INTRODUCTION

The corneal endothelium is embryologically derived from the neural crest and is arrested in the post-mitotic state. Cell loss due to aging or corneal endothelial disorders leads to corneal edema and defective vision. The postnatal total endothelial cellularity of the cornea (approximately 300,000 cells per cornea) is achieved as early as the second trimester of gestation. Thereafter the endothelial cell density (but not the absolute number of cells) rapidly declines, as the fetal cornea grows in surface area[1], achieving a final adult density of approximately 2400 - 3200 cells/mm². [1]

The number of endothelial cells in the fully developed cornea decreases with age up until early adulthood, stabilizing around 50 years of age. [2]

The normal corneal endothelium is a single layer of uniformly sized cells with a predominantly hexagonal shape. This honeycomb tiling scheme yields the greatest efficiency, in terms of total perimeter, of packing the posterior corneal surface with cells of a given area. The corneal endothelium is attached to the rest of the cornea through Descemet's membrane, which is an acellular layer composed mostly of collagen.[2]

The principal physiological function of the corneal endothelium is to maintain corneal clarity by regulating corneal

hydration through passage of solutes and nutrients from the aqueous humor to the more superficial layers of the cornea while at the same time actively pumping water in the opposite direction, from the stroma to the aqueous. This dual function of the corneal endothelium is described by the "pump-leak hypothesis".[3]

Since the cornea is avascular, which renders it optimally transparent, the nutrition of the corneal epithelium, stromal keratocytes, and corneal endothelium must occur via diffusion of glucose and other solutes from the aqueous humor, across the corneal endothelium.[2]

The corneal endothelium then actively transports water from the stromal-facing surface to the aqueous-facing surface by an interrelated series of active and passive ion exchangers. Critical to this energy-driven process is the role of Na^+/K^+ATPase andcarbonic anhydrase. Bicarbonate ions formed by the action of carbonic anhydrase are translocated across the cell membrane, allowing water to passively follow.[4]

Leading causes of endothelial failure include endothelial trauma from intraocular surgery such as cataract surgery. Endothelial failure include both acute intraoperative trauma as well as chronic postoperative trauma, such as retained nuclear fragment in the anterior chamber or malpositioned intraocular lens.[4]

It is well known that during cataract surgery many different factors can generate endothelial damages including the impact of the nuclear fragments, the turbulence generated in the anterior chamber and the volume of the liquid, air bubbles formation, the amount of the ultrasonic energy used and the subsequent temperature increase, contacts with the surgical instruments and the IOL during implantation, the release of free radicals, the length and the features of the incision, the surgical techniques used and the intraoperative complications such as posterior capsule rupture.[5]

The risk of endothelial cell density loss is further enhanced when surgeons have to deal with high-density cataracts, shallow anterior chambers, old age and short eyes.[5]

Viscoelastic materials possess a unique set of properties that result from their chemical structure. These properties enable them to protect the corneal endothelium and epithelium from mechanical trauma and to maintain an intraocular space, such as the anterior or vitreous chambers, even in the face of an open incision. Hence viscoelastic materials have been successfully applied to many areas of ophthalmic surgery, most notably anterior segment surgery, with few complications.[6]

The introduction of ultrasonic phacoemulsifiers has led to a critical reduction in the ultrasounds with the subsequent dramatic improvement of the followability and the holdability. In addition, the development of new viscoadaptive viscoelastic

has provided significant endothelium protection from turbulence, from nuclear fragments and contact with surgical tools.[5]

The OZil Torsional system is a hardware and software upgrade, which includes a dedicated handpiece that produces side-to-side rotatory oscillations of the phaco tip.[7]

Compared with the jackhammer motion in conventional phaco, the OZil Torsional oscillation sheers the lens material with virtually no repulsion, thereby dramatically improving the flow of nuclear material into the phacoemulsification tip, and reducing US energy required for lens removal without compromising efficiency.[7]

Femtosecond laser–assisted cataract surgery provides surgeons an exciting new option to potentially improve patient outcomes and safety. Over many years, 4 unique laser platforms have been introduced into the marketplace. [8]

AIM OF THE WORK

THe aim of the work is to compare between the effect of standard phacoemulsification and microincision intelligent phacoemulsification on corneal endothelium to minimize risk of its loss during cataract surgery.

Chapter 1

ANATOMY AND EMBRYOLOGY OF THE CORNEA

Anatomy of the cornea

The cornea is a transparent avascular connective tissue that acts as the primary infectious and structural barrier of the eye.It forms the anterior 1/6 of the outer fibrous coat.[2]

Together with the overlying tear film, it also provides a proper anterior refractive surface for the eye.[2]

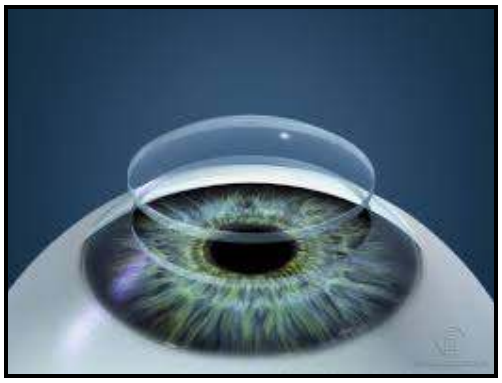

Fig. (1): Human cornea [9]

It is a clear, essentially colorless avascular structure richly supplied with sensory nerve endings that generally subserve touch and pain. There are no lymph vessels or other channels for bulk fluid flow. The interface between the corneal tear film and the ambient atmosphere provides roughly two thirds of the refractive power of the human eye.[2]

The cornea itself is resilient and may be described as viscoelastic in its response to stretching forces. The size, shape, and optical properties of the cornea change little with age. Due to the avascular nature of the cornea, much of its oxygen requirement for metabolic activities comes from atmospheric oxygen dissolved in the tear film .[2]

When the eyelids are closed, oxygen enters the tear film from the superficial conjunctival capillaries. Nutrients such as carbohydrates, vitamins, amino acids, and other substrates are generally delivered through the vascular arcades at the limbus and pass into the corneal stroma or through the corneal endothelium by diffusion or active transport.[3]

Some constituents, such as oxygen and retinale (vitamin A), are found in the tear film and provide nutrition to the cornea. Carbon dioxide and other metabolic end products are similarly removed across the tear film, the corneal endothelium, or through the limbal capillaries.[3]

The newborn infant has a relatively large cornea that reaches adult size by the age of 2 years. It is flatter than the adult cornea, and its curvature is greater at the periphery than in the center. (The reverse is true in adults).[1]

Microscopic anatomy

1) Epithelium

The corneal epithelium covers the front of the cornea. It acts as a barrier to protect the cornea, resisting the free flow of fluids from the tears, and prevents bacteria from entering the epithelium and corneal stroma.[1]

The corneal epithelium consists of several layers of cells (40 Um to 50 Um). The cells of the deepest layer are columnar, known as basal cells. Then follow two or three layers of polyhedral cells, commonly known as wing cells. The majority of these are prickle cells. Lastly, there are three or four layers of squamous cells, with flattened nuclei (Fig.2).[1]

The layers of the epithelium are constantly undergoing mitosis. Corneal epithelial cells have an average lifespan of 7 to 10 days and routinely undergo orderly involution, apoptosis (programmed cell death), and desquamation.[2]

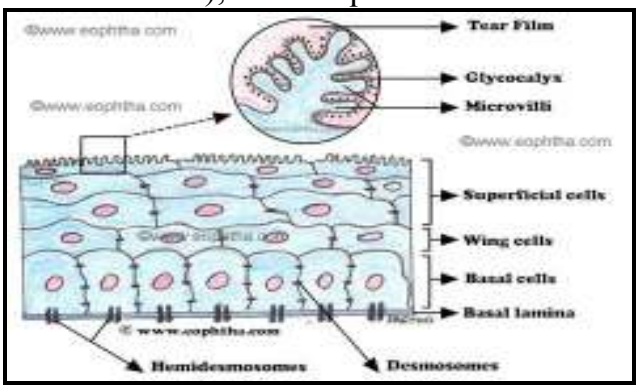

Fig. (2): Layers of corneal epithelium.[10]

This process results in complete turnover of the corneal epithelial layer every week as deeper cells replace the desquamating superficial cells in an orderly, apically directed fashion (fig.3).[1]

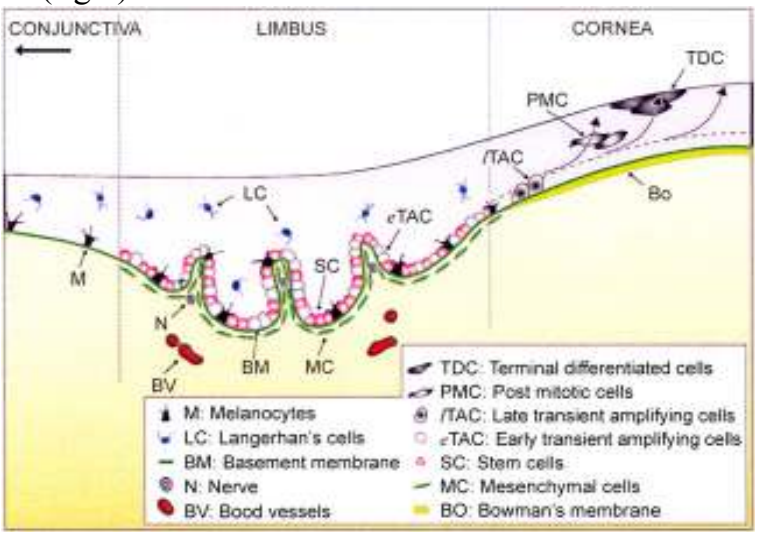

Fig. (3): Hypothetical scheme of limbal stem cell niche. [11]

The epithelial stem cells are the undifferentiated pluripotent cells which serve as an important source of new corneal epithelium. They are found in limbal basal epithelium of palisades of Vogt.[1]

2) Bowman's membrane

The Bowman's membrane (Bowman's layer, anterior limiting lamina, anterior elastic lamina) is a smooth, acellular, non-regenerating layer, located between the superficial epithelium and the stroma in the cornea of the eye. It is composed of strong, randomly oriented collagen fibrils in which the smooth anterior surface faces the epithelial basement

membrane and the posterior surface merges with the collagen lamellae of the corneal stroma proper.[2]

The Bowman's membrane is named after Sir William Bowman (1816–1892), an English physician, anatomist and ophthalmologist, who discovered this membrane.

The adult humans, Bowman's membrane is 8-12 μm thick.With aging, this layer becomes thinner. The Bowman's layer, which (in mammals) is found only in primates and it is absent in cats, dogs, mice .[1]

The function of the Bowman's membrane remains unclear and appears to have no critical function in corneal physiology. Recently, it is postulated that the layer may act as a physical barrier to protect the subepithelial nerve plexus and thereby hastens epithelial innervation and sensory recovery. Moreover, it may also serve as a barrier that prevents direct traumatic contact with the corneal stroma and hence it is highly involved in stromal wound healing and the associated restoration of anterior corneal transparency at the morphological level.[2]

3) Stroma

The stroma accounts for 80 to 90% of the corneal thickness. It is composed of approximately 15% collagen (type 1) by weight. The collagen is arranged in layers or lamellae that run parallel to the corneal surface (Fig.4).[2]

The stroma of the human eye contains 200 to 250 distinct lamella, each layer arranged at right angles relative to fibers in adjacent lamellae.[2]

Each transparent lamellae is 1 to 2 μm thick. Parallel fibers in one lamella are oriented at a different angle than those in adjacent lamellae. Interspersed between the collagen fibrils are proteoglycans (PG), glycoproteins, and salts.[1]

Proteoglycans comprise 4% to 5% of the dry weight of the cornea and have a major role in controlling the hydration, thickness, and transparency of the cornea. Keratocytes are fibrocytes residing in the stroma that secrete PG, collagen, and proteases. Keratocytes can phagocytoze particles and undergo shifts in PG and collagen synthesis in response to injury.[1]

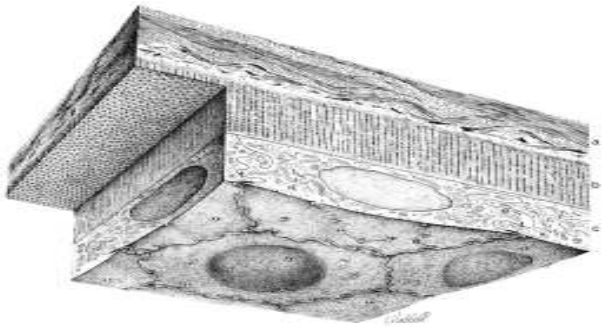

Fig. (4): A figure showing regular fibers of the stroma .[12]

Descement folds are the result of asymmetric swelling of the posterior stroma imposed by the structurally more rigid anterior cornea and structural restriction imposed by the limbus.[1]

Keratocytes are the major cell type of the stroma and are involved in maintaining the ECM environment. They are able to synthesize collagen molecules and glycosaminoglycans while also creating matrix metalloproteases (MMPs), all crucial in maintaining stromal homeostasis.[1]

Most of these keratocytes reside in the anterior stroma and contain corneal"crystallins," representing 25% to 30% of soluble protein in the cells. These crystallins appear to be responsible for reducing backscatter of light from the keratocytes and maintaining corneal transparency.[1]

4) Dua's layer

Researchers at The University of Nottingham have discovered a new layer of the human cornea located at the back of the cornea between the corneal stroma and Descemet's membrane. The new layer has been dubbed the Dua's Layer after the academic Professor Harminder Dua who discovered it.[9]

The new layer that has been discovered is located at the back of the cornea between the corneal stroma and Descemet's membrane. Although it is just 15 microns thick, the entire cornea is around 550 microns thick or 0.5mm, it is incredibly tough and is strong enough to be able to withstand one and a half to two bars of pressure.[9]

The scientists proved the existence of the layer by simulating human corneal transplants and grafts on eyes donated for research purposes to eye banks located in Bristol and Manchester.[9]

During this surgery, tiny bubbles of air were injected into the cornea to gently separate the different layers. The scientists then subjected the separated layers to electron microscopy, allowing them to study them at many thousand times their actual size.[9]

The scientists now believe that corneal hydrops, a bulging of the cornea caused by fluid build up that occurs in patients with keratoconus (conical deformity of the cornea), is caused by a tear in the Dua layer, through which water from inside the eye rushes in and causes waterlogging.[9]

5) Descement's membrane (fig.5)

Descement's membrane, constituting the basal lamina of the corneal endothelium, has a homogeneous appearance on light microscopy but a laminated appearance on electron microscopy due to structural differences between its pre- and postnatal portions. It is about 3 μm thick at birth but increases in thickness throughout life, reaching 10-12 μm in adulthood.[1]

It is composed of a different kind of collagen (Type IV) than the stroma. Descemet's membrane, as the basement membrane for the endothelial layer, is secreted by the single

layer of squamous epithelial cells that compose the endothelial layer of the cornea.[1]

It is also known as the posterior limiting lamina, posterior elastic lamina, lamina elastica posterior, and membrane of Demours. It was named after French physician Jean Descemet.[1]

Significant damage to the membrane may require a corneal transplant as the endothelial cells depend on it for support and cannot re-grow after injury without it.[2]

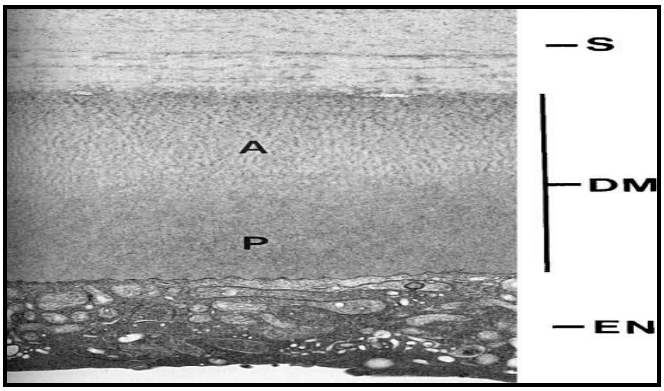

Fig. (5): Micrograph illustrating Descemet membrane (DM) located between the posterior aspect of the corneal stroma (S) and the underlying endothelium (EN). The anterior "banded" region (A) is secreted by the endothelial cells during fetal development and is more highly organized than the posterior "amorphous region" (P), which is secreted after birth. [14]

6) Endothelium

The name endothelium is misnomer. Basically, corneal endothelium is a simple squamous epithelium. The shape of the individual cells is hexagonal which forms continuous mosaic pattern, best seen in specular microscopy (Fig.6).[2]

The endothelial cells are interconnected with each other with various junctional complexes like zonula occludans, macula occludans and macula adherens. These cells possess ion transport system which is known as endothelial pump. These endothelial pumps regulate the water content of corneal stroma.[2]

With ageing, the cell density of the endothelium decreases which is compensated by an increase in cell size (Polymegathism) or shape (Pleomorphism).[2]

The central endothelial cell density decreases at an average rate of 0.6% per year in normal corneas.[1]

As these endothelial cells are involved in corneal hydration (which helps in maintenance of corneal transparency), endothelial cell density below 800 cells/mm^2 leads to corneal decompensation.[2]

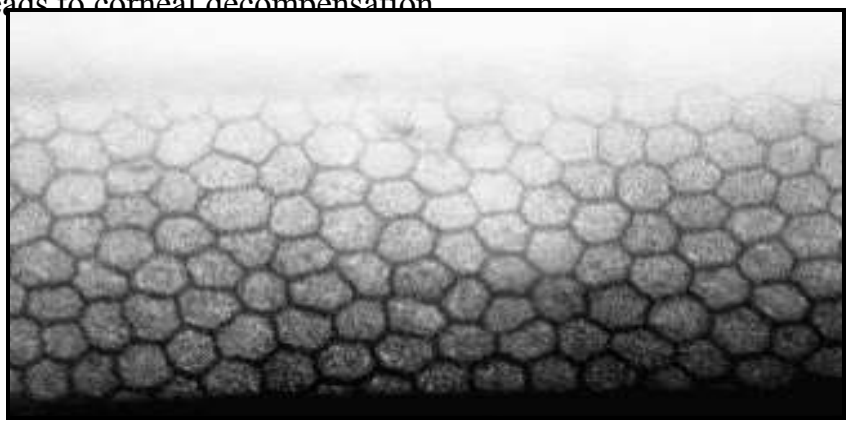

Fig. (6): Specular photomicrograph of normal endothelium. Note the dark well-defined cell borders, the regular hexagonal array,and the uniform cell size.[13]