Surgical Critical Care.net

STEVENS-JOHNSON SYNDROME / TOXIC EPIDERMAL NECROLYSIS

Evidence Based Medicine Guideline

Primary Author: Susan Smith, PhD, APRN-BC
Editors: Michael L. Cheatham MD; Howard G. Smith, MD
Approved: 6/22/2026

SUMMARY
Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are autoimmune diseases causing a severe mucocutaneous reaction characterized by extensive skin sloughing. SJS progresses to TEN based upon the extent of skin loss. SJS/TEN are associated with significant morbidity and mortality. Patient care involves discontinuation of the causative agent/medication and supportive care as the patient's desquamated skin wounds epithelialize. Numerous therapies have been proposed, but none have shown a significant survival benefit over supportive wound care alone.

RECOMMENDATIONS

- **Level 1**
  - **None**
- **Level 2**
  - **Supportive care remains the primary treatment approach for SJS/TEN consisting of wound, ocular and oral care as the wounds epithelialize.**
  - **Diagnosis of SJS/TEN is made using clinical history and physical examination supplemented by punch skin biopsy for pathologic examination and direct immunofluorescence staining.**
- **Level 3**
  - **No survival benefit has been realized from corticosteroids, IVIG, Cyclosporine A, the combination of steroids with IVIG, or plasmapheresis when compared to supportive care.**

INTRODUCTION

Stevens-Johnson Syndrome (SJS) is an acute, life-threatening, T-cell mediated Type IV delayed hypersensitivity mucocutaneous reaction caused by drugs or infections (1-3). SJS was named for Drs. Albert Stevens and Frank Johnson, American pediatricians, who described extensive rash development and multisystem involvement in 1922 (1). The more extensive form, Toxic Epidermal Necrolysis (TEN), was reported by Dr. Alan Lyell, a Scottish dermatologist, in 1956 (1). These are rare, rapidly progressive syndromes with cutaneous, mucosal and systemic manifestations resulting in high mortality and significant morbidity (1-3). Occurrence is unpredictable, affecting all races, genders and ages (3).

Certain populations of patients have a higher risk of disease. The risk of SJS/TEN in females is 1.5 times higher than in males and pregnancy increases the risk to 14% greater than the general population (3). SJS/TEN occurs more frequently in elderly, immunocompromised patients suffering medical comorbidities (4). Medical conditions that potentially increase the risk of SJS/TEN include: liver disease, diabetes, psoriasis, history of past drug reactions or allergies, systemic lupus erythematosus, and malignancy (1,4). A current diagnosis of malignancy increases the risk of SJS/TEN to 30 times the general population (3). Additionally, Black and Asian populations face an elevated risk (3,5). The Han Chinese population allele (HLA-B#15:02) has a strong association with carbamazepine-induced SJS/TEN in Southeast Asia. Human immunodeficiency virus (HIV) and tuberculosis treatment in Africa places this population at a higher risk (1). SJS/TEN is 100 times more likely in people with HIV.

LEVEL OF RECOMMENDATION DEFINITIONS

- **Level 1:** Supported by multiple, prospective randomized clinical trials or strong prospective, non-randomized evidence if randomized testing is inappropriate.
- **Level 2:** Supported by prospective data or a preponderance of strong retrospective evidence.
- **Level 3:** Supported by retrospective data or expert opinion.

The extent of epidermal detachment is the basis for syndrome classification (1,2,6,7):

- SJS: < 10% total body surface area (TBSA)
- SJS/TEN overlap: 10-30% TBSA
- TEN: > 30% TBSA

The incidence of SJS in the United States is 9.2 persons per million, SJS/TEN overlap 1.6 persons per million, and TEN 1.9 persons per million (4,6). Syndrome-associated mortality in the U.S. is 4.8 % for SJS, 19.4 % for SJS/TEN overlap, and 14.8% for TEN (6). Approximately 80% of cases are associated with medication exposure, especially antibiotics, antipyretic analgesics, anti-convulsants and nonsteroidal anti-inflammatory drugs (NSAIDs). More than 300 different drugs and supplements have been implicated. Mycoplasma and viral infections also represent known causes of SJS/TENS, with mycoplasma infection the most common cause of SJS in children. A portion of cases remain without identifiable drug triggers (1,6).

LITERATURE REVIEW

Presentation

SJS/TEN is initially non-specific, typically beginning with fever, headache, rhinitis, cough, malaise, myalgias, and sore throat around 4 weeks following exposure (although skin sloughing can occur more rapidly following exposure to the inciting agent). Within a few days, cutaneous symptoms develop. Macular atypical target lesions first appear as a generalized rash that subsequently progresses to blister formation. Cutaneous necrosis leads to wide-spread epidermal detachment and skin sloughing, resulting in painful, large, open wounds (1,6). Nikolsy's sign, characterized by the detachment of apparently normal skin following light lateral pressure with a fingertip, may be positive (6).

Oral symptoms present as painful erosions or ulcers of lips and oral mucosa. The most frequently observed ocular findings are conjunctivitis, eye pain and photophobia. Corneal defects and pseudomembrane formation may lead to permanent visual impairment (1,6). The mucosa of the lips, mouth, genitalia, respiratory, and gastrointestinal tracts may develop painful ulcerations. The lining of internal organs can also be directly affected leading to pneumonia, colitis, pancreatitis, and liver dysfunction. Electrolyte abnormalities, pancytopenia, hypothermia, dehydration, and life-threatening sepsis are a few of the more common complications of SJS/TEN (1,5).

Diagnosis and Assessment

Diagnosis is based on clinical findings, history of recent medication exposure, exclusion of other diagnoses, and histology. Involvement of two mucous membranes and a positive Nikolsky sign are indicative, but not confirmatory of SJS/TEN. Blistering and epidermal detachment are not sufficient to diagnose SJS/TEN.

Clinical findings can mimic several other disease presentations including:

- Reactive mucocutaneous eruption
- Generalized bullous fixed drug eruption
- Pemphigus vulgaris
- Acute graft versus host disease
- Toxic shock
- Acute generalized exanthematous pustulosis
- Linear immunoglobulin a bullous dermatosis
- Lupus erythematosus
- Drug-induced fixed drug reaction

The "gold standard" for the diagnosis of SJS/TEN is pathologic examination and direct immunofluorescence staining of a punch biopsy of representative skin lesions. Details of performing skin biopsies for the diagnosis of SJS/TEN can be found in the **"Skin Biopsy for Stevens-Johnson Syndrome & Toxic Epidermal Necrolysis"** evidence-based guideline available on SurgicalCriticalCare.net. Histological results should reveal the presence of keratinocyte necrosis, dermal perivascular infiltrates, keratinocyte apoptosis, basal vacuolar subepidermal bullae, and full-thickness epidermal necrosis. Direct immunofluorescence staining is expected to be negative (1,6).

Severity and Prognostics

There are several validated tools available for the assessment of severity and mortality risk due to SJS/TEN. Score of Toxic Epidermal Necrolysis (SCORETEN) is the most frequently utilized tool and has been proven superior to others for predicting mortality risk except in the pediatric population (1,3,6). SCORETEN is a mathematical model

for quantifying seven independent risk factors present on admission including age, history of malignancy, heart rate, epidermal detachment, serum urea, serum glucose and serum bicarbonate (3). It should be calculated on day 1 and 3 of hospitalization (1).

Score of Toxic Epidermal Necrolysis (SCORETEN)

Risk Factor	0 points	1 point
Age	< 40 years	≥ 40 years
Associated malignancy	No	Yes
Heart rate	<120 bpm	≥ 120 bpm
Serum BUN	≤ 28 mg/dL ≤ 10 mmol/L	> 28 mg/dL > 10 mmol/L
Detached or compromised body surface	<10 %	≥ 10%
Serum bicarbonate	≥ 20 mEq/L ≥ 20 mmol/L	< 20 mEq/L < 20 mmol/L
Serum glucose	≤ 252 mg/dL ≤ 14 mmol/L	> 252 mg/dL > 14 mmol/L

SCORTEN Score	Estimated Mortality Rate
0–1	3%
2	12%
3	35%
4	58%
≥ 5	>90%

Other prognostic models include “Age, Bicarbonate, Cancer, Dialysis and body surface area open due to detachment” (ABCD-10) and Re-SCORTEN. The Re-SCORTEN tool combines hematology characteristics with SCORTEN to improve accuracy (4,6). Clinical Risk Score for Toxic Epidermal Necrolysis (CRISTEN) incorporates 10 clinical parameters and patient history on admission (6,7). Ultimately, clinicians must consider findings on serial examinations to assess epidermal detachment and erosions of mucous membranes in conjunction with prognostic models when estimating prognosis.

Management

Initial management begins with prompt withdrawal of the suspected causative agent and all other non-essential medications (1,2). In the absence of universal treatment guidelines, several agents have been administered in attempts to slow or halt progression of the disease (2). Historically, corticosteroids were used to treat SJS/TEN, but studies have found that corticosteroids are associated with higher rates of infection and mortality and do not improve survival (3,6). Corticosteroids have also frequently been employed in combination with other therapies as outlined below (1,6). No survival benefit has been realized from corticosteroids, IVIG, Cyclosporine A or the combination of steroids with IVIG when compared to supportive care alone (2,7).

Intravenous immunoglobulin (IVIG) downregulates the Fas-mediated cascade of keratinocyte apoptosis (1,3,6). There are reports addressing the combination of IVIG and corticosteroids suggesting limited to no benefit, longer hospital stays, acute renal failure, and an increased mortality rate (1-3). IVIG is not indicated in patients with renal impairment (1,3).

There is limited research proposing Cyclosporin A administration as a treatment for SJS/TEN with a meta-analysis reporting lower mortality when compared to supportive care only (2). Chosen for its’ immunosuppressive effect and potential inhibition of apoptosis, Cyclosporin A has been proposed to decrease mortality and hasten time to reepithelialization (1,2). However, significant side effects have been observed such as neutropenia, pneumonia, nephrotoxicity, hepatotoxicity, hypertension and leukoencephalopathy (3,6). Cyclosporin A should be used with extreme caution in patients with pre-existing renal disease or poorly controlled diabetes (1,6).

Tumor Necrosis Factor (TNF) inhibitors may attenuate keratinocyte apoptosis (3). There are emerging reports of increased expression of TNF-a in patients with SJS/TENS. Cautious early reports detail that infliximab and etanercept, administered separately and in combination, may slow progression, support reepithelialization and decrease mortality, but more research is needed (2,3). TNF-a has been administered with and without steroids (1). TNF-a inhibitors increase the risk of opportunistic infections, including reactivation of tuberculosis. Emerging

science identified overactivation of the Janus kinase (JAK)/signal transducer as a key process in SJS/TEN. JAK inhibitors, such as tofacitinib and baricitinib, also inhibit keratinocyte death by suppressing excessive signaling.

Plasmapheresis, a procedure similar to hemodialysis, separates liquid plasma from cellular components containing drugs, cytotoxic factors and inflammatory cytokines, then discards the plasma and mixes the cells with replacement fluids and returns this to the patient (6). There is no evidence supporting a benefit of plasmapheresis in improving mortality or reepithelialization in patients with SJS/TEN (3).

Supportive care remains the primary treatment approach for SJS/TEN consisting of wound, ocular and oral care (1,2,5). Collaboration among the multidisciplinary team and consulting providers is paramount to supporting best outcomes. Rechallenging with the suspect medication is not indicated due to its potential life-threatening consequences. Daily oral, ocular and skin examinations and serial laboratory analysis to follow electrolytes and hematologic parameters are appropriate. Some studies support collection of frequent cultures of the skin (swabs), urine, sputum, and any other drainage. Body temperature and other vital signs must be closely monitored.

There is no consensus on the best wound care approach. Treatment varies greatly from aggressive debridement to a much more conservative anti-shear approach, leaving the denuded skin in place. Pain management is essential for wound care and mobility. Fluid and electrolyte management is essential due to insensible losses and organ involvement. Prophylaxis against stress ulcer prophylaxis and deep vein thrombosis are indicated. Nutritional support is paramount to supporting re-epithelialization and recovery. Mucosal lesions may limit oral intake and enteral nutritional support is indicated when patient's oral intake remains inadequate (1,4,7).

Airway compromise, cited to be present in approximately 40% of patients with SJS/TEN secondary to mucosal sloughing, may result in acute and chronic complications (4). Direct laryngoscopy can help track the extent of disease and guide therapy. Approximately 40% of SJS/TEN patients will require mechanical ventilation leading to an increased risk for pneumonia. Moderate impairment of alveolar dysfunction persists for around 2 months after acute hospitalization.

Prevention of sepsis is critical as it is a major cause of mortality for this population. Absence of natural protective coverage after mucosal and skin sloughing leads to increased nosocomial infections (1,4,6,7). Staphylococcus aureus is the most common bacteria isolated acutely, followed by Pseudomonas aeruginosa in patients experiencing prolonged hospitalization (3).

SJS/TENS places both male and female patients at increased risk of post-renal urogenital complications such as ureteral adhesions, stenosis and scarring, potentially impacting the renal and urinary systems (4). Gynecologic sequelae include vulvar and vaginal adenosis, vaginal stenosis, labial fusion, and even complete vaginal fusion (4,5). Gynecologic interventions are aimed at preventing tissue adhesion. Intravaginal steroids and dilators have been used to prevent long-term complications (5). Consultations with gynecology normally occur in the outpatient setting (4).

Present in 50%-80% of SJS/TEN patients, the most frequent ocular symptoms are conjunctivitis and corneal epithelial defects. Eyelid margin necrosis, epithelial loss of the conjunctiva and pseudomembrane development can lead to symblepharon formation, corneal erosions and even blindness. Chronic ocular sequelae following SJS/TEN may include lacrimal punctal occlusion, ectropion and entropion, trichiasis, distichiasis, severe dry eyes, symblepharon, corneal astigmatism, and photophobia.

Ocular sequela do not always correspond to the extent of skin loss. Treatment should begin as soon as symptoms are noted and not delayed while biopsy results are pending. Ophthalmology consultation is imperative for ongoing management. Early diagnosis and aggressive topical therapy with antibiotic ointment and steroids 4-6 times daily are necessary to prevent further injury and long-term chronic complications. Ophthalmology may perform removal of ocular pseudomembranes and consider amniotic membrane transplantation for severe cases. Amniotic membrane is placed as a patch covering the entire ocular surface to prevent ongoing damage, inhibit inflammation and promote re-epithelialization (3).

Topical Ocular Therapies:

- Topical Antibiotics- Levofloxacin 0.5-1.5% or Moxifloxacin 0.5% eye drops 3-4 times a day
- Topical corticosteroid – dexamethasone 1% or prednisolone acetate1% 2 -6 times daily
- Cyclosporin 0.05%-0.09% drops 2-4 times daily
- Preservative free eye lubricant instilled every hour and PRN (3)

Mental health counseling is essential to assist in processing the pain, disability and fear of recurrence and prolonged hospitalization related to SJS/TEN (1). Visible sequelae include scar formation, nail deformities, and dyspigmentation, similar to patients having suffered burn injuries (1,5). Depression, anxiety, and post-traumatic stress disorder have been reported following clinical recovery (1). Support should not end at hospital discharge (6).

Treatment

- General
  - Obtain medication and exposure history to identify inciting agent and avoid recurrent exposure
  - Confirm suspected allergy is entered in the electronic medical record
  - Discontinue all non-essential home medications
  - Supplemental oxygen prn and follow closely for pulmonary complications
  - Daily laboratory tests (at least initially)
- Wound care
  - Remove detached skin with soap, water and washcloth
  - Apply Mepilex AG to open areas on trunk and extremities; change weekly and as needed
  - Bacitracin to open areas of face or genitalia at least twice daily and prn dryness or soiling
  - If difficulty with voiding due to pain or extensive genitalia lesions, insert indwelling urinary catheter
  - Ocular care (as above)
  - Lip balm prn
  - Nasal saline rinses Q 4 hours prn
  - Perform medical photography to document extent of skin loss
- Pain control
  - Cautious pain management; avoid non-steroidal anti-inflammatory medications (acetaminophen has also been associated with SJS/TEN)
  - Order “Magic Mouthwash” for oral lesion discomfort - diphenhydramine, viscous lidocaine, aluminum, magnesium, simethicone suspension 5 ml swish and swallow before meals and at bedtime (scheduled but may have additional prn order)
- Nutrition
  - Consult clinical nutrition
  - Protein and calorie supplementation with high-calorie, high-protein diet
  - If patient is unable to maintain adequate intake, an enteral feeding tube should be inserted and supplemental nutrition ordered
- Prophylaxis measures
  - Enoxaparin or heparin (based on renal function) for deep venous thrombosis prophylaxis
  - Famotidine for gastrointestinal stress ulcer prophylaxis (watch closely for evidence of gastrointestinal bleeding due to mucosal sloughing)
  - Stool softeners for constipation
- Discharge considerations
  - Follow up with Ophthalmology, Gynecology, Gastroenterology and Dermatology as indicated
  - Avoid all unprotected sun exposure for one year
  - No swimming while any open areas persist
  - Avoid any products suspicious for containing the offending agent
  - Make all providers and family /friends aware of allergy
  - Obtain a Medic Alert bracelet.

Outcomes

SJS/TEN survivors suffer reduced life expectancy of approximately 9 years, hypothesized to result from avoidance of medications considered high-risk of instigating recurrent or worsened response (1). Time to re-epithelialization, mechanical ventilation, organ failure and hospital length of actors are key determinants of outcomes (2,7). Global mortality remains high at 34-50% (1). Ongoing advances leading to improved understanding of immune dysregulation, genetic susceptibility and other related mechanisms offer hope for development of new therapeutic approaches (6,7).

REFERENCES

1. Shah H, Parisi R, Mukherjee E, Phillips EJ, Dodiuk-Gad RP. Update on Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis: Diagnosis and Management. Am J Clin Derm 2024; *25*(6), 891-908.
2. Heuer R, Paulmann M, Mockenhaupt M, Nast A. Systemic immunomodulating therapies for epidermal necrolysis (Stevens-Johnson syndrome/toxic epidermal necrolysis): A systematic review and meta-analysis. J Dtsch Dermatol Ges 2026; 24(1):34-42.
3. Tóth G, Lukács A, Schirra F, et al. Ophthalmic Aspects of Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis: A Narrative Review. Ophthalmol Ther 2023; 1-17.
4. Murphy TJ, Fijany AJ, Swafford EP, Garcia JT, Vyas P, et al. The Outcomes of SJS/TEN: A Nationwide Analysis. J Burn Care Res 2026; *47*(3):723-729.
5. Samynathan A, Thakker S, Shupp JW, Pasieka HB. Stevens-Johnson syndrome/toxic epidermal necrolysis. J Am Acad Derm 2025; 93(4):1161-1172.
6. Watanabe Y, Hama N. Recent advances in the diagnosis and treatment of Stevens–Johnson syndrome/toxic epidermal necrolysis. Allergology International 2025; 74(3):345-355.
7. Daniela Guerrero Carrillo DG. Stevens Johnson Syndrome and Toxic Epidermal Necrolysis Updates on Management 2024; https://doi.org/10.5281/ZENODO.11562846.