Evaluation of The Role of Sutureless Amniotic Membrane in The Management of Ocular Surface and Orbital Disorders

Essay

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The amniotic membrane (AM) is the inner membrane of the placenta that surrounds the fetus in utero and has been used in reconstructive surgery since ١٩١٠ ***(Davis, 1910)***. The AM is a biologic tissue with antiangiogenic, antiscarring, antimicrobial and anti-inflammatory properties that promotes healing of the ocular surface ***(Kheirkhah et al., 2008).***

Although the first documented report of living amniotic membrane transplantation (AMT) for an ocular disorder was published by De Roth in ١٩٤٠ ***(De Roth, 1940)***, little use was seen that used the amniotic membrane for ocular disorders until ١٩٩٥, when Kim and Tseng ***(Kim and Tseng, ١٩٩٥)*** published their results of using cryopreserved amniotic membrane to encourage corneal epithelium regeneration in a rabbit model.

Since then, AM has been increasingly used for ocular surface reconstruction because of its effects of reducing inflammation and maintaining the integrity of the ocular surface ***(Fernandes et al., 2005).***

Currently, AMT has a wide spectrum of ophthalmic clinical applications including ocular surface reconstruction in cases of limbal stem cell deficiency with or without concurrent limbal stem cell transplantation ***(Kheirkhah et al., 2008).***

It is also commonly used in the management of non-traumatic corneal perforations, descematoceles, neurotrophic ulcers and persistent epithelial defects caused by a variety of ocular surface diseases ***(Khokhar et al., 2005).***

Reconstruction of the conjunctival surface after excision of pterygia or other conjunctival lesions can also be completed using AMT ***(Sippel et al., 2001).*** AMT is also used as a

therapeutic bandage contact lens in acute inflammatory conditions and in symptomatic bullous keratopathy ***(Gomes et al., 2005).***

Initially, grafting of the amniotic membrane was solely performed using sutures ***(Kheirkhah et al., 2008).*** Running or interrupted sutures for AM patch fixation have a number of complications and drawbacks:

(a) It is difficult to monitor the epithelialization process.

(b) Protection is lost if AM patch falls off ***(Khokhar et al., ٢٠٠٥).***

(c) Removal of the sutures results in reimpairment of the ocular tissue.

(d) Scar formation persists at least several weeks in the suture sites.

(e) Recent case reports have shown chronic conjunctival inflammation caused by the retained sutures ***(Chung et al., 2006).***

The emergence of biologic adhesives has made sutureless AM a viable and technically easier alternative that avoids suture-related complications ***(Kheirkhah et al., 2008).***

The advent of sutureless and adhesiveless AM device has been an exciting development in ocular surface and orbital reconstruction ***(Kheirkhah et al., 2008).***

The idea of developing a sutureless approach of AM application is not new. John et al on ٢٠٠٠ treated a patient with toxic epidermal necrolysis (TEN) with an AM that was applied

around a symblepharon ring and sutured through the anterior eyelid margins ***(John et al., 2002).***

Tseng et al on ٢٠٠٤ submitted the design of an AM carrier to the US patent office ***(Tseng et al., 2004).*** They also presented results with sutureless AM device ***(Ijiri et al., 2007 and Kheirkhah et al., 2008)*** that is an US food and Drug Administration-approved version called Prokera (Bio- Tissue, Inc., Miami, FL). It is a ring-like plastic ophthalmic conformer, available in two sizes, that incorporates AM between two rims. They reported beneficial effects in patients with acute alkaline burns and partial limbal stem cell deficiency ***(Kheirkhah et al., ٢٠٠٨).***

Prokera is class II medical device comprised of a cryopreserved amniotic membrane (Amnio Graft) clipped into a polycarbonate ring set. It combines the functionality of a symblepharon ring with the biologic actions of cryopreserved amniotic membrane to create a unique treatment option for corneal and limbal wound management ***(http://www.Biotissue.com).***

Prokera can be easily inserted onto the patient's eye without sutures after instillation of anesthetic eye drops to deliver the needed biological actions for suppressing inflammation and promoting healing, as well as acting as a symblepharon ring ***(Kheirkhah et al., 2008).***

Many patients with corneal epithelial defects, Stevens-Johnson syndrome (SJS) and TEN requiring amniotic membrane overlays are old, handicapped or immobile; housed in retirement homes or in intensive medical care units. Thus they are not easily transported and their medical conditions do

not permit them to be brought to the operating room. Therefore insertion of Prokera allows doctors to perform AMT at the acute stage without delay ***(Yoshita et al., 2004 and Ijiri et al., ٢٠٠٥).***

After insertion, Prokera doesn't interfere with topical medications and permits examination of epithelial healing by fluorescein staining and measurement of intraocular pressure by Tono- Pen (Medtronic Solan, Jacksonville, FL) without being removed from the eye ***(Yoshita et al., 2004 and Ijiri et al., ٢٠٠٥).***

Although ProKera contains AM and has been effective at restoring a clear and normal cornea, it should be noted that the diameter of the ProKera only covers the cornea and perilimbal conjunctiva, not the entire ocular surface as sutured AMT does. Although ProKera helps restore corneal epithelial integrity, it is not effective in preventing cicatricial complications in the fornix, the tarsus, and the lid margin. Therefore, ProKera should be considered only if the patient's medical condition is not amenable to the sutured technique. Development of a sutureless device like ProKera that is large enough to cover the entire ocular surface is warranted considering the high ocular morbidity of SJS/TEN ***(Shay E et al., 2010).***

To evaluate the role of sutureless amniotic membrane in the management of ocular surface and orbital disorders.

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AM	*Amniotic membrane*
AMT	*Amniotic membrane transplantation*
AECs	*Amniotic epithelial cells*
CRH	*Corticotrophin releasing hormone*
Fig.	*Figure*
FL	*Florida*
HCG	*Human chorionic gonadotrophin*
HLA	*Human leucocytic antigen*
IHD	*Inner horizontal diameter*
IL	*Interleukin*
IVD	*Inner vertical diameter*
IVIG	*Intravenous immunoglobulin*
INF	*Interferon*
LASEK	*Laser assisted subepithelial keratectomy*
NK	*Natural killer cells*
OHD	*Outer horizontal diameter*
OVD	*Outer vertical diameter*
PRK	*Photorefractive keratectomy*
PMMA	*Polymethylmethacrylate*
SJS	*Steven Johnson Syndrome*
TAC	*Transient amplifying cells*
TEN	*Toxic epidermal necrolysis*
TIMP	*Tissue inhibitors of Metalloproteinases*
TNF	*Tumor necrosis factor*
US	*United States*

(A) Anatomy of the cornea:

The cornea consists of ٥ layers: epithelium, Bowman's layer, stroma, Descemet's membrane and endothelium as shown in ***fig. (1.1) (Chris, 1997).***

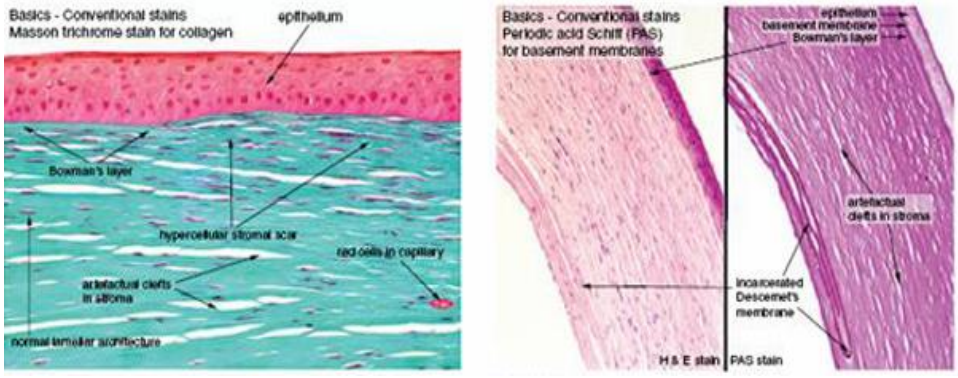

Fig. (١،١) Layers of the cornea *(Chris, 1997).*

Epithelium

The corneal epithelium is a stratified squamous, non-keratinizing epithelium of about ٥ cell layers and ٣٠-٥٠ µm thickness. It is composed of ٣ types of cells: basal, wing and superficial cells as shown in ***fig. (1.2) (Mclaughin et al., 1985).***

The flat superficial cells are organized in ٢ layers with junctional arrangements between adjacent cells. These junctional complexes obliterate the intercellular space and, therefore, serve as an anatomical barrier to the passage of substances into the cornea ***(Mclaughin et al., 1985).***

The surface area of the outermost cells is increased by microvilli that facilitate the attachment of mucin and the tear film ***(Kanski, 2007).***

The polygonal wing cell layer is ٢-٣ cells deep, with an intensive interdigitation of each cell with numerous desmosomal attachments ***(Kanski, 2007).***

The basal cells are aligned perpendicular to the corneal surface and are attached by hemidesmosomes to its own secretory product ٥٠ nm thick basement membrane ***(Yanoff, ٢٠٠٩).***

Basal epithelial cells progressively deform into wing cells and thereafter into surface cells, with a total transit time of around ٧ days ***(Chris, 1997).***

Corneal stem cells reside in the transitional epithelium between cornea and conjunctiva (i.e. the limbus), mainly the superior and inferior limbus, possibly in the palisades of Vogt. They are indispensable for the maintenance of healthy corneal epithelium. They also act as a junctional barrier, preventing conjunctival tissue from growing onto the cornea. Dysfunction or deficiency of limbal stem cells may result in chronic epithelial defects ***(Kanski, 2007).***

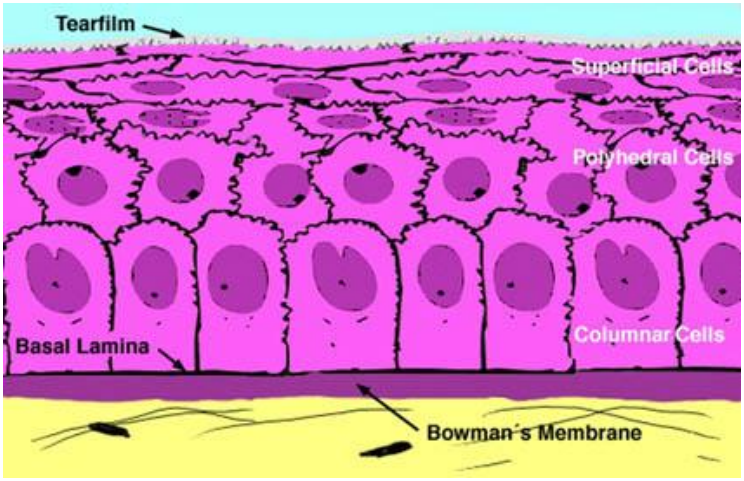

Fig. (١,٢) Histology of the epithelium *(Chris, 1997).*

Bowman's Layer

Bowman's layer is an acellular zone about ٨-١٠ μm thick and contains collagen fibrils arranged randomly as shown in ***fig. (1.3) (Kayes and Holmbey, 1960).*** It is thought to be synthesized by both epithelial cells and by stromal keratocytes ***(Hay and Revel, 1969).***

Posteriorly it merges into the anterior stroma. The function of Bowman's layer is unknown, but it may act as a barrier to corneal invasion by microorganisms ***(Chris, 1997).***

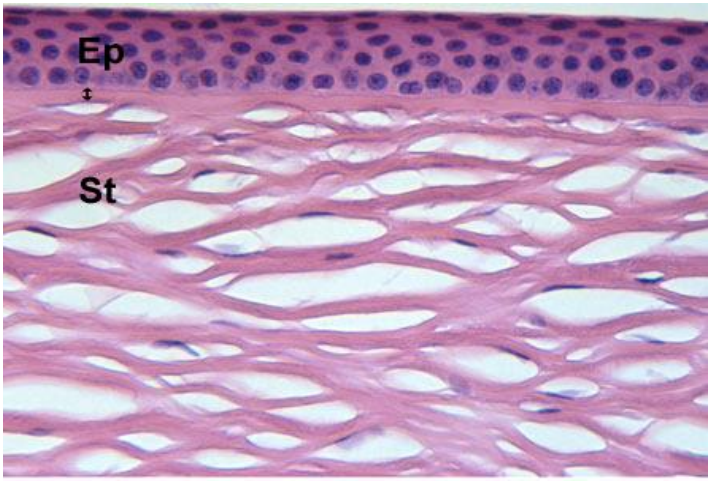

Fig. (١،٣) Histology of the Bowman's layer and the stroma *(Yanoff, 2009).*

Stroma

The corneal stroma comprises over ٩٠٪ of the normal thickness and consists primarily of collagen, stromal cells and proteoglycans. It is approximately ٧٨٪ water. The collagen fibrils are arranged into ٢٠٠-٣٠٠ lamellae parallel to the outer surface, and each lamella extends across the entire breadth of the cornea ***(Maurice, 1984). Fig. (1.4)*** demonstrates the lamellae of the stroma. The spacing between collagen fibrils is