Review Article

The Human Lens: Inception to Excision

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ABSTRACT

The human lens are transparent. With advancement of age, there is a gradual loss of transparency which may lead to cataract formation. Every aging person develops morphological lens changes. However, it is remarkable that only in some patients these circumscribed opacities progress to mature cataracts. The time of occurrence of these opacities also varies widely. There may be huge variations in the morphological manifestations of these age-related lens changes. It is difficult to understand why opacification in some patients is more intense within the anterior cortex, whereas in the others, within the nucleus or within the posterior subcapsular region. These variations of senile cataracts are not inevitably caused due to aging alone but are caused by some other superimposed influences. Despite intensive research going on throughout the world for the factors which determine cataractogenesis; we know little about it. Knowledge about the development and microstructure of the lens is essential for studying the various biochemical and pathological changes occurring in the human lens leading to loss of its transparency. This article reviews the normal gross architecture of the human lens, the development of human lens and its microscopic anatomy, and the factors responsible for cataractogenesis. This article also reviews the evolution of cataract surgery from the ancient couching technique to the phacoemulsification technique.

Key words: Cataract, Cataractogenesis, Couching, Lens

INTRODUCTION

Opacification of the lens of the eye which makes it blind is called cataract.[1,2] The name derives from the Latin word cataracta meaning "waterfall" and the Greek *kataraktes* and *katarrhaktes*, from *katarassein* meaning "to dash down" (*kata*-, "down"; *arassein*, "to strike, dash"). As rapidly running water turns white, the term was later used metaphorically to describe the similar appearance of mature ocular opacities.[3]

The origin of the word cataract mentioned above is however disputed. One meaning is "waterfall" related with the term καταρακτον which the Greeks use for Nile rapids. They thought that the fluid or humor came between lens and iris and disturbed vision. The Greeks also used the term glaucosis for the clouding of pupillary opening caused by coagulation of the eye humors as they thought. Later, the tern hypochyma or suffusion took over the meaning of glaucosis.[4] Physicians at that time thought of cataract as "suffusion" behind the iris, due to the white pupillary reflex produced by mature cataract (Celsus, AD 30). Constantinus Africanus (AD 1018), a monk and an Arabic oculist, introduced the term "cataract" by translating the Arabic equivalent of "suffusion" into Latin "cataracta," which meant "something poured underneath something.,"[3,5]

The ancient Greeks and Romans located the lens in the center of eye. They thought that lens was the principal organ of vision. The anterior position of lens in the eye was described by Galen (130–200), and much later rediscovered in Europe during the renaissance by Bartisch (1583) and Aquapendente (1601). The two later located the lens directly behind the iris without

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any cataract space in between.[4] This article reviews the normal architecture of lens, its opacity, and the evolution of cataract surgery.

ANATOMY OF LENS[1,6,7]

The lens is a transparent and biconvex flexible body that intervenes between the iris in front and the vitreous body behind [Figure 1]. It is circular in outline. It presents anterior and posterior surfaces separated by rounded border, the equator. The central points of both surfaces are called anterior and posterior poles, respectively. The line joining the two poles is called the axis of lens. The lens is devoid of blood supply or nerve supply and obtains nutrition by diffusion from the aqueous and vitreous humor. It is entirely surrounded by capsule. Just beneath the anterior capsule, there is a single layer of epithelial cells. The innermost central part of lens is called nucleus and outer part cortex.[8,9]

THE EYEBALL

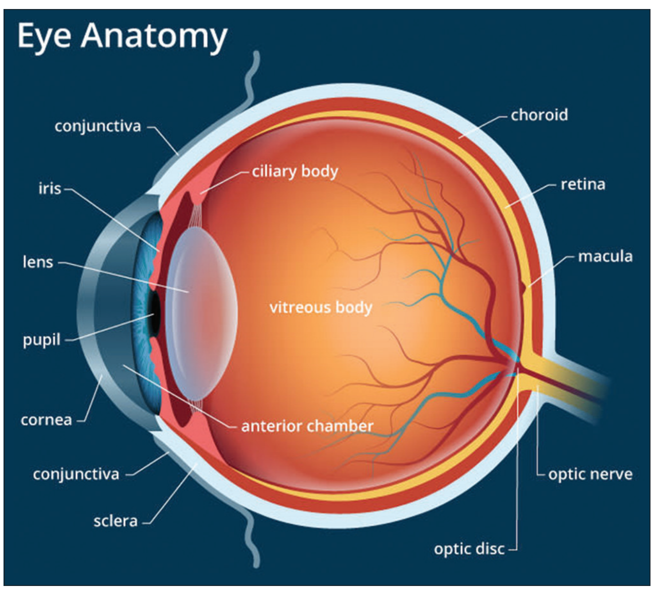

Figure 1: Human eye sectional view

DEVELOPMENT OF LENS

The vertebrate lens develops from head ectoderm overlying the optic vesicle. The association between surface ectoderm and the optic vesicle induces the development of lens plate, or placode which can be seen at 4 mm stage of embryo. The cells of optic vesicle keep on elongating simultaneously. By the 5 mm stage, the lens placode begins to invaginate, forming the lens pit. The optic vesicle also simultaneously gets invaginated, forming the optic cup. The lens pit further invaginates and finally gets detached from the ectoderm to form lens vesicle at 9 mm stage. The embryonic lens hence occupies a space in the concavity of optic cup [Figure 2]. The cells in the posterior portion of lens vesicle elongate to fill the vesicle. These elongated cells form primary lens fibers which eventually lose their nuclei and become the embryonic nucleus of the adult lens. Meanwhile the cells in the anterior part of the vesicle divide actively and become elongated forming secondary lens fibers. The secondary lens fibers elongate toward the anterior and posterior poles of embryonic lens surrounding the embryonic nucleus. The equatorial zone of lens epithelium continues to divide throughout life, producing the cells that differentiate into long lens fibers [Figure 3].

DEVELOPMENT OF LENS

Embryonic lens capsule is seen as a thin basal lamina at 9–10 mm stage. It is synthesized by the epithelium and most superficial lens fiber cells at the posterior surface. Embryonic lens is supplied by blood vessels, tunica vasculosa lentis, and most prominent during 60 mm stage. At about 240 mm stage, vascular system regresses and disappears shortly before birth, leaving the lens without blood supply for rest of life.

MICROANATOMY OF LENS[1,6-8]

The lens capsule is an acellular and elastic structure. It is the thickest basement membrane in the body. It appears to be an anatomical structure that is unchanged throughout life. It surrounds the lens completely and maintains its structural integrity. It receives nutrition from the lens epithelium and fibers, is tough and resistant to traction, and is freely permeable to low molecular weight compounds but restricts movement of larger colloidal material. The main function of capsule is to modify the shape of lens in response to tension on zonules, which is altered during the process of accommodation.

Beneath the capsule, anterior surface of lens is lined by single layer of low cuboidal epithelium. Equatorial epithelial cells elongate and differentiate into lens fibers that turn meridionally and form bulk of lens substance. They are generally hexagonal in shape and nucleated. During the transformation of lens cells into lens fibers, the old fibers in the center lose their nuclei and the new fibers at the periphery possess flattened nuclei. Each lens fiber therefore represents an elongated cell with cell membrane which measures around 8–12 mm at maturity. Sutures of the lens are formed by these fibers arising from the equatorial epithelium which extend anteriorly and posteriorly and meet each other. There are about 2000 lens fibers in adult lens [Figure 4].[1]

Various junctional complexes including desmosomes on the lateral and apical aspects of cell and zonula occludentes are present between the epithelial cells. Another essential feature of lens is an extensive amount of low resistance gap junctions present between fiber cells. These numerous gap junctions help the tissue to function like a syncytium rather than a collection of individual cells. The metabolic and synthetic activity of the lens epithelium is critical for the survival of entire lens.

The harder central part of the lens is known as nucleus and peripheral softer part forms the cortex. Oldest fiber cells are in the center and youngest at the periphery. The laminated structure of lens is due to continuous addition of fibers in the region of equator. Fibers produced here are pushed toward the center of lens and new fibers take their place. This process goes on throughout life. Fiber cell produced at all stages of life from the embryonic stage to the most recent stage are present in the lens.

LENS COMPOSITION[1]

Composition of lens may vary according to the age of lens, and in the given lens according to region selected.

Lens has highest protein content than any biological tissue found in nature.[8] Protein accounts for 33% wet weight of lens, nearly double to that found in other tissues (e.g., brain 10% and muscle 18%). The high concentration of protein is presumably to create a medium of high optical density and therefore high refractive index. Based on solubility in water lens proteins can be divided in two classes. The water-soluble lens crystallines are about 90% while water insoluble proteins consisting of membrane proteins, cytoskeletal proteins, and aggregated crystallines are about 10%.[1,6,9]

The adult human lens contains approximately 66% water which is very low compared to other tissues. Lens capsule contains about 80% water while the water content of the dense nuclear region of the lens is less than that of the outer cortex. There is no significant alteration in lens hydration with aging, but in many forms of cataract lens hydration is dramatically increased. Much of the lens water is in a bound form and less amount in free form.[1]

Other constituents of lens include – amino acids, enzymes, carbohydrates, lipids, potassium and magnesium ions, sodium ions, chloride ions, calcium ions, phosphate, sulfate, bicarbonate and various trace elements including iron, copper, manganese, zinc, and boron.[1]

The cholesterol-phospholipids ratio of human lens fiber membranes is the highest among cell or organelle membranes making the lens resistant to deformation.

Even though the lens has high protein content and is highly refractile, it is transparent.[8] The transparency of lens is largely the result of highly ordered arrangement of macromolecular components of lens cells and small differences in refractive index between light scattering components and the regular arrangement of lens fibers. Even distribution of proteins, that have predominantly lamellar conformation rather than helical, regularity of lens structure and its avascular nature are also responsible for lens transparency.[1]

CATARACT MORPHOLOGY

The beautiful architecture of lens undergoes considerable disruption in the process of cataract development. Cataract is nothing but the loss of transparency [Figure 5]. Since transparency of lens is so highly dependent on protein order and structural integrity, relatively small changes in any of these parameters might lead to development of opacification leading to cataract. Such changes in the lens might include aggregation, changes in tissue hydration, phase separation of molecular components, breakdown of cellular membranes, and changes in structure of cytoskeleton. Most, if not all, of these changes can and do take place during aging and cataract development.[1]

CATARACT SURGERY

There are allusions in the literature that cataract surgery is being performed for two millennia and used to be performed as early as 300 BC with no description of methods and techniques. Couching is the first documented cataract surgery. Early descriptions in history came from India in 600 BC described in ancient Indian Sanskrit manuscripts. In ancient Hindu Medicine, cataract was called “lingnash” and was interpreted as a type of corrupt humor and the teaching of Sushruta

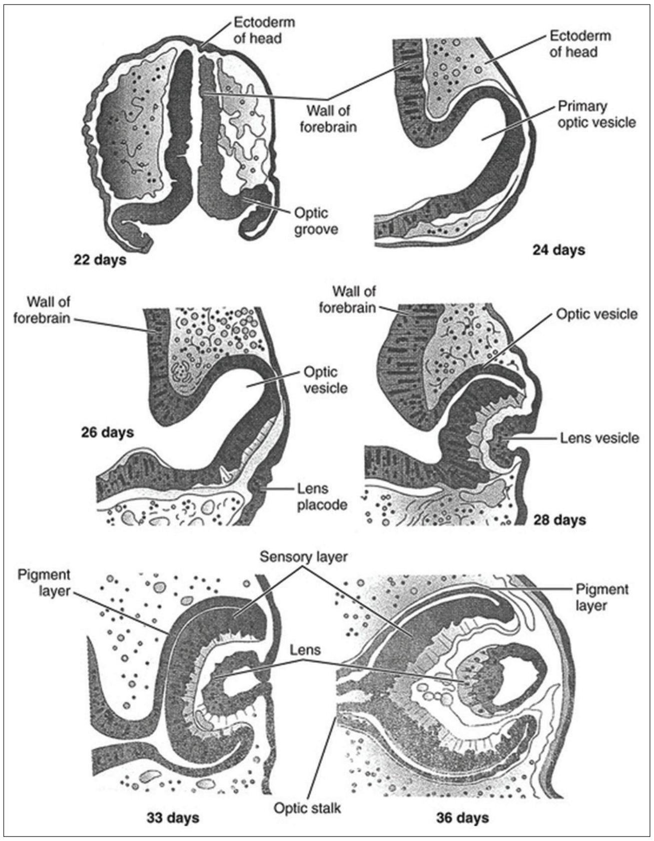

Figure 2: Development of human lens

on its relief by couching are remarkably precise and in detail. He also described a few types of cataracts.[9,11] Physicians used to insert a sharp instrument (a needle or lancet) around 4 mm posterior to the limbus or into clear cornea, pointing toward the whitish opacity. Then, in a downward movement, the lens was dislodged away from the pupil. An assistant held the patient;s head steady while the surgeon inserted a needle into the eye and pushed the clouded lens out of the visual axis, allowing it to rest, or "couch," in the back of the eye.[4,5,12]

Some variations of the couching technique included inserting a hollow needle and "aspirating" the cataract. Cataract extraction by suction was performed by Antyllus, a contemporary of Galen, and extraction was established in China during the 10th century.[4] It was also described by Iraqi and Syrian oculists around 1000 AD.[5] In Rome, archeologists found ancient cataract surgical instruments dating back to the first and second century AD.[13] This technique is also known to have existed in Roman times and continued to be used throughout the Middle Ages and continues to be used in underprivileged "Third World" countries today.[3,14]

Although few early cases of *in situ* lens extraction occurred in Europe, extraction technique was not established until 1753 when a French oculist by the name, Jacques Daviel, (1696–1762) described a new method of cataract surgery which essentially was the first report of a planned extracapsular extraction.[5,4] Daviel performed his first operation of extracapsular cataract extraction on April 2, 1745.[10] Oculists however continued to couch and the extracapsular technique never gained merit until later on in the 19th century. Recognizing that Daviel's method could produce vitreous loss, modern surgeons opted to Sharp's technique, which described the removal of the lens in toto (Intracapsular extraction).[5]

The evolution of cataract surgery took a giant step in 1949 when Harold Ridley, a doctor in England, developed and implanted the first intraocular lens (IOLs). This first IOL was made of a hard plastic material (PMMA) and was designed to imitate the natural human lens. Nowadays, single-piece and all-acrylic foldable lenses are used as IOLs.[13] In the early 1970s, with the introduction of the IOLs and the published results on the complications of absent capsules, surgeons reverted to extracapsular extraction. In the 70s, only emerged new advanced hydrodynamic system, the phacoemulsification technique, which produced high frequency mechanical waves out of an electric current incorporating irrigation and aspiration all in one setting. This technique gained wide popularity due to minimal post-operative complications.

BURDEN OF DISEASE

According to the World Health Organization (WHO) definition of 20/400 vision, approximately 38 million people are blind worldwide. Cataract represents more than 50% of all blindness. About 50% of the general population between the ages of 65 and 75 years has cataracts and that number increases to 70% after age of 75. At least 5–10 million new cataracts occur yearly, throughout the world. It is estimated that more than 1.3 million cataract extractions are performed each year. In India, 4 million new cataract cases are diagnosed annually. The number of people becoming blind from cataracts each year exceeds the number of surgeries performed for cataracts each year. Cataract surgery is the most common operation performed on patients over 65 years of age.

The pathophysiology behind causation of cataracts is complex and yet to be fully understood. In all

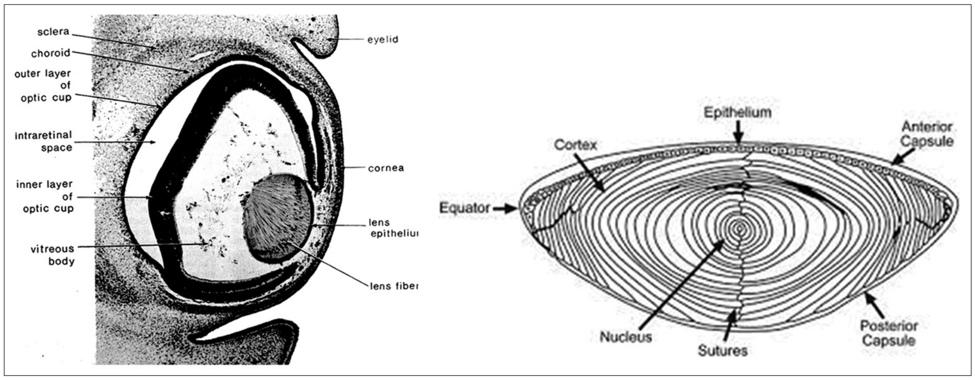

Figure 3: Lens Epithelium and Lens Fibres

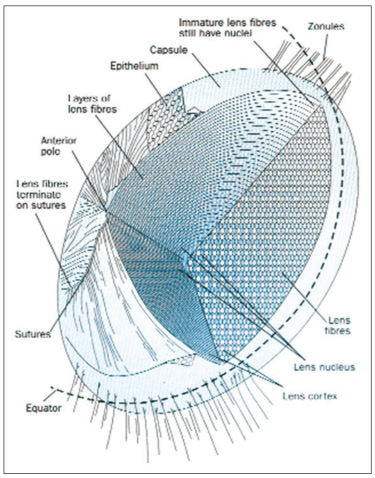

Figure 4: A three-dimensional diagram of lens cut open to reveal layers of lens

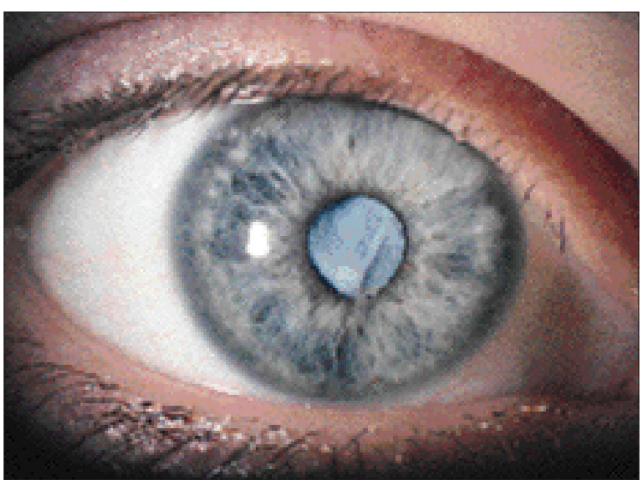

Figure 5: Mature cataract with associated wrinkling of anterior lens capsule

probability, its pathogenesis is multifactorial involving complex interactions between various physiologic processes. These interactions lead to changes in normal morphology, histology, and biochemistry of beautiful transparent lens which gradually loses its transparency leading to advancement of cataract.

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