



MAKING SENSE OF AMNIOTIC MEMBRANES



Push past any feeling of intimidation and allow your patients to reap the rewards of an amazing treatment option.

BY TRACY DOLL, OD, FAAO

Amniotic membranes are useful in treating certain ocular conditions, but if you're confused about when to integrate them into your treatment plan, you're not alone. These medical devices may seem pretty similar, but they're actually quite distinct. This article breaks down the differences between the two main types of amniotic membranes and explains when it would be appropriate to consider the use of an amniotic membrane in the treatment of a particular patient or condition.

AMNIOTIC MEMBRANES: WHAT'S WHAT

The amniotic membrane is the inner lining of the placental tissue of a live donor. Pregnant patients are screened for communicable diseases before the tissue is harvested during an

elective C-section in an FDA-approved protocol. Any donor cells that would cause graft rejection are removed via the preservation and sterilization processes, so nothing is left from the donor that retains the original cellular structure that would cause a reaction.

There are two main types of amniotic membranes used for ophthalmic purposes: cryopreserved and dehydrated (Table). Cryopreserved amniotic membranes have a shelf life of about 2 years and must be stored in a refrigerator or freezer. Dehydrated, or lyophilized (freeze- or air-dried), membranes have a shelf life of about 5 years. This type of membrane is useful if you are working in a location that doesn't have refrigeration, electricity, or water (think military situations).

Application

Applying cryopreserved membranes is similar to inserting a regular contact lens: While the patient looks down, slip the membrane under the upper lid. It will settle and sit on the front surface of the eye (Figure). Many doctors tape the eye afterward to stabilize the membrane. The patient will need to return to your office in 2 to 10 days to have the polymethylmethacrylate (PMMA) ring removed.

It takes more time to place a dehydrated amniotic membrane, and there's a bit of a learning curve to smoothing it out and making sure there are no wrinkles underneath it. Use a Weck-Cel sponge (Beaver-Visitec) to ensure all surfaces are dry; otherwise, the membrane will slide right off. Most doctors use a speculum

to tamp down/rub the dry membrane on the surface of the cornea and then dry off the cornea with the Weck-Cel sponge, as well as the back of the bandage contact lens. Everything that's dry has to stay dry. The dehydrated membrane will dissolve over time, but the patient will need to return to have the bandage contact lens removed.

Bandage contact lenses and dry or lyophilized amniotic membranes, which are freeze-dried, are indicated only for wound coverage. The cryopreserved amniotic membrane retains a key matrix component called heavy chain-hyaluronic acid/pentraxin 3 (HC-HA/PTX3). All by itself, HC-HA/PTX3 is the molecule that does the heavy hitting of actual wound healing. This is the only amniotic membrane option approved by the FDA to promote wound healing. (The other options are only approved for wound coverage.)

The HC-HA/PTX3 molecule works in a variety of pathways. Used in cryopreserved amniotic membranes, HC-HA/PTX3 promotes healing by preventing the growth of fibronectin, which prevents the ability to make scars. HC-HA/PTX3 also has antiinflammatory properties via suppression of TH-1 and

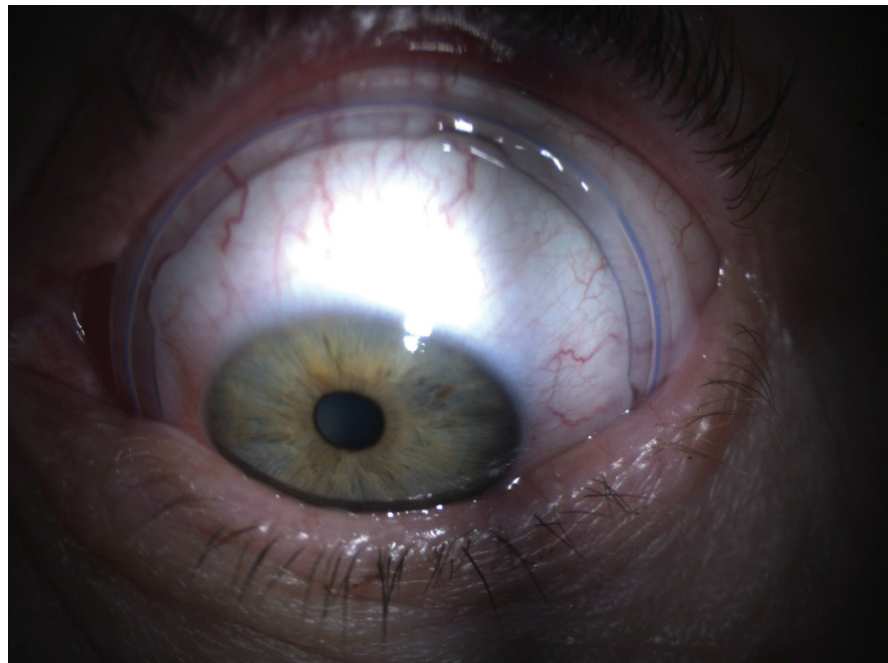


Figure. Application of a cryopreserved membrane. The patient looks down, and the membrane is slipped under the upper eyelid. When the patient looks straight ahead, the polymethylmethacrylate ring centers itself.

TH-17, which are lymphocytes that specifically attack the ocular surface. (They're the same TH-1 and TH-17 molecules that lifitegrast ophthalmic solution 5% [Xiidra, Bausch + Lomb] targets.) Additionally, HC-HA/PTX3 supports the healthy turnover of corneal epithelial stem cells.

Complications

One thing that can get tricky is if you have a patient who reacts to a dry or lyophilized membrane (eg, the membrane sticks to the cornea after it rehydrates). In this case, the only way of removing it is to mechanically scrape it off—or debride the membrane. If a patient isn't tolerating a cryopreserved membrane, you can just pop it out like a contact lens.

The PMMA ring with the cryopreserved amniotic membrane isn't very comfortable. Patients can usually tolerate it, but if you have a patient who is struggling with it and you need to repeat the procedure, you might consider switching to a dry or freeze-dried membrane.

Additionally, some patients (eg, those with blebs) aren't candidates for a cryopreserved amniotic membrane. (Patients with blebs may experience the PMMA ring rubbing on the bleb, which is obviously something you want to avoid.) Also, patients with allergies to any of the ingredients in the cryopreserved solutions (eg, ciprofloxacin or amphotericin B)

AT A GLANCE

- In cases where a bandage contact lens seems to be the go-to treatment option, consider whether an amniotic membrane could offer better results.
- It takes more time to place a dehydrated amniotic membrane than a cryopreserved membrane, and there's a learning curve to figuring out how to smooth the dehydrated membrane out on the cornea.
- If a patient has a bad reaction to a dehydrated membrane, the only way to remove it is to debride the membrane, whereas removal of a cryopreserved membrane requires simply taking it out, as one does a contact lens.
- Amniotic membranes are useful for treating trauma or injury (eg, corneal abrasions), herpetic lesions, and chronic, severe dry eye.

TABLE. Available Amniotic Membranes

AMNIOTIC MEMBRANE	DESCRIPTION/INDICATION	SHELF LIFE	CONTRAINDICATIONS
Cryopreserved			
Prokera Classic/Slim/Plus/Clear (BioTissue)	A corneal bandage designed for treating damaged corneas by creating an environment for regenerative healing	2 years; stored in a refrigerator or freezer	Patients with glaucoma who have filtering blebs
Dehydrated			
AmbioDisk Amniotic Membrane (Corza Medical)	A sutureless, overlay amniotic membrane disk used for ocular surface reconstruction	5 years; stored at room temperature	Not to be used on wounds with evidence of active or latent infection or gangrene
Apollo Amniotic Membrane Allograft (Atlas Ocular)	A chorion-free, amnion-only, sterile human allograft tissue intended for use as a “scaffold” to encourage and enhance ocular tissue repair and regeneration	5 years; stored at room temperature	
Aril Accellular Allograft Amniotic Membrane (Seed Biotech)	An allograft tissue intended for homologous use	See package label for expiration date; stored at room temperature	
Biovance 3L Ocular (Verséa Ophthalmics)	A pure human amniotic tissue with an intact basement membrane intended for use as a biologic membrane covering that provides an extracellular matrix. As a barrier membrane, Biovance 3L Ocular is intended to protect the underlying tissue and preserve tissue plane boundaries.	10 years; stored at room temperature	Patients with a known hypersensitivity to Biovance 3L Ocular. Also should not be used on clinically infected wounds or together with a collagenase product on the wound
BioDOptix Amniotic Extracellular Membrane (Integra LifeSciences)	An allograft tissue intended for homologous use as a protective barrier covering during the repair of soft tissue	5 years; stored at room temperature	Patients with known sensitivity to ethanol and eyes with an active infection
Opticte Amniotic Ocular Matrix (Merakris Therapeutics)	A human extracellular matrix derived from amniotic tissue for the protection of corneal surfaces	5 years; stored at room temperature	
XcellerEYES (Oculus Biologics)	A lyophilized amniotic membrane allograft that is aseptically processed to preserve the native extracellular matrix and endogenous proteins that can be used as a biological barrier or wound cover	Expiration date clearly marked on each package; stored at room temperature	

For complete information on each amniotic membrane, including contraindications, visit the manufacturer’s website.

are not suitable candidates for a cryopreserved amniotic membrane.

INDICATIONS

For some doctors, bandage contact lenses may be the go-to for treating certain trauma cases, but before you reach for this option, take a moment to consider whether an amniotic membrane would be a better choice.

Yes, amniotic membranes take an extra billing step and a bit of patient communication, but don’t deprive appropriate patients the healing benefits that come with their use.

In primary care settings, the most common uses for amniotic membranes are trauma or injury (eg, corneal abrasions) and herpetic lesions. Those who, like me, specialize in dry eye

and don’t see as many urgent cases, are typically caring for patients with chronic conditions and, thus use amniotic membranes a bit differently.

Punctate Keratitis

If you have a patient with superficial punctate keratitis (SPK) that is not responding well or nonresolving, you can place a cryopreserved amniotic

membrane to help keep that cornea healed for quite a few months. It's usually not monotherapy for me in dry eye. I re-epithelialize moderate-to-severe corneas with the Prokera Slim (BioTissue) cryopreserved membrane, and then I try to protect that tissue by attacking the underlying causes of the patient's dry eye. That's the best way I've found to integrate an amniotic membrane into therapy. I find that many therapies are much more comfortable after using Prokera first because you're not dealing with a cornea that's hypersensitive and irritated. So, it tends to be first-line therapy for me in patients with punctate epithelial erosions or SPK of grade three or more.

Dry Eye

Several studies have shown that as few as 3 days of wearing a cryopreserved amniotic membrane can lead to about 3 months of dry eye symptom resolution.^{1,2} This is great for patients who do not have the

ability or the dexterity to instill eye drops or do any home therapy, but it won't fix everything, because the root cause of their dry eye (eg, lifestyle factors, systemic disease, exposure) is still going to be there.

CONSIDER AMNIOTIC MEMBRANES IN YOUR TREATMENT TOOLBOX

Any time you have a cornea that could use some re-epithelialization and healing, consider an amniotic membrane. And if you have a patient with an ocular injury, think about reaching for a cryopreserved amniotic membrane. Keep in mind, too, that this treatment option has antibiotic properties for both Gram-positive and Gram-negative strains of bacteria, so if you're concerned about a patient needing coverage, but you're also worried about infection, an amniotic membrane may potentially be safer than a bandage contact lens. This is why they are great for wound coverage in herpetic cases and the like.

Consider a cryopreserved amniotic membrane over the use of a bandage contact lens if you're looking for actual healing (rather than simply wound coverage) and for reducing scarring, as well as the risk of inflammation and infection.

Still craving additional insights on amniotic membranes? Outside of learning from your local rep, the American Academy of Optometry usually has a workshop at its annual national meeting, and that's coming up in a few months, so keep an eye out. ■

1. John T, Tighe S, Sheha H, et al. Corneal nerve regeneration after self-retained cryopreserved amniotic membrane in dry eye disease. *J Ophthalmol*. 2017;2017:6404918.

2. McDonald MB, Sheha H, Tighe S, et al. Treatment outcomes in the DRy Eye Amniotic Membrane (DREAM) study. *Clin Ophthalmol*. 2018;12:677-681.

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