

# Amniotic membrane grafting for acute ocular involvement in Stevens-Johnson syndrome: Review of perioperative considerations, surgical techniques, and outcomes

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To review the perioperative considerations, surgical techniques, and outcomes of amniotic membrane grafting for acute ocular manifestations in Stevens-Johnson syndrome (SJS) and discuss a novel amniotic membrane grafting method. An online literature search of published articles on amniotic membrane grafting in acute SJS was performed using appropriate keywords on March 1, 2024. The relevant articles were included and analyzed. The review summarizes the relevance of amniotic membrane grafting in the current scenario. It also compares different techniques of amniotic membrane grafting and the ocular surface coverage each procedure provides. A novel technique of amniotic membrane grafting has been discussed with a schematic explanation. It also summarizes the complications of amniotic membrane grafting and their management, and the long-term outcomes of amniotic membrane grafting in preventing chronic sequelae. One should have a lower threshold for doing amniotic membrane grafting in cases with ocular involvement. This prevents the development of long-term sequelae and subsequent corneal blindness.

**Key words:** Acute SJS, amniotic membrane grafting, ocular manifestations

Stevens-Johnson syndrome (SJS) is one of the severe cutaneous adverse drug reactions. Clinically, SJS frequently presents as a disease spectrum rather than an isolated disorder characterized by typical and/or atypical target lesions on the skin with up to 10% epidermal detachment and at least two or more mucosal involvement.<sup>[1]</sup> The other end of the disease spectrum is toxic epidermal necrolysis (TEN) when the extent of epidermal detachment is more than 30%.<sup>[1]</sup> The skin lesions progress over 5–7 days, and in an uncomplicated case, re-epithelialization starts.<sup>[1]</sup> Epidermal detachment area of 10%–30% constitutes the SJS-TEN overlap syndrome.<sup>[1]</sup> Drug-specific HLA associations for the development of SJS-TEN have been detected in various populations.<sup>[2]</sup>

These are rare groups of disorders with a prevalence of 2 per 10 lakh.<sup>[3]</sup> The mortality rate associated with SJS is approximately 1%–5% and that of TEN is to the extent of 25%–30%.<sup>[4]</sup> Considering the severe systemic involvement and relatively high mortality, the primary aim of treatment remains to be patient survival. Other systems, including management of eye-related issues, often take a backseat. The survivors of severe disease at presentation are frequently left with lifelong morbidity due to cicatricial sequelae of the disease involving vital organs such as eyes, upper

gastrointestinal tract (pharynx and esophagus), and male and female external genitalia. We limit our discussion here to ophthalmological manifestations of the disease in the acute stage. In the acute stage, the ophthalmological manifestations are largely due to an extensive inflammatory cascade resulting in the necrosis and sloughing of the ocular surface coupled with the formation of true and inflammatory pseudomembranes.<sup>[5]</sup> Persistent epithelial defects and stromal lysis are not uncommon. If left untreated, these cases often end up with severe cicatricial manifestations. In the eye, the cicatricial changes involving the superotemporal fornix and lacrimal ductules result in the permanent obliteration of lacrimal ductules and thus severe dry eyes. Close apposition of bare palpebral and bulbar conjunctival surfaces results in symblepharon formation and obliteration of conjunctival cul-de-sac. Adhesions between bare lid margins result in the formation of an ankyloblepharon. The exuberant inflammation also poses a threat to the limbal stem cells residing at the basal layer of the limbal epithelium. Inflammatory insult to these cells might result in limbal stem cell dysfunction and deficiency<sup>[6]</sup> that manifest later as a persistent epithelial defect and conjunctivalization, respectively. On long-term follow-up, lid-margin keratinization (LMK) and subsequent

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lid-wiper keratopathy (LWK) have been documented. With this comes the question of whether these long-term sequelae can be prevented. If we change the disease course, the outcomes might improve. This article highlights the preoperative, intraoperative, and postoperative considerations in cases with acute ocular manifestations of SJS undergoing amniotic membrane grafting. This article also highlights the unique surgical technique of amniotic membrane grafting with its advantages over conventional techniques.

## Relevance of AMG in the Current Scenario

Ocular manifestations in SJS are often variable and fulminant, and treatment varies depending on disease severity. Medical management with topical steroids, lubricants, and prophylactic antibiotics has always been the mainstay of treatment.<sup>[7]</sup> Adhesiolysis, forniceal sweeping, and debridement of the loose epithelium have been described previously as surgical interventions in patients with acute ocular manifestations in SJS.<sup>[7]</sup> However, despite these procedures in conjunction with intense topical steroids, the outcomes were dismal, with a significant proportion of patients developing chronic cicatricial complications.<sup>[7]</sup> Initial studies suggested amniotic membrane grafting in the acute stage with either mild or no long-term sequelae.<sup>[8-12]</sup> Similar outcomes were noted in subsequent studies, with better outcomes in patients who received amniotic membrane grafting in the acute stage.<sup>[13,14]</sup> Early use of amniotic membrane in the acute phase of SJS/TEN was found to be effective in mitigating severe vision loss in long-term results. Gregory *et al.* further graded the ocular manifestations that need amniotic membrane grafting.<sup>[15,16]</sup>

The amniotic membrane is said to have anti-inflammatory, antifibrotic, anti-angiogenic, and antibacterial properties.<sup>[17,18]</sup> The extensive inflammatory cascade in the early stage causes severe damage to the limbal stem cells that reside at the basal layer of limbal epithelium. Amniotic membrane owing to its anti-inflammatory properties decreases the inflammation and mitigates the damage incurred to limbal stem cells. This prevents subsequent corneal vascularization and conjunctivalization and thus prevents corneal blindness. The disease course suggests the development of LWK secondary to LMK over the years. Early amniotic membrane grafting covering lid margins can prevent the development of LWK and subsequent corneal blindness.<sup>[16]</sup> The cicatricial complications include conjunctival scarring, cicatricial entropion, trichiasis, etc. Conjunctival scarring at the superotemporal fornix around the lacrimal ductular opening results in severe obliteration of ductules and resultant dry eyes. This can also be prevented by doing amniotic membrane grafting and keeping the amniotic membrane flush with the superotemporal fornix.<sup>[16]</sup>

## Method of Literature Search

We performed a literature search on the PubMed database on March 1, 2024 by using the following keywords: Acute ocular manifestations, SJS, and amniotic membrane grafting using "AND" and "OR." A total of 165 articles were available on search; however, we limited our search to full-text articles written in English. Articles mentioning the management of chronic sequelae and in languages other than English were excluded. A total of 46 articles were finally selected to be

included in the study based on the relevance and availability of articles. Relevance was assessed after reading the abstracts of the articles. To avoid selection bias in selecting the articles, three independent selectors were appointed.

## Indications of AMG in Acute Episode of SJS

Amniotic membrane grafting is indicated if there is a corneal epithelial defect, and/or a conjunctival epithelial defect of >1 cm, and/or a lid margin defect of >1/3<sup>rd</sup> lid margin in at least one lid.<sup>[15]</sup>

## Perioperative Considerations

### General

#### Patient handling

Any category of health caregiver of a patient with SJS-TEN must always adopt barrier methods and use face masks, sterile gowns, and gloves while handling such a patient.

While shifting the patient from bed to another area, it is always preferable not to touch the patient's body parts as friction may give rise to sliding and denudation of the detached skin, which otherwise would serve the purpose of "biological dressing." A safer method of lifting such patients is by holding the corners of the bed linen. If the patient does not have large areas of skin detachment, the palms and soles are not involved with large painful bullae, and the patient can stand on their feet, a wheelchair may be used for shifting.

Special caution is to be taken not to use large pieces of adhesive tape for fixing emergency medical gadgets on the body parts of a patient suffering from SJS-TEN, and all health caregivers must be sensitized. This prevents exposure of the underlying raw skin surface while removing the adhesive tape. The fixation may be done with a small strip of adhesive tape or a roller bandage depending on the type of gadget used and the body part where it is applied.

#### Preoperative, intraoperative, and postoperative challenges (anesthesia-related)

SJS and toxic epidermal necrolysis constitute a spectrum of disorders that can be termed as "acute skin failure."<sup>[19]</sup> These patients need multidisciplinary supportive care for fluid, electrolyte, and temperature management, nutrition, infection control, and analgesia.<sup>[20]</sup> Respiratory involvement is common, caused by bronchial mucositis as well as pneumonia and atelectasis, and may need intensive care.<sup>[21]</sup> This can also progress to chronic obstructive airway disease and bronchiolitis obliterans.<sup>[22]</sup>

Patients with SJS often need anesthetic care for debridement; dressing; grafting; examination under anesthesia; or for a range of ophthalmic interventions such as tarsorrhaphy, mucous membrane graft, amniotic membrane grafting like the current case, Boston keratoprosthesis, and penetrating keratoplasty.<sup>[23]</sup> Apart from the physiological impact of SJS, the physical consequences of widespread exfoliation as well as the pharmacological implications are of concern to the anesthesiologist. These patients benefit from a multidisciplinary approach involving the treating dermatologist, plastic surgeons, ophthalmologists, psychiatrists, intensivists, and anesthesiologists.

SJS is drug-induced in most cases, and it is always important to look for the indication of the specified medication in the given patient. The anesthetic implications of the basic disease may be significant, such as obstructive airway disease or seizure disorder.<sup>[24]</sup> Avoidance of the triggering medication is the cornerstone of treatment of SJS, and the specific as well as the overall list of medications triggering SJS must be borne in mind and avoided [Table 1]. Most drugs in the anesthesiologists' armamentarium, however, do not trigger SJS and have been safely used in these patients [Table 2].<sup>[23]</sup> Concern exists mainly with adjunctive medication such as NSAIDs, paracetamol, and antibiotics. Usually, opioid or regional analgesics are used safely. The antibiotic used must be chosen in consultation with the surgeon and treating dermatologist.

Patients chronically on corticosteroids might need "stress dose" supplementation.<sup>[43]</sup>

Preoperative workup should look for sepsis as it can lead to hemodynamic instability when combined with volume deficit and fluid shift. It is important to assess the fluid status of the patient and resuscitate appropriately to prevent post-induction hypotension. If there is evidence of sepsis, it is reasonable to anticipate the requirement of vasoactive and obtain appropriate central venous access.

Similarly, chances of a fresh infection during the perioperative period are high for these patients, and strict aseptic precautions should be taken in handling and positioning them in the OR, as well as all other procedures and interventions.

As described previously, there is sheetlike peeling of the epidermis on even mild shear pressure (Nikolsky sign). This poses great challenges to shifting and positioning the patient as well as monitoring and IV access. Patients should be shifted carefully using patient transfer mats and minimal handling. Gel or foam padding and creaseless sheets may be used at pressure points to prevent peeling. Similarly, ECG electrodes should be applied on unaffected skin, and if necessary, needle electrodes may be used. BP cuffs can cause pressure necrosis and should be applied over padding or PVC film. Invasive monitoring may be used for longer procedures with anticipated hemodynamic instability.

Intravenous access might be difficult due to denuded skin and dressings. Venous integrity is usually maintained as the involvement is superficial. However, it is difficult to suture any device in the affected areas as it may lead to further epidermal peeling. Past reports have resorted to central venous access to overcome this problem.<sup>[44]</sup>

Patients may have mucosal involvement of the upper and lower airway, extending down to the tracheobronchial mucosa in addition to desquamation and bullous lesions of facial skin. Hence, mask ventilation may be difficult or impossible, and pulmonary aspiration of hemorrhagic debris and slough may lead to pulmonary infiltration, small airway obstruction, and compromised oxygenation. If there is mucosal involvement of the pharynx or larynx, airway instrumentation may carry the risk of injury, bleeding, and loss of airway.

Hence, many past practitioners have chosen to avoid airway instrumentation, using regional anesthesia and/or deep sedation while maintaining spontaneous ventilation with an open airway. However, securing a definitive

airway may be possible with appropriate care and may be essential in anxious or apprehensive patients, major procedures, and in cases with pulmonary involvement. Plan of airway management should be individualized after thorough assessment and weighing the risk of injury or airway loss versus the benefit of avoiding aspiration and hypoxic complications. If airway intervention is chosen, it should be done by an experienced practitioner, with proper visualization using a video laryngoscope or fiberoptic bronchoscopy. While a potentially difficult airway exists, preoxygenation might not be possible as mask seals might be precluded by facial lesions. High-flow nasal cannula/transnasal humidified rapid-insufflation ventilatory exchange has been used successfully in this situation.<sup>[45]</sup> The difficult airway algorithm should be followed with the difficult airway cart kept ready. The use of rocuronium may be considered if mask ventilation is difficult. The use of supraglottic airways has also been described, using a device one size smaller than usual.<sup>[23]</sup> If intubation is chosen, using the smallest reasonable size of the tube may be prudent.

There may be a lot of airway secretions with slough and hemorrhagic debris; thus, proper clearance of secretions and return of airway reflexes is important during extubation. Patients also need close postoperative attention to proper analgesia and pulmonary toileting to prevent postoperative pulmonary complications.

#### *Role of methylprednisolone and IVIG*

Systemic steroids are not a specific treatment option in the SJS-TEN spectrum of disorders. However, in the era when currently used therapies were not available, systemic steroids were the sole drugs in use for the management of SJS-TEN. Usually, oral prednisolone or methylprednisolone can be used for mild cases, and in moderate to severe cases, intravenous dexamethasone or methylprednisolone can be used. The role of steroids in SJS-TEN is in the reduction of inflammatory edema involving vital body parts such as oral, pharyngeal, and genital mucous membranes and the eyes. In a retrospective analysis of eight patients with SJS-TEN treated with methylprednisolone pulse therapy (1 g/day  $\times$  3 consecutive days), the outcome was good as the disease progression was halted on the 3<sup>rd</sup> day of the pulse and there was no mortality at 3<sup>rd</sup> month, though the predicted mortality was 1.6 as per SCORTEN. Moreover, the pro-inflammatory cytokine levels (IFN- $\gamma$ , TNF- $\alpha$ , IL-6, IL-10) were decreased on day 4 post-therapy as compared to the pretreatment level.<sup>[46]</sup>

High-dose intravenous immunoglobulin G (IVIGg) is effective in SJS-TEN by complete inhibition of keratinocyte

**Table 1: List of offending drugs responsible for SJS**

- Allopurinol
- Diclofenac
- Lamotrigine
- Phenytoin
- Carbamazepine
- Sulfamethoxazole
- Amoxicillin/ampicillin
- Levofloxacin
- Ciprofloxacin etc.

**Table 2: Different surgical techniques of amniotic membrane grafting for acute ocular manifestations of SJS that evolved over the years. The table also highlights the area of the ocular surface covered with amniotic membrane in different surgical approaches**

	Procedure of AMT	Anesthesia	Area covered with amniotic membrane	Amniotic membrane apposition to superotemporal fornix	Study design
Kobayashi <i>et al.</i> (2006) <sup>[10]</sup>	Amniotic membrane sutured along lid margin with running 10-0 MFN, with purse string suture around the limbus and with fornix forming bolster sutures near fornices	GA	Advocated lid margin to lid margin coverage	No	Interventional case report
Tandon A <i>et al.</i> (2007) <sup>[12]</sup>	-Amniotic membrane sutured to lid margin with 10-0 MFN sutures, -reflected into fornices and secured with polygalactin sutures and fixed with the silicon bolsters -secured to the cornea and bulbar conjunctiva with 10-0 MFN sutures	GA	Advocated lid margin to lid margin coverage	No	Case report
Gregory DG <i>et al.</i> (2008) <sup>[25]</sup>	-AMG fixed to lid margin with 8-0 nylon -Fixed at fornices with polypropylene sutures with bolsters over skin -Perilimbal purse-string suture	LA	Advocated lid margin to lid margin coverage	No	Case report
Shay E <i>et al.</i> (2009) <sup>[26]</sup>	-10-0 or 8-0 nylon for suturing AMG at lid margin -4-0 Silk or 6-0 Prolene to fix at fornix -10-0 nylon purse-string perilimbal suture	LA	Advocated lid margin to lid margin coverage	No	Diagnostic and surgical techniques
Fu Y <i>et al.</i> (2010) <sup>[27]</sup>	Discussed complete coverage of ocular surface (similar to Shay and Gregory <i>et al.</i> ), though also discussed the role of Prokera and its limitation	-	Advocated complete ocular surface coverage	No	Clinical practice
Shammas MC <i>et al.</i> (2010) <sup>[28]</sup>	-Same as Shay <i>et al.</i> for patients taken to the operating room -Lids addressed same as above; however, used Prokera for corneal coverage for bedside procedures.	-	-	-	Retrospective interventional case series
Shay E <i>et al.</i> (2010) <sup>[29]</sup>	Used ProKera to cover cornea and perilimbal conjunctiva	Topical	Good for corneal epithelial defect healing- no effect on other cicatricial complications	No	Case report
Gregory DG <i>et al.</i> (2011) <sup>[30]</sup>	Used AMG for lids secured externally with running 8-0 Nylon and internally in the fornices with 6-0 Prolene suture and tied externally over soft plastic bolsters and ProKera over the cornea	Under LA in 1 case, GA in the rest 9 cases	Lid margin to lid margin coverage	No	Case series
Barua A <i>et al.</i> (2012) <sup>[31]</sup>	Similar to Shammas <i>et al.</i>	-	-	-	Case report

Contd...

Table 2: Contd...

	Procedure of AMT	Anesthesia	Area covered with amniotic membrane	Amniotic membrane apposition to superotemporal fornix	Study design
Hess TM <i>et al.</i> (2012) <sup>[32]</sup>	AMG fixed to the gray line over the lid margin with 8-0 polysorb sutures, fixed to the fornix with 3-0 SurgiPro sutures secured externally with bolsters	Under GA	Lid margin to lid margin coverage	No	Case report
Hsu M <i>et al.</i> (2012) <sup>[33]</sup>	Used 8-0 nylon sutures to secure AMG at the lid margin and 6-0 proline to secure AMG at the fornix. Nylon sutures in the perilimbal area and over at 4 quadrants over bulbar conjunctiva. Used ring made out of IV tubing to stretch AMG to fornices.	-	Lid margin to lid margin coverage	Yes	Case-control study
Kolomeyer <i>et al.</i> (2013) <sup>[34]</sup>	Used ProKera	Under TA	Only corneal and perilimbal conjunctival coverage	No	Case report
Lopez-Garcias JS <i>et al.</i> (2014) <sup>[35]</sup>	10-0 MFN suture to hold AMG around the limbus. 8-0 vicryl suture to hold at the fornix and lid margin, and symblepharon ring	Under LA	Lid margin to lid margin coverage	No	Prospective study
Pruet CM <i>et al.</i> (2014) <sup>[36]</sup>	Amnion-wrapped symblepharon rings were placed in the cul-de-sac	Under LA	Perilimbal coverage and superior and inferior forniceal coverage	No	Case report
Cheung CS <i>et al.</i> (2016) <sup>[37]</sup>	Used custom-designed symblepharon ring with 4 pairs of drilled holes and an amniotic membrane wrapped around the ring. Double-armed sutures were passed through the rings and when placed over the eye the ring was secured in place with sutures passed through fornices and bolstered over the lids.	--	Corneal, bulbar conjunctival, and superior and inferior forniceal coverage	No	Case report and surgical technique
R Jain <i>et al.</i> (2016) <sup>[38]</sup>	Authors advocated the use of fibrin glue to anchor the amniotic membrane to the underlying ocular surface. BCL was placed at the end	--	Corneal, bulbar conjunctival, and superior and inferior forniceal coverage	No	Review article
Ma KN <i>et al.</i> (2016) <sup>[39]</sup>	The authors used IV tubing to make a symblepharon ring. The author calculated the size of the ring by measuring the palpebral height. No fixed formula to calculate the size of the ring.	GA	Complete ocular surface	Yes	Review article and surgical technique

Contd...

Table 2: Contd...

	Procedure of AMT	Anesthesia	Area covered with amniotic membrane	Amniotic membrane apposition to superotemporal fornix	Study design
N Sharma <i>et al.</i> (2016) <sup>[40]</sup>	The amniotic membrane was draped over the ocular surface followed by fibrin glue injection beneath it. The fornices were swept with a lens hook pushing the amniotic membrane to the fornices. BCL followed by a symblepharon ring was placed.	Topical anesthesia	Covers all surfaces however, subsequent anchorage to the superotemporal fornices is doubtful.	--	Randomized controlled trial
Baş Z <i>et al.</i> (2019) <sup>[41]</sup>	The amniotic membrane was draped over the ocular surface followed by the placement of a symblepharon ring (18 mm). The redundant amniotic membrane was tucked into the palpebral conjunctiva and the excess was trimmed.	Sedoanesthesia	Covers bulbar conjunctiva, superior and inferior fornix, palpebral conjunctiva	No	Case report
Shanbhag <i>et al.</i> (2019) <sup>[42]</sup>	The amniotic membrane was fixed to the ocular surface using a symblepharon ring made out of IV tubing. The same was fixed to the lid margins with cyanoacrylate glue 4 mm away from the lid margin.	Intravenous sedation with topical anesthesia	Complete coverage to lid margins, bulbar conjunctiva, palpebral conjunctiva, and all fornices.	Yes	Retrospective chart review
Zhang <i>et al.</i> (2023) <sup>[23]</sup>	Used a customized symblepharon ring made by 3-D printing technology. The ring was placed over the amniotic membrane	--	Corneal, bulbar conjunctival, and superior and inferior forniceal coverage	No	Retrospective single-center case series
Our technique	Discussed in the peroperative section in detail. It also gives a formula to customize the ring size.	GA	Complete coverage to lid margins, bulbar conjunctiva, palpebral conjunctiva, and all fornices	Yes	Review with surgical technique

N – Total number of eyes enrolled, AMG – Amniotic Membrane Grafting, MFN – Monofilament Nylon, LA – Local Anesthesia, GA – General Anesthesia, IV tubing – Intravenous tubing, BCL – Bandage Contact Lens

apoptosis, as demonstrated in *in vitro* studies. It induces complete inhibition of keratinocyte death in *in vitro* studies and suppresses type IV hypersensitivity reaction and production of cytotoxic markers. A total dose of more than 2 g/kg is used in combination with systemic corticosteroid.<sup>[47]</sup> It can further reduce the chances of fatal complications of SJS-TEN, namely septicemia and immunological hepatotoxicity.<sup>[47]</sup> Analysis of the clinical course of SJS-TEN among Japanese patients has shown that early therapeutic intervention with IVIG (400 mg/kg/day) for 5 consecutive days in combination with corticosteroids induces rapid healing of mucocutaneous lesions.<sup>[48]</sup>

## Ophthalmological

### Preoperative

Logistics: The ophthalmological evaluation in acute conditions is often done at the bedside. The patient cannot be evaluated

on a slit-lamp and needs thorough examination at the bedside. Torchlight examination facilitates examination of the face, periocular area [Fig. 1], and ocular surface. The extent of an epithelial defect is delineated with the help of a fluorescein strip and the blue light of an indirect ophthalmoscope. To have a magnified view, one can use a 20-D lens in addition to an indirect ophthalmoscope focusing over the ocular surface. One can also use a hand-held slit-lamp for examination of the eye.

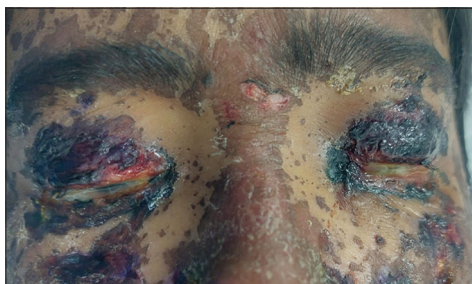
Once the extent of ocular involvement is confirmed, the decision to perform amniotic membrane grafting is made. Indications of amniotic membranes have been mentioned in the previous section. Two large-sized amniotic membrane availability should be confirmed before taking the patient to the operating room. The size of the amniotic membrane should be enough to cover the upper lid margin to the lower lid margin and also drape the bulbar, forniceal, and palpebral conjunctiva. Infant feeding

tube number 10 is used to create rings to secure the amniotic membrane stretched over the ocular surface. The size of the ring is decided based on the horizontal dimension of the palpebral fissure. Once the procedure is planned, the patient and his/her attendants are counseled about the expected outcomes and potential complications of the procedure. It is advised to prepare a SJS kit comprising all the above-mentioned commodities. The contents of the kit have been summarized in the below text.

SJS kit comprises the following:

1. Sterile cotton buds
2. Sterile gloves
3. Infant feeding tube no. 10
4. Fluorescein strip
5. Indirect ophthalmoscope with a 20-D lens
6. Two large amniotic membranes
7. 11 no. blade
8. Sterile sheet
9. Two drapes
10. 5% betadine solution

**Examination:** On cursory examination, blisters/scabs over the face and periocular area can be seen depending on the duration between disease onset and the day at presentation. Extensive inflammatory exudates are often seen at the lid margin with matting of eyelashes and adhesions between lid margins. Care should be taken while opening the eyelids to avoid desquamation of eyelid skin in an attempt to open the eyelids. Sterile cotton buds can be used to open the lids apart. Symblephara and ankyloblepharon are commonly encountered. Thick true

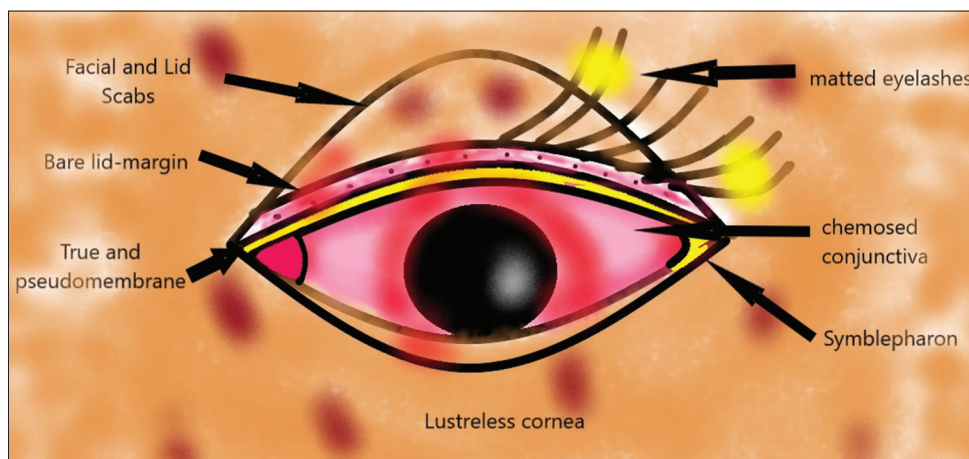


**Figure 1:** Extensive facial and periocular involvement in Stevens-Johnson syndrome/toxic epidermal necrolysis

membrane and pseudomembrane can be visualized over the palpebral conjunctiva. The bulbar conjunctiva is congested and chemosed. Depending on the extent of corneal involvement, it can be clear and lusterless to edematous and opaque [Fig. 2]. Delayed presentation can also result in corneal melt and perforation. The epithelial defect can be extensive involving bulbar and palpebral conjunctiva with or without corneal involvement. The epithelial defect can also extend over the lid margins. At this time, one should start frequent topical steroids (prednisolone 1%), prophylactic topical antibiotics (avoid using drugs known to cause SJS) such as moxifloxacin or levofloxacin (QID),<sup>[44]</sup> lubricants, and topical cyclosporine.

#### *Intraoperative*

The adult palpebral fissure is about 30 mm horizontally. Assuming the cul-de-sac to be a circular space along the fornices (medial, lateral, superior, and inferior) and taking the palpebral fissure horizontally as the diameter of the circle, a circumference of 94.2 mm ( $2\pi r$ ) is calculated. This gives us the length of the tube needed for that particular eye. The ring is made out of the appropriate-sized infant feeding tube number 10. One end of the tube is cut straight and the other beveled; this allows engagement of the beveled end into the straight-cut end of the tube. Amniotic membrane grafting can be done either bedside or in the operating room. If the procedure has to be done bedside, the ring is placed over the amniotic membrane, and the amniotic membrane is wrapped around the ring to form a ring-AMG complex, which can be opened into the cul-de-sac when needed. However, if the procedure is performed in the operating room, the exudative membranes and necrosed conjunctival membranes are first peeled off followed by draping the ocular surface with the amniotic membrane. Fig. 3 shows the trolley prepared in the operating room before amniotic membrane grafting. The amniotic membrane is held in position with the help of the ring<sup>[16]</sup> (video link: <https://youtu.be/qgLiVcW56Oo>). The ring stretches the amniotic membrane and keeps it flush with the fornices. The actual shape of the cul-de-sac is oval and not a circle as assumed while calculating the size of the ring. Considering the height of the cul-de-sac being smaller compared to the width, the excess ring would mold along the superotemporal fornices and facilitate close contact of the amniotic membrane with the superotemporal fornix that harbors the opening of lacrimal ductules [Fig. 4]. The redundant amniotic membrane



**Figure 2:** Acute ocular manifestations of Stevens-Johnson syndrome

can be reflected onto the lid margins following trimming of eyelashes. Thus, the amniotic membrane drapes the ocular surface completely. The ring should preferably be placed with the joint in the ring at the medial canthus. Placement of the joint over the medial canthus facilitates easy removal of the ring. Even in cases with sectoral symblepharon around the ring, it is easy to access the ring medially, and one can open the ring and pull out the tube without causing further damage. A bandage contact lens should also be placed.

#### Postoperative

Postoperatively, it is mandatory to keep an eye on the ocular surface for epithelial integrity and to rule out any infection. It is mandatory to clean the exudates or discharge without pulling the amniotic membrane that is draping the lid margin. Lid mobility is also important to avoid symblephara formation. Over days to weeks, the amniotic membrane starts disintegrating. One has to be able to distinguish between mucoid discharge and disintegrated amniotic membrane and should avoid cleaning the disintegrated amniotic membrane.

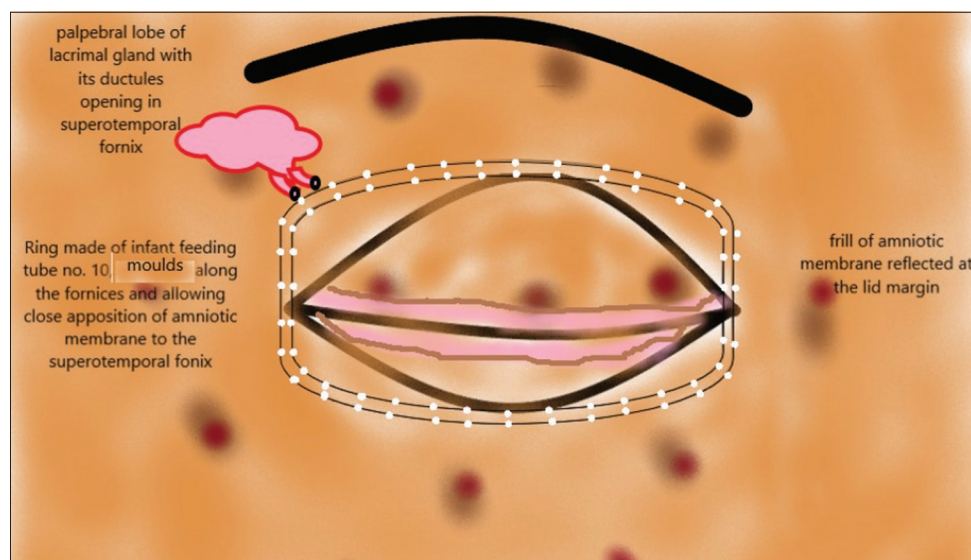


**Figure 3:** A trolley prepared for amniotic membrane grafting in the operating room. The trolley comprises rings prepared out of an infant feeding tube and other instruments necessary for the procedure

Once the amniotic membrane is completely disintegrated and the ocular surface defect has healed, the bandage contact lens and the ring can be removed in an outdoor facility with proper aseptic measures. One can come across adhesions around the ring while removing the ring; in such a scenario, it is better to open the joint and remove the ring. Forceful removal of the intact ring is not recommended because it will be more discomforting to the patient and create raw areas again, which could be detrimental and pose a risk of infection. Topical medications as discussed in the preoperative section should continue; however, the topical steroids (betamethasone/prednisolone phosphate) have to be tapered slowly over 8–10 weeks. This is to tide over the upregulation of tear inflammatory cytokines even after pulse systemic steroids.<sup>[49]</sup> This has to be coupled with a steroid-sparing agent such as cyclosporine 0.05% eye drops.

**A. Surgical technique of AMG in different studies:** There are many studies on surgical techniques of amniotic membrane grafting in acute SJS. Over the years, it was realized that merely having an amniotic membrane in the cul-de-sac is not enough for severe disease;<sup>[34]</sup> rather a complete ocular surface coverage is mandatory. The earlier study by Kobayashi *et al.*<sup>[10]</sup> describes the technique of draping and securing the amniotic membrane from one end to the other sequentially. The technique involves fixing of amniotic membrane to one of the lids first followed by the corresponding fornix, perilimbal episcleral, opposite fornix, and finally to the opposite lid sequentially. With time, the techniques evolved with simpler ways to fix the amniotic membrane over the ocular surface with primary emphasis on complete ocular surface coverage. The ease of doing and less procedure time were next only to the complete coverage. Table 2 summarizes different surgical techniques of performing amniotic membrane grafting in acute SJS.<sup>[10,12,23,25–41,50]</sup>

**B. Complications:** As such, amniotic membrane grafting is always beneficial in such clinical scenarios; however, the inherent complications of the surgical techniques need to be mentioned. Table 3 lists the general complications of all



**Figure 4:** The mechanics of the ring made from an infant feeding tube. The ring stretches the amniotic membrane and keeps it flush with the fornices. The actual shape of the cul-de-sac is oval and not a circle as assumed while calculating the size of the ring. Considering the height of the cul-de-sac being smaller compared to the width, the excess ring would mold along the superotemporal fornices and facilitate close contact of the amniotic membrane with the superotemporal fornix

**Table 3: Complications of the procedure and recommendations for the prevention and management of complications**

Complications	Management	
	Prevention	Treatment
Loss of graft	Diligent and careful cleaning of lid margins and exudates can prevent this.	The procedure needs to be repeated in such a scenario.
graft dislocations	Diligent and careful cleaning of lid margins and exudates can prevent this. One should be able to distinguish between exudates and degenerated amniotic membranes. Avoid undue pull to the graft while cleaning the eye to prevent such complications.	The same graft can be repositioned and fixed firmly using sutures.
lysis of the amniotic membrane before healing of the ocular surface epithelial defect	Excessive inflammation can result in early lysis of the amniotic membrane. Frequent topical steroids following AMG can prevent this.	Redo the procedure to facilitate epithelial healing. <sup>[42]</sup>
secondary bacterial infections	The use of prophylactic antibiotics is indicated to prevent secondary bacterial infection. Foreign materials such as bandage contact lenses (BCLs), and IV tubings over the ocular surface are the predisposing factors.	Frequent topical antibiotics (empirical) should be added in consultation with dermatologists.
Lagophthalmos (specific to our technique)	The oversized infant symblepharon ring made of an infant feeding tube stretches the fornices so much that the patient develops lagophthalmos. This can be prevented by taking a size smaller than the largest calculated size.	Replace the oversized ring with an adequate-sized ring. Perform lateral paramedian tarsorrhaphy and/or place a bandage contact lens.

**Table 4: Long-term outcomes of amniotic membrane grafting for acute ocular manifestations of SJS**

Author/Year	n	Study duration	Study design	Outcome
Mortensen <i>et al.</i> (2023) <sup>[51]</sup>	85 eyes of 42 patients	April 2014–Jan 2022	Retrospective chart review	AMG in severe ocular SSJS/TEN mitigates long-term complications and improves visual outcomes irrespective of dehydrated or cryopreserved amniotic membrane.
Shanbhag <i>et al.</i> (2019) <sup>[42]</sup>	4	Mar 2017–Dec 2017	Retrospective chart review	Long-term outcomes are similar to sutured amniotic membrane
Shanbhag <i>et al.</i> (2019) <sup>[50]</sup>	48 (n=9, who did not receive AMG Vs n=39, who received AMG	Jan 2000–Sep 2017	Retrospective chart review	One should have a lower threshold for AMG in moderate to severe cases, preferably in the first week. This causes a significant decrease in corneal blindness due to SJS/TEN.
Sharma N <i>et al.</i> (2016) <sup>[40]</sup>	n=50 (n=25 in each group)	May 2013–May 2014	Randomized controlled trial	The amniotic membrane decreases inflammation and promotes healing. It prevents the development of chronic ocular surface and lid-margin-related complications. The authors advocated AMT in all cases of SJS/TEN along with standard therapy.

approaches to amniotic membrane grafting.<sup>[42]</sup> The table also mentions the preventive measures to avoid such complications and treatment options to manage complications.

**C. Surgical outcome:** Fewer studies exist on the long-term surgical outcomes of amniotic membrane grafting in the acute stage. Most of the studies are either case reports or case series. Table 4 summarizes the surgical outcomes of the procedure with long-term surgical outcomes from different studies.<sup>[40,42,50,51]</sup>

## Conclusion

To summarize, one should have a lower threshold for early amniotic membrane grafting in patients with ocular complications in acute SJS. A complete ocular surface coverage with the amniotic membrane is mandatory. The surgical techniques may vary, but the most effective and easy-to-do procedure is preferred. The use of an appropriate-sized infant feeding tube facilitates adequate and complete ocular surface coverage by amniotic membrane. The exclusion of fibrin glue decreases the overall cost of the procedure. A precalculated

ring size with a wrapped amniotic membrane can be safely placed in the conjunctival cul-de-sac even at the bedside with minimal manipulation.

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