Amniotic membrane helps ocular surface disease

Cryopreserved and dehydrated membranes offer more therapeutic options

I nflammation is the hallmark symptom of all ocular surface disease, including dry eye disease (DED). Uncontrolled inflammation leads to chronic pain and irritation as well as delayed healing, tissue damage, and vision-threatening complications such as scarring and haze.1

Effective control of inflammation is an important strategy to promote healing, and it is fundamental to my treatment paradigm of dry eye disease.

I have a thriving DED practice within a cornea practice, and every day I see at least one patient seeking dry eye relief despite compliant use of various palliative measures.

Like many other eyecare practitioners, I have embraced the use of amniotic membrane (AM) tissue to control inflammation and rehabilitate the ocular surface for select DED patients as well as those patients who have keratitis, conjunctivitis, and blepharitis.

By Walter O. Whitley, OD, FAAO, MBA

Keep an eye on link between glaucoma and blood pressure

By Benjamin P. Casella, OD, FAAO

While not a systemic disease itself, glaucoma is widely understood to have systemic risk factors.1 Much of the relationship between glaucoma and the human system has to do with the vasculature of the optic nerve itself.

The 1 million or so ganglion cells that converge to make up the optic nerve are similar to other cells in that they must do two things to survive: eat and breathe.

While that is an oversimplification of the two processes, it is essentially accurate.

The cells of the optic nerve depend on the circulatory system for respiration and supply of glucose to make adenosine triphosphate (ATP) and have energy.

So, by definition, anything that negates Glaucoma & blood pressure on page 12

EDUCATE, DON’T SELL TO PATIENTS

By Scott Sikes, OD

ODs must sell from the exam chair. Everyone has heard it, a lot of us have tried it, but how well does it actually work?

Do we as ODs have time to go through all lens options, discuss what makes a particular progressive lens better or worse, and delve into different anti-reflective options? Don’t even get me started on the multiple levels of blue light protection. It’s overwhelming, time consuming, and cumbersome.

So, what’s the solution?

Recently, I have tried to educate patients in my discussions rather than mention specific brands, designs, or features.

By Scott Sikes, OD

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Amniotic membrane grafts help ocular surface disease

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Using amniotic membrane
A decade of experience and impressive outcomes with AM tissue supports my ongoing reliance on this therapeutic intervention, and a growing body of evidence validates my anecdotal observations.

As a proponent and successful user of AM tissue, I sometimes facilitate workshops on this topic. My key message at these events is that there are various types of AM tissue for ophthalmic use, and eye-care providers should try them all. By doing so, clinicians can see for themselves which products provide better clinical results and which fit in best with their overall practice dynamics.

For optometrists who suspect that implanting AM grafts is beyond their level of expertise, nothing could be further from the truth. Implanting an AM tissue graft is as clear cut as applying a contact lens or inserting a punctal plug. When offering patients the option of AM tissue grafts, it can be reassuring to convey that the insertion process is simple.

That being said, it is equally important to manage patient expectations. Let patients know that dry eye is a chronic condition and that while the AM tissue is not a cure-all, it will play a key role among the multiple methods that can be used to manage their conditions.

Cryopreserved vs dehydrated
Cryopreserved AM and dehydrated AM are the two types of AM tissue grafts available for ophthalmic use. Prokera (Bio-Tissue) is the only cryopreserved ophthalmic AM tissue available, whereas several different dehydrated AM tissue grafts are available, including AmbioDisk (Katena) and BioDOptix (Integra LifeSciences).

AM extract autologous serum eye drops are also an option (Regener-Eyes, Regenerative Network International; Genesis; Ocular Science), but they differ from pre-shaped, ready-to-place AM tissue grafts. The primary difference between the two AM tissue categories is how they are preserved. Cryopreserved AM (CAM)—Prokera—must be kept frozen, then brought to room temperature before application. Conversely, heat or chemical processes are used to preserve dehydrated AM (DAM), which is stored at room temperature and must be rehydrated for clinical use.

Prokera is a self-retaining biologic corneal bandage that is fastened to an ophthalmic conformer ring that keeps the graft in place. Placing Prokera takes a few simple steps. I rinse the graft with sterile saline solution to prevent potential stinging from the preservation media and apply topical anesthetic. Then, I hold the upper eyelid, ask the patient to look down, and insert Prokera into the superior fornix.

Next, I pull the lower eyelid down, slide Prokera under the lower eyelid, and check centration under the slit lamp. Tape tarsorrhaphy is optional, but it’s a step that I always include because it helps keep the lid closed, keeps the device in place, and enhances comfort by preventing the patient from blinking.

The membrane dissolves as healing occurs. In my clinical experience, more inflammation there is, the faster the membrane will dissolve and release its biological factors.

I usually follow up with patients in one week, but the membrane may dissolve in

**TAKE-HOME MESSAGE** Amniotic membranes, both cryopreserved and dehydrated, offer choice to patients with ocular surface disease, including dry eye. ODs owe it to themselves and their patients to try different types of membranes, review the literature, and see the results on their own patients. Amniotic membrane is another tool to allow ODs to offer an additional therapeutic treatment options to their patients.

Figure 2A-C. A. A 72-year-old man with postoperative corneal edema five years after complicated cataract surgery. The patient suffers from chronic foreign body sensation and hyperlacrimation. B. Epithelial disruption in a linear-shaped band at 8 o’clock revealed with fluorescein. C. Significant improvement in symptoms and clinical appearance after two days of amniotic membrane therapy. Images courtesy Laurence Craig Thomas, OD
as few as two to three days.

In cases where the graft is still in place at the one-week follow-up, removal is simple: I apply topical anesthetic, pull the lower eyelid down, lift the lower edge of Prokera using a cotton swab or forceps, ask the patient to look down, apply gentle pressure on the upper eyelid, and slide Prokera out.

Placing dehydrated AM requires additional tools, such as a lid speculum, a Weck-Cel sponge, and a bandage contact lens. A bandage lens must be placed on top of the membrane to keep it fixated. Some dehydrated AMs are packaged along with a contact lens; these AMs cannot be used with any bandage lens, only the accompanying lens.

With dehydrated AM graft, apply topical anesthetic, insert a speculum; debride the cornea if indicated; place the membrane basement side down with forceps; center Weck-Cel sponge; place a bandage contact lens on top of it, making sure both are centered; and finally remove the speculum, making sure to avoid disturbing placement of the membrane or contact lens.

The science
AM tissue is a disease-modifying therapy that aids corneal epithelialization, reduces inflammation and fibrosis, prevents structural damage, and boasts antimicrobial properties.\(^2\)

Many of the beneficial effects of AM are attributed to biomolecules, including fibronectin; hepatocyte growth factor (HGF); epidermal growth factor (EGF); basic fibroblast growth factor (bFGF); transforming growth factor (TGF); and collagen types I, III, IV, and V, which are a direct source of corneal regeneration.\(^4\)

This cocktail of natural cytokines enhances tissue thickness, provides a scaffold for epithelialization, and enhances capillary formation—essentially stimulating growth to repair and restore soft tissue.\(^5,6\) What’s more, AM expresses HLA-G, which gives it the ability to graft damaged tissue without triggering an immune response,\(^7\) and naturally blocks the TGF-β receptor responsible for scar tissue development.\(^8\)

While studies show that AM is imbued with these influential cellular power brokers, the anti-inflammatory and regenerative properties associated with these biologics are retained in different amounts or lost depending on the preservation process used. For instance, cryopreserved AM contains (HC)-hyaluronan (HA)/pentraxin 3 (PTX3), the biological compound that is associated with AM’s antiinflammatory, antiscarring, and regenerative properties.\(^9,10\) HC-HA/PTX3 is not, however, present in dehydrated amniotic tissue.\(^11\) This distinction is borne out in the U.S. Food & Drug Association (FDA) labeling of these products: Prokera cryopreserved AM is the only tissue cleared by the FDA for its protective, wound healing, and anti-inflammatory effects.\(^12\)

Relevant research
A 2018 retrospective study demonstrated that a single application of Prokera self-retained cryopreserved amniotic membrane (CAM) can accelerate the recovery of the corneal surface and help reduce signs and symptoms of DED for at least three months.\(^13\)

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This study, known as the Dry Eye and Amniotic Membrane (DREAM) study (not to be confused with the other well-known dry eye DREAM study\(^14\)), looked at 97 eyes of 84 patients who exhibited severe DED despite maximal medical treatments including topical artificial tears, cyclosporine-A, serum, antibiotics, and steroids. Study participants exhibited superficial punctate keratitis, filamentary keratitis, exposure keratitis, neurotrophic keratitis, and corneal epithelial defect.

After 5.4 days of CAM treatment, patients demonstrated an improved ocular surface along with a notable reduction of the severity of their overall Dry Eye Workshop (DEWS) score.\(^15,16\) These findings are consistent with previous studies.\(^13,16\)

AM in my practice
I typically use AM for moderate-to-severe DED patients. If they have been prescribed anti-inflammatory eye drops and oral omega-3 supplements, performed lid hygiene, and had their meibomian glands expressed, but I have not seen healing after one month or more, I will recommend AM.

I always start with CAM and move to DAM only in rare cases in which the patient is intolerant of the conformer ring with CAM. When a patient complains of irritation, it often dissipates within 24 hours.

It has been suggested that proteins in the
Amniotic membrane grafts

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cryopreserved preparations are more plentiful and active,9 and the consistently successful results seen in my practice suggest this is true. However, I also see remarkable results from DAM in select patients.

Keep in mind that when AM is used with recalcitrant DED patients who have advanced disease, at times patients will require several AM tissue grafts consecutively or over a period of months

Nerve regeneration

Patients who have neuropathic corneal pain are also ideal candidates for AM grafts. Morkin and colleagues found that neuropathic corneal pain due to damaged trigeminal nerve terminals significantly improved by about 72 percent within an average of 6 days of CAM treatment.16

John was the first to show that CAM’s increase in corneal nerve density and improved corneal sensitivity is correlated with corneal nerve regeneration.9 Before this study, no therapeutic modality had been shown to regenerate corneal nerves.

In the study, patients exhibited a significant increase in central corneal nerve density for up to three months as well as significant improvement in their DEWS score, pain score, tear film break-up time, fluorescein staining, and Standard Patient Evaluation of Eye Dryness (SPEED) score.

Researchers surmise that the lasting effect of a placement of CAM for DED may be attributed to corneal nerve regeneration given that corneal nerves play a vital role in epithelial regeneration and tear film stability through reflex tearing and blinking.

regeneration, and improve the signs and symptoms of DED, and my own anecdotal observations support this. DAM, too, is effective at improving the signs and symptoms of DED—in my hands and according to anecdotal reports.

Ultimately, eye care providers need to try cryopreserved and dehydrated AM, review the literature, and challenge themselves to decide how to incorporate these tools into their practices to offer additional treatment options to their patients.

REFERENCES