AMNIOTIC MEMBRANE TRANSPLANTATION: AN ADVANCE IN OCULAR SURFACE DISEASE MANAGEMENT

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Background

Amniotic membrane has been around since 1940s when De Roeth used it for repairing conjunctival defects and Sorsby used it for caustic burns. However for reasons that are not very clear, it fell out of favor. Of late a lot of work has been done that has refocused the attention on amniotic membrane and its use in various ocular surface diseases.

How to obtain a graft?

Amniotic membrane is obtained from a placenta delivered through the cesarean section. The amnion is separated from the chorion under strict sterile conditions. This amnion is then processed specially in predefined media after being layered on to nitrocellulose paper with the stromal side on the paper and the epithelial side away from the paper. The cut pieces of the amniotic membrane is preserved at -80^0 C. The donor is screened for viral and other infections. The membrane is then held in quarantine for 4 to 6 months when a repeat serological investigation of the donor is undertaken to avoid the window period of seroconversion. (In the current environment of uncertainty this is very important). The membrane is then ready for release for human use. It is now commercially available in the country.

How does preserved Amnion work?

The amniotic membrane is useful because it has several properties at the surface and molecular llevels.

1) The epithelial surface allows rapid reepithelialisation of the wounded surface. It also alters the stromal microenvironment favorably to allow the epithelial cells to repopulate the surface.
2) It also enhances typical differentiation of the epithelial cells that migrate over it.There is a strong attachment of these epithelial cells to each other and to the amniotic membrane.
3) The epithelial cell attachment to its basement memrbrane suppresses apoptosis.
4) The stromal surface is shown to interact with the corneal stroma and promote down regulation of stromal inflammation. This is attributed to various cell cytokines present in the substance of the membrane. For example the amniotic membrane has been demonstrated to downregulate the release of TGFB a cytokine involved in the inflammatory cycle. This allows the membrane to act like a sink for the inflammatory factors and thus reduces the inflammation that would otherwise follow an injury.
5) It also has anti-angiogenesis properties, it down regulates MAP kinase and upregualtes Angiogenin inhibitors.. This property is also helpful in restoring the ocular surface.
6) It has antiscarring properties too. The down regulation of TGF cytokine and suppression of activation of stromal keratocytes into myofibroblasts is responsible for the reduced scarring effect.
7) It stimulates apoptotic death of inflammatory cells.
8) Tensile strength of the amniotic membrane is very high.
9) It facilitates nerve regrowth.
10) It has non specific mild antimicrobial effects, both antiviral and antibacterial.

Uses

- Ocular surface
- Glaucoma
- Retina
- Cosmetic surgery

Ocular surface

i. Restoration of ocular surface
ii. Limbal stem cell deficiency
iii. Chemical injuries
iv. SJ syndrome
v. Cicatricial disorders
vi. Pterygium
vii. Resurfacing large conj. Defects
viii. Fornix reconstruction
ix. Conjunctivochalasis
x. PEDs
xi. Neurotrophic ulcers
xii. PBK (cases with poor visual prognosis)

Glaucoma

i. Repair of leaking filtering blebs (better than conjunctival advancement - lesser bleb failures, and ptosis and diplopia)
ii. Bleb revision (flat or fibrosed blebs)
iii. Repeat surgery to reduce inflammation and fibrosis

Retina

- Not yet in humans
- rabbit studies - implanted under the retina - useful as replacement for bruch's membrane following removal of choroidal neovas.during submacular surgery

Cosmetic surgery

i. Resurfacing after CO2 laser.
ii. Lid reconstruction

Our experience over the last 2 years has been quite gratifying in the following situations:

- Acute Stevens-Johnson syndrome
- Persistent epithelial defects
- Sterile corneal ulcers
- Large conjunctival defects
- Pterygia
- Glaucoma surgery
- Psuedophakic bullous keratopathy

What not to do?

There are a few potential pitfalls that need to be pointed out so as to avoid unpleasant outcomes:

1. DO NOT use fresh unprocessed membrane, you don't have any knowledge of the viral and / or bacterial contamination of the membrane. Use of contaminated membrane can cause several problems to both the surgeon and the patient. Additionally, in those cases where live membrane is used, **allograft rejection** is possible.
2. DONOT use freeze dried, gamma irradiated membrane for the anti-inflammatory properties. This kind of membrane will only be a patch and nothing more. It is just like a parchment.

Problems with freeze dried, gamma irradiated membrane

- No active growth factors
- No stromal surface specificity
- No anti inflammatory activity
- No epithelial growth support
- Serves only as a PATCH
- Unknown properties

3. DONOT expect any amniotic membrane to work in conditions where you feel that the stem cells of the cornea have been completely destroyed. If you do use for the anti-inflammatory properties, please remember that further surgical interventions will be needed. Amniotic membrane cannot bring back stem cells. It is useful in surgical attempts that involve limbal stem cell transplants as part of the total surface reconstruction.

How is amniotic membrane transplantation performed?

The recipient eye needs to be prepared as per the requirements. For ocular surface reconstruction the epithelium and scarred tissue is dissected and removed to expose the bare corneal stromal and sub-epithelial surface of the conjunctiva. After good hemostasis the bed is ready for the amniotic membrane.

The amniotic membrane is then thawed in the vial. The piece of amnion and the nitrocellulose paper which holds it are taken from the vial. We prefer to take this whole composite onto the eye and outline the needed size. We then cut the membrane while it iis still on the paper. This allows us to easily cut the membrane due to the support offered by the underlying paper. Alternatively, the membrane can be separated from the paper and cut to size after being laid over the ocular surface. The membrane is stitched to the surrounding conjunctiva with 10-0 nylon sutures. In case of symplepharon release the newly created cul-de-sac can be covered with the membrane and sutured to the adjacent tissue.

Amniotic membrane transplantation to reduce wound scarring