INTRODUCTION

The cornea makes the anterior 1/6 of the outer coat of the eye globe and it is responsible for the 40-45 diopters of the refractive power of the eye ***(Bron et al.*, 1997*).***

Stroma of the cornea forms 90% of its whole thickness and it is formed of collagen fibrils which are regularly arranged in lamellae cross each other at regular intervals and these lamellae lie into a proteoglycan ground substance, with little number of keratocytes ***(Linsenmayer, 1981).***

The ectatic conditions of the cornea is due to decrease of the strength of the stroma which causes keratoconus and keratectasia which lead to different degrees of astigmatism and myopia. These conditions can be corrected by different methods and one of them is collagen cross linking by ultraviolet rays together with using riboflavin ***(Wollensak et al., 2003).***

Different ways of the cross linking have been reported by many authors in order to increase the cross links of the corneal collagen and in turn this leads to arrest of the problem of ectatic diseases of the eye and may be also be more efficient than many other managements. The uses of cross linking now also is used to manage other conditions like progressive myopia as it affect the sclera strength. ***(Wollensak et al., 2004).***

AIM OF THE WORK

To review the articles about the new modalities of treatment of different types of corneal ectasia by corneal cross linking and try to spot light its effectiveness and safety which may be a new hope for many of our patients.

Anatomy of the Cornea

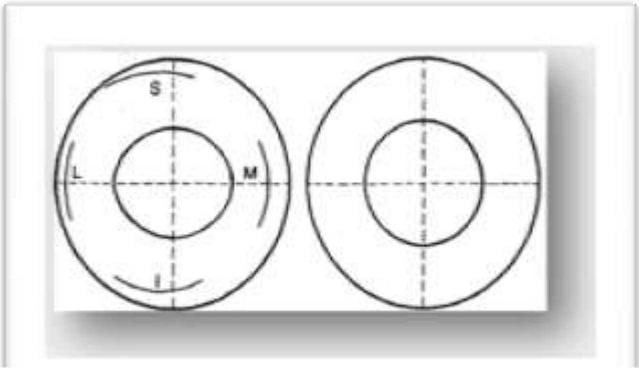
The cornea is a transparent avascular tissue with a smooth, outer convex surface and a concave inner surface, which resembles a small watch-glass **(*Bron et al., 1997*).**

Dimensions and Shape:

The cornea appears elliptical from the front, 11.7mm wide in horizontal meridian and 10.6 mm in the vertical one in adults more curved at the vertical than the horizontal meridian, giving astigmatism ‘with the rule’. The cornea forms a part of what is almost a sphere **(*Maurice, 1970*).**

The posterior surface appears circular, about 11.7mm in diameter. The axial thickness of the cornea is 0.52mm with a peripheral thickness of 0.67mm **(*Bron et al., 1997*).**

The cornea is prolate at its anterior surface with steeper central cornea and a flatter one peripherally. In the central third ‘the optical zone’ the radius of curvature of anterior surface is about 7.8 mm and that of the posterior is 6.5 mm in adult males **(*Bron et al., 1997*).**



(A) (B)

Figure (1): (A) the anterior aspect the cornea is transversely ellipsoid**, (B)** whereas its posterior aspect is circular **(*Bron et al., 1997*).**

Refractive power:

The main function of the cornea is optical; as it forms the principle refractive surface of the eye, accounting for about 70% (40-45 dioptre) of the total refractive power of the eye **(*Bron et al., 1997*).**

The refractive requirements of the eye are met by the high regularity of the anterior surface and the optically smooth quality of the tear film **(*Bron et al., 1997*).**

Corneal transparency

The resistance of the cornea, which provides a protective layer and resists the ocular pressure, is due to the collagenous components of the stroma. The transparency of the corneal stroma is achieved by the regularity and fineness of its collagen fibrils and the closeness and homogeneity of their packing. Water is constantly pumped out of the cornea by its posterior layer via the endothelial pump. This maintains the optical homogeneity and prevents swelling and cloudiness **(*Bron et al, 1997*).**

Surface zones of the cornea:

The corneal surface can be divided into four anatomical zone as shown in figure 2: Central (optical) zone, paracentral zone, peripheral zone and limbal zone**.**

Central zone: The optical zone of the cornea. It is 2.4 mm in diameter.

Paracenteral zone: 6-8mm in diameter.

Peripheral zone: Also called the transitional zone .it is 7-11 mm in diameter.

Limbal zone: It is a ring of cornea, about 0.5 mm in diameter **(*Bores et al., 1993*).**

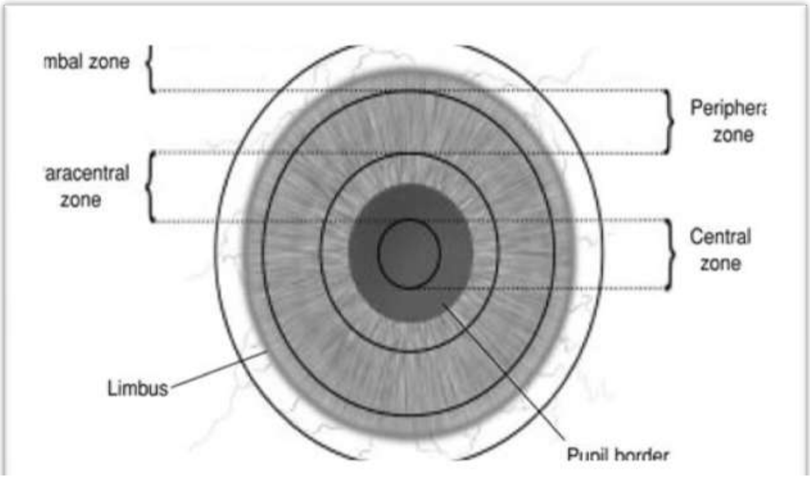


Figure (2): Zones of the human cornea: American academy of ophthalmology, 2003.

Microscopic Structures:

Behind the precorneal tear film there are five layers:

1- The epithelium.

2- Bowman's layer.

3- The stroma.

4- Descemet's layer.

5- The endothelium.

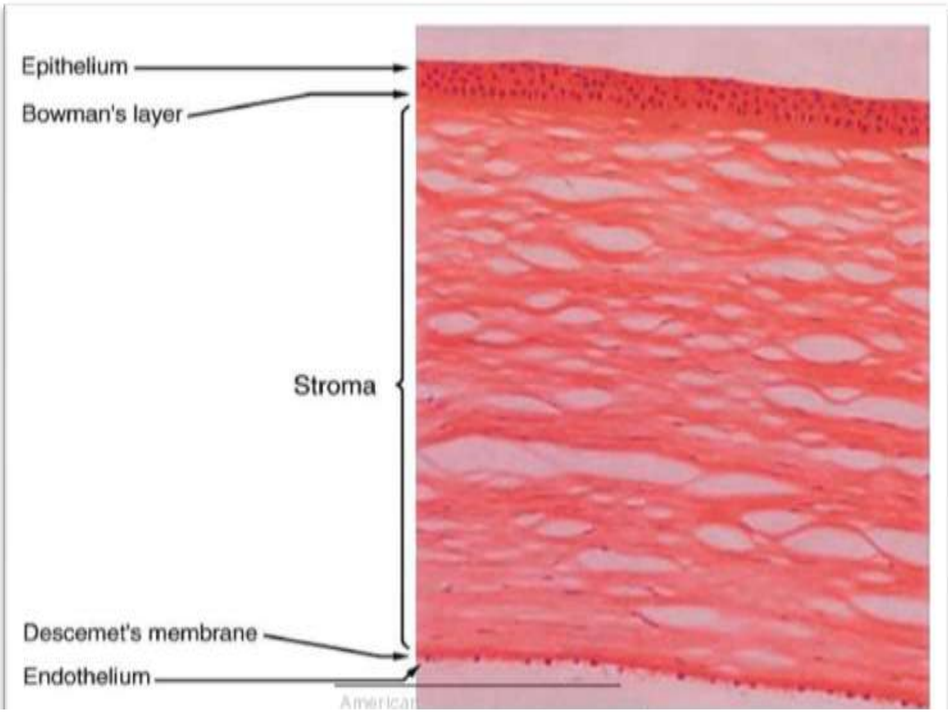


Figure (3): Histological view of the cornea; American academy of ophthalmology, 2003.

[1] The epithelium:

The corneal epithelium is non keratinized stratified squamous epithelium; it is continuous with that of the conjunctiva at the corneal limbus, but differs in possessing no goblet cells. The epithelium is 50-90μm thick and consists of five to six layers of nucleated cells ***(Reinstien et al., 1994*).**

Basal lamina

The basal lamina is secreted by the basal cells which also synthesize the hemidesmosomal structures concerned in the attachment of the epithelium to the basal lamina **(*Gipson et al., 1989*).**

[2] Bowman's membrane

Bowman's layer is a narrow acellular homogenous zone, 8-14 µm thick, immediately adjacent to the basal lamina of the corneal epithelium. The anterior surface is smooth and parallel to that of the cornea ***(Bron et al., 1997).***

Ultrastucturally Bowman's membrane consists of a flattened meshwork of fine collagen fibrils of uniform size, lying in a ground substance. Fibrils diameter (24-27 nm) is less than that of substantia propria. In the posterior region of this layer the fibrils become progressively arranged in their orientation, blending and interweaving with the fibrils of the anterior stroma. Bundles of the stromal lamellae are inserted into the Bowman's layer. The compacted arrangement of the collagen gives great strength for this zone. Bowman's layer is relatively resistant to trauma, both mechanical and infective; once destroyed it is not renewed but it is replaced by coarse scar tissue. It is perforated by many unmyelinated nerve endings in transit to the epithelium ***(Tripathi et al., 1984*****).**

[3] Stroma (Substantia propria)

The stroma forms about 500 µm thick and consists of regularly arranged lamellae of collagen bundles. They lie in a proteoglycan ground substance together with a relatively small population of cells, the keratocytes **(*****Bron et al., 1997*****).**

Transparency of the corneal stroma depends particularly on the degree of spatial order of its collagen fibrils which are small in diameter and closely packed in a regular array. The collagen fibrils themselves are weak scatterer, since their fibril diameter is less than the wavelength of light, and fibril refractive index is close to that of the ground substance. There is little variation in fibril diameter and separation between the anterior and posterior cornea **(*Muller et al., 2001*).**

The stromal fibrils are further organized into bundles, or lamellae, of which there are approximately 300 in the central cornea and 500 close to the limbus. Fibrils within a lamella are in parallel array, except when branching of lamellae occurs. Branching in the horizontal plane occurs throughout the stroma, whereas anteroposterior branching is found only in the anterior third ***(Muller et al., 2001*).**

The anterior and posterior stroma differs in a specific ways. In general the posterior stroma is more ordered; more hydrated, more easily becomes swollen and has a lower refractive index than the anterior stroma. The posterior lamellae are also wider and thicker (100-200 µm wide and 1.0-2.5 µm thick) than the anterior (0.5-30 µm wide and 0.2 -1.2 µm thick). There are also differences in keratocytes morphology. It has been also established that the posterior lamellae of the human corneal stroma are arranged parallel to the plane of the corneal curvature ***(Muller et al., 2001*).**

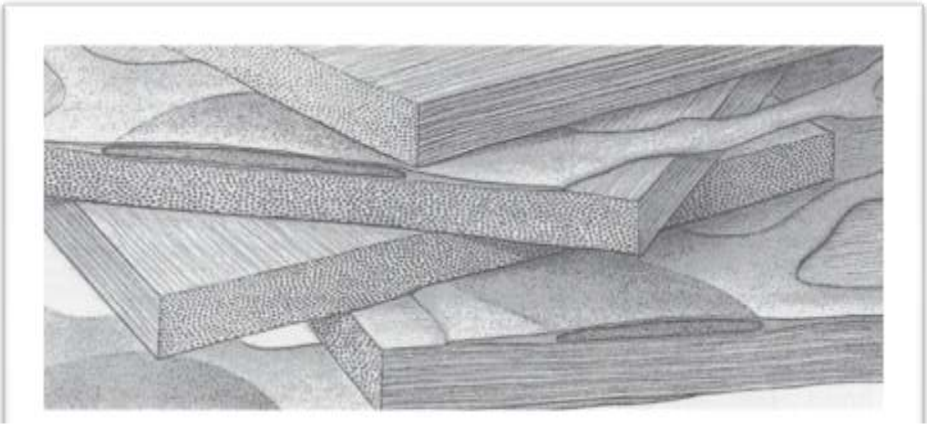


Figure (4): Schematic diagram of corneal stromal lamellae. Collagen fibrils within a lamella are parallel to each other and at right angles to each other ***(Hogan et al., 1997).***

In the anterior stroma there is marked anteroposterior lamellar interweave in which lamellae can be shown to pass obliquely from one layer to another, sometimes passing across several lamellae to reach their destination. A portion of the anterior lamellae are inserted into Bowman's layer and it has been suggested that the later contribute to the formation of the anterior corneal mosaic. It has also been found that anterior stroma 100-120 μm deep to the Bowman's layer, is responsible for the structural stability of this region of the cornea, a feature which is of importance to refractive surgery and possibly for the condition like keratoconus **(*Muller et al., 2001*).**

The keratocytes of the corneal stroma occupy 2.5-5 % of its volume and are responsible for synthesis of the stromal collagen and proteoglycans during development and maintaining it thereafter. In transverse section of the cornea they appear long, thin flattened cells running parallel to the corneal surface. Keratocytes are present all through the cornea, they are found between lamellae; and occasionally within the lamellae. Their stellate processes extend for great distances and frequent connections are made with other keratocytes in the same horizontal plane, usually with a 20 nm gap and sometimes with the formation of maculae occludentes, adherents or gap junction. Anteroposterior connection between keratocytes in adjacent planes does not occur ***(Bron et al., 1997*)**.

The collagen are now defined as a structural protein of the extracellular matrix that contain one or more domains having glycine in every third position of the polypeptide chain. This produces a helical structure that can assemble into a triple helix by associating with two other like helices to result in a rod –shaped macromolecule. The individual collagen chains are covalently cross linked to each other and to other triple helices in the matrix. This results in a super molecular structure with an incredible tensile strength and resiliency **(*Van der Rest, 1991*)**.

[4] Descemet's membrane (Posterior limiting layer)

Descemet's membrane is the basal lamina of the corneal endothelium and is a strong resistant sheet, closely applied to the back of the corneal stroma. Unlike Bowman's layer, it is sharply defined. Although it appears homogenous under light microscopy, it has a laminated structure which may be demonstrated by polarization or electron microscopy ***(Bron et al., 1997)***.

Ultrastructurally in tangential section the membrane appears to consist of superimposed flat plates forming a lamellar pattern of equilateral triangles with sides of about 110 nm. The triangles are interconnected by electron dense nodes and internodes **(*Bron et al., 1997*).**

[5] Endothelium:

The endothelium is a single layer of hexagonal, cubical cells applied to the posterior aspect of Descemet's membrane in a well arranged mosaic pattern. The endothelial cells are 5 μm thick and 20 μm wide in normal corneas, the dimension of the endothelial cells are quite uniform ***(Bron et al., 1997*).**

A gradual decrease in density and increase in shape variation (polymegathism) occur with age: in youth, the cells are predominantly hexagonal in shape in the plane of the cornea but with age become increasingly polymorphic **(*Sherrard et al., 1987*).**

The sub-cellular organisation shows how extremely metabolically active the endothelium is as large number of mitochondria is distributed throughout the cell particularly around the nucleus. Corneal endothelial cells don't proliferate in humans but they proliferate in cell culture systems demonstrating that the cells themselves have mitotic capability. Therefore factors in aqueous humour or in the cellular environment may inhibit proliferation ***(Bron et al., 1997*****).**

The Ectatic Conditions of the Eye

The ectatic conditions of the eye is subdivide into Keratoconus and Post LASIK Keratectasia.

Keratoconus:

Keratoconus (from Greek: *kerato-* horn which is new material specially keratin in the cornea; and *konos* means cone).

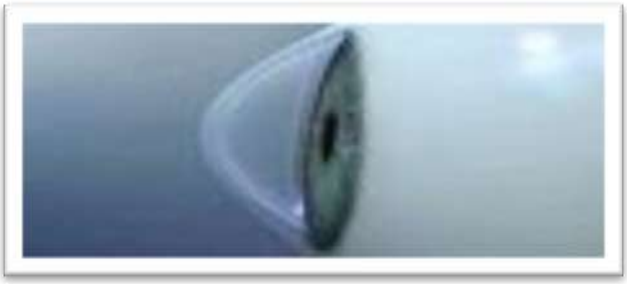


Figure (5): Diagram of Keratoconus ***(Rabinowitz, 1998*).**

Definition

Keratoconus is a degenerative disease of the cornea characterized by a chronic progressive non inflammatory ectasia of the cornea in which a cone like anterior protrusion of the cornea occurs, generally involving the central and inferior paracentral areas. The involved stroma is thin, with decreased tensile strength and may scar. A high degree of irregular myopic astigmatism occurs causing variable amount of visual impairment ***(Leibowitz et al., 1998*).**

Epidemiology of Keratoconus

Incidence: The frequency of Keratoconus vary widely. Most estimates reported about 50 per 100,000 (i.e. 1 per 2000) in white races ***(Wang et al., 2000*****).**

Sex Distribution: Amsler reported a greater prevalence (59.2%) of keratoconus among females in his overall series of 600 cases of keratoconus patients ***(Amsler, 1961*****).**

Age and course: Most patients with keratoconus present between puberty and age 20 years. Keratoconus progresses slowly but continuously for 5 to 10 years and then stabilize permanently ***(Leibowitz et al., 1998*****).**

Familial and hereditary factors: Most cases of keratoconus are sporadic. Hereditary transmission of keratoconus also had been reported. Dominant recessive and irregular transmission all appear to be implicated. A family history can be demonstrated in about 6 to 10 % of cases of keratoconus. **(*****Wang et al., 2000*****).**

Pathophysiology of Keratoconus

The etiology of keratoconus has been investigated frequently but is still largely unknown. Although research work investigating the biochemical and pathological changes at the