If the retina adheres at the margin of the coloboma and becomes folded, it appears doubled up in the cyst. If the fold opens widely, then the subretinal space continues into the lumen of the cyst and the retina is inverted (its outer layers are turned toward the inside of the space). But it is also possible that the pigmentary epithelium itself grows across the open cleft, protrudes and continues to differentiate into retina outside of the eye. In this case, the subretinal space also opens into the lumen of the cyst.

Furthermore, it is possible that pigmentary epithelium as well as the retina itself protrude through the coloboma outside of the eye, in which case the lumen of the cyst communicates with the vitreous body (ectatic coloboma). Atypical cysts can be connected with atypical coloboma, or they originate from overgrowth of the retina in an abnormal direction. There are also congenital serous cysts of the orbit which have no connection with the eye and have as lining an epithelium similar to that of the nasal mucosa, from which it is separated during development and displaced.

10. Megalophthalmos

Megalophthalmos means enlargement of the entire eye. This is a rare event if no other pathologic changes can be found in the large eye. It can also be present without glaucoma. There have been no anatomic examinations to date.

11. Hydrophthalmos

Hydrophthalmos is an enlarged glaucomatous eye due to congenital abnormality of the chamber angle. The eye is enlarged all around and appears spherical. The trabeculae are underdeveloped or are replaced by undifferentiated connective tissue bundles. In other cases, the chamber angle is filled by persistent fetal ligamentum pectinatum, which is present in animals and in the human embryo and atrophies in the course of the development and which consists of loose pigmented tissue with many spaces. Schlemm's canal is entirely or partly absent. In some cases, the iris is peripherally attached to the cornea. The weak corneo-scleral junction is thinned and stretched so that the limbus lies far anterior to the recesses of the chamber angle. Much more rarely the junction is thickened as a sign of compensatory hypertrophy. Bowman's and Descemet's membranes of the thinned cornea are often ruptured, corneal lamellae are hydropic, causing opacities, and a hyaline network may be formed in the anterior chamber. The iris is thickened or atrophic, a connective tissue membrane deposited on its anterior surface can produce ectropion uveae, and endothelium and

Descemet's membrane can proliferate on it if the chamber angle is blocked. The sphincter is thinned, elongated and subdivided. The ciliary body is atrophic, the beginning of the ciliary muscle is displaced posteriorly and only meridional fibers are present. The ciliary processes are thinned and unite with each other and with the posterior surface of the iris. The lens is flat, the zonule stretched and often ruptured and the lens displaced. Nerve fibers and ganglion cells of the retina atrophy and its outer layers disintegrate. A flat, dishlike excavation of the papilla is formed with recession of the lamina cribrosa. The vortex veins are narrowed or occluded and the anterior ciliary veins may be absent as well as Schlemm's canal. The eye may simultaneously show other deformities as coloboma, orbital cyst, and persistent hyaloid artery. Hydrophthalmos can be associated with progressive myopia; in this case, the large eye becomes oval and the posterior sclera is thinned and bulges posteriorly (staphyloma posticum). Hydrophthalmos can be associated with neurofibromatosis and angiomatous formation, especially nevus flammeus of the face. In the case of neurofibromatosis, plexiform neuromas of the lids or orbit and neurofibroma of the ciliary nerves appear. In the case of angiomatous formation, there are capillary angioma of the cheek, the skin of the lids, the conjunctiva, the mucosa of the mouth and throat (capillary nevus), and also angiomatous formation of the meninges and the brain surface, which latter may be reduced in size (Sturge-Weber syndrome). There are never angiomatous changes in the intrinsic eye.

It is open to discussion whether these pathologic changes are coexisting malformations without causal relationship, or whether abnormal nervous influences of the trigeminus produce tissue changes followed by neurofibromatous formation, capillary nevi and hydrophthalmos, as all the affected tissues including the meninges are innervated by the trigeminus.

Hydrophthalmos is considered by some as congenital primary glaucoma, by others as congenital secondary glaucoma, secondary to congenital deformities of the chamber angle obstructing the outflow of the intra-ocular fluid. There are also cases of congenital glaucoma which follow intra-ocular inflammatory

changes and in which the anterior chamber is abolished partly or entirely. These cases can be classified in the group of secondary glaucoma (buphthalmos). The cornea and also the corneo-scleral junction are ectatic and a pannus covers the vascularized and infiltrated cornea, showing hydropic lamellae. The iris is attached to the posterior surface of the cornea and its spaces are widened spongelike, filled with fluid. Sometimes only remnants of the iris are visible, sometimes only the pigmentary epithelium covers the posterior surface of the cornea. Thus, these changes lead over to congenital staphyloma which always produces secondary glaucoma. Although some differentiate between hydrophthalmos and buphthalmos, using the former expression for congenital malformation of the chamber angle with glaucoma and the latter for eyes with congenital inflammatory changes leading to secondary glaucoma, others use both expressions for any condition leading to congenital glaucoma.

12. Congenital Anomalies of Various Eye Structures

The Cornea

The developmental anomalies of the cornea are: (1) absence of the cornea, (2) megalocornea, (3) microcornea, (4) cornea plana, (5) keratoconus, (6) congenital dyskeratosis, (7) congenital defect of the posterior surface, (8) congenital opacities and congenital anterior staphyloma, (9) cysts, (10) embryotoxon and (11) hyaline membranes on the posterior surface.

The cornea is rarely absent in cases of microphthalmos. At the same time the anterior chamber, iris and lens are missing and a sclera-like tissue surrounds the retina.

In megalocornea (keratoglobus, cornea globosa, keratomegalia, anterior megalophthalmos), the cornea is enlarged without increase of the intra-ocular pressure, its diameter is larger and its curvature increased. At the same time, the anterior chamber is deep, the iris atrophic, and the lens often enlarged and cataractous. The condition is male-sex-linked, and hereditary. It is a primary overgrowth without known cause. But such a cornea has not been examined histologically.

Microcornea, anterior microphthalmos, is seen in microphthalmos and coloboma, but is found in also otherwise normal eyes. Frequently the entire anterior eye segment is smaller and only the posterior is normal. The cornea is small in diameter and its curvature increased. As the anterior chamber is shallow, glaucoma is frequent. The anomaly is hereditary and recessive.

The cornea plana is small and flat although the other eye may have normal form. During development, the cornea has, in the beginning, the same curvature as the sclera and bulges only later. If this does not take place, then the cornea remains flattened and has only small refractive power. It is familial.

In keratoconus (conical cornea), the center of the cornea presents a conical bulge. The degenerated lamellae there are thinned, ruptures in Bowman's and Descemet's membranes are frequent and, in a line running around the base of the cone, hemosiderin is deposited in the epithelium and Bowman's membrane (Fleischer's ring). The anomaly, apparently being hereditary familial, appears first during adolescence.

In congenital dyskeratosis of the cornea, the corneal epithelium is hornified and Bowman's membrane is missing. Also other dyskeratoses of the skin exist. The inner lamellae of the cornea may be congenitally defective, probably due to deficient formation of the endothelium, since no inflammatory changes are noticeable. The disturbance would be in the mesoderm. Descemet's membrane is absent. A type of inner ulcer originates. In some cases, also, the adjacent lamellae are irregular and signs of iritis and anterior choroiditis can be seen; endogenous infection transmitted by the placental blood stream is assumed as the cause.

For the origin of the noninflammatory defect of the posterior corneal surface, the theory is mentioned that it originates through delay or failure in the separation of the lens vesicle. Here the disturbance would be in the ectoderm.

Congenital opacities of the cornea, if not produced by entrance of aqueous humor through ruptures of Descemet's membrane in hydrophthalmos, can be brought about by intrauterine inflammation, but also by developmental disturbances in the corneal lamellae; they exist in association with adherent

pupillary membrane, iris coloboma and hydrophthalmos. Interstitial keratitis may already be present at birth and shows infiltration, ingrowth of thin-walled vessels and destruction of lamellae, as do the later appearing forms. It may be caused by syphilitic infection of the fetus but other infections can be the cause. Specific interstitial keratitis occasionally changes the growth of the cornea so that it takes a vertical, oval form.

Congenital anterior staphyloma has similarities to acquired corneal staphyloma. It is usually a partial staphyloma of the cornea with irregular epithelium, absence of Bowman's and Descemet's membranes, and very irregular lamellae and few pigmented cells. Pigment epithelium covers the posterior surface. Ulceration may appear in the cornea. The remaining iris is atrophic and degenerated and adherent to the cornea. The ciliary body is pulled anteriorly and distorted, and the posterior segment of the eye is elongated and shows changes of secondary glaucoma. In many cases, it is the result of intrauterine inflammation and it is probable that a keratitis with a large perforation preceded and the prolapsed iris formed the staphyloma. On the other hand, however, there are cases in which malformation has to be assumed, and which eventually appear to be familial. The disturbance is in the faulty separation of the lens vesicle or in the nondifferentiation of the mesoderm which enters between the surface epithelium and the lens vesicle.

The faulty differentiation of this mesoderm can also produce congenital clefts in the corneal tissue. These pseudocysts are surrounded by embryonal connective tissue which protrudes into the lumen. Displacement of the surface epithelium in the corneo-scleral junction gives rise to epithelial cysts.

In embryotoxon, there is an annular opacity of the deeper layers continuous with the limbal tissue, extending in various amounts into the cornea. It originates by adhesion of the lamina pupillo-capsularis to the cornea. This hereditary malformation has not been examined histologically. Also only described clinically are the congenital hyaline membranes of the posterior surface of the cornea which traverse the anterior

chamber in the form of a network and which apparently originate from the endothelial tissue which grows aberrantly over the chamber angle. They may be remnants of inflammatory processes.

The Sclerotics

The developmental anomalies of the sclera are: (1) blue sclera; (2) congenital scleral cysts and (3) cartilage in the sclera.

Blue sclerotics are found to have a circumscribed or diffuse, very tenuous sclera, the fiber bundles of which are normally formed. Also the cornea can be thinned and Bowman's membrane be absent. On the other hand, the sclera can appear of normal thickness and texture. The blue color is given by the increased transparency of the sclera through which the uveal pigment shines as a dark background through an opaque medium. In the one case, the sclera is very transparent due to its great tenuity; in the other case, due to an assumed structural change which diminishes the opaqueness of the sclera. Blue sclerotics are hereditary familial and often associated with fragilitas ossium (osteogenesis imperfecta, osteopsathyrosis) and otosclerosis or deafness due to a cochlear lesion (van der Hoeve's triad). Frequently the blue sclerotics are associated only with fragilitas ossium or only with otosclerosis. In the former, narrow, widely separated trabeculae develop in the bone, osteoblasts are scarce, cartilagenous cells persist, and the bone is poorly calcified. Numerous spontaneous and abnormal fractures appear, even during intrauterine life and the fractures heal by little bone formation and much fibrous tissue. In the latter, in the otherwise compact labyrinthian capsule, foci of spongy bone develop with large narrow spaces which are fibrous and contain numerous blood vessels. The pathologic bone can extend from the margin of the oval window to the foot plate of stapes and produce ankylosis of the stapes, or it may develop exclusively in the bony capsule of the cochlea and be followed by cochlear degeneration. Widespread disturbance of the mesoderm is assumed as the cause. The frequently recorded hyperplasia of the parathyroid may be its cause, but a disturbance of the calcium and phosphorus metabolism cannot be proved

definitely; a deficiency of phosphorus production is also assumed as possible.

Scleral cysts are lined with flat epithelium of one or several layers and their content is serous fluid. Separated epithelial buds from the cornea or conjunctiva are enclosed in the scleral tissue and form the cyst by proliferation and mucous degeneration or secretion. But not all congenital limbal cysts are of epithelial origin; some seem to be evaginations of the anterior chamber and some outgrowths of Schlemm's canal.

Cartilage, which is normally present in the sclera of lower animals, is found in the human sclera now and then in very malformed eyes and considered as atavistic.

The Iris

The developmental anomalies of the iris are manifold, affect the iris tissue, the pupil and tissue which develops together with the iris but normally disappears again. They are (1) aniridia (irideremia), (2) coloboma of various forms and related malformations, (3) hyperplasia of the anterior iris stroma, (4) anomalies of the iris musculature, (5) congenital heterochromia of the iris, (6) congenital iris cysts, (7) anomalies of the pupillary margin, (8) anomalies of the pupil, and (9) persistent pupillary membrane.

In aniridia, there is an extremely rudimentary iris. The small peripheral stump of the iris consists of very pigmented mesodermal tissue and pigment epithelium which is either everted over the anterior surface, or is turned back with rudimentary iris tissue and attached to the ciliary body. Sphincter and dilator are absent. Schlemm's canal and corneo-scleral trabeculae are present. Usually, uveal trabeculae persist. The iris stump may adhere to the cornea and obliterate the chamber angle. The ciliary processes are occasionally small. The lens remains small, and may show anterior and posterior polar cataract and may be ectatic. Vessels of the often persisting tunica vasculosa lentis adhere to the stump of the iris. The pupillary membrane and hyaloid artery may also persist. The retina shows a deficiency of ganglion cells and absence of a fovea centralis. Aniridia can be present in a normal sized

or microphthalmic eye, but relatively often there is a secondary glaucoma caused by occlusion of the chamber angle and persistence of the uveal mesh-work in the chamber angle (ligamentum pectinatum) which obstructs filtration. The absence of the spongy iris tissue which normally helps partly to eliminate the intra-ocular fluid further increases the tension. Even hydrophthalmos can appear. The anomaly is hereditary and of a dominant character. Two theories are currently considered most likely: one according to which the primary defect is in the ectoderm, the other that the cause is a mechanical hindrance due to persistent tunica vasculosa lentis. If the anlage of the ectoderm in the optic vesicle is inferior, its rim does not form, the ectoderm does not grow further anteriorly from here and also the mesoderm does not develop. If the tunica vasculosa persists, then with the vessels extending from the hyaloid system around the equator, these strands hinder the outgrowth of the iris. If the regression of these embryonal formations stops in only a circumscribed area, then a coloboma of the iris occurs; if the regression stops circularly, an aniridia results. Other theories less well founded are that inflammatory processes play a role, or that the lens long remains in contact with the cornea and thus hinders the outgrowth of the iris.

Colobomata of the iris are, as already mentioned, typical if they correspond with the fetal cleft, and atypical, if they occur elsewhere. Malformations related to coloboma are considered to be a notch in the pupillary margin, a hole in the iris substance (pseudopolycoria, iris dehiscence) or a defect at the ciliary border (iridodiastasis) all of which are also thought to be partial colobomata. Defects in the iris sometimes affect the ectodermal or mesodermal layer alone and are called pseudocoloboma (incomplete coloboma). Considerable clinical information on these changes exists, but no anatomic examination. A notch in the pupillary margin is considered a total coloboma of small degree (notch coloboma). There are cases of one or several congenital holes in the iris in which no trace of tissue is evident. The origin is explained by assuming that the peripheral edges of a notch of the optic cup fuse only at the rim, leaving the depths vacant. Iridodiastasis is

similar to acquired iridodialysis, insofar as an oval or round peripheral defect exists in the iris, bordering the ciliary body, but the pupil remains central and round and the margin of the defect is distinctly outlined. Pits in the iris represent a circumscribed defect of the mesodermal iris tissue, in which only the pigmentary epithelium persists and this is sometimes scant. If the atrophy, which normally forms only the crypts, assumes higher degrees, or if branches of the major circle of the iris do not develop in a circumscribed area, such defects are formed. Sometimes only hypoplasia of the anterior iris layer exists in varying extent. It is possible that mesodermal elements which should form the iris, join the cornea during development.

Hyperplasia of the anterior layer of the iris stroma appears as a persistence of the lamina irido-pupillaris which thickens and extends across the pupillary margin. It can be associated with persistent pupillary membrane which sometimes even adheres to a cataractous lens. The tissue is vascular, dense and cellular, and consists of connective tissue fibers, stroma cells and chromatophores. Sometimes the tissue remains as a congenital dense fibrous membrane with few vessels and without chromatophores and is continuous with the pupillary membrane. A hyaline membrane can extend across the anterior chamber, arising from the posterior surface of the cornea in abnormalities of the cornea and the chamber angle and across the anterior surface of the iris, arising from the latter with abnormality of the anterior layer of the iris.

Disturbances in the development of the iris musculature are absence of the dilator (congenital microcoria, congenital miosis) and hyperplasia and displacement of the sphincter. In the case of a congenitally very narrow pupil, the anterior layer of the pigment epithelium does not develop muscular processes which normally represent the dilator. Or the muscular processes, wherever they develop, are irregular in the iris stroma. Where they are absent, the iris tissue is mucoid. The sphincter can be hyperplastic and show formation of convolutions. It can be developed in an abnormal place.

In heterochromia (anisochromia), the color of both irides is different (heterochromia iridum) or a portion of the iris

shows a different color from the other (heterochromia iridis). The color of the pathologic iris is blue, due to deficiency of uveal pigment. It is hereditary and exists without other pathologic changes of the eye (simple heterochromia), but frequently it is complicated by cyclitis and cataract (complicated heterochromia). Disturbance of the sympathetic nerve is assumed as a cause but also the influence of toxins during the intrauterine life may play a part.

Congenital cysts develop in the iris (1) by implantation of surface epithelium into the mesodermal tissue; (2) as an interspace between both the layers of the pigment epithelium; (3) by immigration of clumps of epithelial cells of the neuroectoderm into the mesodermal tissue; and (4) by attachment of atypical ciliary processes to the posterior surface of the iris. Epithelium displaced by outpouching of the surface epithelium into the mesoderm and severed, or epithelium separated from the lens vesicle and displaced, proliferate in the iris and form cystic spaces by mucous degeneration or intraepithelial secretion. The cysts are situated in the anterior iris and develop towards the anterior chamber. Their anterior wall is thinned, consisting of a hyaline membrane with little iris tissue attached and they are mostly lined with flat epithelium which can also contain cylindrical cells. The posterior wall contains much uveal tissue. The annular sinus (von Szily), which closes in the course of development, is found in the anterior portion of the circumference between both epithelial layers of the optic vesicle. If it remains open, it forms cystic space, lined with pigmented epithelial cells, on the posterior surface of the iris. Less frequently, this interspace, which corresponds with the lumen of the primary optic vesicle, remains open between the two epithelial layers in other places than the anterior circumference. Normally, cells migrate from the neuroectoderm to form the sphincter. They may, instead of forming muscle, form a cyst from pigmented cells which can be surrounded by epithelial cells arranged in the form of rosettes and can show connections with the pigmentary epithelium. Atypical ciliary processes occasionally extend as congenital variation from the posterior surface of the iris and have no connections with the normally developed ciliary body. If such processes form con-

volutions and if their completely pigmented epithelium is attached to the epithelium of the posterior surface of the iris the epithelia join and they can form a completely enclosed cystic space. Cysts of the iris can cause glaucoma.

Anomalies of the pupillary border are: (1) congenital ectropion of the pigment border; (2) hyperplasia of the pigmented margin with formation of the flocculi; and (3) congenital entropion of the iris. The pigmentary epithelium grows actively in the case of the ectropion for some distance across the anterior surface of the iris and is sometimes associated with coloboma. The sphincter is everted. The pigmentary epithelium can be hyperplastic at the pupillary margin to form grape-like clusters of flocculi. The pigmented excrescences of the pupillary margin are rounded nodules or flat, strandlike prolongations. They consist of proliferating pigment epithelial cells, some of which have oval and irregular nuclei. The sphincter is large. On the other hand, vascular connective tissue strands extend into the excrescences of the pigment epithelium and they may have a small lumen. If flocculi are detached, they can float as free pigmented bodies in the anterior chamber. They usually become cystic and possess a fibrous wall with pigment and lymphocytic infiltration, or a wall which consists exclusively of several rows of pigment cells or cells which are free of pigment. In the case of entropion, the otherwise normal pigment epithelium ends before the pupillary margin is reached and the sphincter is normal or is folded backwards, but the iris stroma is inverted at the pupillary margin. Rests of the pupillary membrane may be attached to the lens capsule. At the same time, coloboma can be present.

Anomalies of the pupil appear as corectopia, polycoria and dyscoria. In corectopia (ectopia pupillae), the iris, which otherwise has a normal structure, is very thick in the smaller segment and thin in the larger one. The pupillary margin of the small segment is inverted, continues as a strand in which arteries course and extends to the ciliary body, retina or vitreous body. The zonule is missing in an area corresponding to the small segment, or the strand is attached to it. Often at the same time ectopia lentis exists. The latter may be the

cause for the displacement of the pupil, but in many cases the persistence of embryonal vessels which course from the iris to the vascular system of the vitreous body around the margin of the optic cup probably produces the displacement of the pupil. Also, the abnormal development of the mesoderm at the margin of the optic cup, or intra-uterine inflammatory changes are likely causes. Two or more pupils can be present in the same eye, each surrounded by a sphincter. Such cases have been examined clinically but not anatomically. Congenitally abnormal pupils may be slit-shaped, hourglass-shaped, rectangular or pear-shaped, and may show remnants of the pupillary membrane, coloboma of the iris or abnormal strands. Anomalies in the development of the sphincter can be the cause of these clinically but not anatomically examined congenital deformities.

The persistent pupillary membrane, so common in small degree, is sometimes extensive. It contains open or obliterated thin-walled vessels besides both fine and dense connective tissue, fibrocytes and pigmented cells which contain small nuclei and branching processes, and is of uveal origin. The membrane continues, without a border, into the iris surface. Sometimes only flat, pigmented cells remain as rests of the pupillary membrane on the anterior lens capsule, or occasionally they penetrate the capsule and lie on the epithelium. They contain fine, brown pigment and possess radiating processes and oval nuclei. Congenital capsular cataract in the form of circumscribed white opacities, most of which are in the region of the anterior pole, or, less frequently, at the anterior periphery, frequently coexists with a congenital pupillary membrane, or corresponding adhesion of the lateral capsulo-pupillary membrane. They consist of dense connective tissue with oval nuclei situated on the lens capsule and pigment beneath the lens capsule. It is questionable if they originate by active proliferation or by inflammatory changes, or if they are simply developmental anomalies. In the case of a persistent pupillary membrane, pigmented cells can also be deposited on the posterior surface of the cornea. The pupillary membrane is occasionally adherent to the posterior corneal surface. At the place of attachment, the endothelium

is absent and occasionally also Descemet's membrane. This is either the sequel to an ulcer which perforated during intrauterine life, or the tissue of the cornea or the lamina iridopupillaris did not separate at this circumscribed area during development. An extensive pupillary membrane is frequently present in microphthalmos and may be associated with a coloboma. The congenital pupillary membrane is explained on the basis that the normal atrophy of this tissue does not take place; but inflammatory changes may also play a role. Pigmented bodies, floating freely in the anterior chamber, can originate not only from detached flocculi but also from remnants of the pupillary membrane.

The Ciliary Body

The developmental anomalies of the ciliary body are (1) coloboma, (2) congenital abnormalities of the epithelium, and (3) displacement of the ciliary processes.

The coloboma exists in a typical place or is atypical, is isolated or part of a complete coloboma and affects both epithelium and muscle. As congenital abnormalities of the epithelium are also mentioned the pigmentation of the normally nonpigmented inner layer and the replacement of the inner layer by a convoluted retina-like structure (metaplasia). Displacement of the ciliary processes can take place anteriorly or posteriorly and consists of displacement of the ciliary processes against the ciliary muscle. If the area of the optic cup, from which the ciliary processes normally originate, is pulled, for any cause, anteriorly or posteriorly during development, the ciliary processes are displaced, although the ciliary muscle remains fixed in its normal position. If the iris adheres to the cornea during development, the ciliary processes are pulled anteriorly and choroid covers the inner aspect of the ciliary muscle. Due to a persistent mesodermal membrane or coloboma, the iris may not grow anteriorly, or occasionally, in microphthalmos, the ciliary processes may be displaced posteriorly.

The Choroid

The developmental anomalies of the choroid are coloboma and choroideremia. Colobomata of the choroid are typical and

atypical and macular coloboma, in which apparently the defect is also primarily to be looked for in the choroid. Choroideremia is characterized by complete absence of the choroid and the pigmentary epithelium except in the macular region.

The Retina

The developmental anomalies of the retina are: (1) rosette formation, (2) absence or abnormal development of the macula or fovea centralis, (3) medullated nerve fibers, (4) displacement or metaplasia of retinal tissue, (5) congenital retinal septum and congenital cysts of the retina, (6) atypical folds of the retina, (7) pigmentary retinopathy and Oguchi's disease, and (8) retinal changes in the anencephaly and encephalocele.

Rosette formation is most often seen in microphthalmos and in colobomatous eyes. Tubular formations are seen, lined with cells resembling cyclindrical epithelial cells forming a distinct membrane projecting inward, which membrane is explained as being the folded external limiting membrane. The tubular spaces connect with the subretinal space and are considered to be foldings of the retina, especially of the external nuclear layer. Glial proliferation, formation of cysts and disintegration of the retina, which shows many rudimentary elements, may be added findings. Rosette formation may be easily caused by exposure of the fetus in the uterus to the therapeutic doses of x-rays to the mother. It is due to hyperplasia of retinal tissue, probably with an overgrowth of glial elements. The rosettes of the malformation are distinguished from those in retinoblastoma in that they are spherical in the latter, probably do not contain any external limiting membrane, and are not connected with the subretinal space.

Absence or hypoplasia of the macula is connected with nondevelopment of the fovea and in this way shows persistence of the fetal condition as it contains large ganglion cells, an inner plexiform and an inner nuclear layer. This condition is found in albinism, microphthalmos, aniridia and persistent hyaloid artery. Misplacement of the macula (heterotopia) is observable ophthalmoscopically. The macula is displaced temporally and upwards.

Medullated nerve fibers (opaque nerve fibers) are found in the retina as a developmental disturbance of varying extent. The normal medullated nerve fibers end at the lamina cribrosa where the nerve fibers are nonmedullated under all circumstances; as an abnormality, medullated sheaths may be seen again beyond the lamina in the papilla and in the retina, although otherwise the papilla and retina are normal and only occasionally are other malformations present, as, for example, coloboma.

Retinal tissue can be displaced, or textures can originate which normally are not found in this area (metaplasia). In this manner, inverted retina may be found in place of the pigmentary epithelium and is considered as developed from the latter. This takes place in colobomatous eyes with cysts or in cyclopic eyes. Pigment epithelium can be nonpigmented (leukosis); it is found in this fashion in coloboma of the choroid.

Congenital retinal septum (Mann) is found as a reduplication of the retina which protrudes foldlike into the vitreous body. The retina of the fold is only slightly differentiated and contains proliferating glia and rosettes; pigment epithelium does not partake in the formation of the fold. The fold is often seen in connection with a persistent hyaloid artery. If the primary vitreous adheres to the inside of the optic cup, it hinders the formation of the secondary vitreous in this area, and eventually such a retinal septum is formed. Occasionally, a fold consisting of rudimentary retina extends from the ora serrata in some area behind the lens across to the ora serrata of the opposite side (septum frontale). It is interpreted as detachment of the retina with the formation of strands, or the proliferation of ciliary epithelium which becomes differentiated to rudimentary retina. A congenitally detached retina can form a large cyst, the pathogenesis of which is unknown.

Atypical folds of the retina consist of not completely differentiated retina, containing proliferating glia and connective tissue, and show a strong tendency to extend between the choroid and sclera and into sclera, or even into the optic nerve and its sheaths.

Pigmentary retinopathies of various forms are hereditary familial. Often they develop in adolescence. There is espe-

cially a tendency of the pigment to proliferate into the retina and to fill the perivascular spaces. In Oguchi's disease the retina is found in the area between macula and papilla, nearly exclusively made up of large cones many of which have ectopic nuclei. There is, furthermore, an abnormal layer consisting of syncytial tissue containing many pigment granules between the cones and pigment epithelium. The disease appears as hereditary recessive in Japanese families.

If the eyes are not normal in anencephaly, the ganglion cells and nerve fibers are missing. Sometimes, in their place, there are large cells of embryonal structure. Coloboma, microphthalmos and cysts can exist. Apparently, the brain is present during the early stages of development, the optic vesicles pouch out and soon afterwards disturbances may appear in further development, especially of the cerebrum. Aplasia of nerve fibers and hypoplasia of ganglion cells of the retina can be seen in encephalocele. In rare cases, on the other hand, the anterior portion of the globe can be filled with parts of the brain if an encephalocele protrudes through the sheaths of the optic nerve.

The Optic Nerve

Developmental abnormalities of the optic nerve are: (1) coloboma, (2) inferior conus, (3) peripapillary ectasia, (4) congenital absence of the optic nerve, (5) hypoplasia and aplasia of the optic nerve, (6) enclosure of retinal tissue and pigmentary epithelium within the optic nerve, (7) congenital atrophy of the optic nerve, (8) aberrant nerve fibers, (9) division of the optic nerve, (10) displacement of the papilla (heterotopia) and abnormal shape of the papilla, (11) pseudoneuritis, and (12) abnormality of the central retinal and the ciliary vessels.

Coloboma of the optic nerve is usually a coloboma of its sheaths and may have, as already mentioned, different shapes. There is an evagination of the sheaths and a colobomatous excavation can resemble, in ophthalmoscopic appearance, a glaucomatous one (pseudoglaucomatous excavation) in which the branches of the central retinal vessel climb over the edges of the excavation.

In the area of the inferior conus, the choroid is defective and pigmentary epithelium and retina stop at the margin of

the conus. Usually there is an associated hypermetropic astigmatism. The conus is considered as a primary underdevelopment of the mesoderm in the area of the fetal cleft, with secondary aberration in the arrangement of the retina, the papilla or the vessels; or as primary underdevelopment of the pigmentary epithelium with secondary aberration in the arrangement of the choroid and retina.

Peripapillary ectasia (staphyloma) appears as an ectasia of the sclera around the papilla, which is displaced into the depth of the ectasia. Also, peripapillary atrophy of the choroid appears in the ectasia. It is perhaps a form of coloboma of the optic nerve or of its sheaths or a congenital ectasia of the sclera. These rare cases have been observed clinically, but not examined pathologically.

Congenital absence of the optic nerve is seldom verified in man. In cases of microphthalmos, anophthalmos and cyclopia, it occasionally happens that no optic nerve develops. In this case also, no nerve fibers and no ganglion cells are present, being replaced by glia and vascular mesoderm. Furthermore, the papilla can be absent or there may only be a scleral canal present through which the persistent hyaloid artery passes. In other cases, the retina may be evaginated into the papilla and its sheaths, particularly if there is coloboma present, and pigmentary epithelium may extend into the optic nerve; this occurs in anencephaly, encephalocele, cyclopia and microphthalmos associated with coloboma of the optic nerve.

In still other cases, the optic nerve may only be hypoplastic. When the nerve fibers develop and grow into the optic stalk its cells become glia. These cells of the optic vesicle can, in rare cases, form pigment epithelium and malformed and disorganized retinal tissue which extend to various degrees into the optic nerve.

Congenital optic atrophy shows patches of atrophy in the nerve stem with a normal chiasm and normal visual pathways. It can also occur in encephalocele and microencephaly and its etiology is unknown. It occurs familially.

Aberrant optic nerve fibers by-pass the sheaths in the form of bundles branching in the orbit.

Occasionally the optic nerve divides into two strands, a main stem, and a small accessory bundle which contains the non-crossing fibers.

There is occasionally observed ophthalmoscopically a displacement of the papilla temporalwards, but much more frequently an abnormal shape of the papilla is seen deviating greatly from the round form.

In case of pseudoneuritis, there is an overgrowth of neuroglia. The eye is usually small and hypermetropic. There have been no anatomic examinations except in case of complications which have led to enucleation but which have also distorted the existing abnormality. Remnants of Bergmeister's papilla and remnants of the tissue around the hyaloid artery often exaggerate the changes of the pseudoneuritis.

The abnormalities of the central retinal vessels and of the ciliary vessels in the papilla, the optic nerve and its sheaths are numerous and various. Most of these are examined only clinically and some lie on the border of physiologic variations. Vascular loops of retinal vessels into the vitreous are usually arterial loops. The artery extending from the papilla into the vitreous body returns to the papilla or the retina. Fine tissue, consisting usually of a continuation of the inner limiting membrane, accompanies the artery. In inversion of the disc, the retinal vessels cross the nasal edge of the disc and turn in a temporal direction after coursing nasally for some distance.

Congenital abnormalities of the ciliary vascular system are: (1) cilioretinal vessels, (2) optico-ciliary vessels, and (3) chorio-vaginal veins. The cilioretinal vessels, mostly arteries branching from the circle of Zinn, appear at the margin of the papilla and usually course in the retina to the macula. The corresponding vein goes from the retina into the choroid and continues from there to the ciliary vascular system. Optico-ciliary vessels branch from the retinal vessels of the papilla, extend into the choroid and thence into the ciliary vessels. Occasionally they course behind the lamina cribrosa to the ciliary vessels. A large vein of the choroid may collect the blood from an area of the choroid and extend into the pial sheath of the optic nerve, although normally the blood is eliminated from the

choroid through the vortex vein. Normally, only capillary anastomoses exist between the retinal vessels and the ciliary vascular system. Circumscribed abnormalities appear in this system if these anastomoses assume large dimensions.

The Lens

The developmental anomalies of the lens are: (1) congenital absence of the lens (congenital aphakia), (2) shrunken fibrous tissue cataract, (3) microphakia, (4) lentoid formations, (5) coloboma of the lens, (6) ectopia lentis, (7) anterior and posterior lenticonus, (8) ring cataract, (9) congenital cataract, and (10) persistence of the vascular sheath of the lens.

Sometimes the lens and the zonule are completely absent congenitally or only rests of their tissue are present. It is possible that in a very malformed eye the lens vesicle does not form from the covering epithelium (as in microphthalmos of high degree). In case of congenital corneal staphyloma and congenital dense corneal scars with adherent iris, the lens may be entirely absent or only rudiments may be present in an abnormal position. The lens capsule and rests of the lens substance may be enclosed by the cornea. In this case, the absence of the lens can be primary as a result of imperfect separation of the lens vesicle, but often the absence is secondary, in which case the formed lens has become cataractous, the lens capsule opened and the cataractous lens resorbed almost entirely.

In fibrous tissue cataracts, there is apparently a lens present, but it consists of fibrous tissue and vessels partly enclosed by a capsule inside of which cells can proliferate. Especially in case of severe intra-uterine inflammation which has led to opening of the capsule, connective tissue and vessels of the tunica vasculosa lentis enter through the open lens capsule, and resorption of the lens and its substitution by fibrous tissue from a cyclitic membrane occurs.

In microphakia, the lens is small and spherical; the lens develops insufficiently and the zonule is weak.

Lens-like structures (lentoid formations) can be formed abnormally from ectodermal cells of the iris and the ciliary body.

A coloboma of the lens represents a defect of the lens margin; simultaneously the zonule corresponding to this area is more weakly developed. The lens capsule, epithelium and cell nuclei appear unchanged in the area of the coloboma and only the course of the lens fibers, corresponding to the indentation, is abnormal. Frequently there is a simultaneous coloboma of the uvea or ectopia lentis present. The weakness of the zonule corresponding to the lens coloboma is caused by coloboma of the ciliary body from which the zonule develops and to which it adheres. The typical coloboma corresponds with the fetal cleft, but colobomata also appear at other places on the circumference; in such cases, it is caused by persistent remnants of the tunica vasculosa lentis which obstruct the formation of the zonule and indent the lens by pressure. Coloboma of the lens sometimes develops in an area corresponding to an iridectomy at an early age.

Closely related to coloboma is ectopia lentis, which appears when the zonule is absent in a circumscribed region or only a few thickened fibers are present, in a direction opposite to the displacement. The usually nasally or inferiorly displaced lens is spherical and small. Underdevelopment of the zonule may be the sequel of atrophic changes in the ciliary region or of intra-uterine inflammation, or be caused by persistent mesodermal strands originating from remnants of the tunica vasculosa lentis which can again disappear during fetal life. But a hereditary factor is involved which appears still more distinct if ectopia lentis is associated with widespread mesodermal disturbances of the body. These are arachnodactyly (Marfan's type) and dolichocephaly. If, in case of an ectopia lentis, the zonule tears all around, spontaneous dislocation of the lens is found.

Anterior lenticonus (lentiglobus) consists of a transparent conical elevation of the lens capsule. The cause lies apparently in a weakness of the anterior lens capsule and the anterior zonule. The capsule stretches and the lens substance protrudes. Perhaps there are also ruptures of the capsule present which usually cause cataract. There have been no histologic examinations.

Posterior lenticonus (lentiglobus) consists in a usually opaque spheroidal protrusion of the posterior pole. The posterior capsule is thin and often torn. There is usually present persistent hyaloid artery and the vitreous body contains much fibrous tissue. The nucleus of the enlarged lens is somewhat displaced posteriorly and the partly cataractous cortical substance bulges toward the vitreous body. The defect of the posterior lens capsule, and its resultant weakness, is caused mechanically by traction of the remnants of the hyaloid artery or of rests of the tunica vasculosa lentis; or the defect is developmental, coexisting with weakness of the posterior zonule.

Congenital cataract is very frequent and appears in many forms: (a) as anterior or posterior polar cataract, (b) disc-shaped cataract, (c) nuclear and zonular cataract (lamellar or perinuclear cataract), (d) axial fusiform cataract (Knies), (e) coralliform cataract (Gunn), sutural cataract, (f) punctate cataract, and (g) total and membranous cataract (pseudo-aphakia). Many of these forms, but not all, have been examined microscopically.

Frequently seen is anterior polar cataract which is either flat or protrudes as a pyramidal cataract into the anterior chamber and has adherent strands of pupillary membrane, or is associated with corneal scars; it consists of long lamellar spindle-shaped cells with oval nuclei arranged parallel to the anterior surface of the lens. They represent proliferating subcapsular epithelial cells and are surrounded laterally by large polygonal, often irregular cells which gradually pass into normal epithelium. The long stretched cells degenerate, lose their nuclei, coalesce and form hyaline. This lamellar hyaline tissue, which ultimately simulates connective tissue, shows deposits of cholesterol crystals and calcium. The deeper lens fibers show degenerative changes of differing extent, the fibers disintegrate and there remain granules, Morgagnian globules, and detritus. The epithelial cells of the margin of the anterior polar cataract sometimes start to proliferate and grow underneath the cataract, separating it from the rest of the lens. They secrete on their anterior surface a new cuticular membrane so that the cataract appears entirely enclosed by a homo-

geneous capsule. Anterior polar cataract can be the sequel of perforating corneal ulcer if the lens adheres to the cornea. Corneal endothelium can remain adherent to the cataract and itself form a cuticular membrane so that the cataract appears covered by double homogeneous membranes anteriorly. Anterior polar cataract sometimes follows iridocyclitis. Toxins originating in an inflamed cornea or uvea can damage the epithelial cells and incite them to proliferate, or primarily destroy the lens fibers and secondarily incite the epithelial cells to proliferate. Even without inflammation an anterior polar cataract can develop and is sometimes hereditary. Prolonged contact between cornea and lens during development can be the cause, or more probable are adhesions of remnants of the pupillary membrane and the tunica vasculosa lentis.

Posterior polar cataract appears as a circumscribed opacity of varying extent with disintegration of the lens fibers following opening of the posterior lens capsule; it is frequently associated with persistent hyaloid artery and fibrovascular sheath of the lens. Through a perforation of the lens capsule, fibrous tissue and vessels enter the lens and form a circumscribed mass at the posterior pole, which is surrounded by disintegrated lens fibers; a total cataract can be formed from this area or the entire lens may be replaced by fibrous vascular tissue which finally shrinks (shrunken fibrous tissue cataract).

A disc-shaped cataract is characterized by the absence of a nucleus. The central area is narrow and is closed anteriorly and posteriorly by folded lens capsule, which contains lamellar tissue with spindle-shaped nuclei. In the periphery, the lens fibers have a lamellar arcuate arrangement. It is assumed that the lens fibers which form the nucleus do not develop during embryonal life and are replaced by proliferating epithelium of the lens capsule.

The existence of congenital granular or complete opacities in the center of the lens (nuclear or central cataract) is seen clinically. A transparent or opaque lens nucleus with zonular opacities in the cortex occurs in congenital or hereditary zonular (lamellar or perinuclear) cataract; this has been examined histologically. The opacities appear in a circumscribed lamella,

usually in the layer of the cortex which is the closest to the nucleus. The opacities are circumscribed and often appear in the form of riders. The lens nucleus appears granular and in the adjacent cortical layer there are disseminated irregular patches which contain hyaline globules and granular detritus in clefts which originate from degenerating lens fibers. The damage affects the lens at a time when the nucleus has already developed and lens fibers are being deposited to form the cortex. Injury of the eye during birth can be the cause of zonular cataract. Lacerations of the lens capsule by torsion of strands can produce the circumscribed opacities of the lens.

Opacities of the lens nucleus sometimes appear in the sagittal axis of the nucleus and take different forms. One of these is the clinically observed axial fusiform cataract in which the nuclear opacity continues anteriorly and posteriorly towards a lens pole.

The coralliform cataract, in which axial opacities with enlarged ends radiate from the center of the lens, has been examined histologically. Large masses of crystals, which are assumed to be the protein derivates cystein and tyrosine, are surrounded by degenerated lens fibers which form granular detritus and homogeneous globules. Adhesion of the nucleus to the lens capsule so that it is pulled into a spindle-form on the subsequent growth of the lens, is assumed as the cause of this form of cataract. The clinically observed sutural cataract consists of fine greyish dots which arrange themselves along the suture lines. In a related cataract form, the greyish opacities are arranged in large spots close to the suture lines (anterior axial embryonic cataract). Sometimes the opacities appear to consist of annular elements in the axis of the lens, especially surrounding the sutures, flowerlike (floriform cataract, Koby).

In punctate cataract, numerous opaque grey dots are scattered throughout the cortex of the lens and they consist of granular debris originating from degenerated lens fibers which are surrounded by normal lens fibers. The dots often appear rather bluish (cataracta coerulea).

In total cataract, all lens fibers are degenerated and the entire lens is homogeneous and contains vacuoles filled with granular detritus and hyaline globules, or the lens fibers are swollen, indistinctly outlined and broken up by clefts formed between them, which clefts are filled with fine, granular masses. Sometimes the entire lens is liquefied and contains fatty masses and flocculent material of degenerated lens fibers, although the nucleus remains relatively intact (congenital Morgagnian cataract). Total cataract originates after severe intra-uterine inflammations and rupture of the lens capsule. Especially when the lens capsule is open posteriorly, connective tissue and vessels grow in from the vascular sheath of the lens and can replace the entire lens substance (membranous cataract), or the entire lens is resorbed except for a few remnants (congenital absence of the lens). Many circumstances lead to the formation of congenital cataract. Germ variations, abnormality of the mother and individual disease of the fetus must be considered. Further causes are malnutrition, vitamin deficiency and avitaminosis, disturbances of the calcium metabolism, as by changes of the parathyroid, and, finally, toxic influences from the mother via the placenta, and exposure of the fetus in the uterus to x-rays.

Of the vascular sheath of the lens, usually the posterior portion persists. Often only minimal rests are present and now and then an extensive fibrous vascular membrane persists on the posterior surface of a lens (pseudoglioma). The lens capsule can be eroded, the lens become cataractous and fibrous tissue grow into the lens. If the vascular sheath of the lens persists, the epithelium of the capsule often grows onto the posterior lens pole. The zonule becomes defective when the ciliary processes become attached to the vascular sheath. Vessels of the sheath can anastomose with vessels of the ciliary body, or, around the equator of the lens, with vessels of the iris. Dense connective tissue cells with oval nuclei can adhere, as remnants of the vascular sheath, to the posterior lens capsule to give a circumscribed posterior capsular cataract. Lateral parts of the vascular sheath of the lens persist more rarely;

they are situated at the equator of the lens and connect with tissue of the persistent hyaloid artery posteriorly and the persistent pupillary membrane anteriorly. They often appear as coarse tissue producing defects of the zonule, notching of the iris, coloboma of the iris and lens, and, through adherence to the ciliary body, detachment of the retina and choroid.

The Vitreous Body

The developmental anomalies of the vitreous body are: remnants or anomalies of the primary vitreous, persistent hyaloid artery and congenital cysts of the vitreous.

As remnants of the vasa hyaloidea propria, floating fibrous tissue may be found in the vitreous or may adhere to the posterior lens capsule. As far as clinical observations permit conclusions, such vessels of the vitreous can eventually anastomose. through colobomata and retino-choroidal scars, with choroidal vessels.

A persistent hyaloid artery is often observed clinically but is rarely examined histologically. The entire hyaloid artery, only its posterior end, or only its anterior end may persist. Cases examined histologically show mainly fibrous membranes on the posterior surface of the lens with which the persistent hyaloid artery remains in contact (pseudoglioma). It originates from the papilla as a strand which contains the convoluted thin-walled patent artery surrounded by glial and connective tissue and into which the internal limiting membrane extends from the papilla. This strand passes centrally through the vitreous and is connected to the coarse fibrous vascular membrane of the posterior surface of the lens. Zonule fibers and ciliary processes may adhere and be drawn to it. Its vessels can extend anterior to those of the pupillary membrane and the iris. The posterior lens capsule may be opened, cataract be formed, calcium deposited, the capsular epithelium proliferate towards the posterior lens pole, and, finally, the fibrous tissue enter the lens itself. Together with the hyaloid artery, much mesodermal tissue can proliferate through the fetal cleft and persist in colobomatous or microphthalmic eyes, as enormous

masses that are contiguous with the vascular sheath of the lens. Hemorrhages occur from a persistent hyaloid artery. Occasionally only a stump of the obliterated artery is found extending from the papilla somewhat into the vitreous. Sometimes there is only fibrous tissue on the papilla extending over a vessel into the retina.

Occasionally, cystlike spaces develop in the glial sheath of the persistent artery (hyaloid cysts). Although very frequently a delineated thread representing the anterior end of the hyaloid artery adheres as a hyaloid corpuscle to the posterior surface of the lens nasally from the pole, much more rarely a large mass of fibrous tissue exists that is adherent to the posterior lens surface as the anterior end of the artery (pseudoglioma). It gives rise to posterior capsular cataract or posterior polar cataract. Translucent floating cysts of the vitreous body are considered congenital; their pathology is unknown as they have never been examined histologically.

The Conjunctiva

The developmental anomalies of the conjunctiva are: epitarsus, xerosis, pterygium, cysts, and tumor-like malformations; malformations of the caruncle are: its absence, reduplication and its adhesion to the lid. Most of these changes are observed only clinically. Epitarsus represents a fold of the tarsal conjunctiva which is produced by adhesions of amniotic bands or by intra-uterine conjunctivitis. In xerosis, the surface of the epithelium is congenitally hornified. Pterygium may occur as a congenital and hereditary type. If epithelial folds become separated, cysts are formed. Tumor-like malformations are: fibroma, and subconjunctival neoplasms, consisting of tubuloacinous glands with numerous efferent ducts, surrounded by vascular and nervous tissue containing fat, muscles and cartilage. The caruncle is rarely absent, occasionally also simultaneously with absence of the semilunar fold. Sometimes two caruncles are present. The caruncle can be connected by a skin bridge with the lower lid. This is considered as atavism, as these findings are normal in some animals.

The Eyelids

The developmental anomalies of the lids are: lid coloboma, ectropion, entropion, ankyloblepharon and distichiasis. They are almost exclusively examined only clinically. In lid coloboma, there is a cleft beginning at the lid margin, probably caused by amniotic bands. In ectropion, the conjunctiva extends over the lid margin onto the skin side without positional anomaly of the tarsus; in entropion, the outer skin continues across the lid margin onto the conjunctival side. Ankyloblepharon is present if the upper and lower lids are attached to each other to some extent, often as ankyloblepharon filiforme adnatum, in which there is a fine filiform bridge between the two lids which consists, histologically, of vascular tissue. In distichiasis, there is a second row of cilia which come out at the posterior lid margin and are directed posteriorly. In this case, the Meibomian glands are replaced by irregularly formed rudimentary sebaceous glands which open into the hair follicles of the second row of eye lashes.

The Lacrimal Organs

A congenital anomaly of the tear passages is a congenital tear sac fistula which represents a duct lined by stratified squamous epithelium connecting tear sac and skin.

The Pigment

Congenital pigment anomalies occur as albinism and melanosis bulbi.

In albinism, pigment is absent in the stroma of the uvea, and the pigment epithelium has only a low content of pigment. The pigment granules present are small and clear. Somewhat more pigment is accumulated in the epithelium of the ciliary body and the pigment epithelium of the macular region. The structure of the eye is otherwise normal, except that the fovea is not developed in most cases. In the macula, the nerve fiber layer, outer plexiform layer and nuclear layers are thinned, and the ganglion cell layer and rod and cone layer are widened. The inner limiting membrane dips only in a flat, central indentation. Therefore, mainly a fetal macula persists and no fovea

is present. Partial albinism is rare and only a part of the uvea is free of pigment, for instance, choroid, although the iris is pigmented and the pigmentary epithelium has no pigment. The normal pigment-forming cells do not contain the enzyme necessary for pigment production, or the pigment forming cells are normally developed and even the intracellular granules are present, except that they do not contain stained substance. Albinism is a recessive hereditary trait.

In melanosis bulbi, the pigment of the uvea is enormously developed and pigment appears in ocular tissues which otherwise do not contain pigment. Melanosis can affect most parts of the same bulb or can be restricted to certain parts: to the conjunctiva as melanosis conjunctivae, to the retina as melanosis retinae and to congenital pigmentation of the optic nerve. Although melanosis is rare in the white race, pigmentation is the rule in colored races. But the congenital pigment anomalies must be distinguished from those acquired during life, especially after disease. The conjunctiva shows congenital pigment spots or diffuse melanosis. In the former, pigmented cells are situated subepithelially as groups of spindle-shaped and branching cells in the tissue. Apparently they belong to mesoderm. But also plump and polygonal pigmented cells appear which seem to originate from the epithelium, the basal cells of which are pigmented. The mostly harmless spots now and then cause malignant melanoma. In diffuse melanosis, the pigment of the epithelium is increased; subepithelially there are few pigmented cells; also epithelial cells of the cornea may be pigmented. The pigmentation can continue onto the lid. The subconjunctival and episcleral tissues contain pigment in dots, especially around the entrance of the scleral channels in small circumscribed areas or in larger regions. The pigmentation can extend into the orbit. The pigmented cells are similar to the chromatophores of the uvea, and their processes extend through the connective tissue. Also the sclera can show such chromatophores disseminated in the superficial and middle layers; these chromatophores are found normally in the lamina fusca and are increased in melanosis bulbi. In the iris, especially the cells of the anterior border layer are heavily pigmented. They are seen as flat

cells, as branching chromatophores and as clump cells. The chromatophores of the ciliary body are very numerous and fill the connective tissue septa between the muscle bundles. The choroid, also, is laden with chromatophores. Circumscribed accumulations of chromatophores resemble a melanoma and may give rise to malignancy. Congenital melanosis of the retina also occurs as group pigmentation. The pigmentary epithelium is increased in circumscribed areas and laden heavily with pigment granules. Rods and cones are not developed and pigment cells migrate into the retina, where these cell groups become surrounded by hyaline membranes which are secreted from the cells and correspond to Bruch's membrane. Congenital pigmentation of the optic nerve can appear as uveal and as retinal pigmentation. Sometimes pigment cells of the choroid extend into the papilla together with aberrant choroidal vessels. But pigment epithelium also develops in the papilla, if, from the primitive cells of the optic stalk, characteristic pigment epithelium develops. Sometimes there are crater-like holes in the papilla, the floor of which is lined by pigment epithelium.

13. Congenital Neoplasms

Congenital neoplasms occur as dermoids and teratomas of the anterior segment of the globe and of the orbit.

Dermoid and dermolipoma of the anterior segment of the eye can replace the cornea, be situated at the limbus, in the conjunctiva and in the caruncle. If the dermoid develops before the lens vesicle is separated, a large dermoid consisting of skin with hair follicles, sebaceous and sweat glands, smooth muscle and fat, is seen on a microphthalmic eye which has not formed a Descemet's membrane, anterior chamber, iris or lens. If the lens vesicle is already separated, then a rudimentary lens and iris are present. More frequently noted is circumscribed small dermoid of the limbus, usually situated temporally and inferiorly. It consists of hornifying stratified squamous epithelium with numerous papillae, dense fibrous connective tissue bundles with elastic fibers, smooth muscle fibers, hair follicles, sebaceous

and fat glands and fat. Dermoid of the caruncle has a similar structure. Dermolipoma is occasionally subconjunctival. If the lids are absent and the developing eye is exposed, its anterior surface is then partly or entirely transformed into skin-like tissue. Nonclosure of the lids during development may be the cause of the exposure. Residua of amniotic bands may form a dermoid.

Teratoma contains cartilage and bone, besides fat, nerve tissue, muscles and glands. Dermoid cyst of the orbit is encapsulated and lined by a hornifying epidermis. The capsular tissue shows hair follicles, sebaceous and sweat glands, smooth muscle fibers and fat. The lumen of the cyst is filled with hornified masses, desquamated epithelium and degenerated fatty substance. Calcium, metaplastic bone and cartilage can be deposited in the wall of the cyst. It is derived from invaginated external skin. Teratoma of the orbit can contain elements of the central nervous system, rudimentary eye anlage, epidermis, hyaline cartilage, bone, muscle, rudimentary intestinal tissue and blood spaces. The tissue is mainly of embryonal character. Parts of the tumor become necrotic and calcium is deposited. At times, a rudimentary fetus may replace the orbit and protrude from this area.

READING OF SOURCE MATERIAL

Krause calls congenital encephalo-ophthalmic dysplasia prenatal and neonatal retinopathy with congenital cerebral dysplasia showing microphthalmos, malformations of various parts of the eye, retinal dysplasia, glious membranes and persistent hyaloid artery. The brain shows hypoplasia and agenesis, heterotopia and hydrocephalus.

Dvorak-Theobald found histologically in a case of arachnodactyly thinning of the megalocornea, the iris and trabeculae separated incompletely, underdevelopment of the ciliary body and displacement of the otherwise normal lens.

Histologic examinations of typical coloboma of the uvea are reported by Fischer, Folk.

Koyanagi, v. Szily believe that the primary disturbance is in the ectoderm in formation of coloboma.

van Duyse believes that atypical choroidal coloboma are caused by developmental defects of the ectoderm. First the pigment epithelium and subsequently the choriocapillaris are not developed, then glia proliferates and the choroid becomes aplastic.

The choriocapillaris does not develop and the choroid becomes aplastic in atypical colobomata of the choroid and in coloboma of the macula, according to Collins.

Mann and Ross consider the cause of atypical coloboma of the choroid as inflammatory.

The persistence of connection of the hyaloid artery with ring vessels in the embryo can produce as mechanical obstacle coloboma of the iris, according to Mann.

Calhoun describes a coloboma of the optic nerve as a true hole in the lower portion of the disc accompanied by a cyst consisting of abnormal retinal tissue and pigmentation.

Baurmann reports a case of coloboma of the optic nerve with outpouching of the retina below the optic papilla.

Hidano reports on coloboma of the optic nerve.

Hepburn, Mann, Batten, Davenport, Treacher Collins, Clarke, Greeves and Butler discuss colobomata of the macula.

Janku finds in histologic examination of macular colobomata, inflammatory changes with mesodermal proliferation, destruction of the pigmentary epithelium and degeneration of the overlying retina.

Mann considers also the macular coloboma of inflammatory nature.

Schreiber saw eyes with pure colobomata of the retina with preservation of the pigment epithelium through which large retinal arteries pass into the choroid and return into the retinal layers.

Lloyd distinguishes between extrapapillary coloboma and defective closure of the optic fissure. In the former, the inner layers of the retina are preserved and there is a defect of the pigmented layer, Bruch's membrane and the choriocapillaris.

v. Szily examined anatomically cases of heterotypical conus.

Mann reports microscopic findings in conus and considers nondevelopment of the pigmentary epithelium close to the disc as the primary.

Hagedoorn describes a case with a circumscribed pit in the optic disc in an eye with buphthalmos and pseudoglioma. There was a tissue present which extended hernia-like into the dilated central retinal vein and it was covered with dark-staining nuclei; the shrinking tissue produced a cavity. The central connective tissue meniscus contained aberrant nerve fibers.

Hagedoorn found in grooves of the optic papilla fibrillar tissue from the wall of the artery extending throughout the groove.

Jaensch describes a circumscribed depression of the optic papilla with deep outpocketing of retinal tissue, as its wall consists partially of lamina cribrosa and partially of pia. Only the fiber layer dips into the pocket.

A pit of the papilla of tubular form filled with cells, fibrils and fluid associated with staphyloma of the cornea is described by v. Hippel.

Greer finds the pits or crater-like holes in the optic disc anatomically as evaginations of the pia containing retinal elements.

van Duyse and van Lint express the opinion that the pits of the optic disc are brought about by proliferation of retinal elements into the intermediary tissue at the margin of the disc.

Bergmeister, Blatt, v. Hippel, Stuebel, Wazid Ali Khan, Velhagen report various forms of microphthalmos.

Heine, Rintelen describe microphthalmi with persistent tunica vasculosa lentis and hyaloid artery.

Yudkin reports bilateral microphthalmos with persistent pupillary membrane, tunica vasculosa lentis and hyaloid artery and detachment of the cystic retina containing many rosettes.

Mans describes a microphthalmic eye with absence of parts of the cornea (Bowman's, Descemet's membrane and the endothelium) and absence of the lens. An ectodermal cell complex imbedded in the region of the limbus shows posteriorly traces of a hyaloid artery and a tunica vasculosa lentis.

Cechetto found in a case of apparent anophthalmos a pigmentary epithelium in a rudimentary eye-nodule which gave rise to tumor formation.

v. Hippel found in congenital phthisis bulbi a large mass of connective tissue filling the eye and considers as cause an intrauterine inflammation.

Rogalski describes an anopthalmos in a 10 week old child with open clefts of the face.

Redslob examined a child with a true anophthalmos of the one side and a rudimentary eye of the other side and absence of the optic nerve.

Gallemaerts found in a case of congenital familial anophthalmia in the one orbit a tear gland, fibrous tissue, and numerous pigmented cells, eye muscles and cartilage, in the other no vestige of an eye.

Lenz found marked deformity of the visual cortex in anophthalmos; Stockard finds the visual cortex normal. Also Cosmettatos found the optic center in the occipital lobe normal in a case of congenital anophthalmos in which section through the orbit did not reveal any normal retina.

Rifat reports generalized hereditary deformities in anophthalmos.

Cases of cyclopia are reported by Bachmann, Castaldi, van Duyse, Fischel, Gartner, Hill, Humphrey, Montaldi, Palich-Szántó, Smith and Boulgakow.

Klopstock could recognize all the eye muscles distinctly except the inner rectus in a case of cyclopia.

Humphrey reports a case of cyclopia in a man with one orbit and one optic nerve, but double external rectus and superior oblique, double cornea, pupil, lens and iris. Therefore, the muscles innervated by the oculomotor nerve were fused, although the muscles innervated by the trochlear and abducens nerves separated.

Humphrey finds the cerebral hemispheres remaining vesicular in cyclopia.

The hypophysis is absent in cyclopia, according to Castaldi, Humphrey.

Cyclopia is considered a disturbance of the chemical organization of the embryo at the time when the eye anlage is formed (Villegas and Los Angeles).

Meeker and Aebli describe a case of malformation showing a cyclopian eye, lateral proboscis, cleft palate and cleft lip caused by incomplete separation of monozygotic twins. The eye showed two pupils and the proboscis histologically nasal structure.

A case of triophthalmic diprosopia is described by Cosmettatos.

Chon found in a cryptophthalmos of a 40 day old girl only rudiments of the posterior segment of the globe including remnants of lens, but no cornea and iris. There was no interpalpebral fissure and the covering skin had no muscle, tarsus or meibomian glands. Further, Nichelatti, Perez Llorca report cases of cryptophthalmia.

Kanda found in a case of unilateral anophthalmos a small cyst of the lower lid containing a small lens but otherwise no other recognizable ocular elements. He considers it as cryptophthalmos.

Fischer describes a case in which cornea, anterior chamber and lens were absent congenitally perhaps due to non-invagination of the epithelium.

Halbertsma, Hoffmann, Wajid Ali, Weyman, Wolff report cases of microphthalmos with orbital cysts; van Duyse describes a case of anophthalmos with orbital cyst; v. Hippel describes a case of cyst in cyclopia.

If, in a case of microphthalmos, the true cyst is formed by proliferation of the outer epithelial layer of the optic vesicle corresponding to the dilated subretinal space, the cyst can open secondarily into the vitreous body due to secondary perforation of the wall of the cyst (Koyanagi) or due to artifacts in the histologic preparation (Seefelder).

Forbes describes a microphthalmos with cyst due to failure of closure of the fetal cleft through which the inner layer of the invaginated optic cup protruded.

An orbital cyst with microphthalmos is sometimes filled with ingrowing connective tissue and proliferating neuroglia which can become tumor-like (van Duyse).

Mayou believes that an orbital cyst in microphthalmos is formed by distension of the primary optic vesicle in a time when the optic stalk is not yet closed.

Schmidt found as a rare malformation an eye displaced into the roof of the orbit surrounded by a vascular membrane containing nerve and rounded cells and close to it a cyst containing retina. The orbit had no optic nerve but eye muscles, connective tissue and fat. The malformation apparently originated at a time when the optic cup was formed.

Cohen describes a meningo-encephalocele associated with microphthalmos in a 6½ year old girl. The orbital cyst is meningeal tissue containing glia and neuroblasts.

Orbital encephalocele is reported by Begle, van Duyse, Zeidler.

An encephalocystocele of the orbit in di Marzio's case of a ½ year old girl represented meninges and abnormal brain substance.

Meisner, Seefelder, Theobald and Clapp, Wuerdemann report histologic findings in hydrophthalmos.

Trubin finds the adherence of the lens to the cornea as cause of congenital hydrophthalmos, corneal opacities and anterior lenticonus.

Hagedoorn reports anatomic findings of pits in the papilla in an hydrophthalmos with persistent hyaloid artery and tunica vasculosa lentis.

Wexler and Kornzweig found in a 6 month, premature infant the right cornea ruptured and left buphthalmos with irregular endothelium, the iris adherent to the cornea, Schlemm's canal underdeveloped and the papilla excavated.

Safar reports on causative relations between hydrophthalmos and nevus flammeus.

Byers believes that an inflammation during the intrauterine life precedes the formation of hydrophthalmos, affecting the uvea and leading to obliteration of the excretory passages of the intra-ocular fluid.

Fischer, Hagedoorn, Seefelder describe the development of the cornea.

Kayser has the opinion that a megalocornea can exist without enlargement of the entire eye.

Spanlang describes a dyskeratosis corneae congenita, a cornea with thickened hornifying epithelium, parakeratosis and substitution of Bowman's membrane by connective tissue in a patient with ichthyosis.

Mans finds that in faulty development of the lens, Descemet's membrane and the endothelium do not develop.

Seefelder considers the defect of the endothelium and rupture of Descemet's membrane as cause of congenital opacities of the cornea.

Mans describes congenital corneal opacities caused by defects in Descemet's membrane, the posterior corneal lamellae and the rudimentary lens. The corneal opacities are connected with the faulty formation of the lens.

Hoffmann describes a congenital leukoma without any trace of inflammation and considers it as malformation.

Congenital staphyloma of the cornea is examined histologically by Clausen, Mans, Marchesani, Maschimo, Meisner, Rubert. They all are inclined to consider it rather as malformation than caused by inflammation.

Vrolijk describes a congenital corneoscleral cyst in a 10 year old girl, and considers it as a derivate of vascular structures.

Casanovas finds in a case of blue sclerotics cornea and sclera markedly thin with normally developed fibrils, but less in numbers than normally, and absence of Bowman's membrane. Also, Buchanan finds the sclera and cornea abnormally thin in blue sclerotics, and Chan finds the sclera thinner than normal and of unequal tenuity.

Congenital aniridia is reported by Reitsch, Seefelder, who describes degeneration of the peripheral retina, changes in ganglion cells and absence of the fovea centralis.

Histologic findings in congenital aniridia are reported by Holm.

Holm, Seefelder, Velhagen, believe that aniridia is caused by a primary defect in the development of the neuroectoderm.

Holst finds in congenital miosis histologically an incomplete development of the dilator muscle which has no peripheral attachment wherever a trace of the muscle was detected. In one case a part of the ciliary muscle was found in the peripheral iris.

Holth and Berner find in histologic examination a faulty development of the dilator muscle as cause of congenital miosis.

Merkel describes congenital entropion uveae in a colobomatous eye.

Koch reports on congenital iris cysts.

Cysts originating from the pigment epithelium of the iris, eventually floating as free pigmented bodies in the anterior chamber, are described by Lewis, Evans.

Fuchs finds in anatomic examination of corectopia the presence of a strand of vascularized connective tissue extending from the iris around the pupillary margin to the ciliary body or to the retina.

Zeeman believes that an abnormity of the zonule produces corectopia during the time of the development of the primary vitreous.

Arlt describes cells with small nuclei and many branches containing pigment granules in congenital pupillary membranes.

Mawas and Terrien find congenital pupillary membranes containing chromatophors and covered by pigment epithelium.

Reese describes ciliary processes originating in the iris and finds the dilator muscle interrupted in this area. Such ciliary processes have bridges to the regular processes forming a recessus which may appear as an iris cyst.

Fischer reports congenital displacement of the ciliary body in a microphthalmos.

Seefelder could find rosettes near the papilla. He believes that small cell complexes of the developing retina are separated by the growing nerve fibers and are entirely isolated from the rest of the cells.

Rosettes of the retina are found by Jokl, Velhagen.

Rosettes can be found also in otherwise normal fetal and postfetal eyes (Gilbert, Jaensch, Zuckermann-Zicha).

Goldstein and Wexler found rosette formation in eyes of human embryos exposed to x-ray.

v. Hippel observed medullated nerve fibers in the papilla and also between the rods and cones and the pigmentary epithelium.

Juler and Mann describe a case in which the pigmentary epithelium was nonpigmented (leukosis) and continued also into the optic nerve.

Heine describes a septum frontale consisting of cystic degenerated retina covering the pigment epithelium.

Mann describes a congenital retinal crest consisting of nerve fibers and ganglion cells and hyalin and fibrillar tissue. The fold is in contact with the hyaloid artery. The cause is an abnormality of the closure of the fetal cleft or the primary vitreous adheres to the inner layer of the optic vesicle and the secondary cannot come between them.

Mann describes a congenital reduplication of the retina below, extending into the vitreous body.

Wadenstein describes nonattachment of the retina connected by a cord of glial tissue with the papilla in a premature bi-ovum twin.

Palich-Szántó observed aplasia of the ganglion cells of the retina with absence of the axon cylinders in the retina and optic nerve in case of anencephaly.

Barbieri observed in a case of anencephaly a normal retina, but absence of nerve fibers in the optic nerve.

Brown observed orbital defects and absence of the optic foramen in anencephaly. Eyes in anencephaly are examined further by Rabaud.

Wyburn-Mason reports a case of arteriovenous aneurysm of the mid-brain with vascular nevus of the eye and congenital anomalies of the retina.

The papilla can contain congenital pigment epithelium, according to Juler and Mann.

Hulthquist reports aberrant fascicles of the optic nerve.

A division of the optic nerve into two bundles is reported by Scheerer.

Mann describes the eyes of a fetus in which no lens had developed, but which otherwise appeared normal.

Mann describes a human embryo with open fetal cleft and complete absence of the lens.

Congenital absence of the lens was found in a microphthalmos with staphyloma corneae by v. Hippel.

Fischer reports a cavity in the lens of a human embryo and considers it not as the original cavity of the lens vesicle but as an independent pathologic manifestation of unknown etiology.

Membranous cataract is the result of intrauterine inflammation, according to Findlay, Crisp.

Fischer describes a lenslike structure originating from the epithelium of the ciliary body in a microphthalmos (lentoid).

Anterior polar cataract is examined histologically by Beauvieux and Germain, Lamb, Peters.

Maucione reports cases of congenital pyramidal cataract.

Stein reports histologic examinations of congenital cataract.

Seefelder observed in a case of congenital cataract ruptures of the lens capsule at the equator and posteriorly.

Jaensch found a congenital total cataract in an infant caused by intrauterine inflammation. The lens capsule showed tears by the influence of lysins of the pus cells, the capsular epithelium proliferated and the lens substance shrunk.

Histologic examinations of coralliform cataracts show large crystals surrounded by disintegrating lens fibers. The crystals are, according to Braun, cysteine and tyrosine, according Gifford and Putenney, probably calcium sulphate, according Zentmayer, proteine.

Long and Danielson report congenital cataract and other congenital defects in infants following rubella in the mother.

Cordes describes cataract in an embryo of 7 to 8 weeks after rubeola of the mother.

Cordes and Barber found in an embryo of 8 weeks after rubeola of the mother, retardation of the development of the lens as a toxic agent in the amniotic fluid which attacks directly the lens which is not yet protected by lids.

Gregg reports congenital cataract following German measles in the mother.

Loewenstein reports circumscribed congenital small plaques on the anterior lens capsule consisting of dense connective tissue with pigment granules beneath the capsule.

The lateral parts of the fibro-vascular sheath of the lens persist sometimes as fine, threadlike meshwork, according to Lent and Lyon.

Terry finds in premature infants persistent tunica vasculosa lentis in the form of fibrous membranes behind the lens which frequently is cataractous with persistent patent hyaloid artery, and calls this condition retro-lental fibroplasia. He considers as theoretic cause a precocious increase in the blood pressure at the time when the tunica vasculosa and the hyaloid artery should disappear, due to the too early life outside the uterus, due to dehydration or due to a patent ductus arteriorsus.

Kiewe describes histologically persistent tunica vasculosa lentis and hyaloid arteries.

Reese and Payne report cases of persistent tunica vasculosa lentis which originate from an arrested development, arrested regression and hyperplasia of developing primary vitreous and represents a retrolental fibrous sheath.

Magnus reports persistent tunica vasculosa lentis and persistent hyaloid artery in a microphthalmos with total detachment of the retina.

Marshall saw a case with persistence of the tunica vasculosa lentis, patent hyaloid artery and subsequent buphthalmos.

Leech reports persistent posterior fibrovascular sheath at the posterior pole of the lens in a 4 month old child, which adheres to the ciliary processes and contains rests of the hyaloid artery; he considers fetal iritis as cause.

Lloyd saw in a 5 month old child a mass of connective tissue indenting the lens posteriorly.

Persistent hyaloid artery with thickened sheaths and deposition of connective tissue at the posterior surface of the cataractous lens can give the picture of pseudoglioma. Such cases are reported by Finoff, Gifford and Latta, Heine, Inglis Pollock, Mans, Waetzold.

Claes reports a case of a 4 month old child with pseudoglioma representing remnants of the hyaloid artery, choroidal hemorrhages and detachment of the retina.

Burk describes persistent hyaloid artery as mass of spindle cells of glial origin extending from the optic disc to the posterior surface of the lens. The lens epithelium consisted of several layers of spindle-shaped cells.

Seefelder observed a suppurative conjunctivitis in a 6 month fetus.

Supernumerary caruncle proved histologically is reported by Friedman.

Suarez Villafranca found in a case of congenital coloboma of the upper lid a fistulous track lined with columnar cylindric epithelium in the nasolabial angle with a displaced lower punctum. The malformation probably was formed by failure of the nasal and maxillary bone to coalesce.

Congenital membranous ankyloblepharon consists of epithelium and vascular connective tissue with muscle fibers and many glands, according to Cordero.

The meibomian glands are much smaller than the normal ones in distichiasis and they enter the hair follicles of well-developed accessory cilia, according to Blatt, Claes and Coppez, Frolowa, v. Szily.

Van der Straeten and Appelmans found a completely formed noncalcified tooth in a typical dental sac in the lower lid of a 7 year old boy.

Histologic examination of albinotic eyes are reported by Usher.

Histologic examinations of eyes with melanosis bulbi are reported by Dallos, Davis, Doherty, Friedenwald.

Brons finds the pigment in congenital melanosis bulbi in the conjunctiva, sclera, lamina cribrosa and sheaths of the optic nerve.

Reese describes microscopically melanosis bulbi and finds chromatophores disseminated in the eye tissues outside the uvea.

Melanosis of iris and ciliary body is described by Heine.

Musial describes a case of melanosis of the bulbar conjunctiva with melanosarcoma, and Carlsberg, too, reports melanosis bulbi with melanosarcoma.

An epibulbar dermoid is examined histologically by Stallard and Martin.

Dunnington found multiple dermoids on the eyes of a 2 year old child.

Horner and Cordes found dermoids of the cornea, besides lipoma of the lid and congenital coloboma of the upper lid in a 28 year old woman.

Dermoid cysts of the orbit are reported by Cange and Argaud, Gradle and Stein.

Mann saw a dermoid of the cornea in a microphthalmic eye without iris and lens.

Lijo Pavia and Dusseldorp saw multiple dermoids and dermolipomata with coloboma of the optic nerve in one eye.

Novak, Miller report lipodermoids of the conjunctiva.

Mann describes a congenital fibrolipomatous tumor of the orbit.

Sherman describes a teratoid tumor of the conjunctiva containing glands, nerves and cartilage.

Epibulbar teratomata are described by Scoccianti, Sgrosso, Valude and Offret, Volmer, Williamson-Noble.

Heijl describes teratomata of the orbit.

Morosoff found in a 6 year old boy without visible eyeball a teratoma of the orbit consisting of connective tissue, cartilage, ganglion cells and glia.

Corbett reports a case of congenital teratoma of the orbit in a newborn girl containing neuroglia, various epithelia, bone, cartilage, fat, muscle.

Viana found in a fetus with hydrocephalus unilaterally of the eye the cornea, iris, ciliary body and lens only present as the posterior segment of the eyeball and the orbit was replaced by a tumor containing angiomatous and glandular elements, pigment, cartilage, smooth muscle fibers and sarcoma-like parts, and being in connection with an intracranial glioma. He interprets this tumor composed of ectodermal and mesodermal elements as teratoma.

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Chapter XVII

GLAUCOMA

1. Introduction: The Intra-ocular Pressure

The intra-ocular pressure, which is measured in the scientific experiment with the help of manometers and in the clinic with tonometers, normally shows daily pressure variations as the pressure increases during sleep, is the highest before awakening and decreases afterward to a value which is maintained during the waking state. The pressure is kept at its required height so that the optical function of the eye and its blood circulation remains undisturbed: (1) by the mechanism of Schlemm's canal, which, if disturbed, causes increase of intra-ocular pressure; (2) to a certain degree by the rigidity of the cornea and sclera which show only little elasticity.

Variations of the intra-ocular pressure are possible: (1) by pressure of the extrinsic eye muscles; (2) by changes of the equilibrium level; (3) by altering of the volume of the contents of the eye.

Contraction of the extrinsic striated muscles of the eye and of the lids increase the intra-ocular pressure, and their paralysis decreases it. To a small degree, also, contraction of the smooth extrinsic muscles causes increase of the intra-ocular pressure.

The intra-ocular pressure varies with changes of the pressure in the capillaries, which is regulated by nervous and physico-chemical influences. Increase of the pressure in the carotid arteries, in the vortex veins or in the orbital veins increases the intra-ocular pressure. The colloidal content of the blood of the capillaries is of importance for the intra-ocular pressure. If the colloidal content of the blood is diminished, the intra-ocular pressure goes up. If the intra-ocular fluid is rich in colloids, as in plasmoid aqueous humor, the intra-ocular pressure increases.

The cornea and sclera is distensible to a minimal degree. Therefore, increase of the volume of the eye increases the

pressure considerably, as is the case in dilatation of the capillaries inside of the eye, or in increase of the volume of the vitreous body in changes of its metabolism.

Glaucoma represents a group of pathologic changes, some of which can be observed microscopically, but others of which cannot be demonstrated histologically with certainty, although physico-chemical changes are present in the inner eye. The common features of these abnormal conditions is a more or less extensive increase of the intra-ocular pressure. This increase may be absolute or relative depending upon the particular eye in question. The relative cases are those in which changes appear in the eye, which otherwise are typical of glaucoma; however, increase in pressure cannot be clinically observed. There are even cases of glaucoma which finally become blind but in which the pathologic examination cannot demonstrate definite changes characteristic of glaucoma.

Glaucoma is subdivided into primary and secondary types. In primary glaucoma, the increase in tension appears without preceding visible changes in the eye being found responsible. In secondary glaucoma, the increase of pressure can be traced to preceding visible changes. From one viewpoint, probably all cases of glaucoma are actually secondary. By this is meant that one or various pathologic changes must exist to cause the increased pressure, although these are not known to us at present through lack of very early cases clinically recognized, histologically examined or experimentally investigated, or for other reasons which have until now escaped our observation. A separate position is reserved for congenital glaucoma although it, too, is really a secondary glaucoma.

2. Primary Glaucoma

Primary glaucoma is subdivided according to its clinical appearance into inflammatory, simple and absolute glaucoma. The apparently inflammatory reactions are in reality signs of congestion and they appear acutely with sudden onset and rapidly increase to give severe clinical phenomena, or are found chronically with brief attacks and remissions. Simple glaucoma presents no externally visible changes and is noncongestive. Both

forms may proceed into absolute glaucoma from which there is no return of the increased pressure to normal and the eye remains blind. According to Elschnig, congestive glaucoma is incompensated, and the simple type is compensated; this comparison is taken from the pathology of heart diseases, where in incompensated heart failure congestion appears, and upon compensation the congestion disappears. Secondary glaucoma is often really inflammatory and sometimes also proceeds into absolute glaucoma if the underlying cause cannot be eliminated. To date, the histologically examined eyes belong almost exclusively to the group of absolute glaucomas that became blind and painful and had to be removed; few other eyes with glaucoma have been microscopically examined, especially in the early stages of the disease. It is to be remembered that in secondary glaucoma the findings are manifold corresponding to the underlying primary disease, and that in addition, or as a result, pathologic changes appear which are characteristic of glaucoma. But even eyes enucleated in the course of primary glaucoma show varied pictures, although they have common features more or less characteristic of glaucoma.

Congestive Glaucoma

Congestive (incompensated) glaucoma represents changes in all parts of the globe; many of them are extensive and degenerative and are sequelae of the long-lasting increase of pressure but not at all its cause. The corneal epithelium is edematous. The epithelial cells are separated by fluid droplets, contain vacuoles and show hydropic swelling. Vesicles appear inside the epithelium by rupture of the cells and coalescence of the droplets; epithelium may be exfoliated in layers; the epithelium also becomes thinner in areas and its surface appears irregular. The epithelium, especially in absolute glaucoma, is separated from Bowman's membrane by vesicles (keratitis bullosa). Lymphocytes may appear in the epithelial vesicles and if they are situated in Bowman's membrane, may erode the membrane. In the presence of keratitis bullosa, fine fibrillar connective tissue containing fibroblasts and small vessels proliferates between epithelium and Bowman's membrane (degen-

erative pannus). The pannus may be converted into lamellae and may undergo hyaline and amyloid degeneration. The nerve channels in Bowman's membrane are dilated. The parenchyma of the cornea is in general normal, but the interlamellar spaces may be dilated and interstitial cells degenerated. The endothelium is flattened and irregular, is rarified and proliferates in places, together with proliferation of Descemet's membrane. It is assumed that fluid is pressed into the cornea by the high pressure and finally traverses Bowman's membrane, causing the edema of the corneal epithelium, or that the fluid is expressed from the epithelial tissue, or that primarily the corneal nerves are affected by the increased pressure and the damage leads to trophic disturbances especially in the epithelial cells. Cells and pigment probably originating from the iris may be deposited on the posterior surface of the cornea. Most of the conjunctiva usually becomes atrophic but less frequently it hypertrophies in areas and the limbus usually is infiltrated densely with lymphocytes.

The main characteristic is the apposition of the root of the iris onto the trabeculae of the chamber angle (glaucomatous synechia, anterior peripheral synechia). The base of the iris is turned onto the ciliary body and the loose iris tissue unites with the loose tissue of the anterior surface of the ciliary body. With increase of the synechia, the iris tissue becomes attached to the trabeculae to varying extent, but in the beginning it may be loosened from them; later both grow together. The iris may be pressed further against the posterior surface of the cornea and then the endothelium disappears in the area of the attachment and proliferates on the margin of the adhesion.

Now the tissues of the chamber angle are inseparably united with each other, were it not that a newly formed substance could be visible between them. The iris is often very thinned in the region of the synechia, the trabeculae are compressed, become thinner and sclerotic and their nuclei progressively disappear. The ciliary body is atrophic, its processes and the circular part of the ciliary muscle are pulled anteriorly. At times the iris tissue may be pulled from the synechia, and its tissue may be stretched and show holes. The anterior peripheral

synechia, which is the rule in congestive glaucoma, is rare in non-congestive glaucoma, but as a rule it is found in the end stages of the glaucoma. Frequently it is considered as cause of the glaucoma as the chamber angle is occluded and the aqueous humor cannot flow into Schlemm's canal.

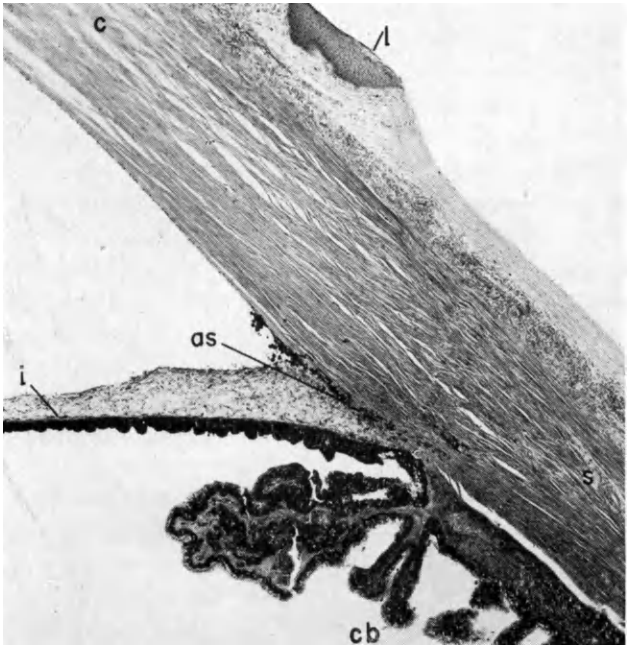

FIG. 58.—GLAUCOMA, ANTERIOR PERIPHERAL SYNECHIA. as, anterior peripheral synechia; c, cornea; cb, atrophic ciliary body; i, iris; l, limbus; s, sclera. 45×.

However, some consider the synechia to be sequela of the increased pressure. It is explained in various manners. Chronic indurating adhesive inflammation of the chamber angle is postulated, but for this there is little evidence in histologic specimens. The iris is said to be pressed (by edematous swelling of ciliary body or by volume increase of the lens, or by both simultaneously) against the trabeculae, and when they stay long enough in contact the chronic irritation ensures that they grow together.

Furthermore, pressure differences between anterior and posterior chambers are assumed as causes of the synechia. If the posterior chamber is overfilled with fluid and the anterior chamber shallow, then the base of the iris is again closer to the trabeculae. This is increased and accelerated when the pupil dilates and the iris is bunched together. Aqueous humor is sucked out of the Schlemm's canal and the root of the iris is sucked still more into the trabeculae. But as already mentioned, in a number of glaucoma cases the chamber angle remains deep and open. In such cases the trabeculae are often sclerotic, pigment and granules in clumps or in cells are attached to them or are deposited into the intertrabecular spaces and other cells may fill them. The various parts of the chamber angle may remain in their places and the recessus be filled up by connective tissue.

In the early stages of glaucoma, the uvea shows stasis and congestion with edema, fibrin and diapedesis of erythrocytes, enormous dilatation of congested vessels and perivascular infiltration. The ciliary processes in particular may swell enormously and press the iris into the chamber angle. In the late stages, the uvea degenerates and atrophies. Cells of the iris degenerate and disappear, chromatophores clump and connective tissue poor in nuclei remains. Iris tissue may be absent entirely in the anterior synechia and only the pigmentary epithelium be present. In addition, proliferative changes may appear. The pigmentary epithelium proliferates at the pupillary margin, forms pigmented posterior synechiae, or ectropion uveae. In other cases, iris tissue grows across the lens as fine vascular sclerotic connective tissue. In this way, posterior synechiae and pupillary membranes are formed into which pigment epithelium migrates. The thin, fibrous membranes with few oval nuclei and vessels arising from the anterior iris layers may establish themselves on the anterior surface of the iris and when they shrink they evert the pigment epithelium; they may also grow over the posterior surface of the cornea.

Pigment epithelium, also, sometimes proliferates on the base of the iris and the ciliary processes and forms projections. On the other hand, pigmentary epithelium disintegrates in some areas and pigment is scattered over iris, corneal endothelium and

the chamber angle. Where mesodermal iris tissue and ectodermal pigmentary epithelium atrophies at the same time, a hole is formed in the iris. The pigment epithelium may be detached from the dilator, both epithelial layers of the pigment epithelium may be separated by a slit, or cystic detachment may occur.

Often sphincter and dilator degenerate and disappear, assumedly because of degeneration of the nerves due to the increased tension. Small circumscribed accumulations of lymphocytes are rare and considered to be caused by stasis, the same as (a) the proliferation of the surface membrane and of the pigmentary epithelium, and (b) alterations in the vessels. Vessels are dilated, their endothelium proliferates and newly-formed vessels appear. Depending on the degree of the degeneration of the eye, sclerosis of the vessels and their surroundings is seen. The media and adventitia undergo hyaline degeneration, endothelium proliferates and the surrounding connective tissue has few nuclei and is sclerotic. In the ciliary body, many muscle fibers disappear and the ciliary processes are thinned and smaller. Hyaline degeneration of the connective tissue and sclerotic changes of the arteries are often senile changes. Granular pigment may be scattered over the ciliary body which may be filled with pigmentary cells. The pigmentary epithelium may proliferate in a flat fashion or may grow out as a whole to form polypoid excrescences containing hydropic cells and small cystic spaces. The capillaries and veins of the choroid are congested, but later the capillaries disappear and other vessels become obliterated over large areas. A small number of lymphocytes may infiltrate the intravascular tissue. The large vessels of the choroid occasionally show proliferation of the intima.

Degeneration of the vessel walls may cause subchoroidal hemorrhages. Vortex veins show, in the early stages, phlebitic processes in addition to thickening of the adventitia, and even thromboses. The proliferating intima may narrow the lumen to a capillary slit. The vessels may be surrounded in the scleral channels by a dense net of spindle-shaped cells interspersed with lymphocytes and fibrillar connective tissue. But they may also remain normal throughout the disease. The myelin sheaths of ciliary nerves degenerate and are replaced by

fibrous tissue surrounded by small groups of lymphocytes. The lamellae of the sclera are sclerotic and the sclera becomes rigid. Fatty degeneration is seen especially in the corneo-scleral junction. Not only the vortex veins but also the veins of Schlemm's plexus and the episcleral vessels show proliferation of their endothelium and are surrounded by lymphocytes due to disturbances of the circulation. Perhaps the changed intra-ocular fluid acting as an irritant plays a role in the origin of the round cell infiltration.

High intra-ocular tension sometimes produces staphyloma of the sclera when ischemic degeneration follows obliteration of the vessels by the proliferating intima. The sclera is thinned and ectatic, lymphocytes, plasma cells and epithelioid cells accumulate, the uvea becomes thin and eventually disappears so that only the pigmentary epithelium remains. Even this may become rarified so that intra-ocular fluid enters between the scleral lamellae and disrupts them.

Staphyloma of the sclera is seen as (1) anterior scleral staphyloma and (2) equatorial staphyloma. The anterior scleral staphyloma is (a) intercalary and (b) ciliary. The intercalary staphyloma lies between iris and ciliary body and encloses the root of the iris; the corneo-scleral junction is stretched and lined by pigmentary epithelium; the staphyloma is bordered anteriorly by the adherent iris and posteriorly by the ciliary body. The ciliary staphyloma is covered on the inside by the stretched and thinned ciliary body. The equatorial staphyloma is formed in the area of the egress of the vortex vein and is lined by atrophic choroid and retina which become united.

The lens of the glaucomatous eye is often enlarged and cataractous with many vacuoles in the disintegrating lens fibers of the cortex. The relative largeness of the lens in relation to the eye is also considered as an occasional cause of the glaucoma.

The vitreous is voluminous and is sometimes pressed, hernia-like, into the posterior chamber and the physiologic cup of the papilla. It seems that the fluid exchange through the border membrane of the vitreous body is restricted in old age and that in this way more fluid is retained in the vitreous body. The

voluminous vitreous presses iris and lens anteriorly and in this way the base of the iris is easily pressed into the recesses of the chamber angle.

In fresh cases, exclusively the nerve fibers and ganglion cell layers of the retina are affected and in advanced cases they are predominantly involved. First vacuolizing degeneration of the ganglion cells and swelling and disintegration of the nerve fibers appear. The nerve fibers and ganglion cell layers finally disappear entirely. The inner nuclear layer is rarified. The outer plexiform layer, the outer nuclear layer and the rods and cones remain intact, but holes in the external limiting membrane may appear; the rods and cones become matted together and lie obliquely. The macula is cystically degenerated and the ganglion cells are rarified or disappear entirely; the cystic degeneration may sometimes also be scattered indiscriminately over the entire retina. The inner limiting membrane is thickened. Connective tissue and glia proliferating in the excavation of the disc may extend onto the neighboring retina. The pigmentary epithelium is sometimes irregular and defective and may even proliferate into the retina. Its cells sometimes show fatty degeneration. The retinal vessels show more or less advanced sclerosis. If circumpapillary glaucomatous halo exists, the retina is thinned in this area and finally consists only of fine fibrillar glia attached to the elastic Bruch's membrane. The pigmentary epithelium here is defective, the choriocapillaris is absent and the choroid is thin and the chromatophores disappear.

Of importance are the changes of the papilla of the optic nerve, especially in the later stages when, with the appearance of the glaucomatous cupping, they become pathognomonic, for the clinical as well as the pathologic diagnosis. But in the beginning, in the acute stage, the opposite is found; there is a neuritis-like swelling of the papilla with varicose swollen nerve fibers and fatty granular cells in some nerve bundles. Vessels are dilated. The swelling of the papilla in glaucoma appears similar to papilledema, but may be differentiated: in papilledema, chiefly fluid poor in protein lies between the nerve fibers which are only slightly edematous themselves, and also trabeculae of

the choroidal lamina cribrosa are convex anteriorly; in glaucoma, the nerve fibers themselves are swollen, there is hardly any fluid between the fibers, and the choroidal lamina cribrosa lies normally or is even compressed. The edematous swelling of the nerve fibers is reversible as long as they are not broken up. As soon as they disintegrate, cavernous degeneration of the optic nerve sets in, since the tissue defect caused by the removal of the disintegrated nerve tissue is not filled by glia. The supporting substance remains with the empty cavities but finally the holes coalesce, and as their last thin walls disintegrate they collapse and disappear. When the increase of tension continues, the nerve fibers and most of the supporting tissues disappear; it is thus that the excavation of the papilla may be formed.

The glaucomatous cup appears in two types: (1) as a more or less deep excavation with atrophy of the nerve fibers and depression of the lamina cribrosa; the margins of the empty-appearing excavation (filled by vitreous) are formed by the scleral channel or at other times by pia and the exposed lamina cribrosa; and (2) as a more or less deep excavation surrounded by the same structures as in the first case, but with the excavation being filled by compressed tissue of the papilla and proliferating fibrillar tissue in different quantity. The first form is mostly found in primary glaucoma, the latter in secondary glaucoma, when inflammatory changes prevail in the anterior segment of the eye. The retina, in which nerve fibers and ganglion cells are now absent, ends with its nuclear layers tapering sharply on the margin of the excavation. The projecting margin of the cup is represented by the end of the elastic Bruch's membrane. The pigmentary epithelium and the choroid, in case they are not degenerated, as they are in the presence of a halo, also extend to this margin. The retina is occasionally pulled over the margin of the excavation and into it. The rods and cones in this case remain in contact with Bruch's membrane. The pre-existing form of the scleral canal determines the form of the excavation. The form of the lateral wall of the excavation is given by the form of the scleral canal and it also determines if and how much the margin of the excavation (corresponding to the margin of the elastic membrane) will overhang. The

walls of the canal may separate from anterior to posterior with its diameter increasing continuously from anterior to posterior and in this case the margin will definitely be overhanging. The lateral walls may be parallel, perpendicular to the aperture, or they may be convergent posteriorly, in which case the cupping will be more dishlike. Furthermore, the course of the canal may not be symmetrical over the entire circumference. The walls of the excavation correspond to the exposed sclera covered by sparse glia. On the nasal side, the central retinal vessels, covered by condensed tissue and bending around the margin of the cup, are pressed toward the medial wall of the excavation. The vessels show sclerotic changes in the form of proliferation of the intima, elastica and adventitia. If the excavation deepens beyond the fornix of the optic nerve sheaths, then the walls are also formed by the pia instead of continuation of the sclera. The floor of the excavation is formed by the compressed lamina cribrosa which is convex posteriorly and which sinks beyond the scleral opening posteriorly along the pia. The trabeculae of the choroidal lamina atrophy and the glial parts largely disappear. The trabeculae of the scleral lamina are sclerotic and have only few nuclei. The small vessels and capillaries of the lamina cribrosa disappear. In rare cases, the excavation is partial, being on one side of the papilla only. On this side, the lamina is displaced posteriorly and the nerve fibers in this area disappear. The excavation becomes atypical if the sclera protrudes on one side, as in the presence of a congenital coloboma of the optic nerve.

The retrolaminar part of the optic nerve becomes atrophic. As far as the central vessels course in the nerve, cavernous degeneration similar to that of the papilla may exist in which the axon cylinders swell, the myelin sheaths disintegrate into droplets, and between still intact nerve fibers and glia holes appear containing detritus. Fatty granular cells may appear. The holes become enlarged simply by disappearance of the nerve fibers; the glia remains normal and the connective tissue structure of the septa is somewhat thickened. Later the glia disappears also, and septa become thinner. The optic nerve usually appears thicker in cross section in the area of the cavernous degeneration.

Further distal progressive degeneration of the optic nerve appears with proliferation of the glia. In this area the optic nerve is thinned in its diameter. Often the nerve fibers atrophy without cavernous degeneration, but they may remain partly intact and run, distorted and tortuous, through the posteriorly displaced lamina cribrosa. Often the retro-laminar optic

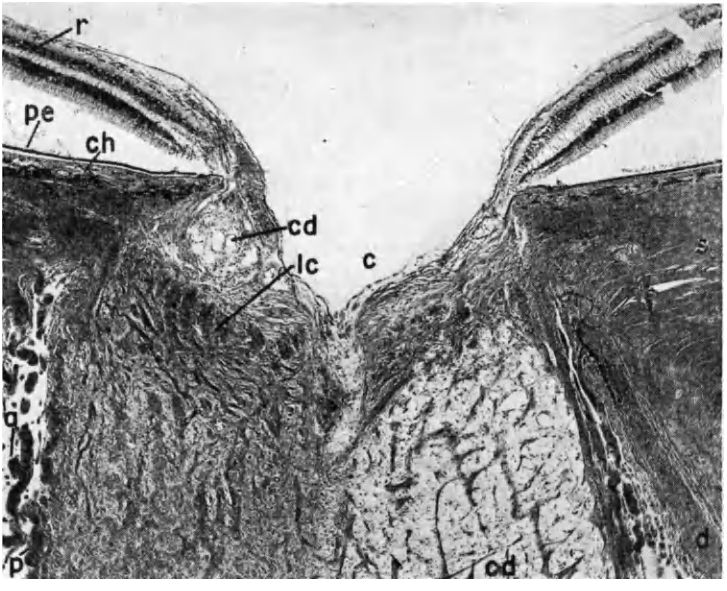

FIG. 59.—GLAUCOMA, CUPPING OF DISC. a, arachnoid; c, cupping; cd, cavernous degeneration; ch, choroid; d, dura; lc, lamina cribrosa; p, pia; pe, pigmentary epithelium; r, retina; s, sclera. 25×.

nerve is condensed and the absent nerve fibers replaced by glia; it may be intensely compressed by the lamina cribrosa which is displaced far posteriorly.

Sometimes a deep physiologic cup extends to the lamina cribrosa; in case of a glaucomatous cupping, the vitreous may be pressed into it and the evagination of the vitreous may be pushed through the lamina cribrosa hernia-like into the retro-laminar part of the optic nerve. The glia and connective tissue lying on the vessels in the physiologic excavation bulge into the vitreous

body, sometimes by proliferation anteriorly from the floor of the excavation. Here, instead of vitreous, the excavation is filled with tissue. There is a more or less compact nucleated tissue in the main formed by compression of the tissue of the papilla, but also produced by proliferating glia and connective tissue. The proliferating tissue may fill the excavation more or less and also protrude into the vitreous body beyond the level of the retina. A connective tissue membrane may separate this tissue from the vitreous body and may also proliferate over the surface of the retina. In this way there may exist a type of retinitis proliferans which is especially marked if due to venous thrombosis and hemorrhages; newly formed vessels may grow from the central retinal vessels into the vitreous. Condensed tissue of the papilla is compressed around the central vessels, and the central connective tisue strand even in the optic nerve stem becomes enormously thickened and more cellular. In case the central vessels are obliterated, the collateral connections to the veins of the optic nerve sheaths become distended. Besides the sclerosis of the central vessels, severe sclerosis of the ciliary vessels can be seen. The pia sometimes shows massive infiltration, hemorrhages, hyaline degeneration and obliteration of vessels. The intervaginal space is obliterated in areas. Glaucomatous excavation may regress as it is filled up by proliferating glial tissue; may regress further by infiltration and separation of the compressed nerve tissue of the papilla, and even further by advancement of the lamina cribrosa and release of the compression of the nerve tissue.

The explanation for appearance of the excavation is given as a mechanical pressure effect wherein ganglion cells and nerve fibers degenerate and especially the latter are stretched and compressed where they pass over the rim of the cup of the papilla. Depending on its inherent weakness and anatomic configuration, the lamina cribrosa is displaced posteriorly to varying extent by increased intra-ocular pressure. If the lamina consists predominantly of glia and the connective tissue trabeculae are rare, it is displaced posteriorly more easily and also succumbs more easily to pressure atrophy. On the other hand, it is said that the excavation is brought about primarily

by cavernous atrophy of the nervous tissue and that the lamina cribrosa sinks posteriorly in empty spaces, when the retrolaminar nerve also has cavernous spaces. By confluence of the caverns, the glaucomatous excavation is formed. The origin of the cavernous degeneration is explained differently. It is assumed that serous fluid is expressed from the nerve tissue by the increased tension, that the vessels are compressed by the high tension and that in this way ischemic softening is produced in the optic nerve. It is also assumed that the fluid in the optic nerve comes from the vitreous body which itself is under increased pressure and from which fluid is pressed through the permeable membrane and into the nerve; it is thought that the fluid is toxic and dissolves the compressed optic nerve tissue.

Noncongestive Glaucoma

The noncongestive (compensated) glaucoma does not show changes in the anterior segment of the eye. The chamber angle is open, shows sclerotic trabeculae and accumulation of pigment. Schlemm's veins may be displaced far anteriorly or behind the trabeculae. In the early stage, perivascular lymphocytic infiltration appears in the episclera and at the vortex veins which show also endophlebitic changes. There is glaucomatous excavation without proliferation of tissue. As the process advances slowly, vacuolated or compressed tissue is often present a long time in the papilla until total excavation appears. The vessels course nasally around the rim of the excavation or freely through the excavation. The vessels supplying the tissue of the papilla and the rarified lamina disappear.

Causes of Primary Glaucoma

Manifold causes are responsible for the appearance of the primary glaucoma. Vascular disturbances are said to be important and they are accompanied by obstacles to the outflow of the intra-ocular fluid. The vascular disturbances produce vascular crises which lead to acute severe stasis or more chronic, less intensive stasis. It is further assumed that simultaneously with these two factors a disturbance of the physiologic regulation

of the intra-ocular fluid must appear to effect the increase in pressure. The intra-ocular fluid, in its production from the capillaries, has to cross a tissue-aqueous barrier consisting of connective tissue, Bruch's membrane and epithelium, and must traverse endothelium and iris tissue in its exit from the chamber. The fluid transport depends upon the normal directive permeability and normal composition of the tissues with corresponding difference of the electric charges of the tissues. If the fluid or the membrane are pathologic, as they are in atrophy and sclerosis, the secretion of the fluid and its elimination is disturbed. The vascular disturbances are in the capillaries and veins. The capillaries are said to show endothelial changes altering the function, which are perhaps caused by changes of the vegetative tonus. Endocrine disturbances and changes in the innervation of the sympathetic nerve supplying the vessels are accused as responsible for the changes of the tonus. The release of a histamine-like substance can produce first localized and subsequently also generalized vascular crises. The capillaries are dilated. There is enormous stasis and protein-rich aqueous is produced. The capillary disturbances are accompanied by venous stasis which is further increased by obstruction of veins by perivascular infiltrates. Sclerotic changes in the veins of the choroid, anterior ciliary veins, and especially vortex veins contribute to the stasis first in the veins and later in the capillaries. The outflow of the intra-ocular fluid is obstructed by closure of the chamber angle by attachment of the iris root to the trabeculae with formation of a peripheral synechia. The adhesions can be caused by inflammatory processes so that the iris is pressed forward by the swollen ciliary body or by a relatively large lens. The filtration in the chamber angle can be obstructed also by sclerosis of the trabeculae, by deposition of pigment in the inter-trabecular spaces (which can also be found in senile eyes, diabetes and detachment of the retina, without increased tension) by deposition of desquamated particles of the lens capsule, by endothelial changes in the canal of Schlemm, by diminished suction action in Schlemm's canal when the ciliary muscle no longer has any influence on the trabeculae and the scleral spur, or when the vessels arising from Schlemm's canal are sclerotic. The loss of

elasticity of the sclera is said to decrease the outflow of the intraocular fluid in the area of the anterior ciliary vessels and the vortex veins. The appearance of increased tension is also related to other causes, especially to excessive secretion of the intraocular fluid, swelling of the vitreous body due to change of its reaction or to increase in protein, osmotic changes of the intraocular fluid with increase of the colloids in a plasma-rich aqueous, which aqueous is thus eliminated from the eye with difficulty.

To the causes of glaucoma which are often hypothetic and several of which perhaps have to act together in different proportions in each special case to produce the disease, predisposing factors of the eye and the entire body are added, causing the appearance of glaucoma. Especially the hyperopic eye with its shallow anterior chamber, whose angle can easily be shut off, is predisposed to glaucoma. Drugs dilating the pupil are able to produce increased tension by closure of the chamber angle by the compressed iris following paresis of the ciliary muscle or vasodilatation. It seems that the capillary system of the glaucomatous eye is disturbed in that its arterial part is narrowed and its venous part dilated with stasis, further dilation and increased permeability following. There are some signs that the glaucoma is part of a general disease, that generalized disease predisposes to its appearance. Acute infectious diseases and focal infections may be predisposing cause. Increased blood pressure and arteriosclerosis are often met with in glaucomatous patients. Vasomotor instability and disturbance of the normal balance between sympathetic and parasympathetic system are said to be characteristic of the glaucomatous individual. The lability of the vegetative nervous system may, in turn, be based on instability of the endocrine system.

3. Secondary Glaucoma

In secondary glaucoma in the majority of the cases there is more frequently an anomaly in the anterior segment of the eye than in the posterior segment causing the increase of the tension. Usually there is found an anterior peripheral synechia, and the glaucoma is congestive (noncompensated). But there is also

transitory increase of tension in some cases, especially in acute eye diseases; and with the cessation of the disease the tension returns to normal. Pathologic lesions producing secondary glaucoma are numerous and unrelated to each other. Secondary glaucoma is produced by: anterior synechia of the iris, corneal staphyloma, acute and chronic inflammations of the uveal tract, trauma, anterior synechia of the lens, swelling of the lens, luxation of the lens, senile exfoliation of the lens capsule and hypermature cataract; it is also caused by obstruction of the central retinal vein, by iris cysts and cysts of the ciliary body, intra-ocular tumor, detachment of the retina, essential atrophy of the iris, epidemic dropsy and obstruction of the veins of the orbit. Experimental glaucoma is also secondary glaucoma.

In most cases of secondary glaucoma, the chamber angle is obstructed. But changes in the iris stroma also decrease the resorption of the intra-ocular fluid. Further vascular changes lead to congestion and stasis and eventually obstruction of the veins. In cases of secondary glaucoma, glaucomatous excavation of the papilla is also found, but the excavation is frequently filled up with proliferating glia and connective tissue and newly formed vessels may grow in from the central retinal vessels. This tissue may, by traction, pull the folded and degenerated retina into the excavation.

An *anterior synechia* of the iris may cause secondary glaucoma, although it does not start peripherally in the chamber angle or is restricted to it. The iris may become attached to the cornea, usually after perforation due to injury or ulcer; less frequently it adheres without perforation and grows to the cornea. After intra-ocular operation, in which the section goes through the limbus, the iris is often incarcerated or prolapsed so that the chamber angle is immediately blocked, often to a great extent. If the pigment epithelium alone, without the anterior surface of the iris, is attached to the corneal lamellae a fistula remains through which intra-ocular fluid filters. When the synechia of the iris is situated centrally, the root of the iris often is attached to the trabeculae and the chamber angle is obstructed. But in such cases the aqueous humor may still penetrate the iris between the trabeculae and drain into Schlemm's canal, or

flow along the veins and out through them. Secondary glaucoma follows probably not only the attachment of the root of the iris to the trabeculae but also inflammatory changes of the chamber angle or increased colloidal content of the aqueous humor itself due to stasis in the veins and capillaries from poor filtration.

Corneal staphyloma formed after partial or total loss of the cornea always leads to secondary glaucoma, since through its formation from the iris, the anterior chamber and the iris itself partly or entirely disappear. If a staphyloma is formed in early childhood the secondary glaucoma causes buphthalmos.

Acute inflammation of the uvea, especially acute iridocyclitis, frequently is associated with increased tension, but in this case the tension rise is seldom permanent. The inflammation may be primary or secondary to inflammation of other parts of the eye, as especially to suppurative keratitis, herpes simplex and herpes zoster and scleritis. The intra-ocular fluid is rich in exudate, is cellular and fibrinous, and is rich in serum and plasma; besides, there is stasis due to congestion of the veins, and perivascular infiltration may increase the stasis by compression of the veins and may obstruct the lymph current in the vascular sheaths. Osmotic and hydrostatic forces which rule the movement of the intra-ocular fluid and regulate the excretion are changed and plasma and cells obstruct the intra-trabecular spaces.

Chronic inflammations of the uvea, and again especially chronic iridocyclitis, produce secondary glaucoma in different ways, either by their sequelae (postinflammatory glaucoma) or by the inflammatory process itself (inflammatory glaucoma). The former is more readily understood and can be proved histologically more easily, although, as treatment of eye diseases becomes more effective, it is perhaps rarer in our time than the latter, which is still hypothetic in many ways. Seclusio pupillae (annular posterior synechia), in which the iris is annularly attached to the lens, prevents the intra-ocular fluid from entering the anterior chamber from the posterior chamber. The fluid collects behind the iris and pushes the iris anteriorly (iris bombée). If the synechiae do not break, the iris pressed to the posterior wall of the cornea finally stays attached to it, after

loss of the endothelium. The iris becomes atrophic and is covered with a newly-formed connective tissue membrane. Total posterior synechia occurs when iris tissue proliferates through disintegrated pigmentary epithelium, or if an extensive cyclitic membrane is formed and the iris grows to the anterior lens capsule in a large area. If this occurs, the blockage of the circulation of the aqueous humor is still more severe. In annular posterior synechia, the anterior chamber is deep centrally and abolished peripherally. In total posterior synechia as the entire diaphragm consisting of iris and lens is pushed anteriorly, the anterior chamber is shallow centrally and deeper peripherally. Inflammatory changes in the chamber angle can cause increased tension without seclusion of the pupil. They cause blockage of the anterior chamber by swelling of the iris and the ciliary body which narrow the chamber angle, and by proliferation of fibrous tissue. The intertrabecular spaces are obstructed first by cells, pigment and fibrin which later may organize to fibrous tissue, first enclosing the trabeculae and finally causing their disappearance. The corneal endothelium may proliferate across the fibrous tissue occluding the chamber angle and secrete a new hyaline membrane.

It can be understood from the above that inflammatory and postinflammatory changes work together in the production of increased tension. But inflammatory changes which neither lead to seclusion of the pupil nor to new formation of connective tissue in the chamber angle may produce attacks of acute or chronic glaucoma. Especially cases of cyclitis (serous iritis, serous cyclitis) of different etiology, caused by foci of infection, heterochromic cyclitis, iridocyclitis after severe burns of the limbus, slow or more acute in their course, may bring about glaucoma. Precipitates, deposition of cells between the trabeculae, and perivascular infiltration appear; the intra-ocular fluid is rich in colloids, and stasis and edema occur in the uveal tissue.

Trauma. Glaucoma may be caused by trauma: (1) by changes set forward by the trauma itself (traumatic glaucoma) and (2) by sequelae of the trauma (posttraumatic glaucoma). Traumatic glaucoma rarely appears after contusion; it is usually seen in

those cases with severe intra-ocular lesions as hemorrhages, dislocation of the lens or the ciliary body, rupture of the choroid and retina. Besides these changes there is found edema and necrosis of different tissues of the eye, infiltration of the scleral channels, disorganization of the walls of intra-ocular vessels and degeneration of ciliary nerves. Different causes are probably responsible for the appearance of the hypertension such as edema, blockage of perivascular lymph spaces, the increased protein content of the aqueous humor, intra-ocular hemorrhages and luxation of the lens. Posttraumatic glaucoma usually follows perforation of the globe. Anterior synechia of the iris or of the lens are formed in central perforation of the cornea; the prolapsed iris may be incarcerated in peripheral perforation of the cornea. Ocular hypertension follows cicatrization of the preceding fistula. Glaucoma appears after intra-ocular operations, especially after cataract extraction, but also after iridectomy. After cataract extraction, hypertension may be caused by incarceration of the iris in the wound, prolapse of the vitreous, postoperative iridocyclitis, ingrowth of the epithelium through the wound into the anterior chamber, large quantities of loose cortical material of the lens in the anterior chamber or intra-ocular hemorrhages. After capsulotomy, the tension may be increased due to iridocyclitis or prolapse of the vitreous; after discission of a soft cataract by enormous swelling of the lens, blockage of the chamber angle by lens particles or iridocyclitis. After iridectomy, the tension is increased by incarceration of the stump in the wound, prolapse of the ciliary body into the wound or incarceration of the lens. In most cases, the chamber angle is occluded; less frequently, the posterior chamber is closed off from the anterior chamber or there is exudation into the aqueous, vascular stasis and congestion.

Anterior synechia of the lens, as already mentioned, produces hypertension. If the central cornea is perforated by ulcer or injury, the lens comes forward and adheres to the cornea; there need be no traumatic cataract or iridocyclitis. If the perforation occurs in early childhood, pyramidal cataract is formed, with adherence of the lens to the posterior surface of the cornea. In

buphthalmos with corneal staphyloma, the shrunken lens or remnants of the capsule may adhere to the staphyloma. In all cases, the anterior chamber is abolished as the iris is pressed against the posterior wall of the cornea, or it partakes in the formation of the staphyloma, or the chamber is reduced to a slit. Sometimes the anterior chamber does not return after glaucoma operation; after damage to the endothelium, the lens unites with the posterior surface of the cornea and malignant glaucoma appears. In congenital microphakia (spherophakia), the lens is small and spherical and bulges through the narrow pupil toward the posterior wall of the cornea, secludes the pupil and prevents the entrance of aqueous humor from the posterior into the anterior chamber.

Swelling of the lens causes hypertension (a) when soft lens material protrudes into the anterior chamber after traumatic or surgical rupture of the lens capsule, or (b) when the lens swells inside the capsule (senile intumescent cataract). In the former case, the intertrabecular spaces are obstructed by loose lenticular masses and peripheral synechia of the iris may arise through iridocyclitis. In the latter case, the iris is pressed toward the cornea and the chamber angle is closed.

Displacements of the lens increase the tension: (a) when the lens is luxated into the anterior chamber and (b) when it is subluxated or luxated into the vitreous. If the lens is luxated into the anterior chamber, it blocks the chamber angle and peripheral anterior synechiae are formed. If the lens is subluxated, the root of the iris is pressed onto the trabeculae by the lens, or the lens may occlude the pupil; also, vitreous can prolapse into the anterior chamber and occlude the pupil, or iridocyclitis may be responsible for the hypertension. Luxation into the vitreous causes toxic degenerative uveitis and the appearance of dense tissue in the chamber angle.

Senile exfoliation of the lens capsule produces glaucoma capsulare. Particles and debris detached from the anterior lens capsule clog the chamber angle.

Hypermature cataract and *Morgagnian cataract* produce irritation of the iris and especially of the ciliary body and cause

closure of the chamber angle. The spontaneous resorption of the lens with or without rupture of the capsule is inclined to lead to secondary glaucoma.

Obstruction of the central retinal vein. Hemorrhagic glaucoma is glaucoma caused by occlusion of the central vein itself, as glaucoma does not appear if only one of its branches is occluded. Hemorrhages appear in the retina, chambers, and sometimes in the vitreous. It is to be differentiated from glaucoma in which there is bleeding into the chambers and the retina due to degeneration of vessels. In hemorrhagic glaucoma, the anterior chamber is filled with plasmoid aqueous, erythrocytes, lymphocytes, and monocytes which fill the chamber angle. The iris in infiltrated with lymphocytes. Besides sclerotic vessels there are many newly formed and easily bleeding vessels in the iris; the iris is covered with a vascular membrane which often also extends over the chamber angle. Endothelium proliferates in the canal of Schlemm. Vortex veins show periphlebitic changes and are occluded by thromboses. The glaucomatous excavation of the papilla is filled with glia and connective tissue. Caverns are found in the retro-ocular optic nerve and glia and connective tissue starts to invade them. Many causes are mentioned for this glaucoma. Veins are congested due to thrombosis and fluid transudes from them, enlarging the chambers and vitreous, pushing the lens and iris anteriorly and closing the chamber angle. The decomposing blood is said to produce toxins which cause inflammation of the iris and proliferation of tissue in the chamber angle. Similar causes may produce secondary glaucoma in arteriosclerotic and renal retinopathy, external exudative retinitis, cyanosis retinae, obstruction of the central artery, and retinitis proliferans.

Cysts of the iris and the ciliary body, and especially, as already mentioned, the ingrowth of the epithelium into the anterior chamber, cause hypertension. Cysts, which increasingly fill with fluid, cause narrowing of the space and finally block the chamber angle. Implantation of epithelium into the anterior chamber covers the chamber angle and prevents the outflow of the aqueous humor; also, the epithelium itself by secretion from the

goblet cells and by cell desquamation adds pathologic substances to the aqueous humor.

Intra-ocular tumor is associated with hypertension for different reasons. Synechia of the iris root may be formed. Iris and lens are moved anteriorly by narrowing of the space or swelling of the vitreous into which more protein is poured out from the congested vessels. Iris and ciliary body are inflamed by toxins of the decomposing tumor, vortex veins and their tributaries from the anterior choroid are obstructed by the growing tumor, or the chamber angle is obstructed by growing tumor or tumor cells.

Detachment of the retina is a rare cause for increased tension. Toxins of the subretinal fluid produce inflammatory changes of the uvea which in turn affect the chamber angle. The detached retina is pulled into the excavation of the papilla. This is sometimes complicated by a conus of a myopic eye or a coloboma of the optic nerve.

Essential atrophy of the iris produces increased tension as the atrophy advances and the resorbing surface of the iris diminishes and is covered by newly formed tissue which shrinks, bridges the chamber angle and obstructs it.

Epidemic dropsy, caused by toxins of polished rice stored in damp heat, produces general edema, dilatation of the heart, peripheral neuritis, dilatation of the capillaries and hemorrhages. Glaucoma appears with dilatation of small vessels in the entire uvea, causing edema and increased albumen content in the aqueous humor. The chamber angle itself remains normal. The toxin is said to be similar to histamin. Dilatation of the capillaries and the increased permeability caused by this substance lead to increase of the osmotic pressure in the intra-ocular fluid.

Venous obstruction in the orbit produces congestion in the eye, increase of albumen of the intra-ocular fluid, swelling of the vitreous, obstruction of the chamber angle and glaucomatous excavation. Further, endo- and periphlebitis and thrombosis of uveal and retinal vessels may occur, increasing the circulatory disturbance of the eye. Different diseases of the orbit lead to

venous obstruction; these are tumor, inflammation, abscess, pulsating exophthalmos caused by arterio-venous aneurysm and hematoma.

4. Experimental Glaucoma

Experimental glaucoma occurs only as secondary glaucoma in animal eyes in which the produced intra-ocular hypertension is kept permanent. Transitory hypertension may be produced in animal eyes in different ways: by increase of blood pressure, by obstruction of the outgoing veins leading to congestion and capillary stasis, by decrease of osmotic pressure in the blood and increase in the aqueous humor, by increase of the fluid content of the eye or by nerve stimulation. In cadaver eyes, excavation of the papilla can be produced by increase of the tension. Ligation of the vortex veins and the anterior ciliary veins causes dilatation of vessels and plasmoid aqueous humor and increases the intra-ocular pressure for a few weeks. Injection of saline solution into the anterior chamber and vitreous increases the intra-ocular pressure for a short time. Injection of irritating and burn-producing fluid, beneath the bulbar conjunctiva, especially close to the limbus, cauterization of the limbus, or punctures and scratches there produce an inflammatory reaction in the chamber angle and its obstruction. Perhaps anterior ciliary veins are damaged and occluded too. Injection of different substances into the anterior chamber obstruct the chamber angle mechanically or produce inflammatory reaction there. To cause this, one may use nondiffusible oils and colloids, bacterial cultures, colloidal nigrosin and india ink. Inflammation in the chamber angle and proliferation of the endothelium with obliteration of the chamber angle can be produced by the action of electrolytes. If a steel needle is introduced as the positive pole into the anterior chamber, the desired success may be attained by electrolysis with a galvanic current of five milliampere. If aqueous humor is removed under sterile conditions, electrolyzed outside of the eye with a steel needle and the electrolytic product (appearing as a dark green mass) is reinjected into the eye, the tension will rise. In rabbits, experimental

buphthalmos occurs following damage of ganglion cells and nerve fibers of the retina.

5. Hydrophthalmos

Hydrophthalmos is a congenital type of glaucoma caused by anomalies of the chamber angle. The trabeculae are either not developed or are only rudimentary. Schlemm's canal is absent or only rudimentarily formed, the scleral spur is undeveloped and the uveal meshwork is abnormally persistent. Deformities of iris and ciliary body are seen. The muscles of the iris are hypertrophied early, and later are deficient. The inner layer of the pigment epithelium is insufficiently pigmented, crypts are missing so that the iris appears thin, the nuclei are relatively numerous, tissue condensed and later the iris atrophies. Partial aniridia may occur. The ciliary body shows fetal structure with scantily differentiated ciliary muscle and a few thin ciliary processes. The connective tissue between the muscle bundles may be increased and infiltration may be present in the ciliary body. Furthermore, changes appear in all parts of the eye. The eye enlarges due to weakness of the outer coats and becomes large and rounded. The cornea appears large and strongly curved. The limbus is abnormally displaced anteriorly in relation to the recesses of the chamber angle, the corneal epithelium is irregular and can show cystic degeneration, and Bowman's membrane is often ruptured and the ruptures are filled with a wide network of fibrils and spindle-shaped cells. Between epithelium and Bowman's membrane, there is a thin, loose pannus. The corneal parenchyma is often hydropic and the lamellae are irregular and become indistinct. Descemet's membrane ruptures. The ends of the rupture are rolled in or protrude into the anterior chamber. The endothelium bridges the defect and proliferates freely or onto the torn Descemet's membrane. The lens remains relatively small. The zonular fibers are stretched and break. Nerve fibers and ganglion cells in the retina disappear. The plexiform layers and nuclear layers are thinned. Hemorrhages may be present. The vessels often appear sclerotic. The choroid is thinned and there are subchoroidal hemorrhages. A flat saucer-shaped excavation of the optic nerve appears with

retrogression of the lamina cribrosa. As the coats of the eye are stretched, the excavation extends over about three times the normal diameter of the papilla. Connective tissue, glia and few vessels may proliferate. The retro-ocular nerve stem is atrophic, the pia and the lamina cribrosa form the floor of the excavation, and the optic nerve sheaths in the beginning course obliquely almost parallel to the sclera.

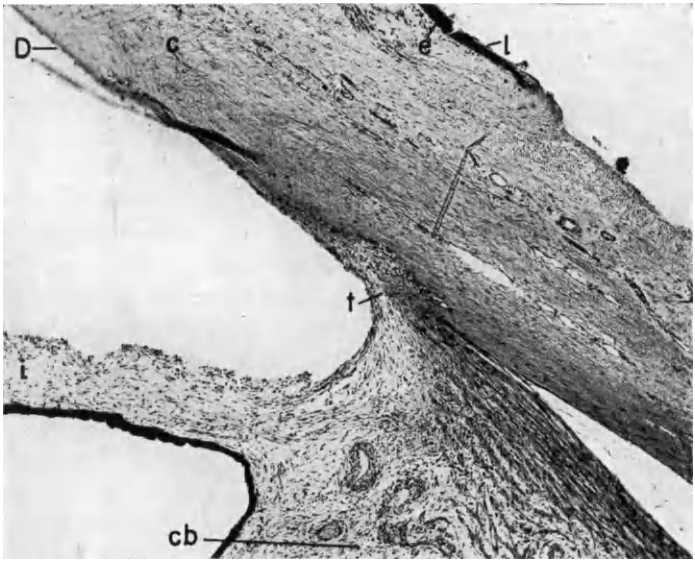

FIG. 60.—CHAMBER ANGLE IN HYDROPHTHALMOS. c, cornea; cb, ciliary body; D, Descemet's membrane; e, epithelium; i, iris; l, limbus; t, rudimentary trabeculae and Schlemm's canal absent. 45×.

Hydrophthalmos is seen combined with other congenital anomalies: (a) with nevus flammeus of the face and (b) neurofibromatosis. In the case of nevus flammeus of the face, in which capillary angiomata are present on the face, intra-ocular capillaries are also dilated and even angiomata of the iris and choroid may exist. The chamber angle is usually, but not always, occluded. Stasis and increased protein content of the aqueous humor may be the primary factors in the production of the hypertension. In Sturge-Weber disease, in which hydrophthalmos

is common, an angiomatous condition of the meninges exists. In the case of generalized neurofibromatosis, neurofibromata of the ciliary nerves exist, too, and the choroid and ciliary body are thickened and contain many oval nuclei and fibrous tissue. Nonmedullated nerve fibers and ganglion cells are present in large numbers. Between these there are oval laminated structures (ovoid bodies). The proliferating cells are thought to be Schwann's cells, and the ovoid bodies rudimentary Meissnerian or Pacinian bodies, or whorls of hyalinized fibroblasts or proliferating nonmedullated nerve fibers. Iris and chamber angle often are underdeveloped. But it must also be mentioned that in both congenital processes glaucoma may first appear in advanced age and then is similar to glaucoma simplex.

Buphthalmos is congenital or acquired in early childhood, secondary glaucoma appearing after perforation of the cornea, iridocyclitis, luxation of the lens or traumatic swelling of the lens. The eyeball is enlarged and rounded; after perforation there may be staphyloma of the cornea, or peripheral anterior synechia, atrophic iris, seclusion of the pupil, luxated lens, secondary cataract, and changes in the posterior segment similar to hydrophthalmos.

6. Annex: Hypotony (Ophthalmomalacia, Essential Phthisis

Hypotony includes cases of differing etiology in which the outstanding clinical symptom is a decrease of the intra-ocular pressure below the norm, usually of high degree. Often the microscopic picture indicates distinctly that the pressure has been decreased during life, but this conclusion cannot always be made from the study of the pathologic changes alone.

In general, the vessels of the uvea appear dilated as they are deprived of the pressure normally exerted on them. This dilatation produces edema, due to outflow of plasmoid fluid from the vessels. The nonpigmented epithelium of the ciliary body becomes vesicular and droplets appear beneath the epithelium of ciliary body and the iris. The aqueous humor becomes richer in albumen. Serous fluid gathers in the suprachoroidal spaces and detaches the ciliary body and choroid. Fluid may also accumu-

late in the subretinal space with subsequent detachment of the retina. The decrease of the intra-ocular pressure may produce papilledema. As the inside pressure onto the outer coats of the eye is diminished, they collapse. The cornea becomes wrinkled and Bowman's and Descemet's membranes are folded and wavy. The sclera appears thickened and shows furrows, corresponding especially to the course of the recti muscles. The fibrous bundles separate. Bruch's membrane is often folded and the pigmentary epithelium is irregular as it fills in the folds. The zonule fibers relax and lens and iris are displaced anteriorly. Diminished secretion of the intra-ocular fluid due to vascular or nervous disturbance is said to be a frequent cause of hypotony. Rarely it appears as a congenital form; it is frequent in myopia if the vitreous body liquefies and the choroid degenerates. It is often found in detachment of the retina when fluid flows through a tear of the retina into the subretinal space and is taken up by the choroid.

Trauma usually decreases the intra-ocular pressure; of course this is true in perforating injury when aqueous humor and, especially vitreous, flow out, but it is also seen in contusion of the eye. Several causes are cited to explain this. The trauma is said to affect directly the small vessels to facilitate the outflow of the intra-ocular fluid, especially when the trabeculae are ruptured. Further, the upset of the normal nervous reflexes disturbs the circulation of the intra-ocular fluid from the vessels to the exit. Inflammation of the ciliary body, and especially formation of a cyclitic membrane with shrinkage of the eye, considerably diminishes the pressure. The intra-ocular pressure is decreased in diabetic coma, but the mechanism is not entirely understood. Perhaps loss of fluid, acidosis, decrease of the blood pressure and influence of toxic substances on the capillaries act together to diminish the intra-ocular pressure. The pressure can also drop under nervous influences. Acute inflammation of the trigeminal nerve in herpes zoster causes acute hypotony; severing of the cervical sympathetic and superior cervical ganglion effects decrease of the intra-ocular pressure. The influence of the endocrine glands on lowering of the intra-ocular pressure is doubtful.

READING OF SOURCE MATERIAL

Duke-Elder and Duke-Elder find increase of the intra-ocular pressure in stimulation of the extrinsic eye muscle by acetyl cholin.

Colombo, Comberg and Stoewer find in humans the intra-ocular pressure increased by stimulation of the facial nerve due to contraction of the orbicularis oculi.

Colle, Duke-Elder and Duke-Elder find that the intra-ocular pressure is very decreased when the eye muscles are paralyzed by curare.

Salvati finds decrease of the intra-ocular pressure after tenotomy of the internal recti.

Friedenwald and Stiehler state that the capillaries of the ciliary body are especially easily permeated.

The volume of the intra-ocular fluid can be changed by injection of anisotonic solutions and in this way also changes of the intra-ocular pressure can be produced (Duke-Elder, Fremont-Smith and Forbes, Marx, Pletnewa, Weekers). According Duke-Elder and Duke-Elder the intra-ocular pressure is decreased if the vitreous body is made experimentally acid and shrinks, and the intra-ocular pressure is increased if the vitreous body is made experimentally alkaline and swells. Meesmann obtained decrease of pressure by injection of isotonic acid solutions into the eye and increase of pressure by injection of isotonic alkaline solutions, but Dominguez always obtained increase of pressure by injection of acid solution as well as alkaline solutions into the eye.

Heesch, Nakamura find that immersion of the eye into acids swells the sclera immensely, compresses the content of the eye and produces enormous increase of intra-ocular pressure.

The changes of the intra-ocular pressure in the course of a day are studied by Hagen, Raeder, Sallmann and Deutsch, Thiel.

Elschnig distinguishes: (1) glaucoma compensatum without changes of the anterior segment of the eye and progressive excavation of the papilla, and (2) glaucoma incompensatum with changes of the anterior segment as (a) prodromal, (b) acute, (c) chronic, (d) absolute. He describes minutely the pathologic changes in eyes of noncompensated glaucoma.

Redslob considers every so-called primary glaucoma as secondary due to intra-ocular circulatory disturbances. Histologically, all cases show corneal precipitates and venous stasis with edema, hemorrhages, tissue proliferation and outpouring of lymphocytes from the blood vessels.

Larsen, Malling, express the opinion that most cases of primary glaucoma are in reality secondary to chronic inflammations of the uvea.

Eyes in acute attacks of glaucoma are examined by Schieck.

Elschnig finds in sudden raise of the intra-ocular pressure a neuritis-like swelling of the optic disk due to entering of fluid from the vitreous body with following hydropic swelling, dissolution of the nerve fibers and formation of glaucomatous excavation.

Friedenwald finds histologically in acute glaucoma, edema and hemorrhagic, serous and fibrinous extravasates in the ciliary body due to damage of the capillaries, which is caused, in his opinion, by toxic histamin-like substances isolated in the aqueous humor.

Zeeman found in eyes with hypermature cataract and acute glaucoma the papilla edematous with some foamy material between the nerve fibers, apparently as product of disintegrating glial tissue, and rounded cells in the chamber angle filled with substances, coming from the lens.

Acute glaucoma is caused by rapidly developing intumescent cataract (Gonzales, Morax.)

Stock saw in an acute glaucoma of four weeks' duration the retina torn at the papilla, as he believes because the optic nerve fibers are stretched over the scleral spur; as they cannot be pulled into the inside of the eye when the lamina cribrosa sinks back they tear and vitreous enters and forms lacunae.

Birnbacher reports primary necrosis of iris and ciliary body causing acute glaucoma.

Talbot finds that in every eye with increased intra-ocular pressure in a few days semispherical bodies appear in Bowman's membrane, and he considers them as lacuna-like spaces around the nerve fibrils.

The aqueous humor becomes more acid in congestive glaucoma, according to Kubik.

Salzmann, describing glaucomatous degeneration of the cornea, finds exfoliation, vesiculation and necrosis of the epithelium, the perforating channels in Bowman's membrane visible, depositions on the membrane, pannus formation and infiltration in the stroma, and Courtis finds vascularization of the cornea and degeneration of the interstitial cells.

The tonofibrils of the corneal epithelium are swollen in glaucoma, according to Mans.

Elschnig states that small spaces originate in the inner layers of the sclera, due to increased intra-ocular pressure, especially in places where the pigment epithelium is deficient, as entering aqueous humor damages scleral lamellae.

Friedenwald considers the rigidity of the sclera in glaucoma rather as sequela than as cause of the glaucoma.

Bergler, Mulder describe cases with extensive adhesion of the iris to the cornea on one side and formation of holes on the other side; Lieskó considers the iris atrophy as cause of glaucoma and not as its sequela.

Peripheral anterior synechia is formed, according to Greeves and McMullen, as the spaces between the trabeculae are filled first with fibrin and cells and that thereafter granulation tissue appears which finally is organized to fibrous tissue. Further, histologic studies of the chamber angle in chronic glaucoma are reported by Herbert.

Early rarification of the macula in primary glaucoma is found by Heine, and Castroviejo, Verhoeff state that the ganglion cells first show degeneration and the macula undergoes cystic degeneration first, then the retina near the ora serrata and later in other regions.

Melanowski believes that the atrophic retina can be displaced into a glaucomatous cupping by shrinkage of newly formed glial and connective tissue of the papilla.

The glaucomatous cupping is caused by pressure and stretching of the nerve fibers as they pass over the margin of the excavation (Kapuczinski), but Evans considers neuritic atrophy with degeneration of the nerve fibers as the primary in the origin of the excavation.

Cattaneo states that the caverns of the optic nerve in glaucoma are caused by hydropic swelling of the nerve fibers due to qualitative and quantitative changes of the aqueous humor and that the newly formed tissue in a glaucomatous excavation, replacing the degenerated nerve fibers, can undergo cystic degeneration (pseudocysts).

Lagrange and Beauvieux compare the cavernous degeneration of the optic nerve to changes of the central nervous system, described by Vogt as état criblé and by Pierre Marie as état lacunaire, which start as degeneration of the nervous tissue near the vessels with enlargement of the lymph spaces, resorption of the myelin and disappearance of the first proliferating glia. They believe that the vessels of the lamina cribrosa and also the choroidal branches of the posterior ciliary arteries are compressed in increased intra-ocular pressure. This leads to ischemia in the nerve tissue and lacunae are formed, similar to the état lacunaire of the cerebrum.

Koyanagi finds caverns of the optic nerve also in orbital tumors and believes that stretching and tearing of optic nerve fibers are the cause of the cavernous degeneration.

Salzmann finds in glaucoma frequently prepapillary proliferation of connective tissue and fine vessels, starting in the center of the excavation of the papilla.

The central retinal vessels sometimes freely bridge the excavation in glaucoma, according to Lagrange and Beauvieux.

Moretti found ossification of the tissue which filled the glaucomatous excavation.

Elschnig believes that a marginal excavation of the papilla without increase of intra-ocular tension is caused also by entrance of aqueous humor.

Redslob finds glaucomatous excavation with and without intra-ocular hypertension. Lacunar spaces appear, due to sclerotic changes of the vessels and venous congestion.

Increase of the elastic tissue, thickening of intima and adventitia in arteries of glaucomatous eyes are similar to those in senile eyes, according to Scheerer.

Latham considers the perivascular infiltration often found in congestive glaucoma as sequela of the stasis.

v. Rényi finds spread and proliferation of pigment besides phagocytosis in glaucoma.

Salzmann finds the lumen of the central retinal vein in the optic nerve progressively narrowed in eyes with absolute glaucoma. The vein is compressed by the artery which is dilated on account of the increased intra-ocular pressure, the central glial meniscus of the papilla or a vitreous herniation. Collateral circulation may develop with the choroidal veins and the veins of the optic nerve sheaths.

Koyanagi describes a case of absolute glaucoma in which the retina has been torn temporal from the optic papilla and is displaced into the papilla. The displacement is caused by traction of the ectatic scleral lamina.

Lamb describes glaucoma with deep anterior chamber in which the chamber angle was occluded by newly formed connective tissue, and he considers toxins as the cause.

Raeder and Harlitz examined a case of atrophy of the face due to inflammatory obliteration of the aorta in the region of the arch. One eye showed a glaucoma simplex with broad anterior peripheral synechiae and marked atrophy of the iris and the ciliary body.

Magitot believes that edema of the ocular tissue due to increased permeability of the capillary walls is responsible for the appearance of glaucoma and the permeability is regulated by the trophic nerves which control the metabolism of the cells. He further states that the glaucomatous atrophy of the optic nerve, which is a descending atrophy with glial proliferation, is caused by changes of the branches of the internal carotid artery supplying the optic nerve. Thalamic excitation provokes a spasm of the vessels, causing edema followed by obliterative degeneration.

Moreu considers glaucoma primarily a disease of the uvea. There exists circulatory stasis in the iris and ciliary body, and the congested iris blocks the chamber angle. He believes that an initial neuro-vegetative dystonia causes the disturbance of the circulation in the uveal vessels, leading to venous stasis, increased capillary permeability and production of albuminous exudate which block the drainage outlets.

Similarly, Arganaraz considers circulatory disturbance of the uvea as cause of glaucoma. Stasis of the vessels is followed by transudation which produces increase of tension.

Disturbances in the circulation of the capillaries resulting in stasis are considered as cause of glaucoma. The disturbance is traced to endocrine factors by Imre, to decrease of the tonus of the sympathetic nerve by Hamburger, to increase of the tonus by Thiel, and to defective regulation by Dieter.

Sondermann finds as origin of primary glaucoma, sclerosing of the sclera with blockage of the outflow of the vortex vein. When the trabeculae of the chamber angle are also sclerosed, Schlemm's canal cannot act any more as safety valve and the intra-ocular tension becomes increased. Schieck, too, believes that compression and occlusion of the veins coming out of the eye cause glaucoma, and glaucoma sets in, according to Friedenwald, if the veins originating from Schlemm's canal are sclerotic and their osmotic pressure disappears.

Elwyn states that the normal pressure of the eye is maintained by central regulation and an effector organ in the eye by means of cholinergic nerves of the parasympathetic nervous system. The effector organ consists of chamber angle, ciliary body and choroidal vessels and maintains a certain volume of fluid in the eye by means of a constellation of electrolytes. Primary glaucoma is a heredo-constitutional functional disease with disturbance of the central regulation resulting in irregular production of the chemical mediator, acetylcholin, in the nerve endings in the effector organ. By that, either the volume of the aqueous or the volume of the blood in the choroidal vessels is increased.

Marin Amat considers glaucoma as reaction of the vagus nerve. It arises when a dysfunction of the locally regulating mechanism breaks the sympathetic-vagotonic balance which regulates the quantity of the in- and outflowing blood in the eye.

Glaucoma is, according to Hess, a neuro-regulatory disturbance, and he believes that the eyeball is represented in the vegetative center of the

diencephalon. The atrophy of the optic nerve develops preferably in persons with asthenia associated with acromegalic features or such with pyknic body with signs of adiposogenital disturbances.

Zondek and Wolfsohn find in certain cases of glaucoma as casual factor pituitary-diencephalic disease acting by means of a disordered circulation in the eye and water retention of its tissue, and they call such a glaucoma "diencephalopathy."

Bloomfield finds that the parasympathomimetic activity is deficient in eyes with chronic simple glaucoma, causing faulty regulation of the intraocular pressure.

Deposition of pigment in the structures of the chamber angle is the cause of glaucoma, according to Barkan, Boyle and Maisler, Levinsohn.

Verhoeff believes that the origin of glaucoma lies in the anterior synechiae and that the vitreous plays a role, too, in the genesis of glaucoma.

Baenziger states that the glaucomatous synechia is caused by increase of pressure in the posterior chamber which is not released fast enough through the pupil.

Melanowski states that the lens pushes the ciliary body against the sclera, causing increased pressure, and Wipper expresses the opinion that the pressure of the lens on a hypertrophic ciliary body causes cyclitis of neuritic character leading to glaucoma.

Schwarzkopf describes multilocular vesicular formations in the ciliary epithelium in glaucoma, which, as he believes, originate from Greeff's vesicles also without paracentesis, and become the cause of the hypotony.

Bennoit believes that the aqueous humor is also eliminated through a slit between the anterior and posterior layers of the iris which continues into the layer of the veins in the ciliary body and choroid. Glaucoma arises when these spaces are blocked. Nordenson finds that the permeability of the hyaloid membrane decreases in old age, leading to mucin retention in the vitreous and causing stasis of the outflow of fluid from the vitreous body, by pushing the lens-iris-diaphragm forward and blocking the chamber angle.

Fortin accuses the ciliary muscle as responsible for glaucoma in case it is no longer able to pull the scleral spur inward, and Herbert describes a system of elastic fibers extending from the ligamentum pectinatum to the ciliary muscles. The elastic pull of these fibers keeps the meshwork open. If this pull is missing, the aqueous humor cannot enter Schlemm's canal. In eyes predisposed to glaucoma, the insertion of the ciliary muscle is relatively far backwards.

Wernicke considers glaucoma as a special form of disseminated sclerosis.

Cords reports histologic findings in secondary glaucoma due to arteriosclerosis in the retina and optic nerve, retinitis proliferans, embolism of the central artery and thrombosis of the central vein.

Fuchs found in secondary glaucoma hydropic swelling of the corneal epithelium with fluid intracellularly.

Monthus and Rochon-Duvigneaud find glaucoma occasionally complicating diabetic retinopathy. A membrane blocking the chamber angle is formed on the anterior surface of the iris.

Duke-Elder and Duke-Elder trace traumatic glaucoma to disturbances of the vasomotor mechanism in the eye.

Tillema describes in traumatic glaucoma rupture through Schlemm's canal and necrosis of the uvea, but also rupture of the lens capsule and prolapse of the vitreous body into the anterior chamber.

Morax finds in traumatic glaucoma, edema and necrosis of uvea and retina and luxation of the lens.

Genet describes a case of glaucoma caused by trauma with the lens luxated and the retina detached. Fox finds post-traumatic glaucoma after cataract extraction, caused especially by incarceration of the iris in the wound, further by obstruction of the chamber angle by large masses of soft, lenticular remnants. Lehrfeld and Reber find posttraumatic glaucoma after iridectomy, needling and cataract extraction. Occlusion of the chamber angle by prolapsed vitreous causes post-traumatic glaucoma, according to Stieren, Urbanek, Vail, and it is caused by ingrowth of epithelium, according to Levine, Vail.

Cases of senile exfoliation of the lens capsule causing secondary glaucoma are reported by Busacca, Garrow, Hoerven, Irvine, Rehsteiner, Trantas, Vogt.

Morgagnian cataract produces secondary glaucoma, probably because the nucleus of the lens rests on ciliary processes and irritates (Knapp).

Weinstein describes cases of absolute glaucoma following thrombosis of the central vein. It is caused by accumulation of pathologic products of the changed metabolism (carbonic, lactic, acetic acids) and swelling of the vitreous.

Evans considers perivascular infiltrations as responsible for secondary glaucoma in intra-ocular tumor.

Maggiore finds inflammatory changes of the uvea in myopia with detachment of the retina and glaucoma, and Fuchs believes that diseases of the ciliary body can produce simultaneously detachment of the retina and glaucoma.

Raeder sees the cause of secondary glaucoma in the subretinal exudate in detachment of the retina. Further, detachment of the retina and glaucoma is reported by Halbertsma.

Epidemic dropsy is a beri-beri-like disease, appearing in Bengal in people eating polished rice, which contains the toxin of the spore-forming bacillus proteophyticus. The dilated capillaries of the uvea, whose endothelium fluid passes easily, produce acute glaucoma with severe edema of the intra-ocular tissue, according to Kirwan, and Kirwan, Kirwan and Mukergee find in such cases enormous dilation of the uveal vessels, edema and increase of albumen in the aqueous humor.

Gazepis noted in glaucoma with pulsating exophthalmos the trabeculae of the chamber angle clogged with mononuclears, plasma cells, pigment-laden phagocytes and free pigment.

Bothman believes that x-ray radiation can produce glaucoma by disintegration of pigmentary epithelium and spreading of the pigment.

Seidel produced glaucoma experimentally by injection of india ink or of colloidal dyes under increased pressure into the anterior chamber, Hamburger by injection of an aqueous solution of nigrosin into the anterior chamber.

Ligature of the vortex veins (Magitot) or the veins back in the orbit (Hiroishi) increased the ocular pressure. If a stasis is produced in all veins

of the head by ligature around the neck (Bonnefon), compression of the thorax (Mazzei), or of the abdomen (Comberg and Stoewer), the pressure in the eye rises.

Histologic findings in glaucomatous eyes after iridencleisis are reported by Holth.

Lagrange reports on glaucoma in early childhood.

Meisner distinguishes hydrophthalmos (1) with deep anterior chamber and developmental anomalies of the chamber angle and (2) with severe developmental anomalies of the entire anterior chamber with extensive adherence of cornea and iris.

Anderson, Cucco, Lamb, Theobald and Clapp report on hydrophthalmos.

Jaensch, Panico find absence of Schlemm's canal as cause of hydrophthalmos, and Lagrange, further, anterior peripheral synechiae which he also considers as developmental anomaly.

Pesme found in a 9 month old infant hydrophthalmos with underdevelopment of Schlemm's canal and hydrocephalos with a miniature ependymal canal, and Seefelder a rudimentary development of the scleral spur and abnormal persistence of the ligamentum pectinatum.

Turkus-Sterlingowa describes gelatinous masses in the anterior chamber of an hydrophthalmos.

Garrow and Lowenstein found in a hydrophthalmos ruptures and fissures and hemispheric bodies in Bowman's membrane and Descemet's membrane appearing in three layers, one true membrane and two newly deposited by the endothelium.

Jahnke found hemangioma of the choroid in glaucoma with nevus flammeus of the face.

Knapp describes a glaucoma in generalized vascular nevus of the face and of the mouth showing proliferation of the iris endothelium with many newly formed vessels of angiomatous type.

Hydrophthalmos with nevus flammeus is examined histologically by Dumphy, Evans and Evans, de Haas, Safar, Weber. The intra-ocular capillaries are dilated and angiomata may be found in the uvea. Schlemm's canal can be absent and the scleral spur and Schlemm's veins displaced posteriorly.

Perera and Stout describe an hydrophthalmos with melanosis of the optic nerve in a 21 month old girl which further showed a neuroepithelioma of the intracranial optic nerve and of the chiasm.

Wiener saw a neurofibroma of the eyebrow with hydrophthalmos showing the chamber angle partly blocked by persistent ligamentum pectinatum and partly absence of Schlemm's canal and thickening of the endo- and perineurium of ciliary nerves.

Oguchi found a tumor-like swelling of the sclera at the posterior pole in an hydrophthalmos consisting of angiomatous tissue and striated muscles. He considers the tumor as epibulbar hematoma.

In hypotony is found histologically edema of the ciliary body by Rados, edema beneath the epithelium of the iris by Carrere, Samajloff, folds of Bowman's membrane by Reis.

Hypotony is found in myopia by Urio, in detachment of the retina by Kleiner, in trauma by Magitot, Weekers, in diabetic coma by Imre, Patek, Poos, in disturbances of glands with inner secretion by Imre, Terrien.

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Chapter XVIII

MYOPIA

Eyes with myopia of a low degree do not differ in structure from emmetropic eyes or eyes with small hyperopia, but in myopia of a high degree there are progressive pathologic changes of the globe.

The globe is elongated in the sagittal axis and frequently is oval. The anterior segment of the globe deviates little from the emmetropic eye, but the posterior segment, starting from the equator is elongated. The posterior pole of the eye and the posterior temporal quadrant are the most ectatic.

The anterior chamber is rather deep and the recessus of the chamber angle extends somewhat farther posteriorly. The ciliary muscle shows an arcuate borderline as the circular portion is little developed. The nucleus of the lens scleroses intensely, especially when the vitreous is liquefied. The junction of the pars plana and the retina proper at the ora serrata is more or less indistinct and the anterior retina shows many oval cystic spaces. In general, the anterior retina is thin, its elements are diminished and often only glial structure remains. Pigment migrates sometimes into the retina, and retina and choroid fuse. The important changes affect the posterior retina and choroid, the optic disc, the vitreous and the sclera. The rods and cones clump together and disappear and the outer nuclei are diminished, vessels disappear and finally a thin membrane consisting of glia remains in the place of the retina. The macula is flattened, especially by thinning of the ganglion cell layer. The pigment epithelial cells are enlarged, multinuclear and vacuolated and may proliferate to glandular-like tubules. Detachment of the retina is frequent, due to cystic degeneration or detachment of the vitreous. The choroid is diffusely thinned, and its vessels are less numerous, lie more distant from each other, their walls are thin and they may obliterate. The choroid may

appear in circumscribed areas, transformed into connective tissue and elastic fibers, and its stroma pigment be decreased. Bruch's membrane is thinned and shows ruptures, through which the pigmentary epithelium proliferates into the choroid, and the retina may bulge into the choroid. Circumscribed small accumulations of lymphocytes are infrequent.

The papilla, its surrounding structures and the optico-scleral canal show important changes. Conus, circumpapillary atrophy of the choroid and obliquity of papilla and scleral canal develop. As a result, the optic nerve fibers course from the retina into the papilla and the scleral canal, temporally in a flat arc and nasally sharply bent around the edge of Bruch's membrane. Although in the normal eye, in general the diameter of the conical scleral canal is smaller on its inner side than on its outer side, in the myopic eye the inner opening of the canal is displaced temporally, and the oblique canal, the form of which becomes irregular resembling somewhat an oblique cylinder, has the wider opening more on its inner side than on its outer side. The inner scleral edge of the canal is temporally flattened to an obtuse angle and projects nasally spurlike far into the optic nerve. The retina is temporally pulled away from the scleral edge and the papilla (distraction), but is nasally pulled over the scleral spur and papilla (supertraction). Together with the retina, the choroid, also, is displaced temporally from the nerve entrance to a various extent and nasally pulled into the papilla. Together with the retina, the pigmentary epithelium and Bruch's membrane, too, is temporally pulled away from the nerve entrance so that a peculiar loop-formation of the nerve fibers originates. The nerve fibers, together with the intermediary tissue, are displaced between retina and choroid, forming a loop with an acute angle at the edge of Bruch's membrane and coursing over the exposed sclera or atrophic choroid into the papilla. It is assumed that the elastic Bruch's membrane splits on its end at the papilla in fine fibers, fanlike, which radiate into the intermediary and interstitial tissue of the optic nerve. As the elastic membrane retracts, it displaces this tissue and with it optic nerve fibers.

Other opinions are that together with the retracting choroid the intermediary tissue is displaced temporally, taking the nerve fibers with it; or that the temporal conus is formed by the inner wall of the scleral canal which is turned anteriorly and temporal-wards, therefore, of a part of the sclera which never was in contact with retina and choroid. The conus temporal margin corresponds generally with the end of Bruch's membrane, where nerve fibers are in contact with the membrane and with dense connective tissue formed by the choroid. The pigmentary epithelium ends usually at the same place with pigment accumulating here and epithelium and glia proliferating and uniting with the choroid. Usually choroid and pigmentary epithelium have disappeared in the region of the conus and therefore the conus appears white ophthalmoscopically. But there are variations. The elastic Bruch's membrane may reach, broken up, into the conus. The choroid may extend into the conus and be atrophic to various extent with islands containing chromatophores and vessels in the conus, which appears ophthalmoscopically in this case pigmented. In the choroid at the margin of the conus, and in the conus itself lymphocytic infiltration may be observed. Occasionally the inner layers of the retina are pulled over the margin of the conus, are folded and appear double. Circumpapillary atrophy of the choroid exists when, in addition to temporal conus, the choroid which extends nasally into the papilla becomes atrophic and transparent too. The optic nerve fibers lying in front of and behind the atrophic choroid produce the white color in the ophthalmoscope picture. Also, nasally, the retina and Bruch's membrane can retract and the nerve fibers show some degree of loop formation. The optic nerve behind the lamina cribrosa turns from its oblique course in the optico-scleral canal to a more straight course. The intraorbital part of the optic nerve is, because of the enlarged globe and the shortened distance to the optic foramen, more curved than normally. The intervaginal space is often dilated, especially on the side opposite the conus.

The vitreous is often liquefied and detached and appears broken up; continuously increasing cavities are formed and the

destruction of the scaffold of the vitreous gives rise to floating particles in the liquid vitreous.

The sclera is thin in the posterior part of the globe more temporally than nasally, due to stretching of the globe or because the sclera itself is congenitally preformed thinner than normally. However, the thinning is progressive. The fibrous bundles of the sclera course in the thinned part meridionally and are thin; circular bundles are missing so that the sclera shows a lamellar structure. Circumscribed areas of the sclera may be very thin and bulge staphyloma-like, appearing clinically bluish as the pigmented atrophic choroid shines through. The thinned retina may extend into the ectasia. An ectasia often appears as a congenital anomaly in the region of the perforating scleral channels.

As a complication of myopia, as already mentioned, detachment of the retina may form; further glaucoma, especially juvenile glaucoma. Hydrophthalmos and myopia may be associated. In this case, the globe is more spherical, enlarged and the sclera is thin all around; however, in hydrophthalmos without myopia, the sclera is mostly thickened. Partial cavernous atrophy of the optic nerve can be seen in myopia. The caverns filled with fluid start behind the lamina cribrosa, extend through the nerve somewhat posteriorly and are followed further backwards by partial simple optic atrophy. The cavernous atrophy in myopia is explained as a sign of simple glaucoma.

It is assumed that progressive myopia is a congenital anomaly of the bulb, but one which makes its appearance in the second decade. The tendency of conus formation which is said to be preformed already in the embryo is believed to be inherited, and so also the obliquity of the optic nerve entrance. Another theory is that an excessive growth of the retina is primary, secondarily causing the stretching of the outer layer of the eye. Probably the stretching happens in an inferiorly preformed outer layer of the eye. This represents the congenital factor and there are additional external factors which introduce and accelerate the process. As the choroid is stretched, vessels disappear and the retina degenerates.

READING OF SOURCE MATERIAL

Bussola describes anatomic findings in myopic eyes.

Giannini describes pathologic changes in high myopia and considers them responsible for the detachment of the retina.

Stocker describes a myopic eye with beginning crescent on the temporal side, supertraction on the nasal side and thinning of the sclera at the posterior pole. He believes that the retina grows more than the sclera and that the latter finally yields.

Stanka found in a case of myopia with detachment of the retina and glaucoma the iris displaced posteriorly, the ciliary body infiltrated and subretinal blood.

Inouye believes that the lamina elastica of the choroid extends somewhat into the papilla with thickening and small hooplike curvature on its end; he finds that the nerve fibers are pulled in a myopic conus beneath the retina by traction of Bruch's membrane and that the choroid lying underneath atrophies.

Buecklers finds similar changes in the senile and myopic circumpapillary atrophy of the choroid: there are cleftlike openings in the fatty degenerated Bruch's membrane, sclerosis of the choroidal tissue and vessels, atrophy and proliferation of the pigmentary epithelium, pointed extensions of the nerve fibers, cystoid degeneration of the ganglion cells and nerve fibers and fatty degeneration of the sclera; the findings depend on variations of the optico-scleral canal. If the canal is oblique, the retina is distracted from the papilla temporally and supertracted over the papilla nasally.

v. Szily observed that the various forms of the papilla are preformed very early in the fetal life, especially with the closure of the fetal cleft. If the intercalary piece of the primitive papilla of the embryo is formed obliquely, the optico-scleral canal is oblique in the developed eye. The myopic form of the optic nerve entrance can be visible already in the embryonal eye.

Scheerer examined the papilla in various age levels and various refractions. He finds on the temporal side, attrition of the scleral margin, lateral bowing of nerve fibers to lie behind the lamina vitrea, retraction of the lamina vitrea and of the pigmentary epithelium and atrophy of the choroid; on the nasal side, supertraction of the lamina vitrea and the pigmentary epithelium and angular cracking of the lamina vitrea and the pigmentary epithelium in all possible refractions and in all ages. Bending of the nerve fibers so that they come to lie behind the lamina vitrea is found also in inverse papillae on the nasal side, even also above and below.

Gilbert finds hernia-like protrusion of the inner nuclear layer into the choroid through defects of Bruch's membrane. The outer nuclear layer is everted.

Sallmann considers the detachment of the vitreous body found in high myopia histologically as important for the origin of detachment of the retina.

Heine concludes from his findings that the sclera in myopia is more thinned than it would be by simple stretching of normally deposited sclera. Bruch's membrane is aplastic and circumscribed atrophic choroidal

foci alternate with proliferative thickening. The macula can be flattened, showing degeneration of the neuro-epithelium.

Hanssen finds the sclera in myops thin at the posterior pole with circumscribed very thin areas. He finds also flat inclusion of glial tissue and nerve fibers between choroid and sclera with shallow ectasia of the latter. He considers those changes as congenital. He finds further cystoid degeneration of the anterior retina giving rise sometimes to detachment of the retina. As the globe is elongated, the S-shaped curvature of the optic nerve in the orbit is still more marked.

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Chapter XIX

INJURIES

Injuries of the eye are of physical and chemical nature. Injuries of physical nature are brought about by contusion and cutting objects. Foreign bodies in the eye may cause injury, as may also such physical agents as cold, heat, electricity and various rays. The eye may be chemically affected by inorganic and organic substances in liquid and gas form.

Many of the injuries are studied only clinically or experimentally, but many are also studied histologically.

1. Contusions

Injuries by contusion are blow, increased air pressure by explosion or projectiles, compression of the skull, as for instance in forceps delivery, or compression of the rest of the body. In contusion, the adnexa as well as the bulb itself may be injured and the latter with or without rupture. The pathologic changes of the adnexa are known nearly exclusively clinically. The lids show hemorrhages from rupture of vessels and lacerations due to rupture of the skin. The conjunctiva may be filled with hemorrhages. The margin of the orbit can be fractured, the tarsus severed perpendicularly and orbit and lid may have emphysema, if air is pressed into the orbit from the paranasal sinuses through the fractured orbital wall. The orbit can be filled with blood, and all its tissues and the bulb pushed anteriorly, but on the other hand, also, enophthalmos can occur if the tissue shrinks and a part of the orbital content is pressed through the fractured floor of the orbit into the antrum. If the injury leads to formation of an aneurism in the orbit, the exophthalmos is pulsating. The eye muscles and nerves of the orbit may be injured. The canaliculi and lacrimal sac may rupture and the nasolacrimal duct may be stenosed by fracture with subsequent dacryocystitis. The lacrimal gland may be luxated, may become atrophied and show dacryops.

Contusion injures by direct effect at the traumatized area or indirectly at a place distant from the area where the force attacks. The mechanical factors alter the form of the bulb, displace it as a whole or its liquid contents only, which conduct the pressure.

Contusion may affect without rupture any part of the bulb in various degree and extent. The cornea is flattened and shows hydropic swelling and fracture of lamellae, blood staining and folds and ruptures of Descemet's membrane. The aqueous humor presses toward the iris, lens and Schlemm's canal. The chambers are often filled with blood coming from the vessels of the iris and ciliary body, when they rupture, or by diapedesis when their walls are paralyzed. Occasionally only albuminous and fibrinous fluid leaves the vessels, filling the chambers as densely stained homogeneous and fibrillar masses; they may stimulate proliferation of connective tissue into the pupil (occlusion membrane). Hemorrhages may disintegrate, forming lipoid and cholesterol, giving rise to proliferation of connective tissue and appearance of phagocytes; the anterior chamber may be filled with newly-formed tissue containing cholesterol crystals (xanthomatosis bulbi).

The iris shows ruptures, affecting chiefly the area of the sphincter, more rarely other parts of the stroma or the pigment epithelium, displacement and inflammatory changes. Hemorrhages may fill the sphincter, and pieces of the iris may be broken off. Iridodialysis is frequent; the iris breaks off in the root from the ciliary body, which becomes atrophic. In iridodialysis, the separated iris shrinks considerably; its tissue is condensed and connective tissue proliferates. The vessels are obliterated and the pigment dispersed and irregular. The trabeculae of the chamber angle may be covered with iris pieces and the intertrabecular spaces blocked. Trabeculae are sometimes torn and the rupture extends into Schlemm's canal. Zonular fibers may break, the lens luxate, the vitreous body prolapse and tissue may grow from the endothelium and anterior border layer of the iris onto the vitreous. Such tissue may also extend into the chamber angle, so that the defect of the iridodialysis is covered. Dense connective tissue can grow over the

anterior surface of the iris, and if it reaches the pupillary margin and shrinks, it may pull the pupillary portion of the iris and the pigment epithelium over the anterior surface of the iris (ectropion uveae, ectropion of the pigment epithelium). If the iridodialysis extends along the entire circumference of the ciliary

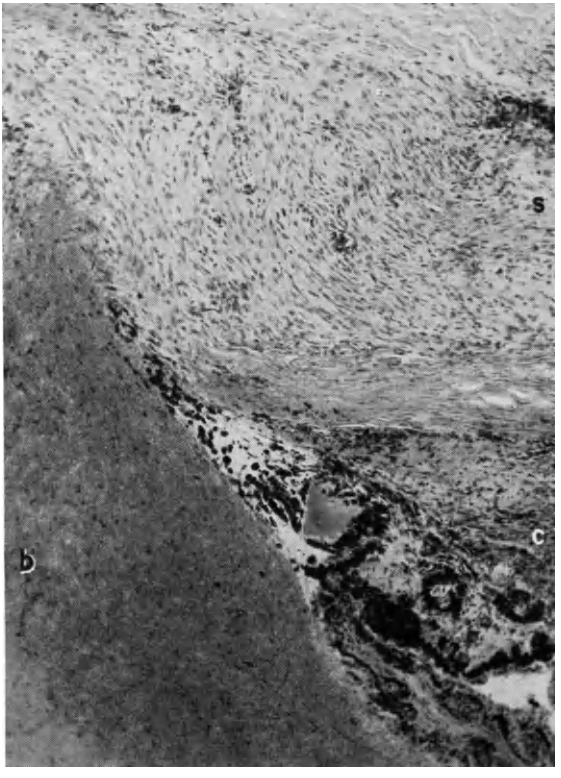

FIG. 61.—ANIRIDIA TRAUMATICA. b, blood in the chambers; c, ciliary body; s, distorted sclera. 75×.

body, traumatic aniridia exists; then the entire iris lies shrunken somewhere in the anterior chamber. In other cases, the iris may be only inverted and retroflected. The posteriorly inverted iris often lies on the ciliary processes and eventually unites with them. The retroflected iris shows pigment epithelium lying on pigment epithelium. In some cases of contusion, pigment may

migrate from the pigment epithelium onto the anterior surface of the lens. The ciliary muscle is sometimes ruptured or muscle fibers become glassy and thickened. The ciliary body often reveals hyperemia and hemorrhages and is detached and displaced posteriorly. Cyclitic membranes may be formed.

The lens shows cataractous changes or displacement and cataract may occur with or without rupture of the capsule. If there is no opening in the capsule present, the cataract is caused by dissociation of the lens protein and water, with swelling and disintegration of lens fibers, formation of vacuoles and appearance of Morgagnian globules. However, in contusion the epithelium may be first destroyed; the aqueous humor has access to the lens and liquefies, through its proteolytic enzymes, the dissoluble lens protein and breaks up the lens fibers. The lens nucleus may also be disorganized, showing spaces filled with fluid, Morgagnian globules and hyaline masses. Frequently the capsule is torn by the force of the contusion and aqueous humor freely enters the lens. In this case, the lens of a young individual is entirely resorbed and the empty capsule sac remains. The nucleus may escape through a large rupture of the capsule, be surrounded by polymorphonuclears, lymphocytes and giant cells and be resorbed. If fibrin is deposited onto the wound of the lens capsule and lens epithelium proliferates, the wound becomes closed. The disintegration of the lens fibers occasionally occurs ringlike around the nucleus or may be limited to a circumscribed area riding on it. Lens epithelium in cataractous lenses often extends to the posterior surface of the lens. If the zonule breaks (usually at the equator of the lens) or connective tissue adherent to the lens capsule shrinks, the lens may subluxate or luxate and is anatomically more spherical. The lens may be partially or totally luxated into the anterior chamber, the lens capsule unite with Descemet's membrane and the cornea be eroded posteriorly. The lens may be luxated into the liquefied vitreous body, may be surrounded by phagocytes and may be attached to the proliferating epithelium of the ciliary body or to the retina by inflammatory tissue. The lens luxated into the vitreous acts in a toxic manner and produces retino-choroiditis. The luxation of the lens is frequently followed by secondary

glaucoma. Contusion may produce hemorrhages into the vitreous, causing formations of strands and membranes here.

Pressure, in case of contusion, can be extended through the aqueous humor and the lens into the vitreous body and the eye bulb be pressed as a whole against the surrounding tissue, so

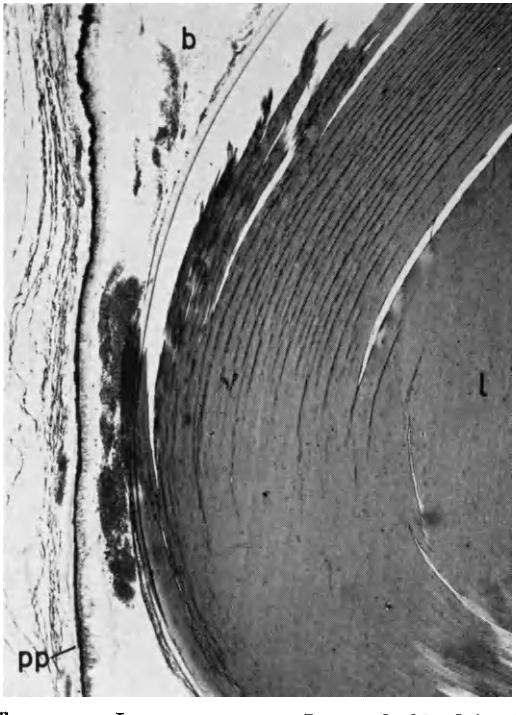

FIG. 62.—TRAUMATIC LUXATION OF THE LENS. b, blood in the posterior chamber; l, lens; pp, pars plana of the ciliary body. 35×.

that alterations in the posterior segment of the bulb arise. In the choroid, hemorrhages and transudations appear; also detachment, pigment alterations and rupture. The paralyzed choroidal vessels appear dilated and filled with blood, serum is poured out by transudation and blood by diapedesis. Accumulation of serous fluid in the suprachoroidal spaces produces detachment of the choroid, which also may be produced by hemorrhages

into the suprachoroidal spaces, when blood vessels rupture. If Bruch's membrane tears, blood flows into the subretinal space. In this case, organizing connective tissue and proliferating vessels become attached to the retina, which degenerates and from which glia grows into the proliferating tissue (chorioretinitis proliferans, choroiditis hyperplastica). The choriocapillaris is interrupted, the outer retinal layers atrophy and pigment wanders from the pigment epithelium into retina and choroid. But also without rupture of Bruch's membrane, rupture of the choroid and perhaps simultaneously of the retina may appear. The inner layers of the choroid appear separated; frequently also the pigment epithelium is interrupted and proliferates on the margin of the rupture. Finally, scar tissue appears in the choroid, the pigment epithelium often forms multiple pigmented and nonpigmented epithelial ducts and the covering retina may atrophy to a thin membrane. Shrinking scars can cause secondary detachment of the retina or the choroid.

The retina may show edema, holes in the macula, ruptures, detachment and hemorrhages. The edema affects the inner layers of the retina, containing minute fluid-filled spaces and small hemorrhages (commotio retinae, Berlin's opacity). It is caused perhaps by hitting of the retina by the vitreous body or perhaps by sudden reflex narrowing of the vessels followed by intensive dilatation. The contusion first produces ischemia of the retina by constriction of the vessels, but soon dilatation follows, causing hemorrhages. A hole in the macula follows edema with formation of cysts which coalesce and rupture. Therefore, histologically, either a severely cystic degenerated retina is found in the macula with a small amount of serous fluid in the subretinal space, and proliferation of the pigment epithelium, or the retina is torn and the lips of the tear rolled up toward the vitreous. The retina may tear also in other areas, either due to a severe subretinal hemorrhage, or by overstretching, with and without rupture of the choroid. If retina and choroid are torn at the same time, usually they become attached to the sclera by proliferating tissue. Rupture of the retina alone usually causes detachment, which sometimes is caused also by

shrinking membranes in the vitreous body formed after hemorrhages. Dialysis of the retina occurs occasionally on the ora serrata.

The optic nerve may show neuritic changes, be torn off in the optico-scleral canal, or atrophy. The contusion neuritis is seen as edema of the papilla accompanied by hemorrhages. In case of avulsio nervi optici, the optic nerve is torn off from

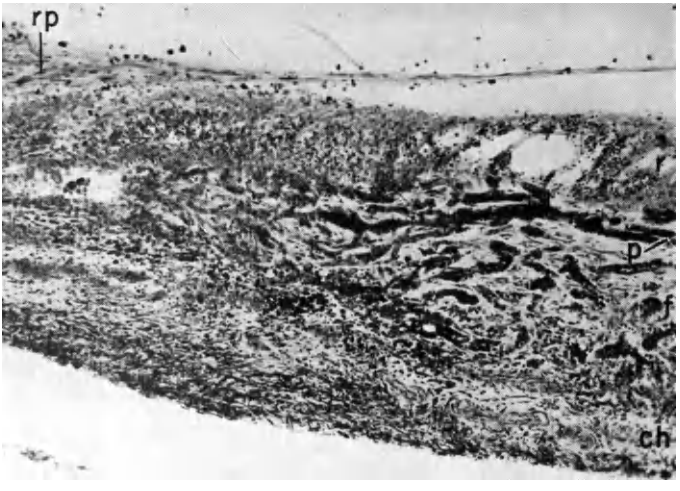

FIG. 63.—CHORIORETINITIS CAUSED BY TANGENTIAL TRAUMA OF THE GLOBE. ch, fibrosed choroid; f, newly formed fibrous and glial tissue; p, proliferating tubular shaped pigment epithelium; r, disintegrated retina; rp, retinitis proliferans. 70×.

the optico-scleral canal, partly or entirely, is covered by hemorrhages and degenerates. The optic nerve atrophies secondarily in alterations of the retina and if the retro-bulbar portion of nerve is damaged.

Gun shot injuries of the eye often produce severe changes, also, even if the globe is not ruptured or hit directly. The globe is smashed or filled with extensive hemorrhages if the bullet hits the globe directly. But the projectile may pass through the orbit tangential to the globe, which is then rotated, indented, and pushed toward the wall of the orbit. The retina may be detached or the choroid torn, followed by hemorrhages, exudation and

scar formation. Degeneration and proliferation produces a scar of the retina and choroid consisting of dense connective tissue and glia and layers of pigment epithelium (chorioretinitis sclopetaria). If tissue proliferates from the choroid into the retina and further budlike into the vitreous body, chorioretinitis proliferans exists.

Contusion frequently damages the globe with rupture of its outer layers and may produce a direct or indirect rupture of the bulb. The sclera usually ruptures where it is thinned by perforating channels, either by direct force or indirectly as the bulb is pressed toward the orbital walls. The rupture is most frequently located at the limbus, running concentric to it, and extends from within outward. The trabeculae rupture, their edges curl inward and Schlemm's canal is opened. Sometimes this is all that happens, but often the rupture extends through the channels of the anterior ciliary veins onto the episclera and conjunctiva which finally also may tear. In contrast to this typical scleral rupture, atypical scleral ruptures happen infrequently. They are rarely meridional in the posterior segment of the eye, at the equator or in ectatic areas of the sclera. The cornea may also burst and the corneo-scleral junction tear. Iris, ciliary body, vitreous body, choroid and retina may prolapse into the wound, depending partly on the place of the rupture. It bleeds into the tissue of the eye. Iris may break off partly from the ciliary body (iridodialysis), or completely and be thrown out of the eye (traumatic aniridia). The lens may luxate into the vitreous body or out of the eye. The luxated lens can be situated beneath the intact conjunctiva or in Tenon's space, or may be lost entirely. The capsule may stay intact or tear and the lens may escape from the capsule. If the lens is luxated subconjunctivally, connective tissue membranes proliferating from the episclera are formed around the lens which usually is surrounded by hemorrhages. The lens may become cataractous, shrink and calcify or its capsule may be eroded by phagocytes, giant cells and proliferating blood vessels and the lens may be resorbed. Retina and choroid are usually detached if they are not prolapsed. Endophthalmitis and sympathetic ophthalmia may be sequelae. The wound in the

sclera can close by scar tissue from the episclera and choroid, but uveal tissue may be incarcerated, leading to the formation of a staphyloma.

The globe can be damaged by contusion of the skull, in which fractures and hemorrhages occur. The optic nerve is damaged directly, the nerve fibers degenerating and disappearing in the

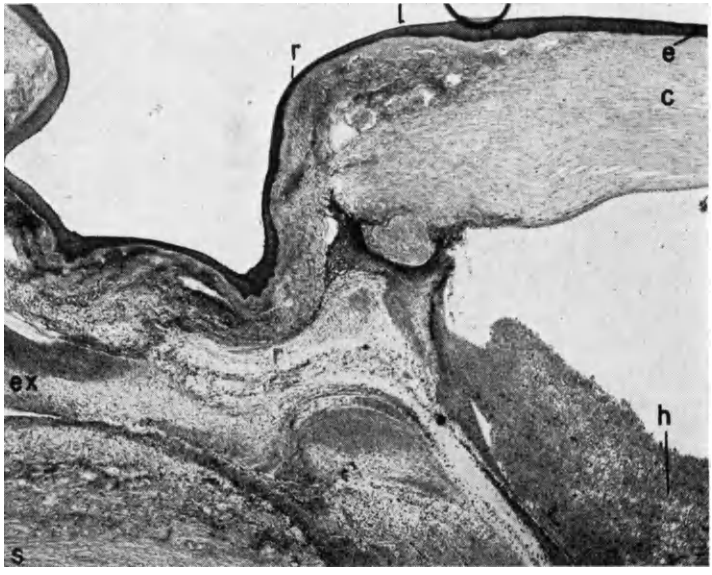

FIG. 64.—SCLERAL RUPTURE. c, cornea; e, epithelium; ex, exudate; h, hemorrhage; l, limbus; r, rupture; s, sclera. 30×.

area of the injury, and the degeneration of the nerve fibers continues toward the papilla. In case of hemorrhages into the sheaths of the optic nerve, papilledema sets in, which can also be caused by extensive intracranial hemorrhages with increased tension.

Compression of the chest produces angiopathia retinae traumatica. Retinal hemorrhages, coagulation of globules in the retina, and edema of the papilla are seen. It is caused by stasis in the veins of the skull and neck and suddenly increased cerebral pressure.

Bone fractures occasionally cause fat emboli in vessels of the retina, choroid and optic nerve. Specific staining reveals the small vessels of the retina, the chorio-capillaris and capillaries of the optic nerve filled with fat droplets. The nerve fibers and ganglion cell layer, may be edematous.

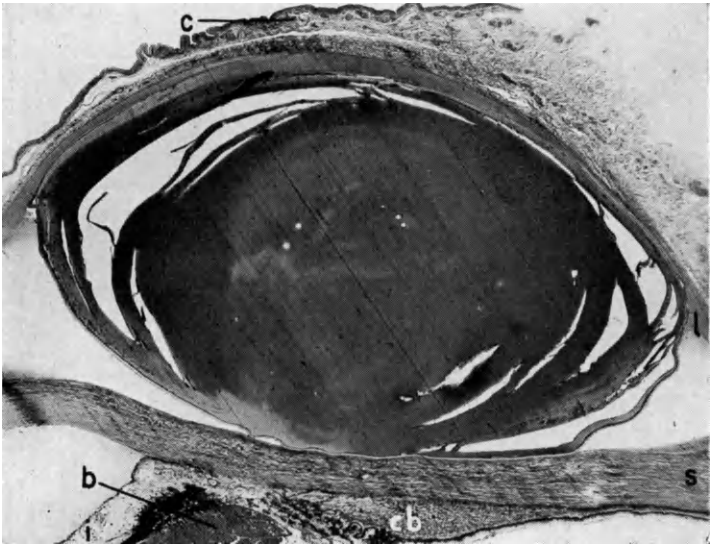

FIG. 65.—SUBCONJUNCTIVAL LUXATION OF LENS. b, blood in the posterior chambers; c, conjunctiva; cb, ciliary body; i, iris; l, lens; s, sclera. 12×.

2. INJURIES FROM CUTTING OBJECTS

Cutting objects produce superficial and perforating injury of the eye and its adnexa. Damages of the ocular tissue produced by cuts are in many instances studied only clinically or experimentally.

Superficial wounds caused by cuts affect cornea, sclera and conjunctiva. The cornea may show an erosion only or deeper reaching defects, in case of infection a suppurative ulcer, and nonsuppurative inflammation in case of noninfectious foreign bodies. In erosion, the epithelium is defective but regenerates soon; also, Bowman's membrane may be injured, which does not regenerate. Recurrent erosion shows ballooning degen-

eration of the epithelium. A cut can form a deep-reaching wound channel which is closed by fibrin and finally by regeneration of tissue from the fixed cells. A part of the cornea, including epithelium, Bowman's membrane, and the adjacent lamellae may be cut off, and if this defect is not infected it can be filled up by regenerating tissue. If an erosion or other defects of the cornea are infected, a suppurative ulcer of a serpigenous or mycotic ulcer type may form, but under certain circumstances herpes corneae, epidemic keratoconjunctivitis or disciform keratitis may appear. Foreign bodies of any kind, metallic, inorganic or organic, may heal in, without irritation, or perhaps produce a circumscribed necrosis and discoloration, some proliferation of fixed cells in surrounding tissue, the formation of capillaries, immigration of polymorphonuclears and the formation of a connective tissue capsule. Iron, copper, stone, glass particles, powder dust, wooden splinters, hairs or straw, are seen as foreign bodies.

Wounds of the sclera heal if not infected by regeneration from the episclera. Foreign bodies, such as iron or copper, may heal in or produce choroiditic foci. Wounds of the conjunctiva are covered by fibrin and granulation tissue, which may grow across the surface and organize. If the palpebral and bulbar conjunctiva are affected simultaneously in opposing areas, symblepharon arises, firmly attaching the lid to the globe. If lymph vessels are cut off, lymph cysts are formed. Healed in foreign bodies are surrounded by a cellular connective tissue capsule, or produce epithelial cysts by epithelial implantation, or cause foreign body granulomas, e.g., caterpillar hairs.

A perforating injury in a cut causes severe damage in all parts of the eye, especially if foreign bodies enter and remain in the eye. The ocular tissues show pathologic changes caused by the injury itself, followed by regeneration and scar. But not infrequently, complications set in (infection and glaucoma). Foreign bodies damage mostly by chemical alteration.

The perforated cornea shows hydropic swelling at the lips of the wound which roll in, are separated or override. In other cases, sclera and conjunctiva are perforated. Iris may prolapse into the wound. The lens becomes cataractous by injury of the

capsule and luxates if the zonule is broken. The ciliary body may prolapse or be detached and it may bleed from it into the chambers and vitreous body. The vitreous body may be detached or prolapse and also the retina and choroid. Sometimes a double perforation is seen, one in the anterior and the other in the posterior segment of the bulb. Corneal and scleral wounds often heal without prolapse of intra-ocular tissue, the cornea by proliferation of fixed cells and regeneration of lamellar tissue by these cells, the sclera by proliferation of fine fibrillar tissue from the episclera and the choroid. But if the wound margins of the sclera override, buds of cellular and vascular connective tissue proliferate into the vitreous body. Iris, lens, ciliary body and vitreous body prolapsing into a corneal wound can unite with the corneal tissue. Fistulae and cysts are formed if the surface epithelium or lens are incarcerated in the wound. Ciliary body, choroid and retina may be incarcerated in a wound of the sclera uniting with its tissue. Fistulae and cysts can also be formed in the sclera.

Defects of the iris do not heal and the wound remains dehiscent. But sometimes endothelium and pigment epithelium proliferate and even an iridodialysis may close.

Wounds of the ciliary body are covered with fibrin which is substituted by connective tissue. In large, dehiscent wounds, dense shrinking connective tissue scars appear, causing atrophy of the ciliary body and, furthermore, atrophy of the bulb.

Wounds of the vitreous body remain open and are lined by condensed vitreous substance. If much of the vitreous body is lost, it shrinks, becomes dense and detached. Then cells proliferate into the cavity from the ciliary body and retina. Connective tissue, glia and vessels proliferate in case of hemorrhages into the vitreous.

Wounds of the lens capsule are usually dehiscent and the margins are curled up. Aqueous humor enters the lens and causes cataractous disintegration and resorption of the lens substance. Occasionally, the capsule defect is covered with blood and iris, fibrin is poured out, the capsular epithelium proliferates over the defect, pigmented cells from the iris grow in, and also lymphocytes and polymorphonuclear cells enter.

A severed retina does not unite, but the edges of the wound may stay attached to the choroid.

Serous iritis, suppuration of the tissues and the chambers, sympathetic ophthalmia and secondary glaucoma are seen as complications of cutting injuries.

In serous iritis, the posterior surface of the cornea is covered with precipitates consisting of lymphocytes and monocytes. The iris and the ciliary body are infiltrated with lymphocytes diffusely or in circumscribed nodules. Lymphocytes may also appear in the chamber angle, Schlemm's canal and anterior ciliary vessels and the retina show periphlebitis.

Suppurative inflammation is accompanied by infiltration of the corneal wound with polymorphonuclears, occasionally by a ring abscess of the cornea; polymorphonuclears and fibrin appear in the anterior chamber, iris and ciliary body. The lens may contain pus cells if the capsule has been opened. If the suppuration extends into the vitreous body, endophthalmitis exists, and, if the inflammation progresses further, panophthalmitis showing pus cells in the retina, uvea and sclera also, and extending into the orbital tissue. Depending on the intensity and extension of the acute inflammation, phthisis or atrophia bulbi is the end result. Atrophy may be restricted to the anterior segment of the eye as the cornea flattens, posterior synechiae appear and the iris thickens without formation of cyclitic membranes.

In case chronic uveitis develops, sympathetic ophthalmia may follow.

Seclusion of the pupil produces secondary glaucoma. It can also be produced by iris prolapse followed by anterior synechia.

3. Foreign Bodies

If a foreign body remains in the eye, suppuration can set in if germs adhere to the foreign body. The foreign body damages the tissue by cutting it and by chemical attack.

The infected foreign body produces a circumscribed suppuration where it is located. A foreign body enclosed in the lens may form an abscess here. From the area of the infection the suppuration may extend throughout the globe, but the irritation

may also be only minor to form a granuloma around the foreign body.

Frequently, inorganic foreign bodies remaining in the eye are dissolved by the tissue fluids and act chemically. A piece of iron in the eye has often been found to cause siderosis bulbi. Apparently, the carbon dioxide of the tissue dissolves the iron.

Ferous oxide bicarbonate is formed, from which ferric hydroxide precipitates, uniting with the albumen to ferric albuminate. The iron is deposited in the tissue most densely around the foreign body (direct siderosis), but it is also carried through the tissue fluid to distant parts of the eye (indirect siderosis). The foreign body usually is surrounded by granulation tissue. The presence of iron in the tissue can be recognized by the rusty stain, but can also be proved in smallest quantities by special stain (Perlia's Prussian blue stain). In the cornea iron is deposited in the epithelium, fixed cells, trabeculae and on the posterior surface of the cornea. In the iris, it is found in stroma cells, in the pigment epithelium, in the sphincter and dilator muscles. In the ciliary body, iron enters the epithelium and the inner surface of the ciliary muscle. It is found in the capsular epithelium of the lens. The vitreous body becomes dense, shows membranes and may be detached. The supporting cells of the retina are filled with iron and the nervous elements degenerate. The pigment epithelium contains iron and proliferates, and pigment enters the retina. Iron is found in all parts of the choroid, except the choriocapillaris.

If a piece of copper is in the eye, it is usually surrounded by polymorphonuclears and later by granulation tissue. Copper is deposited in the cornea, between Descemet's membrane and the endothelium, also in the epithelium and fix cells. It appears in different parts of the uvea. In the lens, it is found in the epithelium and between the lens fibers. In the retina, nervous elements become necrotic, the supporting tissue proliferates and blood-filled cysts may be present. The pigment epithelium proliferates and pigment migrates. The papilla is swollen and infiltrated and in sequence the optic nerve atrophies. Copper also can be proved by a special staining method. (Potassium ferrocyanide and acetic acid form brown copper ferrocyanide.)

Quicksilver produces fibrinous suppurative inflammation and may be encapsulated in connective tissue. Lead particles are surrounded by abscess or granulation tissue, containing fibrous tissue and giant cells. Glass and stone particles may heal in without irritation if they are not infected or produce hemorrhages. Only in the retina do pigment cells collect around them, supporting tissue proliferates and nervous elements degenerate.

Organic foreign bodies such as wood, parts of plants, cilia and bone particles, produce, if they are not infected, foreign body granulomas containing many lymphocytes, epithelioids, connective tissue and giant cells which surround the foreign bodies closely.

4. Injuries Due to Agents of Physical Energy

The eye may be injured by physical energy such as cold, heat and electricity; the damage is seen clinically and experimentally, but no histologic examinations have been made. However, there are examinations of eyes injured by radiational energy (sun, infra-red and x-rays).

Sunlight produces hyperemia of retina and choroid, rods and cones adhere to the pigment epithelium and the outer plexiform layer and the papilla appear edematous.

Infra-red rays apparently produce the heat lamellae of the lens in which the surface layers of the lens capsule break off.

Radium and x-rays cause desquamation of the epithelium of conjunctiva and cornea; frequently only islands of cells with clumped and disintegrated nuclei remain. The limbus is infiltrated with plasma cells; the corneal parenchyma shows alteration of its cells. Stroma cells and pigment epithelium of the iris degenerate, the latter with formation of vacuoles, and lymphocytic infiltration and newly formed capillaries appear. The ganglion cells of the retina swell, contain vacuoles, small granules and globules and the nuclei shrink, disintegrate and show chromatolysis. Also, glia cells are vacuolated and their nuclei disintegrate; their fibrils clump and break up in particles and granules. The endothelial cells of the vessels are vacuolated. Human fetuses exposed intra-uterine to x-rays show hydropic

swelling of lens fibers and disintegration of epithelial cells of the lens and rosette formations in the retina.

5. Injuries by Chemicals

If chemicals injure the eye, (a) primary burn appears with coagulation and liquefaction of the protein, and local increase of temperature, (b) infiammatory changes as reaction, and (c) regeneration as scar formation follows. Injuries by acids, alkalis, lime, metals, organic compounds and gases are observed.

Acids entering cornea and conjunctiva produce swelling and disintegration of the epithelium, disappearance of Bowman's membrane, coagulation of corneal lamellae, necrosis with subsequent formation of ulcers, and endothelial cells show balloon degeneration. Blood appears in the anterior chamber from hyperemic iris vessels. The lens epithelium is affected. The damage of cornea and conjunctiva can be followed by symblepharon and pseudopterygium.

Alkalis entering conjunctiva and cornea produce necrosis, disappearance of Bowman's membrane, ingrowth of newly-formed vessels and hemorrhages, accumulation of polymorphonuclears in cornea and anterior chamber and disintegration of the endothelium. The iris is infiltrated with polymorphonuclears and lymphocytes and the pigment epithelium is destroyed; cataract sets in. In the chamber angle and on the posterior surface of the cornea, connective tissue may be deposited. Hemorrhages may appear in the inner layers of the retina.

Lime burns are frequent. Calcium apparently forms with the protein a compound from which it can no longer be dissolved. The conjunctiva becomes necrotic, the corneal epithelium disintegrates and Bowman's membrane is destroyed, corneal lamellae swell and disintegrate and lymphocytic infiltrates appear; corneal scars are formed and vessels grow in. The chamber angle often obliterates and the intra-ocular tension increases. Circumscribed necroses are seen in the sclera. The iris is infiltrated with lymphocytes. Occasionally periphlebitis of the retina and papillitis is seen.

Metals are resorbed by the conjunctiva and cornea, if they are instilled into the conjunctival sac, but they may be deposited

also in the deep tissues of the eye if they are resorbed during occupation or medication and they may enter the interior of the eye as perforating foreign bodies. Most of the cases are only examined clinically or the pathology is studied in animal experiments. The metals affecting the eye are iron, copper, quicksilver, lead, zinc, magnesium, chromium. Some are deposited in crystals or amorphous granules in the tissues, some produce ulcers of the cornea, vascular alterations and injure the nervous substance.

A number of organic compounds of daily use and taken as medication may damage the eye externally and intrinsically. Most injuries are studied clinically and occasionally in animal experiments. Injuries are seen by indelible pencil, alcohol, chloroform, creosote, lysol, aniline, formaline, naphthalene, animal and plant poison as venom poison and tobacco.

Gases may burn locally or damage by inhalation, especially the nervous substance. These injuries are studied clinically and in animal experiments. Carbonmonoxide, sulfur hydrogene, carbon-sulfate and fumes of various origin are found as damaging causes. Histologic examinations have been made of eyes injured by poison gas. It may produce circumscribed necrosis of the conjunctiva and tarsus, perforation of the cornea due to necrosis of the parenchyma with desquamation of the epithelium, pyknosis, and disintegration of the lamellae. The limbus is densely infiltrated with lymphocytes and vessels enter the corneal remains from all sides. Uveal vessels may thrombose and the retina show edema and disintegration. The thrombosis may extend into the orbit.

READING OF SOURCE MATERIAL

Magnus observed dacryops after severing of the efferent ducts of the tear gland and formation of fistula (dacryops fistulosus).

Injured efferent ducts of the tear gland obliterate and the gland undergoes fibrous degeneration, according to Wiedersheim.

Zeidler describes a case of extensive melanosis of the conjunctiva following a superficial gun-shot injury.

Klein finds as chronic post-traumatic syndromes leading to enucleation, nonspecific infiltrating iridocyclitis, chronic septic endophthalmitis, epithelial implants, chronic hemophthalmos, extensive contusion necrosis, late

toxic iritis after detachment of the retina of long standing, endogenous iridocyclitis and sympathetic ophthalmia.

Rones and Wilder report nonperforating eye injuries in soldiers leading to a great variety of pathologic changes and find chronic endophthalmitis as the most frequent event.

Ascher finds hemorrhages into the posterior chamber in contusion of the eye.

D'Amico observes occasionally homogeneous gelatinous albuminous and fibrinous transudate in the anterior chamber of perforated eyes. The transudate is poured out from paralytic vessels of iris and ciliary body and is called pseudoluxation of the lens.

Caspar, Gifford, Jaensch, Soudakoff report xanthomatosis bulbi in injured eyes; Shapira reports steatosis bulbi.

Rohrschneider found in an injured eye freely floating cholesterol crystals in the chambers and in the vitreous and fatty deposits in retina and choroid, originating from old vitreous hemorrhages.

Velhagen found in an atrophic bulbus following injury cell shadows in the vitreous and deeply staining masses of radiating rods which he considers as crystallinic structures.

Lamb describes a case of iridodialysis from contusion with a tear reaching far into the ciliary body.

Radnot found in an injured eye the luxated lens adherent to the detached retina.

Histologic findings in commotio retinae 48 hours after the accident is reported by Roscin.

Osterberg found in a case of acute traumatic chorio-retinitis (Siegrist) histologically thickening of the adventitia and media of the ciliary vessels accompanied by a low-grade infiltration, complete degeneration of the retina into a glial membrane, disintegration of the pigment epithelium, ruptures in Bruch's membrane, absence of the choriocapillaris and sclerosis of the large choroidal vessels. He considers hemorrhages as cause of the changes.

Reis saw a case of rupture of the sclera and cornea with folding of the latter.

Scharizer observed in an eye with rupture of the sclera also ruptures of the central retinal artery and vein; the blood eroded a cavity of the type of an arterio-venous aneurysm.

Schaefer describes an atypical indirect equatorial rupture of the sclera caused by a cow-horn; further, Casanovas reports atypical ruptures of the sclera.

Michail, Velhagen report traumatic intrascleral cysts.

Abramowicz reports traumatic corneo-scleral cysts extending into the anterior chamber, lined with corneal epithelium.

Balacco saw an epithelial papilloma of the anterior chamber, ingrowing through a small perforation of the cornea.

Tooker describes epithelial implantation cysts of the posterior chamber following injury.

In D'Amico's case of subconjunctival luxation of the lens, the latter was free of the capsule and cataractous and the uvea was inflamed.

D'Amico found in a case of subconjunctival luxation of the lens the latter softened and resorbed leaving a space communicating with the anterior chamber.

Nista examined histologically eyes with pyramidal cataract after perforation.

Michail, Pitsch report ossification of the lens due to proliferating cyclitic membranes, and Herrenschwand reports ossification of the globe after injury.

Miceli describes ruptures and hemorrhages in the optic nerve sheaths with compression of the nerves in fracture of the base of the skull.

Jaensch found bilateral hematoma of the optic nerve sheaths following injury of the cavernous sinus.

Pallin found in a 21 year old man with head injury without fracture, intracranial hemorrhages and subdural and subarachnoidal hemorrhages of the optic nerve, hemorrhages in the perichoroidal spaces, choroid, subretinal space, retina and in front of the retina and papilla. Retinal and choroidal vessels show defects from which it had bled.

Urbanek describes histologic findings of fatty embolies of the eye in the central vessels of the optic nerve, in capillaries of the retina and in the choriocapillaris and orbital vessel, in three cases with multiple bone fractures.

Poos reports a knife injury of the limbus with luxation of the lens and detachment of the retina at the ora serrata.

Mansilla found extensive hemorrhage covering the iris, ciliary body and vitreous following an injury by a twig.

Gourfein reports an epibulbar papilloma in an eye with leukoma corneae appearing 40 years after an injury.

Kosena finds frequently in injured eyes transitional forms of sympathetic ophthalmia and septic endophthalmitis.

Reese and Khorazo report a case of endophthalmitis due to B. subtilis following injury.

Michaelson and Kraus saw in war injuries of the eye proliferating choroidal tissue projecting into the vitreous through a gap in the overlying retina.

Rocco found in an injured eye a foreign body of the form of a protective cap of a tape measure.

Hamilton observed bacillus Welchii infection in cases of intra-ocular foreign bodies.

Gsell and Gsell report a corneal abscess caused by a foreign body followed by perforation of Descemet's membrane and beginning endophthalmitis.

Fejer describes abscess around a ferric foreign body in the eye.

Finnoff describes traumatic cyclodialysis in an eye with intra-ocular foreign body and siderosis.

Jess, Lamb, Mayou Pusey, Paulo Filho, Sebas and Giardulli report siderosis bulbi.

Kranz finds in siderosis corneae mainly the basal cells of the epithelium filled with iron.

Narog found in a siderotic cataract small yellowish granules containing iron.

Loewenstein and Foster describe in an eye with siderosis exudate in the retina containing much iron and an avascular bandlike formation on its outer surface which they call posterior degenerative pannus.

Guist reports a case of xenogenous siderosis bulbi and finds depositions of iron in the uninjured retina and choroid and sclera where it is carried through the intact retina.

According to D'Amico, only exogenous siderosis exist. Iron ions coagulate cytoplasm particles and thus form siderin pigment. He sees in this process the tendency of the tissue to transform the highly poisonous iron ion in a more complex less poisonous product. The heaviest damage appears when iron is located in the ciliary body, as it is fastest dissolved here. Siderin is distributed by the tissue fluid and can cause death of cells. The nervous elements of the retina are the most affected.

Clausen, Coppez, Jess, Weiss find in chalcosis copper in the cornea, in a thin layer between the lens capsule and the epithelium, in and between lens fibers, on the posterior capsule, on the zonule fibers, in the retina and in the tissues in the vicinity of the foreign body. All tissues show inflammatory changes.

Hertel reports a vitreous abscess due to a piece of lead and a foreign body granuloma around a wood splint.

Hertel reports lead in the eye producing an uveitis resembling sympathetic ophthalmia.

Berger found a foreign body tubercle around a stone spicule at the limbus. It contained fibroblasts, monocytes and hyaline degenerated vessels.

Gredsted finds in the nodules of the conjunctiva caused by plant hair, infiltration of lymphocytes, plasma cells, polymorphonuclears, fibroblasts and giant cells around the hairs.

Velhagen saw inclusions of plant cells appearing as hexagonal cells containing pigment granules in the cornea of an eye injured by wood. The plant cells were surrounded by a membrane containing giant cells; the eye showed endophthalmitis.

O'Brien found a cilium in the vitreous surrounded by giant cells four days after the injury; an eyelash in the eye can produce a cyst (Bonnet and Paufique).

Exfoliation of the zonule lamella in glass-blowers is examined anatomically by Busacca, Riedl, Schnyder, Vogt.

Hoffman finds after injury by x-rays narrowing of the arteries and dilatation of the veins and capillaries in retina and choroid, cystic degeneration of the retina, chromatolysis and vacuolization of its ganglion cells and destruction of nuclei and cells.

Grzedzielski finds in x-ray cataract in man degeneration of the epithelium of the lens capsule, swelling of lens fibers at the equator and formation of vacuoles.

Schlaegel examined eyes of atomic-bomb casualties and finds the epithelium of the cornea desquamated and vacuoles in the cortex of the lens as sequelae of the radiation, and serous, suppurative inflammation in the uvea and nodular infiltration of the retina due to systemic disturbances and invasion of bacilli into the eye.

Hertel reports acid and alkali burn of the eye.

Alagna found in hydrocyanic acid intoxication atrophy and degeneration of the retina and the optic nerve.

Kiss finds after ammonia burn the iris diminished to a small membrane consisting of amorphous masses and narrow spaces, the anterior chamber

filled with connective tissue, the lens capsule folded and lens fibers disintegrated to amorphous masses.

Hertel finds histologically after injury of the eye with ammonia, swelling and atrophy of iris and ciliary body.

van der Hoeve found severe uveitis with hypopyon due to burn with carbid.

Purtscher describes in a case of lime burn crystallinic deposits between the corneal lamellae. He considers them as organic calcium compounds.

Hollum found in a case of arsenic poisoning the corneal epithelium irregular, Bowman's membrane completely destroyed and the anterior cornea replaced by a vascular fibrous tissue.

Iritzer-Braun found in an injury of the orbit with an indelible pencil necrosis of the tissue, and could extract from the tissue a substance having a spectrum similar to methyl-violet.

Herrenschwand describes histologic changes following a wasp sting. The cornea showed absence of the epithelium and Bowman's membrane, its lamellae were necrotic and showed abscess formation and polymorphonuclears and fibrin filled the anterior chamber; the eye also showed depigmentation of the iris, vacuolization and karyolysis of the pigmentary epithelium and proliferation of the lens epithelium.

Yoshida found vacuolization and hyaline degeneration of the sphincter following a wasp sting of the eye.

Lundsgaard reports a bee sting in the region of the ciliary body leading to nearly total depigmentation of the ciliary body.

Histologic examination of eyes injured by war gases are reported by Jess.

Mustard gas burns show, according to Uhde, histologically the epithelium of the cornea destroyed, Bowman's membrane wrinkled, edema and cellular infiltration of the stroma, formation of fibrous scars and the endothelium detached from Descemet's membrane.

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Chapter XX

SURGERY AND ITS COMPLICATIONS

Eyes and their adnexa are rarely examined after successful operations unless death occurs accidentally a short time after surgery. Eyes are sometimes removed and examined histologically after operations if they have become blind through complications, are painful or the fellow eye is in danger. Complications often produce changes of the eye which are similar to those arising spontaneously in local or generalized disease, or which appear after perforating injury of the eye.

Eyes are examined after cataract operation, operation for glaucoma, detachment of the retina, evisceration, removal of intra-ocular foreign bodies, and after optico-ciliary resection. Complications appear and are histologically examined after cataract operations and capsulotomy, after operation for glaucoma, for detachment of the retina, evisceration, removal of intra-ocular foreign bodies, after optico-ciliary resection, muscle operations, and tear sac operations.

1. Cataract Extractions

The picture seen in eyes after cataract surgery varies considerably, depending on the type of cataract and the operation performed. After extraction of a noncomplicated cataract, the corneal epithelium is often irregular; it may be edematous with formation of vesicles and erosion may appear; Bowman's and Descemet's membrane are folded. The posterior corneal lamellae and Descemet's membrane are folded perpendicular to the section (keratitis striata). There is a linear, oblique scar starting close to the ending of Descemet's membrane on the posterior surface of the cornea, traversing inwardly the lamellae of the cornea, and outwardly the sclera and the limbal tissue. The wound heals by primary intention. Depending on the procedure, there is either a small peripheral hole in the iris, a

peripheral coloboma or a complete iris coloboma. After intracapsular extraction, the pupillary aperture is filled by vitreous and the anterior border layer of the vitreous often protrudes into the anterior chamber, sometimes hernia-like. After extracapsular extraction, there is aftercataract of various extent. Soft cataractous masses may be found in the anterior chamber and on the posterior surface of the cornea; behind the pupillary opening there may be the more or less empty sac of the capsule which encloses, at the equator usually, a greater amount of cataractous substance known as Soemmering's ring. After extraction of a complicated cataract, there are additional changes of the eye representing the ocular disease causing the cataract, as iridocyclitis, choroiditis, retinitis, detachment of the retina or glaucoma.

Complications may arise during or after any type of cataract operation, intracapsular or extracapsular extraction, discission of a soft cataract, or following linear extraction. They are frequent during and after surgery upon a complicated cataract. Complications arising during cataract extraction are: (1) intralamellar section; (2) iridodialysis; (3) prolapse of the vitreous body; (4) expulsive hemorrhage; and (5) luxation of the cataract. They may appear during the operation and destroy the eye immediately, or may become noticeable in the course of time through their sequelae. Complications arising after cataract surgery are: (1) extensive hemorrhage in the anterior chamber, vitreous and ocular tissues; (2) dehiscence of the wound; (3) incarceration and prolapse of the iris in the wound; (4) incarceration of the lens capsule in the wound; (5) prolapse of the vitreous; (6) iridocyclitis; (7) sympathetic ophthalmia; (8) endophthalmitis phacoanaphylactica; (9) infectious endophthalmitis and panophthalmitis; (10) ingrowth of epithelium; and (11) detachment of retina. A large number of these changes cause secondary glaucoma. Detachment of the choroid is common and temporary, but as it is usually of no consequence it must not be considered as a complication. Sometimes there is a longer lasting hypotony without other disturbances. If the operated globe remains soft a long time for any cause, papilledema sometimes appears.

As a complication during the operation, one may have a section that is intralamellar; that is, the anterior chamber is not opened and the section remains exclusively in the cornea. It can happen that the iris is torn away from the ciliary body to varying extent (traumatic iridodialysis). Vitreous may prolapse through the wound and may spread over the surface of the globe; it is seen as a condensed strand extending into the wound after it is healed. Bleeding may occur into the chambers or other parts of the eye; most severe and fatal for the eye is what is known as an expulsive hemorrhage. If the intra-ocular pressure is high and the vessel walls are degenerated, the sudden drop of the tension when the eye is opened produces the severe hemorrhage which fills and dilates the suprachoroidal spaces. The bleeding is often from a long ciliary artery, the long ciliary nerve is pushed aside and the hemorrhage usually extends into the anterior segment of the eye. Choroid and retina are displaced toward the center of the eye by the blood. Such a hemorrhage may still encapsulate and organize. But usually the hemorrhage continues and pushes the contents of the eye—cataractous lens, iris, ciliary body, vitreous body, retina and choroid—through the wound and out of the eye. If the eye is not enucleated or eviscerated, a phthisic stump results. Occasionally, especially if the section is too small, the cataract may be luxated into the vitreous body; this may happen in extra- as well as in intracapsular extraction. A cataract, if luxated in the capsule, may float in the vitreous body or adhere to the ciliary body and retina, and be tolerated a long time, although it may ultimately lead to retinochoroiditis and secondary glaucoma. A cataract luxated without its capsule acts as a foreign body and becomes surrounded by polymorphonuclears, lymphocytes, giant cells and granulation tissue.

Complications after cataract surgery are numerous and depend on the type of cataract and the operation. Cataract in diabetes, iridocyclitis or glaucoma frequently lead to complications, Extraction of the lens in high myopia is often followed by complications, especially detachment of the retina. Some complications even start during the operation itself, as, for example, the incarceration of iris in the wound; but many appear after some

lapse of time. Hemorrhages from vessels which are cut during the operation appear five to six days later. The anterior chamber can be entirely filled with blood. If this is not resorbed, blood staining of the cornea may follow or organizing tissue be formed in the anterior chamber. Less frequently, hemorrhages appear in the posterior chamber, vitreous body, retina or choroid. Sometimes the wound is dehiscent and filled with fibrin through

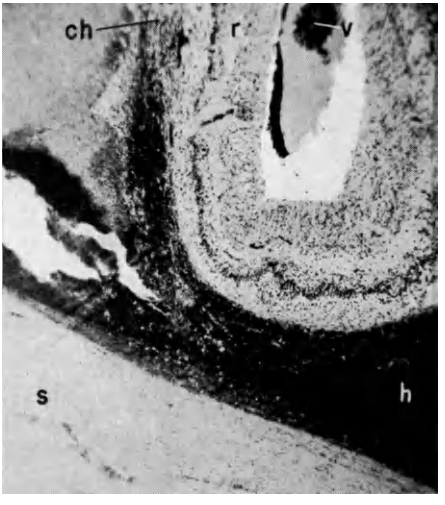

FIG. 66.—EXPULSIVE HEMORRHAGE. ch, detached choroid; h, suprachoroidal hemorrhage; r, detached retina; s, sclera; v, vitreous body. 50×.

which intra-ocular fluid may seep out, and this is only slowly and incompletely organized. The result is a high astigmatism of the cornea. Fibrous strands may extend from the dehiscent wound of the cornea onto the iris. The outer aspect of the wound may close, but its inner lips may stay open a long time. However, the most frequent complicating incident is the incarceration of iris in the wound and iris prolapse. The iris turns into the wound and its anterior surface grows to the cornea after forming granulations which organize. Iris prolapse exists in various degrees. The prolapsed iris is covered with fibrin, forming granulations which organize and form lamellar tissue covered by epithelium. The inner surface of the iris prolapse is often

lined by vitreous. Secondary glaucoma often develops as a sequel. Lens capsule can lie rolled up in the wound and prevent its closure; it is surrounded by lymphocytes and granulations. The vitreous may be prolapsed into the wound and become a dense fibrous strand or it may extend through the pupil into the anterior chamber, which may be entirely filled with vitreous. In both cases, secondary glaucoma can supervene: in the former case by blocking of the chamber angle; in the latter case by obstruction of the pupil and formation of an iris bombée in which the iris is pressed peripherally against the cornea and the chamber angle is closed. Chronic iridocyclitis occurs in different degrees. If posterior synechiae to the lens capsule are formed, secondary glaucoma may eventually be caused by seclusion of the pupil. Cyclitic strands may form. Sympathetic ophthalmia may develop with all its characteristic features; it is more frequent if the iris or lens capsule is incarcerated in the wound. If soft lens material remains after extracapsular extraction or after discission of a soft cataract in the eye, this may become inflamed. The soft lens masses may become attached to the posterior surface of the cornea, lie on the trabeculae in the chamber angle and raise the tension by mechanical obliteration of the exit; they may fill the pupil and be enclosed in the sac of the capsule. The irritation of the protein substance which is dissolved produces inflammation of the uvea which takes a severe form if the eye is sensitized to lens substance. This is especially the case if the lens of the other eye has been previously opened. The iris and ciliary body and eventually also the choroid are densely infiltrated with lymphocytes. Some feel this inflammation has an allergic nature, but others consider it to be purely toxic. As in postoperative iridocyclitis, sympathetic ophthalmia and endophthalmitis phacoanaphylactica, the infiltration of the uvea preponderates and the exudation is minimal; the infiltrating cells are mainly lymphocytes and the posterior surface of the cornea is covered with small precipitates. In bacterial infection of the chamber, endophthalmitis sets in and is characterized by exudation of polymorphonuclears and fibrin from the uvea into the anterior and posterior chambers and perhaps also into the capsule sac and from uvea and retina

into the vitreous body. As the inflammation progresses, panophthalmitis follows and the end is phthisis bulbi. The endophthalmitis is usually caused by infection from the conjunctiva and through the wound, but it may be caused also by metastatic foci from the body (for instance from infected roots of teeth). As a sequel to the ingrowth of epithelium, the wound is lined by stratified squamous epithelium and intracorneal cysts, or corneal fistula may exist. The epithelium, containing goblet cells, proliferates further into the anterior chamber and covers

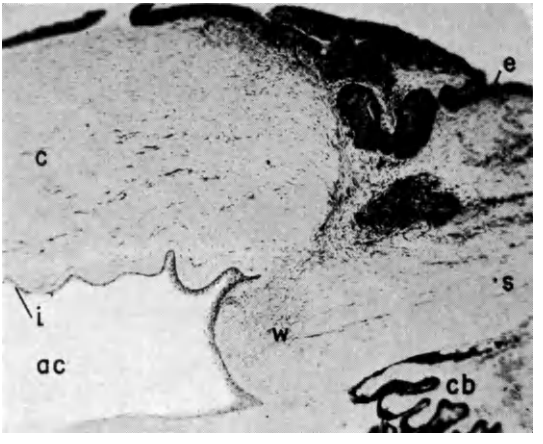

FIG. 67.—INGROWTH OF EPITHELIUM INTO THE ANTERIOR CHAMBER. ac, anterior chamber; c, cornea; cb, ciliary body; e, epithelium; i, ingrowing stratified epithelium; s, sclera; w, wound. 50×.

and replaces the endothelium; lines the chamber angle; grows across the iris, secondary cataract, fibrous connective tissue which forms on the iris, remains of the cataract, and across the pupil. Eventually, chamber cysts are formed and as the intra-ocular fluid has no egress, secondary glaucoma supervenes. Detachment of the retina occurs in some cases after extracapsular or intracapsular extraction and after discission of soft cataract, but usually in myopes and after loss of vitreous. Probably besides the changes in the vitreous, also cyclitic strands are responsible for the detachment.

It might be mentioned that after irrigating the anterior chamber with irritating fluids, corneal lamellae swell and may disintegrate so that lasting opacities are formed. Corneal ulcers, usually marginal, caused by infection from the conjunctiva are transient.

2. Needling

Following discission of an aftercataract (capsulotomy) complications may appear, as iridocyclitis, prolapse of the vitreous, endophthalmitis, hemorrhage or retinal detachment. Traction on the ciliary processes during needling produces iridocyclitis and the ciliary body is filled with lymphocytes and fibrinous exudate. The vitreous body may extend into the wound or prolapse into the anterior chamber. In case of iridocyclitis and prolapse of the vitreous, secondary glaucoma may follow. Infection may lead to endophthalmitis. If the secondary membrane is very vascular, bleeding may occur from the vessels and the organization of the hemorrhage by dense connective tissue may make the discission futile, or may cause increased tension. The retina can be torn off by pulling upon the secondary membrane. But, also, the prolapsed vitreous may form dense membranes and cause, by their contraction, detachment of the retina.

3. Glaucoma Operations

Surgical procedures for glaucoma are numerous. Most employed are iridectomy, sclerotomy, corneo-scleral trephining (Elliot), sclerectomy (Lagrange), iridencleisis (Holth), cyclodialysis (Heine) and trabeculotomy (Barkan). There are many modifications as well as combinations of these operations.

In iridectomy, the iris is often torn off at its root with result that the anterior surface of the ciliary body lies free, in case there is no anterior peripheral synechia, or the iris just lies on the trabeculae without adhering to them. In case the iris and trabeculae are firmly united, then the iris is cut off and the stump remains attached to the posterior surface of the cornea. The stump does not show any proliferation or scarification like the pillars of the iris. The usually atrophic iris shows some lymphocytic infiltration and proliferation of tissue at the pupillary

margin, forming posterior synechiae. If the corneal section goes obliquely through the limbus it is done with a knife or keratom; it goes perpendicularly through episclera and sclera if done as an incision ab externo. It is more likely that in the latter case the iris is separated at its base. The iridectomy is apparently most efficient if the peripheral synechiae are loosened. But the free wound surface of the iris, with opening of its interstitial spaces, often seem to suffice to absorb the intra-ocular fluid and to remove it. Sclerotomy is performed as anterior or posterior sclerotomy. In anterior sclerotomy, there is an oblique linear wound through the limbus; in favorable course, the trabeculae of the chamber angle are also incised simultaneously. In posterior sclerotomy the lamellae of the sclera are separated by the perpendicular section which continues through choroid and retina into the vitreous. The slit usually remains open for a very long time and filters into the episclera underneath the conjunctiva, probably by incarceration of vitreous. In sclerectomy, a small corneo-scleral piece at the limbus is resected and here there remains a gap, usually with oblique somewhat irregular walls. There is some tendency to close by outgrowth and new formation of lamellar tissue. The borders of the gap are anteriorly and centrally the cornea where Bowman's membrane ends and peripherally the sclera; posteriorly and centrally the borders are the cornea (Descemet's membrane and endothelium of which are sectioned), and peripherally the sclera and the ciliary body. Over the gap there is a subconjunctival filtering scar. Its tissue is loose, or consists of a meshwork of fine fibrils, few cells and empty communicating spaces. The tissue appears myxomatous and many fibrils are swollen. Further, there is an iridectomy and the iris is usually cut at its root. Corneo-scleral trephining gives a similar picture except that the margins of the gap in the sclera are usually parallel, perpendicular and regular.

In iridencleisis and its related iridotasis, the oblique wound through the limbus is dehiscent, goes through limbus, sclera and cornea and is lined by the everted iris. The iris is attached to the chamber angle and the posterior surface of the cornea and bends around the margin of the section of the cornea into the

conjunctival wound. It grows to the peripheral wall of the corneal section. The pigment epithelium if turned anteriorly faces the central wall of the filtering canal and has no tendency to unite with the mesoderm of the cornea; in the opposite, it frequently proliferates subconjunctivally and even onto the opposite side. The overlying tissue shows the loose myxomatous tissue of the filtering scar. If, in iridencleisis, a complete iridectomy is done or only a basal piece of the iris is excised, there is either a small complete iris coloboma, or the coloboma is only peripheral as in iridotasis, in which case a central piece of the iris remains with the sphincter intact and a normally situated pupil. In cyclodialysis, the ciliary muscle is separated from the scleral spur and trabeculae from the ciliary body. The anterior chamber then communicates with the suprachoroidal space between the sclera and the separated suprachoroid. Also, arteries entering into the ciliary muscle through the sclera are severed. The drainage of the aqueous into the suprachoroidal space, as well as the atrophy of the ciliary body due to severing of the blood supply is said to cause the decrease in the tension. In trabeculotomy the corneo-scleral trabeculae are incised and Schlemm's canal thus communicates with the anterior chamber.

Complications during and after glaucoma surgery vary, depending upon the type of operation. Some operations have complications more often, others hardly at all. Unfortunately, the operations with less complications are not always the more successful, as related to their lasting effectiveness in lowering the tension. The complications are (aside from technical errors like faulty section, iridodialysis, tearing of the conjunctival flap): (1) inflammations, (2) early and late infections, (3) dehiscence of the wound, (4) inclusion of the iris and ciliary body, (5) hemorrhage, (6) cataract formation, and (7) luxation of the lens. Iridocyclitis of low degree with formation of posterior synechiae is frequently seen. Sometimes there is a fibrinous exudation because of venous stasis. In secondary glaucoma in which there are already inflammatory changes, the inflammation may flare up and this might have severe sequelae such as formation of pupillary membrane, cataract, detachment

of the retina through a cyclitic membrane and finally may cause sympathetic ophthalmia.

Exogenous infection causes endophthalmitis. The infection may be introduced during the operation or later from an infected conjunctival sac, especially when the wound is dehiscent. Metastatic infections from a distant focus are infrequent. Late infections may appear in fistula-forming operations. In infection of the conjunctival sac, bacteria may enter through the thin, cystic conjunctiva into the fistula and into the anterior chamber, producing suppuration in the chambers and even in the vitreous body. The wound may stay open after iridectomy and be ectatic. It may remain open after the surgery or the closed wound may burst, especially if the pressure in the vitreous increases; the dehiscence of the wound may also be the result of incarceration of iris and especially of the ciliary body. Sometimes there is an iris prolapse. Frequently the chamber angle is blocked and the intra-ocular pressure increases irreparably. Especially may the incarcerated and adherent ciliary body occlude the fistula. In every event, scleral staphyloma may be the result. Hemorrhages appear in the chambers, retina and choroid. Through the sudden reduction of the high intra-ocular pressure, vessels inside the globe may burst. But the vessels may also become dilated and congested, and the hemostasis may produce, by formation of large quantities of plasmoid intra-ocular fluid, irreparable increase of the pressure (malignant glaucoma). Accumulation of much blood in the globe, in itself, increases the pressure, makes the wound burst, and, if the hemorrhage is in the suprachoroidal space, pushes the contents of the eye out through the wound (expulsive hemorrhage). In less severe cases, blood staining of the cornea may follow; organization of the blood in the chambers may be followed by xanthomatosis of the eye. Hemorrhages into the retina and especially into the macula are accompanied by severe sequela for vision. Injury to the lens capsule by instruments during the operation, as also spontaneous rupture of the capsule caused by decrease of the intra-ocular pressure, are followed by cataract formation. Subluxation and luxation of the lens

have severe sequelae for the eye. The lens may be incarcerated between the iris root and the ciliary body to block the chamber angle. Its equator may lie in the wound or the fistula and occlude them. Sometimes only the ruptured capsule lies in the wound. The sequela is incompensated glaucoma (malignant glaucoma). Detachment of the choroid is frequent and harmless and in some cases there is long-lasting hypotony.

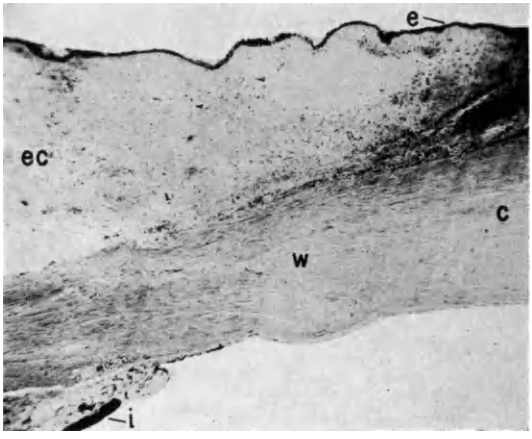

FIG. 68.—IRIDECTOMY. c, cornea; e, epithelium; ec, edematous conjunctiva; i, iris stump; w, wound. 50×.

4. OPERATIONS FOR DETACHMENT OF THE RETINA

Surgical procedures for detachment of the retina are numerous and every method used has many modifications. Complications during and after the operation are found, but not in all groups, and in some hardly any. Today the almost exclusively and universally performed operation is the closure of the retinal hole and formation of chorioretinal adhesions surrounding the tears; also much used is excision of bands of sclera with resultant shortening of the globe. Other methods like the temporary evacuation of the subretinal fluid by puncturing the sclera or permanent drainage by formation of trephine openings, or introduction of metal wires and hair into the subretinal space and formation of chorioretinal adhesions by introduction of irritating substances under the retina, are now rarely performed and have only historic interest. The closure of the retinal hole

and the formation of chorioretinal adhesions is done nowadays almost exclusively by diathermy; there is swelling hyaline degeneration and necrosis of the scleral lamellae around the puncture. The adjacent choroid shows small hemorrhages and contains fibrin and some cellular exudate of lymphocytes, plasma cells and giant cells, and histiocytes proliferate. Sometimes Bruch's membrane is broken in several places. The pigment epithelium is disintegrated. Minimal granulations proliferate in the choroid and in the subretinal space. The adjacent retina shows disintegration of rods, cones, nuclear layer; polymorphonuclears,

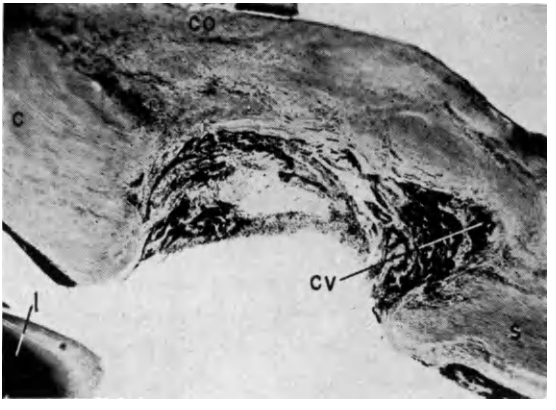

FIG. 69.—ELLIOT'S TREPHINING. c, cornea; cb, ciliary body incarcerated in the trephine hole; co, conjunctiva; l, lens; s, sclera. 50×.

monocytes and lymphocytes may lie on the inner limiting membrane. The margin of the retinal hole is attached to Bruch's membrane by fibrin and cells. In case a piece of sclera is removed, the overlying retina and choroid are folded and the lips of the sclera are kept together by tissue proliferating from the choroid and episclera. If the coagulation by diathermy is too intense, severe uveitis sets in with exudation into the vitreous; much fibrin is formed and many cells appear. If heavy coagulation is done at the ora serrata, severe cyclitis follows with the formation of a cyclitic membrane. The organization of the exudate in the vitreous and of the cyclitic membrane lead to atrophia bulbi. This complication is also responsible for the appearance of cataract. Occasionally there is heavy bleeding

from the choroid during or after the operation, if large vessels, especially the vortex veins, are injured.

During a keratoplasty, the underlying tissue, as the lens or iris, can be injured by the instruments. Iris or lens can prolapse into the wound and as the intra-ocular pressure is decreased, there can be much intra-ocular bleeding and even expulsive hemorrhage. The transplant can be lost or, under certain circumstances, it can disappear into the interior of the eye.

The transplant may be pushed out and intra-ocular tissue prolapse, and eventually a staphyloma may be formed in the further course of the disease. Iris can be incarcerated between transplant and cornea, producing granulations and causing vascularization of the transplant. The transplant can disintegrate and become opaque. Blood vessels can grow into the transplant from the surrounding cornea, also without adherence of the iris, causing opaqueness of the transplant. Intra-ocular infection is rare.

5. Evisceration of the Globe

After evisceration, there remains a scleral stump resembling that seen in phthisis bulbi. It sometimes contains uveal elements. Parts of the sclera are occasionally necrotic. The necrotic part is hardly stained and is surrounded by polymorphonuclears. Complications to be mentioned are: (1) orbital cellulitis and (2) sympathetic ophthalmia. Suppuration present in the bulb before the evisceration may continue along the optic nerve and produce meningitis or extend through the sclera, especially in panophthalmitis, into the orbit, causing thrombophlebitis in the septa. If uveal tissue remains behind, it may show typical sympathetic ophthalmia with lymphocytes, accumulations of epithelioid cells and occasional giant cells; the scleral canals are infiltrated with lymphocytes and the optic nerve may contain lymphocytic nodules. Frequently sympathetic ophthalmia has already begun by the time evisceration is done.

6. Extraction of Foreign Bodies

If an intra-ocular foreign body cannot be extracted, the fate of the eye depends upon the kind of foreign body, its location, the extent of the injury or a simultaneously existing acute sup-

purative or chronic, even sympathetic inflammation. From the extraction itself, even if it is successful, or after the extraction, complications may set in. Complications are seen more frequently, of course, if nonmagnetic foreign bodies are extracted with instruments than if magnetic foreign bodies are removed by the magnet. Severe hemorrhages may occur which imperil the eye if they are in the vitreous body. Formation of a traumatic cataract occurs if the lens is perforated by the foreign body, whether it remains in the lens or is extracted. Foreign bodies located in the posterior segment of the eye, if they injure the retina or must be extracted through the sclera, may produce retinitis proliferans, proliferating retinochoroiditis and detachment of the retina.

7. Opticociliary Resection

Opticociliary resection, which is only infrequently done, and in which the optic nerve and the surrounding ciliary nerves are severed with sometimes a part being resected, is often examined histologically, particularly to study the regeneration of nerves. The central nerve endings grow out and proliferate into the sclera. They do not always use the old nerve sheaths, but enter the sclera in small bundles. The outgrowing nerves occasionally form neurinoma.

8. Squint Operation

During and after surgery on external eye muscles, accidents are rare. The sclera may be incised, or the globe perforated by sutures; in case of infection, inflammations of the uvea are seen which may progress to circumscribed abscess, and even to panophthalmitis. Corneal ulcers and, now and then, marginal degeneration of the cornea with shallow dimples occur; these, perhaps, are the result of impaired nutrition when blood vessels are severed. Granulomas of the operated muscles frequently occur, usually as reaction to the sutures. Infection of the orbit may also occur.

9. Tear Sac Operations

In tear sac operations, either (1) a direct connection between the tear sac and nose is performed externally (according to

Toti) or internally (according to West-Polyak), or (2) the tear sac is totally extirpated. If the operation is done for chronic dacryocystitis, using the method of Toti or West-Polyak, acute inflammation may follow (dacryophlegmon). In both operations for formation of a communication with the nose, the surrounding structures can be infected, as can also the orbit and the meninges. Not rarely, in the latter case, a tear sac fistula appears. Then the mucosa of the tear sac is connected with the skin by a sinus which is lined by stratified squamous epithelium. Either inflamed mucosa, which was not removed, or inflamed ethmoidal cells, which surround the lacrimal fossa, are the cause.

READING OF SOURCE MATERIAL

Fuchs describes as unintentional injuries in cataract extractions incarceration of the iris, iridodialysis, blood on the zonule, orbicularis ciliaris, in the suprachoroidal space, in iris and ciliary body, desquamation of the iris- and ciliary epithelium, incarceration of the lens capsule, tears and dialysis of the retina and luxation of the lens into the vitreous body.

Safar describes histologically in an eye with luxation of the lens nucleus into the vitreous happening during a cataract extraction, rests of the lens nucleus in the anterior chamber surrounded by foreign body giant cells and a very vascular membrane.

Birch-Hirschfeld finds in expulsive hemorrhage severe changes in choroideal veins.

Samuels finds postoperative nonexpulsive subchoroidal hemorrhage caused by rupture of the long posterior arteries; the eyes succumb due to lack of blood supply and increased intra-ocular pressure.

Tooke describes following a cataract extraction incarceration of the iris in the wound with blockage of the chamber angle causing secondary glaucoma and choroidal and retinal detachment.

Truc and Dejean describe cases of sympathetic ophthalmia following cataract extraction.

Corrado, Damel and Aroub, Morax, Papolczy, Szekely report implantation of epithelium into the anterior chamber after cataract extraction.

Fuchs describes in an eye operated for cataract peculiar giant cells and double refracting fibers which he considers as cotton.

Payne reports microscopic findings after various glaucoma operations, as paracentesis, posterior sclerotomy, iridectomy, iridencleisis and trephining. In no case was a peripheral anterior synechia released.

Besso thinks that the decrease of the intra-ocular tension after iridectomy is due to atrophy of the ciliary body. The circumlental space becomes enlarged, the vessels of the bulb and the secretion of the aqueous humor are diminished.

Cases of cyclodialysis are examined histologically by Elschnig, Grosz, Kronfeld, Loddoni who finds the connection between chamber angle and suprachoroid patent through months.

Tooke found following an iridectomy the formation of the cyst in the wound due to incarceration of the iris stump.

Sallmann observed frequent injuries of Descemet's membrane in glaucoma surgery (iridectomy, iridencleisis and cyclodialysis).

The filtering scars after trephining are histologically examined by Holth, after iridencleisis by Gjessing, Holth, Ismet who found microscopically the hole after trephine operation blocked with inflammatory debris without proliferation of the surrounding tissue.

Dusseldorp describes herniation of the vitreous following trephining (Elliot).

Sympathetic ophthalmia appears after iridectomy (Samuels), after sclerectomy (Samuels) after Elliot's trephining (Schoenenberger), after iridencleisis (Leatherwood).

Speciale-Cirincione describes ingrowth of epithelium into the anterior chamber following glaucoma operations.

Weekers and Weekers found that the microcoagulation of the ciliary body damages the ciliary processes with the least trauma at the place where the aqueous humor is produced.

Levkojewa describes pathologic changes following Gonin operation and found the sclera circumscribed necrotic, the ciliary body atrophic, scar formation in the suprachoroid and round cell infiltration of the choroid, Bruch's membrane destroyed and the entire retina detached.

Stallard finds in an eye successfully treated by diathermy for retinal detachment buds of granulation tissue perforating Bruch's membrane and fixing the retina hooklike. Diathermy close to the ora serrata causes proliferation of fibrous tissue into the circumlental space.

Reese observed cases of cystic degeneration of the macula following successful surgery for detachment of the retina.

Potechina found in an exenterated eye a cyst lined with conjunctival epithelium.

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INDEX

Note: To avoid duplication and keep the index within a practical length, certain pathologic conditions are not indexed separately (or if so, only briefly and generally), but are fully indexed with the pertinent part of the eye under the heading "Pathology" (e.g., specific inflammations, neoplasms, etc.). *Italic* numbers in parentheses indicate figure references.

Pathology