

Stevens - Johnson Syndrome and Toxic Epidermal Necrolysis

By Hosam Sheha, M.D., Ph.D. and Scheffer C. G. Tseng M.D., Ph.D.



POP 1st Day

Supplies for Procedure

1. Sterile lid speculum
2. Sterile gloves
3. Anesthetic drops
4. Antibiotic drops
5. Sterile scissors
(provided with the ProKera™ device)
6. Sterile forceps
(provided with the ProKera™ device)
7. ProKera™ (by Bio-Tissue™) call for info:
1-888-296-8858

Overview

Stevens-Johnson Syndrome (SJS) is an immune-complex-mediated hypersensitivity disorder which typically involves the skin and the mucous membranes.¹ SJS is a serious systemic disorder with the potential for severe morbidity and even death. Significant involvement of oral, nasal, eye, vaginal, urethral, GI, and lower respiratory tract mucous membranes may develop in the course of the illness.² The severe variant of SJS showed extensive skin involvement resulting in toxic epidermal necrolysis (TEN). Although SJS/TEN is considered one of the most devastating ocular surface diseases which causes corneal damage and threatens vision, management of ocular involvement may be compromised because more attention is directed to maintaining the vital functions during the acute stage. Furthermore, upon eye examination of patients suffering SJS/TEN at the acute stage it is difficult to recognize hidden conjunctival inflammation and ulceration deep in the fornix and tarsus. Inadequate control of ocular surface inflammation and ulceration at the acute stage will set in a vicious cycle, leading to the chronic stage of scarring (cicatrix), which then contributes greatly to subsequent corneal complications.^{3,4}

Although systemic corticosteroids are commonly used and shown to be of some benefit in ameliorating systemic manifestations of the acute phase of SJS and TEN,⁵ its therapeutic effect has never been demonstrated in a controlled trial. Furthermore, retrospective studies demonstrate no benefit of corticosteroids or higher rates of morbidity and mortality in corticosteroid-treated patients.^{6,7} Cyclosporin A⁸ and plasmapheresis⁹ have been proposed as alternatives. Recently, IV immunoglobulin has also been advocated for both SJS¹⁰ and TEN.¹¹ Despite these measures, specific attention to suppress ocular surface inflammation and to promote early epithelialization has not been considered. A recent retrospective study verified that the extent of lid margin keratinization and tarsal scar (as a result of cicatricial complications) is highly correlated with sight-threatening corneal complications.¹²

Amniotic membrane transplantation has been used as a temporary graft (or patch) during the acute stage, defined as the first two weeks, of chemical and thermal burns. It can suppress inflammation and prevent subsequent scarring in the later stage.¹³⁻¹⁵ Amniotic membrane has also been used as a temporary graft in patients with acute SJS/TEN with^{16,17} (23, 16) or without^{12,18} corneal involvement in the acute stage to suppress inflammation and facilitate wound healing, resulting in restoration of a normal and healthy ocular surface and sight.

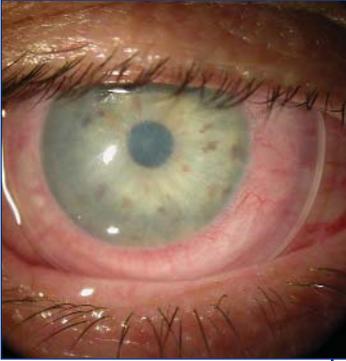
A new medical device recently approved by the FDA, PROKERA® (Bio-Tissue, Miami, FL), can facilitate the early delivery of the needed biological effects of cryopreserved amniotic membrane at the bedside or clinic without sutures. This delivery mechanism for cryopreserved amniotic membrane is an important utility in treating this devastating disease at the acute stage.

In conclusion, transplantation cryopreserved amniotic membrane performed in the acute phase of SJS/TEN can be highly effective not only in reducing inflammation and preventing scarring in the conjunctival and corneal surfaces and in restoring corneal epithelial integrity in eyes even when the hidden inflammation and ulceration is not detected. As a result, it prevents sight-threatening cicatricial complications at the chronic stage.¹⁷

ProKera™ sizes:

| Catalog # | Size |
|-----------|-------|
| PK-15 | 15 mm |
| PK-16 | 16 mm |

FAQs



ProKera™ Inserted in eye

Key Insertion Steps:

- Use a lid speculum to open the eye
- Administer anesthetic drops
- Insert ProKera™ into the upper lid, and then tuck it under the lower lid
- Administer prophylactic antibiotic drops



POP 4th Day



POP 10th Day

What is Stevens-Johnson Syndrome (SJS) and what are the symptoms?

Stevens-Johnson Syndrome is a serious, potentially life-threatening skin disease. With Stevens-Johnson Syndrome the sufferer can first experience non-specific symptoms, such as headaches, aching body, fever, and cough. Then a rash may develop over the face and trunk, which then spreads to other parts of the body. The rash is patchy and spreads. Blistering can then appear, usually in places such as the eyes, mouth, nose and genital areas, and the mucous membrane becomes inflamed. Because some of the above symptoms can be found in many other diseases, it is important to consider SJS in the differential diagnosis due to its severe morbidity.

What is Toxic Epidermal Necrolysis (TEN)?

Toxic Epidermal Necrolysis is another variation of the disease. With this variation the skin also begins to peel away in large amounts. This leaves the sufferer looking as though the patient has burns. There is a significant risk of infection and fluid can profusely leak out in the places where the skin has come away.^{19,20}

What are the differences between Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)?

SJS and TEN (Toxic epidermal necrolysis) are characterized by identical clinical signs and symptoms, identical treatment approach, and identical prognosis.

Several classification schemes have been reported, the simplest (French, Allergol Int, 2006) breaks the disease down as follows:

- SJS - A "minor form of TEN," with less than 10% body surface area (BSA) detachment
- Overlapping SJS/TEN - Detachment of 10-30% BSA
- TEN - Detachment of more than 30% BSA

Patients with 90% skin detachment and diagnosed with TEN may have none or only mild ocular involvement with excellent prognosis, and patients with 10% skin detachment may have severe ocular involvement with blinding consequences, and vice versa.²¹

What is the main cause of SJS/TEN?

The most common cause of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis is through an allergic drug reaction. The drugs that are usually responsible for these reactions include: Penicillin family, some non-steroid anti-inflammatory drugs (NSAIDS), Allopurinol, Phenytoin, Carbamazepine, barbiturates, anticonvulsants, and sulfa antibiotics. The onset of symptoms in drug related Stevens-Johnson Syndrome may not appear for one or two weeks after first taking the drug. Reaction to drugs is by far the most common cause of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis.

What causes SJS/TEN in children?

Medication is usually the cause of the disease of Stevens-Johnson Syndrome in children. However, this condition can stem from other unknown causes. Some of the medications that have been linked to SJS in children include children's Motrin, Advil, and other ibuprofen based drugs. These drugs have received highly negative publicity on a number of occasions after being identified as the cause in a range of cases where children have become seriously ill with SJS.²²

FAQs (continued)

Who can diagnose SJS/TEN?

A dermatologist is the most likely clinician to establish the diagnosis, with or without biopsy. Severe cases may require the involvement of a burn specialist or plastic surgery specialist. Internal medicine, critical care, or pediatrics consultants direct inpatient care.

A consultation with an ophthalmologist is mandatory when there is ocular involvement. Even if the eye is closed, one cannot assume the eye is not involved. Bedside examination is inadequate to assess ocular involvement because hidden inflammation and ulceration in the fornix and tarsus may not be visible when eyelids are not everted. Due to the severe ocular morbidity of this disease at the chronic stage, it is advised to assume all victims of SJS/TENS have ocular involvement until a thorough ocular examination can be performed.

Are there any laboratory tests for diagnosing SJS/TEN?

Skin biopsy is the only diagnostically helpful laboratory study. Serum levels of tumor necrosis factor- α , soluble interleukin 2-receptor, interleukin 6, and C reactive protein typically are elevated in patients with SJS; however, none of these serologic tests is used routinely in diagnosing and managing SJS.

What is the differential diagnosis of ocular SJS?

Although there are other diseases that may present cicatricial complication such as Chemical burns, Conjunctivitis, Keratoconjunctivitis, Atopic Dermatitis, Trichiasis, Entropion, Ocular Rosacea, Sarcoidosis, Scleritis, Sjogren Syndrome, Squamous Cell Carcinoma and Trachoma, SJS/TEN has a characteristic clinical presentation different from these diseases.

How is SJS treated?

Upon diagnosis of SJS, the doctor will first need to identify the cause of the disorder, as this will determine the treatment and steps required. If the disease has occurred as a reaction to medication, the patient should stop taking the medication immediately. Treatment may take place in the burns unit at the hospital depending on the severity of the symptoms. It is important that anyone with this type of disease is treated in the cleanest environment, as this is a disease that leaves both adults and children open to secondary infections. If you have already contracted an infection on top of the SJS, the doctor may also need to administer antibiotics.

The treatment for a patient with SJS can vary depending on the health of the person and the severity of the disease. Fluid replacement and topical steroids may be needed, and the doctor may also administer oral and eye exams and treatments. For eye problems, it is important to consult ophthalmologists to consider early (within the first two weeks) intervention with amniotic membrane transplantation.

What are the complications of SJS/TEN?

Ophthalmologic: Corneal ulceration, anterior uveitis, panophthalmitis, blindness

Gastroenterologic: Esophageal strictures

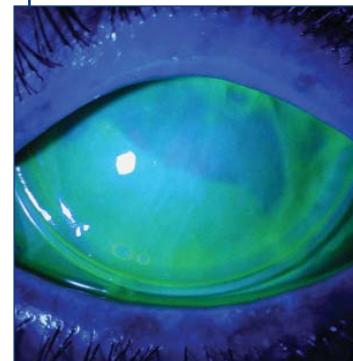
Genitourinary: Renal tubular necrosis, renal failure, penile scarring, vaginal stenosis

Pulmonary: Tracheobronchial shedding with resultant respiratory failure

Cutaneous: Scarring and cosmetic deformity, recurrences of infection through slow-healing ulcerations

How can SJS/TEN be prevented?

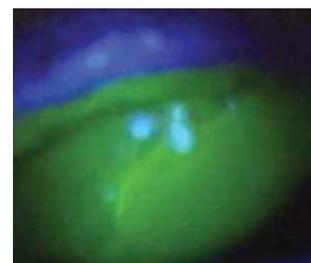
Early recognition and avoidance of possible offending agents may reduce the incidence and/or severity of SJS/TEN.



ProKera™ with fluorescein staining



POP 9th Day



POP 9th Day OD



POP 9th Day OS

References

- 1) Stevens AM, Johnson FC: A new eruptive fever associated with stomatitis and ophthalmitis. Report of two cases in children. *Am J Dis Child* 1922; 526-533.
- 2) French LE: Toxic epidermal necrolysis and Stevens Johnson syndrome: our current understanding. *Allergol Int* 2006 Mar; 55(1): 9-16.
- 3) Belfort R Jr, de Smet M, Whitcup SM, et al. Ocular complications of Stevens-Johnson syndrome and toxic epidermal necrolysis in patients with AIDS. *Cornea* 1991;10:536-8.
- 4) Power WJ, Ghoraishi M, Merayo-Llodes J, et al. Analysis of the acute ophthalmic manifestations of the erythema multiforme/Stevens-Johnson syndrome/toxic epidermal necrolysis disease spectrum. *Ophthalmology* 1995;102:1669-76.
- 5) Patterson R, Miller M, Kaplan M, et al. Effectiveness of early therapy with corticosteroids in Stevens-Johnson syndrome: experience with 41 cases and a hypothesis regarding pathogenesis. *Ann Allergy* 1994;73:27-34.
- 6) Halebian PH, Corder VJ, Madden MR, et al. Improved burn center survival of patients with toxic epidermal necrolysis managed without corticosteroids. *Ann Surg* 1986;204:503-12.
- 7) Roujeau JC, Stern RS. Severe adverse cutaneous reactions to drugs. *N Engl J Med* 1994;331:1272-85.
- 8) Arevalo JM, Lorente JA, Gonzalez-Herranda C, Jimenez-Reyes J. Treatment of toxic epidermal necrolysis with cyclosporin A. *J Trauma* 2000;48:473-8.
- 9) Egan CA, Grant WJ, Morris SE, et al. Plasmapheresis as an adjunct treatment in toxic epidermal necrolysis. *J Am Acad Dermatol* 1999;40:458-61.
- 10) Prins C, Vittorio C, Padilla RS, et al. Effect of high-dose intravenous immunoglobulin therapy in Stevens-Johnson syndrome: a retrospective, multicenter study. *Dermatology* 2003;207:96-9.
- 11) Viard I, Wehrli P, Bullani R, et al. Inhibition of toxic epidermal necrolysis by blockade of CD95 with human intravenous immunoglobulin. *Science* 1998;282:490-3.
- 12) Di Pascuale MA, Espana EM, Liu DT, et al. Correlation of Corneal Complications with Eyelid Cicatricial Pathologies in Patients with Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis Syndrome. *Ophthalmology* 2005; 112:904-912.
- 13) Kim JS, Kim JC, Na BK, et al. Amniotic membrane patching promotes healing and inhibits protease activity on wound healing following acute corneal alkali burn. *Exp Eye Res* 2000;70:329-37.
- 14) Meller D, Pires RT, Mack RJ, et al. Amniotic membrane transplantation for acute chemical or thermal burns. *Ophthalmology* 2000;107:980-89; discussion 990.
- 15) Kobayashi A, Shirao Y, Yoshita T, et al. Temporary amniotic membrane patching for acute chemical burns. *Eye* 2003;17: 149-58.
- 16) John T, Foulks GN, John ME, Cheng K, Hu D. Amniotic membrane in the surgical management of acute toxic epidermal necrolysis. *Ophthalmology* 2002;109:351-360.
- 17) Kobayashi A, Yoshita T, Sugiyama K, et al. Amniotic Membrane Transplantation in Acute Phase of Toxic Epidermal Necrolysis with Severe Corneal Involvement. *Ophthalmology* 2006;113:126-132.
- 18) Roujeau JC: Stevens-Johnson syndrome and toxic epidermal necrolysis are severity variants of the same disease which differs from erythema multiforme. *J Dermatol* 1997 Nov; 24(11): 726-9
- 19) Lyell L. Toxic epidermal necrolysis: an eruption resembling scalding of the skin. *Br J Dermatol* 1956;68:355-61.
- 20) Roujeau JC. The spectrum of Stevens-Johnson syndrome and toxic epidermal necrolysis: a clinical classification. *J Invest Dermatol* 1994;102:28S-30S.
- 21) Ball R, Ball LK, Wise RP, et al: Stevens-Johnson syndrome and toxic epidermal necrolysis after vaccination: reports to the vaccine adverse event reporting system. *Pediatr Infect Dis J* 2001 Feb; 20(2): 219-23.

Provided by

The Ocular Surface Research & Education Foundation (OSREF)

Visit www.osref.org to view the Ocular Research & Education Foundation's full library of medical education material

For additional clinical information, contact Scheffer C.G. Tseng, M.D., Ph.D. by phone at 305-274-1299 or by e-mail at stseng@ocularsurface.com.