

Review

Current Advances in the Medical Management of Stevens-Johnson's Syndrome

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Abstract

Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are potentially life-threatening type IV immune reactions characterized by systemic inflammation mediated by cytotoxic T lymphocytes resulting in epidermal detachment and extensive necrosis. Although infrequent, the main concern across the SJS/TEN spectrum is its mortality, morbidity and associated financial burden. To date, there are no definitive recommendations regarding optimal treatment regimens; therefore, early diagnosis, prompt withdrawal of the culprit drug, and interdisciplinary consultations are vital to avoid disease progression. It is hard to assess the efficacy of novel therapies when the "conventional", well-founded therapies with corticosteroids and cyclosporine are still under investigation. However, optimal posology is still under debate, as well as possible combined therapies. Other drugs that have shown to have a possible beneficial effect, like etanercept and n-Acetylcysteine, are still under investigation, given the insufficient number of investigations and small samples. New pharmacological approaches have been proposed in the last decade to improve outcomes across the SJS/TEN spectrum. This review aims to analyze novel approaches for SJS/TEN and assess their efficacy and safety compared to currently available treatments.

Keywords: Stevens-Johnson syndrome; toxic epidermal necrolysis; medical treatment; corticosteroids; cyclosporine



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1. Introduction

Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and SJS/TEN overlap are severe phenotypes within the same spectrum of severe epidermal necrolysis [1]. They are classified according to the percentage of detached or detachable body surface area (BSA): SJS involves <10% BSA, SJS/TEN overlap involves 10–30%, and TEN involves >30% [2]. This distinction is clinically important because baseline severity, complications, and mortality differ across the spectrum. Any phenotype may also involve extracutaneous organs, complicating treatment and recovery [3].

SJS/TEN is rare; as a result, it is difficult to establish accurate epidemiological data without involving substantially large populations [4]. The incidence of SJS/TEN is between 1 and 6 cases per one million people [5,6]. These conditions are known for affecting individuals of all ages, but the highest incidence is in adults older than 40. Moreover, Asian

and black people have an increased risk of developing SJS/TEN [7,8]. Likewise, most cases tend to appear in winter or early spring, which correlates with seasonal antibiotic prescriptions [4]. Regarding its etiology, 50–95% of the cases are directly related to medication exposure; however, infectious and idiopathic causes can represent up to 20% of the cases, depending on the examined population [9]. While numerous drugs are tagged as a possible cause of SJS, the most frequently associated drugs are anticonvulsants, antibiotics, and nonsteroidal anti-inflammatory drugs (NSAIDs) [10].

Although infrequent, the principal concern across the SJS/TEN spectrum is its mortality, morbidity and associated financial burden. Mortality has shown an increase depending on the severity of the presentation and is substantially higher in TEN than in SJS. Moreover, patients with these conditions have a very prolonged length of stay and high care costs, scaling up to US\$57,000 per patient [7]. To date, there are no definitive recommendations regarding optimal treatment regimens; therefore, early diagnosis, prompt withdrawal of the culprit drug, and interdisciplinary consultations are vital to avoid disease progression [11]. New pharmacological approaches have been proposed in the last decade to improve outcomes across the SJS/TEN spectrum. This review aims to analyze novel approaches towards SJS/TEN and assess their efficacy and safety compared to currently available treatments.

2. Methods

A narrative literature search was performed in PubMed/MEDLINE and Google Scholar from database inception to 15 September 2026. Search terms combined “Stevens-Johnson syndrome”, “toxic epidermal necrolysis”, and “SJS/TEN overlap”, “treatment”, “corticosteroids”, “cyclosporine”, “intravenous immunoglobulin”, “etanercept”, “plasma-pheresis”, “JAK inhibitors”, “IL-15”, “granulysin”, “HLA”, and “SCORTEN”. English-language clinical studies, systematic reviews, meta-analyses, and relevant guidelines were considered, with priority given to comparative studies and clinically relevant outcomes. Because this was a narrative review, no formal meta-analysis was performed.

3. Stevens-Johnson Syndrome: Is There Space for Novel Strategies?

The first step for proper management of SJS/TEN is establishing the diagnosis. As simple as it might sound, this represents a formidable task. First, no current available guideline, neither the Indian nor the British variant, provides clear diagnostic criteria for this condition [12,13]. To further complicate matters, making differential diagnoses only by clinical variables is nearly impossible. The most distinctive hallmark of SJS is the involvement of mucous membranes, which distinguishes it from other conditions like erythema multiforme; however, it is not pathognomonic [14]. Although no available test can diagnose SJS by itself, a skin biopsy can help to rule out other conditions. A histopathology analysis reporting full-thickness epidermal necrosis, subepidermal bulla, and scanty inflammatory infiltrate in the papillary dermis is supportive of SJS/TEN [15].

The immunopathogenesis of SJS/TEN is driven by a drug-specific, Type IV delayed-type hypersensitivity reaction where the immune system destroys skin and mucous membrane cells. It begins when a culprit medication or its metabolite interacts with specific Human Leukocyte Antigens (HLA Class I) on antigen-presenting cells. This interaction forms a complex that alters cell-surface peptides, activating clonally expanded cytotoxic CD8⁺ T lymphocytes and natural killer (NK) cells. Once activated, these immune cells infiltrate the skin and flood the local tissue with massive amounts of highly destructive cytotoxic proteins, most notably granulysin, alongside perforin and granzyme B. Concurrently, upregulated Fas-Fas Ligand (FasL) interactions and key pro-inflammatory cytokines—such as tumor necrosis factor-alpha (TNF- α) and interferon-gamma (IFN- γ)—amplify the signal,

leading to widespread, full-thickness keratinocyte apoptosis and programmed necroptosis. This occurs when monocyte-derived Annexin A1 binds to Formyl Peptide Receptor 1 (FPR1) on keratinocytes, triggering a highly inflammatory lytic cascade mediated by RIP3 kinase pathways [16,17].

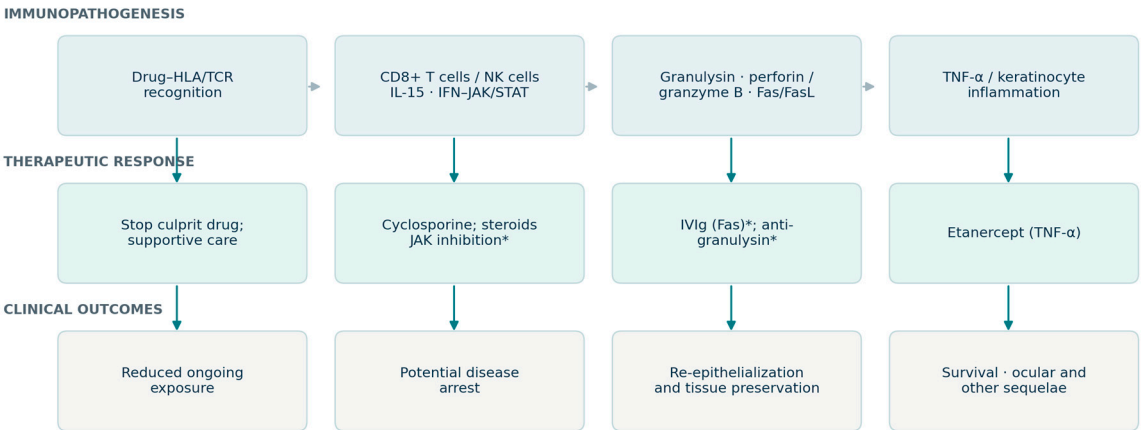
Likewise, the severity-of-illness score for TEN (SCORTEN) is a mortality prognostication tool for epidermal necrolysis. It was developed in 2000 by a team in France, using 165 patients to identify significant variables via a logistic regression model and 75 patients to internally validate the results. From this model, the researchers identified seven equally weighted parameters that are risk factors for death: age > 40 years, malignancy, heart rate > 120 beats per minute, initial percentage of epidermal detachment > 10%, serum urea > 10 mmol/L, serum glucose > 14 mmol/L, and bicarbonate < 20 mmol/L. However, SCORTEN is a prognostic rather than a treatment-selection tool; its calibration may vary across populations, and it does not eliminate confounding in observational treatment comparisons [18].

Treatment workup typically includes both general and pharmacological measures. Considering the high prevalence of drug-induced SJS/TEN, early withdrawal of the suspected drug is central to treating SJS/TEN. It has been extensively demonstrated that earlier drug withdrawal is associated with a better prognosis; likewise, drugs with longer half-lives have increased mortality risk [19]. Maintaining body temperature, proper fluid-electrolyte balance, and an aseptic environment are crucial [15]. Coverage of the denuded skin reduces wound infections and improves its healing, especially when using biomembranes [20]. Compromise of other organs is relatively frequent, mainly concerning the ophthalmologic system; therefore, early interdisciplinary consultation is crucial to avoid further complications [21,22]. Early ophthalmologic assessment and close monitoring are essential because ocular sequelae are a major source of long-term morbidity. In patients with significant eyelid margin involvement, pseudomembranes, or corneal or conjunctival epithelial defects, early amniotic membrane transplantation should be considered during the acute phase to reduce ocular surface scarring and vision-threatening complications [22] (Figure 1).

Regarding medical treatment, recommendations remain heterogeneous, and most interventions lack high-certainty comparative evidence. Systemic corticosteroids are widely used in some regions, particularly early in the disease course, but their mortality benefit remains controversial because studies vary in dose, timing, and case mix [23–25]. Initial therapy with high-dose steroids, like methylprednisolone pulses (MPP), has significantly decreased mortality in 377 American patients [26]. However, no randomized trials have established the comparative efficacy of steroids, but most available data suggest that it is the most promising alternative [27]. Second in frequency is cyclosporine, which significantly decreases disease progression because of its mechanism of action related to granulysin and keratinocyte apoptosis [28]. Other approaches, including tacrolimus, intravenous immunoglobulin (IVIg), N-acetylcysteine (NAC), biologic therapy, and plasmapheresis, have also been used and are reviewed below [29] (Figure 2).

Systemic corticosteroids have long been used in SJS/TEN. Earlier studies raised concerns about infection, delayed wound healing, and mortality [30], whereas later observational studies and meta-analyses suggested possible benefit, particularly when therapy is initiated early [31]. However, heterogeneous regimens, treatment timing, supportive care, and patient populations prevent a firm conclusion regarding mortality benefit. Potential benefit must be balanced against infectious, metabolic, and wound-healing complications. Increased survival rates, decreased complications, and improved clinical course were the benefits of corticosteroids and cyclosporine. No other drugs tested within newer studies had significant improvements compared to supportive therapy alone [32–34].

A Integrated immunopathogenesis and therapeutic targets



B Therapeutic window across the clinical course

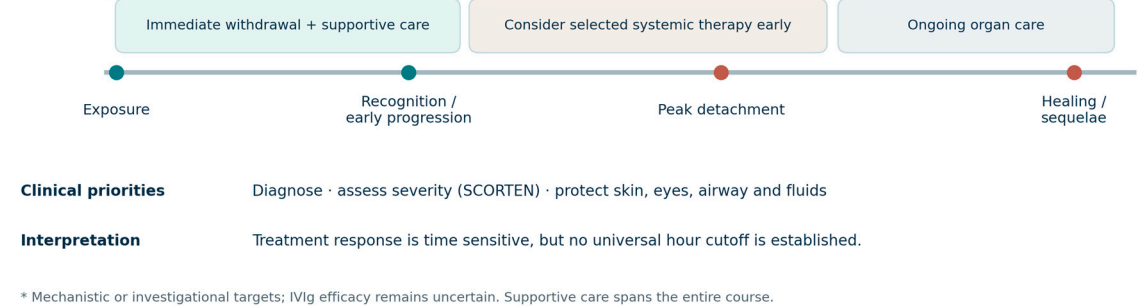


Figure 1. (Panel (A)) Integrated immunopathogenesis–therapeutic target map in three layers: immune mechanisms, therapeutic responses, and clinical outcomes. (Panel (B)) Schematic therapeutic window across the clinical course of SJS/TEN. The timeline is conceptual rather than scaled to hours or days. Immediate culprit-drug withdrawal and multidisciplinary supportive care remain priorities throughout; systemic therapies require individualized assessment, and emerging targets are investigational.

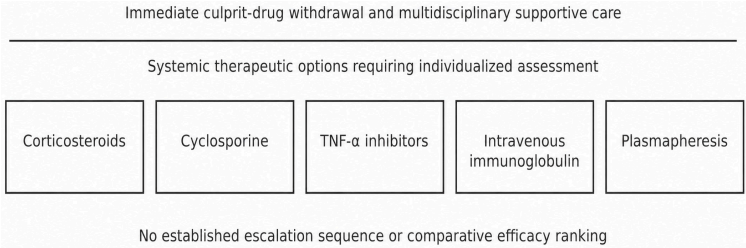


Figure 2. Therapeutic options for Stevens-Johnson syndrome and toxic epidermal necrolysis. Prompt culprit-drug withdrawal and multidisciplinary supportive care are foundational. Systemic therapies are displayed without an escalation sequence or ranking of comparative efficacy; their use requires individualized assessment of disease severity, treatment timing, contraindications, and the limitations of the available evidence.

Recent evidence suggests that, when corticosteroids are selected, early short-course or pulse regimens may be preferable to prolonged exposure. It is well-established that corticosteroids increase the risk of infections and delay wound healing. These disadvantageous effects are more likely to appear in long-term therapies [35]. A small sample study reported that short-term therapy with dexamethasone pulses was associated with favorable outcomes in patients with SJS/TEN; however, the small sample resulted in non-significant findings [35]. However, a more recent study by Micheletti et al. [26] demonstrated that MPP for five consecutive days and high-dose IVIg therapy significantly increased the surviv-

ability of patients with SJS. A systematic review and network meta-analysis reported that combination therapy with corticosteroids and IVIg may reduce mortality risks in patients with SJS/TEN overlap and TEN [36].

Current evidence regarding the benefits of IVIg is controversial. The most extensive study regarding this subject, the European Study of Severe Cutaneous Adverse Reactions (EuroSCAR), reported that IVIg did not improve mortality compared with supportive care alone [32]. However, a recent meta-analysis reported that high-dose IVIg (>2 g/kg) significantly decreased the mortality of selected patients across the SJS/TEN spectrum [37]. Notably, IVIg dosages in the previous study were significantly different, which could explain the divergence. Nevertheless, further randomized controlled trials are required to establish whether IVIg improves clinically important outcomes in SJS/TEN. A systematic review concerning the dosage of IVIg found that higher doses were associated with reduced mortality; however, after adjustment by a multivariate logistic regression model, dosage did not correlate with outcomes [38]. However, in contrast, Indian studies have reported IVIg is neither cost-effective nor supported by evidence [29]. Overall, IVIg should be described as an option with uncertain efficacy rather than as an established mortality-reducing therapy.

Cyclosporine has shown potentially favorable mortality and healing signals in observational studies and meta-analyses [39,40]. Moreover, Gilbert et al. [41] reported few adverse effects, but the available evidence does not establish cyclosporine as uniformly low risk. Comparative cohorts have reported lower standardized mortality ratios and shorter re-epithelialization or hospital stays than with IVIg or supportive care. Along these lines, patients with high SCORTEN scores, a predictive mortality score, receiving cyclosporine had significantly lower mortality than what was predicted by the score [42]. Cyclosporine may therefore be considered in selected patients after assessment of renal function, infection risk, drug interactions, and other contraindications; residual confounding and small sample sizes limit certainty [28].

On the other hand, skin lesions in SJS/TEN contain high levels of TNF- α [43], which leads to the hypothesis that TNF- α inhibitors like etanercept could be potentially useful. Evidence for etanercept now extends beyond isolated case reports and includes case series and retrospective cohorts. Available studies suggest faster disease arrest or re-epithelialization in some patients, but differences in design, timing, and co-interventions limit certainty [44,45]. Additional comparative studies are required to define its effect on mortality and safety.

Other novel alternatives like NAC have been implemented in a handful of cases. NAC has been reported only in case reports and very small series. It should therefore be considered experimental or investigational; efficacy, safety, and optimal dosing have not been established. [46]. Along these lines, Saavedra et al. [47] reported a case of SJS receiving 600 mg TID that had a very satisfactory evolution. Nonetheless, similar to TNF- α , NAC efficacy and safety need to be further analyzed through randomized controlled trials. It is important to mention that the results when using immunoglobulins and TNF- α inhibitors are time-dependent, so earlier use could generate greater clinical benefits [48].

Lastly, plasmapheresis (PP) removes circulating drugs, metabolites, cytokines, and other soluble mediators [49]. Case series and uncontrolled studies have reported clinical improvement, but these designs cannot establish efficacy [50,51]. A systematic review found insufficient high-quality evidence to recommend PP routinely [52]. Furthermore, negative results have been reported when combining IVIg and PP, and the recent cohort summarized in Table 1 did not show a mortality or length-of-stay benefit [53]. Evidence supporting combination treatment with IVIg and PP is insufficient, and no clear added benefit has been demonstrated. PP may be considered as rescue therapy in selected refractory cases, but this remains based on low-certainty evidence (Table 1).

Table 1. Potential therapies for the Stevens-Johnson syndrome.

Study [Ref]/ Design/Population	Comparator and Timing	Main Outcomes	Adverse Effects	Certainty and Limitations
Yang et al. [48] Multicenter retrospective; <i>n</i> = 139 <i>SJS/TEN</i>	Corticosteroid monotherapy; TNF- α inhibitor $\leq$ 13 days or IVIg $\leq$ 7 days from rash onset	Earlier disease arrest and re-epithelialization; no significant difference in hospitalization	Not reported systematically in the summarized results	Low: retrospective allocation, heterogeneous therapies, residual confounding
Yoon et al. [45] Single-center, retrospective cohort study utilizing electronic medical records. <i>n</i> = 118	Intervention Group: 44 patients (37.3%) who received etanercept. Comparator Group: 74 patients (62.7%) who did not receive etanercept (standard/alternative care). Timing: Etanercept was administered at a median of 5 days following the onset of cutaneous symptoms.	Efficacy: No statistically significant differences were observed between the groups regarding age at onset, SCORTEN (severity score), overall mortality, survival, or length of hospital stay.	Not explicitly detailed	Lack of Randomization: Being a retrospective observational cohort, it is prone to selection and confounding biases and sample size
Hasan et al. [54] Case series; <i>n</i> = 3 <i>severe cutaneous drug reactions</i>	No control group; IV NAC with or without IVIg; timing heterogeneous	Clinical improvement described	No major treatment-related adverse effects reported in the small series	Very low: three cases, mixed interventions, no comparator
Senda et al. [53] Retrospective cohort; <i>n</i> = 256 <i>severe SJS/TEN</i>	Plasma exchange versus no plasma exchange; administrative database	No reduction in in-hospital, 30-day, or 50-day mortality; no shorter stay	Not captured in sufficient clinical detail	Low: retrospective design, coding limitations, residual confounding

Recent mechanistic work has expanded interest beyond TNF- α inhibition. Interferon-JAK/STAT signaling, IL-15, granulysin, and the PD-1/PD-L1 axis are potential therapeutic or biomarker pathways [24,25,55]. JAK inhibitors, including baricitinib and tofacitinib, have emerging translational and early clinical evidence in studies with a small number of patients in which a single-cell multiomic analysis was performed in drug-induced SJS/TEN [56]. Likewise, depleting LAG3+ cells using specialized monoclonal antibodies (such as GSK2831781) has successfully reduced inflammation and improved barrier integrity in other T-cell-driven skin pathologies like psoriasis without compromising safety. Translating this approach to SJS/TEN could selectively eliminate the sessile, tissue-damaging memory T-cell pools responsible for severe epidermal detachment [57]. Whereas IL-15 blockade and anti-granulysin strategies remain experimental, the PD-1/PD-L1 pathway requires caution because immune-checkpoint inhibition may itself precipitate severe cutaneous adverse reactions. These approaches should therefore be presented as investigational rather than established treatments.

HLA pharmacogenomics forms the backbone of precision prevention in SJS/TEN and provides a preventive link between pathogenesis and clinical care. In drug-induced SJS/TEN, HLA class I-mediated antigen presentation and cytotoxic CD8+ T-cell responses are important pathogenic mechanisms, and specific HLA alleles confer substantial risk in selected drug-population combinations. However, these associations do not account for all cases; infection-associated and idiopathic presentations are also reported, and the absence of a recognized HLA risk allele does not exclude the diagnosis [9,16,17]. Associations such as HLA-B*15:02 with carbamazepine-related SJS/TEN and HLA-B*58:01 with allopurinol-related severe cutaneous adverse reactions support genotype-guided prescribing in selected populations [58]. A negative test does not eliminate risk and does not replace clinical vigilance.

In summary, most available studies are retrospective, including small or heterogeneous populations, and differ in treatment timing, dose, supportive care, and outcome definitions. These limitations increase the risk of selection bias and confounding by indication. Mortality should therefore be interpreted against baseline severity, preferably using observed versus SCORTEN-predicted mortality, rather than crude mortality alone [31]. The three studies summarized in Table 1 also differ substantially in design and sample size.

4. Conclusions

The SJS/TEN spectrum represents a diagnostic and therapeutic challenge for physicians. Even after several decades, there is still no consensus regarding the optimal therapy for this condition. It is hard to assess the efficacy of novel therapies when the “conventional” therapies are still under investigation. Corticosteroids and cyclosporine are frequently used, but their benefits depend on patient selection and remain supported mainly by observational evidence. However, optimal posology is still under debate, as well as possible combined therapies. Other drugs that may have a beneficial effect, such as etanercept and NAC, are still under investigation, given the limited number of studies and small sample sizes. In general, available guidelines focus on the withdrawal of the culprit drugs and supportive care, which is the foundation of SJS/TEN management. Further research is needed to define the role of novel and conventional therapies using phenotype-specific, severity-adjusted, and safety outcomes.

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Abbreviations

The following abbreviations are used in this manuscript:

BSA	Body Surface Area
IVIg	intravenous immunoglobins
MPP	methylprednisolone pulses
NAC	N-acetylcysteine
NSAIDs	nonsteroidal anti-inflammatory drugs
PP	plasmapheresis
SJS	Stevens-Johnson syndrome
TEN	Toxic Epidermal Necrolysis
TNF- α	Tumor Necrosis Factor Alpha

References

1. Schneider, J.A.; Cohen, P.R. Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: A Concise Review with a Comprehensive Summary of Therapeutic Interventions Emphasizing Supportive Measures. *Adv. Ther.* **2017**, *34*, 1235–1244. [CrossRef]
2. Lerch, M.; Mainetti, C.; Terziroli Beretta-Piccoli, B.; Harr, T. Current perspectives on Stevens-Johnson syndrome and toxic epidermal necrolysis. *Clin. Rev. Allergy Immunol.* **2018**, *54*, 147–176. [CrossRef]

3. Yamane, Y.; Matsukura, S.; Watanabe, Y.; Yamaguchi, Y.; Nakamura, K.; Kambara, T.; Ikezawa, Z.; Aihara, M. Retrospective analysis of Stevens-Johnson syndrome and toxic epidermal necrolysis in 87 Japanese patients—Treatment and outcome. *Allergol. Int. Off. J. Jpn. Soc. Allergol.* **2016**, *65*, 74–81. [\[CrossRef\]](#)
4. Frey, N.; Jossi, J.; Bodmer, M.; Bircher, A.; Jick, S.S.; Meier, C.R.; Spoendlin, J. The Epidemiology of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in the UK. *J. Investig. Dermatol.* **2017**, *137*, 1240–1247. [\[CrossRef\]](#)
5. Chan, H.L.; Stern, R.S.; Arndt, K.A.; Langlois, J.; Jick, S.S.; Jick, H.; Walker, W.M. The incidence of erythema multiforme, Stevens-Johnson syndrome, and toxic epidermal necrolysis. A population-based study with particular reference to reactions caused by drugs among outpatients. *Arch. Dermatol.* **1990**, *126*, 43–47. [\[CrossRef\]](#)
6. Yang, S.C.; Hu, S.; Zhang, S.Z.; Huang, J.W.; Zhang, J.; Ji, C.; Cheng, B. The Epidemiology of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in China. *J. Immunol. Res.* **2018**, *2018*, 4320195. [\[CrossRef\]](#)
7. Hsu, D.Y.; Brieve, J.; Silverberg, N.B.; Silverberg, J.I. Morbidity and Mortality of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in United States Adults. *J. Investig. Dermatol.* **2016**, *136*, 1387–1397. [\[CrossRef\]](#)
8. Yang, M.S.; Lee, J.Y.; Kim, J.; Kim, G.W.; Kim, B.K.; Kim, J.Y.; Park, H.-W.; Cho, S.-H.; Min, K.-U.; Kang, H.-R. Incidence of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis: A Nationwide Population-Based Study Using National Health Insurance Database in Korea. *PLoS ONE* **2016**, *11*, e0165933. [\[CrossRef\]](#)
9. Schwartz, R.A.; McDonough, P.H.; Lee, B.W. Toxic epidermal necrolysis. *J. Am. Acad. Dermatol.* **2013**, *69*, 173.e1–173.e13. [\[CrossRef\]](#)
10. Zimmerman, D.; Dang, N.H. Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN). In *Oncologic Critical Care*; Springer International Publishing: Cham, Switzerland, 2019; pp. 267–280.
11. Singh, G.K.; Mitra, B.; Arora, S.; Akhoun, N.; Verma, R.; Sharma, P.; Mitra, D. A retrospective, 5-year, clinicoepidemiological study of severe cutaneous adverse reactions (SCARs). *Int. J. Dermatol.* **2021**, *60*, 579–588. [\[CrossRef\]](#)
12. Creamer, D.; Walsh, S.A.; Dziewulski, P.; Exton, L.S.; Lee, H.Y.; Dart, J.K.G.; Setterfield, J.; Bunker, C.B.; Ardern-Jones, M.R.; Watson, K.M.T.; et al. UK guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults 2016 (print summary-Full guidelines available at <http://dx.doi.org/10.1016/j.bjps.2016.01.034>). *J. Plast. Reconstr. Aesthetic Surg.* **2016**, *69*, 736–741. [\[CrossRef\]](#)
13. Gupta, L.K.; Martin, A.M.; Agarwal, N.; D'Souza, P.; Das, S.; Kumar, R.; Pande, S.; Das, N.K.; Kumaresan, M.; Kumar, P.; et al. Guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis: An Indian perspective. *Indian J. Dermatol. Venereol. Leprol.* **2016**, *82*, 603. [\[CrossRef\]](#)
14. Williams, R.; Hodge, J.; Ingram, W. Indications for intubation and early tracheostomy in patients with Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. *Am. J. Surg.* **2016**, *211*, 684–688.e1. [\[CrossRef\]](#)
15. Schwartz, R.A.; McDonough, P.H.; Lee, B.W. Toxic epidermal necrolysis: Part II. Prognosis, sequelae, diagnosis, differential diagnosis, prevention, and treatment. *J. Am. Acad. Dermatol.* **2013**, *69*, 187.e1–187.e16, quiz 203–204.
16. Marks, M.E.; Botta, R.K.; Abe, R.; Beachkofsky, T.M.; Boothman, I.; Carleton, B.C.; Chung, W.-H.; Cibotti, R.R.; Dodiuk-Gad, R.P.; Grimstein, C.; et al. Updates in SJS/TEN: Collaboration, innovation, and community. *Front Med.* **2023**, *10*, 1213889. [\[CrossRef\]](#)
17. Justice, J.; Mukherjee, E.; Martin-Pozo, M.; Phillips, E. Updates in the pathogenesis of SJS/TEN. *Allergol. Int.* **2025**, *74*, 361–371. [\[CrossRef\]](#)
18. Bastuji-Garin, S.; Fouchard, N.; Bertocchi, M.; Roujeau, J.C.; Revuz, J.; Wolkenstein, P. SCORTEN: A severity-of-illness score for toxic epidermal necrolysis. *J. Investig. Dermatol.* **2000**, *115*, 149–153. [\[CrossRef\]](#)
19. Garcia-Doval, I.; LeCleach, L.; Bocquet, H.; Otero, X.L.; Roujeau, J.C. Toxic epidermal necrolysis and Stevens-Johnson syndrome: Does early withdrawal of causative drugs decrease the risk of death? *Arch. Dermatol.* **2000**, *136*, 323–327.
20. Ramakrishnan, K.M.; Sankar, J.; Venkatraman, J. Role of biological membranes in the management of Stevens Johnson syndrome—Indian experience. *Burns J. Int. Soc. Burn Inj.* **2007**, *33*, 109–111. [\[CrossRef\]](#)
21. Kompella, V.B.; Sangwan, V.S.; Bansal, A.K.; Garg, P.; Aasuri, M.K.; Rao, G.N. Ophthalmic complications and management of Stevens-Johnson syndrome at a tertiary eye care centre in south India. *Indian J. Ophthalmol.* **2002**, *50*, 283–286.
22. Metcalfe, D.; Iqbal, O.; Chodosh, J.; Bouchard, C.S.; Saeed, H.N. Acute and Chronic Management of Ocular Disease in Stevens Johnson Syndrome/Toxic Epidermal Necrolysis in the USA. *Front. Med.* **2021**, *8*, 662897. [\[CrossRef\]](#)
23. Pasricha, J.S. Corticosteroids in toxic epidermal necrolysis. *Indian J. Dermatol. Venereol. Leprol.* **2008**, *74*, 493, author reply 493–495. [\[CrossRef\]](#)
24. Watanabe, Y.; Hama, Y. Recent advances in the diagnosis and treatment of Stevens-Johnson syndrome/toxic epidermal necrolysis. *Allergol. Int.* **2025**, *74*, 345–355. [\[CrossRef\]](#)
25. Murillo-Casas, A.D.; Zwiener, R.; Giavina-Bianchi, P.; Pardo-Manrique, V.; Villarreal-González, R.; Patricia Monge-Ortega, O.; Velásquez-Lopera, M.M.; Silva-Espinosa, D.L.; Castillo-Loaiza, S.M.; Muñoz-García, L.E.; et al. Latin American guidelines for the diagnosis and treatment of Stevens-Johnson syndrome and toxic epidermal necrolysis. *World Allergy Organ. J.* **2025**, *18*, 101046. [\[CrossRef\]](#)

26. Micheletti, R.G.; Chiesa-Fuxench, Z.; Noe, M.H.; Stephen, S.; Aleshin, M.; Agarwal, A.; Boggs, J.; Cardones, A.R.; Chen, J.K.; Cotliar, J.; et al. Stevens-Johnson syndrome/toxic epidermal necrolysis: A multicenter retrospective study of 377 adult patients from the United States. *J. Investig. Dermatol.* **2018**, *138*, 2315–2321. [\[CrossRef\]](#)
27. Houschyar, K.S.; Tapking, C.; Borrelli, M.R.; Puladi, B.; Ooms, M.; Wallner, C.; Duscher, D.; Pfürringer, D.; Rein, S.; Reumuth, G.; et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: A systematic review and meta-analysis. *J. Wound Care* **2021**, *30*, 1012–1019. [\[CrossRef\]](#)
28. Singh, G.K.; Chatterjee, M.; Verma, R. Cyclosporine in Stevens Johnson syndrome and toxic epidermal necrolysis and retrospective comparison with systemic corticosteroid. *Indian J. Dermatol. Venereol. Leprol.* **2013**, *79*, 686–692. [\[CrossRef\]](#)
29. Kumar, R.; Das, A.; Das, S. Management of Stevens-Johnson Syndrome-Toxic Epidermal Necrolysis: Looking Beyond Guidelines! *Indian J. Dermatol.* **2018**, *63*, 117–124. [\[CrossRef\]](#)
30. Kelemen, J.J.; Cioffi, W.G.; McManus, W.F.; Mason, A.D.; Pruitt, B.A. Burn center care for patients with toxic epidermal necrolysis. *J. Am. Coll. Surg.* **1995**, *180*, 273–278.
31. Roujeau, J.C.; Bastuji-Garin, S. Systematic review of treatments for Stevens–Johnson syndrome and toxic epidermal necrolysis using the SCORTEN score as a tool for evaluating mortality. *Ther. Adv. Drug Saf.* **2011**, *2*, 87–94. [\[CrossRef\]](#)
32. Schneck, J.; Fagot, J.P.; Sekula, P.; Sassolas, B.; Roujeau, J.C.; Mockenhaupt, M. Effects of treatments on the mortality of Stevens-Johnson syndrome and toxic epidermal necrolysis: A retrospective study on patients included in the prospective EuroSCAR Study. *J. Am. Acad. Dermatol.* **2008**, *58*, 33–40. [\[CrossRef\]](#)
33. Zimmermann, S.; Sekula, P.; Venhoff, M.; Motschall, E.; Knaus, J.; Schumacher, M.; Mockenhaupt, M. Systemic Immunomodulating Therapies for Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. *JAMA Dermatol.* **2017**, *153*, 514–522. [\[CrossRef\]](#)
34. Brüggem, M.C.; Le, S.T.; Walsh, S.; Toussi, A.; de Prost, N.; Ranki, A.; Didona, B.; Colin, A.; Horváth, B.; Brezinova, E.; et al. Supportive care in the acute phase of Stevens-Johnson syndrome and toxic epidermal necrolysis: An international, multidisciplinary Delphi-based consensus. *Br. J. Dermatol.* **2021**, *185*, 616–626. [\[CrossRef\]](#)
35. Kardaun, S.H.; Jonkman, M.F. Dexamethasone pulse therapy for Stevens-Johnson syndrome/toxic epidermal necrolysis. *Acta Derm. Venereol.* **2007**, *87*, 144–148. [\[CrossRef\]](#)
36. Tsai, T.Y.; Huang, I.H.; Chao, Y.C.; Li, H.; Hsieh, T.S.; Wang, H.H.; Huang, Y.-T.; Chen, C.-Y.; Cheng, Y.-C.; Kuo, P.-H.; et al. Treating toxic epidermal necrolysis with systemic immunomodulating therapies: A systematic review and network meta-analysis. *J. Am. Acad. Dermatol.* **2021**, *84*, 390–397. [\[CrossRef\]](#)
37. Barron, S.J.; Del Vecchio, M.T.; Aronoff, S.C. Intravenous immunoglobulin in the treatment of Stevens-Johnson syndrome and toxic epidermal necrolysis: A meta-analysis with meta-regression of observational studies. *Int. J. Dermatol.* **2015**, *54*, 108–115. [\[CrossRef\]](#)
38. Huang, Y.C.; Li, Y.C.; Chen, T.J. The efficacy of intravenous immunoglobulin for the treatment of toxic epidermal necrolysis: A systematic review and meta-analysis. *Br. J. Dermatol.* **2012**, *167*, 424–432. [\[CrossRef\]](#)
39. Valeyrie-Allanore, L.; Wolkenstein, P.; Brochard, L.; Ortonne, N.; Maître, B.; Revuz, J.; Bagot, M.; Roujeau, J. Open trial of ciclosporin treatment for Stevens-Johnson syndrome and toxic epidermal necrolysis. *Br. J. Dermatol.* **2010**, *163*, 847–853. [\[CrossRef\]](#)
40. Shah, R.; Chen, S.T.; Kroshinsky, D. Use of cyclosporine for the treatment of Stevens-Johnson syndrome/toxic epidermal necrolysis. *J. Am. Acad. Dermatol.* **2021**, *85*, 512–513. [\[CrossRef\]](#)
41. Gilbert, M.; Scherrer, L.A. Efficacy and safety of cyclosporine in Stevens-Johnson syndrome and toxic epidermal necrolysis. *Dermatol. Ther.* **2019**, *32*, e12758. [\[CrossRef\]](#)
42. Kirchhof, M.G.; Miliszewski, M.A.; Sikora, S.; Papp, A.; Dutz, J.P. Retrospective review of Stevens-Johnson syndrome/toxic epidermal necrolysis treatment comparing intravenous immunoglobulin with cyclosporine. *J. Am. Acad. Dermatol.* **2014**, *71*, 941–947. [\[CrossRef\]](#)
43. Yao, L.; Su, X.; Liu, L.; Qi, Y.; Wei, B.; Ma, R.; Du, X. Recent developments in the research of Stevens-Johnson syndrome and toxic epidermal necrolysis: Pathogenesis, diagnosis and treatment. *Eur. J. Med. Res.* **2025**, *30*, 453. [\[CrossRef\]](#)
44. Pham, C.H.; Gillenwater, T.J.; Nagengast, E.; McCullough, M.C.; Peng, D.H.; Garner, W.L. Combination therapy: Etanercept and intravenous immunoglobulin for the acute treatment of Stevens-Johnson syndrome/toxic epidermal necrolysis. *Burns J. Int. Soc. Burn Inj.* **2019**, *45*, 1634–1638. [\[CrossRef\]](#)
45. Yoon, I.; Natarelli, N.; Toothman, M.; Mhaskar, R.; Correa, L.; Lin, A. 71032 Evaluating Etanercept for the Treatment of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis. *J. Am. Acad. Dermatol.* **2026**, *95*, AB204. [\[CrossRef\]](#)
46. Redondo, P.; de Felipe, I.; de la Peña, A.; Aramendia, J.M.; Vanaclocha, V. Drug-induced hypersensitivity syndrome and toxic epidermal necrolysis. Treatment with N-acetylcysteine. *Br. J. Dermatol.* **1997**, *136*, 645–646. [\[CrossRef\]](#)
47. Saavedra, C.; Cárdenas, P.; Castellanos, H.; Contreras, K.; Castro, J.R. Cephazolin-Induced Toxic Epidermal Necrolysis Treated with Intravenous Immunoglobulin and N-Acetylcysteine. *Case Rep. Immunol.* **2012**, *2012*, 931528. [\[CrossRef\]](#)
48. Yang, H.; Yuan, L.; Zhao, B.; Lin, Y.; Zhang, M.; Feng, T.; Qin, Y.; Zhao, P.; Zheng, Y.; Zhu, G. Evidence of a Therapeutic Window for TNF- α Inhibitor and Intravenous Immunoglobulin Benefits in Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis Treatment: A Multicenter 6-Year Retrospective Study. *J. Allergy Clin. Immunol. Pract.* **2026**, *14*, 1087–1093.e3. [\[CrossRef\]](#)

49. Košťál, M.; Bláha, M.; Lánská, M.; Košťálová, M.; Bláha, V.; Štěpánová, E.; Malý, J. Beneficial effect of plasma exchange in the treatment of toxic epidermal necrolysis: A series of four cases. *J. Clin. Apher.* **2012**, *27*, 215–220. [[CrossRef](#)]
50. Egan, C.A.; Grant, W.J.; Morris, S.E.; Saffle, J.R.; Zone, J.J. Plasmapheresis as an adjunct treatment in toxic epidermal necrolysis. *J. Am. Acad. Dermatol.* **1999**, *40*, 458–461. [[CrossRef](#)]
51. Narita, Y.M.; Hirahara, K.; Mizukawa, Y.; Kano, Y.; Shiohara, T. Efficacy of plasmapheresis for the treatment of severe toxic epidermal necrolysis: Is cytokine expression analysis useful in predicting its therapeutic efficacy? *J. Dermatol.* **2011**, *38*, 236–245. [[CrossRef](#)]
52. Jacobsen, A.; Olabi, B.; Langley, A.; Beecker, J.; Mutter, E.; Shelley, A.; Worley, B.; Ramsay, T.; Saavedra, A.; Parker, R.; 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**, *3*, CD013130. [[CrossRef](#)]
53. Senda, A.; Fushimi, K. Effectiveness of early treatment with plasma exchange in patients with Stevens-Johnson syndrome and toxic epidermal necrolysis. *Sci. Rep.* **2024**, *14*, 2893. [[CrossRef](#)]
54. Hasan, J.; Rabbani, R. Intravenous N-acetylcysteine in severe cutaneous drug reaction treatment: A case series. *SAGE Open Med. Case Rep.* **2020**, *8*, 2050313X20934708. [[CrossRef](#)]
55. Hasegawa, A.; Abe, R. Recent advances in managing and understanding Stevens-Johnson syndrome and toxic epidermal necrolysis. *F1000Research* **2020**, *9*, 612. [[CrossRef](#)]
56. Nordmann, T.M.; Anderton, H.; Hasegawa, A.; Schweizer, L.; Zhang, P.; Stadler, P.C.; Sinha, A.; Metousis, A.; Rosenberger, F.A.; Zwiebel, M.; et al. Spatial proteomics identifies JAKi as treatment for a lethal skin disease. *Nature* **2024**, *635*, 1001–1009. [[CrossRef](#)]
57. Gibson, A.; Ram, R.; Gangula, R.; Li, Y.; Mukherjee, E.; Palubinsky, A.M.; Campbell, C.N.; Thorne, M.; Konvinse, K.C.; Choshi, P.; et al. Multiomic single-cell sequencing defines tissue-specific responses in Stevens-Johnson syndrome and toxic epidermal necrolysis. *Nat. Commun.* **2024**, *15*, 8722. [[CrossRef](#)]
58. Mushiroda, T. Pharmacogenetic biomarkers associated with risk of developing severe drug eruptions and clinical implementation of HLA genetic testing. *Allergol. Int.* **2025**, *74*, 380–385. [[CrossRef](#)]

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