Aetna considers preserved human amniotic membrane transplantation or limbal stem cell transplantation for ocular surface reconstruction medically necessary in members with limbal deficiency (hypofunction or total loss of stem cells) refractory to conventional treatment when the member has any of the following conditions:

- Total loss of stem cells (one eye involvement only)
  - Chemical/thermal injuries of the ocular surface
  - Contact lens-induced keratopathy or toxic effects from lens-cleaning solutions
  - Corneal limbal dermoid
  - Multiple surgeries or cryotherapies to the limbal region
  - Stevens-Johnson syndrome
Hypofunction of stem cells (one or both eyes can be involved)

- Aniridia (hereditary)
- Bullous keratopathy
- Chronic limbitis
- Keratitis associated with multiple endocrine deficiency (hereditary)
- Neurotrophic keratopathy (neuronal or ischemic)
- Peripheral corneal ulcerative keratitis (including Mooren's ulcer)
- Pterygium (primary and recurrent) and pseudopterygium

Aetna considers amniotic membrane transplantation for the treatment of conjunctivochalasis medically necessary when conservative therapies (e.g., artificial tear drops, and antibiotic/steroid drops) have failed.

**Note:** Allogeneic amniotic membrane-derived grafts include AmbioDisk, AmnioGraft, Artacent Ocular, and Prokera.

Aetna considers amniotic membrane transplantation and limbal stem cell transplantation experimental and investigational for the following indications (not an all-inclusive list) because its effectiveness for indications other than the ones listed above has not been established.

- Bacterial keratitis
- Gelatinous drop-like corneal dystrophy (also known as subepithelial amyloidosis of the cornea)
- Restrictive strabismus
- Retinal detachment
- Use in trabeculectomy for primary open-angle glaucoma

Aetna considers combined HLA-matched limbal stem cells allograft with amniotic membrane transplantation experimental and investigational as a prophylactic approach to prevent
corneal graft rejection following penetrating keratoplasty because the effectiveness of this approach has not been established.

Aetna considers sural nerve grafting for the treatment of neurotrophic keratitis experimental and investigational because the effectiveness of this approach has not been established.

Aetna considers allogeneic corneal epithelial stem cell transplantation for the treatment of limbal stem cell deficiency and other indications experimental and investigational because the effectiveness of this approach has not been established.

Aetna considers combined amniotic membrane transplantation and umbilical amnion for the treatment of infectious scleritis experimental and investigational because the effectiveness of this approach has not been established.

Aetna considers combined heparinized-amniotic membrane with growth factors for the treatment of corneal alkali burns experimental and investigational because the effectiveness of this approach has not been established.

Aetna considers the use of human amniotic membrane plug for the treatment of macular hole and macular hole retinal detachment experimental and investigational because the effectiveness of this approach has not been established.

**Background**

The normal ocular surface is covered by corneal and conjunctival epithelium. The corneal epithelium is well-known for its rapid self-renewal process, with ultimate tissue regeneration relying on the existence of stem cells located in

https://aetnet.aetna.com/mpa/cpb/200_299/0293.html
the limbal epithelium (the junction zone between the corneal and conjunctival epithelia). Total loss or hypofunction of the stem cells can occur as a result of certain conditions that cause damage or alteration of the corneal surface (termed limbal deficiency). Normal healing of corneal epithelial defects is prevented and a unique pathological state ensues manifested by poor epithelialization (persistent defects or recurrent erosions), chronic stromal inflammation (keratitis mixed with scarring), corneal vascularization, and conjunctival epithelial ingrowth. Since some of these features can be found in other corneal diseases, the sine qua non for making the diagnosis of limbal deficiency is the existence of conjunctival epithelial ingrowth onto the corneal surface. Clinically, this pathologic state can be confirmed by detecting conjunctival goblet cells on the corneal surface through the use of impression cytology.

Persistent corneal epithelial defects refractory to conventional treatment remain a therapeutic challenge that often requires surgical intervention. For those with hypofunction of limbal stem cells, treatment is directed at altering the microenvironment to maintain and activate the remaining stem cell population. For those conditions leading to a total loss of stem cells in 1 eye, limbal autograft transplantation is performed by taking a graft from the healthy fellow eye to replace the lost stem cell population. Obviously, this procedure is not applicable with patients having bilateral diffuse limbal involvement.

The transplantation of human amniotic membrane has been added to the therapeutic armamentarium. Amniotic membrane obtained from cesarean deliveries is prepared and cryopreserved under sterile conditions and can be sutured onto the ocular surface. Amniotic membrane-covered surfaces have been shown to induce rapid re-epithelialization (in 2 to 4 weeks) to a smooth and wettable surface and reduce inflammation, vascularization, and scarring, thus allowing successful surface reconstruction.
For partial limbal deficiency with superficial involvement, amniotic membrane transplantation (AMT) alone has been shown to be sufficient and superior to autograft limbal transplantation (ALT) because there is no need to administer cyclosporine. For total limbal deficiency, additional ALT is needed, and AMT has been shown to enhance successful engraftment of ALT by preparing the perilimbal stroma and reducing inflammation and vascularization.

Espana et al (2003) evaluated the long-term outcomes of epithelial debridement and AMT for pain and discomfort relief in patients with symptomatic bullous keratopathy and poor visual potential. This retrospective study included 18 eyes (18 patients) with bullous keratopathy presenting with intractable pain or discomfort and poor visual potential. After epithelial debridement, all eyes had AMT with the basement membrane side up. During a mean follow-up of 25.1 months +/- 9.6 (SD) (range of 12 to 45 months), pain relief, epithelial healing, and visual changes were analyzed. Pain relief was obtained in 88% of patients; 66% of eyes had complete resolution of ocular discomfort starting soon after the first post-operative day. One eye had evisceration for persistent pain 10 months post-operatively. Corneal epithelial healing was complete in all except 1 eye. Remaining complaints included foreign-body sensation (5%), tearing (11%), and photophobia (5%). The authors concluded that AMT was a safe, effective, and long-lasting treatment modality for intractable pain associated with chronic bullous keratopathy in eyes with poor visual potential. It can be an alternative to conjunctival flaps for the long-term management of patients with bullous keratopathy in whom corneal transplantation is not indicated.

Chansanti and Horatanaruang (2005) assessed the outcomes of AMT for symptomatic relief in patients with bullous keratopathy. This retrospective study included 17 eyes (17 patients) with bullous keratopathy presenting with intractable pain or discomfort. Symptomatic relief epithelial healing, and visual changes were analyzed. During the follow-up period of
14.1 +/- 11.9 months (range of 1 to 36 months) after AMT, 14 eyes of 17 eyes (82.4 %) with intolerable pain pre-operatively had pain relief post-operatively. Corneal epithelial healing was complete in all except 2 eyes; 1 of which had evisceration because of severe corneal ulcer, and the other underwent penetrating keratoplasty soon after AMT. The authors concluded that AMT is a safe and effective treatment modality for pain relief associated with chronic bullous keratopathy. It can be an alternative to conjunctival flap, with better cosmetic appearance for the management of patients with bullous keratopathy.

Srinivas et al (2007) examined the effectiveness of AMT in relieving pain and discomfort in patients with painful bullous keratopathy and its role in improving vision in eyes with visual potential. A total of 7 eyes of 7 consecutive patients with painful corneal conditions were included in a retrospective interventional non-comparative case-series study. Pain relief, epithelial healing, and visual changes were evaluated. Pain relief and freedom from discomfort were considered for the success of the surgery. The mean follow-up was 26.57 weeks (range of 11 to 53 weeks). Pain relief was achieved in all 7 (100 %) eyes. Associated symptoms including foreign body sensation, photophobia, and tearing subsided significantly in all patients starting soon after the first post-operative day. Vision improved in 5 (71.42 %) patients. The authors concluded that AMT is an effective alternative for the management of patients with painful bullous keratopathy.

In a prospective, non-comparative interventional case-series study, Georgiadis et al (2008) reported the findings of cryo-preserved human AMT for the management of symptomatic bullous keratopathy. Consecutive cases with symptomatic bullous keratopathy for more than 12 months not amenable to conservative treatment were managed with AMT. Patients were recruited over a 5-year period in 1 referral center. Only 1 eye of each patient (the worse affected eye in bilateral cases) was operated. A 360-degree conjunctival peritomy was
followed by removal of the diseased corneal epithelium. Amniotic membrane was transplanted over the cornea as a patch and sutured to the free conjunctival edges. Primary outcome measures were ocular pain and epithelial defects; secondary measures were visual acuity (VA) and ocular surface inflammation. Four out of 85 recruited cases did not complete the minimum observation of 12 months and were excluded from the study. The mean follow-up period for the remaining 81 cases was 21 +/- 4.2 months (range of 14 to 34 months). Seventy-one (87.6 %) eyes became asymptomatic with healed epithelium, 7 required repeated AMT and 3 underwent penetrating keratoplasty. Visual acuity improved in 64 (79 %) patients and remained unchanged in 14. No complications were recorded. The authors concluded that AMT is a safe and effective treatment for symptomatic bullous keratopathy when penetrating keratoplasty is not available. It has been shown to alleviate pain, promote corneal epithelialization and reduce conjunctival inflammation whereas in some cases it may also improve VA.

Chawla et al (2010) compared the safety and effectiveness of photo-therapeutic keratectomy (PTK) and AMT for symptomatic relief in painful bullous keratopathy. A total of 25 eyes (25 patients) with symptomatic bullous keratopathy and poor visual potential were randomized into 2 groups. In the PTK group (n = 13) after manual epithelial debridement, 100-microm excimer laser ablation was performed. In the AMT group (n = 12), the corneal epithelium was scraped and cryopreserved amniotic membrane with basement membrane side up was secured with 10-0 monofilament nylon sutures. All patients were followed-up for at least 6 months. Outcome parameters included symptomatic relief, time taken for surface re-epithelialization, change in corneal thickness, and complications. At 6-month follow-up, a significant decrease was seen in the symptom scores from the baseline level in both the PTK and AMT groups (p = 0.011 and 0.017, respectively) with no difference between the groups (p = 0.593). Complete epithelialization was noted 2 weeks post-
operatively in 13 of 13 eyes in the PTK group as compared with 8 of 12 eyes in the AMT group (p = 0.023). However, this difference was not significant at the end of 3 weeks (p = 0.288). One eye in the AMT group developed staphylococcus epidermidis keratitis. The authors concluded that both PTK and AMT are comparable in providing symptomatic relief in patients with bullous keratopathy and poor visual potential.

In a retrospective, interventional case series study, Strube et al (2011) reported the use of AMT in patients with restrictive strabismus. Chart review of 7 consecutive patients (8 eyes) who developed restrictive strabismus after peri-ocular surgery and were treated with surgical removal of restrictive adhesions and placement of an amniotic membrane transplant. Main outcome measures were intra-operative findings to explain the mechanism of restrictive strabismus, and clinical post-operative results, including ocular alignment, ductions and versions, symptom relief, and resolution of diplopia. Restrictive strabismus occurred after surgery for pterygium, retinal detachment, orbital floor fracture, dermoid cyst, and dermatochalasis. Restrictive strabismus was due to a combination of conjunctival contracture, fat adherence, or rectus muscle contracture. All patients developed post-operative scarring, with failed additional standard surgery to remove the adhesions, including 1 patient treated with mitomycin C for recurrent scarring after pterygium. Re-operation using AMT was associated with improvement of ocular motility in 6 of the 7 patients; 1 patient had recurrence of scarring with persistent diplopia. The remaining 6 of 7 patients had no significant recurrence of scarring, and motility remained stable during the follow-up period of 5 to 13 months. The authors concluded that AMT may be an useful tool in the treatment of restrictive strabismus. Prevention of conjunctival scarring and fat adherence during primary surgery remains the best option. Findings of this small study need to be validated by well-designed studies.
In a prospective, randomized study, Stavrakas et al (2012) examined the effectiveness of AMT on improving the outcomes of trabeculectomy in primary open-angle glaucoma (POAG). A total of 59 eyes affected by POAG were enrolled in this study: 32 eyes underwent amnion-shielded trabeculectomy (study group) and 27 eyes underwent trabeculectomy without any anti-metabolites (control group). Success was defined as intra-ocular pressure (IOP) less than 21 mm Hg without any medications at 24 months follow-up. The 2 groups were compared in terms of IOP, bleb morphology, bleb survival and risk of failure, glaucoma medications, and complications. There was no statistically significant difference in terms of post-operative IOP between the 2 groups and at 24 months median IOP was 15.5 mm Hg for the AMT group and 16.0 mmHg for the control group. Post-operative reduction of IOP was 8 mm Hg for the AMT group versus 6 mm Hg for the non-AMT group (p = 0.276). Two patients from the study group developed IOP greater than 21 mm Hg in contrast to 7 patients from the classic trabeculectomy group. The study group had 61.0 % less risk of developing IOP greater than 21 mm Hg (p = 0.203). No major complications in the AMT group were observed. Amniotic membrane transplantation blebs were diffuse with mild vascularization. The authors concluded that in patients with POAG, AMT showed favorable effects on bleb survival, however data failed to provide firm evidence that AMT could be used as a routine procedure in trabeculectomy.

The outer surface of the eye is covered by 2 distinct cell layers: (i) the corneal epithelial layer that overlies the cornea, and (ii) the conjunctival epithelial layer that overlies the sclera. These cell types are separated by a transitional zone known as the limbus. The corneal epithelial cells are renewed every 3 to 10 days by a population of stem cells located in the limbus. Limbal stem cell transplantation (LSCT) has been employed for corneal generation (Health Quality Ontario, 2008).
Ram et al (2010) examined the long-term clinical results of cell therapy in patients with burn-related corneal destruction associated with limbal stem-cell deficiency. These investigators used autologous limbal stem cells cultivated on fibrin to treat 112 patients with corneal damage, most of whom had burn-dependent limbal stem-cell deficiency. Clinical results were assessed by means of Kaplan-Meier, Kruskal-Wallis, and uni-variate and multi-variate logistic-regression analyses. They also assessed the clinical outcome according to the percentage of holoclone-forming stem cells, detected as cells that stain intensely (p63-bright cells) in the cultures. Permanent restoration of a transparent, renewing corneal epithelium was attained in 76.6 % of eyes. The failures occurred within the first year. Restored eyes remained stable over time, with up to 10 years of follow-up (mean of 2.91 +/- 1.99; median of 1.93). In post-hoc analyses, success -- that is, the generation of normal epithelium on donor stroma -- was associated with the percentage of p63-bright holoclone-forming stem cells in culture. Cultures in which p63-bright cells constituted more than 3 % of the total number of clonogenic cells were associated with successful transplantation in 78 % of patients. In contrast, cultures in which such cells made up 3 % or less of the total number of cells were associated with successful transplantation in only 11 % of patients. Graft failure was also associated with the type of initial ocular damage and post-operative complications. The authors concluded that cultures of limbal stem cells represent a source of cells for transplantation in the treatment of destruction of the human cornea due to burns.

In a retrospective, consecutive cohort study, Miri et al (2010) evaluated the long-term results of LSCT in patients with ocular surface (OS) disease. Case records of 27 eyes of 26 patients (19 males and 7 females) who presented with unilateral or bilateral total limbal stem cell deficiency and treated at the Department of Ophthalmology were examined. All eyes that were treated with LSCT and that had at least 1-year follow-up were included. There were 12 auto-limbal and 15 allo-limbal
transplants. Of the latter, 9 were from living related donors (LRDs) and 6 were from cadaver donors (CDs). A total of 9 eyes underwent LSCT and penetrating keratoplasty (PKP), and 11 eyes underwent LSCT and AMT. Cataract extraction with implant was carried out in 4 eyes. Some eyes had more than 1 associated procedure; 9 eyes had LSCT only. Patients with allo-limbal transplants also received systemic immunosuppression. Surgical success was measured by the duration for which a healthy corneal epithelium was maintained after LSCT. Visual success was measured by improvement VA in the operated eye during the follow-up period. The follow-up period of all eyes was up to 119 months (mean of 38 +/- 35.9 months, median of 24 months). Survival of LSCT, as determined by the maintenance of healthy corneal epithelium until last follow-up, was seen in 22 eyes (82 %). The surface failed within 3 months in 4 eyes (1 with LRD and 3 with CD) and after 43 months in the 5th patient (with CD). Subsequently, 6 eyes required PKP to achieve their maximum visual potential. The VA (measured in decimal fraction) improved over a period of 1 year from a mean of 0.121 (SD of 0.184) pre-operatively to a mean of 0.313 (SD 0.348) post-operatively. The authors concluded that limbal stem cell transplantation, in isolation or in combination with other procedures, is effective in improving corneal clarity and vision. Autografts have the best long-term outcome followed by LRD allografts. Cadaver donor allografts have a comparatively poor outcome. This may partly reflect the difference in case mix between unilateral and bilateral OS conditions.

The Work Loss Data Institute’s 2010 clinical practice guideline on “Eye” listed amniotic membrane transplantation as well as kerato-limbal allograft/LSCT as procedures that were considered and recommended for the management of individuals with occupational eye injuries.

In a retrospective study, Sangwan et al (2011) evaluated the effectiveness of xeno-free autologous cell-based treatment of limbal stem cell deficiency. This study included 200 patients,
above 8 years of age, with clinically diagnosed unilateral total limbal stem cell deficiency due to OS burns treated between 2001 and 2010. A small limbal biopsy was obtained from the unaffected eye. The limbal epithelial cells were expanded ex-vivo on human amniotic membrane for 10 to 14 days using a xeno-free explant culture system. The resulting cultured epithelial monolayer and amniotic membrane substrate were transplanted on to the patient’s affected eye. Post-operative corneal surface stability, visual improvement and complications were objectively analyzed. A completely epithelialized, avascular and clinically stable corneal surface was seen in 142 of 200 (71 %) eyes at a mean follow-up of 3 +/- 1.6 (range of 1 to 7.6) years. A 2-line improvement in VA, without further surgical intervention, was seen in 60.5 % of eyes. All donor eyes remained healthy. The authors concluded that autologous cultivated limbal epithelial transplantation using a xeno-free explant culture technique was effective in long-term restoration of corneal epithelial stability and improvement of vision in eyes with OS burns.

In a retrospective, non-comparative, case-series study, Huang et al (2011) evaluated outcomes of allo-limbal transplantation from living-related donors to treat partial limbal deficiency secondary to ocular chemical burns. This study included 17 patients (17 eyes) with partial limbal deficiency (less than or equal to 50 %) secondary to ocular alkali burns (11 eyes) or acid burns (6 eyes). Recipient eyes were treated by removing the conjunctivalized pannus. Superior limbal grafts (mean length of 3 to 5 clock hours) from HLA antigen-matched living-related donors were transplanted into deficient areas of recipient eyes. No recipients received systemic cyclosporine A therapy. Main outcome measures included corneal re-epithelialization, reduction in vascularity, improved corneal clarity, and best-corrected visual acuity (BCVA). All eyes achieved epithelialization a mean (SD) of 10.1 (1.9) days after surgery. Corneal re-epithelialization, reduction in vascularity, and improved corneal opacity were seen in all eyes. No eyes demonstrated recurrent epithelial defects or fibro-vascular
tissue, but gradual recurrence of peripheral corneal vascularization was observed in 7 eyes during the follow-up period. Allograft rejection developed in 3 eyes (17.6 %), all of which were successfully treated; BCVA improved in all eyes, and 10 eyes (58.8 %) had achieved BCVA of 0.5 or better (greater than or equal to 20/10 Snellen) at the last follow-up visit. The authors concluded that transplantation of limbal tissue from live-related donors successfully reconstructed the ocular surface. Long-term graft survival in patients with partial limbal deficiency secondary to ocular chemical burns can be accomplished without the use of systemic immunosuppression.

In a prospective, non-comparative, interventional case-series study, Marchini et al (2012) investigated the long-term effectiveness of auto-limbal transplantation in patients with limbal stem cell deficiency. A total of 16 eyes from 16 patients with severe, unilateral limbal stem cell deficiency caused by chemical burns were included in this study. Autologous ex-vivo cultured limbal stem cells were grafted onto the recipient eye after superficial keratectomy. Main outcome measures included clinical parameters of limbal stem cell deficiency (stability/transparency of the corneal epithelium, superficial corneal vascularization and pain/photophobia), VA, cytokeratin expression on impression cytology specimens and histology on excised corneal buttons. At 12 months post-surgery, evaluation of the 16 patients showed that 10 (62.6 %) experienced complete restoration of a stable and clear epithelium and 3 (18.7 %) had partially successful outcomes (re-appearance of conjunctiva in some sectors of the cornea and instable corneal surface). Graft failure (no change in corneal surface conditions) was seen in 3 (18.7 %) patients. Penetrating keratoplasty was performed in 7 patients, with VA improving up to 0.8 (best result). For 2 patients, regeneration of the corneal epithelium was confirmed by molecular marker (p63, cytokeratin 3, 12 and 19, mucin 1) analysis. Follow-up times ranged from 12 to 50 months. The authors concluded that grafts of autologous limbal stem cells cultured onto fibrin
glue discs can successfully regenerate the corneal epithelium in patients with limbal stem cell deficiency, allowing surgeons to perform successful cornea transplantation and restore vision.

In a retrospective case-series study, Basu et al (2012) reported the clinical outcomes of repeat auto-limbal epithelial transplantation in patients with recurrence of limbal stem cell deficiency after a failed primary procedure. The study included 50 patients, above 8 years of age, with clinically diagnosed unilateral limbal stem cell deficiency following ocular surface burns. Following failure of primary surgery all patients underwent a repeat limbal biopsy from the unaffected eye. The limbal cells were expanded ex-vivo on a human amniotic membrane substrate for 10 to 14 days using a completely xeno-free explant culture technique. The resulting cultured epithelial monolayer and amniotic membrane were transplanted onto the patient's affected eye. All patients underwent a comprehensive ophthalmic examination of both eyes at every follow-up visit. Post-operative corneal surface stability, change in VA, and complications were objectively analyzed. At a mean follow-up of 2.3 +/- 1.4 (median of 1.96, range of 1 to 7.5) years, 33 of the 50 recipient eyes (66 %) maintained a completely epithelialized, avascular, and clinically stable corneal surface. A 2-line improvement in VA was seen in 38 of the 50 recipient eyes (76 %). None of the donor eyes developed any clinical features of OS disease, conjunctival over-growth of the donor site, or decrease in vision throughout the follow-up period. The authors conclude that repeat autologous cultivated limbal epithelial transplantation successfully restores corneal epithelial stability and improves vision in eyes with recurrence of limbal stem cell deficiency, following failed primary surgery for ocular burns, without adversely affecting donor eyes.

Gelatinous drop-like corneal dystrophy (GDLD), also known as subepithelial amyloidosis of the cornea, is a rare autosomal recessive disorder. Gelatinous drop-like corneal dystrophy is
rare in many countries, but relatively prevalent in Japan. The
typical finding of GDLD is grayish, mulberry-like, protruding
subepithelial depositions with a prominent hyper-fluorescence
of the cornea. Histologically, GDLD corneas are characterized
by subepithelial amyloid depositions that were identified as
lactoferrin by amino acid sequencing analysis. In 1998, the
TACSTD2 gene was identified as a causative gene for this
disease through a linkage analysis and a candidate gene
approach. To-date, 14 reports have demonstrated 21
mutations comprised of 9 missense, 6 nonsense, and 6 frame-
shift mutations from 9 ethnic back grounds. Currently, it is
hypothesized that the loss of TACSTD2 gene function causes
decreased epithelial barrier function, thereby facilitating tear
fluid permeation into corneal tissue, the permeated lactoferrin
then transforming into amyloid depositions via an unknown
mechanism. For the visual rehabilitation of patients with
GDLD, ophthalmologists currently employ various types of
keratoplasties; however, almost all patients will experience a
recurrence of the disease within a few years after such
interventions. Wearing of a soft contact lens is sometimes
considered as an alternative treatment for GDLD (Kawasaki
and Kinoshita, 2011).

In a non-comparative interventional case-series study,
Movahedan et al (2013) reported the outcomes of allograft
LSCT for recurrent GDLD. A total of 4 eyes of 3 consecutive
patients with recurrent GDLD underwent allograft LSCT; 2
eyes underwent concomitant penetrating keratoplasty while
the other 2 underwent simultaneous superficial keratectomy.
Main outcome measures were best spectacle corrected visual
acuity, IOP and corneal clarity. Patient age ranged from 28 to
63 years. Mean follow-up after surgery was 23 ± 10 (median
of 22; range of 12 to 36) months. Mean VA improved from
2.70 ± 0.61 logMAR pre-operatively to 1.05 ± 0.06 logMAR at
final post-operative visit (p = 0.066). Intra-ocular pressure was
normal in all eyes at baseline and remained within normal
limits at all post-operative visits. All corneas remained smooth
and clear during the follow-up period with no episode of
rejection or recurrence. All patients maintained ambulatory vision until final follow-up. The authors concluded that the findings of the present study provided further evidence that LSCT may be an effective therapeutic alternative in patients with GDLD. These findings need to be validated by well-designed studies.

Mooren's ulcer is a chronic ulcerative inflammation of the cornea. The exact pathogenesis remains unclear; but it can or will lead to loss of vision if untreated. Severe pain is common in patients with Mooren's ulcer and the eye(s) may be intensely reddened, inflamed and photophobic, with tearing. There are a number of therapies employed for the treatment of this condition (e.g., anti-inflammatory drugs (steroidal and non-steroidal), cytotoxic drugs (topical and systemic), conjunctivectomy as well as cornea debridement (superficial keratectomy)). However, there is no evidence to show which is the most effective amongst these treatment modalities.

Lavaju et al (2013) reported a case of Mooren's ulcer treated with AMT supplemented with autologous serum eye drops. A 22-year old male presented with history of pain, redness, watering and diminution of vision of the right eye for 1 year. Examination of his eyes revealed the BCVA of 6/60 and 6/6 in his right and left eyes, respectively. Slit-lamp examination of the right eye showed a peripheral ulcer extending from 2'0 to 11'0 clock positions with peripheral thinning and the features suggestive of Mooren's ulcer. The condition did not improve with topical steroids and cyclosporine A eye drops. Therefore, 360-degree conjunctival peritomy with cauterization of the base was performed. Since there was no obvious improvement, AMT was done with supplementation of autologous serum eye drops 20 % 4 times a day. The patient showed symptomatic improvement in 1 week. There was cessation of the progression of the ulcer and decreased vascularization. One month later, a small corneal perforation was noted and was managed well with cyanoacrylate glue and bandage contact lens application. At 9 months of follow-up,
the patient was symptomatically better, the ulcer had healed, the vascularization had decreased and the anterior chamber was well formed. The authors concluded that AMT appeared to be a promising treatment of Mooren's ulcer refractory to immunosuppressive therapy. Addition of autologous serum eye drops seems to be an effective supplementary therapy.

Schallenberg et al (2013) reported on a retrospective case-series of patients treated with systemic immunosuppressive therapy and additional AMT. Medical records from 7 patients (11 eyes), 4 males and 3 females, with severe progressive Mooren's ulcer were analyzed retrospectively. The mean follow-up was 88.4 ± 80.8 months (range of 12 to 232 month). A HLA-typing was performed in all patients. A systemic immunosuppressive therapy was administered in all patients. The amniotic membrane was transplanted after the base of the ulcer was resected. Multiple AMTs were necessary in 6 patients. The visual outcome of all patients was poor. No patient achieved a VA better than 20/630 Snellen chart; 5 patients were positive for HLA-DQ2 and 4 patients were positive for HLA-DR17(3). The authors concluded that the aggressive and highly inflammatory form of Mooren's ulcer is difficult to treat and the progression of the disease is hard to influence positively even under systemic immunosuppressive therapy. Therefore, the main intention of therapy is to achieve a stable epithelialized corneal surface without the risk of perforation. They stated that AMT is not able to cure severe forms of Mooren's ulcer. However it supports the immunosuppressive therapy in acute situations as in critical corneal thinning.

In a Cochrane review, Alhassan et al (2014) evaluated the effectiveness of the various interventions (medical and surgical) for the treatment of Mooren's ulcer. These investigators searched CENTRAL (which contains the Cochrane Eyes and Vision Group Trials Register) (The Cochrane Library 2013, Issue 5), Ovid MEDLINE, Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid
MEDLINE Daily, Ovid OLDMEDLINE (January 1946 to June 2013), EMBASE (January 1980 to June 2013), Latin American and Caribbean Literature on Health Sciences (LILACS) (January 1982 to June 2013), the metaRegister of Controlled Trials (mRCT) (www.controlled-trials.com), ClinicalTrials.gov (www.clinicaltrials.gov) and the WHO International Clinical Trials Registry Platform (ICTRP) (www.who.int/ictrp/search/en). They did not use any date or language restrictions in the electronic searches for trials. They last searched the electronic databases on June 4, 2013. These researchers planned to include randomized controlled trials (RCTs) or discuss any prospective non-RCTs in the absence of any RCTs. The trials included would be of people of any age or gender diagnosed with Mooren's ulcer and all interventions (medical and surgical) would be considered. Two authors screened the search results independently; they found no studies that met their inclusion criteria. As these investigators found no studies that met their inclusion criteria, they highlighted important considerations for conducting RCTs in the future in this area. The authors concluded that they found no evidence in the form of RCTs to assess the treatment effect for the various interventions for Mooren's ulcer. They stated that high quality RCTs that compare medical or surgical interventions across different demographics are needed. Such studies should make use of various outcome measures, (i.e., healed versus not healed, percentage of area healed, speed of healing, etc.) as well as ensuring high quality randomization and data analysis.

Capozzi and colleagues (2014) examined if the use of combined HLA-matched limbal stem cells allograft (LAT) with AMT is a safe and effective prophylactic surgical procedure to prevent corneal graft after PKP. These investigators reported the case of a 17-year old patient with a history of congenital glaucoma, trabeculectomy and multiple corneal graft rejections, presenting total limbal cell deficiency. To reduce the possibility of graft rejection in the left eye after a new PKP, a 2-step procedure was performed. At first the patient
underwent a combined HLA-matched LAT and AMT and then, 10 months later, a new PKP. During 12 months of follow-up, the corneal graft remained stable and smooth, with no sign of graft rejection. The authors concluded that in this patient, the prophylactic use of LAT from HLA-matched donors and AMT before PKP, may result in a better prognosis of corneal graft survival. These preliminary findings need to be validated by well-designed studies.

In a systematic review, Shen and colleagues (2020) examined the safety and effectiveness of trabeculectomy along with AMT for the treatment of glaucoma. This review was carried out using RevMan 5.3. These investigators searched PubMed, Embase, and the Cochrane Library and included studies published until September 2019. The treatment group included patients with AMT and trabeculectomy (group A), and the control group had only trabeculectomy (group B); only RCTs were included. The outcomes were IOP, complete success rate, number of anti-glaucoma medications, and complications. A total of 5 studies, including 174 eyes (87 eyes in the AMT group and 87 eyes in the control group), were eligible in this review. The parameters had no significant difference in heterogeneity between the AMT and control groups pre-operatively. In the AMT group, the mean IOP was significantly lower at 3 and 12 months after operation (p < 0.0001 and p = 0.02, respectively), while the number of complete successes in the AMT group was significantly higher at 6 and 12 months (p = 0.02 and p = 0.003, respectively) compared with the control group. Complications, including a flat anterior chamber and hyphema, appeared to be decreased in the AMT group compared to the control group (p = 0.02 and p = 0.02, respectively). No differences were observed in the number of anti-glaucoma medications, hypotony, encapsulated bleb, or choroidal detachment. The authors concluded that the findings of this review suggested that AMT is a safe and effective treatment in combination with trabeculectomy in glaucoma for its stable IOP level, high success rate, and low incidence rate of complications. Moreover, these researchers
stated that although only prospective studies were included, some limitations should not be overlooked. First, not every article explained the randomized strategy explicitly and convincingly. Second, some factors, such as the size of glaucoma, treatment before operation, surgeon skills, and surgical methods, could have affected these findings. Third, for lack of an abundant number of eligible cases, some statistics were unable to be acquired, and a limitation exists regarding visual ability and other vision aspects.

Pelegrin et al (2008) reported the importance of early surgical treatment of corneal ulcers associated with vernal keratoconjunctivitis (VKC) which may potentially produce severe lesions and permanent visual sequelae. The authors presented the case of a child with corneal ulcer in plaque who did not respond to medical treatment and had a good response to surgical treatment. A superficial keratectomy with an amniotic membrane patch was performed. A rapid post-operative epithelialization with a final good visual acuity was achieved. The authors concluded that although amniotic membrane grafts following keratectomy have been described as a successful treatment in deep ulcers, in cases with slight stromal thinning, the amniotic membrane patch may be enough to achieve epithelialization. They stated that this procedure avoided the presence of the remains of membrane under the epithelium, which may affect post-operative corneal transparency.

Miranda-Rollon et al (2009) presented the case of a 46-year old man diagnosed initially with atypical adenoviral conjunctivitis and advanced marginal queratolysis with risk of perforation. The final diagnosis was gonococcal keratoconjunctivitis. The patient was successfully treated with amniotic membrane transplant, topic and systemic ceftriaxone (50 mg/ml and 1 gram/12 hours intravenous). The authors concluded that gonorrhea must be suspected in cases of torpid evolution conjunctivitis.
Gris et al (2010) compared the effectiveness of conjunctival resection versus conjunctival resection with amniotic membrane graft (AMG) in patients with superior limbic keratoconjunctivitis not responsive to medical therapies. In a retrospective and comparative study, 16 eyes of 9 patients with long-lasting superior limbic keratoconjunctivitis who were refractory to medical treatment were included. Conjunctival resection was performed in 8 cases, and conjunctival resection with AMG was performed in 8 cases. Subjective symptoms, biomicroscopic signs, and impression cytology were evaluated both pre- and post-operatively. The mean follow-up period was 46 months, ranging from 1.5 to 6 years. After surgery, all cases undergoing conjunctival resection and 7 of 8 cases undergoing conjunctival resection with AMG remained asymptomatic. One case undergoing conjunctival resection with AMG experienced recurrence, requiring re-operation 2 years later (conjunctival resection without AMG). In this patient, complete disappearance of symptoms and signs was achieved during a 4-year period of follow-up after the second surgery. No intra- or post-operative complications were observed in either group. Pre-operative impression cytology disclosed severe squamous metaplasia, and goblet cells were markedly decreased in all patients. Post-operative impression cytology 3 months after surgery did not show any significant improvement in squamous metaplasia in either of the groups. The authors concluded that conjunctival resection and conjunctival resection with AMG are effective and safe surgical procedures. Despite the potential benefits of the AMG, this procedure did not provide additional advantages in this study.

In a retrospective study, Guo et al (2013) evaluated the outcome of surgical resection and amniotic membrane transplantation (AMT) for treatment of refractory symptomatic giant papillae in vernal keratoconjunctivitis (VKC). A total of 13 eyes of 9 patients with refractory giant papillae associated with corneal shield ulcer and/or punctate epithelial erosions who underwent surgical resection of the papillae combined with AMT to cover the tarsal conjunctival defect were included...
in this analysis. During 14.2 ± 4.2 months of post-operative follow-up, smooth tarsal conjunctival surface was achieved in all cases, with no recurrence of the giant papillae in any eye. Corneal shield ulcers and punctate epithelial erosions healed within 2 weeks after surgery and did not recur during the follow-up. Best-corrected visual acuity improved from 0.26 ± 0.21 logarithm of the minimum angle of resolution pre-operatively to 0.02 ± 0.04 logarithm of the minimum angle of resolution post-operatively (p = 0.01). Three patients experienced recurrence of VKC symptoms, but without giant papillae, which could be well controlled by topical medications. The authors concluded that surgical resection combined with AMT is an effective procedure for treatment of refractory giant papillae in patients with VKC.

Yang et al (2013) evaluated the use of surgical treatment with amniotic membrane for long-term atopic keratoconjunctivitis. Damaged corneas were repaired with various techniques: AMT, amniotic membrane coverings, amniotic membrane fillings (AMFs), and amniotic membrane inlay fillings, the latter of which were combined with glycerol-preserved corneal transplants. This retrospective study was conducted on 37 eyes belonging to 37 patients with atopic keratoconjunctivitis. Thirty-two patients were classified into 4 groups according to surgical technique; 5 patients undergoing medical management served as controls. Surgical outcome was measured by recovery time and long-term visual improvement. In all surgical eyes, integrity of ocular tissues was effectively restored and symptoms were reduced at 24.4 ± 13 days post recovery. Mean best-corrected visual acuity improved from 0.6 ± 0.2 to 0.198 ± 0.16 logarithm of the minimum angle of resolution (p < 0.001). There were no intra-operative or post-operative complications, with the exception of 2 recurring cases, both controlled by medication. Recovery time of the control groups lasted 52 ± 16 days. In controls, mean best-corrected visual acuity improved from 0.74 ± 0.15 to 0.54 ± 0.29 logarithm of the minimum angle of resolution (p ≤ 0.05). The vision improvement has significant difference for
surgical treatment vs medical. (Mann-Whitney U-test, U = 119, p < 0.05, 1-tail test). Vision improvements remained stable during a mean follow-up period of 21.7 ± 3.8 months. The authors concluded that patients suffering from severe chronic atopic keratoconjunctivitis and its complications can benefit from suitable surgical treatments: transplants, covers, fillings, or corneal graft surgeries supplemented with AMFs.

Ijiri et al (2007) evaluated how sutureless amniotic membrane patches may affect visual functions in normal human eyes. A total of 10 sets of sutureless amniotic membrane patch manufactured as ProKera were inserted in 1 eye of 6 normal patients. Four sets (1 each) were inserted in 4 patients, while 6 sets (3 each) were inserted in 2 patients. Uncorrected distant and near visual acuities, color vision, amniotic membrane thickness measured by pachymetry, and total symptom scores were compared before and after insertion. Within 30 minutes after insertion, mean distant visual acuities decreased from -0.22 +/- 0.06 to 0.92 +/- 0.45 logarithmic minimum angle of resolution (logMAR). Among 10 sets of PROKERA inserted, the largest optotype (1.0 logMAR) of the near vision chart could not be recognized in 5, but color vision evaluated by Panel D-15 was still preserved in all. Total symptom scores increased to 47.8 +/- 9.1 points (maximum, 100 points). Among symptoms, total scores for foreign body sensation (17.8 +/- 3.6) and blurred vision (17.8 +/- 4.4) were high. Loss of distant visual acuity and increases of symptom scores were not correlated with amniotic membrane thickness, of which the mean was 67.6 +/- 25.2 mum. However, amniotic membrane that was less opaque tended to provide relatively good visual acuities. The authors concluded that because of the relative non-transparency of sutureless amniotic membrane patches in PROKERA, distant and near visual acuities decreased in normal human eyes. The foreign body sensation noted after insertion is primarily derived from the rigid supporting skirt.
Pachigolla et al (2009) reported the safety and effectiveness profile of sutureless and adhesiveless amniotic membrane device (ProKera, Bio-Tissue, Inc., Miami, FL) in the management of various ocular surface and orbital disorders. A total of 20 eyes of 20 patients underwent placement of 21 ProKera implants between March 2006 and July 2007 at the University of Texas Southwestern Medical Center were included in this study. Patient demographics, indications for placement, and duration of ProKera retention were recorded. Outcomes measured included corneal epithelial healing, visual acuity, patient tolerance, and adverse events. ProKera was most commonly used in patients with corneal neovascularization with or without limbal stem-cell deficiency (10 eyes). Other indications included recurrent pterygium or pseudopterygium (3 eyes), anophthalmic orbit contraction (2 eyes), persistent epithelial defects (2 eyes), severe thinning in a corneal ulcer (1 eye), benign hereditary intra-epithelial dyskeratosis (1 eye), and band keratopathy (1 eye). The mean duration of ProKera retention was 25.3 days (range of 0 to 125) visual acuity improved in 12 eyes (60%). Immediate adverse events included residual epithelial defects after removal (5 eyes) and spontaneous extrusion of the implant (4 eyes). Six patients (30%) reported eye pain or headache and 4 eyes (20%) had recurrence of the primary pathology. The authors concluded that sutureless and adhesiveless AMT is a safe and effective method to promote healing and reconstruction of the ocular surface and orbit with minimal side effects. Recurrence of the underlying primary pathology remains a concern. The advent of a newer, softer conformer ring may improve patient tolerability and limit discomfort. However, keratoconjunctivitis is not one of the conditions that were treated by ProKera in this study.

In a case report, Shay et al (2010) described the efficacy and limitation of ProKera for treating acute ocular manifestations of toxic epidermal necrolysis (TEN). ProKera was inserted in both eyes at day 10 after onset of ocular symptoms in a 5-year old boy suffering from acute TEN, manifesting conjunctival
inflammation, large conjunctival defects, pseudomembrane formation, and total corneal epithelial defects. At 9-month follow-up, insertion of ProKera resulted in complete re-epithelialization, clear corneas, and vision of 20/20 in both eyes. However, because ProKera only covered the cornea and peri-limbal conjunctiva, these 2 eyes still showed some conjunctival inflammation several months after discharge from the hospital. Eventually, 1 eye showed mild lid margin keratinization and cicatricial entropion, and both eyes showed trichiasis. The authors concluded that these data suggested that ProKera, when inserted during the acute stage of TEN, may be effective in healing corneal epithelial defects and preventing corneal sequelae. Because of the limited area covered, ProKera may not prevent cicatricial complications in the fornix, tarsus, and eyelid margin as effectively as sutured AMT. Again, this case study did not address the use of ProKera for keratoconjunctivitis.

Suri et al (2013) evaluated the indications and outcomes of ProKera in the management of ocular surface disorders. These investigators performed chart review of patients who had ProKera implantation for ocular surface disorders between June 2008 and May 2012 at 3 ophthalmology practices in Philadelphia, PA. The parameters evaluated included age, sex, indication for AMT, any other combined procedure, duration of retention of amniotic membrane, the effect of amniotic membrane on ocular surface healing, follow-up time, and complications. There were 35 eyes of 33 patients with a mean age of 68.2 ± 19.5 years (range of 17 to 99 years). There were 25 male patients, and median follow-up was 110 days (mean of 164.6 days; range of 30 to 960 days). The indication for insertion of ProKera was non-healing corneal ulcers of infective origin (group 1) in 9 eyes (25.7%), neurotrophic keratopathy (group 2) in 11 eyes (31.4 %), chemical injury (group 3) in 5 eyes (14.3%), and other indications (group 4) in 10 eyes (28.6 %). Complete or partial success was seen in a total of 44 %, 64 %, 80 %, and 70 % eyes in groups 1 to 4, respectively. Discomfort with the device
was seen in 6 (17.1 %) of 35 eyes, and recurrence of primary pathologic condition occurred in 5 (14.3 %) of 35 eyes. The authors conclude that ProKera treatment is easy to use and reasonably well-tolerated, with moderate success in corneal ulcers and encouraging results in acute moderate chemical injury. Recurrence of primary pathologic condition was seen particularly associated with neurotrophic keratitis and dry eye syndrome. It is unclear how many patients had keratoconjunctivitis.

**Conjunctivochalasis**

Meller et al (2000) examined if preserved human amniotic membrane can restore the large conjunctival defect created during surgical removal of conjunctivochalasis (CCh). Amniotic membrane transplantation (AMT) was performed at 2 facilities in 40 consecutive patients (47 eyes) with symptomatic CCh refractory to conventional treatments. The majority of patients were elderly (73.1 +/- 9.7 years) and women (75 %). Over a follow-up period of 6.9 +/- 4.3 months, 46 (97.8 %) eyes recovered smooth, quiet, and stable conjunctival surfaces. Epithelial defects healed in 16.5 +/- 7.3 days. Episodic epiphora was resolved in 24 of 30 (83.3 %) eyes and improved in 5 other eyes. Notable relief was also noted for such symptoms as fullness or heaviness (19/19, 100 %), sharp pain (6/6, 100 %), redness (14/17, 88.2 %), tiredness (17/20, 80.9 %), itching (11/13, 78.6 %), blurry or decreased vision (6/8, 75 %), burning (8/13, 61.5 %), foreign body sensation (8/13, 61.5 %), and crust formation (1/2, 50 %). Complications included focal inflammation of the host conjunctiva adjacent to the graft (6 eyes), scar formation (5 eyes), and suture-induced granuloma (1 eye). The authors concluded that AMT can be considered as an effective means for conjunctival surface reconstruction during removal of CCh.

Georgiadis and Terzidou (2001) presented their experience with the use of preserved human amniotic membrane on patients with epiphora caused by CCh. A total of 12 patients,
7 women and 5 men, aged 56 to 72 years (mean of 61 years) were referred with chronic epiphora. In all patients, no punctal ectropion was present, the lacrimal pathway was patent, and the dye disappearance test was abnormal. All patients had already undergone various therapies including multiple irrigations of the lacrimal system, antibiotic drops, steroid drops, and artificial tear drops. In all patients, CCh, which was not previously diagnosed, was evident on slit-lamp examination. After surgical removal of the excess conjunctiva, preserved human amniotic membrane was placed over and sutured with 10-0 nylon continuous suture to the free conjunctival edges. During the post-operative period, artificial tear drops and steroid/antibiotic drops were applied. Improvement of the epiphora was evident from the first post-operative day. After removal of the suture 10 to 15 days (mean of 12 days) after surgery, no patient complained of epiphora. The dye disappearance test was normal. During the follow-up period, which ranged from 6 to 11 months (mean of 8 months), no patient complained of epiphora and no CCh was detected in the area in which human amniotic membrane was transplanted. The authors concluded that in their experience, AMT greatly improved symptoms of epiphora caused by CCh.

Kheirkhah et al (2007) showed poor adhesion between the conjunctiva and the sclera in eyes with superior CCh and introduced a new surgical approach by reinforcing adhesion between the conjunctiva and the sclera for correcting this deficiency. After conjunctival peritomy and removal of the loose Tenon remnants, "Tenon reinforcement" for conjunctival adhesion to the underlying sclera was achieved by AMT with fibrin glue (group A, 9 eyes of 6 patients) or 10-0 nylon sutures (group B, 8 eyes of 6 patients) in 17 eyes of 12 patients with refractory superior CCh. The mean age of patients was 68.2 +/- 9.8 years (range of 54 to 80 years). Superior CCh was associated with a superior limbic keratoconjunctivitis (SLK)-like clinical feature before surgery and found to exhibit dissolved Tenon capsule during surgery in all patients. During a mean
follow-up of 3.7 +/- 1.9 months after surgery, all eyes achieved smooth conjunctival surface without any sign of CCh. Complete resolution of symptoms was seen in 9 eyes (52.9 %) and significant resolution in 8 eyes (47.1 %). There was no significant difference between groups A and B in improvement of symptoms and signs. No complications related to surgery were noted during follow-up. The authors proposed that loose and dissolved Tenon tissue was correlated with the development of superior CCh, which may result in an SLK-like appearance by blink-related micro-trauma. Moreover, they stated that reinforcement of conjunctival adhesion onto the sclera by AMT with either fibrin glue or sutures is effective in alleviating symptoms and signs in eyes with superior CCh.

Maskin (2008) evaluated the hypothesis that the therapeutic effect of AMT ocular surface reconstruction in the setting of symptomatic temporal CCh is through improved tear clearance. A total of 12 eyes with delayed tear clearance by the fluorescein clearance test in the setting of symptomatic temporal CCh were subjected to surface reconstruction by using AMT and evaluated for the effect on delayed tear clearance, symptoms, surface erosions, artificial tear use, VA, and tear strip wetness. Amniotic membrane transplantation of temporal symptomatic CCh did not improve tear clearance; however, it significantly improved symptoms (Fisher exact test, p = 0.001), surface erosions (Fisher exact test, p = 0.008), and log minimal angle resolution VA (Fisher exact test, p = 0.007) and reduced artificial tear use (Fisher exact test, p = 0.015). There was also an improvement in tear strip wetting, but this did not reach statistical significance. The authors concluded that relief of symptoms and improvement in clinical signs after AMT for symptomatic temporal CCh was not caused by improved tear clearance.

Furthermore, EyeWiki (last updated December 24, 2014) stated that “In addition to pterygium surgery, AMT has been used for other conjunctiva reconstruction techniques. Conjunctiva tumors have been removed and the remaining
defect was revised with amniotic membrane. Surgical use of AMT for the revision of scars and symblepharon have been reported. In cases of conjunctivochalasis that fail medical therapy, AMT has been used to reconstruct the ocular surface.

Also, the Cochrane Consulting Group (last updated April 14, 2014) noted that “In the surgical treatment of conjunctivochalasis, the removal of conjunctival folds results in a large elliptical defect in the conjunctiva, which is repaired with 1 or 2 layers of amniotic membrane covered with conjunctiva, and sutured in place. Sometimes tissue glue is used. Amniotic membrane provides a scaffold for cell regrowth into the defect and promotes patient recovery.”

**Bacterial Keratitis**

In a prospective RCT, Tabatabaei and colleagues (2017) examined if early AMT improves the outcomes among patients with bacterial keratitis. A total of 49 eyes from 49 patients with bacterial keratitis received routine antibiotic therapy followed by double-layer AMT during 2 to 5 days after start-up of the medications and the second group of 50 eyes from 50 patients only received routine anti-bacterial therapy. The main outcomes including VA, corneal healing time, scar size, hypopyon size and duration as well as the depth of corneal opacity and neovascularization were followed-up for a 6-month period. In addition, Langerhans cells density and tectonic procedures were documented during the healing period. The results indicated statistically significant better BCVA ($p < 0.001$), uncorrected VA ($p < 0.001$), as well as contact lens corrected VA ($p < 0.001$) at 6 months in the case group compared to control group. Corneal healing time, the depth of corneal opacity, hypopyon size and duration were not significantly different in the case group while the scar size ($p < 0.001$) was significantly smaller. In addition, significantly less corneal vascularization at 6 months ($p < 0.001$) and Langerhans cells density ($p < 0.001$) at 1 month were
observed in the case group. The authors concluded that early use of AMT in treatment of patients with bacterial keratitis was associated with better outcomes compared to antibiotic therapy alone. They stated that more comparative studies to investigate the probable side effects as well as the cost-benefit of this method are needed.

Current bacterial keratitis guidelines from the American Academy of Ophthalmology (AAO, 2013) have no recommendation for amniotic membrane transplantation as a treatment for bacterial keratitis per se. However, they do indicate that, if there is a persistent epithelial defect and the infection is under control, adjunctive therapies to rehabilitate the ocular surface should be instituted, such as amniotic membrane coverage, as well as lubrication, antibiotic ointment, bandage contact lens, and tarsorrhaphy.

Sural Nerve Grafting for Neurotrophic Keratitis

In a prospective, observational, case-series, single-center study, Weis and colleagues (2018) reported their center’s experience in treating neurotrophic keratitis (NK) through corneal neurotization using nerve transfers and sural nerve grafts in the adult population. A total of 6 consecutive patients (5 men and 1 woman) with severe NK were evaluated. All patients had complete corneal anesthesia in the neurotrophic eye; 3 patients had unstable epithelial disease with recurrent breakdowns despite maximal medical and standard surgical management; 3 presented with dense scarring of their cornea. These patients were surgically treated using nerve transfers and sural nerve grafts for neurotization of the neurotrophic eye. Subjects were evaluated for corneal sensation, epithelial breakdown, and VA. Mean participant age was 57 years (SD 19) with a mean denervation time before the procedure of 23 months (SD 20). Patients were followed-up for a minimum of 6 months following the procedure, with a mean follow up time 12 months (SD 4.2). All patients had improved corneal sensation within half a year following the procedure; 5 patients (83 %)
demonstrated improved VA. Of these patients, 3 (50%) had improved VA with no further surgical intervention; 1 patient underwent cataract extraction 13 months after neurotization and another underwent amniotic membrane grafting 17 months after neurotization. The authors concluded that their experience suggested that corneal neurotization using nerve transfers and sural nerve grafts for patients suffering from deteriorating neurotrophic keratitis was a safe procedure in adults. It successfully restored corneal sensation in all patients and improved VA in most patients. These preliminary results need to be validated with well-designed studies with larger sample size and longer follow-up.

**Allogeneic Corneal Epithelial Stem Cell Transplantation for Limbal Stem Cell Deficiency**

Campbell and colleagues (2019) stated that limbal stem cell deficiency (LSCD) is a disease resulting from the loss or dysfunction of epithelial stem cells, which seriously impairs sight. Autologous limbal stem cell transplantation is effective in unilateral or partial bilateral disease but not applicable in total bilateral disease. An allogeneic source of transplantable cells for use in total bilateral disease can be obtained from culture of donated cadaveric corneal tissue. In a controlled multi-center study, these researchers examined the feasibility, safety, and efficacy of allogeneic corneal epithelial stem cells in the treatment of bilateral LSCD. Patients were randomized to receive corneal epithelial stem cells cultured on amniotic membrane (AM): investigational medicinal product (IMP) or control AM only. Patients received systemic immunosuppression. Primary end-points were safety and VA, secondary end-point was change in composite ocular surface score (OSS). A total of 16 patients were treated and 13 patients completed all assessments. Safety was demonstrated and 9/13 patients had improved VA scores at the end of the trial, with no significant differences between IMP and control groups. Patients in the IMP-arm reported significant, sustained improvement in OSS, whereas those in
the control-arm did not. Serum cytokine levels were measured during and after the period of immune suppression and these investigators identified strongly elevated levels of CXCL8 in the serum of patients with aniridia, which persisted throughout the trial. The authors concluded that the this 1st RCT of allogeneic corneal epithelial stem cells in severe bilateral LSCD demonstrated the feasibility and safety of this approach; and this intervention warrants further study in larger sample sizes in a phase-III clinical trial. These researchers also stated that new studies would also benefit from concentrating on a single disease group to eliminate some of the variables in this study.

**Amniotic Membrane Transplantation and Limbal Stem Cell Transplantation for Corneal Limbal Dermoid**

Pirouzain (2013) reviewed the data in the published literature concerning the medical and surgical management of pediatric limbal dermoids. Current standard medical treatment for grade I pediatric limbal dermoids (ie, with superficial corneal involvement) is initially conservative. In stages II (ie, affecting the full thickness of the cornea with/without endothelial involvement) and III (ie, involvement of entire cornea and anterior chamber), a combination of excision, lamellar keratoplasty, and amniotic membrane and limbal stem cell transplantation are advocated. Combinations of these approaches seem to yield better and more stable long-term ocular surface cosmesis and fewer complications in comparison with traditional methods of excision and lamellar keratoplasty. The author stated that management of amblyopia (i.e. occlusion treatment, chemical penalization with/without spectacle wear, etc) must continue after surgical excision to yield optimal results when or if the surgery is done at a younger age.

Cho and colleagues (2018) noted that limbal dermoids are choristomas known as congenital benign tumors found in abnormal locations. Despite the benign nature, enlarging
limbal dermoids may cause visual abnormalities by cornea infiltration with fat component, visual axis invasion, gradually induced corneal astigmatism, and finally result in anisometropic amblyopia. These investigators reported a rare case of progressive, large pediatric corneal limbal dermoid in a newborn, managed with tissue glue-assisted monolayer AMT. Subject was a 1-day old male baby (gestational age of 36±6 weeks; birth body weight, 2,785 g) presented to the authors’ clinic with a whitish mass on his right eye since birth. Ocular examination revealed a solid, whitish-yellow, and ovoid mass with central keratinized epithelium over the superior limbus; the lesion covered 2/3 of the cornea with rapid progression in size. The final pathological examination revealed that the lesion was composed of keratotic lining squamous epithelium resembling epidermis, underling dermal fibrotic connective tissue, and mature fat. The patient underwent deep lamellar excision followed by mitomycin C (MMC) soaking (0.2mg/ml, 3 mins) and tissue glue-assisted monolayer AMT with the ring conformer at 2 months of age. The ring conformer was smoothly removed 2 weeks after the operation. The patient showed a smooth healing process with less pain and rapid corneal re-epithelization. The ocular surface was stable during the follow-up visits, and no complications were detected. Only mild post-operative scarring over the incision wound was observed. The authors concluded that although a combination of excision, lamellar keratoplasty, and multi-layer AMT and limbal stem cell transplantation was advocated for the treatment of grade-II and grade-III pediatric corneal limbal dermoids, the procedure used in this study offered an alternative surgical approach. However, because of the large size of the lesion and the young age of the patient, the management of amblyopia with visual rehabilitation and corneal transplantation was still needed in the future.

**Amniotic Membrane Transplantation and Limbal Stem Cell Transplantation for Ocular Chemical Injury**

https://aetnet.aetna.com/mpa/cpb/200_299/0293.html
Westekemper and associates (2017) analyzed the morphological and functional outcomes of patients receiving AMT after ocular chemical burn. These researchers performed a retrospective analysis of all patients treated for acute ocular chemical burn between 1998 and 2008 in 2 participating centers. Ocular chemical burns were classified by Roper-Hall and Dua classifications. A total of 72 eyes of 54 consecutive patients aged 37.3 years (± SD 11.6 years) were included in this cohort study; 7 chemical burns were acid burns, 61 were alkaline and 4 were of unknown origin. In 37 eyes (51.4 %), AMT was applied within the first 6 days following injury. Mean follow-up time was 36.4 months (median of 18.5; 1.3 to 117.3 months). Overall, 29 eyes (40.3 %) achieved a BCVA of LogMAR 0.2 (0.63 decimal) or better at final visit. Complete 360° LSCD occurred in 33 eyes (45.8 %), while partial LSCD occurred in 21 eyes (29.2 %). The authors concluded that AMT was an effective adjunctive treatment in the management of acute ocular chemical burns to support epithelial healing and restore ocular surface integrity with potential to improve vision. However, these investigators stated that long-term debilitated vision remained in those with severe burns complicated by LSCD.

In a randomized, parallel-controlled, clinical trial, Eslani and colleagues (2019) compared the outcomes of conventional medical treatment versus combined medical treatment and AMT in the management of patients with Roper-Hall grade IV ocular chemical injury. A total of 60 eyes of 60 patients with Roper-Hall grade IV ocular chemical injury with a minimum follow-up of 12 months were enrolled in the study. Patients were randomly assigned to 2 groups -- Group 1 (30 eyes) received topical preservative-free lubricating gel and drops, chloramphenicol, betamethasone, homatropine, oral vitamin C, and doxycycline; Group 2 (30 eyes) received AMT on the entire ocular surface in addition to the medical treatment provided in Group 1. The main outcome measure was time to complete corneal epithelialization; secondary outcome measures were BCVA and neovascularization in the central 5
mm of the cornea. Mean follow-up time was 20.3 ± 2.5 months (13 to 24 months). Corneal epithelial defects healed within 72.6 ± 30.4 days (21 to 180) in Group 1 versus 75.8 ± 29.8 days (46 to 170) in Group 2 (p = 0.610). Mean BCVA was 2.06 ± 0.67 logMAR (0.4 to 2.6) versus 2.06 ± 0.57 logMAR (1 to 2.9) in Groups 1 and 2, respectively (p = 0.85).

Group 1 developed more central corneal neovascularization (22 eyes; 73.3 %) compared to Group 2 (16 eyes; 53.3 %), however, it was not statistically significant (p = 0.108). The authors concluded that in comparison to conventional medical therapy, AMT combined with medical therapy did not accelerate corneal epithelialization or affect final VA in severe chemical injuries.

**Amniotic Membrane Transplantation / Limbal Stem Cell Transplantation for the Treatment of Retinal Detachment**

Caporossi and colleagues (2020) described a new surgical technique, using a human amniotic membrane patch, in 2 cases of retinal detachment with para-vascular retinal breaks over patchy chorio-retinal atrophy in pathologic myopia, already underwent pars plana vitrectomy with the internal limiting membrane peeling for myopic foveoschisis. A 23-G pars plana vitrectomy was performed. A human amniotic membrane patch was implanted under the neuroretina to seal the posterior retinal break. Standard silicone oil tamponade was performed at the end of the surgery. The patients were positioned face down after the operation for the 1st week.

Optical coherence tomography (OCT) scans were used in the follow-ups. The 2-week post-operative OCT showed a new tissue growth over the human amniotic membrane patch. The 3-months OCT showed the new tissue entirely covering the human amniotic membrane plug; VA improved from 20/2000 (2 LogMAR) to 20/250 (1.1 LogMAR) 3 months after the operation in both patients. The silicone oil was extracted 2 months after surgery, and no recurrences were observed. The patient's VA remained stable at 20/250 after the silicone oil extraction. The authors concluded that in these complex
cases, human AMTX could be a valid option, when internal limiting membrane has already been peeled in previous surgeries, to seal the posterior retinal breaks over high myopic chorio-retinal atrophy, with encouraging results. These preliminary findings need to be validated by well-designed studies.

Furthermore, an UpToDate review on “Retinal detachment” (Arroyo, 2020) does not mention amniotic membrane transplantation and limbal stem cell transplantation as management options.

**Combined Amniotic Membrane Transplantation and Umbilical Amnion and for the Treatment of Infectious Scleritis**

Syed and Rapuano (2020) reported the outcomes of 2 cases of infectious scleritis with severe scleral thinning managed using combined mechanical debridement, cryopreserved umbilical amnion (UA) and AMT, and anti-microbial therapy. Subjects were 2 patients who presented with severe infectious scleritis with progressive scleral melts secondary to Pseudomonas aeruginosa subsequent to pterygium surgery and intravitreal injection, respectively. Surgical debridement was followed by UA grafting, AMT, and anti-microbial therapy. Epithelialization and vascularization were observed within 1 to 4 weeks post-operatively. At last follow-up of 5 to 6 months, the structural integrity of the sclera remained preserved with no infection recurrence, graft necrosis, or wound dehiscence. The authors concluded that the findings of this case series highlighted the utilization of UA grafting along with AMT and topical and systemic antibiotics to preserve the globe in cases of severe infectious scleritis. These preliminary findings need to be validated by well-designed studies.

**Combined Heparinized Amniotic Membrane and Growth Factors for the Treatment of Corneal Alkali Burns**
Zhao and colleagues (2020) noted that ocular chemical burns are potentially blinding ocular injuries and require urgent management; AMT is an effective surgical treatment partly because AM is a rich source of growth factors (GFs) that can promote epithelialization and wound healing. However, GFs will be gradually lost and insufficient after preparation process and long-time storage, leading to unsatisfactory therapeutic effects. These researchers presented a modified AM (AM-HEP) for the supplement and sustained release of GF by surface grafting heparin for treatment of ocular chemical burns. Heparin grafting rate and stability, microstructure, physical property, and sustained release of epithelial growth factor (EGF) of AM-HEP were characterized. Biocompatibility and ability to promote corneal epithelial cell growth and migration were evaluated and compared with a biological amnion, which is available on the market in-vitro. The therapeutic effects of AM-HEP combined with EGF (AM-HEP@EGF) in-vivo had been evaluated in a model of mouse corneal alkali burn. The results indicated that heparin was introduced into AM and maintain stability over 3 weeks at 37°C. The modification process of AM-HEP did not affect microstructure and physical property after comparing with non-modified AM. EGF could be combined quickly and effectively with AM-HEP; the sustained release could last for more than 14 days. AM-HEP@EGF could significantly promote corneal epithelial cell growth and migration, compared with non-modified AM and control group. Faster corneal epithelialization was observed with the transplantation of AM-HEP@EGF in-vivo, compared with the untreated control group. The corneas in the AM-HEP@EGF group exhibited less inflammation and were more transparent than those in the control group. The authors concluded that the findings from in-vitro and in-vivo experiments demonstrated that AM-HEP@EGF could significantly enhance the therapeutic effects. These preliminary findings need to be validated by well-designed trials in human.

Human Amniotic Membrane Plug for the Treatment of
Macular Hole and Macular Hole Retinal Detachment

In a retrospective, interventional, comparative case-series study, Yadav and colleagues (2020) described the surgical outcomes of macular holes (MHs) by inserting a human amniotic membrane (hAM) plug. A total of 10 patients who had undergone hAM plugging for a MH were included in the study; 7 patients had idiopathic full-thickness MHs, 1 patient had traumatic MH, and 1 patient each had a MH-induced retinal detachment and combined retinal detachment. The control group included 10 cases with similar configuration and duration of MHs treated with the inverted peeling of the internal limiting membrane technique. All patients underwent a standard 3-port, 25-G transconjunctival pars plana vitrectomy and hAM plug transplantation in the subretinal space under the MH. The anatomic and functional outcomes were assessed at 4 weeks post-surgery. At the 4-week follow-up visit, all the MHs in the hAM plug group achieved hole closure, whereas 80% of the eyes in the control group were able to achieve hole closure. Improvement of 0.1 logMAR vision was noted in 8 of the 10 patients. At the 4-week follow-up visit, the external limiting membrane and ellipsoid zone layer continuity over the hAM was defined only in 1 case. No significant difference was observed between the hAM plug group and controls in visual and anatomical responses. No complications following hAM transplantation such as rejection, endophthalmitis, or hypotony were noted following surgery. The authors concluded that subretinal hAM graft transplantation could be a useful option in the repair of primary or refractory MHs not only for achieving anatomic closure but also for the accompanying visual improvement.

The authors stated that the small number of cases (n = 10), short follow-up time (4 weeks), and varied set of indications were the major limitations of this trial. This study of 10 new cases added to a very small number of published cases of hAM plugged MHs. These researchers stated that further studies are needed to determine the efficacy of this new
technique, and more intra-operative and post-operative analyses would be useful to understand the interaction between the amniotic membrane and the retina.

In a retrospective, interventional, case-series study, Huang and associates (2020) examined the surgical outcomes of cryo-preserved and dehydrated hAM graft transplantation for the treatment of MH and MH retinal detachment (MHRD) repair. This trial was carried out in 2 hospitals. Two types of hAM grafts, namely, the dehydrated form (AmnioGen, HCT Regenerative, Taiwan) and the cryo-preserved form (AmnioGraft, Bio-Tissue, Miami, FL), were consecutively used in MH surgeries. Anatomical and functional outcomes between the 2 types of hAM grafts were compared. A total of 17 patients (mean age of 62.1 ± 10.0 years, 9 (52.9 %) men) were enrolled. Of them, 11 patients had persistent MHs, 3 had MHs without prior surgery, and 3 had MHRD. A cryo-preserved hAM graft was used in 10 patients, and a dehydrated hAM graft was used in 8 patients; 1 patient used a cryo-preserved hAM in the 1st MH surgery and a dehydrated hAM in the 2nd surgery for extra-macular hole with retinal detachment. After a 6-month follow-up, 13 (76.5 %) patients had sealed MHs. The average visual acuity (VA) of cases with sealed MHs improved from 1.38 ± 0.62 to 1.12 ± 0.47 logMAR (p = 0.03). In the other 4 cases with persistent MHs, 3 had graft dislocation and 1 had a re-opened MH with graft contraction. There were no significant differences in closure rate (80.00 % versus 71.43 %, p = 0.68) or VA improvement (0.19 ± 0.37 logMAR versus 0.15 ± 0.41 logMAR, p = 0.85) between the 2 kinds of hAM graft. The authors concluded that these preliminary findings from case-series studies showed that both cryo-preserved hAM and dehydrated hAM were feasible alternative grafts for the treatment of persistent or recurrent MHs’ both approaches had similar anatomical and functional outcomes. Moreover, these researchers stated that this study was limited by the small sample size (n = 17). They
stated that further studies with longer follow-up periods are needed to confirm the clinical application of hAM grafts and examine the differences between the 2 types of hAM graft.

### CPT Codes / HCPCS Codes / ICD-10 Codes

*Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":*

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CPT codes covered if selection criteria are met:</strong></td>
<td></td>
</tr>
<tr>
<td>65778</td>
<td>Placement of amniotic membrane on the ocular surface; without sutures</td>
</tr>
<tr>
<td>65779</td>
<td>single layer, sutured</td>
</tr>
<tr>
<td>65780</td>
<td>Ocular surface reconstruction; amniotic membrane transplantation, multiple layers</td>
</tr>
<tr>
<td>65781</td>
<td>limbal stem cell allograft (e.g., cadaveric or living donor)</td>
</tr>
<tr>
<td>65782</td>
<td>limbal conjunctival autograft (includes obtaining graft)</td>
</tr>
<tr>
<td><strong>CPT codes not covered for indications listed in the CPB:</strong></td>
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</tr>
<tr>
<td><strong>Sural nerve grafting - no specific code:</strong></td>
<td></td>
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<tr>
<td><strong>Other CPT codes related to this CPB:</strong></td>
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<tr>
<td>65450</td>
<td>Destruction of lesion of cornea by cryotherapy, photocoagulation or thermocauterization</td>
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<tr>
<td><strong>HCPCS codes covered if selection criteria are met:</strong></td>
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<tr>
<td>V2790</td>
<td>Amniotic membrane for surgical reconstruction, per procedure</td>
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<tr>
<td><strong>ICD-10 codes covered if selection criteria are met:</strong></td>
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<table>
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<tr>
<th>Code</th>
<th>Code Description</th>
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<td>Benign neoplasm of cornea [dermoid]</td>
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<td>D31.12</td>
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<td>H11.001 -</td>
<td>Pterygium of eye</td>
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<td>H11.069</td>
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<td>H11.811 -</td>
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<td>H11.829</td>
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<td>H16.001 -</td>
<td>Corneal ulcer</td>
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<td>H16.079</td>
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<td>H16.231 -</td>
<td>Neurotrophic keratoconjunctivitis</td>
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<td>H16.239</td>
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<td>H18.10 -</td>
<td>Bullous keratopathy</td>
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<td>H18.13</td>
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<tr>
<td>H18.40 -</td>
<td>Corneal degeneration</td>
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<td>H18.49</td>
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<tr>
<td>H18.50 -</td>
<td>Hereditary corneal dystrophies</td>
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<td>H18.59</td>
<td></td>
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<tr>
<td>H18.821 -</td>
<td>Corneal disorder due to contact lens</td>
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<td>H18.829</td>
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<tr>
<td>L51.1</td>
<td>Stevens-Johnson syndrome</td>
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<tr>
<td>Q13.1</td>
<td>Absence of iris</td>
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<tr>
<td>T26.00x+</td>
<td>Burns and corrosion confined to eye and adnexa</td>
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<tr>
<td>T26.92x+</td>
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ICD-10 codes not covered for indications listed in the CPB:
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<th>Code</th>
<th>Code Description</th>
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<td>E08.3521</td>
<td>Diabetes mellitus with retinal detachment</td>
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<td>E08.3539, E08.3541</td>
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<td>Code</td>
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<tr>
<td>H16.8</td>
<td>Other keratitis [bacterial] [neurotrophic keratitis]</td>
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<tr>
<td>H18.59</td>
<td>Other hereditary corneal dystrophies [gelatinous drop-like corneal dystrophy]</td>
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<td>H33.001 - H33.8</td>
<td>Retinal detachments and breaks</td>
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<tr>
<td>H35.721 - H35.729</td>
<td>Serous detachment of retinal pigment epithelium</td>
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<td>H35.731 - H35.739</td>
<td>Hemorrhagic detachment of retinal pigment epithelium, right eye</td>
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<tr>
<td>H40.1110 - H40.1194</td>
<td>Primary open-angle glaucoma</td>
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<tr>
<td>H44.2C1 - H44.2C9</td>
<td>Degenerative myopia with retinal detachment</td>
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<tr>
<td>H50.0 - H50.9</td>
<td>Strabismus and other disorders of binocular eye movements [restrictive]</td>
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<tr>
<td>Z94.7</td>
<td>Corneal transplant status [penetrating keratoplasty]</td>
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**Allogeneic corneal epithelial stem cell transplantation:**

**CPT codes not covered for indications listed in the CPB:**

**Allogeneic corneal epithelial stem cell transplantation - no specific code:**
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<tr>
<th>Code</th>
<th>Code Description</th>
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<tbody>
<tr>
<td>ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):</td>
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<tr>
<td>H18.891 - H18.899</td>
<td>Other specified disorders of cornea [limbal stem cell deficiency]</td>
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<td></td>
<td>Amniotic membrane transplantation and umbilical amnion:</td>
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<tr>
<td></td>
<td>CPT codes not covered for indications listed in the CPB:</td>
</tr>
<tr>
<td></td>
<td>Amniotic membrane transplantation and umbilical amnion - no specific code</td>
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<tr>
<td>H15.001 - H15.099</td>
<td>Scleritis [infectious scleritis]</td>
</tr>
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<td></td>
<td>Combined heparinized-amniotic membrane with growth factors:</td>
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<tr>
<td></td>
<td>CPT codes not covered for indications listed in the CPB:</td>
</tr>
<tr>
<td></td>
<td>Combined heparinized-amniotic membrane with growth factors - no specific code</td>
</tr>
<tr>
<td>T26.60XA - T26.60XS</td>
<td>Corrosion of cornea and conjunctival sac, unspecified eye</td>
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<td></td>
<td>Corrosion of cornea and conjunctival sac, right eye</td>
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<tr>
<td></td>
<td>Corrosion of cornea and conjunctival sac, left eye</td>
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<tr>
<td>Human amniotic membrane plug:</td>
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<tr>
<td>CPT codes not covered for indications listed in the CPB:</td>
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</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
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<tr>
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</tr>
<tr>
<td>H33.001</td>
<td>Retinal detachments and breaks</td>
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<tr>
<td>H33.8</td>
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<tr>
<td>H35.341</td>
<td>Macular cyst, hole, or pseudohole</td>
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<tr>
<td>H35.349</td>
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</tbody>
</table>

**Human amniotic membrane plug – no specific code**

ICD-10 codes not covered for indications listed in the CPB (not all-inclusive):

The above policy is based on the following references:


https://aetnet.aetna.com/mpa/cpb/200_299/0293.html


and primary closure for pterygium excision.


72. Suri K, Kosker M, Raber IM, et al. Sutureless amniotic membrane ProKera for ocular surface disorders:


AETNA BETTER HEALTH® OF PENNSYLVANIA

Amendment to
Aetna Clinical Policy Bulletin Number: 0293 Corneal Graft and Amniotic Membrane Transplantation, Limbal Stem Cell Transplantation, or Sural Nerve Grafting for Ocular Indications

There are no amendments for Medicaid.