

DRUGS ARE ONLY PROVEN CAUSE SJS/TEN

1. **“Stevens–Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and SJS–TEN overlap are severe mucocutaneous conditions, *mostly caused by reactions to drugs.*”**

(Torres-Navarro, I, et al. Systemic therapies for Stevens-Johnson syndrome and Toxic Epidermal Necrolysis: a SCORE-TEN Based Systematic Review and Meta-analysis. *J Eur Acad Dermatol Venereol.* 2021 Jan;35(1):159-171.)

2. **“Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) is a rare, *severe drug reaction* associated with significant mortality.”**

(Wang, LL, et al. Long-term sequelae from Stevens-Johnson syndrome/toxic epidermal necrolysis in a large retrospective cohort. *J Am Acad Dermatol.* March 2021; 84 (3): 784-786.)

3. **“Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis Syndrome (TENS) are severe and *potentially lethal adverse drug reactions* characterized by acute inflammation and subsequent necrosis of the skin, mucous membranes, and ocular surface.**

(Sanford, A, et al. ALDEN Based Determination of Culprit Drugs in Stevens-Johnson Syndrome: A 15-year Single Center Review. *American Burn Association 52nd Annual Meeting*, 2019, S96.)

4. **“Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are considered *a delayed-type hypersensitivity reaction to drugs.*”**

(Lerch, M. et al. Current Perspectives on Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. *Clin Rev Allergy Immunol.* 2018 Feb;54(1):147-176.)

5. **“Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are considered the most severe types of *cutaneous adverse reactions to drugs*, with high morbidity and mortality rates.”**

(Olteanu, et al. Severe Physical Complications among Survivors of Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis. *Drug Saf* (2018) 41:277–284.)

6. **“Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are rare but life-threatening mucocutaneous diseases that predominantly occur as *adverse reactions to newly administered drugs.*”**

(Frey, et al. Epidemiology of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in the UK. *Journal of Investigative Dermatology* (2017) 137:1240-1247.)

7. **“Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are severe adverse reactions to drugs that cause a life-threatening eruption of mucocutaneous blistering and epithelial sloughing.”**

(Lee, HY, et al. Long-term Complications of Stevens–Johnson syndrome/toxic epidermal necrolysis (SJS/TEN): The Spectrum of Chronic Problems in Patients who Survive an Episode of SJS/TEN Necessitates Multidisciplinary Follow Up. *British Journal of Dermatology* (2017) 177:924–935.)

8. **“The reaction is usually initiated by, and primarily directed against, drugs.”**

(Roujeau, JC. Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. *Drug Safety*, 2013 36:145-146)

9. **“In the current classification, drugs appear to be the only cause of SJS/TEN.”**

“A large body of evidence suggests that TEN is an adverse drug reaction resulting from a specific alteration in drug metabolism.”

“By contrast, there is no association between TEN and other viral infections, including human Herpesvirus 6 and 7, cytomegalovirus and parvovirus B19.”

(Paquet, et al. New Insights in Toxic Epidermal Necrolysis (Lyell’s Syndrome) Clinical Considerations, Pathobiology and Targeted Treatments Revisited. *Drug Safety* 2010; 33(3):189-212.)

10. **“While SJS and TEN are almost exclusively attributed to drugs, EEMM is mainly triggered by infectious agents and infection.”**

“About 5 % of patients with SJS and TEN are infected with HIV, yet neither HIV infection nor other infections appear to be independent risk factors for SJS and TEN.”

(Mockenhaupt, M. Severe drug-induced skin reactions: clinical pattern, diagnostics and therapy. *J Dtsch Dermatol Ges* 2009; 7(2):142-60.)

11. **“We conducted a pooled analysis combining the data from these 2 studies to determine medication risk factors of SJS/TEN in children 15 years of age or younger. The aims were to (1) describe the characteristics of cases, (2) determine if drugs suspected to be risk factors in the general population were confirmed among children, and (3) investigate if other drugs or factors were associated with these diseases in children.”**

“Nonmedication factors have also been hypothesized to increase the risk of SJS/TEN: HIV, herpesvirus or *Mycoplasma pneumoniae*, radiotherapy, lupus erythematosus, and collagen vascular disease.

“We did not confirm any suspected nonmedication risk factors.”

“Our study did not show any significant association with recent herpes infection.”

(Levi, et al. Medications at Risk of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Children: A Pooled Analysis. *Pediatrics*, 2009; 123(2): e297-e304.)

12. **Reviewed 61 patients between 1985-1995. “All cases of TEN were attributable to drugs.”**

“All three of the disorders [EM, SJS & TEN] have been linked to drugs, with TEN being exclusively attributed to this factor.”

(Foreman, et. al. Erythema Multiforme, Stevens-Johnson syndrome and Toxic Epidermal Necrolysis in Children. *Drug Safety* 2002; 25(13): 965-972.)

13. **“The generally proven cause of TEN is an adverse drug reaction resulting from a specific formation of toxic drug metabolites, perhaps in the skin itself.”**

(Paquet, P, et al. Treatment of Drug-induced toxic epidermal necrolysis (Lyell's syndrome) with intravenous human immunoglobulins. *Burns*, 2001: Sep;27(6): 652-655.)

14. **“Both diseases [SJS & TEN] are primarily, if not solely, caused by drugs.”**

(Garcia-Doval, et. al., “Toxic Epidermal Necrolysis and Stevens Johnson Syndrome: : does early withdrawal of causative drugs decrease the risk of death? *Arch Dermatol*, 2000 136:323-327.)

15. **“*The herpes simplex virus is not a cause of Stevens Johnson syndrome, which is clearly related to a drug in over two thirds of cases.*”**

(Roujeau, JC Severe Drug-Induced Blistering Disorders. *Rev. Rhum. [Engl. Ed.]*, 1997; 64(1):5-9.)

16. **“SJS and TEN usually with mucous membrane involvement are characterized by blisters provoked by epidermal necrosis and arising on discrete or confluent macules widespread or predominant on the central parts of the body. *Herpes virus has no role in this severe disorder, which is mainly provoked by drug reactions.*”**

(Roujeau, JC. Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis are Severity Variants of the Same Disease which differs from Erythema Multiforme. *Journal of Dermatology* 1997; 24:726-729)

17. **“EM, SJS & TEN may represent variants of the same disease process. ... The more severe the reaction, *the more likely it is that it has been drug-induced.*”**

(Knowles, et. al. Serious dermatologic reactions in children. *Current Opinions in Pediatrics* 1997; 9:388-395.)

18. **“...Stevens Johnson syndrome is usually drug-induced.” *There are no alternative causes of TEN that are not related to drugs.*”**

(Roujeau, et. al. Severe Cutaneous Reactions to Drugs. *NEJM* 1994; 331(19):1271-1285.)

19. **“Drugs are considered as the most important, *if not the only, cause of TEN.*”**

(Correia, O, et al. Evolving Pattern of Drug-Induced Toxic Epidermal Necrolysis. *Dermatology* 1993; 186:32-57.)

20. **“Accumulated clinical evidence *points to drugs as the most important, if not the only cause of TEN.*”**

Roujeau, JC. Toxic Epidermal Necrolysis (Lyell syndrome): Review. *J Amer Acad Dermatol.* 1990; 23(6), part 1:1039-1061.)

21. **“[T]he consensus from the TEN international workshop in Creteil, France, in 1985, was that to date, *no cause other than drug has been clearly documented.*”**

(Roujeau, JC. Clinical Aspects of Skin Reactions to NSAIDs. *J. Rheum.* 1987 (Suppl. 65):131-134.)