

# Improving the evaluation of patients with Stevens-Johnson Syndrome and toxic epidermal necrolysis

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## Background

- Stevens-Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe, mucocutaneous adverse reactions typically induced by medication that results in extensive necrosis and detachment of the epidermis.<sup>1</sup>
- SJS and TEN exist as a continuum and are classified by the percent of body surface area (BSA) involved:<sup>2</sup>
  - < 10% of BSA involved - SJS
  - 10-30% of BSA involved - SJS/TEN overlap
  - >30% of BSA involved - TEN
- Fortunately, SJS/TEN is a rare condition with an estimated incidence of 5-6 cases per million individuals per year.<sup>3</sup>
- Risk factors for SJS/TEN include HIV, connective tissue disease, malignancy, older age, and Black or Asian ethnicity.<sup>4-8</sup>
- High-risk medications include allopurinol, lamotrigine, sulfamethoxazole, carbamazepine, and phenytoin.<sup>5</sup>
- The overall mortality for patients with TEN is greater than 30%.<sup>8</sup>
- The most common cause of death in these patients is sepsis.<sup>9</sup>
- Commonly identified pathogens include *S. aureus* and *P. aeruginosa*.<sup>10</sup>

## Objective

In this study, we aim to identify risk factors that may expedite the diagnosis and subsequent treatment of SJS/TEN and/or better prognosticate disease severity.

## Methods

We are performing a retrospective analysis on 4,475 patients seen at an HCA Healthcare facility in the United States.

### Inclusion Criteria

- Primary diagnosis of SJS, SJS/TEN, or TEN
- Age: 18-88
- Years: 2015-2022
- HCA patient

### Collected Labs

- CMP
- Mg
- Phos
- CBC + Eosinophils
- Hgb A1c
- Procalcitonin

### Analysis

Analysis will be performed by the HCA national research team with the intent of finding an association with SJS/TEN continuum

## Images



## Discussion

- SJS/TEN is usually preceded by a non-specific prodrome including fever, coryza, cough, sore throat, conjunctivitis, and myalgias. A set of tests with proven positive and negative predictive value for SJS/TEN would allow for earlier recognition of the disease.
- Early identification of SJS/TEN is crucial for minimizing morbidity and mortality.
- Prompt withdrawal of the culprit drug in SJS/TEN, particularly *before* the first definitive dermatologic signs, has been associated with lower mortality and better prognosis.<sup>13</sup>
- Immediate transfer to a burn unit allows for necessary supportive care and improves survival.
- If used, adjuvant pharmacotherapies such as cyclosporine or TNF blockers must be initiated early in the course of disease for notable benefit.<sup>14</sup>
- Without early and aggressive supportive measures, the patient is at risk of fatal complications such as sepsis, ARDS, shock, or DIC and debilitating long-term sequelae such as widespread scarring, lung disease, and blindness.

## References

- Roujeau JC, Stern RS. Severe adverse cutaneous reactions to drugs. *N Engl J Med*. 1994 Nov 10;331(19):1272-85. doi: 10.1056/NEJM199411103311906. PMID: 7794310.
- Bastuji-Garin S, Rzany B, Stern RS, Shear NH, Naldi L, Roujeau JC. Clinical classification of cases of toxic epidermal necrolysis, Stevens-Johnson syndrome, and erythema multiforme. *Arch Dermatol*. 1993 Jan;129(1):92-6. PMID: 8420497.
- Sekula P, Dunant A, Mockenhaupt M, Naldi L, Bouwes Bavinck JN, Halevy S, Kardaun S, Sidoroff A, Liss Y, Schumacher M, Roujeau JC, RegiSCAR study group. Comprehensive survival analysis of a cohort of patients with Stevens-Johnson syndrome and toxic epidermal necrolysis. *J Invest Dermatol*. 2013 May;133(5):1197-204. doi: 10.1038/jid.2012.510. Epub 2013 Feb 7. PMID: 23398396.
- Yang C, Mosam A, Mankalia A, Dlova N, Saavedra A. HIV infection predisposes skin to toxic epidermal necrolysis via depletion of skin-directed CD4+ T cells. *J Am Acad Dermatol*. 2014 Jun;70(6):1096-102. doi: 10.1016/j.jaad.2013.12.025. Epub 2014 Mar 12. PMID: 24629995.
- Mockenhaupt M, Viboud C, Dunant A, Naldi L, Halevy S, Bouwes Bavinck JN, Sidoroff A, Schneek J, Roujeau JC, Fichtner A. Stevens-Johnson syndrome and toxic epidermal necrolysis: assessment of medication risks with emphasis on recently marketed drugs. The EuroSCAR-study. *J Invest Dermatol*. 2008 Jan;128(1):35-44. doi: 10.1038/sj.jid.5710103. Epub 2007 Sep 6. PMID: 17805550.
- Gillis NK, Hicks JK, Bell GC, Daly AJ, Kanetsky PA, McLeod HL. Incidence and Etiology of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in a Large Cancer Patient Cohort. *J Invest Dermatol*. 2017 Sep;137(9):2021-2023. doi: 10.1016/j.jid.2017.05.010. Epub 2017 May 23. PMID: 28549653; PMCID: PMC5900641.
- Chabzy G, Madini C, Haddad C, Lebrun-Vignes B, Henery F, Ingen-Housz-Oro S, Gonzalez-Chiappe S, Wolkenstein P, Chosidow O, Mahr A, Fardet L. Incidence of and mortality from epidermal necrolysis (Stevens-Johnson syndrome/toxic epidermal necrolysis) in France during 2003-16: a four-source capture-recapture estimate. *Br J Dermatol*. 2020 Mar;182(3):618-624. doi: 10.1111/bjd.18424. Epub 2019 Oct 22. PMID: 31396952.
- Hsu DY, Brieve J, Silverberg NB, Silverberg JI. Morbidity and Mortality of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in United States Adults. *J Invest Dermatol*. 2016 Jul;136(7):1387-1397. doi: 10.1016/j.jid.2016.03.023. Epub 2016 Mar 30. PMID: 27039263.
- Revuz J, Penso D, Roujeau JC, Guillaume JC, Payne CR, Wexler J, Touraine R. Toxic epidermal necrolysis. Clinical findings and prognosis factors in 87 patients. *Arch Dermatol*. 1987 Sep;123(9):1160-5. doi: 10.1001/archderm.123.9.1160. PMID: 3632000.
- de Prost N, Ingen-Housz-Oro S, Duong TA, Valeryie-Allanore L, Legrand P, Wolkenstein P, Brochard L, Brun-Buisson C, Roujeau JC. Bacteremia in Stevens-Johnson syndrome and toxic epidermal necrolysis: epidemiology, risk factors, and predictive value of skin cultures. *Medicine (Baltimore)*. 2010 Jan;89(1):28-36. doi: 10.1097/MD.0b013e3181c94290. PMID: 20075702.
- Harris V, Jackson C, Cooper A. Review of Toxic Epidermal Necrolysis. *International Journal of Molecular Sciences*. 2016; 17(12):2135. https://doi.org/10.3390/ijms17122135
- Lienhojva, R. J. (2022). Disease severity and status in Stevens-Johnson syndrome and toxic epidermal necrolysis: Key knowledge gaps and research needs. *Frontiers in Medicine*, 9, 901401.
- Garcia-Dovai I, LeCleach L, Bocquet H, Otero X, Roujeau J. Toxic Epidermal Necrolysis and Stevens-Johnson Syndrome: Does Early Withdrawal of Causative Drugs Decrease the Risk of Death? *Arch Dermatol*. 2000;136(3):323-327. doi: 10.1001/archderm.136.3.323
- Y.K. Heng, H.Y. Lee, J.-C. Roujeau. Epidermal necrolysis: 60 years of errors and advances. *British Journal of Dermatology*, Volume 173, Issue 5, 1 November 2015, Pages 1250-1254, https://doi.org/10.1111/bjd.13989

This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.

- Images show diffuse erythema, flaccid blisters, and erosions on the trunk and extremities