Amniotic Membrane Transplantation for Reconstruction of the Conjunctival Fornices

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Purpose: To describe the clinical outcome of amniotic membrane transplantation (AMT) for fornix reconstruction in a variety of ocular surface disorders.

Design: Noncomparative interventional case series.

Participants: Seventeen eyes in 15 patients with symblepharon. Four eyes had ocular-cicatricial pemphigoid, two eyes had symblepharon after pterygium excision, four eyes had chemical or mechanical trauma, two eyes had strabismus surgery, two eyes (one patient) had Stevens-Johnson syndrome, one eye had toxic epidermal necrolysis, and two eyes (one patient) had chronic allergic conjunctivitis.

Intervention: The subconjunctival scar tissue was dissected from the episclera, and the freed conjunctival flap was recessed to the fornix. A layer of amniotic membrane (AM) was applied to cover the exposed episclera. The fornical edge of the membrane was anchored with sutures passing through the full thickness of the lid.

Main Outcome Measures: A deep conjunctival fornix, lack of motility restriction.

Results: The mean follow-up period was 37 ± 24 months (range, 9–84 months). Complete fornix reconstruction was demonstrated in 12 of 17 eyes (70.6%), whereas 2 eyes had a partial success, and 3 eyes (3 patients) had recurrence of symblepharon with restricted motility. In eyes that demonstrated partial success or failure, the underlying etiology was either an autoimmune disorder or a recurrent pterygium. The most successful outcome was observed in eyes with symblepharon associated with trauma.

Conclusions: AMT is an effective method of fornix reconstruction for the repair of symblepharon in a variety of ocular surface disorders. Future modifications, including an epithelial cellular component on the AM (conjunctival autograft or ex vivo expanded epithelial stem cells) may improve the outcome of this surgical procedure. *Ophthalmology 2003;110:93–100 © 2003 by the American Academy of Ophthalmology.*

Progressive scarring of the conjunctiva may lead to obliteration of the fornices and formation of symblepharon in a variety of ocular surface disorders. These include surgical trauma after pterygium or lid surgeries; chemical burns; autoimmune disorders such as ocular-cicatricial pemphigoid (OCP), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis; infectious disorders such as adenoviral membranous conjunctivitis or severe end-stage trachoma; and inflammatory conditions such as Sjögren's syndrome and sarcoidosis.[1] Severe symblepharon may lead to further surface breakdown as a result of impaired or ineffective blinking by causing entropion or lagophthalmos and disturb the integrity of an adequate and stable tear film by obliterating the tear meniscus. In some instances, symblepharon may cause restrictive diplopia.

The surgical procedure to correct symblepharon involves excision of the scar tissue and application of a tissue substitute to cover the palpebral or bulbar surface of the defect. This is usually followed by an additional procedure to prevent readhesion, such as insertion of a conformer or a symblepharon ring,[2] application of β-irradiation,[3] subconjunctival injection of mitomycin-C,[4] or conjunctival or mucous membrane grafting,[1] skin grafting,[5] or silicone sheet implants.[6,7] Conjunctival autografting may be limited by lack of a healthy tissue or bilateral involvement, whereas grafted oral mucous membranes may shrink or cicatrize. β-Irradiation can prevent recurrence but fail to restore a healthy conjunctival surface and may cause scleral necrosis, whereas foreign material implants are limited by inflammatory response and are removed after a few weeks.

The amniotic membrane (AM) is the innermost layer of the placenta and consists of a thick basement membrane and an avascular stroma. It can be used as a substrate to replace damaged mucosal surfaces and has recently been used successfully for reconstructing corneal[8–12] and conjunctival[13–16] surfaces damaged by various insults in various ocular surface disorders.[17] It was recently found to be effective in reducing recurrence after extensive pterygium removal[18,19] and to repair symblepharon associated with

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The senior author (Scheffer C. G. Tseng) has obtained a patent (USTO 09/027.109) in the preparation and clinical uses of human amniotic membrane and has a proprietary interest in Bio-Tissue, Miami, Florida.

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Table 1. Patients' Data and

No/Age/Gender	Eye	Diagnosis	Symblepharon Location	Past history, Previous Procedures
Symblepharon in autoimmune disorders				
1/60/M	OD	OCP	Inferior	Multiple entropion repairs
2/72/F	OS	OCP	Superonasal, inferonasal, and temporal	Optic atrophy after excision of meningioma
3/61/F	OD	OCP	Inferior	Subconjunctival MMC
4/69/M	OS	OCP	Inferior	
5/46/F	OD	SJS	Superotemporal, inferotemporal	
	OS		Superotemporal	
6/41/F	OS	TEN	Inferior	Ectropion repair
7/35/M	OD	Allergic conjunctivitis/ hay fever	Superonasal and inferonasal, both eyes	Motility restriction
	OS			
Symblepharon after ocular surgery				
8/41/M	OD	S/p pterygium surgery	Inferior	Diplopia, motility restriction
9/43/M	OS	S/p pterygium surgery	Superonasal	Two surgeries for pterygium (first with β-irradiation; second with limbal autograft) motility restriction, diplopia
10/41/F	OS	S/p strabismus surgery	Superior	Multiple procedures for Duane's syndrome type II
11/46/F	OD	S/p strabismus surgery	Inferonasal and superonasal	Multiple procedures for congenital esotropia
Symblepharon after ocular trauma				
12/45/M	OS	Chemical burn	Inferior	Multiple procedures of KLAL, AMT, PKP, and Bearveldt implant
13/26/M	OD	Chemical burn	Inferior	
14/5/F	OS	Obstetric trauma (forceps delivery)	Inferotemporal and superotemporal	Multiple strabismus procedures; oral mucosa graft for symblepharon
15/45/M	OS	Thermal burn	Inferonasal	

AMT = amniotic membrane transplantation; CF = counting fingers; ED = epithelial defect; F = female; HM = hand motions; KLAL = keratolimbal penetrating keratoplasty; SJS = Stevens Johnson syndrome; S/p = status post; TEN = toxic epidermal necrolysis.

pterygium.[20] These studies have shown that amniotic membrane transplantation (AMT) facilitates epithelialization and reduces inflammation, vascularization, and scarring. Herein we report the outcome of AMT for fornix reconstruction in patients with pathogenic symblepharon.

Patients and Methods

Patients

After obtaining informed consent, symblepharon lysis followed by amniotic membrane graft was performed in 17 consecutive eyes (15 patients) at the Bascom Palmer Eye Institute from 1993 to 1999. Surgeries were approved by the Medical Science Subcommittee for the Protection of Human Subjects in Research of the University of Miami School of Medicine (Institutional Review Board). Indications for the surgical correction of symblepharon included motility restriction with diplopia; unstable tear film as a result of an obliterated fornix with ocular irritation symptoms; or as part of preparing the ocular surface for transplantation of limbal epithelial stem cells. Clinical data concerning patient demography, preoperative examination, surgical procedure, postoperative follow-up, and the final outcome and complications were retrieved in a prospective manner by use of an itemized data form. The same surgeon (SCGT) performed all surgical procedures. All patients were photographed before surgery and at various visits postoperatively. Outcome measures included the maintenance of a stable fornix depth throughout the follow-up period, lack of recurrence of scar tissue, and resolution of preoperative motility restriction. Surgical success was defined as the appearance of a deep fornix without recurrence of scar tissue after 6 months of follow-up and resolution of preoperative motility restriction. Partial success was defined as focal recurrence of scar tissue or a band, but with overall maintenance of a deep fornix, and lack of recurrence of preoperative motility restriction. Failure was defined as recurrence of the scar tissue and persistence of any preoperative motility restriction at last follow-up.

Surgical Outcome

Visual Acuity		Follow-up (Months)	Surgical Outcome	Comments
Preoperatively	*Postoperatively*			
20/40	20/40	72	Success	
HM	HM	40	Success	
20/25	20/25	16	Success	
20/100	CF	15	Failure	AMT repeated 1 month later with partial success
20/200	20/60	48	Success	Focal keratinization, corneal ED
20/50	20/30	46	Partial success	Reoperated 2.5 years later with AMT
20/40	20/25	22	Failure	Recurrence
20/50	20/20	14	Success	
20/25	20/25	12	Success	Pyogenic granuloma, resolved after steroid injection
20/20	20/20	24	Failure	Diplopia remained after second AMT performed 6 months later
20/20	20/20	84	Partial success	Residual motility restriction
20/50	20/30	9	Success	
20/30	20/20	60	Success	
HM	HM	15	Success	Repeated KLAL/PKP/AMT 5 months later, resulting in improved vision of 20/50; pyogenic granuloma excised
20/300	20/20	37	Success	Partial limbal stem cell deficiency
NLP	NLP	61	Success	Optic neuropathy associated with obstetric trauma
20/60	20/30	72	Success	

allograft; M = male; MMC = mitomycin C; NLP = no light perception; OCP = ocular cicatricial pemphigoid; OD = right eye; OS = left eye; PKP =

Symblepharon Lysis and AMT

All patients were anesthetized with a retrobulbar block. Several drops of 1:1000 epinephrine were applied to the ocular surface to achieve vasoconstriction and prevent excessive bleeding. A 4-0 nylon suture was placed in the midportion of the tarsal plate of the lower (or upper) lid to apply traction (Fig 1A). The subconjunctival scar tissue was dissected off from the perilimbal area, and the remaining epithelium-lined conjunctival flap was freed from the underlying bulbar sclera and the adjacent conjunctiva. This pedicle flap was recessed to the deep fornix so that it covered the palpebral surface of the lid. In cases in which the surrounding host tissue tended to carry preexisting inflammation or to be associated with more inflammatory activity (e.g., pterygium, OCP, and SJS), subconjunctival injections of long-acting triamcinolone acetonide (10–12 mg in total) were given along the edges of the excised conjunctiva in several depots.

The method of AM preparation and preservation has been previously described.[9,11,13] In this study, preserved human AM was obtained from Bio-Tissue (South Miami, FL).[11] After thawing, the AM was removed from the filter paper and placed over the conjunctival defect with the basement membrane side up. The smooth basement membrane side of the AM could be distinguished from the sticky stromal side by touching it with a Weckcel sponge (Edward Weck & Co, Inc., Research Triangle Park, NC). The AM was trimmed to fit the entire conjunctival defect, including the bulbar surface of the fornix and the deeper portion of the palpebral aspect of the fornix. The membrane was then secured to the recessed conjunctival edge with a few interrupted or a running 9-0 Vicryl sutures so that its margin was placed under the conjunctival margins to facilitate epithelial growth over the membrane (Fig 1B). This membrane was then tugged to the deep fornix by a muscle hook anchored to the palpebral side of the fornix by passing two or three double-armed 6-0 Vicryl sutures through the full thickness of the lid and secured to the skin with silicone bolsters (Fig 1B). The rest of the membrane was then secured and flattened to the bulbar aspect by interrupted 10-0 nylon sutures with superficial scleral bites. Care was taken to avoid trapping blood under the membrane. Postoperatively, all patients were

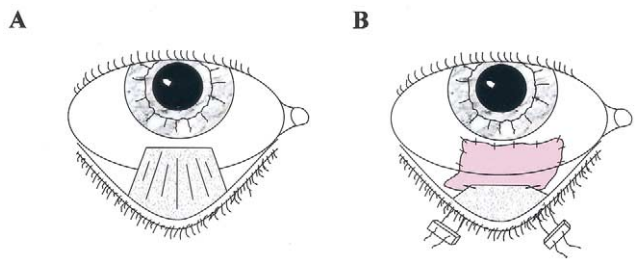


Figure 1. Schematic drawing of amniotic membrane transplantation for reconstruction of the lower fornix after symblepharon lysis. **A,** Preoperative demonstration of the scar tissue extending from the palpebral aspect of the fornix to the bulbar perilimbal area. **B,** The symblepharon is dissected from the perilimbal edge with the removal of subconjunctival fibrous tissue from the bulbar aspect. This freed conjunctival flap is recessed to the fornix to be used as a mucosal surface to cover the palpebral surface of the fornix. Amniotic membrane graft (pink) is sutured to cover the bulbar conjunctival defect by interrupted sutures with episcleral bites and secured to the deep fornix by passing two double-armed mattress sutures through the full thickness of the lid and tied over the skin with bolsters.

treated with topical Pred-Forte (1% prednisolone acetate, Allergan, Irvine, CA) every 2 hours for 1 week and tapered off in a period of 4 to 6 weeks. Topical Ocuflox (0.3% ofloxacin, Allergan, Irvine, CA) was applied three or four times a day until full epithelialization of the AM was evident. Full epithelialization was determined on the first postoperative visit when no fluorescein staining was demonstrated over the amniotic membrane. Sutures were removed during the second or third postoperative week. When areas of marked fibrovascular proliferation or congested conjunctival vessels were noted, especially at the excised edges, subconjunctival injections of triamcinolone acetonide in the amount of 4 to 8 mg were administered in the office.

Results

The demographic data, clinical presentation, and surgical outcome are summarized in Table 1. There were 17 eyes in 15 patients (8 men, 7 women). The average age was 45 ± 16 years (range, 5–72 years). The mean follow-up period was 37 ± 24 months (range, 9–84 months). The patients were subdivided further into three major groups according to the underlying etiologies associated with symblepharon (i.e., autoimmune disorders, after ocular surgery, and after ocular trauma). The first group of seven patients (nine eyes) included four patients with OCP, one patient with SJS, one patient with toxic epidermal necrolysis, and one patient with chronic allergic conjunctivitis. The second group of four patients (four eyes) developed symblepharon after previous surgeries for pterygium (two patients) and strabismus (two patients). The third group included four patients (four eyes). Two patients developed symblepharon after alkali burns. One patient had forceps injury at birth, which involved proptosis, extensive conjunctival lacerations, and restrictive ocular motility, necessitating several strabismus procedures. The fourth patient had a thermal burn from hot metallic shrapnel after hammering of a hot metal rod.

In eight patients, multiple surgical procedures previously had been performed to correct the underlying disorder or associated ocular surface problems. These included repair of lid malposition (ectropion or entropion), excision of recurrent pterygium, correction of strabismus, allogeneic limbal stem cell transplantation, oral mucosa transplantation, or subconjunctival injection of mitomycin-C into the scar tissue.

AMT achieved successful fornix reconstruction in 12 of 17 eyes (70.6%). In all 17 eyes, complete epithelialization of AM was observed 3 weeks after surgery, resulting in a noninflamed appearance of the surgical site. In these 12 eyes with successful results, the fornix was deep, and no recurrences were observed. The visual acuity improved after surgery in eight eyes, remained stable in eight eyes, and deteriorated in one eye with OCP as a result of disease progression. Motility restriction was noted in three eyes preoperatively. Of them, two eyes remained with restrictive motility at last follow-up, and one eye had normal ocular movements after surgery.

Partial success was demonstrated in two eyes, and failure was observed in three eyes. Patients who experienced a failure or a partial success had symblepharon associated with autoimmune disorders (three of nine eyes) or previous surgery (two of four eyes), whereas all four eyes that had developed symblepharon secondary to chemical or mechanical trauma resulted in a successful outcome. Two of the three failed eyes were reoperated on at 1 and 6 months, respectively, after the initial procedure. One of the two reoperated eyes had partial success after the second procedure, and in the second eye no improvement was observed as a result of recurrence of the scar tissue. In the third eye that failed, recurrence of the symblepharon was not associated with motility restriction or with ocular irritation symptoms. In two eyes (cases 7 and 12), pyogenic granuloma developed in the first 3 months after surgery and was managed with topical corticosteroid injection (case 7) or with surgical excision (case 12). In two eyes (cases 3 and 12) subconjunctival injection of triamcinolone was needed to control areas of marked inflammatory activity.

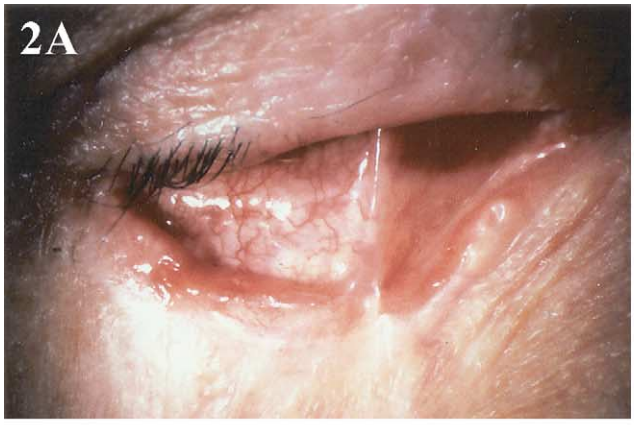
Case Reports

Case 1. A 60-year-old male with OCP complained of increasing ocular irritation as a result of unstable tear film caused by entropion secondary to an inferior symblepharon (Fig 2A) despite previous multiple entropion repairs. Excision of the subconjunctival scar tissue in the symblepharon was performed from the inferior perilimbal area, followed by recessing the bulbar conjunctival tissue to the fornix and placement of an AM graft to cover the bulbar conjunctival defect. Complete epithelialization over the AM graft was evident 2 weeks after the surgery (Fig 2B), with a deep fornix (Fig 2C). Six months after surgery, the patient maintained a deep fornix with total resolution of his ocular symptoms (Fig 2D). Reactivation of OCP activity occurred 4 years later and was controlled with oral cyclophosphamide. However, the symblepharon did not recur during 6 years of follow-up.

Case 3. A 61-year-old woman with OCP had ocular irritation

Figure 2. A, A 60-year-old male with inferior symblepharon associated with ocular cicatricial pemphigoid. **B** and **C,** Two weeks after symblepharon lysis with amniotic membrane transplantation, there was complete epithelialization over the amniotic membrane graft and a deep fornix. **D,** Six months after surgery, a deep fornix remained with resolution of ocular irritation symptoms. The symblepharon did not recur after 6 years of follow-up.

Figure 3. A, An inferior symblepharon in the right eye of a 61-year-old woman with ocular cicatricial pemphigoid. **B** and **C,** Two weeks after surgery, the graft was epithelialized, and the excision area was quiet. **D,** A year later, she had a deep and quiet inferior fornix with a stable tear film and reduced symptoms.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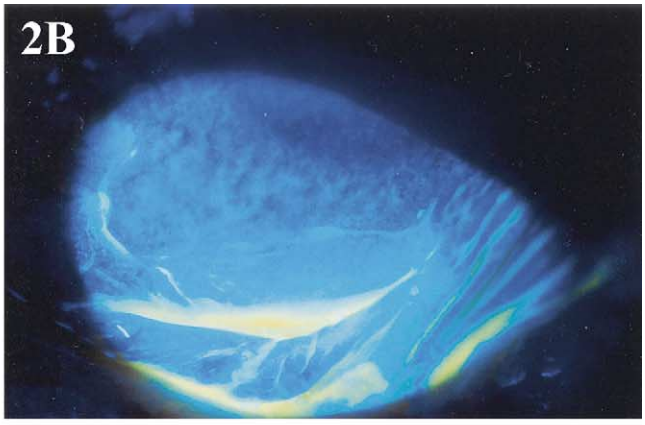
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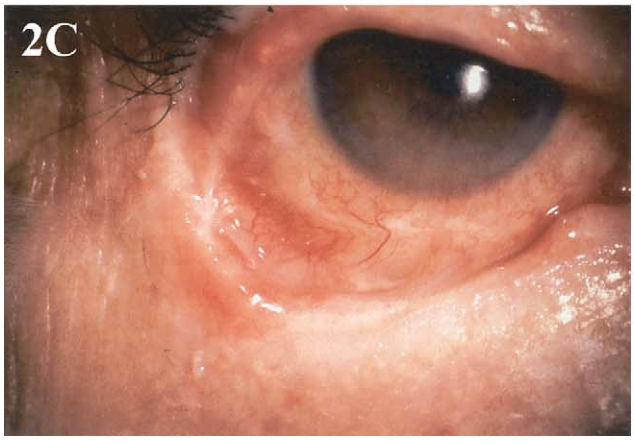
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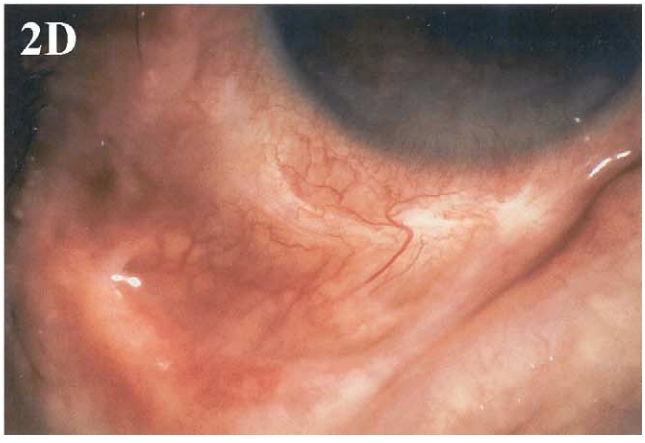
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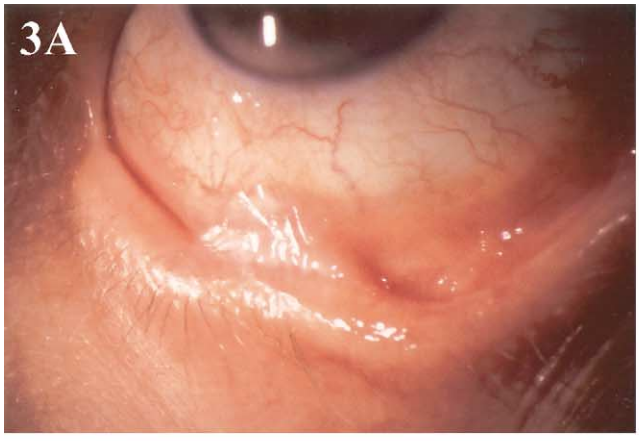
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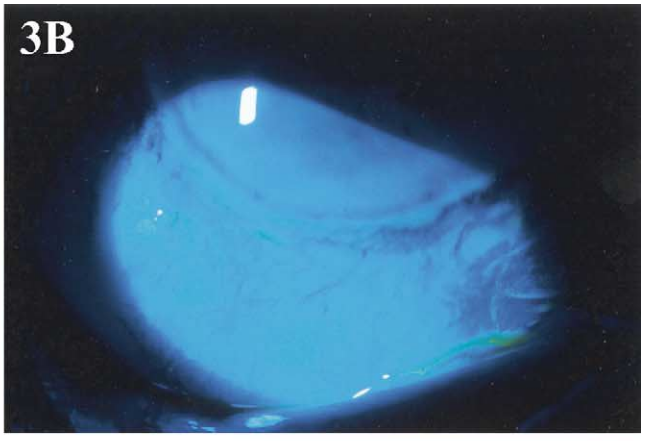
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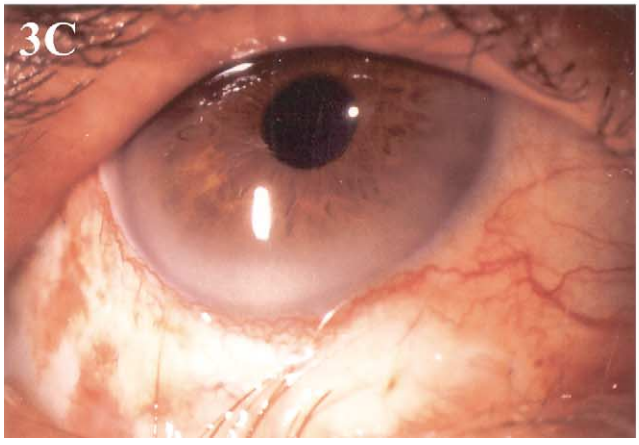
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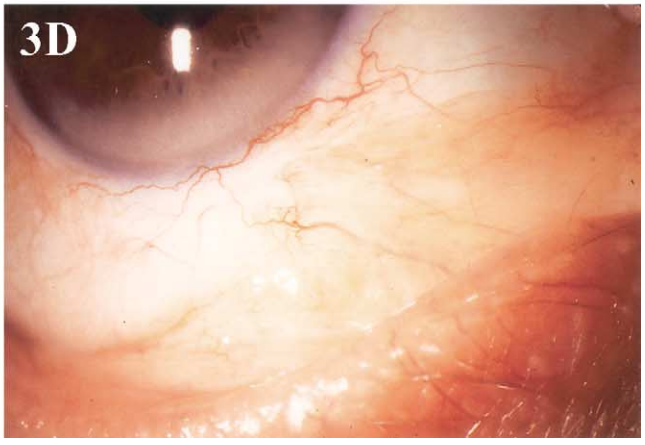
3D

as a result of foreshortening of her inferior fornix predominantly in the right eye (Fig 3A). She received a subconjunctival injection of mitomycin-C to the inferior fornix without any improvement. Three months later, fornix reconstruction with AMT was performed. The AM-covered defect was completely epithelialized, resulting in a quiet and deep fornix 2 weeks after surgery (Fig 3B, C). Increased conjunctival inflammation was noted in the conjunctiva adjacent to the surgical incision 2 months after surgery. This was managed with a local triamcinolone acetonide injection and systemic cyclophosphamide (200 mg a day) for 1 month, when cyclophosphamide was replaced with mycophenolate mofetil (CellCept), 1 g twice a day for 6 months. A year after surgery, she had a deep and quiet inferior fornix (Fig 3D) and a stable tear film, and her symptoms were largely eliminated.

Case 5. A 46-year-old woman with SJS had shortening of the inferior fornix with a temporal symblepharon in the right eye (Fig 4A) and a superotemporal symblepharon of the left eye. She had a successful fornix reconstruction with AMT in her right eye, with almost complete healing at 2 weeks (Fig 4B). Focal keratinization of the tarsal conjunctiva caused a corneal epithelial abrasion and was managed with topical 0.01% retinoic acid ointment. A quiet fornix and a freely mobile globe were observed 2 months (Fig 4C) and 3 years (Fig 4D) later. The left eye had a similar surgery but experienced recurrence, which was reoperated 2.5 years later with an AM graft with a successful outcome.

Case 12. A 45-year-old male with an alkali burn in his left eye had limbal stem cell deficiency with conjunctivalization of his cornea and symblepharon of the inferior fornix. He had previously undergone several procedures of allogenic limbal transplantation combined with a penetrating keratoplasty and AMT, which failed. As an initial step to prepare the ocular surface for a later stem cell transplantation, fornix reconstruction with AMT was performed. A stable deep fornix with no recurrence of the scar tissue was evident during the first 5 postoperative months. Therefore, repeated limbal allograft transplantation, combined with penetrating keratoplasty and AMT, was performed, resulting in visual acuity of 20/50.

Discussion

The formation of symblepharon may destabilize the tear film by interfering with eyelid blinking and tear meniscus formation, by reducing the size of goblet cell–containing conjunctiva, by facilitating mechanical trauma caused by lid malposition and misdirected lashes, and by limiting the ocular motility. Symblepharon as such further aggravates the underlying pathology and directly accounts for the patient's symptoms of discomfort. Furthermore, without being first corrected, such symblepharon is a major obstacle, if not a contraindication, for the ensuing corneal transplantation and ocular surface reconstruction.

Procedures to correct symblepharon are numerous, suggesting that each variation has its limitations. For example, buccal or labial grafts are associated with unsatisfactory results, because they occupy a large space in the fornix, and they may shrink with time. Silicone sheets, plastic wraps, conformers, and rings may be associated with recurrence once the implant is removed. Application of β-irradiation or mitomycin-C may result in scleral ischemia or necrosis. A healthy conjunctival autograft is ideal to use, but its availability is limited in patients with a bilateral and diffuse disease such as OCP or SJS. A promising alternative to the preceding conventional therapies should possess the dual actions of restoring the normal conjunctival tissue in the symblepharon-lysed area and preventing the underlying cicatricial processes leading to readhesion.

In this study we report that AMT is an effective surgical method for symblepharon repair and can maintain a deep fornix and scar-free environment with complete or partial success in 14 of 17 eyes. Although, historically, symblepharon repair was the first indication described in the literature for the use of AM grafts, this report is the first large series that presents the results of fornix reconstruction with AMT. Our results differ from those first reported by de Rötth in 1940,[21] who used *live* fetal membrane (i.e., amnion and chorion together) in the treatment of symblepharon. de Rötth reported successful fornix reconstruction in one of six patients, whereas grafts in the others dissolved in 10 weeks. The discrepancy may be attributed, in part, to his inclusion of live cells and chorion, leading to an unwanted allograft rejection. When appropriately separated from the chorion and maintained in a medium containing Dulbecco's modified Eagle's medium and glycerol, at a temperature of $-80°$ C, the AM is a substrate without live cells. We and others have reported that AMT can successfully be used as an alternative to a conjunctival graft for conjunctival surface reconstruction after removal of large conjunctival lesions such as pterygium,[13,18–20] conjunctival intraepithelial neoplasia, tumors, scars,[14] and conjunctivochalasis.[22] It should be noted that the reconstructed area can be very large as long as the underlying bed is not ischemic and the adjacent host conjunctiva remains normal. This concept is supported by our finding that eyes with a more favorable outcome had symblepharon associated with a previous surgical procedure or trauma; in these, insult was remote, and there was no ongoing inflammatory activity in the host conjunctiva.

The therapeutic effect of AM may involve three key actions that work synergistically in suppressing fibrosis, reducing inflammation, and promoting epithelialization. We have reported that AM stromal matrix suppresses transforming growth factor-β signaling, proliferation and myofibroblastic differentiation of normal human corneal and limbal fibroblasts,[23] and normal conjunctival and pterygium body fibroblasts.[24] This action explains why AMT helps reduce scars during conjunctival surface reconstruction,[14] and may play a role in preventing fibroblast activation. The AM stromal matrix also suppresses the expression of certain inflammatory cytokines that originate from the ocular surface epithelia, including interleukin-1α (IL-1α), IL-1β,[25] IL-2, IL-8, interferon-γ, tumor necrosis factor-α, b fibroblast growth factor, and platelet-derived growth factor (Bültmann S, et al. Invest Ophthalmol Vis Sci 1999;40 [Suppl]:S578), (Heiligenhaus A, et al. Invest Ophthalmol Vis Sci 2000;41[Suppl]:S56), (Tsay RJF, et al. Invest Ophthalmol Vis Sci 2000;41[Suppl]:S454). The suppression of inflammation is a key element in the prevention of further fibrovascular proliferation and scar formation in the conjunctiva. Furthermore, AM supports the normal phenotype of a nongoblet conjunctival epithelium in culture,[26,27] and AMT maintained a normal conjunctival epithelium with goblet cell differentiation in vivo.[26] In this regard, it is superior to buccal or nasal mucous membrane grafts, whose epithelia are different from that of the conjunctiva.

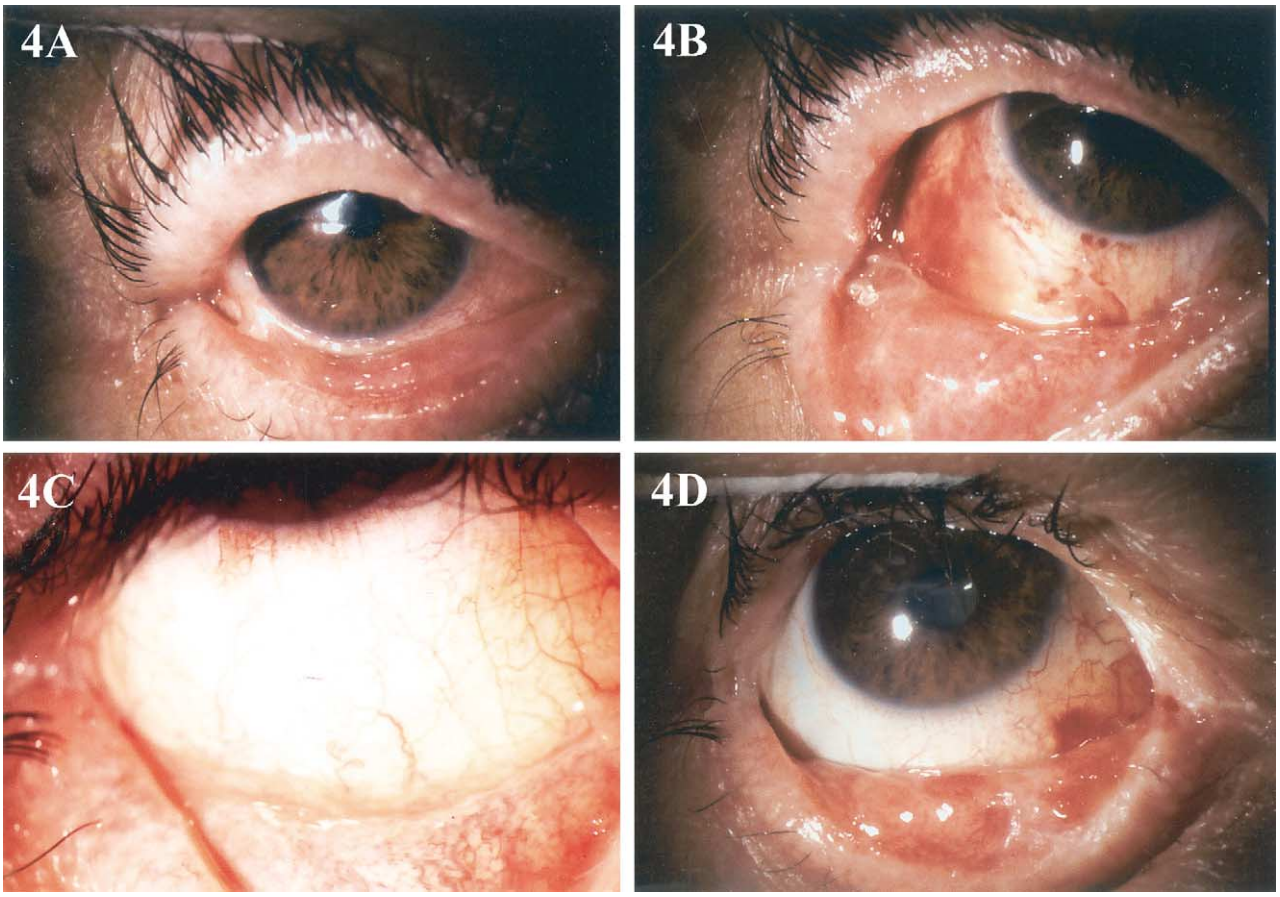

Figure 4. A, A 46-year-old woman with Stevens-Johnson syndrome was seen with foreshortening of the inferior fornix and a temporal symblepharon in the right eye. She also had a superotemporal symblepharon of the left eye. **B,** After a successful fornix reconstruction in her right eye, the amniotic membrane was epithelialized at 2 weeks. **C,** A quiet fornix and a freely mobile globe were observed at 2 months. **D,** Three years after surgery, the fornix is deep and quiet.

In contrast, we noted that the cases with recurrence or only a partial success had an underlying disease that is known to be associated with relentless inflammation such as OCP, SJS, toxic epidermal necrolysis, or a recurrent pterygium. We believe that continuous exposure of the conjunctival fibroblasts to a host of inflammatory cytokines[28–31] will create an ongoing cicatricial process that eventually will overcome the beneficial effect of AM, and hence limit the success of AMT in fornix reconstruction. For those with ongoing inflammation such as OCP or in some cases of SJS, systemic immunosuppression remains to be the mainstay of therapy in preparation of such eyes for reconstruction.[32,33] In the case of pterygia, we recently reported that inflammatory cytokines activate the pterygium body fibroblasts to overexpress metalloproteinases types I and III[31] (i.e., to a phenotype resembling that of the head fibroblasts).[34] Therefore, such measures as intraoperative and postoperative long-acting corticosteroids to suppress the ongoing inflammation are effective in reducing the recurrence rate for both primary and recurrent pterygia after AMT.[18] It should be noted that extensive removal of the fibrovascular tissue is also crucial to promote the success of AMT in pterygia.[18] Nevertheless, in this study the host scar tissue was not removed but rather recessed to the fornix after symblepharon lysis. Thus, we wonder whether the remaining scar tissue may be responsible for the failure in our patients. Another adjunctive measure may involve the use of mitomycin-C to suppress the ongoing cicatricial process mediated by inflammation as recently suggested for OCP.[4] New therapies are needed to control inflammation mediated by immune dysregulation while yielding minimal or no side effects.

Even if the inflammation of the cicatricial process can be fully suppressed and controlled, there will be advanced cases in which the success of AMT is limited. This is because AM used as a substrate still relies on the migration, growth, and differentiation of the epithelial cells from the adjacent host conjunctiva. Therefore, the efficacy of AMT is curtailed whenever the host conjunctiva is diffusely keratinized or the population of conjunctival epithelial stem cells that are enriched in the fornix[35] is severely deficient in such cicatricial diseases as OCP, SJS, and toxic epidermal necrolysis. Future exploration is thus needed to determine whether it is also possible to expand conjunctival epithelial stem cells by AM in vivo[11] and ex vivo[36,37] in a manner similar to that practiced in various corneal diseases with total limbal stem cell deficiency. Meanwhile, because the location of conjunctival epithelial stem cells is uncertain,

AMT may be augmented by the addition of free conjunctival autografts sutured on top of the AM grafts. This method is already used by our group in recurrent pterygium surgery and may be implemented in symblepharon correction as well.

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