Amniotic Membrane Transplantation for Ocular Surface Reconstruction

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History of Amniotic Membrane Transplantation

Amniotic membrane, or amnion, is the innermost layer of the placenta and consists of a thick basement membrane and an avascular stromal matrix. Amniotic membrane transplantation has been used as a graft or as a dressing (patch) in different surgical subspecialties in early literature. In the English-language literature, a live fetal membrane including both amnion and chorion was first used by De Rotth in 1940 as a graft for conjunctival surface reconstruction. Probably due to the inclusion of live cells and the chorion, the success rate was low, i.e., one out of six cases, treating symblepharon and conjunctival defect. In 1940 Brown proposed the use of rabbit peritoneum as a temporary patch to cover the acutely burned ocular surface in order to promote healing and prevent spread of necrosis. Based on this idea, in 1946 and 1947, Sorsby et al. used chemically processed “dry” amniotic membrane, termed “amnioplastin,” as a temporary patch for treating acute ocular burns. They showed that the earlier the intervention, the shorter the hospitalization. Although a remarkable success was noted, amnioplastin had to be applied repeatedly. For reasons still not clear, the use of amniotic membrane disappeared from the literature. As early as 1965, Roper-Hall reviewed the subject of chemical burns and concluded “other materials have been advocated from time to time as temporary grafts with varying enthusiasm.”

In 1995 Kim and Tseng reintroduced amniotic membrane for ophthalmic uses. In a rabbit model they showed that 40% of corneas with total limbal deficiency can be reconstructed by replacing the conjunctivalized surface with a preserved human amniotic membrane. As will be described in detail, encouraging results have since been reported by a number of investigators (see Figure 20.1). We attribute such a surge of interest in this new surgical procedure to an improved method of processing and preservation, which has maintained the inherent properties of the amnion.

Mechanisms of Action

The guidelines and operation standards concerning the procurement, processing, and distribution of such a tissue as amniotic membrane, are reported by the Food and Drug Administration, USA (Final Rule: Screening and Testing of Donors of Human Tissue Intended for Transplantation, July 29, 1997), and recently reviewed by Dua. When appropriately processed and preserved (see Figure 20.2), the amniotic membrane can be used for a number of indications, either as a graft to replace the damaged ocular surface stromal matrix, as a patch (dressing) to prevent unwanted inflammatory insults from gaining access to the damaged ocular surface, or a combination of both. Recent reports indicate that potential action mechanisms might include those summarized in Table 20.1.

Compositionally, the basement membrane component of the amniotic membrane resembles that of the conjunctiva. The basement side of the membrane is an ideal substrate for supporting the growth of epithelial progenitor cells by prolonging their life span and maintaining their clonogenicity. This action explains why amniotic membrane transplantation can be used to expand the remaining limbal stem cells and corneal transient amplifying cells during the treatment of partial limbal deficiency and to facilitate epithelization for persistent corneal epithelial defects with stromal ulceration. In tissue culture, amniotic membrane supports epithelial cell growth from explant cultures or other cultures, and maintains their normal epithelial morphology and differentiation. The resultant epithelial cells/amniotic membrane can be transplanted back to reconstruct the damaged corneal surface in humans and in rabbits. The amniotic membrane can also be used to promote nongoblet cell differentiation of the conjunctival epithelium. These data explain...
why conjunctival goblet cell density is promoted following amniotic membrane transplantation in vivo.\textsuperscript{20}

The stromal side of the membrane contains a unique matrix component that suppresses TGF-\(\beta\) signaling, as well as proliferation and myofibroblast differentiation of normal human corneal and limbal fibroblasts\textsuperscript{21} and of normal conjunctival fibroblasts and pterygium body fibroblasts.\textsuperscript{22} This action explains why amniotic membrane transplantation reduces scar formation during conjunctival surface reconstruction,\textsuperscript{23,24} prevents recurrent scarring after pterygium removal,\textsuperscript{25–29} and reduces corneal haze following phototherapeutic keratectomy (PTK) and photorefractive keratectomy (PRK).\textsuperscript{30–32} Although such an action is more potent when fibroblasts are in contact with the stromal matrix, a lesser effect is also noted when fibroblasts are separated from the membrane by a distance,\textsuperscript{21} suggesting that some diffusible factors might also be involved besides the insoluble matrix components in the membrane. In line with this thinking, several growth factors have been identified in the amniotic membrane.\textsuperscript{33} The stromal matrix of the membrane can also exclude inflammatory cells by stimulating them into rapid apoptosis\textsuperscript{31,32} and contains various forms of protease inhibitors.\textsuperscript{34} This action explains why stromal inflammation is reduced after amniotic membrane transplantation\textsuperscript{11,23} and why corneal neovascularization is mitigated,\textsuperscript{35} actions important for preparing the stroma for supporting limbal stem cells to be transplanted either at the same time or later.\textsuperscript{10,26,36–39}

This action also explains why keratocyte apoptosis can be reduced, and hence why stromal haze is prevented in PRK or PTK by amniotic membrane.\textsuperscript{30–32} Future studies are needed to resolve the exact action mechanism.

![Figure 20.1. History of English-language literature on amniotic membrane transplantation in ophthalmology.](image1)

![Figure 20.2. Histology and preparation of amniotic membrane. Amniotic membrane (Am) is the innermost layer of the placenta (A) and consists of a thick basement membrane (BM) and an avascular stromal matrix (M), which is apposed to vascularized chorion (C).](image2)