AMNIOTIC MEMBRANE
Many ocular applications; research needed to define limits

by Howard Larkin in Vienna

Amniotic membrane has many qualities that make it attractive for ophthalmology. It provides trauma protection with little immune response; it encourages epithelialisation of damaged cornea and conjunctiva, and suppresses inflammation, neovascularisation and cicatrisation, which helps keep recovering corneas clear and ocular tissues free of obstructive scar tissue or abnormal blood vessels. It may even help the conjunctiva grow.

As a result, amniotic membrane has been used in a long list of ophthalmic procedures. It is particularly useful for grafted and patched epithelial ulcers and defects, protecting the epithelium following PK, limbal transplants, treating partial limbal deficiency, reducing calcium deposits in band keratopathy and after corneal EDTA treatment, and for immediate treatment of chemical burns. It has also been successfully used to culture corneal limbal epithelium for transplant.

“I think we all consider it a part of our standard surgical armamentarium,” ESCRS president Jose Guell MD, Barcelona, Spain, told the second annual EuCornea Congress.

However, the mechanisms of action of amniotic membrane are poorly understood, Dr Guell noted. As a result, “I honestly believe it is currently being used far in excess of its true useful potential.”

For example, it is not suitable in cases of complete limbal deficiency, should not replace conjunctival grafts for pterygium, is not a useful patch for pseudophakic corneal oedema and cannot be substituted for corneal stroma, he said. While it has been used to suppress scar formation in glaucoma filtering surgery, its track record is poor in these applications.

“I think we need to take into account these limitations.”

Mechanisms of action
Derived from donor tissue from the amniotic sac, amniotic membrane was used experimentally as far back as the 1940s, and was used clinically in ophthalmology beginning in the early 1990s. In 1995 it became more widely available as preservation problems were overcome. Dr Guell pointed out that some of the mechanisms of action for amniotic membrane are inferred from its composition rather than proven scientifically in relation to ophthalmic surgery.

“We all thought preserved membrane to be an inert tissue with no viable cells and with very low biological activity.”

Nonetheless, different parts of the amniotic membrane have different properties with implications for surgical applications. The epithelium has the highest concentration of growth factors and is the best substrate for culturing limbal cells of undifferentiated epithelial phenotype. Consequently, the membrane is typically placed epithelium side up in cases where rapid epithelium is desirable.

The basal lamina, which remains after any type of preservation, is made up of collagen, laminin and fibronectin similar to the conjunctiva. It promotes epithelial cell migration, strengthens adhesions to basal cells, induces epithelial differentiation, and prevents apoptosis.

The stromal matrix suppresses inflammatory signalling factors, traps inflammatory cells from other tissues and induces their rapid apoptosis, and contains anti-inflammatory and anti-angiogenic proteins and protease inhibitors. It reduces inflammation locally, and is effective in treating inflamed tissues. Stromal side-up transplants remain clear.

Surgical strategies
As a graft, amniotic membrane can replace absent stromal matrix and provide a basement membrane for epithelial growth, Dr Guell said. As a patch, it protects the ocular surface from external insults and provides biological factors to reduce inflammation and promote epithelialisation. In combination, epithelial side-up membrane at the periphery covered by stromal side-up at the centre ensures that epithelial cells migrating from the conjunctiva will grow only at the periphery rather than growing over the cornea, as can happen with a single membrane.

There are many indications for amniotic membrane as a corneal graft, the most common being persistent epithelial ulceration and bullous keratopathy, Dr Guell said. He cautioned, however, that simply using membrane as a patch has only a temporary effect on bullous keratopathy. It may improve the epithelium, but after a few months the bulli reappear. All of the diseased epithelium must be removed and the membrane used as a patch to support conjunctival epithelial growth. As a corneal graft in combination with a corneal patch, it also can be used to treat neurotrophic ulcer.

The most common indication for amniotic membrane is as a patch, Dr Guell said. It is very effective for persistent corneal endothelial defects and promoting epithelialisation after PK in older and diabetic patients.

“We can improve early post-op epithelialisation. In a case with perforation we use all of our weapons, PK, membrane, and Avastin, to improve the behaviour of the eye. In eyes where we do limbal transplantation we also use the membrane to protect the epithelial surface.”

In a keratoconic eye, Dr Guell has used amniotic membrane to improve epithelialisation after scraping the epithelium. For partial limbal deficiency after extended contact use amniotic membrane can be used to encourage re-growth.

“It does not make sense to use membrane on complete limbal deficiency because the membrane will not afford limbal cells.”

For acute chemical calcification, amniotic membrane can control inflammation and allow re-epithelialisation if it is applied within a few hours of the injury, Dr Guell said. But typically, patients don’t come for two or three weeks, and then it is too late.

Culturing limbal cells from a fellow eye for transplant is a new indication. Dr Guell believes more will emerge as research progresses. He suggested that a group be formed to compare studies and standardise evaluation of ocular surface disease, such as the number of clock hours of limbal deficiency.

“Our understanding of the best method of preservation for the membrane and its mechanisms of action still needs significant research.”

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