# VANDERBILT VUNIVERSITY

## MEDICAL CENTER

**Guideline:** Management of patients with suspected Stevens-Johnson Revised Date: July 2025 Syndrome (SJS)/Toxic Epidermal Necrolysis (TEN) Review Date: July 2027

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#### Introduction

Stevens-Johnson syndrome (SJS) and Toxic epidermal necrolysis (TEN) are rare (1-10 per million people per year) severe, life-threatening mucocutaneous reactions characterized by painful erythematous rash, bullae, and erosions secondary to T-cell mediated hypersensitivity. They typically follow medication changes but may also be secondary to infection, malignancy, or idiopathic. Characteristic features include a prodrome of fever and lethargy followed within weeks to days of inciting event, presence of coalescent erythematous macules with purpuric centers, painful/tender blistering and <a href="mailto:epidermal">epidermal</a> detachment which is worse with light pressure (Nikolsky's sign), and ocular and mucosal involvement.

#### **Definitions:**

- Stevens Johnson Syndrome (SJS): Blisters/detached skin < 10% total body surface area (TBSA). Not all areas of erythema or rash are included in the percentage. Only sloughed areas or those with positive Nikolsy sign (epidermal detachment) are included.
- SJS-TEN Overlap: 10-30% TBSA
- Toxic Epidermal Necrolysis: >30% TBSA

Acute complications include infection, fluid losses, sepsis, and shock, as well as pneumonia, dysphagia, renal dysfunction, hepatitis, and death (20-30%). Ocular complications, mucosal stenosis (tracheal, esophageal, anal, vaginal, etc.), scarring, hypo- and hyper-pigmentation, as well as other skin and nail changes may occur in the chronic setting among survivors. <sup>III</sup>

#### Objectives

Provide guidance on the initial workup of patients with suspected SJS/TEN. Provide suggested management of patients with confirmed SJS/TEN.

#### Scope

Standardizing the workup and management of patients with confirmed or suspected SJS/TEN.

#### **Audience**

All providers caring for burn patients.

#### Guidance

- I. Management of referrals from outside hospitals via Access Center
  - A. If referral does not have definitive diagnosis of SJS/TENS:
    - Standard access center call will take place with the addition of photographs of the affected areas emailed to the access center and forwarded to the burn provider on call.
    - Burn provider on-call will review and if they believe the diagnosis is likely to be SJS/TEN, burn surgery will accept transfer to VUMC ED or directly to Burn ICU for evaluation and management.
    - If burn provider on-call does not believe that the condition is consistent with SJS/TEN and the referring facility does not have access to dermatology, then the transfer center will connect referring facility with VUMC Dermatologist

- on call to assess whether transfer to VUMC for the dermatologic condition is warranted.
- If there is any discrepancy, the patient may be transferred to the VUMC ED for evaluation and appropriate disposition. Burn surgery and dermatology will be consulted upon arrival.
- B. If referral is from an inpatient unit WITH biopsy-confirmed SJS/TEN:
  - Patients requiring ongoing hospitalization for their wounds may be accepted as a direct admission to the BICU using standard operating procedures.
  - SJS/TEN may be accepted at any stage, but patients who show clear signs of healing/resolution or minimal wound burden may be considered for clinic follow up at burn provider discretion.
- II. Initial Evaluation of the patient with possible SJS/TEN
  - A. Primary Survey (ABCs)
  - B. Complete history and physical exam paying particular attention to current medications, recent medication or dosing changes, recent illnesses, timing and progression of rash, history of independent risk factors for SJS and TEN (including immunosuppression/HIV, active cancer, common causative agents). Exam should include evaluation of the type of rash, presence and coalescence of blisters, presence of a Nikolsky's sign, and percent %TBSA that has already sloughed or would with slight pressure. Ocular and mucosal involvement must also be evaluated.
  - C. Recommend that all patients with suspected SJS/TEN have a consult by the burn surgery team. The burn surgery resident should staff the case with the burn fellow and burn surgeon in a prompt manner.
  - D. The hallmark of appropriate care is *immediate* cessation of offending agent and initiation of supportive care. When the offending agent is not obvious, the Algorithm for assessment of drug causality in epidermal necrolysis (ALDEN) mechanism may be employed (Appendix A)<sup>iii</sup>.
  - E. In patients in whom SJS/TEN is the likely diagnosis, the patient should be admitted to the burn ICU.
    - Airway/Breathing: Sloughing of the oral mucosa or bronchial tree can
      present a significant problem for the maintenance of an airway and
      appropriate gas exchange. Patients with difficulty controlling their
      secretions and/or difficulty phonating or with a muffled voice shouldbe
      considered for intubation in addition to those patients that meet
      traditional criteria for intubation and mechanical ventilation.
    - 2. Circulation: Patients with SJS/TEN <u>DO NOT</u> require aggressive fluid resuscitation unlike patients with large thermal burns. Fluid resuscitation should be based on the patient's physiologic status at the time of admission and their response to fluid administration. In patients with >20%TBSA involved, a Foley catheter should be placed for monitoring urine output and possible prevention of mucosal stenosis if the urethra is involved.
    - 3. Severity: The Severity-of-illness score for TEN (SCORTEN) is a highly accurate predictive model for mortality and should be calculated on the day of admission. (Appendix B).<sup>iv</sup>

Factors contributing to this include the following:

- i. Age>40
- ii. Malignancy
- iii. Tachycardia
- iv. >10% TBSA
- v. Serum urea >10mmol/L
- vi. Serum glucose >14mmol/L
- vii. Serum bicarbonate <20mmol/L

#### 4. Consultations:

- Dermatology: This is a required consult for all suspected cases of SJS/TEN
- ii. Ophthalmology: This is a required consult for all patients with SJS/TEN. $^{\lor}$
- iii. Gynecology: In female patients with concern for involvement of their vaginal or labial mucosa, a gynecology consultation is recommended for evaluation and *possible* management with vaginal dilators and/or packing as well as steroid cream.
- iv. Urology: A Foley catheter should be placed for patients with difficulty urinating (dysuria, hematuria, inability to void) as they may have sloughing of their GU tract. In this case, a urology consultation should be placed at time of Foley insertion to manage a potential urethral stricture.
- v. Allergy: This is a *required* consult for all suspected case sof SJS/TEN prior to discharge
- 5. Nutrition: If possible, oral feeding should be continued after admission. If a non-intubated patient is unable to swallow or unable to consume adequate calories (for example, in severe stomatitis), a feeding tube should be placed and tube feeds started. All intubated patients should have a feeding tube placed and tube feeds started onadmission.
- 6. Wound management: Based on % open TBSA
  - i. A Lund Browder is required on all patients with suspected SJS/TEN within 24 hours of admission.
  - ii. For SJS/TEN, as involvement progresses, the Lund Browder needs to be updated.
- 7. There are no consensus guidelines for wound care in SJS/TEN beyond minimizing additional tissue damage and preventing shearing injury. (Enescu CD, Elder AJ, Deirawan H, Moossavi M. To Debride or Not to Debride: A Review of Wound Management for Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. Cureus. 2024 Mar 1;16(3)) Prophylactic debridement of devitalized epidermis has not been shown to have improved outcomes compared to leaving detached skin in place. Unlike burns, there may be epidermal cells that are detached but may not be entirely necrosed or damaged. Therefore, there may be a benefit to leaving detached epidermis in situ once the blister fluid is evacuated as viable cells may aid in re-epithelialization.

- 8. Removal of blister fluid has been shown to be beneficial through removal of cytokines within the fluid, minimizing the risk of spreading separation, and allowing the epidermis to serve as a biological dressing.
- 9. Wound care: Conservative wound care includes gentle cleaning with topical antimicrobial cleanser to remove bioburden (particularly staph aureus and pseudomonas). Blisters are lanced or deflated and the epidermis is allowed to adhere to the wound bed. The wounds are then covered in a durable dressing (such as synthetic, biologic, or nanocrystalline silver-coated dressings) and changed per protocol taking care to minimize shear.
- 10. Operative or more aggressive debridement would be at the discretion of the burn surgeon with consideration of the patient's clinical course.
- 11. Systemic Management: Immediate cessation of all potential inciting agents is paramount to recovery. Additional systemic therapy should be discussed in conjunction with dermatology. Immunomodulating medications, such as etanercept, have shown promising results compared to IVIG or steroids although studies are small. (Wang et al. Randomized, controlled trial of TNF-α antagonist in CTL-mediated severe cutaneous adverse reactions. 2018; Jacobsen A, Olabi B, Langley A, et al. Systemic interventions for treatment of Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and SJS/TEN overlap syndrome. Cochrane Database Syst Rev. 2022). Use of these agents must be a discussion between the burn surgeon, dermatology, and the intensivist.
- 12. Prevention: Preventing recurrence of SJS/TENS involves identification of the inciting agent and mitigating risk of re-injury. A consult to Allergy will be placed prior to discharge as there are multiple factors (including genetic predispositions) that can be evaluated to reduce risk of recurrence.
- 13. Research: Multiple, concurrent clinical trials are occurring on this patient population and every patient suspected of having a diagnosis of SJS or TEN must be screened by the research teams. As soon as the patient is accepted or arrives, the research team must be paged at (615) 831-4277. If the patient is coming from outside the hospital, any information about them should be relayed to the research team by phone and by email (sis@vumc.org), as appropriate (i.e., Images, MRN, etc.)
- F. In patients in whom SJS/TEN is possible but not a clear diagnosis, a punch biopsy will be performed by the dermatology service. This biopsy should be taken at an edge of sloughed tissue to involve normal tissue as well.
  - 1. If the patient is admitted to another service, and the burn service should be consulted and will follow as needed and make recommendations. If the diagnosis is not SJS, the burn team will sign off. If the diagnosis is SJS/TENS, burn surgery will assume care and the patient will be transferred to an appropriate bed in the burn unit.
  - 2. If the patient is a consultation from the ED and SJS is suspected, burn surgery will admit the patient and manage until biopsy results are confirmed. ICU vs. floor admission will be at the discretion of the attending physician(s). If, after biopsy, the diagnosis is not SJS, the patient

will be transferred to an appropriate medicine team with dermatology consultation.

G. In patients in whom the diagnosis is not SJS/TEN, the burn service may sign off at the discretion of the consulting surgeon with a recommendation for dermatology consultation.

<sup>i</sup> Lerch M, et al. Current perspectives on stevens-johnson syndrome and toxic epidermal necrolysis. Clinical Rev Allergy Immunol 2018; 54 :147-176

<sup>&</sup>quot;Charlton OA, et al. Toxic epidermal necrolysis and stevens-johnson syndrome: a comprehensive review. Adv Wound Care. 2019;9 (7):426-439

Fouchard N, et al. SCORTEN: A Severity-of-Illness Score for Toxic Epidermal Necrolysis. J Inv Derm 2000;115(2):149-153

iv Sassolas B et al. ALDEN, an algorithm for assessment of drug causality in Stevens-Johnson Syndrome and toxic epidermal necrolysis: comparison with case-control analysis. Clinical pharmacology and therapeutics 2010; 88(1): 60–68

<sup>&</sup>lt;sup>v</sup> Saeed HN, Chodosh J. Ocular manifestations of Stevens-Johnson syndromeand their management. *Current opinion in ophthalmology*. 2016;27(6):522-529

## **Appendix A**

Criterion	Values	Rules to apply	
Delay from initial drug	Suggestive +3	From 5 to 28 days	-3 to 3
component intake to	Compatible +2	From 29 to 56 days	
onset of reaction (index day)	Likely +1	From 1 to 4 days	
(macx day)	Unlikely -1	> 56 days	
	Excluded -3	Drug started on or after the index day	
		In case of previous reaction to the same drug, only changes for: Suggestive: +3: from 1 to 4 days Likely: +1: from 5 to 56 days	
Drug present in the body on index day	Definite 0	Drug continued up to index day or stopped at a time point less than five times the elimination half-life <sup>a</sup> before the index day	-3 to 0
	Doubtful -1	Drug stopped at a time point prior to the index day by more than five times the elimination half-life <sup>a</sup> but liver or kidney function alterations or suspected drug interactions <sup>b</sup> are present	
	Excluded -3	Drug stopped at a time point prior to the index day by more than five times the elimination half-life <sup>a</sup> , without liver or kidney function alterations or suspected drug interactions <sup>b</sup>	
Prechallenge/rechallenge	Positive specific for disease and drug: 4	SJS/TEN after use of same drug	-2 to 4
	Positive specific for disease or drug: 2	SJS/TEN after use of similiar drug or other reaction with same drug	
	Positive unspecific: 1	Other reaction after use of similar <sup>c</sup> drug	
	Not done/unknown: 0	No known previous exposure to this drug	
	Negative - 2	Exposure to this drug without any reaction (before or after reaction)	
Dechallenge	Neutral 0	Drug stopped (or unknown)	-2 or 0
	Negative - 2	Drug continued without harm	
Type of drug (notoriety)	Strongly associated 3	Drug of the "high-risk" list according to previous case-control studies <sup>d</sup>	-1 to 3
	Associated 2	Drug with definite but lower risk according to previous case-control studies <sup>d</sup>	
	Suspected 1	Several previous reports, ambiguous epidemiology results (drug "under surveillance")	
	Unknown 0	All other drugs including newly released ones	
	Not suspected -1	No evidence of association from previous epidemiology study <sup>d</sup> with sufficient number of exposed controls <sup>c</sup>	
Other cause	Possible –1	Intermediate score = total of all previous criteria	-11 to 1
Juier cause	rossible -1	Rank all drugs from highest to lowest intermediate score	-1
		If at least one has an intermediate score > 3, subtract 1 point from the score of each of the other drugs taken by the patient	

<sup>&</sup>lt;0, Very unlikely; 0-1, unlikely; 2-3, possible; 4-5, probable; ≥6, very probable

ATC, anatomical therapeutic chemical; SJS, Stevens-Johnson syndrome; TEN, toxic epidermal necrolysis

<sup>&</sup>lt;sup>a</sup> Drug (or active metabolite) elimination half-life from serum and/or tissues, taking into into account kidney function for drugs predominantly cleared by kidney and liver function for those with high hepatic clearance. <sup>b</sup> Suspected interaction was considered when more than five drugs were present in a patient's body at the same time. <sup>c</sup> Similar drug = same ATC code up to the fourth level (chemical subgroups). <sup>d</sup> Definitions for "high risk," "lower risk," and "no evidence of association" in Methods

## **Appendix B**

Independent prognosis factors of TEN.			
Variables	Odds ratio (95% CI <sup>a</sup> )	p-value	
Age (≥ 40 y old)	2.7 (1.0–7.5)	0.05	
Heart rate (≥ 120 per min)	2.7 (1.0-7.3)	0.04	
Cancer/hematologic malignancy	4.4 (1.1–18.0)	0.04	
BSA <sup>b</sup> involved at day 1			
< 10%	1		
10-30%	2.9 (0.9–8.8)	0.04	
> 30%	3.3 (1.2–9.6)		
Serum urea level (> 10 mmol per liter)	2.5 (0.9–7.3)	0.09	
Serum bicarbonate level (< 20 mmol per liter)	4.3 (1.1–16.0)	0.03	
Serum glucose level (> 14 mmol per liter)	5.3 (1.5–18.2)	< 0.01	
SCORTEN	2.45 (2.26–5.25)	< 10-4	

<sup>a</sup>Confidence interval; <sup>b</sup>BSA, body surface area detached. SCORTEN represents the number of abnormal parameters among the seven independent prognosis factors (a weight of 1 was assigned to each independent parameter), odds ratio corresponds to one score points.

## Mortality rates and relative risks according to the SCORTEN

SCORTEN	N No. of patients	Mortality rate		Odds ratio (95% CI*)
		Percent	95% CI	(93% CI)
0–1	31	3.2	(0.1–16.7)	1
2	66	12.1	(5.4-22.5)	4.1 (0.5-35.2)
3	34	35.3	(19.8-53.5)	14.6 (2.0-138.0)
4	24	58.3	(36.6-77.9)	42.0 (4.8-367.0)
≥ 5	10	90.0	(55.5–99.8)	270.0 (15.0-487.0)

<sup>a</sup>Confidence interval, SCORTEN represents the number of abnormal parameters among the seven independent prognosis factors (a weight of 1 was assigned to each independent parameter).