INTRODUCTION

The cornea is a membrane that forms a barrier between the eye and external environment.

The cornea is formed of six layers,their arrangement from outwards inwards are:

1. Epithelium.
2. Bowman's layer.
3. Stroma (substantia propria)
4. Descemet's membrane.
5. Dua's layer
6. Endothelium.

New corneal layer (Dua's layer), which is a novel, well-defined, acellular, strong layer in the pre-Descemet's part of the cornea. This separates along the last row of keratocytes in most cases performed with the big bubble (BB) technique. Its recognition will have considerable impact on posterior corneal surgery and the understanding of corneal biomechanics and posterior corneal pathology such as acute hydrops, Descemetocele and pre-Descemet's dystrophies ***(Rahman et al., 2012).***

The cornea is a multi-laminated tissue, consisting of an anterior stratified squamous “tight” epithelium (about 50µm thick), a tough collagenous stroma, and a posterior “leaky” monolayer of active pumping endothelial cells (about 5µm thick). Its combination of remarkable strength and transparency is due to highly organized micro-structure and nano-scale of the stroma. On the micro-scale, the stroma comprises 250-400 lamellae containing type (I and V) heterotropic collagen fibrils arranged in meridional, horizontal and circumferential directions ***(Jaycock et al., 2005)***.

These two factors (anatomy and material properties) will reflect the biomechanical behavior of the cornea in response to forces such as the intra ocular pressure (IOP) and surgical interventions.

Finally, this behavior will result in a specific shapefor the cornea that determines its opticaloutcome.Hence, its effect on the vision ***(Luce et al., 2005).***

Corneal biomechanics are related to corneal response to an applied force, they are important for maintaining corneal health and follow up of progression of diseases and outcome after refractive surgeries, and also critical for IOP.

Some of corneal biomechanical parameters:

1. **Elasticity:** ability of the cornea to deform with complete reversibility, and is the ratio between stress and strain, it is not time dependent.

2. **Viscosity:** is the resistance of the material to flow or deform, and it is time dependent.

3. **Corneal hysteresis:** (CH) phenomenon is a result of viscoelastic dampening in the cornea due to the combined effect of the corneal thickness and rigidity. In other words, the tissue's ability to absorb and dissipate energy.It is not stiffness and not represent elasticity.

4. **Corneal resistance factor (CRF):** is an empirical function, there is negativecorrelation with CH and CRF with the age.

5. **Central corneal thickness (CCT)**: CCT was the primary factor used for screening candidates for refractive surgery. Patients with thinner corneas are considered to be at higher risk for developing post-LASIK corneal ectasia. However, due to the large and easily identifiable differences in hysteresis between normal and compromised corneas, this metric value provides a more accurate characterization of the biomechanical state of the cornea than does the measure of CCT.

This observation is coupled with the fact that CH is only weakly correlated with CCT. Hysteresis and CCT are related but are not measurements of the same biomechanical parameter ***(Ambrosio et al., 2007)***.

It has been shown that the elastic and viscoelastic properties of the cornea are related, making possible the use of the hysteresis measurement to arrive at a more accurate measurement of IOP less influenced by corneal properties such asCCT.

And does not appear to drop artificially post-laser in situ keratomileusis (LASIK), present a complete characterization of the cornea's biomechanical state, which has potential uses in screening refractive surgery candidates and predicting outcomes ***(Liu et al., 2005)***.

The exact mechanism which maintains the corneal contour itself is not known,but may be due to the passive distension of corneal tissues which is maintained by the corneal mass, the elastic properties of corneal tissue and the mechanical force acting on this tissueIOP. However individuals, and these parameters have been widely accepted as important when measuring, rigidity or elasticity of corneas are known to vary greatly between IOP ***(Luce et al., 2005)***.

New devices can measure corneal biomechanics:

1. The Ocular Response Analyzer (ORA) is a new devicewhich is an adaptation of the non-contact tonometer that allows measurement of IOP as well as new measurements called CH and corneal resistance factor CRF ***(Shimmyo et al., 2003)***.

The ORA determines corneal biomechanical properties using an applied force–displacement relationship. An air jet similar to that used in traditional air-puff tonometers generates force/pressure on the cornea. To distinguish between corneal biomechanical properties and IOP ***(Martinez et al., 2006).***

Unlike conventional tonometers, ORA make a dynamic measurement which includes two applanation events enabling the device to gain information about the cornea's response to the air pressure pulse ***(Wells et al., 2008)***.

It provides several variables as the Goldmann-correlated IOP, corneal-compensated IOP, CRF, and CH ***(Martinez et al., 2006)***.

2. A New Tonometer–The Corvis ST Tonometer:

The Corvis ST (CST), a newly developed tonometer with features of visualization and measurement of the corneal deformation response to an air impulse.

The CST offers an alternative method for measuring IOP. IOP measurements taken with these devices may not be interchangeable ***(Fabian et al., 2012).***

AIM OF THE WORK

Our aim is to review literatures about corneal biomechanics, its importance, factors affecting it, and its measurements, using new devices enabling us topredict the results and the complications after the surgery. In addition, it gives us an accurate measurement of IOP.

ANATOMY, PHYSIOLOGY AND BIOCHEMISTRY OF THE CORNEA

Anatomy

Gross anatomy:

The cornea is a transparent, avascular tissue. The anterior corneal surface is covered by the tear film, and the posterior surface is directly bathed by the aqueous humor. The transparent cornea is continuous with the opaque sclera and semitransparent conjunctiva. The transitional zone between cornea and sclera is the richly vascularized limbus ***(Anthony et al., 2003)***.

The adult cornea measures 11 to 12 mm horizontally and 9 to 11 mm vertically. It is approximately 0.56 mm thick at the center, and increases gradually toward the periphery where it is about 1 mm thick. The radius of curvature of the anterior surface is about 7.7 mm horizontally and 7.8 mm vertically, and that of posterior surface is about 6.9 mm ***(Snell et al., 2003)***.

The refractive power of the anterior surface is about +48 diopters (D) and that of the posterior surface -4 Dand so the mean refractive power is 44±2 D. Thus, the cornea provides about 3/4 of the total refractive power of the eye which is about 60 D ***(Snell et al., 2003)***.

Microscopic anatomy of the cornea:

It is formed of six layers, their arrangement from outwards inwards are:

1. Epithelium.
2. Bowman's layer.
3. Stroma (substantia propria).
4. Pre-Descemet (Dua's layer).
5. Descemet's membrane.
6. Endothelium.

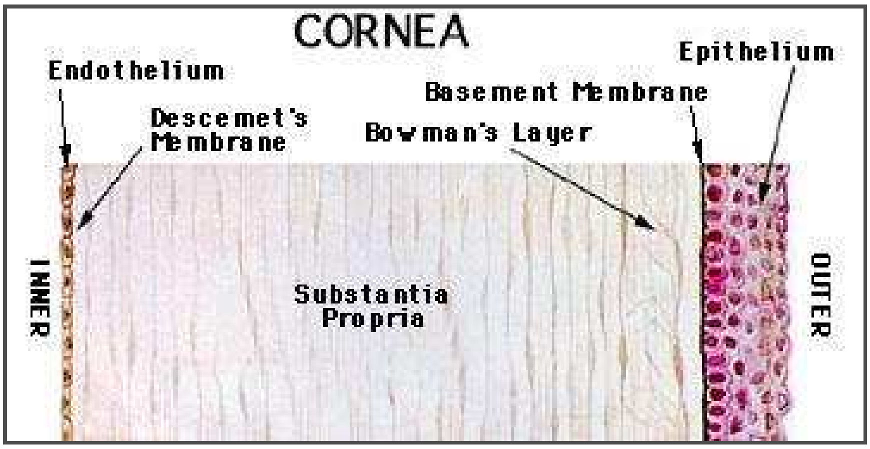

Figure (1): The corneal layers ***(Anthory et al., 2003)***.

1- Epithelium:

It consists of stratified, squamous, non-keratinized cells of about 60 µm thickness about 10% of the total thickness of the cornea. The corneal epithelium consists of five to six layers of three different types of epithelial cells.The basal cells are the deepest and stand in a palisade like manner on a basal lamina, representing the generative layer of the epithelium. The basal cells are columnar with rounded heads and flat bases. Each nucleus is oval and parallel to the cell`s long axis. The second layer (the wing cells) consists of polyhedral cells, convex anteriorly, which cape the basal cells, and send processes between them. The long axis of their nuclei is parallel to the corneal surface. The next 2-3 layers are also polyhedral and become wider and increasingly flattened towards the surface. The surface cells have largest surface area which is greater at the periphery; they retain their nuclei and do not show keratinization. Their nuclei projects posteriorly leaving the surface perfectly smooth ***(Anthory et al., 2003)***.

2- Bowman's layer:

It is a narrow, acellular homogenous zone, 8-14 µm thick, immediately subjacent to the basal lamina. The anterior surface is smooth and parallel to the corneal surface. It consists of a meshwork of collagen fibrils of uniform size, lying in a ground substance. The compacted arrangement of the collagen offers a great strength of this zone. Bowman's layer is relatively resistant to trauma, once destroyed it is not renewed but replaced by coarse scar tissue ***(Smolek et al., 1993)***.

3- Stroma (substantia propria):

It is about 500 µm thick and forms about 90% of the cornea.Itconsists of extracellular matrices, keratocytes (corneal fibroblasts), and nerve fibers. Cellular components occupy only 2to 3% of the total volume. The rest is occupied by extracellular matrices; collagen and glycosaminoglycans. Collagen occupies more than 70% of the dry weight of the cornea. The collagens are primarily collagen type I, with lesser amounts of types III, V and VI ***(Tripathi et al., 1998)***.

Collagens are stiff fibrous molecules, and one of the more abundant proteins throughout the body. Keratocytes synthesize a pro-α–chain of collagen. Three molecules of pro-α-chain are hydroxylated, glycosylated, and finally assembled to a procollagen triple helix structure. These procollagens are secreted into the extracellular space, and propeptides at both ends of collagen molecules are cleaved to form collagen molecules. Collagen molecules self-assemble into fibrils with a diameter of 10 to 300 nm. These fine collagen fibrils further assemble into collagen fibers. Stromal collagen fibers are characteristicallyextremely uniform in diameter (22.5 to 35 nm) andthe distance between them is also uniform and constant (41.4 nm). The regular arrangement of collagen fibers in the stroma contributes to corneal transparency. Any disturbance in the uniformity of the fixed interfiber distance, as in stromal edema or scarring, may cause loss of corneal transparency ***(Tripathi et al., 1998)***.

4-Pre-descemet layer (Dua'slayer)

Dua et al. (2014) examining 31 human donor sclerocorneal discs, including 6 controls to define a novel pre-Descemet's layer in the human cornea with the big bubble (BB) technique. There is a novel, well-defined, acellular, strong layer in the pre-Descemet's cornea. This separates along the last row of keratocytes in most cases performed with the BB technique. Its recognition may have considerable impact on posterior corneal surgery and the understanding of corneal biomechanics and posterior corneal pathology such as acute hydrops, Descemetocele and pre-Descemet's dystrophies.

Dua et al. (2014) examined the peripheral part of the pre-Descemet's layer by electron microscope and found that beams ofcollagenemerged from the periphery of the pre-Descemet's layer (PDL) on the anterior surface of the Descemet's membrane and divided and subdivided to continue as the beams of the TM. Long-spacingcollagenwas seen in the PDL and TM.Trabecularcells (CD34-ve) associated with basement membrane were seen in the peripheral part of the PDL and corresponded to the start of the separation of the collagen lamellae of PDL.Collagen VI was present continuously in PDL and extended into the TM. Matricellular proteins were seen predominantly in the TM with only laminin extending into the periphery of PDL.

5- Descemet's membrane:

It is the basal lamina of the corneal endothelium. It is 10-12 µm in thickness. It is a strong resistant sheet, closely applied to the back of the corneal stroma, from which it is sharply defined, and it is the plane of separation used for lamellar keratoplasty. Its major protein is type IV collagen. The glycoprotein and proteoglycan contents are responsible for the brilliant pink staining with periodic acid Schiff reagent ***(Tripathi et al., 1998)***.

6- Endothelium:

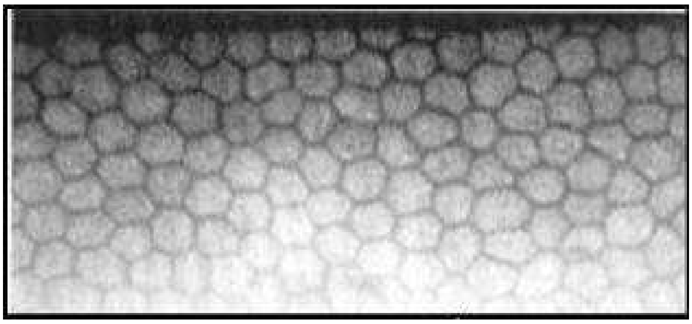

Figure (2): The Endothelium ***(Gipson et al., 1994)***.

The corneal endothelium is a single layer of 400 000 to 500 000 low cuboidal cells that when viewed from the anterior chamber surface, forms a hexagonal mosaic on Descemet's membrane, Fig. (2) ***(Gipson et al., 1994)***.

Cells are 4 to 6 µm in height and 20 µm in width. The cells lateral walls are extremely tortuous and interdigitate with extensive folds and finger like projections. Numerous gap junctions along the lateral membranes provide cell to cell cytoplasmic communication.Unlike corneal epithelium; the endothelium is not a self-renewing cell layer as the number of endothelial cells decreases with age ***(Gipson et al., 1994)***.

Physiology

Epithelium:

The functions of the corneal epithelium are firstly to form a barrier between the environment and the stroma, secondly to form a smooth refractive surface through interaction with the tear film. The superficial two layers of flattened cells encircled by tight junctions (Zonula occludens) serve as a semi permeable, high resistant membrane that prevents the movements of fluid from the tears in to the stroma and protects the cornea and the intraocular structures from infection ***(Zigman et al., 1979)***.

Stroma:

Arrangement of the collagen fibers in the stroma is the principal factor that determines corneal transparency. Both the diameter of each collagen fiber and the mean distance between collagen fibers are quite homogeneous and measure less than half ofthe wavelength of the visible light (400 to 700 nm). This anatomic relationship is thought to be responsible for the fact that the incident ray scattered by each collagen fiber is cancelled by the interference of another scattered ray, which allows it to pass through the cornea ***(Mourice et al., 1987)***.

Endothelium:

The main physiological functions of the corneal endothelium are to maintain an effective barrier from the aqueous humor to maintain the metabolic pump, and ultimately, to maintain the corneal transparency. The integrity of the endothelial cell junction establishes the barrier and is the most important factor in controlling the endothelial metabolic pump, which is located on the lateral walls of the endothelial cells ***(Jayccock et al., 2005)***.

Biochemistry

The corneal stroma contains 75-85%water (on a wet weight basis). The remaining solids, 20-25% ***(Whitacre et al., 1993)*** constituted mainly of collagen, other proteins, and glycosaminoglycans (GAG) or mucopolysaccharides. The skeleton of the corneal stroma is primarily made up of corneal fibrils, nearly organized and with a periodicity of 64 to 66 nm. They are typically 25-30 nm in diameter. Four collagen types have been identified: type I (50-55%), III (< 1%), V (8-10%) and VI (25-30%). These collagen fibrils are fairly similar to tendon and skin collagen, containing high nitrogen, glycine, proline, and hydroxyproline content ***(Birk et al., 1988)***.

Collagen synthesis:

Corneal collagen is formed during embryonic and early postnatal development, resulting in a very little synthesis of collagen in a normal adult stroma. It is suspected that types III collagen is synthesized by the endothelial cells, which deposits in the growing Descemet's membrane of a neonatal cornea ***(Jester et al., 2005)***.

The other three types I, V and VI appear to be synthesized by stromal derived fibroblasts. It is further speculated that types VI collagen, due to its unusual structure and role as a space-filling element, may be involved in the development of the transparency of the neonatal cornea ***(Jester et al., 2005)***. Anterior stroma lamellae run obliquely and randomly across the cornea, often starting at the limbus and terminating at Bowman's membrane where they interweave with the collagen within Bowman's membrane. In contrast, the posterior lamellae are thicker, wider, and have a more ordered limbal to limbal arrangement, running preferentially in the inferior-superior and medial-lateral meridians. At the limbus, corneal stromal lamellae interweave with scleral collagens taking a circular course that is thought to account for the increased thickening of tissue in this region (Fig.3) ***(Meek et al., 2001).***