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THE CORRELATION OF OPHTHALMIC PATHOLOGY AND THERAPEUTIC PROGRESS IN THE PAST 25 YEARS

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Submitted in Partial Fulfillment
for the
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College of Medicine
University of Nebraska
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CHAPTER I

INTRODUCTION

Vesalius was able to leave a great gift for medical science just because he had enough courage to disregard old traditions and investigate disease by doing post mortem examinations. Our present scientific progress is also based on examinations of the bodies, tissues of the diseased, of experimental animals and correlation of the proven pathology, with signs seen prior to death and therapeutic methods and agents used. Ophthalmology is just a part of the whole medicine but highly integrated with other specialties because so many pathological conditions and events in the human body leave characteristic changes in the eye visible during life, and some can be found after death. In reverse, just a few ocular conditions may leave their signs somewhere else further from intraorbital structures.

Gross and microscopic examination of the enucleated eye in ophthalmology has the same meaning as autopsy and tissue examination in general pathology. Our failures, mistakes, inevitable conditions and progress in therapeutic methods, surgical as well as pharmaceutical, are clearly reflected in the specimens which, when seen by an experienced eye reveal a great deal of information. My past experience in this particular field inspired me to look into this source of information and present gained knowledge to the general practitioner of the United States, and particularly Nebraska. I refer to the most common conditions and failures which cause the eye to become enucleated; also to point out how much can be gained by proper recognition of pathology in the doctor's office, proper administration of therapeutic aid and proper use of today's drugs

which have progressed so much in the past couple of decades.

During the past twenty-five years, in the section of Pathology of the Department of Ophthalmology, University of Nebraska College of Medicine, six hundred and seventy pathological specimens have been accumulated. This great increase in number and variety is a sign of expansion even under unsatisfactory conditions and should be accredited to the head of this particular section of the department.

Of the vast majority of the specimens submitted from the physicians doing ophthalmic surgery all over Nebraska, just a few of these are specimens of animals used for some sort of investigation. It should be noted that the majority of the cases submitted to surgery were first seen by general practitioners. There are numerous occasions where the general practitioner tried at first to treat the diseased organ and when he became lost in the complexity of developing pathologic process, turned it over to the physician specially trained in ophthalmology. There were other cases also where the destructive injuries were of such a degree and extension that it was impossible to save the eye.

The classified list (Table No. I) of pathological specimens does not reflect the actual pathology found but the final diagnosis of the conditions that resulted in the eye to be enucleated and also specimens of ocular adnexa involved by their own particular pathology or extended from the eye.

As we see from this simple list, marked by names and numerals,

TABLE NO. I

Lesions of Bulbus Oculi

Secondary glaucoma	186
Primary glaucoma	27
Congenital glaucoma	7
Traumatic perforation	68
Corneal ulcer	22
Phthisis	46
Panophthalmitis	11
Sympathetic ophthalmia	5
Acute anterior uveitis	1
Post-operative expulsion hemorrhage	3
Retrolental fibroplasia	1
Toxoplasmosis	1*
Coat's disease	1
Malignant melanoma of the choroid	46
Malignant melanoma of the iris	6
Malignant melanoma of the ciliary body	5
Metastatic adenocarcinoma in the uveal tract	1
Retinoblastoma	20**
Bowen's disease	2
Ectopic lacrimal land in the eyeglobe	1
Benign melanoma of the choroid	3
Benign melanoma of the iris	1
Benign melanoma of the ciliary body	1
Intraocular neurofibroma	1
Hypertensive retinopathy	1***
Polyarteritis nodosa	1***
Papillary edema	1***

* No organism demonstrated, based upon the clinical history and x-ray findings.
** Recurrences included.
*** Autopsy specimens.

we can realize that within the past twenty-five years, many eyes were lost and the majority of them were lost only because we were not in a position to save them. Looking through this list, two major groups dominate the numbers, one is secondary glaucoma and the other is malignant tumors of the eye.

Secondary glaucoma is the major result of various complications

in a diseased eye and particularly in an inflamed one. Tumors are prone to arise from the apparently normal tissue, in an unknown manner, and even with the recent advances in medicine we are still looking for a cure. The same is true in inflamatory conditions. Discovery os new fields in different branches of science adds to our knowledge in combatting diseases, but at the same time it brings new thoughts and questions, broadening some subjects which previously appeared so simple.

TABLE NO. 2

Lesions of and from the Ocular Adnexae

Cavernous hemangioma of the orbit	1
Erythroleukemic infiltration of the conjunctiva	1
Mixed tumor of the lacrimal gland	6
Metastatic adenocarcinoma on the lid	1
Epithelial cyst of the conjunctiva	2
Granulation tissue	4
Cavernous hemangioma of the lid	1
Basal cell carcinoma of the lid	5
Squamous cell carcinoma of the lid	2
Cutaneous benign papilloma of the lid	6*
Extrabulbar intraorbital malignant melanoma	1
Xanthelasma	6
Chalasion	5
Sebaceous cyst of the lid	4

*
One case of premalignant cutaneous papilloma.

For a better understanding and realization of the progress made in medicine, I would like to go through the history of medicine, touching just the major points, primarily paying attention to the events important to ophthalmology or directly connected with it. This will help us to appreciate things that were discovered and

placed into our hands in the past quarter century and years prior to it when each simple step took hundreds of years.

CHAPTER II

EARLY HISTORY OF THERAPEUTIC PROGRESS

B. C.

2250 - Code of Hammurabi (Babylon) describes precisely the fees for eye treatment and consequences in case of unsuccessful treatment.

2000 - Writings of King Chammurapi (Egypt) mentions operations on the eye.

1500 - Ebers Papyrus (question that this dates back as far as 3400 B.C.) Dynasty, gives a fairly definite description of cataract (this one is incorrect), epiphora, trachoma and its sequellae and treatment for these conditions.

900 - Coptic Medical Papyrus has this prescription for the eyes (1).

Armenian Borax	10 Obols
White Lead	2 Obols
Pepper	1 Obol
Ginger	1 Obol
Verdrigis	2/3 Obol
Starch	2 Obols
Salammoniac	1 Obol

Pound them well, strain through a fine sieve; apply to the eyes which are dim and they will become quite clear.

460 - Hipprocrates Birth - Hipprocrates describes anatomy of the eye as being made from three membranes which were distended by ocular humors named aqueous, vitreous and crystalline; describes optic nerve but does not know its function. His theory for various conditions consists mostly of restricted diets and hot foot baths. "Blepharoxysis" is used for granulations on the lids (Trachoma) and this is done by rubbing the conjunctival surface of the lids with Milesian Wool and wound on a stick of wood. (Basically this same treatment for Trachoma survived up to the Sulfonamide period)

300 - London Papyrus describes what seems to be Trachoma and remedies for ingrowing eyelashes. They include Lizzard's Blood, Bath's Blood, clipping the lashes or pulling them out until the eyes improve.

A. D.

29 - Celsus' book, "De Medicina", reveals a somewhat different type of treatment from that previously used. He advocates Collyria of different kind for each condition known to him, (Collyria was a small bar of medicine dissolved in water or oil just before use); for mydriosis - purgation, pterygium - surgical excision, docryocystitis - complete resection of the sac which is followed by cautery. Trichiasis and distichiasis by burning out the hair

follicles with a hot needle; lagophtholmos by surgery based on contracture of the scar tissue, cataract - by couching (actually dislocating cataractous lens). He evidently does not understand what the actual opacity is or where it exists, nor does he understand the hypermetropia produced by displacing the lens.

131-201 - Galen writes "Optics", "Diagnostics of the Eye" and "Anatomy and Physiology of the Eye". He believes that eye coats are extensions of the brain, "Crystalline Body" essential for vision, hypochymata (cataracts) are formed between crystalline humor and the cornea; the lens is nourished by the vitreous body, the vitreous body is nourished by extension from the brain, making a thin coat around it, (apparently retina) and this one is nourished by a net-like membrane which he calls choroid. Next comes the sclera-tendinous sheath, which, from the description seems to be what is now called Tennon's Capsule, (first time described in the literature) and extension from the periosteum for protection of the eye, (now Conjunctiva). He uses the name "Iris", but its meaning is different. This, to our understanding, he calls "Hragoeides, (grape skin). The cornea, believed by Galen, is derived from the meningeal sheats of the brain; and the pupil, is filled with air. In physiology of the vision in his thoughts are that "Visual Rays" are initiated from the brain, go through all transparent parts of the eye towards object, then the rays reflect this same way back and are transmitted by the retina and the optic nerve back to the brain; but how all this happens is a mystery to him. Cataract treatment is performed by vigorously shaking the patient's head.

850-860-932 - Rhases discovers reaction of the pupil to the light as "In the middle of the icy humor (iris) appears a hole which now dilates and now contracts, according to how the icy humor feels the need of the light; it contracts when the light is strong, and dilates in obscurity. The hole is the pupil and the membrane is the uvea"(5: 576).

960 - Ammar starts "extraction" of the cataract with the needle entering through the sclera and aspirating liquified lens material.

965-1036 - Alhazen is the first who proves that "angle of incidence is equal to the angle of reflection, and that the perpendicular to the plane of incidence, the incident ray and the emergent ray, all lie in this same plane" (5: 578). He is also the first to teach that "visual rays pass not from the eye to the object, but from the object to the eye, and that an infinite number of rays are emitted or reflected, as the case may be, from each and every point comprised within the surface of that object" (5: 578).

1018-1087 - Constantinus Africanus invents the word "Cataracta". (Greeks used the word "Hypophyma" and Romans, "Suffusio".) He translates many Arabian Medical books into Latin.

1027 - "Ali Ben Osa, Erinnerungsbuch fur Augenärzte, aus arabischen Handschriften übersetzt und erläutert".

1313 - Alexander de Spine re-invents convex glasses with frames.

1317 - Salvino degli Armati made glasses and fitted them to the patients.

1399 - Beginning of 'Acta Facultatis Medicae Vennensis". May 6th.

1452 - 1519 - Leonardo da Vinci first compared the action of the eye to the camera obscura.

1462 - Hieronymus Brunschwyck describes removal of the magnetic metallic imbedded foreign body from the eye by means of magnet or lodestone.

1500 - Berengario da Capri for the first time describes correctly conjunctiva, proving also that conjunctiva is not an extension of periosteum.

1504 - Vesalius born. He discovers that removed crystalline lens act like convex lens.

1517 - Pope Leo X is known to have worn concave lenses for myopia.

1519 - Publication of Friesen's "Spiegl der Artzny" and "Synonima".

Felix Platter writes that received images in the eye are projected upon retina and not upon the optic disc as previously described by Leonardo da Vinci.

1550 - Hollerius prescribes spectacles for myopia.

1559 - Caspar Stromayer publishes in Sudhoff "Ophthalmic Treatise".

1560 - Franciscus Maurolycus describes myopia, hypermetropia and the optics of the lens, and also proves that Galen's doctrine of Crystalline lens, as being the most important organ for vision, is incorrect.

1564 - Eustachius discovers abducens nerve and suprarenal glands.

1575 - Pare introduces artificial eyes.

1583 - George Bartisch publishes his book "Ophthalmodouleia das Augendienst", ancestor of all modern textbooks; and is also the **1st** first to remove the eye in toto.

1584 - Sir Walter Ralpigh demonstrates curare which he brought from Guiana.

1585 - Guillemeau publishes treatise on diseases of the eye.

1590 - Invention of compound microscope by Hans and Zacharias Jansen.

1600 - Fabricius of Aquapendente demonstrates and describes correct position of the crystalline lens.

1604 - Johann Keple first demonstrates inversion of optic image on the retina.

1619 - "Oculus" by Christoph Scheiner is published.

1635 - Descartes proves that accommodation depends upon the change in form and thickness of the lens.

1644 - Descartes publishes treatise on dioptrics and reflex action.

1656 - Rolfink proves that cataract is clouding of the lens.

1662 - Meibom discovers and describes Meibomian glands.

1664 - Willis publishes his "Cerebri Anatome" in which he classifies bulbar nerves.

1689 - Leeuwenhok di covers and describes anatomy of the cornea and rods in the retina.

1697 - Pacchiomi discovers glands (Pacchioni bodies) in the dura matter.

1704 - Jean Mery observes and describes reflection from the pupil of a cat's eye submerged in water.

1705 - Michel Brisseau first performs autopsy on dead soldier who had cataract and automatically proves that cataract is an opacity in the lens itself - "Mirabile dictu" he explains in his script. All together he performs five autopsies to prove his doctrine about cataract. Maitre-Jan, co-worker of Michel Brisseau, supports very energetically ideas about his findings.

1713 - Anel for the first time probes lacrimal ducts.

1722 - St. Ives is the first who removes cataract "en masse" from the living subject by dislocating cataractous lens into Anterior Chamber and then removing it through corneoscleral incision.

1728 - Introduction of operative artificial pupil by Cheselden.

1730 - Improvement of cataract operation by Daviel.

1745 - Daviel does the cataract operation on patient by the name of Brother Felix, Hermit of Aiguille from Provence and during operation accidentally breaks the lens capsule, spilling loose cortical material into the anterior chamber. He then opens the anterior chamber and washes the loose opaque material out, (extracapsular extraction). On April 8, 1747, while operating on patient M. Garion, he meets with the difficulty of dislocating the lens, so he makes a lower corneosclera incision and removes the lens in toto (intra-capsular extraction). The section is made using lance and scissors and cornea lifted with forceps (5).

1752 - De la Faye invents corneosclerar section made by the knife.

1756 - Publication by Nicolas Audri on infraorbital neuralgia.

1773 - First professorate in ophthalmology errected in Vienna occupied by Joseph Barth under the title of "Professor der Augenheilkunde".

1780 - Benjamin Franklin invents bifocal lenses.

1786 - Description of exophthalmic goiter by Parry.

1794 - Oct. 31. Publication upon colorblindness by Dalton.

1798 - Joseph Beer invents iridectomy (Vienna) and describes it in 1805.

1801 - Publication on Astigmatism and states undulatory theory of light by Thomas Young. First ophthalmologic journal is printed by Himly and Schmidt in Braunschweig and Jena.

1804 - Royal London Ophthalmic Hospital founded. (1805?)

1816 - Beer describes luminosity of the pupil in albino and invents new term, "Amaurotic cat's eye".

1829 - Introduction of print for blind by Louis Braille.

1830 - Sir William Mackenzie first recognizes increased intraocular pressure, essential symptom of glaucoma.

1831 - Homatropin produced by Dadenburg.

1833 - Geiger and Hesse isolate atropin.

1839 - Beer observes and describes reflection seen in case of aniridia. Velpeau reintroduces ancient method of lacrimal sac extripation. Dieffenbach performs tenotomy on the living patient.

1840 - Basedow describes exophthalmic goiter and associates both conditions.

1841 - Guerin describes operation of advancement (resection), but his described procedure is not accepted because of danges involved.

1842 - Publication of treatise on Strabismus by Dieffenbach.

1842 - Nikolaus Meyer for the first time describes removal metallic intraocular foreign body from the eye applying magnet to the wound of entrance in the sclera.

1843 - Kuchler invents test chart for visual acuity. Frommuller, general practitioner, invents trial case.

1845 - Kussmaul first to explain why fundus is not visible normally and that eye's refractive power prevents it from seeing.

1846 - Cumming first observes fundus reflection in artificially dilated pupil.

1847 - Brucke (Vienna) first to observe fundus, using his own constructed instrument where he passed tube through the flame of the candle while lookin into pupillary aperture.

1851 - Hermann Helmoltz, (Konigsberg) invents ophthalmoscope and describes it in 43 paged book "Beschreibung eines Augenspiegels zur Untersuchung der Netzhaut im lebenden Auge".

1852 - Ruete reports in his work, "Der Augenspiegel und der Optometer" the indirect method of ophthalmoscopy. Rekoss publishes article "Rekoss Discs" describing the rotary discs containing lenses in Vierord's Archiv.

1853 - Epkens construets mirror with the hole in the center for ophthalmoscopy.

1854 - Jaeger publishes complete standardized test charts for visual acuity. British Medico-Surgical Review, Vol. XIV, p. 426, "Report on Ophthalmoscope" stating that Babbage, seven years prior invented ophthalmoscope; report by Thomas Wharton Jones.

1854 - Foundation of Archiv fur Ophthalmologie by von Graefe. Discovery of the function of vaso-dilatory nerves by Claude Bernard.

1855 - Von Graefe introduces iridectomy for glaucoma.

1857 - First ophthalmologic society meets first time in Brussels from September 13th to 16th. Strangely enough, this first society was not of a local character but international and was called "First International Ophthalmologic Congress".

1857 - Introduction of operation for strabismus by Von Graefe.

1859 - Discovery and analysis of spectrum published by Kirchhoff and Bunsen.

1859 - Von Graefe describes embolism observed in retinal vessels. Dixon first makes incision through all layers of eyeglebe for extraction of the intraocular foreign body with magnet.

1862 - George Critcheti in Heidelberg Congress reports safe advancement operation. Sir William Bowman introduces method and gradation of digital intraocular tonometry.

1862 - Publication of the studies on astigmatism and presbyopia by Danders.

1863 - Weber induces lacrimal probe combined with knife.

1864 - Von Mooren of Dusseldorf, introduces "preliminary iridectomy" to cataract extraction.

1865 - Isolation of eserin by Vee and Leven.

1866 - Von Graefe publishes description on sympathetic ophthalmia.

1867 - Publication treatise on physiological optics by Helmoltz.

1870 - Description by Saemisch of Serpinginous ulcer of the cornea.

1874 - McKeown first nserts tip of the magnet into the vitreous for removal of the ntraocular foreign body.

1875 - Julius Hischberg constructs first electromagnet for extraction of magnetic intraocular foreign body.

1884 - Crede introduces silver nitrate (Argentum Nitricum) installation into conjunctival sac for newborn. Cocaine used in eye surgery by Carl Koller.

1897 - Hirschberg introduces Holocain.

1900 - Gartner introduces tonometer.

1905 - Braun introduces novocain.

1906 - Barany publishes his theory on vestibular nystagmus.

1909 - Ehrlich introduces his "Kugel 609" - Salvarsan.

1911 - Gullstrand received Nobel Prize for optical research.

CHAPTER III

THERAPEUTIC AGENTS DURING PAST TWENTY-FIVE YEARS

As we looked through the pathology in the first chapter we were able to see a great variety of conditions for which the eye had to be enucleated, but taking the last twenty-five years as a whole, we would not be able to see what had been done in connection with medical progress. In order to see clearly the influence of it in certain conditions and diseases, it is necessary to divide these twenty-five years into three periods; the period before Sulfonamides became available for clinical use (1929-1937); the period when we had Sulfonamides (1938-1945); and the period when antibiotics started to reach our sick. The last period actually extends up to the present time in a modified form. Correlating the introduction of new therapeutic agents, we will be able to see which conditions were eliminated, which became more rare, and how surgery was made safer.

Today's art of healing is greatly simplified by advancements in therapeutic agents, highly specialized methods of examination and surgery. Most of the young physicians do not fully appreciate the present drugs and highly advanced technical aides in our profession, not realizing how much work, skill and ingenious thinking has been put into medical progress within the past few years. Just a quarter of a century ago very few had but a slight idea about possible developments in the treatment of the diseases. For many years since microorganisms were discovered as being the source of diseases, many different methods have been used to try to destroy them without doing any harm to the host.

The first major success in this particular field was reached

by Dr. Ehrlich, with his miraculous "Kugel No. 606" - Salvarsan, which was finally found and evaluated in 1909. This product proved to be effective against spirocheta pallida, but the toxicitity to the host meant great caution had to be used in order to avoid harm to the patient. The chemical name for Salvarsan is dioxy-diamido-arseno-benzol-dihydrochloride, which was the origin for the later drug, Neosalvarsan (in this country called Neoarsphenamine) and this proved to be less toxic.

Market advancements before 1929 were also made in the field of vaccination, making history in the discovery of smallpox prevention. Immunization sera for diphtheria was introduced from logical observations and conclusions made by Friedrich Löffler, and this was the actual scientific development of the idea used by Mithridates IV, King of Pontus, who sed gradually increasing amounts of poison in order to protect himself from a large dose of it.

The Schick test came to life in 1913 and immunology was introduced. Serum against tetanus was evaluated and first used during World War I. In 1924, Dr. Albert Claudette made a strain of weakened T. B. bacillus, opening a wide, new field of progress. Fighting a disease with another disease, initiated by a Viennese doctor, Julius Wagner, Jauregg, showed great promise. The idea of focal infection and slow toxin excretion harming the organism was realized and attacked by means of surgery.

Presulfo Period
1929 - 1938

This period in this country and also in Nebraska, lasted up to 1938. This time ocular surgery was already well advanced but the greatest menace of all was infection of any kind, which often ruined the most perfect surgical results.

In this period the main drugs to combat infection of any kind were compounds of silver or mercury, such as Silver Nitrate, Collargol, Protargol, Argyrol, Ammoniated Mercury, Ophthalmic Ointment, Yellow Mercuric Oxide Ointment, Mercuric Oxycyamide, Phenylmercuric Nitrate, Nitromersol, Mercurochrome and others as: Medicinal Zinc Peroxide, Ethyl Hydrocuprein , Hydrochloride, Bensalkonium Chloride. All these drugs were successfully used and some of them helped to control infections but they were far from good. In connection with these "bacteriastatic agents" (as they were then called but which actually should be termed as graded strength disinfectants), dry and moist heat were used, also infra-red short wave irradiation and some corrosives. Copper Sulfate and Silver Nitrate Crystals were used in the treatment of trachoma. Trichloro-acetic Acid was employed in the cauterization of prolapsed uveal tissue or ulcerating lesions. Tincture of Iodine was used in combatting Dendritic Ulcer of the Cornea and is still considered the best treatment at the present time. Boric Acid in combination with Zinc Sulfate and occasionally with Epinephrine, was widely used as eyedrops for irritation or infectious conditions.

Primary glaucoma medical and surgical treatment was already well advanced, based on scund judgement and drugs such as Pilocarpine, Eserine, Mecholyl and Prostigmine. Buffer solutions were also ad-vanced and in this part of the continent it was accepted solution developed by Gifford and used as artificial tears and as a vehicle for some drugs.

Otherwise, treatment around 1929 was mostly symptomatic and diseases such as infectious lesions in the body or the eye were attacked indirectly by local exploration of chemically harmful medicine which usually not only destroyed the microorganisms, but also damaged the tissue in the area of application. Another basic method was the support of organism or by creating a physiological status enabling the body to fight the infection.

Period of Sulfonamides
1938 - 1946

A relatively sudden and sharp turn took place in 1932 when Dr. Gerhard Domagk discovered a chemotherapeutic agent which opened new possibilities and hopes for the future in the method of combatting macroorganisms in the living host. The first of this type of drug was developed under the protection and support of T. G. Farbenindustrie in Germany. Dr. Domagk named this drug "Prontosil". It was a dark red dye compound consisting of 4-sulfonamido-2, 4-diamino-azobenzene (6). According to the combined reports in German literature published on December 20, 1932, it appears that this compound was actually found two years prior and during this time it was clinically evaluated. Soon after, multiple improved similar compounds were developed that have less toxicity and more bacteriostatic power. They were thrown onto the market under different names such as, Albucid Uliron, Cibasol, etc. Improvement of the basic compound is still in progress, even at the present time. Chronologically, soon after Domagk, french scientist J. Trefouiel, F. Nitti and D. Bovett, discovered that para-amino-benzenesulfonamide was also affective. In 1936, Dr. Leonard Colebrook, very sarcastically criticized the newly developed drug as being unscientific and unconvincing. Out of curiosity he started to investigate this new drug by using it in Queen Charlotte's obstetrical hospital on the cases of puerperal sepsis, and later had to admit that this drug was one of the best he ever used. He even carried

his work further by establishing necessary doses in order to reach the necessary concentrations in the blood for the best possible curative effect. But at any rate his first unfavorable report left a bad impression in England and the Western Hemisphere and temporarily blocked the way for this new drug in those countries. In spite of Colebrook's propaganda, Buttle, Gray and Stephenson, also in England, became interested in this new compound and soon published observations on cases of meningococcus meningitis, reporting wonderful results (6). At this time the United States also opened its doors for investigation in the use of this drug. Soon after, this compound was used in trying to combat other microorganisms and was found to be successful against gonococcus, pneumocoocus, haemolytic streptococcus, and staphylococcus.

New compounds were investigated and given to the ill. A. J. Ewins and M. A. Phillips succeeded in making an effective compound consisting of 2-sulfamilylaminopyridine in abbreviated form called Sulfapyridine. In 1939, Sulfathiazole, (2-Sulfanilylaminothiazole) came into use, and in 1941, Sulfadiazene (2-Sulfanilamidopyrimidine), then Sulfaguanidine (2-Sulfanilaminoguanidine), Sulfasuccidine (Succinyl-2-Sulfanilaminothiazole).

Delayed introduction of Sulfanamides in this country opened this new period here just about 1938 and by 1939 they were beginning to be used in the eye diseases (8). In the first place, administrations of sulfonamides was just systemic in different inflamatory conditions of the eye and its adnexa, and proved to be a good agent

in control of infection seated in the tissues well supplied by blood. This raised the problem of administration of sulfonamides to the surface area or parts of the eye where no blood supply is persent, and in this way the topical administration of sulfonamides was investigated and advanced. From my own experience I remember that in 1942 we used to grind a tablet of Cibasol and this powder was placed on the conjunctival sac. Soon we realized that this way secondary damage of the cornea occasionally occurred, apparently caused from too high a concentration of chemical compound. Then we tried to dissolve tablets in normal saline and used as drops. Soon after, ophthalmic preparations appeared on the market. Preparations used for topical administration were of great variety and of different carrying vehicles. The most common and most useful were liquid solutions, and for prolonged action, ointments. The following sulfo compounds were in use in ophthalmology: Sulfocetamide, 5-10% ointment and 30% solution, Sulfathiazole, Sulfamylon, etc.

Bacteriostatic action of sulfonamides was investigated thoroughly and the following conclusions were, that it prevents multiplication of pathogenic microorganisms suseptible to this drug, giving the host's organism time and a chance to phagocityze them and to develop immune bodies specific for these microorganisms.

In eye conditions, systemic use of sulfonamides is effective only where the drug can reach the tissues by blood or diffusion. It has to be mentioned that interesting observations have been made

that Sulfadiazine easily diffuses into aqueous humor and Sulfathiazole shows practically no diffusion. Topical administration of sulfonamides requires 30% of Sulfocetamide in order to have enough penetration through the cornea in order to reach the adequate concentration in the anterior chamber.

It should be mentioned that effective concentration of sulfonamides depends on several factors:

1- The rate of absorption of this drug.

2- Factors of diffusion.

3- Rate and degree of excretion or elimination.

4- Extent of acetylation. (7)

It is known that protein bound and acetylated sulfonamides are not available for therapeutic action and just free sulfonamides act upon microorganisms. Sulfonamide action upon the microorganisms is based upon inhibition of essential enzyme systems involved are those which have to do with oxidation-reduction process of metabolism. Sulfonamides and its derivitives arrest mitosis in high form of life and individual cells increase in size above the normal because of inability to divide under the influence of these components, until finally they reach such a size that they break down. It is also proven that sulfonamides are effective against some anaerobic microorganisms inhibiting their respiratory process.

Period of Antibiotics

1946 - 1954

Already in 1877, Pasteur observed and concluded that antrax bacillus does not survive in soil because of the peculiar interaction of other microorganisms. This was the first known observation made about competition of survival among minute organisms, giving further impulse and start of the period now known as antibiotic period.

Bacillus brevis was the first microorganism to serve in this progress when in 1939 Dubos made an extract from what was then called Thyrotrisin, and demonstrated that it destroyed certain cultures of some pathogenic gram-positive microorganisms.

Penicillium notatum was noted to have inhibitory or destructive action on bacteria. This observation was made by Fleming, who after long years of work, came out with a new drug and introduced a new era in the history of the healing art. This drug was called Penicillin and was used in the second world war among United States service men. The civilian population started to receive penicillin in very small amounts at the end of 1944 and it became fully available by 1946 (9).

The ice was broken and new antibiotics were investigated and released into the market at a very rapid rate, and the better known following antibiotics were Streptomycin, Dehydro-streptomycin, Chloramphenicol, Aureomycin, Terramycin, etc.

Their action upon the microorganisms is different than of

sulfonamides. Sulfonamides are bacteriostatic agents whereas antibiotics are bactericidal in higher concentrations, but they are bacteriostatic, like sulfonamides, in low concentration. Bacteriostatic action of the sulfonamides is an interference with fission of the microorganism by combining themselves with proteins containing sulfhydryl groups, cysteine and thioglycolic acid. The antibiotics bactericidal action is based upon interference with development of bacteria by inhibition of essential metabolic functions, and this, in some cases, acts upon cell division and some may interfere with vitality of the cell. Penicillin, for example, inhibits the synthesis of derivative of nucleic acid which is an active participant in transport of the certain amino acids through the wall of the cell. Streptomycin, on the other hand, acts by blocking of the reaction between pyruvate and oxalacetate in Krebs condensation cycle. Combination of two or more drugs has its advantages where two different components act simultaneously upon different phases of metabolism. Combination of Streptomycin and P A S is proven as highly efficient. Using in combination, Bacitracin with Penicillin, it requires much smaller doses of each in order to reach full bactericidal therapeutic effect. On the other hand, combination of Penicillin and Chloramphenicol is dangerous because microorganism is held in the state of suspended animation until Penicillin is excreted, and Penicillin is only effective against dividing cells, whereas Chloramphenicol inhibits the cell division, and where there is no cell division, penicillin does not

have any chance to act upon the sensitive stage of life of such microorganisms.

When the antibiotics were started to be used at the bedside, enthusiasm was so great that sulfonamides were practically thrown out the window, but soon disadvantages became apparent in the form of allergic manifestations, decreasing susceptibility of some microorganisms. Decreased susceptibility or "acclimatising" to the antibiotics theory is that few organisms survive while under the influence of the antibiotic and start to propagate a new strain with changed metabolic complement of enzymatic system. Other thoughts are that in this same genus of microorganism, there are individually stronger microorganisms and these, when they survive, propagate a strain which has no weak fellows and in this way a new, more resistant population becomes dominant. Another thought is that antibiotics induce mutation which forces the change of metabolic mechanisms by which organisms live and multiply.

Many physicians make a great mistake at this particular point by using indiscriminately, antibiotics were actually they are not needed, or administering inadequate amounts so that under this inadequate level of drug, many organisms, even susceptable to this drug, survive and create new antibiotic resistant strains of organisms. Another false method in the use of antibiotics, not as common as the one mentioned above, is that the physician, thinking that certain infection appears to him as not very serious, starts the treatment with a low dose of antibiotics and as days go by he realizes that

the condition of the patient is not improving, maybe even getting worse, and then, paralell to this picture, he increases the amount of the antibiotic. Finally he reaches amount of the drug which really should help but actually does not. The answer here again lies in a clear and simple pattern. This acts upon microorganisms just like immunization of the children against tetenus or diphtheria and giving booster shots. For example, colon bacillus, in case of improper treatment, can become resistant against streptomycin to a thousand times the original lethal concentration, within a week, where M. tuberculosis, on the other hand, needs about three months of improper treatment until it becomes streptomycin-fast (7).

Some of the microorganisms are not susceptible to antibiotics because they produce specific enzymes which actually destroy active antibiotic agents. A good example is E. coli, which contains large amounts of the enzyme called Penicillase which very rapidly inacti-vates Penicillin. A similar enzyme was also found in a great variety of mold-like flora. Here we face another problem; the coexistance of many microorganisms in the human body, of which a great number are real pathogens, and the resulting balance of all these organisms prevents production of the disease. In case of antibiotic therapy, susceptible organisms are eliminated, and this way the coexistance balance is upset. Recently we are finding more and more reports in medical literature about such complications where pathogenic organism used to be in the normal flora of the body as non-pathogen, pre-dominant are from the group of the fungus, and when the balance is

upset, they take the upper hand, start to multiply very rapidly, invading the organism of the host. Sound judgement and proper use, even of these miracle drugs, is necessary. Overconfidence can often bring a tragedy upon a fellow patient.

Therapeutic Agents of Today

For some time, sulfonamides were pushed out of the medical field in the period of great joy, expectancy and confidence in new rising antibiotics. It soon was realized that they can not give everything we need to combat the infections and diseases pro-duced by microorganisms. Sound thinking and judgement brought them back and both antibiotics and sulfonamides, with equal import-ance, became our main weapon against the disease-producing organisms. At the present time we have a great variety of compounds in use and most important are summarized with indications as to which organisms they are most useful against (Table No. 3).

Antibiotic activity against viruses appears unsuccessful because they do not have any intrinsic metabolic activity. But borders of viruses are not certain and we have the impressions that some of the larger viruses, like chlamydozoaceae, may be influenced by antibiotics so that the course of the disease can be altered and similar action is also observed in the group of Rickettsial diseases.

Practically all antibiotics are effective against microorganisms in the stage of active growth. Aureomycin, Terramycin, Chloramphenical are bacteriostatic while Penicillin, Streptomycin and just recently introduced, the new drug, Erythromycin, are bactericidal in sufficient concentrations and bacteriostatic in lower concentrations. From this observation and conclusion it seems it would be rational to use proper antibiotics in active or progressing infectious process and all chronic conditions due to microorganisms should be treated

TABLE NO. 3

THERAPEUTIC AGENTS - HOW THEY ARE USED
AGAINST MICROORGANISMS IN OPHTHALMOLOGY

	Penicillin	Streptomycin	Aureomycin	Chloramphenicol	Neomycin**	Terramycin	Polymyxin	Bacitracin	Tyrothricin	Erythromycin***	Sulfonamides	Remarks
Micrococcus Pyogenes Var. Aureus	A	B	B	B	C	B	E	B*	B*	A		
Micrococcus Pyogenes Var. Albus	A	B	B	B	E	E		B*	E	A		
Neisseria Gonorrhaea	A	B	B	B	E	B	E	B*	E	A	AB	
Neisseria Meningitidis	A	O	B	E	E	E	B*	B*	E	B*	AB	
Neisseria Catarrhalis						B	E	E			A	
Streptococcus Pyogenes	A	B	B	B	E	B	O	B*	B*	A	B	
Streptococcus Salivarius	A	B	B	E	E	B	O	B*	B*	A	B	
Streptococcus Mitis	A	B	B	E	E	B	O	B*	B*	A	B	
Streptococcus Bovis	A	B	B	E	E	B	O	B*	B*	A	B	
Streptococcus Lactis	A	E	B	E				B*				
Streptococcus Faecalis	E	B	A	E	E	B	O	E	E			
Streptococcus Liquefaciens	E	B	A	E	E	B	O	E	E			
Streptococcus Anaerobius	A		B			B		B*	E			
Corynbacterium Diptheriae	A	E	E	E	E	E	O	E	E	A		Antitoxin
Corynbacterium Xerose				E		E		E				

Explanation of symbols at end of chart.

(Con't.)

TABLE NO. 3

	Penicillin	Streptomycin	Aureomycin	Chloramphenicol	Neomycin**	Terramycin	Polymyxin	Bacitracin	Tyrothricin	Erythromycin***	Sulfonamides	Remarks
Erysipelothrix Erysipeloidis	A	C										Use both for Synergistic Action.
Escherichia Coli	C	B	A	A	C	B	B*	C				
Aerobacter Aerogenes	C	B	A	A	C	B	B*	C				
Klebsiella Pneumoniae	E	A	A	A	C	C	B*			A		
Klebsiella Azaenae		C					E					
Proteus Vulgaris	E	A	E	B	C	C	C	C	C			
Pasteurella Multocida	E	C	E	E		E	B*	C			A	In combination with Streptomycin.
Pasteurella Tularensis	C	A	A	B	E		E				B	In comb. with Streptomycin.
Haemophilus Influenzae	E	A	A	A	C	B	B*	B*			B*A	
Moraxella Lacunata			A									
Bacillus Anthracis	A	C	B	E	E	C	E	E	E			
Clostridium Septicum	A	C	E	C						A		
Clostridum Novyi	A	C	B	C				E		A		
Clostridium Sporogenes	A	C	E	C	C	E	C	E		A		
Clostridium Perfringens	A	C	B	C	E	E	C	B*		A		
Clostridium Tetani	A	C	C	E	C	E	C	E	E	A		Antitoxins
Clostridium Histolyticum				C				E		C		
Mycobacterium Tuberculosis	C	A	E	E	B*	E	C		E			Streptomycin with PAS or Sulfones
Nocardia Asteroides	A	B		E								

(Con't.)

TABLE NO. 3

	Penicillin	Streptomycin	Aureomycin	Chloremphenicol	Neomycin**	Terramycin	Polymyxin	Bacitracin	Tyrothricin	Erythromycin***	Sulfonamides	Remarks
Nocardia Madurae												??
Actinomyces Bovis	A	B		E							A	Use both
Actinomyces Israeli	A	O	B					E			A	Use both
Borrelia Vincentii	A	O	B							A		
Herpes Simples and Zoster						B						
Chlamydozoa Trachomalis						B					A	
Pseudomonas Aeruginosa	O	A	B	C	C	B	B*	B*	O		B	

A - Drug of choice
B - Effective
B* - For topical use and drug of choice in case drug marked "A" is not available for topical use.
C - Effectiveness not certain
E - Effective just in vitro
O - Not effective

** Neomycin produces a lease of hypersensitivity reactions (10, 11, 12).

*** Reports on Erythromycin are incomplete at the present time. There are reports of some investigation available and it is certain that this drug, in many infections, is superior to other drugs, especially when microorganisms become resistant to another antibiotic and they are in the range of the spectrum of Erythromycin. A last report (23) is on concentrations in the eye when given systemically. It is as follows:

TABLE NO. 3 (Con't.)

Studies Done on Rabbits

Time After Injection	In Serum	Aqueous	Vitreous
1 hour	1.92	0.24	0.06
2 hours	9.96	0.24	0.06

He further reports that in "eye infections due to 'Ilotycin' (trade name for Erythromycin) susceptible organisms have responded quite favorably to doses of 200-400 mgm. every six to eight hours". Approach can be chosen as systemic or topical, depending on the location of the infected area. Clinical trial was given and favorable results were obtained in acute and chronic conjunctivitis, keratitis, dacryocystitis, meibomitis, marginal blepharitis, corneal ulcer and ophthalmia neonatorum (prophylactic use). Hypersensitive reactions, according to their report, are rare.

with sulfonamides in case these microorganisms are susceptible to them.

Now enters the question as to how we can determine which kind of organisms we have in a particular case. In the first place, organisms have certain properties that produce certain symptoms or complexes of symptoms or diseases. In case it is difficult to recognize them from just the clinical history and picture, there are a few simple suggestions briefly summarized (see appendix), giving suggestions as to when certain organisms can be expected, how to determine their presence, and other important microscopic features seen in the specimen. Until such an answer is reached, a patient may be treated with some antibiotic or sulfonamide or whatever seems feasible, based upon logical thinking, clinical history and the presenting features of his condition.

Desoxycorticosterone, Cortisone and Hydrocortisone finally were found useful in ophthalmic practice. Their action can be classified into major groups; alternating effect upon inflammatory response and alterneting effect upon allergic response. Cortisone changes the inflammatory response in many instances, such as bacterial infections, chemical irritation, inflammation due to foreign protein and thermal burns. Its action produces such changes that can be observed in histologic preparations. It reduces the inflammatory process by diminishing leucocytic infiltration, transudation, capillary thrombosis and hemorrhage, delays phagocytosis and delays fibroblast proliferation eo ipso inhibits formation of the scar. This action of Cortisone is the same elsewhere, as in the eye. It must be mentioned that such an alternation, in case of active infection, may have very serious results because all the natural mechanisms of defense are inhibited and invasion of microorganisms is facilitated. Destruction of the organ by infectious inflammatory process may follow and even generalized bacteremia can be the final result in case of imprudent use of Cortisone.

Further, Cortisone alters hypersensitivity reactions in the form of protection by diminishing generalized organism response to the antigen. Antibody formation is influenced but it seems that production of the substance, which gives rise to the hypersensitivity response, is just moderately altered by Cortisone. Here we should keep clearly in mind the difference between hypersensitivity and

immunity. Cortisone and Corticotropin do not inhibit antigen and antibody reaction follows; Cortisone is no help in anaphylactic shock; neither changes the local histamine reaction although they do diminish the reactivity to histamine of tissues altered by allergic disease (11). To conclude these statements it is possible to state that Cortisone is helpful in delayed reactions but not in immediate hypersensitivity reactions, in which drugs of choice are antihistaminic preparations.

Dr. Hoods summarizes clinical usefulness in his article (13) as follows:

> "(a) In certain inflammatory conditions of the eye, especially those affecting the cornea, uveal tract, and external eye, the parenteral administration of ACTH or cortisone, or the topical administration of cortisone, is followed in a high percentage of cases by a dramatic control of the inflammatory and exudative phases of disease. These agents do not affect the cause of the disease but rather influence the reaction of tissues to the cause or to the irritant.
>
> "(b) In many favorably influenced there is a definite tendency for the inflammation to recur after cessation of treatment.
>
> "(c) In certain edematous and inflammatory conditions, especially secondary glaucoma, inflammations of the retina and optic nerve, and edematous corneal grafts, and also probably in syphilitic interstitial keratitis, the action of cortisone and ACTH is variable and cannot be accurately predicted.
>
> "(d) In some haemorrhagic and exudative conditions (Coat's disease, Eales' disease, malignant exophthalmos, diabetic retinopathy and retrolental fibroplasia) no consistent therapeutic results have as yet been demonstrated.
>
> "(e) In degenerative disease, whether of the cornea, retina, or uveal tract, these agents are totally ineffective (13)."

Curare and curare-like agents, investigated by Dr. McIntyre, also reached ophthalmology. Two years ago Dr. Kirby stated that he

very extensively uses this drug in ophthalmic surgery with very good results (14). More physicians apparently became interested in these drugs producing muscle-relaxing properties, which are so important in the precise surgery in ophthalmology, giving the surgeon a better chance to proceed with the operation without any disturbance from the patient. Antihistamines found their value in ophthalmology, also in instances where the release of histamine or histamine-like substances is the cause of the symptoms.

Hyaluronic acid also began being used in ophthalmology by adding it to local anesthetics and reports in the majority are favorable. This is also used in degenerative keratitis. Streptokinase, Streptodornase and Trypsin were brought into the market but they are still not safe enough for use in ophthalmology.

Today, antibiotics and sulfonamides are equally important as weapons against infections, plus recent additional drugs, some which partially changed the outcome of the disease process. One of these is Cortisone which first was widely used, and many complications were apparent until the accurate action of this drug was finally realized, and its use was discontinued in conditions where microorganisms may invade or spread and local suppressed inflammatory reaction would not be able to bar the destructive action of such an invasion.

On this basis the study of pathology will be divided into these three basic periods with intention to demonstrate, for teaching personnel, how this progress in healing arts influenced treatment

and to point out, for the physician in practice, the most common conditions in our state. Knowing this, the professor will stress certain points while teaching the students, and the physician in practice will have an idea as to what happens to the eye and how he would be able to prevent complications.

CHAPTER IV

DISCUSSION OF THE PATHOLOGIC PROCESS IN THE EYE

To present all the information about the microscopic preparations accumulated during the past twenty-five years in this department, it was necessary to re-examine all of them. The reason for this was that, just in the past few years, specimens sent to this institution were accompanied by clinical history. Many early preparations apparently were not examined at all or had descriptive terminology which could not be understood by the physician of today. Because of lack of many clinical histories, my presentation is based purely on pathological findings in order to avoid confusion. In some cases it was difficult to rebuild the possible chain of events in the diseased eye and in such cases Dr. Gifford helped to make the final touches.

I have divided these twenty-five years into three major periods and have discussed briefly the progress of drugs which so greatly changed our attitude and methods of treatment. The found pathology I also divided accordingly into three groups and shall correlate the changes into a certain pattern, bringing out the advantages of our progress and finally to bring out some problems that we have to face to find the way for further improvement. I shall limit myself to the conditions of the eyeglobe itself, leaving out adnexa pathology. The presenting pathology of the eyeglobe is classified in Tables No. 1 and 4. In addition to these 469 specimens, there are also specimens of ocular adnexa from which few are from major clinical importance. In this group of conditions the progress of medical therapeutic agents is not as well reflected as in inflammatory conditions of the eyeglobe. Here, more or less, we can see

the educational progress of our physicians and alertness in recognizing malignant lesions and realizing the importance of the early surgery. The following list is again divided into the same periods as above for the sake of uniformity. (See Table 2 and 5)

These specimens of adnexa represent pathology submitted to this department, but knowing that many such lesions, when operated upon, are sent to general pathologists and never reach our hands it should be mentioned that they are more common than can be expected from this list.

Any kind of trauma causes an inflammatory process in the tissue. This can be physical, chemical, or thermal trauma or induced by pathogenic microorganisms. Before I start to analyze the pathology in detail in each particular group of pathogenic processes in the eye, I shall present the general concept of inflammatory events and basic morphology occurring in the eye. The reason for this is that the eye, being a highly specialized organ in its parts, and its reaction, as broken down into specific structures of the eye, reacts differently to the trauma and even to different kinds of trauma; repair has a different pattern for each specified part of the eye. Pain, swelling, heat and redness cannot be forgotten as the classical sign of inflammation. Increased blood flow to the inflamed area results in increased temperature and redness. Transudation and exudation into the eyeglobe may alter the physiological balance of the fluid exchange and result in increased intraocular pressure. If inflammation occurs in the adnexa, visable swelling is apparent.

TABLE NO. 4

LESIONS OF THE EYE
(No. & % of cases)

Diagnosis Based on Microscopic Examination	1929-1937	%	1938-1945	%	1946-1955	%	Total	%
Secondary Glaucoma	40	37.5	56	42.6	89	38.7	185	39.5
Perforating Corneal Ulcer	10	19.3	5	3.8	7	3.0	22	4.7
Panophthalmitis	3	2.87	4	3.0	4	1.7	11	2.3
Acute Anterior Uveitis			1	.8			1	.2
Sympathetic Ophthalmia			3	2.3	2	.9	5	1.1
Traumatic Perforation	14	13.1	16	12.2	38	16.6	68	14.5
Phthisis	11	10.3	12	9.2	23	9.9	46	9.8
Coat's Disease					1	.4	1	.2
Primary Glaucoma	3	2.8	12	9.2	12	5.2	27	5.8
Congenital Glaucoma	2	1.9	2	1.5	3	1.3	7	1.5
Toxoplasmosis			1	.8			1	.2
Postoperative Expulsive Intra-ocular Hemorrhage			1	.8	2	.9	3	.7
Retrolental Fibroplasia			1	.8			1	.2
Hypertensive Retinopathy*	1						1	.2
Periarteritis Nodosa					1	.4	1	.2
Papillary Edema***					1	.4	1	.2
Malignant Melanoma of the Choroid	12	11.2	11	8.4	23	9.9	46	9.8
Malignant Melanoma of the Iris					1	.4	1	.2

TABLE NO. 4

(Con't) (No. & % of cases)

Diagnosis Based on Microscopic Examination	1929-1937	%	1938-1945	%	1946-1955	%	Total	%
Malignant Melonoma of the Ciliary Body			2	1.5	3	1.3	5	1.1
Malignant Melanoma of the Limbus					1	.4	1	.2
Retinoblastoma***	5	4.7	1	.8	14	6.1	20	4.3
Bowen's Disease	1	.9			1	.4	2	.4
Benign Melanoma of the Choroid	1	.9	2	1.5	1	.4	4	.8
Benign Melanoma of the Iris					1	.4	1	.2
Ectopic Intraocular Lacrimal Gland					1	.4	1	.2
Metastatic Adenocarcinoma in the Uveal Tract	1	.9					1	.2
Intraocular Neurofibroma					1	.4	1	.2
TOTAL	107	99.9	131	100	231	100	469	100

* Autopsy Specimen
** Autopsy Specimen of the patient who had cerebellopontine tumor
*** Recurrences included

Pain is due to pressure or stretching of the tissues or compression of the nerve endings. Migration of the white cells is a protective process, also exudation which can have low or high protien content, precipitation of fibrin, and because of local damage, diapetesis of the red blood cells may occur. The process of healing reflects itself in fibroblast activity, new vascularization, and changing

morphology of the white blood cells.

The inflammation in itself can be classified into three major groups - acute, subacute and chronic. The cellular morphology is the indicator for classification while examining microscopically. The clinical picture is based upon certain findings, such as appearance, local and general reaction, laboratory studies and clinical evaluation of responses to the specific treatment.

Acute inflammation is characterized by polymorphonuclear leucocytes which actively take part in phagocytosis of the microorganisms and cellular debris. Their action is based upon proteolytic enzymes.

Allergic manifestations, and infestations with parasites, represent increased amounts of eosinophils; for some unknown reason they also are seen in subacute endophtholmitis (27).

Chronic inflammatory cells are predominantly lymphocytes. Their increase in number usually is parellel with rising antibody titers. The second important cell in chronic inflammation is the plasma cell, appearing later than lymphocytes. This cell is usually not seen in the bloodstream. At the side of the lesion this cell slowly undergoes degenerative mutation, first becoming a so-called plasmocytoid cell and then known as Russell body.

In case of conjunctivel inflammation, lymphocytic follicle proliferation is very active, giving, in certain conditions, characteristic velvet-like appearances.

In acute inflammatory lesion and also in the stage of subacute inflammation, after polymorphonuclear leucocytes appear, mononuclear

TABLE NO. 5

LESIONS OF THE OCULAR ADNEXAE

	1929-1937	1938-1945	1946-1955	Total
	No. of cases			
Mixed Tumor of the Lacrimal Gland	3	1	2	6
Extrabulbar Intraorbital Malignant Melanoma*	1			1
Basal Cell Carcinoma of the Lid	4	1		5
Squamous Cell Carcinoma of the Lid	2			2
Metastatic Adenocarcinoma in the Lid			1	1
Cavernous Hamangioma in the Retrobulbar Space**	1			1
Cavernous Hemangioma of the Lid		1	1	2
Erythroleukemic Infiltration of the Conjunctiva	1		2	3
Cutaneous Benign Papilloma***	2	1	2	5
Granulation Tissue	1	1	2	4
Xanthelasma	1	3	2	6
Chalazion	1		4	5
Epithelial Cyst of the Conjunctiva	1	1		2
Sebaceous Cyst of the Lid		1	3	4
TOTAL	18	10	20	48

* No other malignant melanoma tumors were found.
** Eye was removed and no pathology found.
*** One case of premalignant papilloma in the period of 1929-2937.

wandering cells, better known as microphages, will follow. Their function is also phagocytic, especially for cellular debris, including hemoglobin, lipoids and degenerated polymorphonuclear leucocytes.

Foreign body reaction, T B, lues, Boeck's sorcoid, and sympathetic ophthalmia, are accompanied by fixed tissue microphages (epithelioid cells). They usually form a nest, known as granuloma or giant cells, also called foreign body giant cells, or in some instances, Langhan's giant cell.

Seldom seen in ocular inflammatory lesions are mast cells and basophils. Their function and significance is not well understood.

Repair processes are signified by fibroblasts which are derived from connective tissues and form the scar. Endothelial cells originate from fixed tissues or capillaries giving origin to new blood vessels and granulation tissue.

The greater majority of disease-producing microorganisms are found as saprophyter existing on the epithelial surfaces. Of these, the most common are colon bacilli (Escher. coli) in the intestinal tract, streptococci, pneumococci and other gram negative cocci on the mucous membranes of the mouth, and micrococci (staphylococci) on the surface of the skin. Saprophytic microorganisms, in case they invade the body, may produce an inflammatory process locally, or even a specific disease. This invasion has different characteristics for each organism, attacking in its own way the living cell; Example: Pasteruella tularensis proliferates intracellularly and Brucella suis in the mesodesmal endothelium of the vessels. Reaction to the invaded microorganism is often specific for the invading microorganism and invaded tissue; T B and lues are characterized by epithelioid cells or so-called granulamotous reaction; while the

most common pathogens, like streptococcus, staphyloccus and pneumococcus, causes pyogenic reaction.

Toxin-producing organisms, important in ophthalmology, are tetanus and diphtheria; one in case of injury and the other a possible manifestation on the conjunctiva.

An entirely different origin inflammatory process should be mentioned in this specific field of medicine and this is due to hypersensitivity. In the process of developing acquired resistance to certain noxious agents, organisms may become hypersensitive and, playing a major role as in immunity, this is a response of the antibodies to the antigens. It seems that in acquired immunity, antibodies change the microorganisms so that they become more susceptible to the antibacterial agents of the organism. Hypersensitivity, on the other side, appears to reach such an alternation that antibodies alter the cells of the body so that by introduction of antigens these cells are damaged by combined action of antigens and antibodies, evoking inflammatory effects which can be localized or generalized. A. R. Rich (24,25) classifies hypersensitivity into two major groups; the anaphylactic state and the bacterial hypersensitivity.

He further subclassifies the anaphylactic state into (a) Anaphylactic reaction, (b) Arthus phenomenon, and (c) Pollen type hypersensitivity. Anaphylactic reaction is rarely seen in the human being, which is characterized by rapid development of urticaria and erythema in case specific protein is injected into the skin. Further, if a larger amount is given, the result is serum sickness

PANOPHTHALMITIS, SIDEROSIS, & TRAUMATIC CATARACT

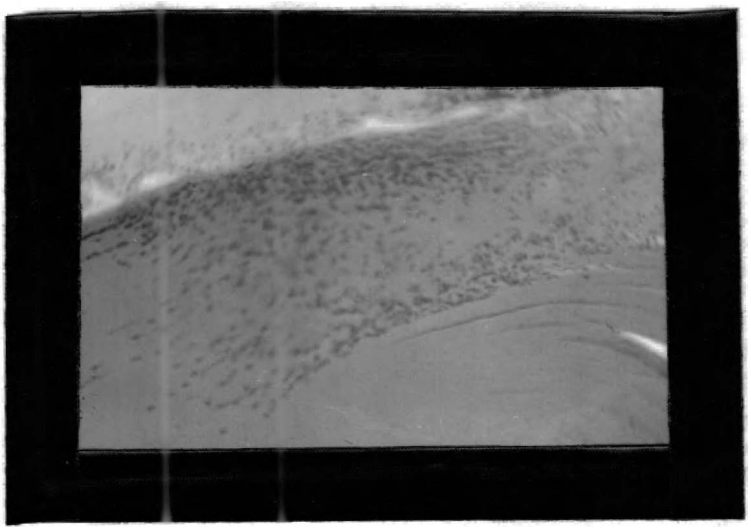
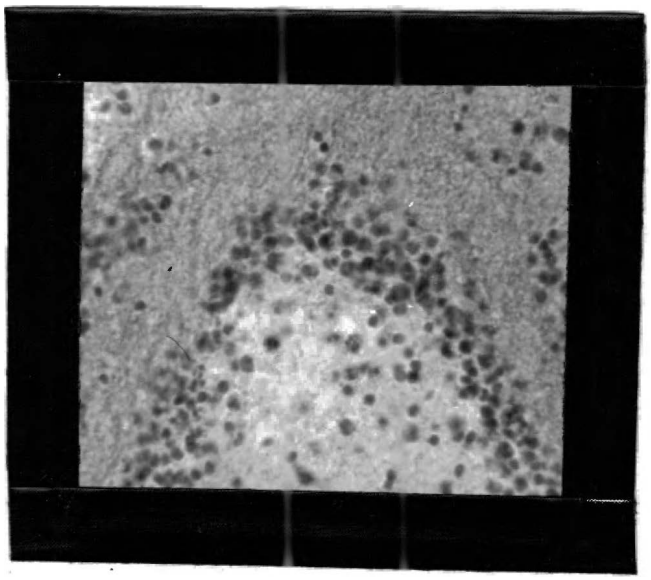


Fig. 1

Case No. 582. Male, 26 years old. Eye was struck by something while working under car engine six days prior to enucleation. X-rays demonstrated metallic foreign body in the eye. Removal with giant magnet was unsuccessful. Subsequent acute inflammatory process forced removal of the eye. Enucleation in 1952.



Examination - Perforation of the globe at 8 o'clock near the limbus. Anterior chamber is filled with purulent exudate containing primary polymorphonuclear leucocytes and some red cells. Marginal tissue of the wound is necrotic and packed with polymorphonuclear cells, this same cellular morphology is present in the iris and ciliary body (Fig. 1A & 1B).

(con't.)

Fig. 1A

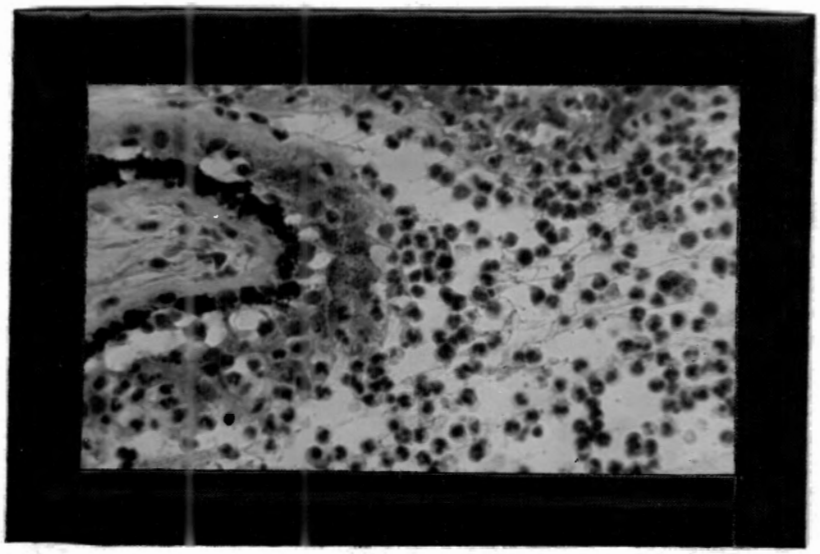


Fig. 1B

Lens capsule is ruptured and cortex invaded also by polymorphonuclear cells (Fig.) and there is cataract formation at the point of rupture of the capsule. Retina is detached with hemorrhages underneath. Vitreous and retina are also moderately invaded by polymorphonuclear cells. Ferrous foreign body found just behind the ciliary body with marked local siderosis of the tissue.

and if such protein reaches the blood stream and is dispersed throughout the body anaphylactic shock and death result. Protein, or a substance containing protein, is usually a sensitizing agent. In some instances inorganic chemicals, believed forming a new complex with the already present protein in the body, then becomes foreign to the organism of the host.

Arthus phenomenon is an exaggerated reaction basically similar to the anaphylactic state. Here the site of damage occurs in involuntary muscles and vascular endothelium, and this actually is responsible for local changes found in this type of reaction.

Clinically similar, Shwartzman's phenomenon should be differentiated because this one does not depend on specific antigen antibody combined reaction and the local pathological changes are different, as "A marked degree of venous and capillary dilatation and engorgement. This is immediately followed by severe hemorrhage, and shortly thereafter, there occurs a striking edema and intense leucocytic infiltration", (26) resulting in vascular prestasis and stasis, thus producing occlusion of the vessels and blocked nutrition. Origination for this particular area is followed by local necrosis.

Polen type hypersensitivity is produced not only by pollens but also by other proteins. Here, side effects are conjunctiva, nasal mucosa, sinus linings, bronchioles and the skin.

Bacterial hypersensitivity or hypersensistivity to infection can be local or systemic and is delayed and progressive. This type is produced by contact of the body with living or dead whole bacteria

ENDOGENOUS ENDOPHTHALMITIS

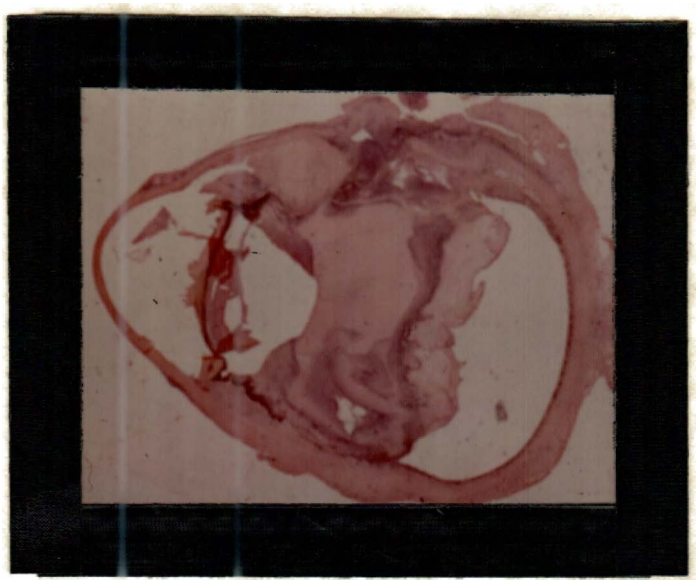


Fig. 2

Case No. 645. Male, 73 years old. Episode of influenza six weeks previous. Eye became inflamed since and vision was gone shortly after. Generalized orbital edema was found; very marked deep and superficial in infection; anterior chamber filled with bloody coagulum. Translumination suggested opaque mass within the eye. Eye is blind. Enucleation, 1953.

Microscopic examination reveals edematous sclera with necrotic perforation (upper part in Fig. 2). AC* filtration angle filled with blood. Complete posterior synecchiae. Lens shows incipient cataract. Cyclitic membrane formed from young fibrous tissue and many fibroblasts. Vitreous cavity is filled with disorganized vitreous and residual fragments of the retina. Episcleral tissue thickened with multiple new vessels. Iris, ciliary body, vitreous space, choroid, sclera around perforation and episcleral tissue are heavily infiltrated predominantly by lymphocytes and plasma cells and few polymorphonuclear leucocytes and giant cells.

*Anterior chamber.

or virus only; but, where hypersensitivity is already developed, response can be obtained with that specific bacterial protein or intact bacteria. Differentiation of this type of hypersensitivity from Arthus phenomenon is based upon that in Arthus type, hypersensitive response is not elicited by introducing intact bacteria. Hypersensitivity to the infection can manifest itself in local, focal and generalized, or systemic reaction.

In our specialty, there is a wide variety of ocular conditions due to hypersensitivity phenomena. One of them is endogenous endophthalmitis which has shown rapid increase in recent years.

In closing, it should be mentioned that there were several deaths reported (17: 74) that followed repeated intravenous infections of thyphoid vaccine which is usually used in ophthalmology as a non-specific protein therapeutic agent.

As I stated, processes of inflammation and repair have some characteristic pattern for each structural part of the eye. Conjunctiva has unkeratinized epithelium which may very rapidly form a hornified layer of the cells when exposed to drying conditions as in lagophthalmos, lack of lacrimal glands, or, a well known condition - keratitis sicca. The cornea is very sensitive to the fluid exchange in balance. A 20% increase of fluid in the cornea results in clouding. Endothelial distrophy is the major cause of such disturbances seen in infections, disturbances of the ophthalmic branch of the fifth nerve, and glaucoma.

Each layer of the cornea also has its own properties. Complete

loss of epithelium is not serious, if infection can be prevented, and usually grows back within 24 to 36 hours. Bowman's membrane consists primarily of collagen; its characteristics are that in case of injury it is repaired by fibrous scar producing corneal opacities. It also has a tendency to become calcified in prolonged local disturbances or generalized disturbances of calcium metabolism.

Descement's membrane is mesodermal in origin and consists of the separate layers - outer, elastic and inner cuticular. Repair usually takes place primarily by fibrous tissue which later is completely or partially replaced by proliferation of the cells existing at that place and usually clearing the opacity to a certain extent. In case the cornea is under prolonged irritation or has extensive damage, new vascularization usually takes place.

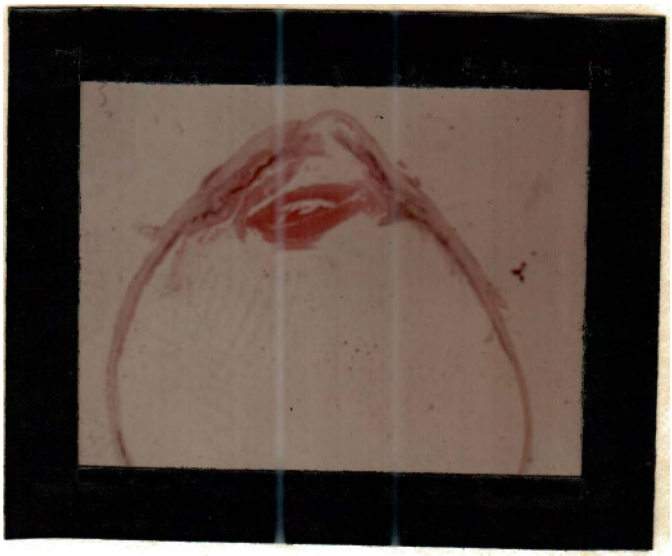
The sclera is a fibrous covering of the eye which is practically avascular; in contrast, the episcleral tissue is highly vascular. Infection from inside the eye, or outside, usually penetrates the sclera along the blood vessels, being called perivascular infiltration. This same pattern is also followed by malignant tumors. The sclera itself is very resistent to any disease process but in case it becomes invaded, treatment is difficult because of lack of direct blood supply. The sclera, being fibrous in origin, often takes part in the generalized diseases of tendons and their sheats; Example: lues, tuberculosis, rheumatic fever, gout and other collagen diseases. A wound of the sclera is repaired by fibroblast migration.

Anatomical structure of the lens consists of three major parts,

CLINICALLY SYMPATHETIC OPHTHALMIA

MICROSCOPICALLY PANOPHTHALMITIS

Fig. 3



Case No. 377. Male, 63 years old. Fellow eye was removed because of destructive injury with a nail. 3 wks. later this eye became inflammed and developed secondary glaucoma. LaGrange sclerectomy was performed without effect. Enucleation 2 wks. later, 1944.

Local purulent inflammatory process when surgical section was made. Anterior periferal synecchiae completely occludes filtration angle. Lens capsule ruptured and shows cataractous changes. Iris, ciliary body and choroid are infiltrated by lymphocytes and epithelioid cells with few giant cells. Retina has prevascular infiltration of this same cellular morphology and multiple area of necrosis. Fig.3A represents area when lens capsule was ruptured and demonstrates amount of cellular infiltration which are polymorphonuclear leucocytes.

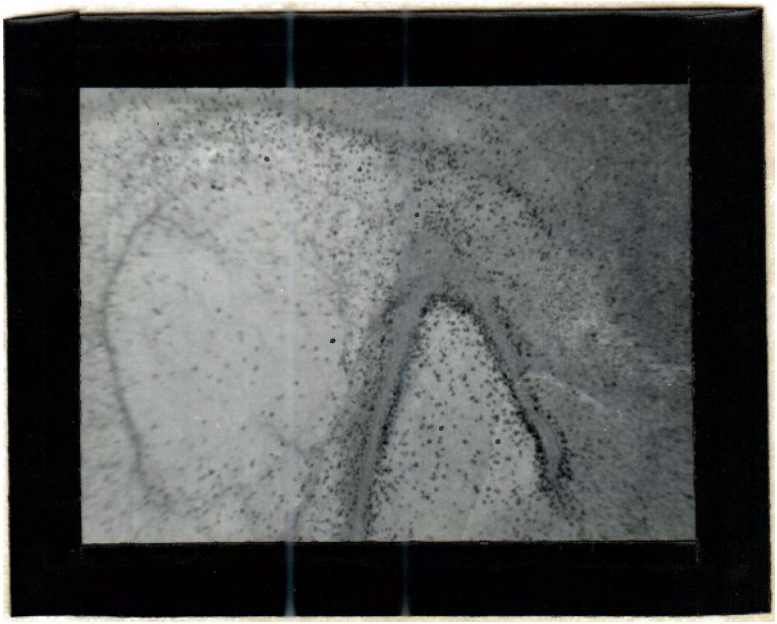


Fig. 3A

COAT'S DISEASE

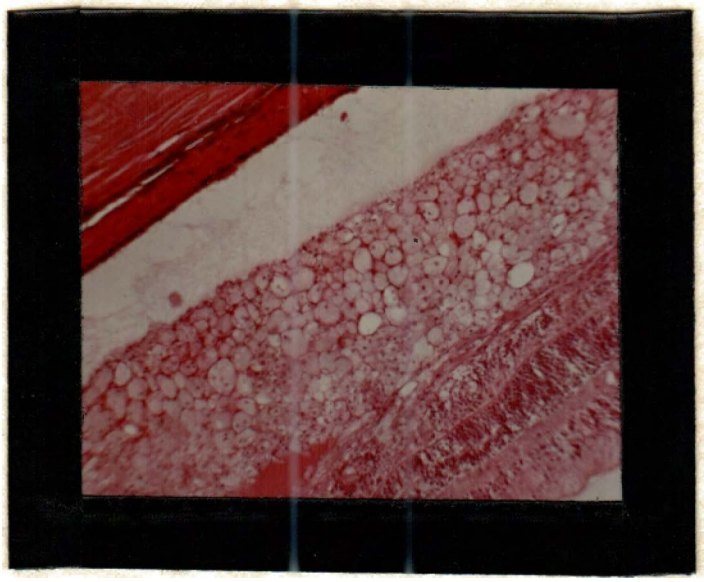


Fig. 4

Case No. 603. Female, 3 years old. No history of trauma or other diseases. Eye enucleated because found yellowish elevated lesion in the fundus and retinoblastoma was suspected. Enucleation - 1952.

Microscopically the only change found were thickening of the retina with cyst-like spaces and some areas dearranged cellular pattern (Fig. 4) and in one area reveals subretinal large collection of so called foamy cells or bladder cells surrounded by small amount of exudate (Fig. 4 & 4A). Choroidal vessels were congested and perivascular spaces showed lymphocytic infiltration.

Cause of this condition is just speculative, but is of importance because this disease frequently gives in to more pathologic changes like deposit of cholesterol crystals, spontaneous intraocular hemorrhages, formation of hyalinized sheats and sooner or later ends with secondary glaucoma.

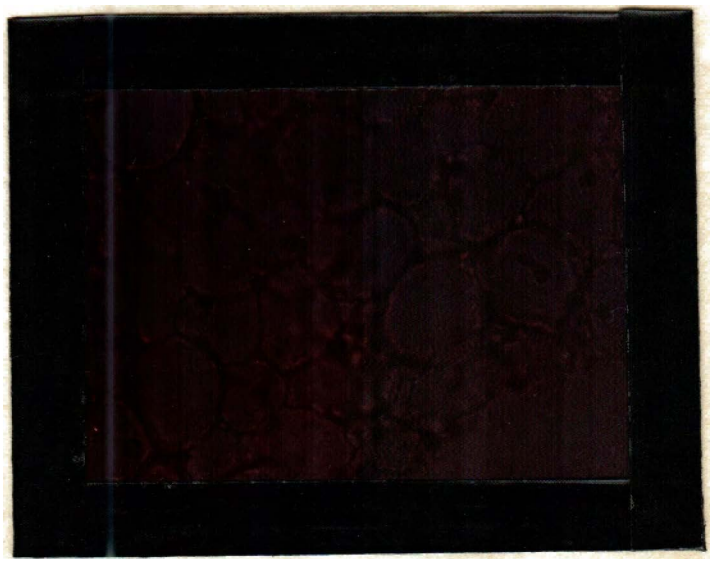


Fig. 4A


page 58 enlarged

these being: capsule, cortex and nucleus. Each one responds differently to trauma. The lens capsule, under the influence of inflammation of the neighboring parts of the eye, undergoes proliferation of the subcapsular epithelium. The cortex, in the process of aging, undergoes sclerotic changes and condensation which gives a clinical picture of nuclear sclerosis. Knowing the pattern of the growth makes it clear why this mainifestation is apparent in the middle of the lens. In case of injury or inflammatory process, the lens cortex undergoes liquefaction, the character and rapidity depending on multiple factors including severity of inflammation, length of time, age of patient, extent of injury, or disturbance of normal physiology supporting metabolism of the lens. All these changes produce lens opacities. The most commonly seen cataracts are senile. Secondary cataracts may be associated with scleroderma, idiocy, myotonia gravis, diabetes, tetanus, rickets, inborn faulty metabolism of galactose, deficiency of riboflavin and tryptophane, poisoning with 2-4 Dinitrophenol or Thallium, radiation, infrared rays, trauma, etc.

The vitreous and its metabolism is the least known part of the eye. It seems that the vitreous does not have any active metabolism and in the event that microorganisms invade, it is found to be very good culture media. Infection in the vitreous is the most difficult to cope with because penetration of the drug is practically nil. There is no blood or lymphatic supply and if anything reaches it, it reaches just by diffusion. Metabolic waste products from adjacent

structures may be taken up by the vitreous and result in crystalized soaps of calcium or cholesterol representing a clinical picture known as asteroid hyalitis. Floaters occasionally seen in the vitreous are condensations of vitreous sheats due to aging, subclinical trauma or neighboring inflammatory conditions. In case of vitreous atrophy, it is replaced by aqueous.

The iris is often involved in one or another kind of inflammatory condition and injury. The reticulo-endothelial system of the iris takes an active part in phagocytosis of the microorganisms. Postinflammatory adhesions of the iris play a major part in ocular complications by upsetting normal circulation of the aqueous. A very specific characteristic of the iris is that its fibrous tissue does not proliferate if traumatised, cut or infected; as a result we do not see any scar formation in this particular organ of the eye.

The ciliary body has its peculiarities too. Its epithelium takes part in aqueous formation and selective reabsorption of it. Long standing inflammation stimulates epithelial growth or production of exudate which forms cyclitic membrane when organized and is in the anterior surface of the lens, or if this is in the posterior surface of the lens, the fibrous bands pull off the retina and further complete distortion and disorganization of the eye, this known as phthisis bulbus oculi.

Choroid is composed of the blood vessels and connective tissue with some pigment in it. Because of its structure, this is most

common place in the eye for metastatic tumors and embolic inflammatory lesions. Close proximity of the retina explains parallel involvement in such incidents but an abudnance of blood in the choroid gives healing a better chance while in the retina collateral circulation is poor and the damage done here usually is greater. The choroid is also a common place for primary malignant melanoma. Sclera, from one side and Bruch's membrane, from the other side, keep such tumors limited a relatively long time to the space but they can ultimately be invaded.

Two different structural layers compose the retina. One, which embryologically is originated from the outer wall of the optic vesicle, is a pigment layer and next to the inner wall of the vesicle is a sensory layer which is again subdivided into another seven layers. Aging first reflects itself in the region of the orra serrata by formation of H. Blessig cysts, and seccnd, distinctive features in senile macular degeneration. Trauma, inflammation and degenerative changes result in glial proliferation, formation of copora amylacea, cytoid bodies, edema, exudation, retinal neovascularization, cystoid degeneration and proliferation of the pigment.

CHAPTER V

SECONDARY GLAUCOMA

The largest and most dominating group presenting the chief cause for enucleation among the specimens is secondary glaucoma. Multiplicity of pathology found in the eye with secondary glaucoma is amazing and I shall discuss each one of these changes separately as I feel that in many instances, complicating factors which actually resulted in secondary glaucoma, could have been prevented, especially at the time when treatment and modern means of examination are available. In some cases, secondary glaucoma again can be a manifestation of space occupying lesions and making further investigation imperative.

As we follow Tables No. 6, 7, 8, 9, and 10, listing pathologic changes among the specimens listed under secondary glaucoma, we can see that a great majority of these cases are traumatic, bearing complicating sequellae and secondary infection; the second group were more or less primary inflammatory conditions and their complicating changes; finally, the last group, which consists of miscellaneous pathology pre-existing prior to the final disease, or an intercurrent addition to the sum of all pathologic changes.

Contusion of the eyeglobe is one of the more common cases of secondary glaucoma which often results in eventual enucleation. The presence of anterior chamber hemorrhage and diminished vision is the most common presenting clinical sign. The flow through Schlemm's canal may be occluded by hemorrhage itself or secondary membranes formed during the organization of this hemorrhage. In the presence of anterior chamber hemorrhage, the introcular pressure

TRAUMATIC INJURY WITH SUBSEQUENT
SIDEROSIS ENDING WITH SECONDARY GLAUCOMA

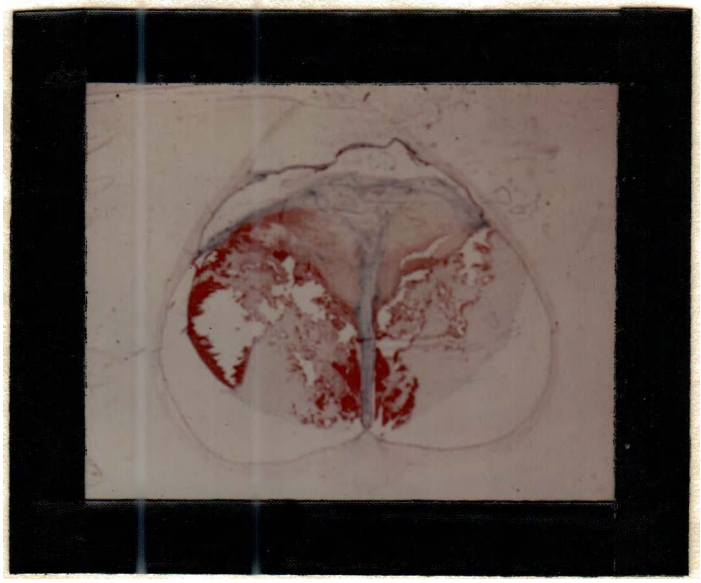


Fig. 5

Case No. 548. Male, Age 40, was struck in the eye while pounding with hammer on file at age 15. Foreign body entered through cornea, was extracted. Infection developed in the panophthalmitis which gradually subsided. 25 years later eye became very painful. Examination revealed 40 degrees exotropia, no LP, iris yellowgreen, AC shallow and hazy, heavy pupillary membrane. Tension 34 mm. Hg. Enucleation in 1952.

Corneal vascularized scar. Multiple lymphocytic KP's. Dense anterior peripheral synecchiae. Atrophy of iris and ciliary body. Enclosed in cyclitic membrane are remnants of lens capsule. Complete detachment of the retina which is disorganized and beneath it massive hemorrhage and exudate. Very marked siderosis in the uvea, corneal epithelium, retina and Schlemm's canal. Diffuse infiltration of inner structures by lymphocytes.

OBSTRUCTION OF CENTRAL VEIN, SECONDARY GLAUCOMA

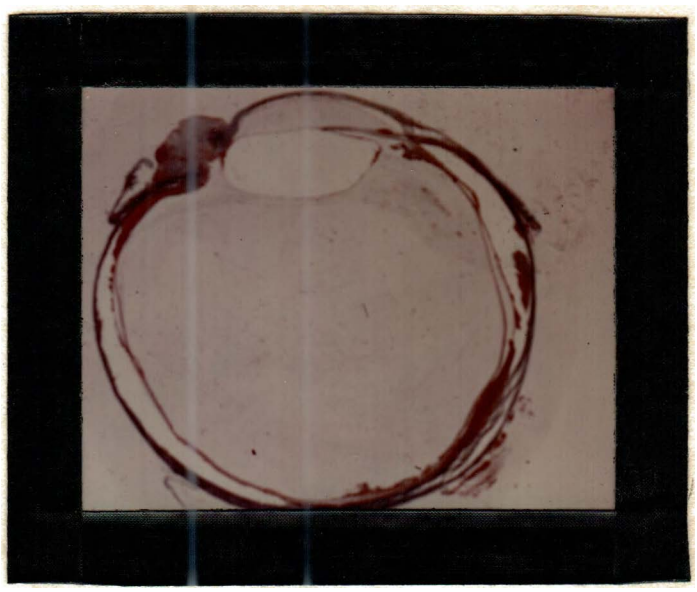


Fig. 6

Case No. 606. Female, 76 years old. Pain in the eye of 6 weeks duration. Somebody outstate did trephine operation. At present time eye has LP, tension 64 mm. Hg. Enucleation 2 days later - 1953; with diagnosis absolute glaucom .

Microscopic: Cornea is irregular, at the limbus trephine opening closed by prolapsed ciliary body and fibrous mass. Filtration angle obliterated by anterior synecchiae. Lens has cataractous changes in the cortex. Areas of hemorrhage in the vitreous and most in suprachoroidal space and in the retina. Marked cystic degeneration of the retina. Marked glaucomatous cupping. Central vein occluded in the area of lamina cribrosa, revealing accumulation of sub-endothelial lipid containing cells, multiple fibrous plaques and thickened outer coating.

increases, blood pigment penetrates into the cornea end damages the corneal endothelium which further upsets the normal balance of intraocular fluid exchange. Hemosiderin deposits change transparency of the cornea and make it appear greenish.

The iris and ciliary body may be injured by blunt trauma of the eyeglobe. Irregularity of the pupil is observed in such cases or mydriasis which follows rupture of the sphincter. Cyclodialysis with massive hemorrhage as well as iris rupture are serious complications and need special attention.

Contusion contrecoup effect upon the retina produces specific changes characteristic of this kind of trauma. Retinal tears with detachment, retinal edema, which later ends in cystoid degeneration, and retinal hemorrhages are the most common findings. The fovea is the most sensitive place in case of commotio retinae and tears are most common in the area along the orra serrata. Retinal hemorrhages are absorbed or are followed by massive glial proliferation. The lens can be involved also. Contusion cataract, with or without rupture of the lens capsule and dislocation of the lens which can be complete or incomplete, can dislocate anteriorly or posteriorly.

Perforating injuries in themselves do not produce the secondary glaucoma; but when perforation is not severe enough and does not require immediate enucleation the scleral or corneal wound heals reestablishing continuity of the outer covering of the eyeglobe, changes in the eye due to trauma, introduced infection, secondary changes, retained intraocular foreign body, massive intraocular

hemorrhage, prolapse of the intraocular tissue, inplantation of epithelial cyst in the anterior chamber; or traumatic cataract upsets the normal physiology of the eye. A more specific description of all traumatic injuries to the eye will be discussed in a later chapter.

Infection and secondary changes which follows it are the most common causes of secondary glaucoma. Infection can be introduced by a perforating injury, by a superficial inflammatory lesion penetrating through the cornea by endogenons or on the basis of hypersensitivity.

Keratitis and corneal ulcers often produce secondary so-called irritation iritis and sterile hypopyon. When a corneal ulcer perforates, microorganisms invade the intraocular space, resulting in acute purulent iritis. Endogenous purulent iritis is rare. When the iris heals during the inflammatory process, connective tissue increases on the stroma. The posterior surface of the iris gets bound to the lens because fibrinous exudate, which develops during the inflammatory stage, is organized; a similar process goes on also in the anterior surface and complete or incomplete obliteration of the anterior chamber angle occurs. Besides bacterial-purulent iritis there is another form of iritis, correctly called inflammatory reaction of the iris. This one is due to noxious agents present in the host's body, such as protein from broken down organisms, some absorbed from intestinal tract and some coming from local infection, and in some instances the origin and even media precipitating such inflammatory

reaction cannot be found or its origin is obscure. In any case, such patients should be checked for possible concurrent systemic infection like syphilis, tuberculosis, sarcoid, etc. This type of inflammatory reaction may also follow injection of antigens to which the patient is sensitive or during active therapy of lues. In this particular group there are three clinically known types. One is multiple minute lesions which can be found microscopically. Externally there can be seen mild scleral congestion and there are practically no subjective complaints. Where these lesions heal, they produce minute foci of fibrons and small adhesions to the lens. The only trouble is that this focal inflammatory reaction recurs every month or year, in a matter of day in rare cases, the final result is complete posterior synecchiae and possibly anterior peripheral synecchiae and finally ends in secondary glaucoma. The second type is that which usually starts abruptly. The lesions are slightly larger and are easily seen with the naked eye. They can be single or multiple and run as acute inflammation leaving perma-nent damage to the iris and post-inflammatory adhesions but which can be prevented if the case is under substantial medical care. Recurrences in this type are rare. The third type starts suddenly and as a violent inflammation. The anterior chamber is usually packed with inflammatory cells and occasionally with fibrin. Marked scleral injection, occasional hemorrhages in the anterior chamber, edema of the iris with marked congestion of its vessels, and small hemorrhages in the anterior chamber complete the picture. The

disease is self-limited and signs and symptoms subside rapidly. Recurrences are common varying from two to three month intervals up to several years. Under good care this type usually does not develop any complications. Photophobia is the main complaint from the patient's point of view. Microscopically, in all these three types of inflammatory reaction of the iris, the cellular pattern predominantly consists of lymphocytes and wandering mononuclear leucocytes dominate the picture. Another type of iritis which often ends in secondary glaucoma is called heterochromic iritis. This disease is practically always unilateral. Its course is very mild but consequences can be serious. During the disease, translucent keratitic precipitates can be observed in the opacities in the anterior vitreous. After repeated attacks the iris loses its pigment. Cataracta complicata and secondary glaucoma is the ending result. In these cases, secondary glaucoma usually is permanently cured by cataract extraction. Etiology of this disease is obscure but it is believed, and some believe that it is confirmed by animal experiments, that it is due to a disturbance of ocular sympathetic innervation without apparent Horner's syndrome. However, if patient has Horner's syndrome at birth, depigmentation of the iris of this particular eye usually occurs without any signs of iritis and people who have acquired Horner's syndrome do not show any changes of the iris nor do they develop such an iritis. Ciliary body inflammation by itself is a rare condition and its etiology is obscure. The specific reactions of the ciliary body epithelium and cyclitic membrane formation

has been described. Clinically, patients are found to have deep scleral injections, vitreous opacities and visual disturbances.

Involvement of the ciliary body and iris in inflammatory processes is called iridocyclitis and by some, anterior uveitis. Here the combined clinical features can be observed and the most dangerous complications are anterior peripheral and posterior synechia and anterior chamber hemorrhages resulting in secondary glaucoma; cyclitic membrane formation causing destructive changes of the eye; and finally phthisis and secondary cataract which also may produce secondary glaucoma.

Endophthalmitis may be exogenous or endogenous. Exogenous is usually the result of traumatic perforating injuries, or penetrating ulcerations and, in this particular occasion, the corneal ulcer. Exogenous endophthalmitis will be discussed in more detail in a chapter about perforating injuries. Endogenous endothalmitis is fairly well known as to its clinical behavior and pathological findings but its etiology is not very clearly understood. Bacterio-logical examination of fluids or tissue, taken from such an eye, fail to give us the answer. Its classification depends on the past ex-perience and correlation with pathological findings. Based upon this it is classified into granulomations and nongranulomations. Cellular morphology was previously described and on this basis two types can be differentiated adding the typical clinical pictures characteristic for each type and adding the acuteness of the condition.

Polymorphonuclear cells in the anterior chamber fluid do not agglutinate and keratitic precipitates, seen under the slit-lamp, are fine. Such a cornea appears frosted with a mignifying aid. In contrast to this, lymphocytes form clumps in the aqueous and keratitic precipitates appear larger when examined with the slitlamp or ophthalmoscope. The largest keratitic precipitates are seen with the presence of epitheloid cells, macrophages and endo-thelial phagocytes, which can be seen even with the naked eye.

A granulomotous uveitis onset is usually insidious. Vascular reaction is slight to moderate. The iris shows nodularity and is especially clearly seen at the pupillary margin but it loses its normal pattern of trabeculation. Secondary cataract possible and posterior synechia are common. Anterior chamber cellular morphology is dominated by epitheloid cells with increased amounts of protein in the aqueous.

A nongranulomatous uveitis onset is acute. Extreme photophobia, lacrimation, blurred vision or even pain, are prominent complaints of the patient. Scleral injection and congestion can be seen very markedly on examination. The iris does not lose its trabeculation pattern but loses its clear appearance or may have a grayish hue and iris vessels are dilated. There is very prominent anterior chamber flare or may even have already visible fibrinous or gelatinous exudate. Posterior or anterior synecchia may occur after few recurrences. During the acute stage, intraocular pressure can be elevated because heavy exudation in the anterior chamber blocks outflow of the aqueous.

Panophthalmitis is a purulent infection of the interior eye. Some ophthalmic pathologists use this term for indication of any purulent infection, regardless of the extent, as long as it is inside the eye. My understanding and use in this paper is that panophthalmitis is a bacterial-purulent infection of the interior eye with all internal structures more or less involved in the inflammatory process, but not indicating that the whole eye is in the state of suppuration. The reason for this is that sometimes we can have, for example, bacterial iritis due to perforation, but without any inflammatory reaction in the retina or inflammatory cells in the vitreous. In this case, I certainly feel that the term panophthalmitis is not justified. On the other hand, when the iris is actively involved in a purulent inflammatory process, and I see cellular inflammatory reaction throughout all the structures, I feel that this term is proper.

Panophthalmitis is usually an infection with virulent pathogenic microorganisms, very rapid in its developement and destructive in action. In case perforation is small enough or is sealed by scar formation, or blocked by prolapsed intraocular tissue, secondary glaucoma is the result. Inability to control the infection necessitates enucleation of such an eye because of the danger of extension into adjacent structures, destruction of the eye by acute inflammatory processes or sympathetic ophthalmia.

Vitreous abscess is one of the worst complications because antibacterial agents cannot, in sufficient concentrations, reach

pathogenic organisms present in the vitreous.

In case acute infection is controlled and secondary glaucoma subsides, the process usually goes into subacute and then chronic stages and usually results in phthisis bulbus oculi. Its clinical picture is of the most violent inflammation, corneal edema, very marked injection and congestion of scleral and conjunctival vessels, edema of the conjunctiva and possibly of the lids and periorbital tissue. The inside of the eye usually cannot be seen because of a whitish-yellow purulent material present in the anterior chamber. General malaise, pain, severe headaches and vomiting are not uncommon symptoms associated with violent panophtholmitis.

Another very important factor producing secondary glaucoma in intraocular hemorrhage is anterior chamber hemorrhage and its causes, already described, and the mechanism producing secondary glaucoma explained.

The wear and tear which blood vessels can withstand are principally dependent on their inherited characteristics and signs of it usually manifest themselves in the senium. In case these signs are found in younger persons, two etiologic factors should be considered; (1) inherited deficiency of the vessel wall and, (2) intensification of wear and tear causing the vessels to become prematurely senile. One of the most important factors in premature changes is the persistent increase in blood pressure or attacks of narrowing of the peripheral arterioles producing temporary nutritional and oxygen supply deficiency to prearterioles and capillaries,

ESSENTIAL IRIS ATROPHY

Fig. 7

Case No. 628. Female, 70 years old, poor vision noted 1.5 years ago, blind for past 6 months. Secondary glaucoma. The iris shows extensive atrophy of the stroma with only pigment layer remaining stretched across from limbus one one side, half way to the periphery on the other. The rest of the iris stroma is thin with few vessels remaining. Enucleation in 1953.

Essential iris atrophy is one of the causes of secondary glaucoma. It is believed that this is congenital vascular disturbance of the minor circle of the iris, a mechanical stretching of the iris which causes narrowing and occlusion of the radial arteries with a nutritional disturbance, c ngenit l anomaly or local abiotrophy (17: 379). Secondary glaucoma du to progressive essential atrophy of the iris is resistant to treatment, is unilateral and more common among women.

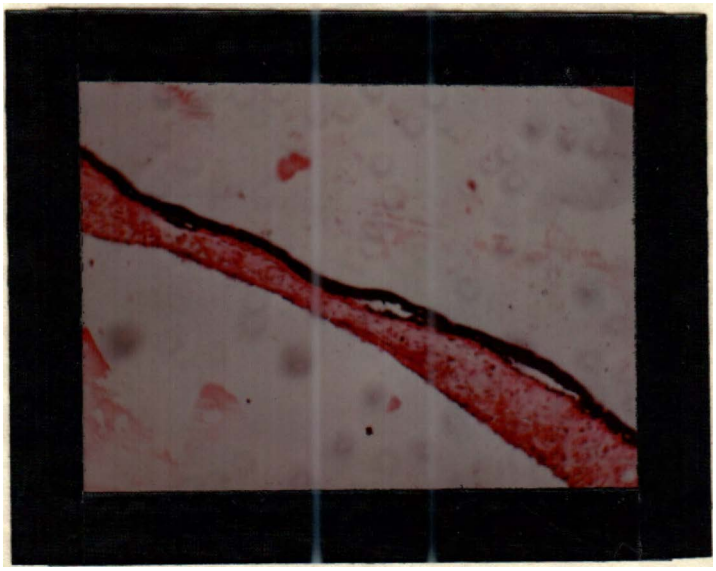


Fig. 8

Case No. 636. Male, no history present. Enucleation - 1953. Iris is thin, irregular loss of stroma, decreased amount of blood vessels, marked loosening of pigment layer. Secondary glaucoma.

which, in turn, initiates primary changes in the vascular wall and afterwards the process takes its course (local vasomotor constriction). Under the conditions following should be listed eclampsia and pre-eclampsia, Raynaud's disease, migrane, mitral stenosis, severe hemorrhage, severe anemia, poisons such as tobacco, excessive intake of coffee (Sedan Foyle), Quinine, polycythemia vera, beri beri glaucoma, lues, angioneurotic hypertension, Bright's disease (constant suboxidation), Renal amiloidosis, periarteritis nodosa, chronic lead poisoning, polycystic kidneys, and tumors of the adrenal medulla.

As Aschoff describes, "We understand by arteriosclerosis a chronic disturbance of the vessels which becomes irreversible on reaching its climax in vessels impaired by changes attending the process of aging with resulting deformation of lumen and brittleness of the vascular wall."(27)

According to Elwyn's explanation (28), arteriosclerosis manifests itself by an increase in the connective, also elastic tissue of the intima and reduplication of the marginal elastic layer, sometimes showing increased connective tissue in the muscularis, all together resulting in the thickening and hardening of the walls. The elasticity of such a vessel is greatly reduced and in the process of advancing pathology, stretching of the vessel wall occurs with resulting temporary dilatation of the vessel and producing a tortious pattern of the vascular tree.

Basic pathological patterns of the sclerotic vessel consists of atherosis, hyalinosis, lipoidosis and nodular deformation. The

process itself is different in various vessels. The well developed intima of the artery first shows a deposit of fat and lipoids in the cells of intima and a very fine lipoid deposit in the ground substance; at the same time, a gelatinous transformation of the ground substance occurs. Such an area of fatty infiltration slowly increases in size and the center becomes liquified, forming an atheromatous plaque. Parallel with this process, a localized proliferation of elastic and connective tissue takes place between the endothelium and atheramatous plaque which prevents the liquified material from breaking into the lumen of the vessel. In case such atheroma breaks into the lumen, an atheromatous ulcer is formed, initiating the focus of thrombus formation. In atheromatons plaque, fatty acids are set free and attract calcium which becomes deposited in this lesion and so processes of lipoidosis, atheroma plaque formation, calcinosis, and nodular thickening of the intima constitutes the picture of the arteriosclerotic vessel.

The pathological process and progress in the arteries of the extremities is different. Here the primary process is deposition of calcium in the ground substance of the connective tissue surrounding the muscle fibers. As the deposit of calcium deposit increases it forms plates which usually arrange themselves in a circular manner.

Again, pathologic progress in arterioles and precapillaries is different. Here the process consists of a deposition of hyaline and hyalinisation of the basal membrane underneath the endothelium.

EXFOLIATION OF THE LENS CAPSULE, SECONDARY GLAUCOMA

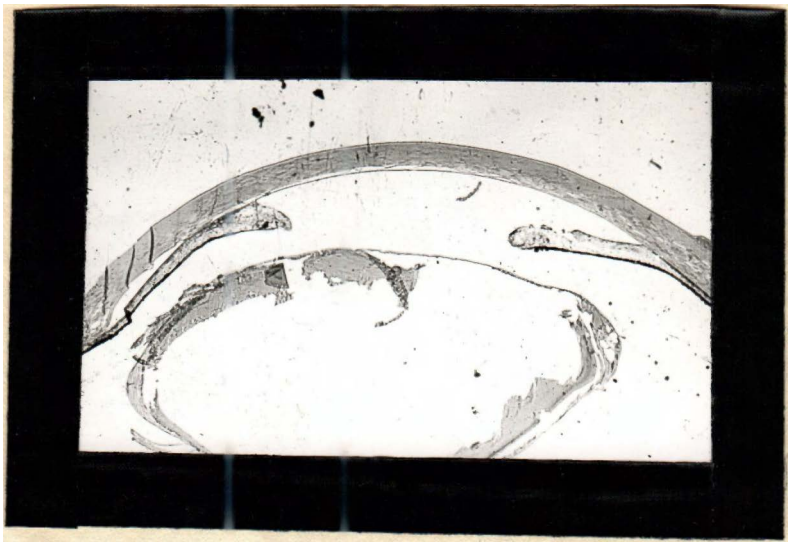


Fig. 9

Case No. 659. Female 80 ye rs old. Progressive loss of vision for past 5 years, painful eye for last 6 months. Cornea clinically cloudy, no LP, AC shallow. Tension over 90 mm. Hg. Enucleation, 1953. Fig. 9 microscopically early bullous keratophothy. Extensive anter-ior peripheral cynecchiae. Reduplication of corneal endothelium in AC angle. Ciliary body is atrophic with advanced hyalinization. Lens is cataractous. Anteri r surface of the lens capsule, ciliary process and posterior surfac of the iris are covered with "baumartig" (branching-arborization) precipitated material.

Fig. 10

Courtesy of
Dr. Gifford

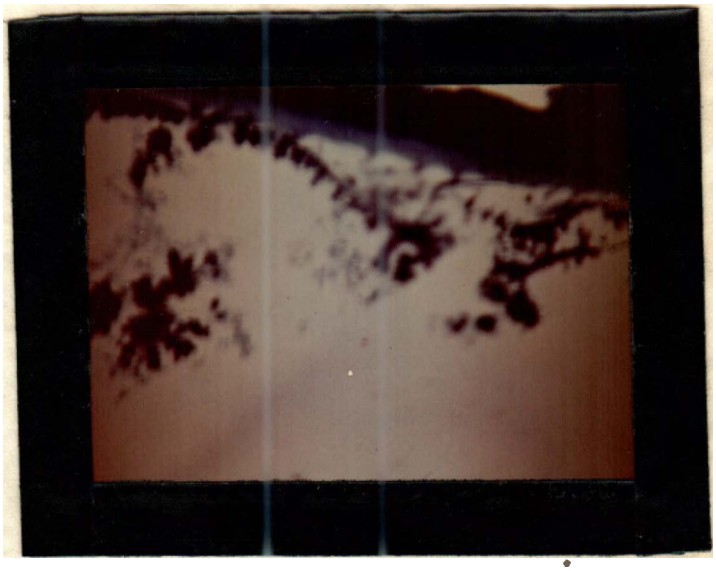


Fig. 10A

Courtesy of
Dr. Gifford

Exfoliation of the le s capsule* causes secondary glaucoma or is found in eyes with prematurely advanced cataracts. In case such a lens is not removed, ye sooner or later goes into status of glaucoma. Etiology of condition known as exfoliation of the lens is not known.

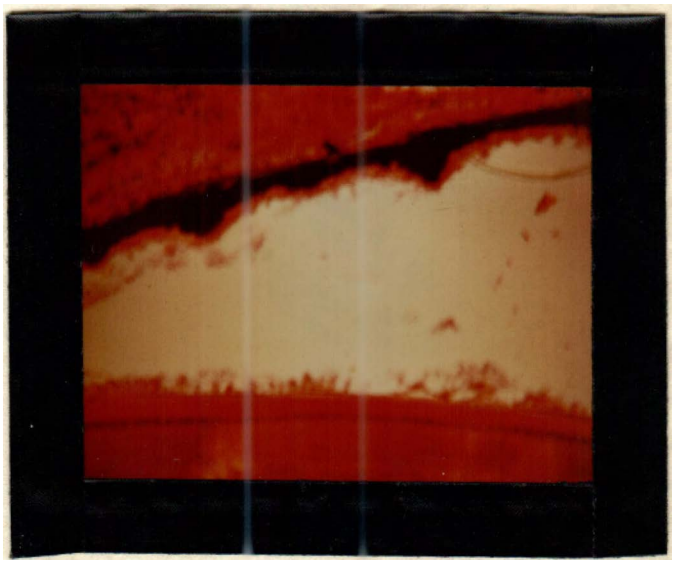


Fig. 11

Courtesy of
Dr. Gifford

* More than three years ago I expressed the opinion that this is not exfoliation of th lens c psule but substance is precipitated on these surfaces. M present professional status does not permit me to express my opinion about the etiology of this condition.

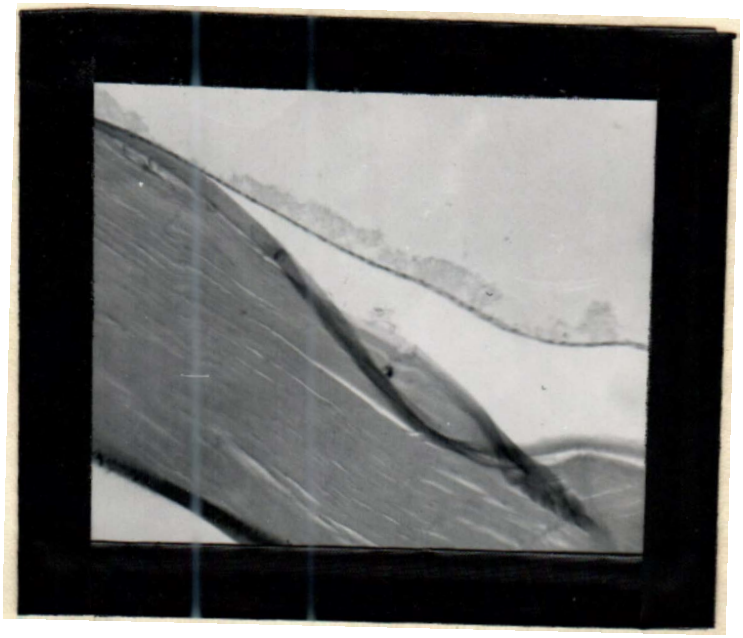


Fig. 12

Figures 10, 10A nd 11 demonstrate the characteristic arborization in cases of exfoliation of the lens capsule.

Figure 12 represents si ilar pattern precipitate in case of chromic endophthalmitis complicated by secondary glaucoma.

Following through multiple microscopic slides it seems that it begins with fibrinoid precipitate but fibroblasts of different maturity, up to fibrills and mature fibrous cells, are also found. The fats and lipoids are found in hyaline material. These changes are basic signs following a disturbance in the nutrition of the arteriole just as the primary deposit of fat in the elastic vessel and calcium in the muscular vessel are results of local disturbances in nutrition.

Diabetes mellitus is responsible for vascular changes characteristic in this particular disease; in addition, producing arteriosclerosis, it demands special discussion. Anyone can recognize the specific vascular changes characteristic for diabetes. The etiology of this pathology is obscure.

It is my belief that diabetes mellitus, in which the mechanism for the maintenance of normal bloodsugar is inherently deficient, instead of retaining its normal stability throughout the life, becomes unstable at birth, in early or middle life. This cause of the instability is not to be found in the effector organs, such as liver, pancreatic islands or peripheral vegetative nerve system but it is to be found in the mechanism as a whole or in its central regulation in the brain. Furthermore, gross pathological changes in the brain cannot be found because this is an inherited weakness of the proper gearing of the individual parts of this mechanism which is already present in the germ plasm. The etiology of blood vessel changes in this condition is also obscure. One thing which

appears certain is that dilatation and prestasis in the terminal vessels are responsible for initiation of the characteristic vascular changes in diabetes mellitus.

Visible arteriosclerotic manifestations in the fundus of the eye, such as, tortuosity of the vessel walls and variations of the arterial light reflex, are important clinically and can be explained in the prior described events occurring in the wall of the blood vessel. Secondary glaucoma, in this case, is a result of intraocular hemorrhage due to the sclerotic process gradually diminishing the lumen of the vessel; occlusion occurs when the bloodflow is so slow that it becomes extremely concentrated and finally coagulates; or obliteration of the vessel occurs, because of encroaching wall tissue into the lumen and obstructing it; or by local thrombus formation initiated by a sclerotic plaque broken into the lumen. Embolic occlusion of the retinal vessels is very rare.

When, in the process of phlebosclerosis, the retinal vein becomes occluded massive hemorrhages, retinal and optic disc edema results. Vision fairly rapidly becomes greatly diminished. At first, some cases have reactive hypotony of the eye but in a few months, in spite of the therapy, the majority of cases develop secondary glaucoma.

The last major secondary glaucoma-producing factor is the intraocular tumor. Benign intraocular tumors which do not grow at all or grow very slowly, cause no symptoms if they are not located in vital points of vision or do not disturb normal biophysiology

SECONDARY GLAUCOMA DUE TO SIDEROSIS

Fig. 13

Case No. 520. Female. No history present. Enucleation in 1950. Foreign body found in ciliary body, size 2x2 mm. which by histochemical reaction identified as iron. Corneal epithelium is discolored by dissolved iron particles (Fig. A), also very marked discoloration is present throughout the whole retina, iris muscles and ciliary body. A.C. trabecular meshwork and Schlemm's canal is packed with orphous discolored material. Ciliary body and iris show atrophic changes. Cataractous lens is dislocated posteriorly. There is recession of the lamina cribrosa.

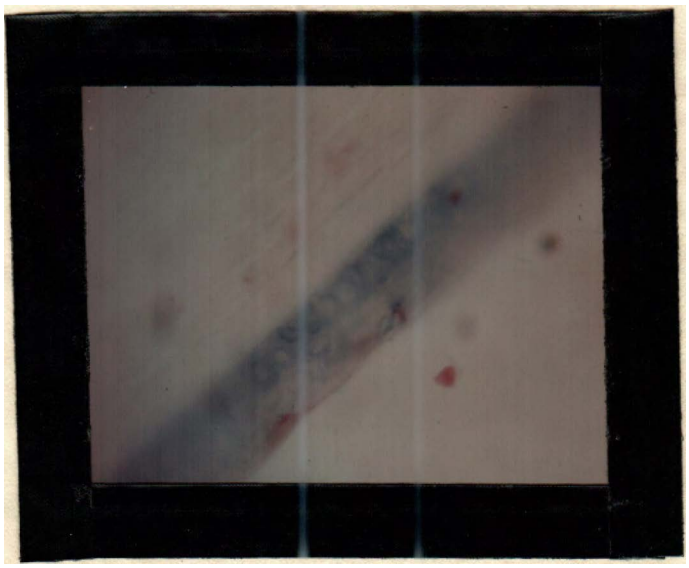


Fig. 13A

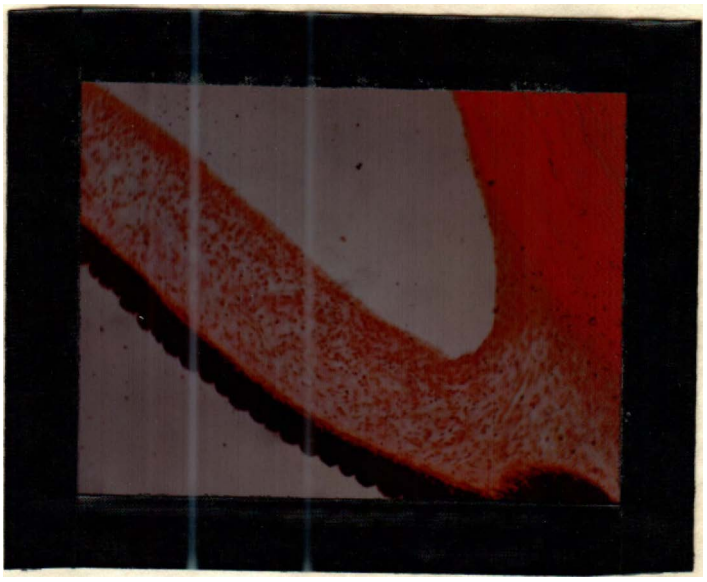


Fig. 14

Case No. 521. Female; ge of the patient not given. Eye has been larger since infancy. Vision LP, tension 56 mm. Hg.

Fig. 14 represents filtration angle which in deep, chamber angle is obliterated by the iris tissue which starts in area at the end of Descement's membrane, increased fibro tissu amount fills the trabeculae. Schlemm's canal not dem nstrated.

of the eye. Malignant tumors, if the eye is not enucleated early enough, sooner or later produce a true picture of secondary glaucoma. Tumors will be discussed in more detail in a later chapter.

Eyes which had to be enucleated because of uncontrolled increased intraocular pressure have many different interesting pathological findings. From the summarized tables following we can see exactly what was taking place in such an eye. Injuries and infections and their complications, dominating the field of causes, reflects clearly the necessity to look soberly into the problems of preventive measures against injuries and to look for more effective ways and means of controlling the inflammatory process in case of infection or inflammatory reactions from which some are not yet completely understood.

Loss of an eye because of secondary glaucoma, during the past twenty-five years totaled 185 from 469 cases, or 39.5%. This is a very impressing percentage. But how does it look when it is broken down into definite periods where medical science really made its steps forward? In the pre-sulfo period, we have 107 specimens from which 40 of them were labeled secondary glaucoma, or 37.5% of the total; in sulfonamide period the total specimen count shows 131, secondary glaucoma, 56, result - 42.6%; and finally the last period of antibiotics in combination with sulfonamides, the number of specimens being 231, of these, 89 were glaucoma cases and the result as 38.7%. Actually there is an increase of cases. Why?

TABLE NO. 6

INCIDENCE OF TRAUMA IN SECONDARY GLAUCOMA

	1929-1937	%	1938-1945	%	1946-1955	%	Total	%
Traumatic Contusion	8	20	9	16.1	7	7.8	24	12.9
Traumatic Performation	11	27.5	13	23.2	18	20.2	42	22.7
Surgical Perforation	3	7.5	5	8.9	5	5.6	13	7
Chemical Trauma	-	-	1	1.8	2	2.2	3	1.7

TABLE NO. 7

TRAUMATIC LESIONS IN EYES WITH SECONDARY GLAUCOMA

Aphakia	4	10.0	6	10.7	10	11.2	20	11.4
Displacement of the Lens	2	5.0	1	1.8	10	11.2	13	7.0
Traumatic Cataract	6	15.0	4	7.1	20	22.5	30	16.8
Surgical Extracapsular Cataract Extraction	1	2.5	3	5.4	4	4.5	8	4.3
Prolapse of Inner Contents of the Eye	5	12.5	-	-	2	2.2	3	1.7
Retained Foreign Body	6	15.0	1	1.8	10	11.2	17	9.2
Siderosis	4	10.0	1	1.8	8	8.9	13	7.0
Retinal Detachment	11	27.5	9	16.1	21	23.6	41	23.2

TABLE NO. 8

VASCULAR LESIONS IN SECONDARY GLAUCOMA

	1929-1937	%	1938-1945	%	1946-1955	%	Total	%
Intraocular Hemorrhage*	23	57.5	18	32.1	32	35.8	73	39.5
Central Vein Occlusion**	5	12.5	3	5.4	8	8.9	15	8.7
Anterior Chamber Hemorrhage***	7	17.5	3	5.4	5	5.6	15	8.1
Central Artery Occlusion	-	-	-	-	1	1.1	1	0.6
Proliferating Retinopathy	1	2.5	2	3.6	5	5.6	8	4.3
Rubiasis Iridis	1	2.5	1	1.8	3	3.3	5	2.7

* Intraocular hemorrhage is usually traumatic; some cases should be considered but not included here because there was no history and it happened that in sections made for microscopic examinations no occlusion was possible to demonstrate.

** Cases included with definite history or findings under microscopic examination.

*** Cases where just anterior chamber hemorrhage was present.

By analysis of the microscopic preparations made from the specimens enucleated because of secondary glaucoma, we can see that that (Table No. 6) 20% of the eyes which suffered contusion in the presulfo period were enucleated; 16.1% in the sulfo period and just 7.8% in the period of antibiotics. There is no direct connection of this particular lesion with the progress of therapeutic agents, but indicates improvement of general therapeutic management and indirectly for new drugs which frequently prevents secondary

TABLE NO. 9

INFLAMMATORY LESIONS IN SECONDARY GLAUCOMA

	1929-1937	%	1938-1945	%	1946-1955	%	Total	%
Corneal Ulcer - Perforated	5	12.5	2	3.6	1	1.1	8	4.3
Active	5	12.5	3	5.4	1	1.1	9	4.9
Healed	4	10.0	8	14.3	2	2.2	14	7.6
Active Keratitis	4	10.0	-	-	1	1.1	5	2.7
Iritis (only)	6	15.0	2	3.6	1	1.1	9	4.9
Anterior Uveitis (Iridocyclitis)	23	57.5	14	25.0	10	10.1	47	25.4
Endophthalmitis	2	5.0	9	16.1	30	33.6	41	22.2
Panophthalmitis	9	22.5	3	5.4	3	3.4	15	8.1
Vitreous Abscess	-	-	-	-	1	1.1	1	0.6

TABLE NO. 10

POST-INFLAMMATORY CHANGES IN CASES OF SECONDARY GLAUCOMA

Posterior Synecchiae	8	20	3	5.4	1	1.1	12	6.2
Anterior Peripheral Synecchiae	17	42.5	9	16.1	6	6.7	32	17.3
Iris Bombé	-	-	1	1.8	5	5.6	6	3.1
Cyclitic Membrane	2	5.0	1	1.8	3	3.3	6	3.1

---

invasion of microorganisms when superficial layers of the eye coating are interrupted.

Traumatic perforation which ended in secondary glaucoma also shows a decline of 27.5% in the presulfo period, 23.2% in the sulfo period and 20.2% in the antibiotic period. Here it reflects definite improvement of management of perforating lesions inspite of a marked increase, as you see in a later chapter, in the number of violent traumatic injuries in recent years.

Surgery and its safety are reflected in numerals representing postsurgical complications which usually are of an inflammatory nature and as a result of it, ended in secondary glaucoma as follows: 7.5% in the presulfo period, 8.9% in the sulfo period and 5.6% in the antibiotic period. It seems that the use of antibiotics post-operatively achieved this progress.

Chemical trauma shows an increase in number in recent years but this is because more chemical compounds are used now in the household than 20 years ago and it does not reflect directly on our progress in management. Knowing the approximate amount of cases nowdays and 12 years ago when I just started to work in the eye hospital in Lithuania I dare to state that a comparatively much greater part of such cases are cured now than were then.

Table No. 7 represents the traumatic lesions which complicated the process of healing or contributed factors partially or totally in the development of secondary glaucoma. From pathological changes which may complicate the primary injury in the loss of the lens, keeping about this same level in numbers, extracapsular cataract extraction and retinal detachment later shows a marked increase

this being contributed by an increase of traumatic cases. A similar pattern, retinal detachment, also shows traumatic cataract which frequently initiates increased intraocular pressure and, contributing culture media for microorganisms, helps spread the infection because therapeutic agents usually do not reach the inside of the disorganized mass of the lens material. Prolapse of the inner contents of the eye, which is more common in recent years, shows declining numbers because surgical management supported with antibiotic therapy very frequently gives good results.

Retained foreign bodies and siderosis goes hand in hand because most of the foreign bodies were of the iron origin. Siderosis may alone cause secondary glaucoma and toxicity of dissolved iron is not explained completely at the present time. The technique of the removal of foreign bodies in many cases is greatly advanced. About 20-30 years ago metallic foreign bodies were left in the eye; now they are removed and such an eye is given a chance of recovery and is usually supported by antibiotic therapy.

Dislocation or subluxation of the lens is a possible factor initiating secondary glaucoma. This, as with traumatic injuries of the eye, is increasing in number. Extraction of such a lens is the only treatment known and this has to be accomplished as soon as possible.

Vascular lesions can be secondary to trauma or infectious processes in the eye or can be primary factors initiating secondary glaucoma. Looking through Table No. 8, we see that of the eyes with

secondary glaucoma had one type or another of intraocular hemorrhage or vascular lesions which can be responsible for the development of this condition. The later group includes central vein occlusion which shows a definite increase in recent years; rubeosis iridis has a similar pattern and proliferating retinopathy. Central vein occlusion, as stated previously, is a condition of the senium, giving only an impression that our average age and tension of our civilized life is increasing. Therapeutic agents and the management of this condition is still unsatisfactory. Proliferating retinopathy is a result of some trauma which can be mechanical or infectious. It is increasing too, indicating that more eyes survive after serious damage and have time to develop this secondary condition of repair, or can go along with condition of rubeosis iridis because both conditions are found in diabetes mellitus and can be precipitating factors of secondary glaucoma. Its increase in number indicates that management of the diabetic patient is better today and patients survive longer, having time to develop these changes in the eye. Much can be said about this condition, but prevention of it at the present time is not very advanced and many studies are needed in this field.

Inflammatory lesions found under microscopic examination are summarized in Table No. 9. Superficial and anterior segment of the eye inflammatory lesions demostrate clearly the effect of new drugs. These are corneal lesions, iritis, and iridocyclitis. Perforated corneal ulcer, found in 12.5% in the presulfo period,

dropped to 3.6% in the sulfo period and finally to just 1.1% in the antibiotic period. A very similar pattern is seen in cases with active corneal ulcer. Keratitis, due to infection, was common before sulfonamides were put to use and just one accidental case was found in recent years of the antibiotic period.

Iris and ciliary body involvement in inflammatory processes shows a definite decline with advancement of new drugs, dropping from 72.5% in the presulfo period to only 11.2% in the antibiotic period.

A reverse picture is presented in two inflammatory lesions of the eye. These two lesions are panophthalmitis and endophthalmitis. Panophthalmitis shows a decline as new therapeutic agents are started but endophthalmitis is increasing in number.

Panophthalmitis, as was discussed earlier in this chapter, is an inflammatory condition of the eye structures due to bacterial invasion or, in other words, a purulent inflammatory process. This lesion is progressively controlled by new drugs as demonstrated in Table No. 9, being found in 32.5% of the eyes with secondary glaucoma in the presulfo period, 5.4% in the sulfo period and just 3.4% in the antibiotic period.

Endophthalmitis, in some instances, has an unknown origin but it seems that when more eyes are saved by controlling the purulent infection, very often these eyes go into a sterile inflammatory process and end with secondary glaucoma or phthisis. Here it seems to be the actual cause, inspite of new drugs and better surgical

technique, for secondary glaucoma still being as high in frequency as it is.

Table No. 10 represents the complications that occur during or as a result of the inflammatory process. All of these changes may be the factors of irreversibility of secondary glaucoma when the healing process is completed. Actually, these changes are just part of a natural repair mechanism during the inflammation but they upset the physiological mechanism of fluid circulation by obstruct-ing normal channels of flow. These changes show definite decline with the therapeutic progress of drugs and keeps approximately parallel with declining inflammatory lesions of the cornea, iris and ciliary body. In other words, our present drugs may be admin-istered in the anterior segment of the eye and have sufficient concentration to achieve control of infection.

In conclusion of this chapter we can say that secondary glau-coma is still and will be one of the major factors for enucleation of the eye as long as our preventive measures do not reach larger masses of the population because trauma and secondary infection is a major factor in initiating secondary glaucoma. Drugs that we have now are effective in the anterior segment of the eye but studies are necessary concerning the way to reach adequate concentrations in the parts of the eye where fluid exchange is slow.

Endophthalmitis presents a new task to our profession. It needs to be better clarified with a development of therapeutic agents. The surgical progress is adequate in combination with therapeutic

agents in our hands.

Secondary glaucoma in association with intraocular tumors will be discussed in a later chapter.

CHAPTER VI

TRAUMATIC INJURIES OF THE EYE

From a total of 469 enucleated eyes in the last quarter century, 220, or 46.9% were due to trauma with all the complications possible to be expected with injuries. Ninety-one of them were taken out because of immediate destruction of the eye during the trauma or because of early complications. All of the eyes had perforating injuries. Eighty-two had delayed complications and were enucleated because of secondary glaucoma. Thirty-three healed after trauma but underwent degenerative changes and reached the stage of phthisis.

Having such a great number of cases where injury directly caused immediate loss of the eye, or initiated further complications, I feel the subject of trauma to the eye should be discussed in detail.

Nebraska, primarily an agricultural state besides having a fairly well developed industrial center right here in Omaha, has its typical injuries particular to this part of the country. Besides the injuries of professional character there are a few which are from carelessness and some which come from the fact that the state legally permits children to own and use firearms.

Professional hazards and their results are reflected in injuries such as steel particles penetrating the eyeglobe, blast injuries, cattle's horns, cattle's tails, corn stalks, branches, etc., all of which occurs among laborers, factory workers, road gangs, farmers, etc. Among children, which are represented in a high number, the BB gun accidents are far greater than any other, such as knife wounds, toys, milk bottles, etc. Chemical injuries are seen quite often in office practice, but the present modern treatment in most

cases are saved and do not reach that stage of complication which would necessitate enucleation.

I visited a few factories and corporations in the immediate vicinity just to satisfy my own personal curiosity and was left with an impression which forces me to say that the use of preventative measures and the teaching of workers to protect themselves is low in comparison with industry in eastern states and that in Germany before the war.

To clarify the possible pathology in case of injury, I shall discuss it stressing the injuries found among eyes lost in our area. To keep some order in discussing this particular problem it is necessary to divide them into penetrating or perforating and nonpenetrating or nonperforating injuries. Perforating injuries can be due to laceration, rupture, surgical incision, punctures and injuries caused by foreign bodies which have enough velocity to penetrate through the lids, cornea or sclera. The seriousness of a perforating injury depends on extent, depth and structures involved. Laceration type injuries mostly involve the cornea. Sudden loss of the anterior chamber fluid causes prolapse of the iris or even the lens. Laceration may be large enough so that it involves the sclera and ciliary body. Blunt force of sufficient violence causes rupture of the globe. Destruction in this type of injury is usually great. Rupture of the ocular coats occurs at the point of the force implied, countrecoup at the point of weakness, or according to the motion of fluid and semifluid contents of the eye, which can be

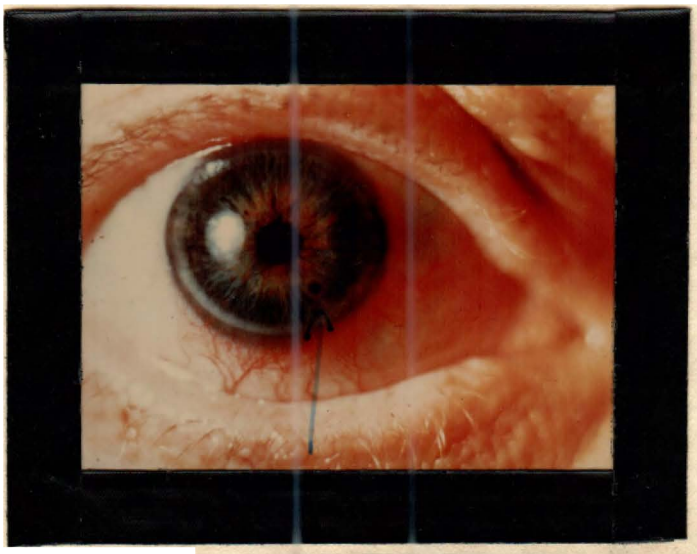


Fig. 15

Corneal Foreign Body.

Courtesy of Dr. S. Sugar.

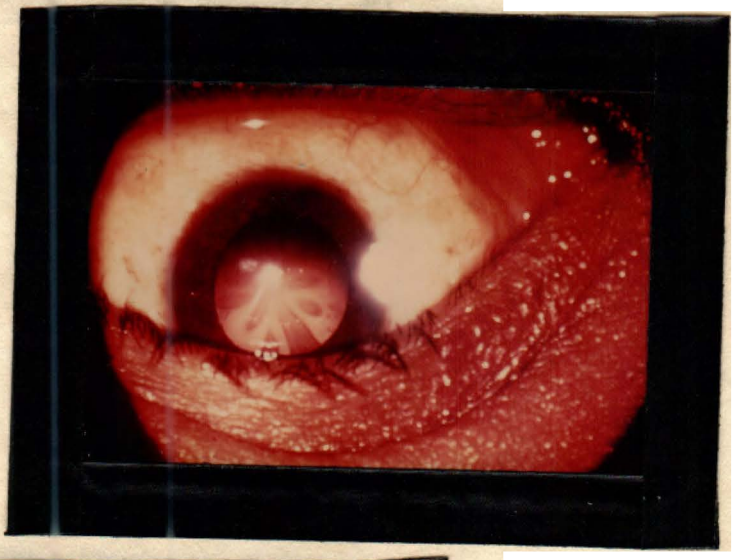


Fig. 16

Anterior Dislocation of the Lens.

Courtesy of Dr. Vickery

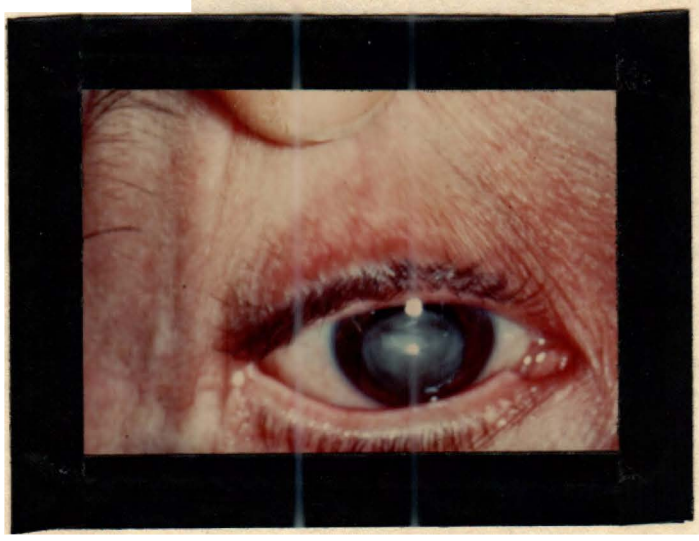


Fig. 17

Dislocation of the Lens.

Courtesy of Dr. Vickery

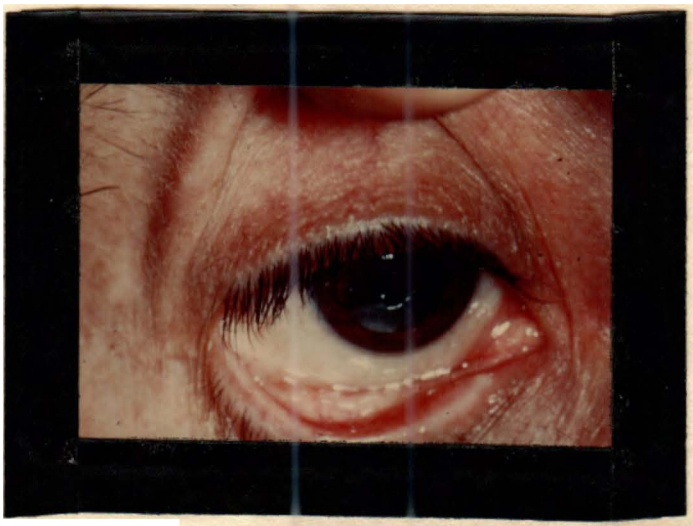


Fig. 18

Dislocation of the Lens.

Courtesy of Dr. Vickery

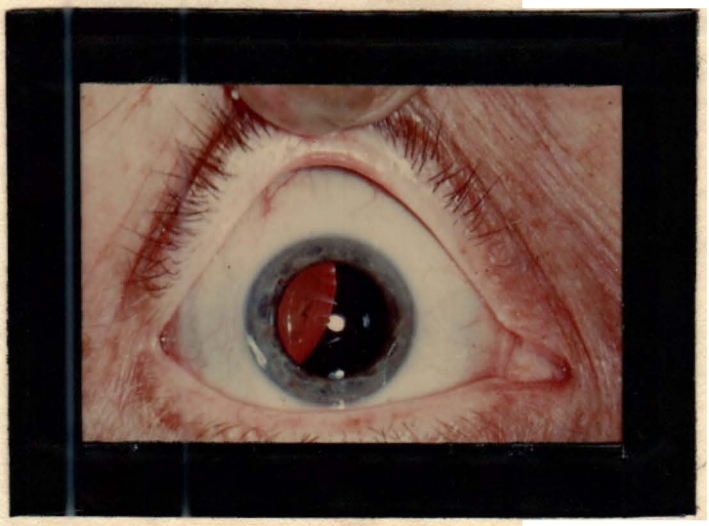


Fig. 19

Dislocation of the Lens.

Courtesy of Dr. Vickery

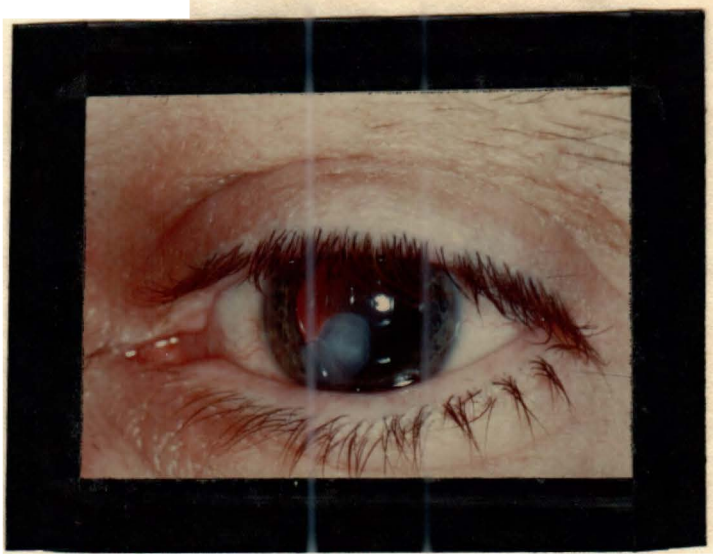


Fig. 20

Corn al Ulcer

Courtesy of Dr. Judd.

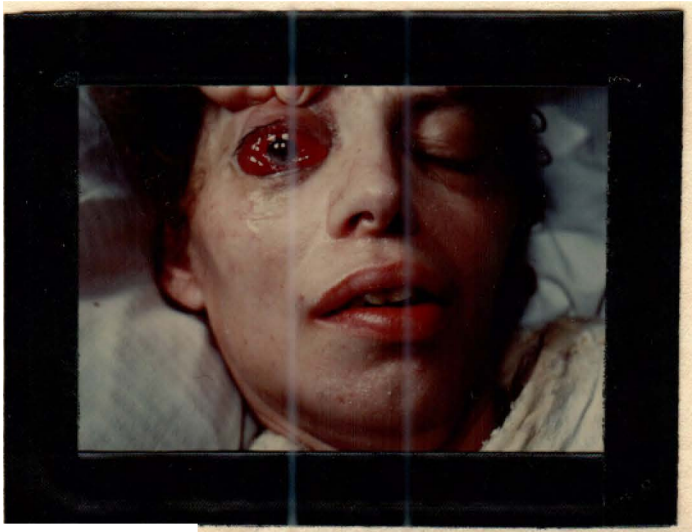


Fig. 21

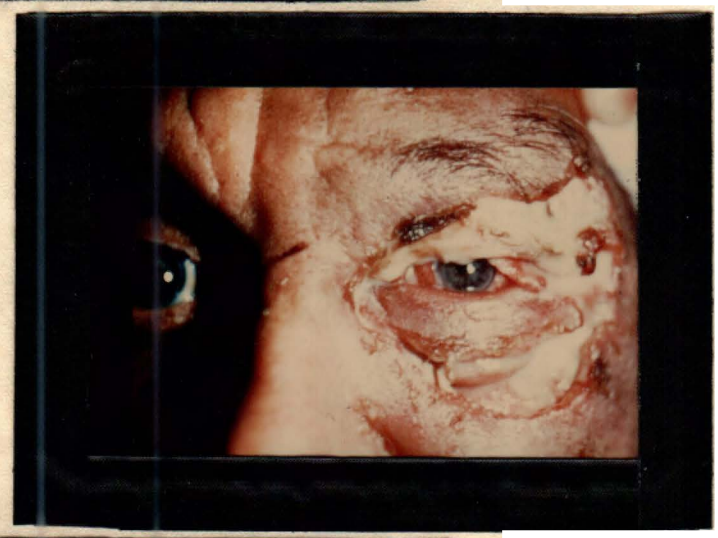
Traumatic Evulsion of the Eye.

Courtesy of Dr. Rasgorshek

Fig. 22

Chemical Trauma

Courtesy of Dr. Sugar



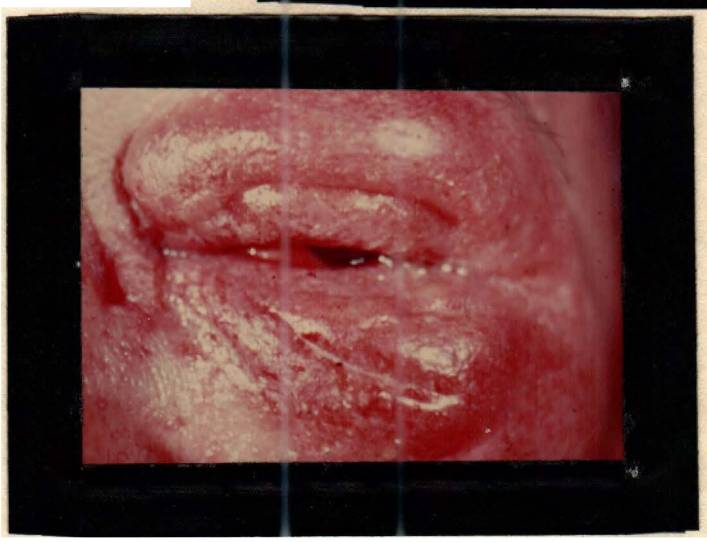


Fig. 23

Hypersensitivity Reaction.

Courte y of Dr. Judd

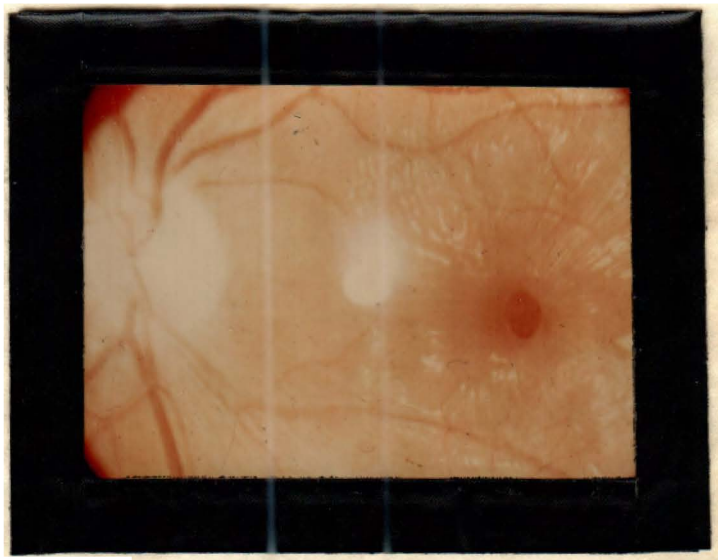


Fig. 24

Macular Hole
after Contusion

Courtesy of
Dr. Vickery

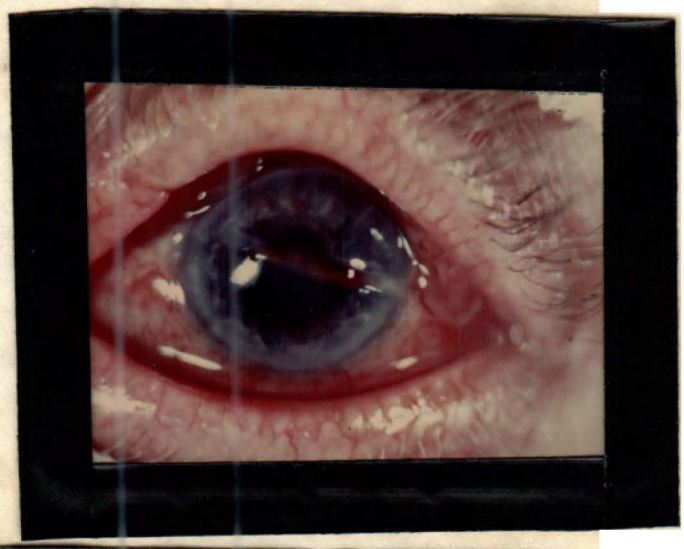


Fig. 25

Corneal
Laceration

Courtesy of
Dr. Judd

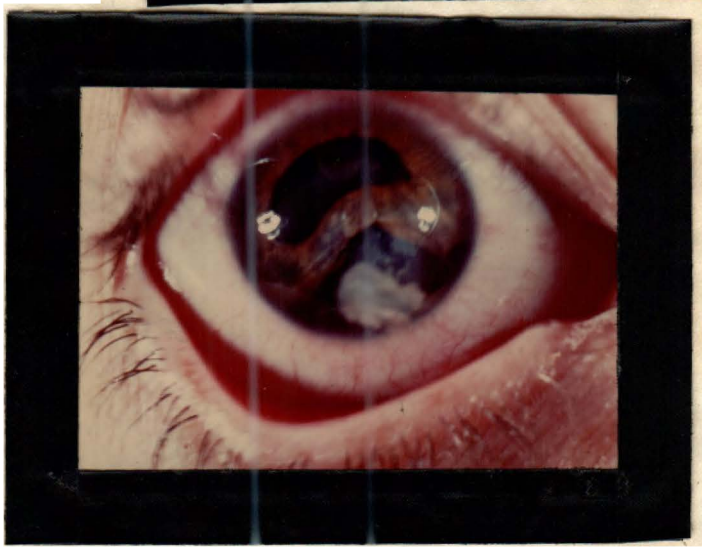


Fig. 26

Traumatic Rupture
of the Root of
the Iris.

Courtesy of
Dr. rrison

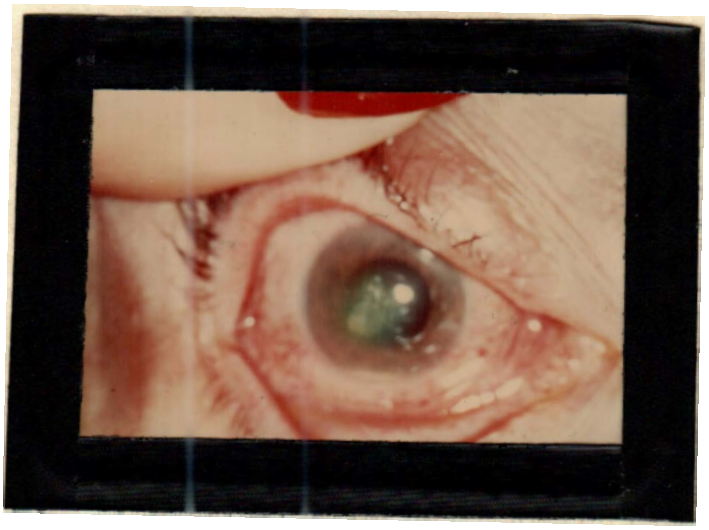


Fig. 27

C rneal Ulcer.

Court sy of Dr. Judd

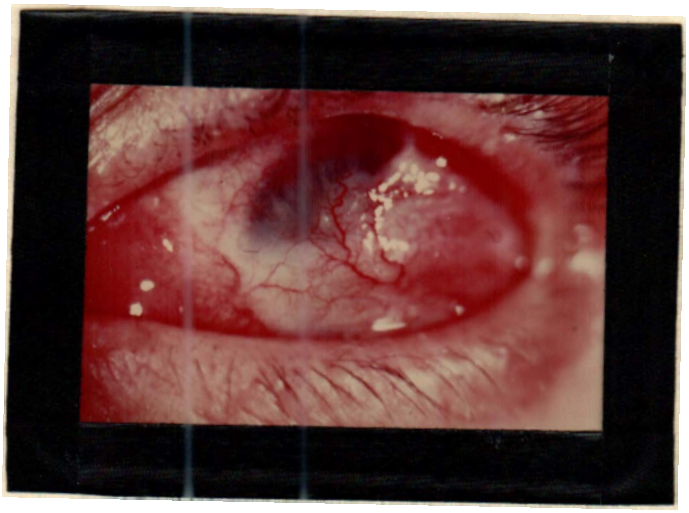


Fig. 28

Late Results of Chemical Trauma.

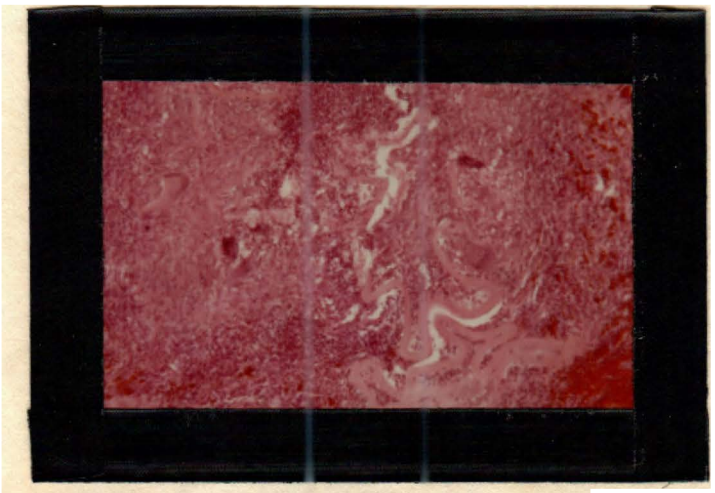
Courtesy of Dr. Judd

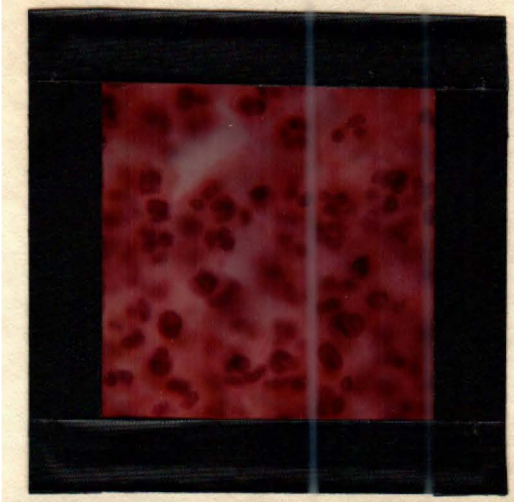
proven by physiomathematical calculations.

In case of surgical wounds, the most commonly involved structures are the lens capsule and iris. Prolapse of the vitreous or uveal tissue causes the most complications resulting in delayed wound healing, secondary infections and downgrowth of the epithelium.

Punctures are the most treacherous injuries of all. Externally they usually appear insignificant and very often heal per primam faciem, but what is left from this little wound often causes considerable grief to the physician and sometimes the loss of the eye to the patient. It has to be emphasized here that puncture wounds cannot be taken lightheartedly. It must be realized that the depth of penetration and the potential infection are two major problems which must usually be coped with. Such injury may involve the cornea, iris, lens, vitreous, choroid, sclera and the track of the injuring object may end somewhere in the retro-orbital tissue or even in the intracranial cavity. It is very possible that in such cases, pathogenic organisms were seeded all along the path of the penetrating object and here we have the problem on our hands which can be serious immediately or become serious when we think that we have taken care of this small wound somewhere in the cornea. Purulent meningitis, intracranial abscess, suppuration of the retrobulbar tissue and acute panophthalmitis may be the end result. Punctures penetrating the ethmoidal or frontal sinuses open spaces which are seldom steril. Involvement of the lacrimal ducts needs early recognition in order to prevent suppuration and scarification strictures,

PANOPHTHALMITIS FOLLOWING PERFORION INJURY





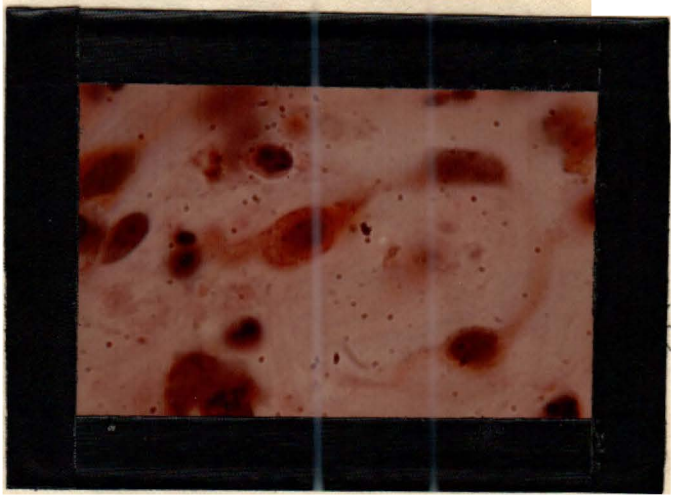


Fig. 29

Case No. 639. Male, 6 years of age.

Eye was struck by dart. Local physician treated this eye by local administration of drugs for three days until patient was admitted to the hospital. On admission, temperature was 102° F., some rigidity of the neck, periorbital edema and purulent material filled entire conjunctival sack covering the eye, AC was filled with yellow purulent exudate, iris not visible, intraocular tension low. Micrococcus pyogenes and*

--Fig. 29A

* gram positive rods were cultured. Systemic antibiotic therapy rapidly brought temperature to normal and meningeal signs disappeared. Ten days later, patient was dismissed and ordered to come

(con't) Fig. 29B

PANOPHTHALMITIS FOLLOWING PERFORION INJURY
(con't.)

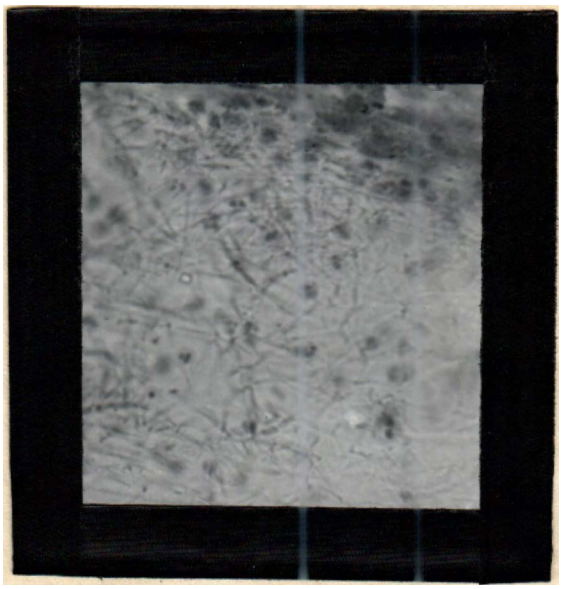


Fig. 29C

(con't. from p. 74a)
back in six weeks to have this eye enucleated. Enucleation, 1953.

Eye underwent phthisic changes and stayed moderately inflammed inspite antibiotic therapy.

Microscopically, perforation found near the center of the cornea. AC shallow and iris and residual of the lens material with capsule adherent to the posterior surface of the cornea (Fig. 29). Practically all cortical material absorbed and capsule is wrinkled. Dense cyclitic membrane. Shallow AC filled with fibrin coagulum with polymorphonuclear cells (Fig. 29C). Iris necrotic and also infiltrated by polymorphonuclear cells (Fig. 29D). Fig. 29A demonstrates cellular morphology predominant cell being polymorphonuclear leucocytes and a few plasma cells. Fig.29B shows young fibroblasts, polymorphonuclear cells & lymphocytes found in forming corneal scar.

Fig. 29D

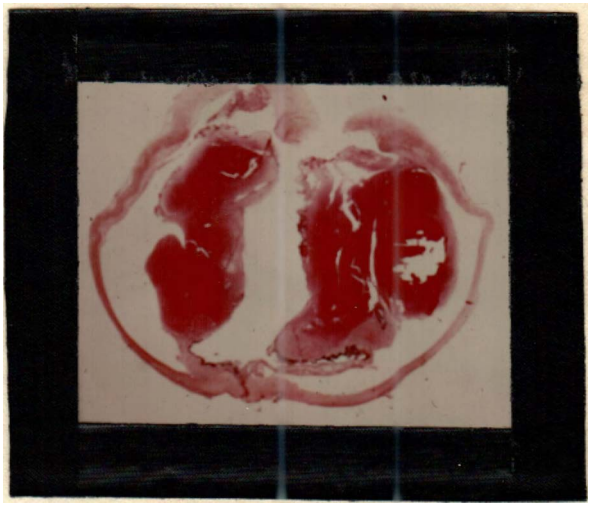
or, if severed, need recognition as soon as possible to establish the continuity of them.

The same must be said of intraocular foreign bodies. Very often, intraocular foreign bodies are very small and the majority of them are metallic. The wound, in such a case, is very small, but infection, injury of vital parts of the eye, and toxicity of the foreign bodies-intraocular-should be kept in mind. Among cases of eyes examined with retained foreign bodies was one with a piece of button, two with a BB pellet, one with multiple gravel pieces from explosion, two of plant origin, one brass, one copper and the rest had iron origin foreign bodies. The majority of magnetic foreign bodies can be removed by using a giant magnet. In case the original injury is not too great and there are no secondary complications, fair or even good vision may be expected, but in case of massive hemorrhage or infection, enucleation is very often necessary. In-fection may be controlled sometimes and the eye saved, but even then there is a great chance that the eye will go into progressive degen-eration and end with phthisis.

Ferrous retained foreign bodies and its alloys results in siderosis. The degree of siderosis and the time it starts depends on the number of particles, solubility, position in the eye and their encapsulation. It is a generally accepted thought that siderosis develops one year after such a foreign body enters the eye globe (17: 169), but in our own collection we have one case where definite siderosis was demonstrated three weeks after the accident and more in less than one year

TRAUMATIC INJUR WITH LOSS OF INNER CONTENTS OF THE EYE

Fig. 30



Case No. 573. Female, 11 years old. ye was struck with golf ball, immediate enucleation - 1952.

Multiple laceration through cornea and sclera. Around lacer tion there were already polymorpho-nuclear leucocytes infiltration.(Fig. 30 A) Whole globe was filled with blood (Fig. 30B). In the corneal wound were prolapsed iris & fr gments of lens capsule. There was no retina and very little of vitreous.

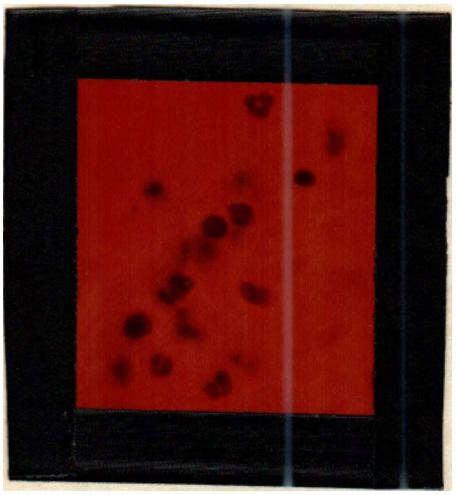


Fig. 30

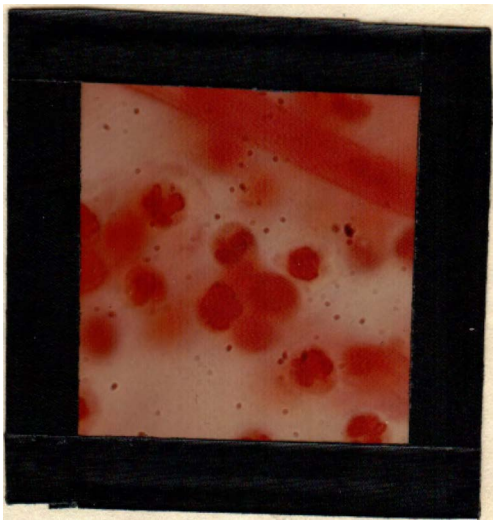
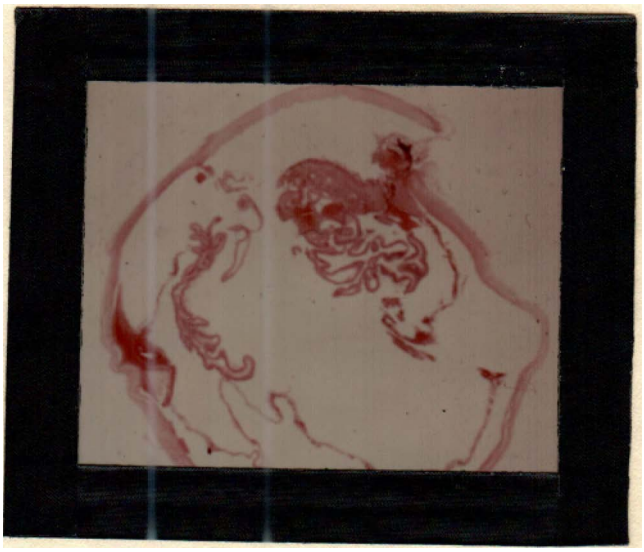


Fig. 30B

TRAUMATIC PERFO TION WITH LOSS OF INTRAOCULAR STRUCTURES



Case No. 559. Female, Age two years. Her older brother dropped milk bottle and fragment of the glass flew, penetrating through he lids and perforating the eye. Enucleation next d y - 1951.

Fig. 31 represents the extent of destruction done by such trauma. Lens an part of the iris absent. Wound is 5 mm. long in anterior segment of the eye. Prolapsed tissue in the wound consists of iris ciliary body and some vitreous; all prolapsing tissues and edges of the wound are heavily infiltrated by polymorphonuclear leucocytes. Vitreous is filled with detached and disrupted retina; also choroid is separated by ubchoroidal hemorrhages.

Dissolved ferrum are taken up by the cells and epithelial structures take up the greatest part. The toxic effect of the ferrous ion is very strong and under its influence the retina under-goes rapid atrophy, the retinal vessels become occluded and may cause cataract formation and secondary glaucoma is very frequently an end result of siderosis.

Copper and brass are as toxic as iron, producing similar reactions in the eye. Being non-magnetic, such foreign bodies present special problems in their removal.

Eyeglobe injuries by blunt objects may cause contusion, or, if severe enough, rupture of the globe. Rupture of the globe in this instance usually is associated with great amounts of destruction of the structures inside the eye and also prolapse of the inner ocular tissues.

Contusion without disruption of the sclera may also result in magnifold destructive lesions of the structures inside the eye. The most common are: retinal detachment, intraocular hemorrhages, rupture of the iris sphincter, rupture of the iris at the pupillary margin or at the root, a tear through the scleral spur, retinal and preretinal hemorrhages, rupture of the choroid which has a characteristic location between the optic disc and macula, and dislocation of the lens. Later sequellae from contusions are also multiple as in contusion cataract, which, as a rule, is rosette-like in appearance and located in the posterior cortex. Hemorrhage in the anterior chamber frequently results in formation of secondary

membranes which block the anterior chamber angle and produce secondary glaucoma. Secondary glaucoma may also be the result of intraocular hemorrhage in the posterior part of the eye. Counter-coup force in instances of contusion produces a known feature called commotio retinae. Marked edema of the retina is very frequently associated with hemorrhages in different sizes and locations. Such a retina undergoes a more or less degenerative process after such injury and hemorrhages are absorbed or organized into membranes mixed with glial tissue producing a known picture of traumatic proliferative retinopathy. Retinal tears most commonly occur along the ora serrata and retinal detachment follows the accumulation of the fluid.

Thermal, particularly chemical burns of the eye and the lids, is fairly common in this state. Such injury produces necrosis of the involved structures and heals by dense scar formation, which distorts the lids or produces adhesions between the eyeglobe and the lids, this being known as symblepharon. Corneal burns are followed by ulceration, slow healing and formation of the opacities.

From the chemical agents most commonly causing injuries of the eyes are lime, lye, ammonia, sulfuric acid and phenol. The most unpredictable burns are produced by alkali and at first they do not look severe but a few hours later the extent of damage increases due to the inability of the tissues to neutralize, and acid penetration is limited by a buffering reaction.

Radiant energy also plays an important role in producing ocular lesions but their damage very seldom induces such lesions that it

would be necessary to enucleate the eye, but sometimes contributes to the initial factor for further complications or impairs the normal function of this organ. Types of radiant energy that should be mentioned are visible light and its fractions and ionizing radiant sources.

Direct visible light in excess injures the retina and leaves permanent scotomas. Injury here occurs because of large amounts of energy concentrated on relatively small areas producing a burn-ing effect on the spot. Coagulation occurs in the cells of this area and death of those cells follows. This is usually seen among people who have lost their lenses because of cataracts as the lens absorbs a great deal of infrared waves. Ultraviolet ray damage to the eye is superficial and produces a known pathological picture named keratoconjunctivitis rivealis. Healing, if not complicated by infection, is usually rapid.

Roentgen and radium damages are now rare because past experience has taught about dangers and protective measures were applied. The most common complication from such sources of irradiation was and still is secondary cataract or loss of eyelashes or eyebrows when, for therapeutic reasons, this area has to be irradiated. Retinal lesions in the form of exudates and hemorrhages are observed among the patients requiring whole body irradiation.

One more source of energy that produces injury to the eye and is quite common is electric shock. Resulting damage ranges from acute conjunctivitis--effect of ultraviolet light--and directly--

cataracts that develop with great rapidity producing diffuse cloudiness of the lens.

TABLE NO. 11

TRAUMATIC INJURIES

	1929-1937	%	1938-1945	%	1946-1955	%	Total	%
Perforating Injuries	25	52.1	35	56.4	79	71.9	139	63.3
Contusion	9	18.7	13	21.0	15	13.7	37	16.7
Thermal and Chemical Injuries	-	-	1	1.6	3	2.7	4	1.8
Surgical Perforations	14	29.2	13	21.0	13	11.7	40	18.2
TOTAL	48	100.0	62	100.0	110	100.0	220	100.0

TABLE NO. 12

REASONS FOR ENUCLEATION

	1929-1937	%	1938-1945	%	1946-1955	%	Total	%
Secondary Glaucoma	22	45.9	28	45.2	32	29.1	82	37.6
Irrepairable Injury	14	29.2	21	33.8	56	50.9	91	41.7
Phthisis	9	18.8	8	12.9	16	14.6	33	15.0
Other Complicating Factors	3	6.2	5	8.1	6	5.4	14	6.7
TOTAL	48	100.0	62	100.0	110	100.0	220	100.0

Table No. 11 represents types of injuries which, directly or because of infection or other post-traumatic complications, resulted in enucleation of the eye. The majority of eyes enucleated because of traumatic injuries and sustained perforating injuries show a very marked increase in number in recent years. The answer to this is that progressing mechanization of our life is not followed by increased security devises or safety education of the general population. The same can be said in cases of contusion and chemical injuries which also show a marked increase of incidence. Surgical perforation of the eyeglobe shows increased safety and is easily reflected in figures as therapeutic agents advanced with the use of sulfonamides.

Reasons for enucleation are summarized in Table No. 12, where secondary glaucoma, due to trauma, post-traumatic infection or post-inflammatory changes, produce increased intraocular pressure, showing interesting changes in the different periods. Presulfo and sulfo periods have almost identical numbers; the antibiotic period shows a marked decline indicating that inflammation due to infection in some cases was possible to control.

An entirely different picture represents itself in the pattern of numerals where the eye was removed because injury was too great or too violent and the eye was impossible to save and was taken out immediately or a short time after trauma occurred indicating the same as in Table No. 11, that more and more accidents occur as mechanization advances.

TABLE NO. 13

PATHOLOGICAL FINDINGS IN THE EYES ENUCLEATED BECAUSE OF TRAUMATIC INJURIES OR POST-TRAUMATIC COMPLICATIONS

	1929-1937	%	1938-1945	%	1946-1955	%	Total	%
Perforation of the Cornea	1[illegible]	35.4	33	53.2	75	68.2	115	52.3
Perforation of the Sclera	[illegible]	12.5	13	20.9	57	51.9	76	34.6
Destruction of the Eyeglobe	[illegible]	8.3	1	1.6	4	3.7	9	4.1
Prolapse of the Iris	[illegible]	12.5	2	3.2	19	17.3	27	12.3
Prolapse of the Ciliary Body	[illegible]	4.2	1	1.6	10	9.1	13	5.9
Loss of Entire Intraocular Cataracts	[illegible]	4.1	-	-	3	2.8	5	2.3
Traumatic Aphakia	[illegible]	6.3	5	7.1	13	11.8	21	9.5
Prolapse of the Vitreous	[illegible]	8.7	2	3.2	9	8.2	15	6.8
Surgical Aphakia	[illegible]	4.1	4	6.5	3	2.8	9	4.1
Traumatic Iridodialysis	[illegible]	-	-	-	4	3.7	4	1.8
Traumatic Cyclodialysis	[illegible]	-	1	1.6	3	2.8	4	1.8
Dislocation of the Lens	[illegible]	4.1	1	1.6	12	10.9	15	6.8
Rupture of the Choroid	[illegible]	2.1	-	-	-	-	1	.5
Traumatic Cataract	15	31.3	16	25.7	39	35.5	70	31.8
Retinal Detachment	16	33.3	11	17.7	26	23.7	53	24.1
Traumatic Aniridia	1	2.1	2	3.2	4	3.7	7	3.2
Retained Foreign Body	8	16.6	7	11.3	26	23.7	41	18.6

TABLE NO. 13

(con't.)

	19[illegible]-19[illegible]	%	1938-1945	%	1946-1955	%	Total	%
Siderosis	[illegible]	14.[illegible]	2	3.2	11	10.0	20	9.1
Intraocular Hemorrhage	1[illegible]	29.[illegible]	8	12.9	24	21.9	46	20.9
Anterior Chamber Hemorrhage	[illegible]	14.[illegible]	3	4.9	4	3.7	14	6.4
Postoperative (after Catarect Extraction) Expulsive Hemorrage		-	1	1.6	1	.9	2	.9
Panophthalmitis	1[illegible]	33.[illegible]	10	16.1	16	14.5	42	19.1
Endophthalmitis	[illegible]	19.[illegible]	8	12.9	28	25.5	45	20.5
Acute Iridocyclitis	[illegible]	8.7	9	14.5	4	3.7	17	7.7
Corneal Ulcer	[illegible]	14.[illegible]	5	7.1	1	.9	13	5.9
Hypopion	[illegible]	6.[illegible]	1	1.6	-	-	4	1.8
Vitreous Abscess	[illegible]	2.1	2	3.2	2	1.8	5	2.3
Sympathetic Ophthalmia	[illegible]	-	3	4.9	-	-	3	1.4
Anterior Synecchiae	[illegible]	12.[illegible]	12	19.3	6	5.5	24	10.9
Posterior Synecchiae	[illegible]	8.7	4	6.5	2	1.8	10	4.5
Cyclitic Membrane	[illegible]	4.[illegible]	-	-	4	3.7	6	2.7
Staphyloma	[illegible]	4.[illegible]	3	4.9	6	5.5	11	5.0
Phthisis	[illegible]	19.[illegible]	8	12.9	16	14.5	33	15
Ossification	[illegible]	8.7	4	6.5	4	3.7	12	5.5
Calcification	[illegible]	2.1	1	1.6	3	2.8	5	2.3
Amyloid Bodies	[illegible]	2.1	-	-	4	3.7	5	2.3
Cholesterol Crystols	[illegible]	2.1	-	-	2	1.8	3	1.4
Secondary Glaucoma	1[illegible]	29.[illegible]	25	40.3	26	23.7	65	29.5
Bullous Keratopathy	[illegible]	6.[illegible]	-	-	-	-	3	1.4
Endothelial Dystrophy		-	1	1.6	-	-	1	.5

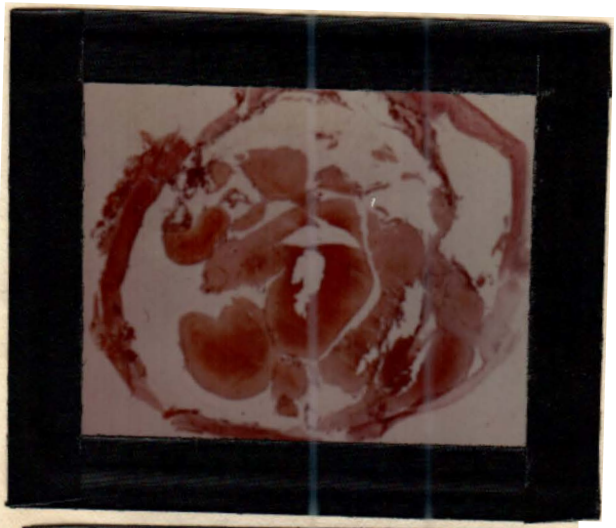


Fig. 32

Case No. 531. Male. Dynamite blast injury, Enucleation this same day. 1949. Fig. 32 speaks for itself showing degree of destruction. Massive hemorrhage filled the vitreous and all tissues were edematous. It is remarkable that this eye was enucleated just a few hours after accident. Polymorphonuclear cells were found throughout all tissues in a great number (Fig. 32A).

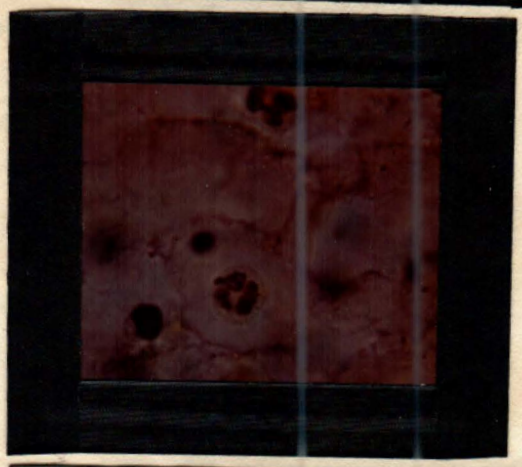


Fig. 32A

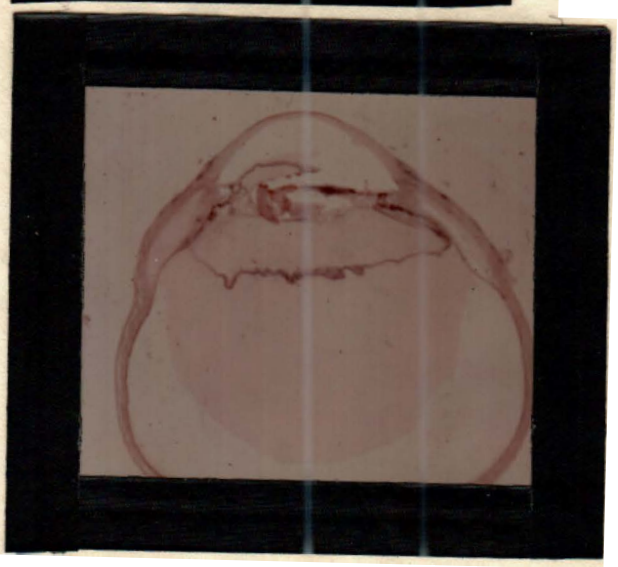


Fig. 33

TRAUMATIC PERFORATION, INTRAOCULAR FOREIGN BODY,
PANOPHTHALMITIS, VITREOUS ABSCESS

Case No. 473. Male, 46 years old. While pulling a nail, a piece of it penetrated the eyeglobe. One month later, enucleation, 1950. Section does not show the side of penetration. Foreign body found, size 3x4x2 mm. KP's on the posterior surface of the cornea. Filtation angle and Schlemm's canal are packed with lymphocytes and plasma cells. Extensive posterior synecchiae and organized membrane (Fig. 33A). Cataractous lens in subcapsular area is invaded by polymorpho-nuclear cells (Fig. 33B). Ciliary body is detached and disorganized. Vitreous is disorganized and there is formed vitreous abscess with predominantly polymorphonuclear.

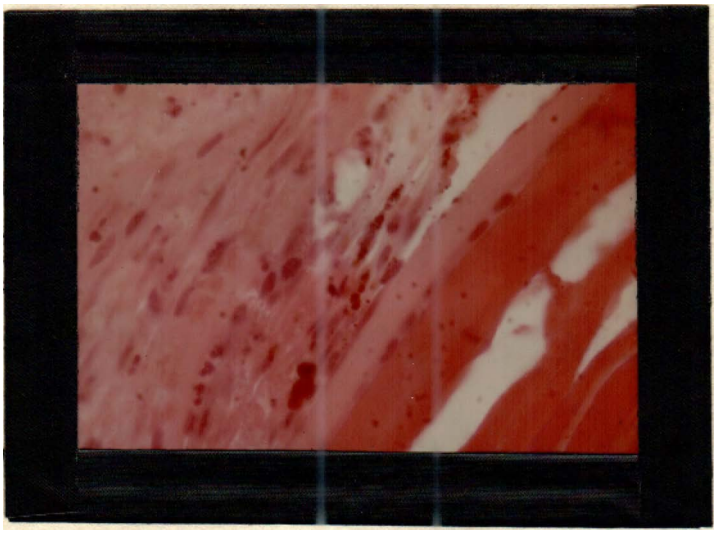


Fig. 33A

Fig. 33B

(Con't) cells, a few lymphocytes and red cells. Uveal tract shows in-eipient siderosis.

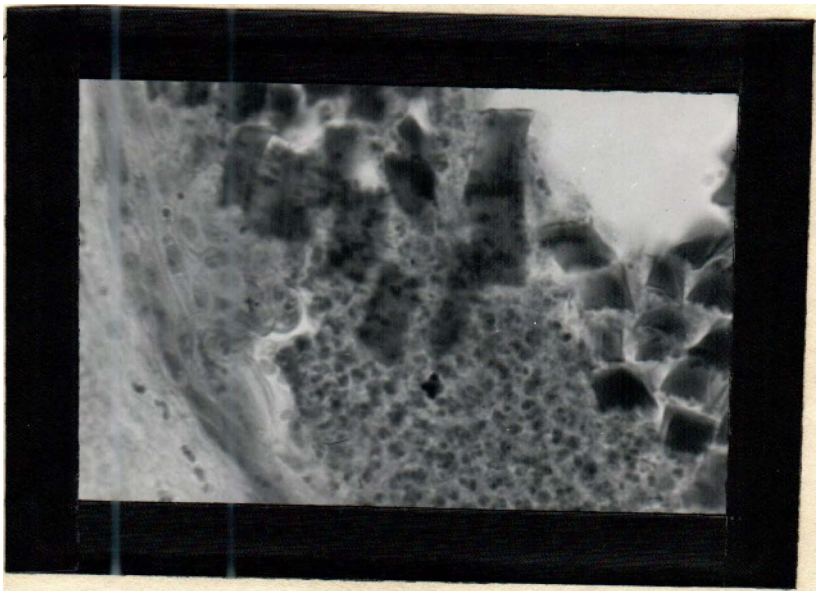


TABLE NO. 13

(con't.)

Retained Foreign Bodies

I -Ferrum (34), II -Cuprum (1), III -Brass (1), IV -Plant origin (2), V -Gravel (1), VI -BB Pellet (2), and VII -Button Fragment (1).

Phthisis which follows traumatic injury can not be evaluated according to the pattern of the three periods within the past twenty-five years because this condition, in many cases, was tolerated by the patient for many years before such an eye was removed.

Table No. 13 represents all the microscopic findings summarized and computed for each separate lesion found in the removed traumatized eye. The first group shows the degree of injury. Looking through the figures and compairing them for each period we see a very marked increase of more serious and extensive lesions in the last period and this presents the same answer as before, that in recent years we have more violent forces injuring the eye.

The second group represents the inflammatory lesions associated with trauma and our interest lies in demonstrating our progress.

In spite of more extensive injuries in the recent years we see that purulent infection of the whole eye, panophthalmitis, shows a definite decline as new, more specific drugs are advanced.

In the presulfo period, 33.3% of the enucleated eyes, because of trauma, showed purulent infection meaning that microorganisms invaded the eye and this infection was not controlled. In the sulfo period the number decreased to 16.1% and finally in the antibiotics period, reached as low as 14.5%, in spite of more extensive lesions as was demonstrated above.

A reversed picture is presented in the case of endophthalmitis. This inflammatory process is not known as well as it should be, but it seems that when bacterial invasion is controlled, tissue reaction and advancing changes are carried further as sterile, acute, sub-acute or chronic inflammation, which usually changes the physiology of the eye to such an extent that in this case the eye ends with secondary glaucoma or phthisis. If the eye became badly infected in the presulfo period it was enucleated as is shown in the group of panophthalmitis. Now the bacterial infection is more frequently controlled and such an eye has more chance to develop endophthalmitis, secondary glaucoma or phthisis.

Anterior segments and corneal lesions due to microorganisms were very effectively eradicated by new drugs as is apparent from the figures in this table.

The vitreous abscess does not give any conclusive evidence, but it is well known from clinical experience, that bacterial invasion into the vitreous is usually disasterous to the affected eye because no antibiotic can adequately concentrate it that would bacteriocidal, and the vitreous represents itself as a very good culture media.

The third group in this table summarizes the postinflammatory changes in the traumatized eye. All these changes are expected in any eye which has had any inflammatory process. Secondary glaucoma was covered in a previous chapter and the phthis will be discuss later.

In closing this chapter it is clear that many eyes which became infected were saved. Entophthalmitis requires more studies, expecially in regard to tissue reactions of sensitizing agents and their prevention. Advancing mechanized life should also be followed by increasing perfection of protective measures and safety education of the whole population.

CHAPTER VII

CORNEAL LESIONS

Before sulfonamides and antibiotics, corneal ulcers were one of the most difficult inflammatory lesions of the eye to cope with. Corneal ulcers are of great variety and their presenting pathological and clinical picture is different in each case. Basically, from the clinical standpoint they can be divided into marginal, central, serpiginous and ring abscess of the cornea.

Marginal ulcers usually are caused by micrococcus and Koch-Week's bacillus which is an epithelial parasite and is seen under the microscope as a minute gram negative slender rod. This kind of ulcer starts at the margin in the corneal epithelium or under the epithelium, initially forming a small abscess. It has no tendency to spread to the center of the cornea. Recurrences in this particular type of ulcer is common. This lesion under a microscope shows predominantly polymorphonuclear cell infiltration and the destruction of epithelium and stroma beneath. When macrophages reach the lesion, repair is accomplished by scar formation and vascular invasion from the limbus.

Central corneal ulcers are more serious because the opacities left after healing usually interfers with normal vision. Fungus and multiple pyogenic microorganisms may produce such a lesion. The most common organisms are: beta hemolytic streptococcus, klebsiella pneumoniae, Friedaender's bacillus, pyocyaneus, diplobacillus de Petit, and neisseria gonorrheae. This type of ulcer tends to penetrate deep into the cornea; it undermines and forms an abscess and occasionally results in perforation. Polymorphonuclear cells are

PERFORATED CORNEAL ULCER FOLLOWED BY PANOPHTHALMITIS

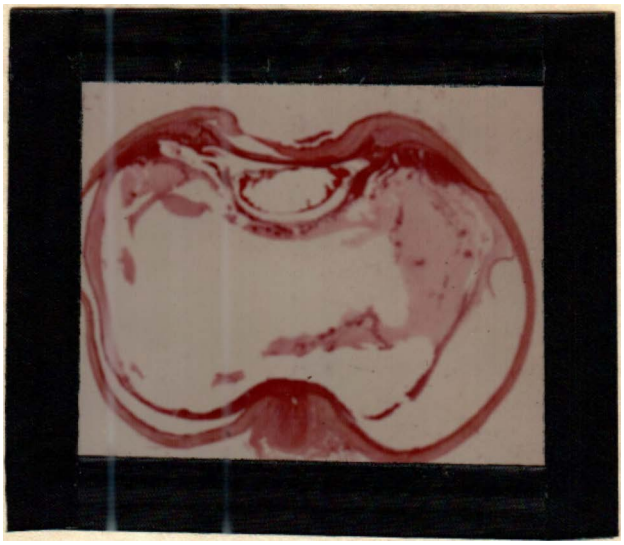


Fig. 34

Case No. 373. Male, 82 years old. This eye was traumatized by a calf's horn. Corneal ulcer with perforation. Enucleation in 19 5. Cornea perforated in the center and the defect is closed with young organized fibrous tissue mixed with many p lymorphonuclear leucocytes; this same cellular infiltra ion is seen in the remaining cornea. The anterior chamber is shallow and filled with purulent exudate which ext nds behind the cataractous lens. These same cellular morphology, polymorphonuclear leucocytes, are found in great numbers throughout the iris, ciliary body, retina, choroid and even the optic nerve. Necrotic changes are found throughout all inner eye structures.

PERFORATING CORNEAL ULCER

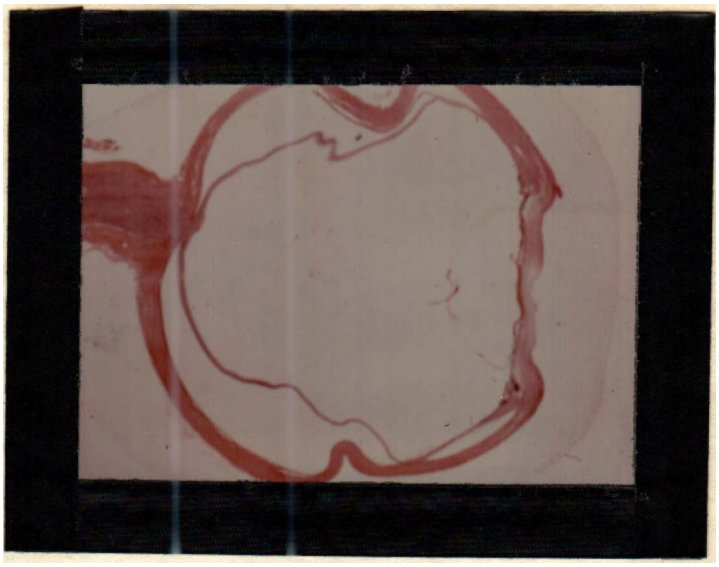


Fig. 35

Case No. 670. Male, 70 years old. History of rheumatoid arthritis of 20 years duration and keratitis sicca for four years. Recurrent corneal ulcer which responded well to antibiotic therapy. During the last episode of corneal ulcer, patient did not consult physician for one month at which time diagnosis of ulcer ante perforationem was made. Enucleation in 1954.

Microscopic - The central area of the cornea shows complete necrosis filled with polymorphonuclear leucocytes and iris pigment. The anterior chamber is completely obliterated and extensive posterior synecchiae are present. The anterior surface of the iris also shows polymorphonuclear cell infiltration. The remaining cornealepithelium shows marked keratinization.

abundant in this lesion and participation in the inflammatory process is seen in the iris and ciliary body. Sterile cell accumulation in the anterior chamber is common. Microorganisms for identification are found in the periphery of the ulcer. In case of perforation, panophthalmitis may follow or if healing of the perforated ulcer takes place when the perforation is sealed by prolapsed iris, corneal staphyloma is the result.

Aspergillus nigrus corneal ulcer—we have one specimen of such a lesion—is equally invasive and perforation is common.

Ring abscess is caused by pyogenic microorganisms of high virulence. A characteristic microscopic picture is that of complete necrosis of the deep layers in the center of the cornea with less lesions in the superficial layers. Massive infiltration by polymorphonuclear cells is usually seen throughout all the layers of the cornea. Usually, endothelium and epithelium is gone, but Bowman's and Descemet's membranes are intact except for the small opening of perforation. This is most destructive of the lesions of the cornea and very often results in the further spread of infection after perforation.

Corneal ulcer very seldom starts with intact epithelium but the most minute disruption of epithelial continuity may serve as the port of entrance for pathogenic microorganisms.

We have 60 specimens in our collected series which demonstrate active or healed corneal lesions, making 12.5% of the cases of enucleated eyes.

Perforated corneal ulcer takes first place with all possible complications which may be associated or follow the perforation. From these are panophthalmitis, endophthalmitis, anterior uveitis, and others like anterior staphyloma, synecchiae, cyclitic membrane, etc.

Tables No. 14 and 15 represent very well how such lesions were influenced by sulfonamides and antibiotics with 22.4% before the sulfonamide period, 18.3% during the time sulfonamides were available and just 4.7% of all enucleated eyes during the time that antibiotics started to be used. Secondary complications also show a definite decline.

TABLE NO. 14

CORNEAL LESIONS

	1929-1937	1938-1945	1946-1955	Total
Perforated Corneal Ulcer	8	7	3	18
Corneal Ulcer Ante Perforationem	4	4	1	9
Active Corneal Ulcer	2	3	2	7
Perforated Corneal Ulcer Healed Previously	2	5	2	9
Trachoma with Ulceration	1	1	1	3
Complicated Dendritic Ulcer	-	1	-	1
Ring Abscess of the Cornea	-	1	-	1
Healed Nonperforated Corneal Ulcer	2	1	1	4
Corneal Ulcer Due to Aspergillus Nigrus	-	-	1	1
Deep Active Kerotitis	6	1	-	7
TOTAL	24	24	11	60
Total eyes enucleated	107	131	231	469
in percent	22.4	18.3	4.7	12.5

TABLE NO. 15

PATHOLOGY FOUND ASSOCIATED WITH CORNEAL LESIONS

	1929-1937	1938-1945	1946-1955	Total
Panophthalmitis	7	2	2	11
Endophthalmitis	1	3	1	5
Acute Anterior Uveitis	7	7	4	18
Subacute Anterior Uveitis	2	1	-	3
Chromic Anterior Uveitis	1	3	-	4
Cyclitic Membrane	1	-	-	1
Secondary Cataract	2	2	1	5
Posterior Synecchiae	2	1	1	4
Anterior Peripheral Synecchiae	4	1	1	6
Anterior Staphyloma	-	2	1	3
Secondary Glaucoma	6	6	2	14
Phthisis	2	1	-	3
Prolapse of the Iris	2	3	2	7
Retinal Detachment	1	-	-	1
Intraocular Hemorrhage	1	2	1	4
Foreign Body in the Cornea	1	-	-	1

CHAPTER VIII

PHTHISIS BULBUS OCULI

Phthisis bulbus oculi is understood in pathology as shrunken eyeglobe. The phthisic eye usually does not produce any symptoms for a long period of time but after many years becomes more and more irritable and finally so painful that enucleation becomes necessary. This final stage is called phthisis dolorosa (27: 363).

The process of shrinking is initiated by perforating injuries, retianed foreign bodies, recurrent inflammation which can be endogenous or exogenous, and contusion (see Table No. 16).

The development of shrinkage of the eye is based upon progressive pathologic changes going on primarily in the ciliary body and the vitreous. Disorganization by trauma of any kind fails to produce an adequate amount of intraocular fluids and the eye becomes soft. Highly vulnerable vitreous, for this reason, undergoes progressive atrophy usually due to contracture of the scar tissue which forms in the eye as an attempt of repair after mechanical or inflammatory trauma. Decreasing intraocular pressure and scarification upsets the vascular system which is going into obliterative changes. The retina is pulled off by scar tissue and hyaline-like material accumulates beneath and parallel to it; hyaline degeneration starts in the choroid and further calcification and ossification takes place.

Analysis of the specimens shows that 46 enucleated phthisic eyes occur out of a total of 469 making 9.8%. The presulfo period shows 11.1% of the total number of eyes enucleated; in the sulfo period, 8.4%; and in the antibiotic period, 9.5%. These figures, as they are, are inconclusive for a statement about therapeutic

TABLE NO. 16

PHTHISIS INITIATED BY FOLLOWING CONDITIONS AND THEIR COMPLICATIONS

	1929-1937	1938-1945	1946-1955	Total
Surgical Perforation	2	2		
Perforating Injury	4	3	14	
Perforating Injury ith Retained Foreign Body	1	1	4	6
Perforation of the Corneal Ulcer	2	1		
Recurrent Endophthalmitis	2		1	
Chemical Burn Perforation			1	1
Endogenous Panophthalmitis		2	2	
Contusion	2	2		4
TOTAL	13	11	22	46
Total Eyes Enucleated	107	131	231	469
Phthisic Eyes in %	11.1	8.4	9.5	9.8

progress, but when we look closer into other figures (Table No. 16) we see that in spite of a marked increase of traumatic injuries, the number of phthisic eyes is relatively smaller and there is a definite decrease of corneal inflammatory lesions resulting in phthisis. Surgical perforations were also exposed to more dangers because of the inability to control infection before chemotherapeutics and antibiotics appeared. Endogenous endophthalmitis, it appears, has not been influenced by therapeutic progress.

The whole picture of this discussion presents the conclusion that in spite of an increasing number of traumatic cases, relatively fewer eyes reach a destructive form of phthisis bulbus oculi due to progressing therapeutic factors.

ENDOGENOUS IRIDOCYCLITIS
(Endophthalmitis)
SUBSEQUENT ATROPHY OF THE GLOBE

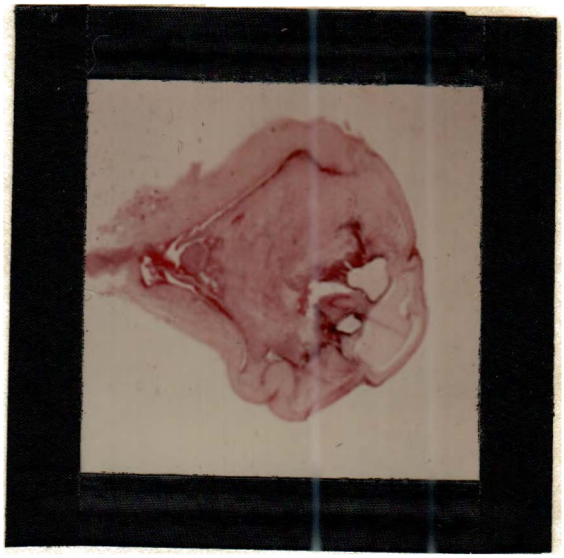
Fig. 37

Case No. 655. Female, 37 years old. Rheumatoid arthritis of ten years duration. Eye gradually lost vision associated with pain and redness. Enucleation in 1954.

Cornea vascularized and scarified in the level of Bowman's membrane. Anterior chamber practically completely obliterated by anterior synecchiae. Iris and ciliary body are displaced anteriorly and show marked disorganization and infiltration by lymphoc tes. Lens shows cataractous changes. Anterior segment of the choroid also shows some leucocytic infiltration. Retina shows marked atrophy and most of the vessels are occluded.

PHTHISIS AFTER CHEMICAL TRAUMA.

Case No. 625. Male, 67 years of age. Lime burn 47 years prior to enucleation. For pa t two years eye became irritable and finally painful. Enucleation - 1953.

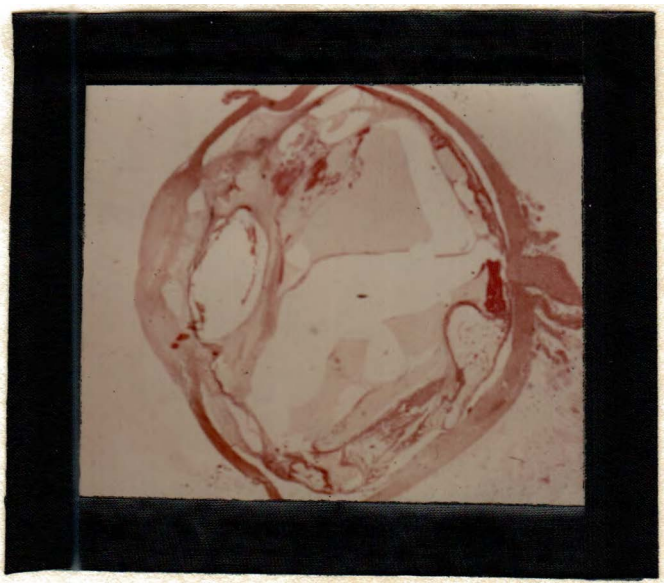


Phthisic eye, cornea thickened and vascularized. Inner structures of the eye are grossly and microscopically disorganized and infiltrated by plasma cells, various ma turity fibroblasts and few lymphocytes. Few areas of recent hemorrhages. Bone formation is advanced.

Fig. 38

TRA MATIC TINAL DETACHMENT FOLLOWED BY PHTHISIS

Fig. 39

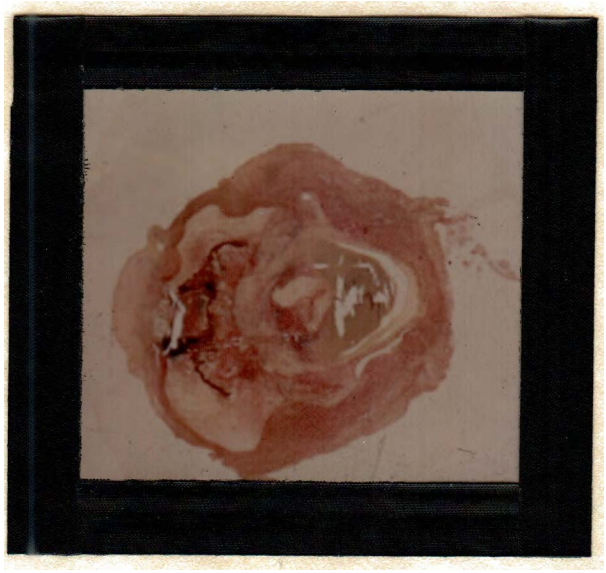


Case No. 338. Female 76 years old. Traumatic detachment of retina, 36 yrs. Painful eye for past 3 mos. Previously soft eye became ha d.

Cornea is thickened and vascularized. AC is filled with organized exudate which contains ne vessels, lymphocyte & plasma cells. Postinflammatory Pupilery membrane fuses with cyclitic embrane enclosing cataractous lens. Retina detached and mostly replaced by glial tissue. Subretinal and sub-choroidal hemorrhages of recent origin. Choroid is fibrosed and shows plasma cell and lymp ocytic infiltration. Bone formation is present in and along the deg nerated choroid.

SIDEROSIS AND PHTHISIS BULBUS OCULI

Fig. 40



Case No. 513. Male, 44 years old. Was hit in the eye by something while hammering on a sickle bar. 2 days later first unsuccessful attempt to remove foreign body which wa located in the eye & measuring 1xlxl mm. 5 days after trauma, one fragment was removed. 2 days later x-ray showed residual fragment; by that time severe panophthalmitis developed. 3 months after trauma, phthisis, no LP, painful, enucleation in 1949. (Fig. 40). Enucleated eye measured 19 mm. AP diameter, 17 mm. vertically and 15 mm. horizontally. Perforation injury at the limbus, down growth of corneal epithelium, marked infiltration by lymphocytes. Cornea highly vascularized. Foreign body particles demonstrated in ciliary body (Fig. 40A), ferr us discoloration - siderosis prominant in epithelium of ciliary body, iris and anterior chamber angle. Remnant lens capsule is folde and enclosed into cyclitic membrane which is adherent to disorgani ed detached retina. Lymphocytes are numerous throughout all structures except sclera. There is atrophy of the nerve. Generalized endophthalmitis.

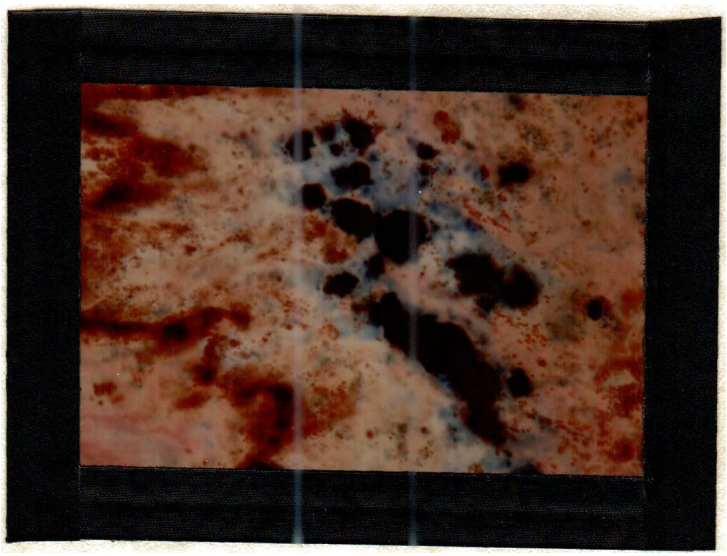


Fig. 40A

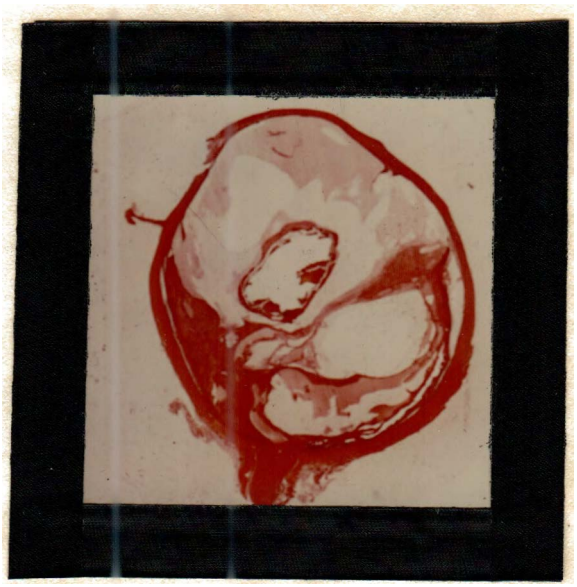


Fig. 41

Case No. 404. Female, a e 13. At age of three months noted that affected eye as turning in, and eye appeared to be smaller. At age 13 sharp pain in this eye for two weeks. No light perception, 1/3 of normal size, cornea scarified. Anterior periferal synecchiae, pupil very small. Roetgen reveals multiple areas of calcification in the cranial cavity. Enucleation in 1946.

Anterior-posterior measurement of the eye 17 mm. Extensive anterior synecchiae. Fibrosis of iris and ciliary body. Dislocated cataractous lens in the vitreous. Retina disorganized with very marked gliosis. Early bone forma-tion between retina and choroid. Marked irregular pig-ment proliferation of the r etinal pigment.

CHAPTER IX

TUMORS OF THE EYE

Malignant melanoma of the uveal tract takes first place, in our selection, among tumors found in enucleated eyes.

Malignant melanomas arise from Schwann cell, stromal melanoblast or nevus cell. Benign melanomas have the same origin (29: 221). Benign melanoma may also become malignant spontaneously, irritated by an inflammatory process or trauma. A predominant theory exists that all malignant melanomas have their start in pre-existing benign melanoma (29: 223).

Malignant melanomas are classified on the basis of the cell type, pigment, and argyrophic fiber content (17: 399). Spindle A is the most malignant type. It has a spindle shaped cell and a narrow nucleus with an ill-defined nucleolus. Second in malignancy is Spindle B which is distinguishable from Type A by a more oval nucleus and a well defined nucleolus. Third in malignancy is the so-called fascicullar type in which cells are arranged in a fascicullar pattern. The epitheloid type is next having a large round cell, varying in size, with acidophilic homogeneous cytoplasm nuclei, sometimes more than one, and a well defined nucleoli. The last type is a so-called mixed type which may have two or more of the above described types of cells. Malignancy of this last type can vary greatly depending on its structural basis.

As there is no known drug to destroy this malignant lesion, early recognition and surgical intervention is essential. At the presnet time, nation-wide statistics show that about 15% of the patients die within one year after enucleation of the eye with malignant melanoma, and five-year survival does not exceed 50% (17: 388).

The tumor next in frequency is retinoblastoma. This malignant tumor is found in the eyes of children with an average age being two years old. Reese (29: 67) reports from his series that the youngest patient who had retinoblastoma was one month old and the oldest, 11 years old. Werhoeff reports one case, 48 years of age, having true retinoblastoma (30: 643).

It is fairly well proven that retinoblastoma has hereditary tendencies but a great number of sporadic cases were observed where the family history was apparently negative.

Retinoblastoma usually has a multiple origin and arises from either external or internal nuclear layers of the retina, and also has a tendency to appear in both of the eyes of a patient. Microscopically, this tumor is classified in two types: one is made up of undifferentiated retinoblast and the other of a spongioblastic series forming so-called true rosettes. Pseudorosettes are distinguished from true rosettes by the way the cells are arranged; pseudorosette is the condition where cells surround a small vascular channel, while true rosettes do not have the vessels in the middle.

Retinoblastoma of the pseudorosette type grows faster and more commonly undergoes necrosis in the parts further from the vascular channel. True rosette retinoblastoma is a slower growing type.

Retinoblastoma in the first stage grows by direct extension but later, tumor cells break off from the surface of the mass and may implant anywhere in the eye that they have sufficient nutrition to survive and multiply on. The most common sites of such transferred

MALIGNANT MELANOMA OF THE CHOROID

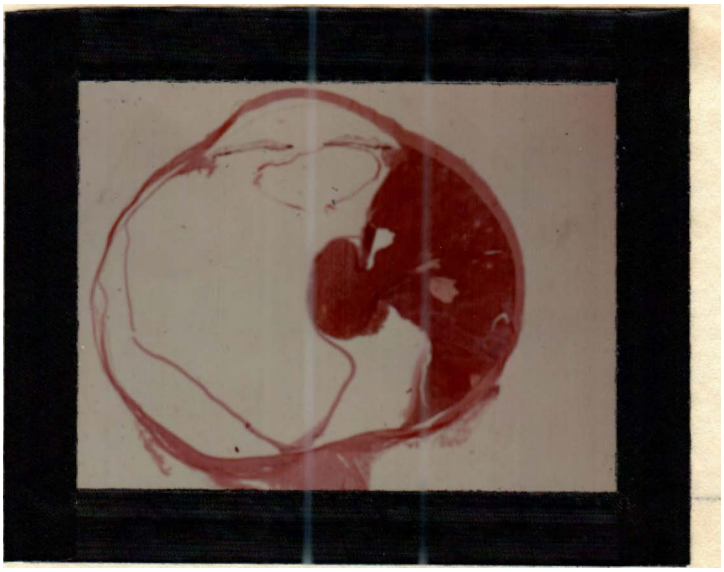


Fig. 42

Case No. 661. Male, 65 years of age. Four years prior the enucleation, a failing vision was noted in this eye. Seen by ophthalmologist just shortly before enucleation. At that time he had questionable light perception. Translumination indicated large intraocular mass. Ophthalmoscopically, mass seen protruding into half of vitreous. Tension 14 mm. Hg. Enucleation in 1953. ig. 42 represents size and location of the tumor which occupies temporal half of the globe and has ped·enucleated dome on top, extends from ciliary body almost up to optic nerve; retinal detachment is present behind the tumor. Tumor is heavily pigmented and cellular pattern is fascicular of spindle type cells. Fig. 42B represents sections where tumor is invading along blood vessel chanel through the sclera.

Prognosis in this case is poor.

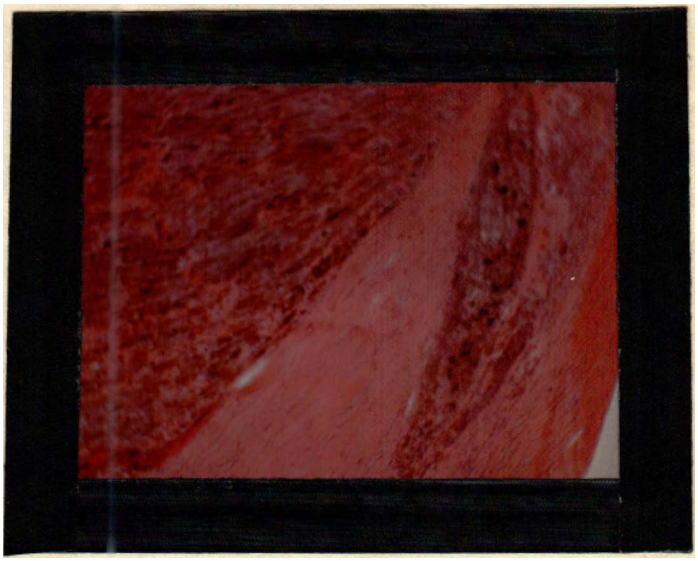
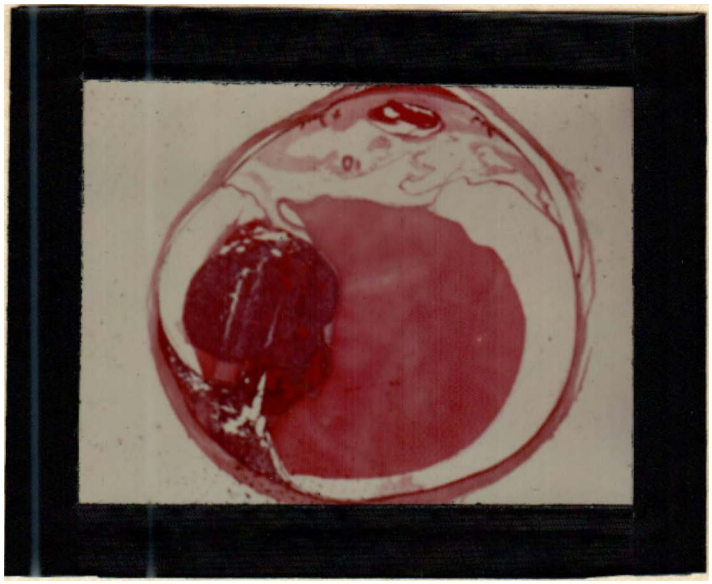


Fig. 42B

MALIGNANT MELANOMA OF THE CHOROID

Fig. 43



Case No. 599.
No clinical history with the specimen.
Enucleation in 1951.

Fig. 43 represents gross view of the eye with the tumor arising from posterior temporal side of the choroid, which appears to be ped enucleated. Tumor is very heavily pigmented and highly vascular. Retina is completely detached and space is replaced by fluid with high protein content. Side of invasion into sclera can be seen in Fig. 43A.
Prognosis: poor.

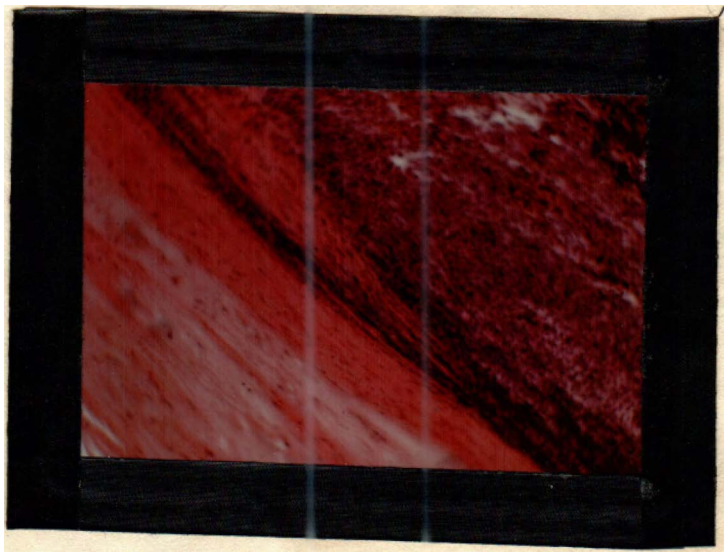


Fig. 43A

MALIGNANT MELANOMA OF THE CILIARY BODY

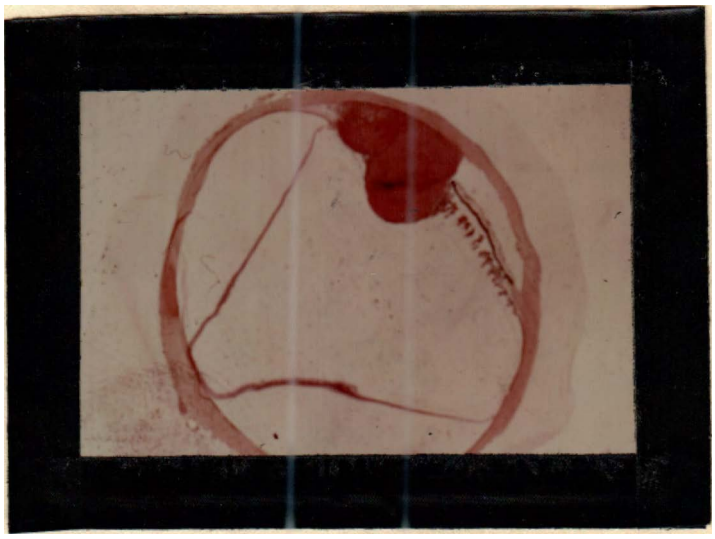


Fig. 45

Case No. 387. Female, age 63 years. Patient noted failing vision two months before enucleation. Examination revealed bulging of the iris at the root. Gonioscope showed brownish mass covered with small vessels behind the iris. Enucleation in 1946.

Figure 45 represents the gross picture and location of the tumor. Anterior chamber angle is invaded by tumor. AC contains moderate amount of loose pigment particles. Fig. 45A represents origin of the tumor which is highly vascular.

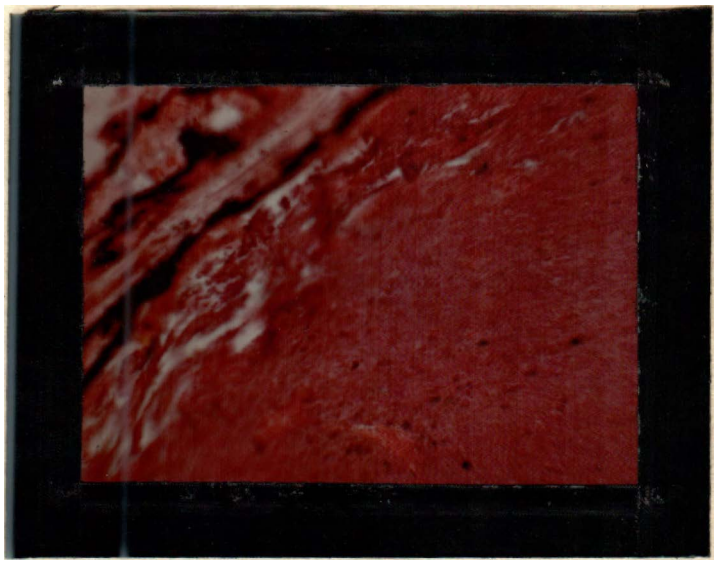


Fig. 45A

BOWEN'S DISEASE

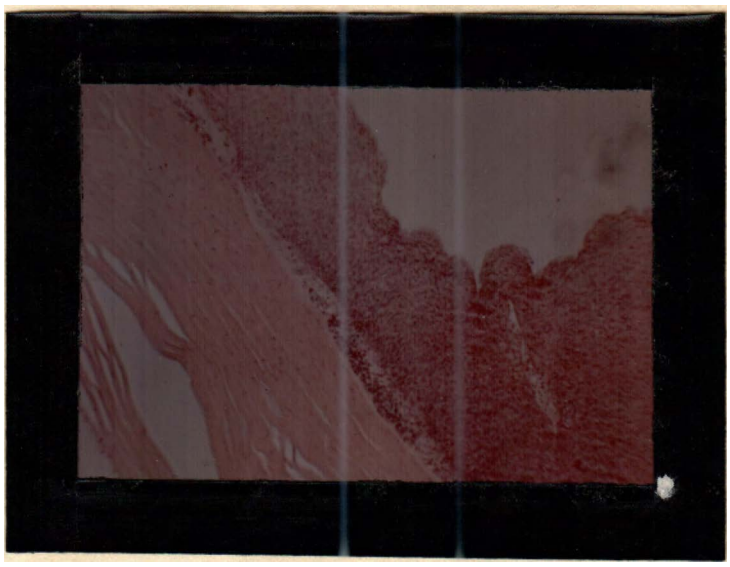


Fig. 46

Case No. 169. Male, 68 years old. Injury of the cornea one year prior the enucleation. One month after trau-ma growth on the cornea was noted. Diminishing vision since trauma. Vis-ion at the time of enucleation -light perception. Enucleation in 1934.

Fig. 47

Case No. 402. No-clinical history known. Enucleation in 1946.

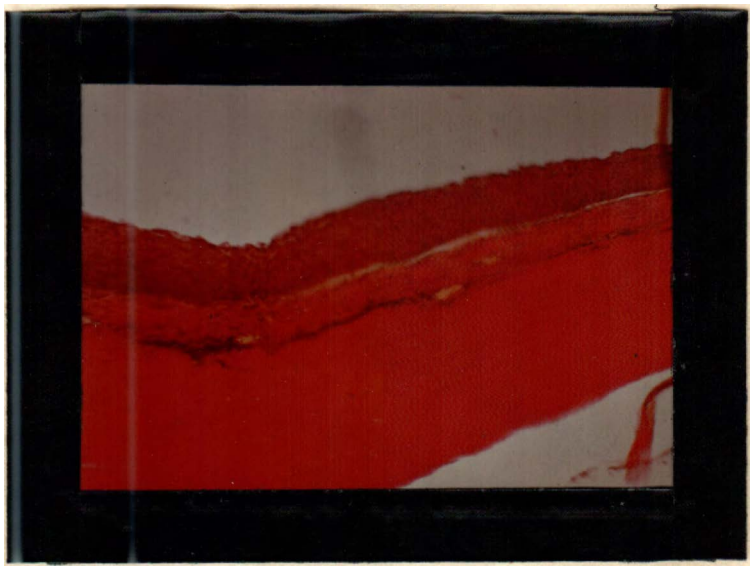


Fig. 46, 47, and 47A represent intraepithelial epithelioma of the cornea or known also as Bowen's disease. Pictures represent just part of the corneae. This neoplasm is considered as premalignant lesion which may become frank squamous cell carcinoma and characterized by pleomorphism, loss of basal polarity, inflammatory reaction in stroma (Fig. 47), disappearance of basement membrane, vacuolated cells with hypercromic nuclei and cells with multiple nuclei. In both cases, neopl sm has destroyed Bowman's membrane, clearly seen in Fig. 47A. (p. 93e)

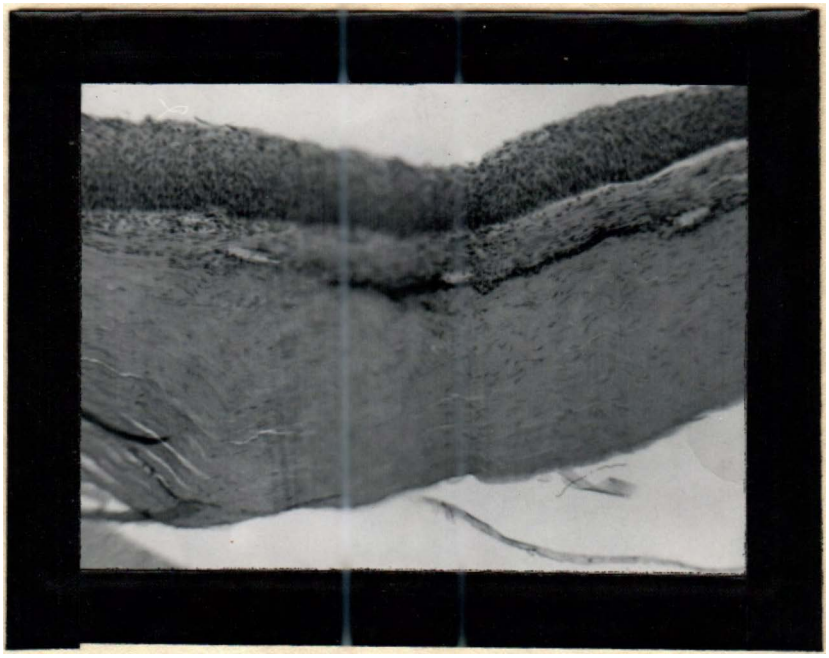


Fig. 47A

MALIGNANT MELANOMA OF THE IRIS

Fig. 48

Case No. 466. Male, 70 years old, gradual loss of vision of one year. Vision 20/160, eliptical mass in the iris between 9 and 11 o'clock. Cataractous lens. Surgically broad biopsy of the iris taken and cataract extraction done. Pathologic report -malignant melanoma, immediate enucleation of the eye - 1946.

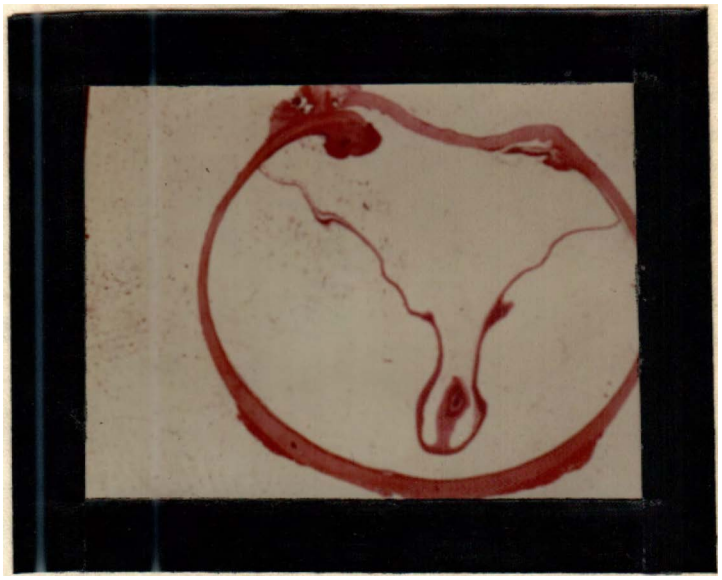


Figure 48 represents gross view of the eye tumor being extended into ciliary body but no invasion into the sclera. Tumor is lightly pig-mented and is of spindle subtype B. Surgical suction with silk sutures clearly seen in Fig. 48A (p. 93f). Prognosis: favorable.

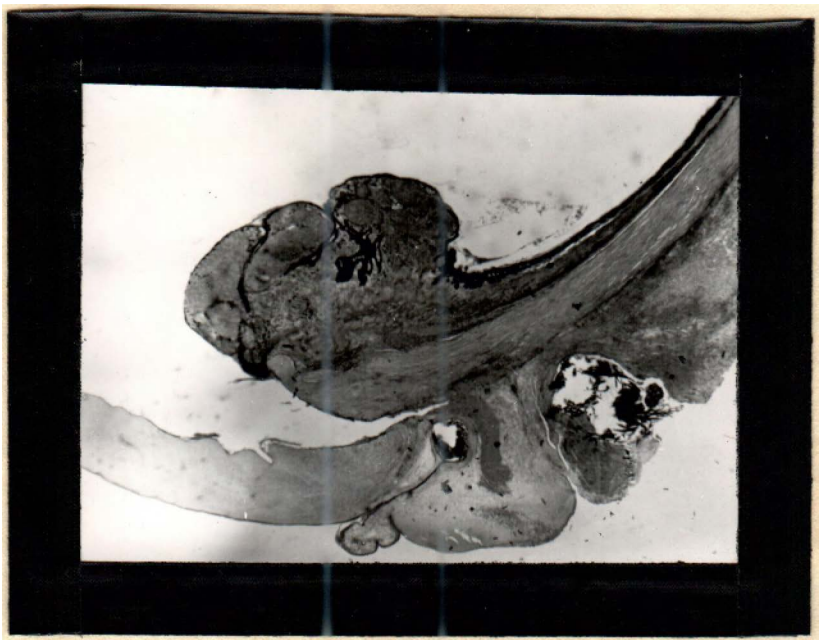


Fig. 48A

RETINOBLASTOMA

Fig. 49

Case No. 514. Female two years of age. Parents noticed hollow appearance of the globe and took her to the physician who referred the patient to an ophthalmologist. Findings: 10D elevated retina by whitish mass with dilated vessels. Enucleation followed; three months later local recurrence in the orbit followed. Roentgen therapy foll wed but 6 months later patient's general status started to deteriorate rapidly, multiple subcutaneous masses appeared over the side of the face and head. Symptomatic treatment started to comfort the distress. Enucleation - 1951.

RETINOBLASTOMA

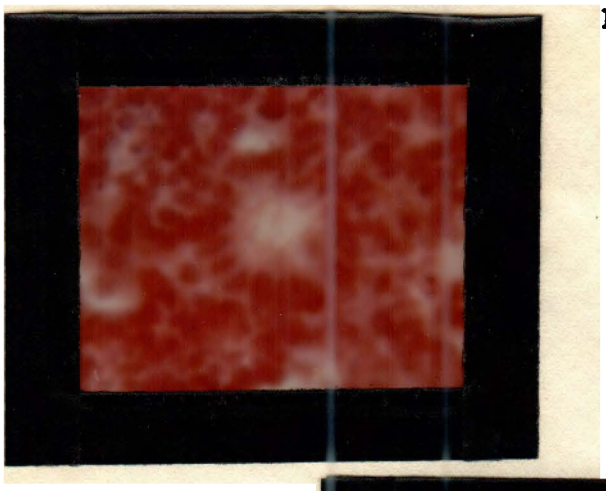


Fig. 49A

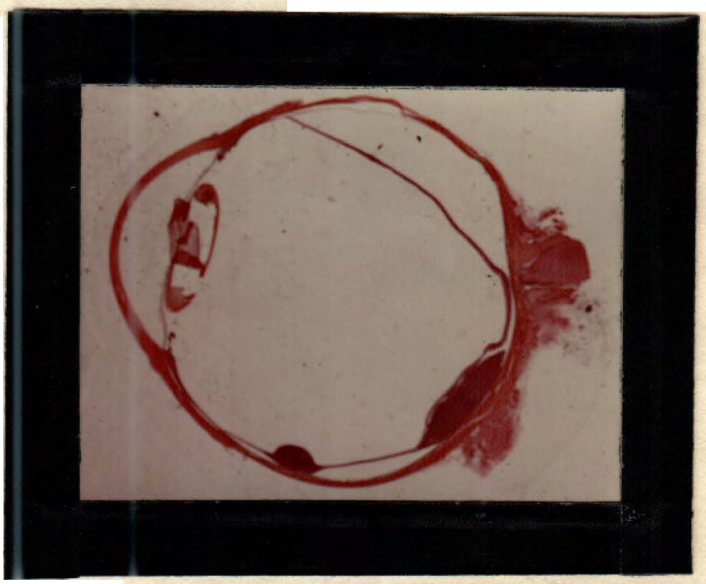


Fig. 50

Case No. 649. Female, 2 years of age. History of eye turning in at 3 1/2 mo. duration. Ophthalmoscopic examination revealed two pinkish-white areas superior and temporal to the disc. Elevation 5D. Examination five days later showed increase in size of these lesions. Enucleation in 1953.

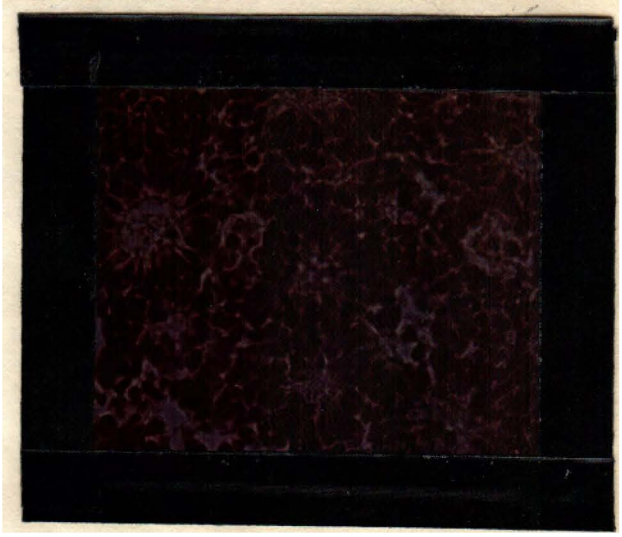


Fig. 50A

This tumor of childhood occasionally observed at birth. Can be unil t-eral. Retinal detachment

(con't.)

tumor itself or intraocular hemorrhage usually is observed.
Fig. 49 - Origin of the tumor near the optic disc, sections showed invasion. Tumor itself protruding far into the inner of the eye retina is detached. Lamina Vitrea destroyed and multiple invasions into the choroid. Multiple independent origins of other smaller masses of tumor.
Fig. 50 represents very well, multilocular origin of tumor.
Fig. 49A and 50A - Cellular pattern of retinoblastoma, true rosettes.

implants are: Choroidal surface, iris, ciliary body and, occasionally, the filtration angle. When a tumor breaks into the choroid, rapid growth occurs because of the very rich blood supply. Retinoblastoma has one specific characteristic that has predilection for the invading optic nerve (29: 81), this being one of the most important factors that should be remembered in regard to therapeutic evaluation.

Local extension of the tumor, if not treated, is usually not limited to the eyeglobe itself. It breaks through the sclera, invades intraorbital structures and orbital bones, and reaches as far as the brain structures. Distant metastases are common and they are bloodborn.

Early diagnosis and proper therapy is essential. Therapy usually consists of enucleation and irradiation of the fellow eye and, in some cases, a combination of enucleation and irradiation. To make a diagnosis of retinoblastoma or to suspect one is not difficult, but because of the early age of the patient, he is brought to the physician after the tumor manifests itself in the pupil, or distorts the eye in size or shape. The usual color of the endophy-tum type tumor is pinkish with a creamy hue, with blood vessels on the surface; on rare occasions it may be white with visible vessels. Appearance helps to make the diagnosis. The exophytum type, which is rarer and starts in outer layers of the retina, if the tumor does not break through the retina, presents a picture of funnel shaped retinal detachment without any visible hole in the retina. Calcium deposits frequently occur and can be demonstrated by x-ray examination.

This is one test offers not much help in confirming the diagnosis before therapeutic intervention. In advanced cases of secondary glaucoma further complications lead to buphthalmos. Secondary cataract may confuse the picture by the first impression but complete examination, a good history and knowing the age of the patient will aid in arriving at the correct diagnosis.

Another malignant tumor worth discussing is the mixed tumor of the lacrimal gland. The mixed tumor of the lacrimal contains epithelial and mesenchymal elements and occasionally some transitional tissue which is how this tumor received such a name.

Under the microscope this tumor appears to be composed of epi-thel ium forming cords and al veoli with some mucous present in the lumen. Stroma is of the myxomatous type occasionally found with particles of bone or cartilage. The tumor is encepsulated but the capsule has elements of the malignant tumor. Depending on the histological pattern, mixed tumors may be more or less malignant. Tumors having a well developed capsule and more myxomatous stroma are definitely radioresistant. Tumors in which epithelial elements prevail and grow in adenoid cystic formation usually have an ill defined capsule, are more malignant and tend to invade neighboring structures including the bone, and are moderately radiosensitive.

A patient with such a tumor usually requires complete orbital exenteration followed by irradiation and in cases where bone is involved removal is also necessary.

The prognosis for the patient with a mixed tumor of the lacrimal

TABLE NO. 17

INTRAOCULAR AND INTRAORBITAL TUMORS

	'1929-1937	'1938-1945	'1946-1955	Total
Malignant Melanoma of the Uveal Tract*	15	14	27	51
Retinoblastoma**	5	1	11	17
Malignant Melanoma of the Limbus	-	-	1	1
Bowen's Disease	1	-	1	2
Metastatic Adenocarcinoma in the Uveal Tract	1	-	-	1
Extrabulbar Intraorbital Malignant Melanoma***	1	-	-	1
Benign Melanoma of the Uveal Tract	3	-	1	4
Benign Epithelioma of the Ciliary Body	1	-	-	1
Intraocular Neurofibroma	-	-	1	1
Ectopic Intraocular Lacrimal Gland	-	-	1	1
Mixed Tumor of the Lacrimal Gland****	4	1	1	6
Cavernous Hemangioma of the Orbit	1	-	-	1
Invasion of Squamous cell Carcinoma Into the Orbit	1	-	-	1

*This includes six cases of malignant melanoma of the iris and five cases of the ciliary body. One case had distant metastases.
**Includes three recurrences.
***Origin unknown, no history.
****Includes one recurrence.

gland is poor. Local invasion through the bone and into the brain is the most common cause of death.

Intraepithelial epithelioma, also known as Bowen's disease, is not common. This lesion is more prevalent among males and can be seen in an average age of sixty years. Bowen's disease is completely intraepithelial and under the microscope one can see a marked variation in the size and shape of the cells proliferating from basal cells. This lesion does not have invasive character-

istics but there is a possibility of metastases; therapy in this condition in surgical, accomplished by complete excision of the lesion. Irradiation therapy is of no value.

TABLE NO. 18

ASSOCIATED FINDINGS WITH TUMORS

	'1929-1937	'1938-1945	'1946-1955	Total
Invasion into Adjacent Tissue Structures	12	14	19	45
Invasion into the Orbit	4	3	1	8
Retinal Detachment	4	4	16	24
Intraocular Hemorrhage	3	1	2	6
Secondary Glaucoma	7	5	4	16
Anterior Chamber Hemorrhage	3	1	2	6
Anterior Synecchiae	1	-	-	1
Bullous Keratopathy	-	1	1	2

Malignant tumors of the eye, as we see from Table No. 17, are dominated by malignant melanoma, the second place taken by retinoblastoma and the third, an extrabulbar intraorbital tumor--mixed tumor of the lacrimal gland. For the sake of uniformity, figures are divided according to the three periods of therapeutic progress even though we have no drugs to cure these lesions except surgery and irradiation therapy.

None of these tumors can be prevented at the present time and the physician's most important task is early detection of such tumors so that permanent cure may be achieved by means of surgery or surgery combined with irradiation.

Table No. 18 gives a general idea of when the physician detects these tumors and the figures do not show very pleasant features. The majority of the malignant tumors revealed a spread beyond original structural barriers; large numbers had detached retinas, intraocular hemorrhages and secondary glaucoma. All these signs show that the tumor was large enough to produce secondary glaucoma or hemorrhage because of necrosis or invasion; retinal detachment because of bulk sufficient to raise the retina, or accumulation of the fluid. Much can be said of the importance of early detection but more important is knowing that such lesions do exist, that they are comparatively common, and the thing to do is to look for them.

CHAPTER X

SENILE MACULAR DEGENERATION

Senile macular degeneration in one of the ocular conditions caused by vascular changes of the aged. This particular condition is fairly common among older individuals of both sexes. Among 1,041 patients over sixty years of age who sought medical advise because of nonpainful failing vision, it was found that 11.24% had senile macular degeneration (15: 145). Dr. O. C. Anderson (15) estimates that if the population over sixty years of age would be taken as a whole, 2.26% would have this condition.

Senile macula degeneration changes in the fundus can usually be without recognized difficulty during ophthalmoscopic examination of the eye, especially when using redfree light.* Many different types are described and the ophthalmoscopic appearance is of a great variety.

Drusen is one of the commonest findings; they are yellowish or reddish in color, sharply circumscribed and usually it is difficult to distinguish one from another. Drusen are not pigmented and produce visual disturbances just in the cases where they are in the macula itself or very close to it. In case no drusen can be seen in the macula and the other findings suggest that they should appear, usually an examination using redfree light will reveal not only already fully developed drusen but also drusen in their early formation. Drusen, under redfree light, usually appear as light flecks and they are especially prominent in contrast to other fundus structures. Increased pigmentation of very fine distribution is

* My own experience and also widely used among European ophthalmologists.

found to be in the areas between the drusen and appear darker than the rest of the fundus where no drusen are present. Increased amounts of pigmentation can be seen between the long standing drusen. Pigment, in such cases is irregularly dispersed as coarse gramules. Glial and fibrous proliferation also takes place.

It is not necessary to have drusen in senile macular degeneration. In some cases, only increased irregular pigmentation or only scar formation can be seen. In another, forms like hole formation or so-called disciform macular degeneration is a presenting picture.

The wear and tear of the vascular bed during a lifetime produces changes in the vessels which are characteristic of the aged. These changes result in prestasis, stasis, and finally, in complete occlusion of the minute vessels causing anoxia and inadequate nutrition of the areas supplied by these particular vessels. These changes, in return, cause the degeneration of the structural tissues of the eye visible both grossly and under microscope.

The elements of the retina takes certain patterns, limiting the membranes and the Mueller fibers become thicker. Diminution of the neuronal elements and glial proliferation takes place and the pigment migrates into these areas. Vacuoles appear between the inner nuclear and outer plexiform layers and by coalescence form cystoid spaces appearing as a tunnel in the flat preparation of the retina. The Drusen, amyloid bodies located in the fiber layer, according to Dr. Weil (16:11) are formed after the cells die "by

precipitation of intrescellular colloid substance" or, "by degeneration of the axis cylinders". However, some believe (17: 47) that these drusen result from degenerative changes in the glial cells. Mucoid material is predominant in these bodies.

The cystoid degeneration of the macula is rare. Complete loss of the retinal tissue is visible microscopically. Two types are the most common. One, which German medical literature calls Pigment Verschieburg, is where irregular areas of pigmentation are interlaced with areas of increased pigmentation. These changes occur in the pigment layer of the retina along with irregular colloid excrscences on the Bruch's membrane. Over the areas of depigmentation, neuroepithelium of the retina is usually damaged and if these changes occur in the macular area, vision is greatly impaired. Arteriosclerotic changes of the vessels in the form of hyaline deposits and fibrosis after is possible to demonstrate.

The second type is one of disciform senile macular degeneration. The initial pathology here is also primarily based upon aging vessels in the form of weakening vascular walls and at the stage of stasis, hemorrhage by diapetesis or serous exudation. Bruch's membrane breaks and an accumulation of serous or serosanguinous fluid detaches the epithelium pigment of the retina. When a sanguinous element is predominant in such exudate, the resulting organization being massive proliferative changes. Three elements are found in this proliferating tissue. The first is fibroblastic; the second is endothelial, derived from damaged blood vessels; and the third is glial, originating

from rupture of the pigment layer of the retina. Irregularly distributed fragments of destroyed epithelium pigment is found in this scar which will occasionally proliferate locally. In this same group is the circinate type in which the pathological process is the same except that its maximum changes are in the periphery of the involved area. This type and its subtype have disciform configuration when seen through an ophthalmoscope.

Prognosis in the case of senile macular degeneration should be looked upon from two points of view. One is the lesion itself which is not good because if the patient is seen with a fully developed picture of this condition it must be known that the lesion cannot advance much further. The other view is that when the condition is in just incipient stage. Many try to stop the progress of degeneration with nicotinic acid, nicotinic acid in combination with Metrazol, or just Potassium Iodide (KI). It has not been proven yet that these drugs stop the progress but no harm is usually done either. The patient should be assured that complete blindness is not possible from this condition but no known therapeutic intervention will improve the vision. Special telescopic glasses are helpful in some cases to aid in adequate reading vision.

This chapter is presented, not because I have seen senile macular degeneration in our microscopic preparations, but because I feel it necessary, based on my past experience while working in the eye clinic of our University where I observed numerous patients sent for cataract surgery who did not have cataracts at all.

Gradual and painless loss of vision has more causes than the cataract. One of the most common is senile macular degeneration and chronic simple glaucoma. It takes little time to inspect the fundus, look at the optic disc and macula, dilate the pupil and check the whole fundus. Such an examination would preserve the physician's good reputation and the patient would not be impressed by false hopes. If a physician does not look for an intraocular lesion, it may be that he does not know any better but who is to blame. In my opinion it is the school he attended to acquire his basic knowledge in the art of healing.

CHAPTER XI

SUMMARY

Gross and microscopic examination of the diseased organs and their tissue represents one of the best sources of proof of our mistakes or of progress in the art of healing. For this reason, this particular source of information was chosen to present the influence of new drugs on diseases of the eye and parallel with this, to point out the most disasterous eye conditions in this state in order to bring particular attention to them for presentation to medical students.

For the reader's appreciation, the most important events are presented from the history of therapeutic and diagnostic progress starting as far back as 2250 B.C. up to the years before sulfonamides were used as therapeutic agents.

The last 25 years are divided into three periods:

1. Presulfo period - from 1929 to 1937.
2. Period of sulfonamides - 1938-1945.
3. Period of antibiotics - 1946-1955.

Treatment of eye conditions before the sulfonamide period was based mainly on different compounds of silver, mercury, zinc, tincture of iodine and supportive therapy in the form of radiant energy. Pilocarpine, Eserine and Mecholyl had then been used for primary glaucoma and are even now major drugs used for this condition.

Dr. Domagk, in 1932, announced for the first time an effective proven sulfonamide. It took six years before drugs of this group were put into use in this country, due to misinterpretations regarding original work done with early compounds of sulfonamides.

As people became interested in improving this drug, their adverse effects were rapidly eliminated by making new compounds with similar bacteriostatic action as the original. Sufonamides were first used systemically but powders and crystals were soon applied to the surfaces and ointments were used for topical installation in the conjunctival sac.

The first observation of the present day antibiotic agents were published by Pasteur in 1877 but not until World War II was the new useful drug, Penicillin, presented by Fleming. This drug became available for civilian population in Nebraska in 1946. New multiple antibiotic from many different sources were investigated and the suitable ones were released on the market.

Antibiotic action is bactericidal if in sufficient concentration but in low concentration it is like one of the sulfonamides--bacteriostatic. Combinations of two or more antibiotics are useful in many instances with the exception of Penicillin and Chloramphenicol because they have an interfering action with each other. Some organisms became resistant to antibiotics as was the case with sulfonamides.

When antibiotics were first used, enthusiasm about them was so great that sulfonamides were practically forgottan. Today, both types of drugs are equally accepted to control certain types or groups of microorganisms. Today's most common antibiotics are compaired in Table No. 3 as to their usefulness against the more common microorganisms.

Cortisone and other corticotropic drugs also found their place

in ophthalmology. States of hypersensitivity allergy and nonpurulent inflammatory lesions are altered by this type of drug.

Curare and curan-like agents have a limited use in ophthalmology.

Table No. 4 represents the final diagnosis made by microscopic examination which was assumed as the reason for enucleation. From 469 cases, 39.5% were enucleated because of secondary glaucoma; 14.5% were irrepairable traumatic injuries; 9.8%, malignant melanoma; 9.8%, phthisic eyes; 4.3%, retinoblastoma (recurrences included); 4.7%, corneal ulcer, and others in diminishing numbers.

Inflammation resulting from trauma and invasion by pathogenic or endogenous organisms are the major factors in the destructive process of the eye. It can be classified into acute, subacute or chronic cellular morphology.

Hypersensitivity and allergic states also play a major role in ocular pathology and as yet is not very well understood. Hypersensitivity reaction can be induced by any foreign protein or by inorganic chemicals which may form, in the body, new components with proteins of the host already present which then become foreign to this organism.

Each structural part of the eye reacts differently to trauma. Corneal epithelium regenerates very rapidly, Bowman's membrane always heals by forming an opaque scar, Descement's membrane, by a scar which has a tendency to clear or become vascularized. Very extensive lens injuries result in cataract formation; injuries of the retina, by glial proliferation and new vascularization.

Secondary glaucoma has very multiple initiating factors but

the most common is inflammation which can be caused by many factors. The most common are traumatic, exogenous and endogenous inflammation. Postinflammatory and post-traumatic changes upset the normal physiology of the eye and ocular pressure increases. Massive hemorrhages accompany trauma and act as a space occupying substance, blocking the filtration angle or forming secondary membranes. Intraocular hemorrhages may also occur in the senium because of arteriosclerosis or in diabetes mellitus where typical changes predispose the vascular tree to occlusion and new vascularization in the retina and iris.

Siderosis, tumors and displacement of the lens may upset the physiology of the eye causing intraocular pressure to increase.

The second most common cause for enucleation is traumatic injury. They play a major part in producing secondary glaucoma, and also often force the eye to be enucleated because of extensive destruction. If the eye heals and does not develop secondary glaucoma it may go into the degenerative process known as phthisis. From 469 specimens, 220 or 46.9%, microscopically showed signs of traumatic injury. Eighty-two of them, or 37.6%, ended with uncontrolled secondary glaucome; 33, or 15% became phthisic; and 91, or 41.7%, were enucleated immediately or within a short time because of extensive irrepairable destruction of the globe. Most of the traumatic injuries occurred because of carelessness or were to children who were permitted to handle dangerous tools.

Corneal inflammatory lesions, very common before 1938, have become rare since sulfonamides and antibiotics have been put to use for this condition. The corneal ulcer is well represented among

these specimens with all possible complications, such as, perforation, prolapse of the iris, staphyloma, the invasion of microorganisms into the inner eye, and phthisis.

Phthisis bulbus oculi is the final result of a traumatized eye if the eye survives extensive traumatic lesion or a massive inflammatory process and does not develop uncontrolled secondary glaucoma. The primary pathological changes occur in vitreous and ciliary bodies; the vitreous shrinks, the ciliary body undergoes a degenerative process and does not produce an adequate amount of aqueous causing the eye to become hypertonic. Further changes include degeneration of all structures of the eye and subsequent calcium deposition and ossification.

Sulfonamides, antibiotics, Cortisone and improved surgical technique have markedly altered the picture of ocular pathology. Inflammatory lesions due to pathogenic microorganisms are, in most instances, controlled as long as such lesions are in the structural parts of the eye where these drugs can be administered in adequate concentration. Vitreous and lens present the most difficult problem. Even the most recent drugs are of little value when organisms invade these structures because of poor concentration in these structures, since the already present organisms are then the source of continuous focus in the eye.

Endophthalmitis, which is the inflammatory process due to hypersensitivity, shows a marked increase, a reverse proportion to purulent infections. From the histories of these patients there is definite indication that this condition develops after the purulent inflam-

matory process is controlled--eo ipso this is the pathologic process due to a hypersensitivity phenomenon to proteins of destroyed organisms which left debris behind.

Secondary glaucoma also shows an increase and it is visible from computed tables that more eyes survive acute inflammation or physical trauma. Consequently, because we have learned to destroy pathogenic microorganisms but have not learned to prevent the seoondary changes in the eye that follow such lesions, there are more damaged eyes available to develop this condition.

Malignant melanoma is the most commonly found tumor of the eye with 51 cases. The second in frequency is retinoblastoma with 17 specimens.

Malignant melanoma usually arises from the choroid and for a period of time is confined to this space. Retinal detachment was found in 24 cases; invasion into adjacent structures such as the sclera and retina or penetrations of the sclera was found in 45 cases, secondary glaucoma in 16 cases.

Retinoblastoma is a childhood tumor. Its rapid growth and local invasion is common. Survival is possible only when far reachinh extensions or metastases are not present.

Medical progress in the group of tumors is reflected in different ways which are actually poorly demonstrable but the physician should be more alert and detect these lesions as early as possible.

Senile macular degeneration is of importance because of the prognostic value to the patient. This lesion, I believe, is a result of a decreased blood supply to the macula because of senile changes of the vascular tree.

CONCLUSION

Sulfonamides and antibiotics have solved many problems. A great majority of the microorganisms producing diseases may be controlled by these drugs. The incidence of developing strains of sulfonamide-antibiotic resistant microorganisms are rare if these components are use properly.

Corneal lesions are almost completely healed if, in the stage where no major damage has occurred, these lesions are caused by microorganisms sensitive to these drugs. This same can be said for similar inflammatory lesions in the other parts of the eye that are well supplied with blood. Topical or systemic use concerns the location of the lesion and proper judgement as to which drug should be used. The vitreous and lens present a major problem in treatment if they become invaded by microorganisms.

Preventive use of sulfonamides and antibiotics have saved many eyes in spite of the fact that we lost many eyes to infection because of improper handling.

Many different kinds of traumatic injuries cause the loss of eyes and the incidence shows a definite increase in recent years. The major post-traumatic complication is secondary glaucoma which also shows a marked increase during the periods of sulfonamides-antibiotics because of invasion of microorganisms being better controlled in traumatized eyes which then develope a combination of post-traumatic and postinflammatory changes, upsetting the normal physiology of the, and thus it goes into the stage of secondary glaucoma or phthisis.

Sterile inflammatory lesions due to tissue sensitization to the foreign protein shows a reverse ratio to the purulent lesions which are controlled by new drugs. Investigation in this field is desirable.

Malignant melanoma, among our specimens, in many instances shows that invasion to adjacent tissues was present. Physicians and medical students should keep in mind that early recognition of such a lesion may save many lives.

Our medical schools should present the serious and more common lesions of the eye; also, other common diseases should be presented in more detail to impress upon the students, who will become general practitioners in this state, the sound basic management of such conditions.

APPENDIX

This additional appendix is given for those who will try to make the correct diagnosis of inflammatory lesions of the eye. There are a few suggestions which can be easily carried out in a moderately equipped office of the general practitioner in this country.

BACTERIOLOGY OF THE EYE AND EXTERNAL DISEASES
(Modified from Frederick H. Theodore, M. D.)

Cultures: In practical office bacteriology, cultures are generally reserved for:

(1) chronic conjunctivitis, (2) chronic blepharitis, (3) recurrent chalazia, (4) unusual or resistant types of acute infections, and (5) corneal ulcers.

A cotton swab moistened with broth is touched to the conjunctiva and then immediately inoculated upon blood and mannitol agar. The lid is cultured separately.

Staphylococcus "A" (toxic) is distinguished from staphylococcus "B" (non-toxic) by:

(1) pigment formation, (2) hemolysis, (3) positive coagulase test, (4) fermentation of mannitol, and (5) liquefaction of gelatine.

Tests 1, 2, and 4 are easily performed and generally suffice. The presence of staphylococcus "A" indicates staphylococcus toxoid or vaccine.

OUTLINE OF SLIDE DIAGNOSIS
(Modified from Dr. Thygeson)

Giemsa stain for epithelial scrapings:

1. Label slide with diamond marking pencil.
2. Fix in methyl alcohol for 3-5 minutes.
3. Immerse in coplin jar contining 40 cc. of dilute Giemsa solution (1 drop of Giemsa to 1 cc. of distilled water), for 1 hour. (Alternate technique: 1 drop of Giemsa to 2 cc. of distilled water and stain overnight.)
4. Quickly pass slide through two jars of 95% ethyl alcohol and allow to dry.

Polymorphonuclear exudates occur in:

1. All bacterial infections of the conjunctiva, except N. Catarrhalis, and Diplobacillus (Morax-Axenfeld) which is characterized by much fibrin and no mucus.
2. Fungi-streptothrix.
3. Certain "intermediate" viruses: (a) trachoma, (b) inclusion conjunctivitis, (c) lymphogranuloma venereum.

Mononuclear exudates (usually small lymphocytes) occur in the following virus infections:

(1) epidemic kerato-conjunctivitis, (2) acute follicular conjunctivitis of Beal, (3) molluscum contagiosa conjunctivitis, (4) herpes simplex conjunctivitis, and (5) verruca vulgaris conjunctivitis.

Eosinophiles and Basophiles occur in allergic conjunctivitis (usually of long standing):

(1) vernal catarrh, (2) hay-fever conjunctivitis, (3) atropine conjunctivitis, and (4) other drug, consmetic, and non-specific allergies.

In pilocarpine and eserine sensitivity and in phlyctenular kerato-conjunctivitis no eosinophilia occurs.

Diagnostic findings in trachoma:

(1) plasma cells in scrapings and exudates, (2) follicular expression (easily obtained):

(a) lymphoblasts (from germinal center), (b) macrophages (Leber cells), and (c) necrotic cells.

(In non-trachomatous follicles - expressed with difficulty - only small lymphocytes are found.)

Keratinized epithelium - (cells stain reddish; nuclei are absent or degenerated) occur in:

(1) avitaminosis, (2) exposure due to cicatricial changes or radiation, and (3) kerato-conjunctivitis sicca (also shows an increase in goblet cells and excessive mucus with absence of pus cells).

Note: Keratinization of epithelium is normal at lid margin, so there is no source of material.

Epithelial inclusions of ocular importance:

(1) Elementary bodies 150-200 millimicra in size.
(2) The following stain with Giemsa: (a) elementary bodies of trachoma (cytoplasmic), (b) inclusion conjunctivitis (cytoplasmic), and (c) lymphogranuloma venereum (cytoplasmic).
(3) Special stains needed for: (a) herpes simplex (intranuclear), (b) herpes zoster (intranuclear), and (c) vaccinia (cytoplasmic).

Cocci

Gram positive:

(1) Scattered, round, clumps or pairs; never on living epithelial cells - Staphylococcus.
(2) Pairs or short chains - Streptococcus.
(3) Lancer-shaped diplococci (end to end) - Pneumococcus.
(4) Varying-sized minute coccoid orgainsms - Streptothris.
(5) Large round bodies, varying in size, budding - Yeast.

Gram negative:

(1) Numerous coffee-bean intracellular diplococci, (side to side) found on living epithelial cells - Gonococcus or meningococcus.
(2) Similar morphology, not intracellular nor epithelial parasites, little pus - N. Catarrhalis.

Bacilli

Gram positive:

(1) Pleomorphic, large, curved; epith. parasite - C. Diphtheriae.
(2) Similar morphology; not epith. parasite - C. Xerosis.
(3) Short, fat, clubbed - C. Hoffmanni.
(4) Branching forms and filaments - Streptothrix.

Gram negative:

(1) Large diplobacillus, numerous, no pus - Morax-axenfeld.
(2) Always single, encapsulated - Friedlander.
(3) Large rod - Coli.
(4) Minute cocco-bacillus; not epith. parasite - Influenza.
(5) Minute slender rod from corneal ulcer - Pyocyaneous.
(6) Minute slender rod; epith. parasite - Koch-weeks.
(7) Large fusiform bacillus (pos.) & spirilli (neg.) - Vincent's.

Common causes of bacterial conjunctivitis:

Hyperacute Purulent: Gonococcus or meningococcus.
Acute Catarrhal: Staphylococcus "A", pneumococcus, influenza, and streptococcus.
Subacute: Pneumo, influenza, staph. "A", strept., Morax-Axenfeld.
Chronic: Staph. "A", Morax-Axenfeld.
Post-operative: Staph. "A", (mainly).
Conjunctivitis or Newborn: Staph. "A", pneumo., inclusion virus, influenza, lacrimal infection, coli, strept., gonococcus.

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