

Nursing Care of Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis in Children

Abstract

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are rare, life-threatening, and rapidly developing skin diseases that are generally triggered by medications and characterized by epidermal separation and mucosal involvement. The cause of epidermal damage is the apoptosis of keratinocytes. This damage is frequently caused by medications or infections. The most common cause of infection is *Mycoplasma pneumoniae*. The most common drugs that cause damage are anticonvulsants, sulfonamide group antibiotics, and non-steroidal anti-inflammatory drugs. The disease starts with symptoms such as fever and flu symptoms. Mucosal involvement begins within 1-7 days. Although there are many options for treatment of the disease, there is no drug with proven efficacy. Systemic treatment and appropriate nursing care are recommended in the approach to the disease. Recently, intravenous immunoglobulin (IVIG) and corticosteroids have been considered as an effective treatment. In nursing care, protecting the skin from infections, providing optimal body temperature, providing appropriate oral and eye care, and pain management are among the primary issues. The aim of this study is to provide up-to-date information about pathophysiology, clinical signs, treatment, and nursing care of SJS and TEN, for which early diagnosis and treatment are important due to the lack of its own unique symptoms and clinical picture to the literature by reviewing the related literature.

Keywords: Steven-Johnson syndrome, Toxic epidermal necrolysis, Nursing care

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Introduction

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN) are rare, severe, life-threatening, and rapidly developing skin adverse reactions that are usually induced by medications and characterized by epidermal separation and mucosal skin rash.¹ SJS and TEN are distinguished based on the involvement percentage of body surface. If the involvement is less than 10%, the diagnosis of SJS is established; if it is around 10-30%, it is SJS/TEN overlap; and more than 30% is involved, it is TEN.² SJS and TEN are less seen in children than adults.³ Even though their incidence rates are not exactly known, it is estimated that there are 0.4-1.9 million cases of SJS and TEN per year. Their incidence rates are approximately equal in girls and boys.⁴ Antoon et al.⁵ reported that the incidence rate was 6.3 per hundred thousand for SJS, 0.7 per hundred thousand for SJS/TEN overlap, and 0.5 per hundred thousand for TEN. While incidence of the disease is higher in the age group of 11-15 years, its mortality rate is higher between 0 and 5 years. Risk of death is higher in adults when compared to pediatric population.⁶ It has been reported that the mortality rate of pediatric patients is 0% in SJS, 4% in SJS/TEN, and 16% in TEN. Sequelae such as pigmentation disorder on the skin, adherence in the genital organs, and vision problems in the eye remain in many living patients.^{6,7}

The causes of SJS and TEN include malignancies, collagen tissue diseases, genetics, immunological disease, infections, and drugs. In children, SJS and TEN are triggered by drugs at the rate of 60-90%. SJS and TEN are the most severe side effect associated with drugs. The most common drugs causing the disease are antiepileptic (60%), antibiotic (26.6%), and non-steroidal anti-inflammatory and chemotherapeutic drugs.^{7,8} Examples of drugs that can lead to SJS and TEN are sulfonamides, phenobarbitals, carbamazepine, lamotrigine, oxycam group non-steroidal anti-inflammatory drugs, nevirapine, and allopurinol.^{7,9} Recent studies have revealed that penicillin is among potential triggering drugs.^{7,10} Side effects of the drug usually appear within the first 2-8 weeks after onset of drug use.^{7,11} Vaccines can also very rarely cause disease.¹²

One of the most common causes in etiology of pediatric SJS and TEN is infections. These infections are *Mycoplasma pneumoniae*, cytomegalovirus, Epstein-Barr virus, herpes virus, rickettsia, and Hepatitis A.¹³⁻¹⁵ 25-50% of SJS cases are idiopathic.¹³ It has been determined that the disease recurs in children at a certain level and recurrence possibility of the disease is higher in adults than young children.¹⁴ Its risk is higher in the presence of immunodeficiency or autoimmune disease in individuals with Human Leukocyte Antigen B*1502 and Human Leukocyte Antigen B*1501 (HLA-B*1502 and HLA-B*1501) genotype from Human Leukocyte Antigen (HLA) types.⁹ In a study conducted by Okubo et al.¹⁶ with pediatric patients in the United States, they determined that hospital admission rates were higher in those who were aged between 15 and 19 years, male, black children, and children from very low-income families.

Early diagnosis of SJS/TEN is an important issue due to the lack of its specific clinical picture and its high mortality rates. Recent studies have presented evidence to examine the pathogenesis, clinical presentation, treatment, and impact of SJS/TEN as well as the importance and effectiveness of its nursing care in order to reduce its mortality and morbidity.^{9,11,14} Number of studies on SJS and TEN in Turkish literature for nurses is limited.



Figure 1. The child diagnosed with SJS.

Therefore, the aim of this review is to present up-to-date information about treatment and nursing care upon review of the literature of the last 10 years using the keywords SJS and TEN.

Pathogenesis

Even though pathogenesis of the disease is still not exactly clarified, it is thought to be associated with genetic predisposition and immunological mechanisms. Those taking part in genetic predisposition are HLA alleles. Being an aromatic antiepileptic drug, carbamazepine is one of first drugs that can bind to HLA in drug-induced SJS. Ou et al.¹⁷ have reported that there is a strong correlation between carbamazepine-induced SJS/TEN and HLA-B*1502 from HLA types in Chinese society. This correlation is not valid for all Asian populations. No correlation has been found between carbamazepine-induced SJS-TEN and HLA-B*1502 genotype in Koreans and Japanese.¹⁷ An European study also revealed no correlation between HLA-B*1502 genotype and carbamazepine-induced SJS/TEN in Hispanic Caucasian populations. The same study revealed that carbamazepine-induced SJS/TEN was associated with HLA-A*1101 genotype.¹⁸ In their study, Khor et al.¹⁹ found that HLA-B*1502 and HLA-A*3101 had a significant correlation with carbamazepine-induced SJS/TEN in Indian population of Malaysia. A correlation was determined between allopurinol-induced SJS/TEN and HLA-B5801 genotype in Japan society. However, this correlation was not found in European society.¹¹ These findings have revealed the necessity of conducting genetic test for both genotypes before prescribing carbamazepine in the population of India.¹⁹ Drug-induced SJS and TEN can be caused by dysregulation of cellular immunity. Cytotoxic T lymphocytes and natural killer (NK) cells can identify drugs and metabolites presented by class I HLA on keratinocytes. When these immune cells are activated, cytotoxic signals such as Fas/Fas ligand, perforin/granzyme B, and granulysin, which mediate keratinocyte apoptosis and detachment of skin and mucous membranes, are released.¹¹ In the samples taken from blisters in the body of the patients, cytotoxic CD8+ T lymphocytes are seen.⁷ Cytotoxic CD8+ T cells and cytotoxic T cells are the most important cells in the fluid inside the blisters in the initial period in SJS and TEN patients. At later stages, monocytes become dominant.²⁰ Activation of cytotoxic T lymphocytes and secretion of cytokines with natural killer cells are thought to cause widespread epidermal and mucosal necrosis.²¹

Clinical Findings and Complications

The prodromal symptoms of the disease are the symptoms of flu infection such as unwellness and fever which appear before the onset of the disease and last for 1-7 days.^{11,20} Skin lesions generally start within several days. Erythema, erosion, and pseudomembranes gradually develop in the mucous membranes of the mouth, nose, eyes, anal, and genitals.^{11,22} Bullous lesions usually occur on the skin and mucous membranes of patients within 12 h.²²

When erythema is the main skin finding (Figure 1), Nikolsky's sign may help establishing diagnosis even though it is not specific to SJS/TEN.^{11,22} Nikolsky's sign refers to epidermal separation developing as a result of exerting a tangential pressure to erythematous and blister-free parts of skin. Besides skin involvement, multiple organ systems especially in the cardiovascular, respiratory, and gastrointestinal systems may be involved in the patient. The ocular surface is one of the frequently affected areas as the mucosal surface in TEN. There is no correlation between the severity of epidermal separation and the severity of ocular findings.¹¹ Eye involvement is an important factor of morbidity in children. Since eye involvement causes xerophthalmia, corneal damage, and scar in children, some patients may have long-term sequelae.^{3,23} Involvement of more than 30% of body involvement, comorbid renal failure, sepsis, epilepsy, bacterial infections, and malignancy are associated with high risk of death. The rate of need for support devices such as ventilatory and dialysis is also higher in these patients.^{5,6,23} Chatproedprai et al.²⁴ reported that the most common skin finding was dyspigmentation in terms of long-term skin sequelae in SJS and TEN overlap cases. In the same study, when comparing with SJS group, SJS/TEN overlap cases had a more significant morbidity in skin, eye, and genital organs of SJS/TEN overlap cases. Deaths occur in SJS and TEN primarily due to chronic respiratory failure. However, the underlying factors for respiratory complication are unknown. Obliterative bronchiolitis rarely develops after SJS and TEN and causes long-term morbidity.³ Obliterative bronchiolitis is a severe respiratory complication and results in obstruction of peripheral airway lumen.²⁵ Sato et al.²⁶ reported that the complication of obliterative bronchiolitis developed in one child among 15 pediatric cases. When obliterative bronchiolitis is progressive and severe, it results in a process leading to lung transplantation.³ Genitourinary involvement is quite common in children suffering from SJS and TEN. Urethral stricture may rarely develop in these patients.²⁷ Score of Toxic Epidermal Necrosis (SCORTEN) is the scoring system frequently used to determine severity of the disease. Scoring is based on seven prognostic factors: age, malignancy, body area affected, tachycardia, urea, glycaemia, and serum bicarbonate level.

It is possible to calculate SCORTEN within 24-72 h. However, SCORTEN is not a scoring that is exactly accepted for children.⁷ Sorrel et al.²⁸ found that this scoring was useful for determining morbidity in pediatric patients having a SCORTEN value of four or higher points.

Treatment and Nursing Care

Management of the disease includes early diagnosis, immediate termination of the causative drug, initiation of supportive care as soon as possible, early consultation from fields such as dermatology and ophthalmology, and hospitalization of the patient in the pediatric intensive care unit without losing time. Early intervention reduces morbidity and mortality.²⁹ Healthcare professionals from many fields should work collaboratively in the management of SJS/TEN.²⁵ Nursing care should include supportive care for symptoms such as infection protection and body temperature management, wound care, nutrition, and oral-eye care. This syndrome, which requires immediate hospitalization, may be

traumatic for the child and his family. Therefore, care should be provided to the children and their family based on family-centered care approach.

Treatment

Even though many options are available for treatment of individuals suffering from SJS-TEN, there is no reliable drug with high evidence level. It is treated with corticosteroid, IVIG, cyclosporine, plasmapheresis, and TNF- α inhibitors.¹¹ Sibbald et al.³⁰ reported in a single-center retrospective study that the combination of steroid and IVIG may be useful. Wang et al.³¹ reported that in patients with moderate SJS and TEN, TNF- α inhibitors provided skin healing in a short time and a decrease in the incidence of gastrointestinal bleeding compared to corticosteroids. Cyclosporine is thought to reduce mortality in adults and children compared to high-dose IVIG.^{32,33} In their study, Gavigan et al.³⁴ revealed that the TNF- α inhibitor etanercept, used in the treatment, was beneficial and accelerated the re-epithelial formation. Chahal et al.¹² determined that the use of etanercept in treatment reduced edema and progression of the disease discontinued within 24 h. In their study, John et al.³⁵ demonstrated that the use of cyclosporine provided re-formation of epithelial tissue. Chafanska et al.²¹ reported that when IVIG treatment was used with other treatment combinations or independent TNF- α inhibitors, it recovered rapidly symptoms of the disease. However, in their study, Antoon et al.³⁶ compared length of hospital stay, mortality, and mechanical ventilation with the use of steroid and IVIG in SJS and TEN and found no correlation among them.

Nursing Care

Nursing care has an important place in management of this disease. This is because nurses have a key role in epithelialization process, prevention of infection, and psychological and socio-cultural aspects. Nursing care is also supportive care. Supportive care includes wound care, fluid-electrolyte management, nutritional support, body temperature management, eye care, pain control, and respiratory maintenance.^{20,29} In their study, Trommel et al.³⁷ reported that the most common nursing issues were wounds, problems in vital functions, dehydration and fluid imbalance, pain, secretion problems, and fever. Also, consciousness disorders, anxiety or panic, sleep, and rest problems were seen in patients. Hypothermia, oral mucosa, and eye problems were experienced by the children during hospitalization. Scaly skin appearance, skin rashes, hypo- hyperpigmentation, loss of nail, and swallowing problems were also observed after re-formation of epithelial tissue.

Infection Protection and Body Temperature Management

Patients with SJS/TEN should be isolated in the early period and necessary measures should be taken in order to protect them against infection.³⁸ Room temperature should be 30-32°C in order to prevent epidermal heat loss. Patients should be protected from hypothermia for wound healing.^{11,14} Moreover, the increase in energy need of pediatric patients should be taken into consideration.¹¹

Wound Care

Whole body of the patients should be washed with sterile water two times per day. Wound irrigation should be performed with hot sterile water, saline, or dilute chlorhexidine in a sterile way. More than one nurse should take part in the care of the child during wound care and body bathing to protect him/her from infections. It is important to maintain sterility in terms of eliminating the infection, which will accompany the child, thus shortening the hospitalization period and increasing the speed of recovery.

In wound care, the patient's large bullae should be drained and the small bullae should be healed without touching them. Pressure mattresses and many dressing types such as moisturizing and moisture-retaining ointments, silver or antibiotic impregnated non-adhesive, biological, biosynthetic, nanocrystalline silver dressings such as silver nitrate or chlorhexidine wound dressings on the infective wound, and collagen dressings are used in wound care.^{14,20,29,38,39} McCarthy and Donovan⁴⁰ (2016) reported that silicone silver foam dressings containing silver sulphate are used in patients with SJS/TEN and successful results were obtained.

The use of foam dressings is beneficial as it reduces skin trauma and pain due to the low frequency of change. The advantage of nanocrystalline dressings is that they prevent the pain associated with change in dressing since there is no need for change for seven days.³⁸ In a literature review comparing effectiveness of different wound dressings, no difference was found in terms of period of wound healing. The researchers have emphasized that dressings which stay in the wound site for a long time and do not need to be changed frequently are beneficial for patient comfort.⁴¹

Nutrition

Early transition to oral nutrition and high calorie intake as in wound injuries are crucial in care of SJS and TEN. Electrolyte and protein balance should be provided in nutrition.^{19,29} In case of lack of oral nutrition, enteral nutrition should be considered. Dietary content of patient should be planned and prepared with a dietitian.

Eye Care

Eye care should be moisturized daily.³⁷ Eyes should be cleaned regularly and artificial tear drops should be applied to the eye every 1-2 h. Drops with corticosteroids and antibiotics can be used to reduce inflammation.^{20,29} Topical antibiotics and corticosteroids prevent ocular complications.⁴² In their retrospective study, Xiang et al.⁴³ suggested that eye drops containing dexamethasone may be the conventional treatment for lacrimal system obstructions. Early amniotic membrane application is effective in preventing eye complications in the pediatric group.³⁰

Oral Care

There is no standardization in oral care; however, oral cleaning, debridement, and supragingival cleaning should be performed with oral gels and solutions (chlorhexidine 0.12% and lidocaine 2% gel).¹⁰ In their study, Barea-Jiménez et al.¹⁰ observed that the use of Dapsone 5% gel recovered lip lesions.

Pain and Possible Infection Management

Pain management includes the use of analgesia and topical anesthesia. Applications that will directly press on open wound areas should be avoided and an appropriate position should be given to the patient.¹¹ Urogenital areas should be observed for adherence.³⁸ The use of prophylactic antibiotics is not recommended.²⁹

Information and Emotional Support

Providing appropriate information and emotional support to patients and their families is important in the acute management of the disease. Quality of life of patients has become impaired and psychosocial complications may develop.²⁰ The psychosocial effects of post-traumatic stress disorders and issues such as absenteeism and stigmatization in children as well as returning to school should be examined in nursing care.⁴⁴ The studies have demonstrated that the disease will recur in children to a certain extent and that the recurrence rate of the disease will be higher in adolescents compared to young children. Families should be informed about this issue.¹³

Conclusion

SJS and TEN are rare, life-threatening, and rapidly developing skin diseases that are characterized by epidermal separation and mucosal skin rashes and have a high rate of mortality. They are usually induced by drugs, primarily anticonvulsants, sulfonamide antibiotics, and non-steroidal anti-inflammatory drugs. Early diagnosis of the disease and the patients' referral to intensive care or burn units in a short time and coordinated work of all disciplines reduce mortality and morbidity. Systemic treatment and appropriate nursing care are recommended in the management of the disease. Supportive treatments such as protection from infections in care, compliance with aseptic conditions, eye, mouth and skin care, as well as nutritional support are effective method of treatment. SJS-TEN may recur depending on the intake of the same drug. Families of surviving patients and themselves should be informed about the drugs and their derivatives that cause the disease. Nursing care has an important place in recovery.

Informed Consent: Informed consent was obtained from the mother of the patient who participated in the study.

Peer-review: Externally peer-reviewed.

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References

- Mockenhaupt M. Stevens–Johnson syndrome and toxic epidermal necrolysis: Clinical patterns, diagnostic considerations, etiology, and therapeutic management. *Semin Cutan Med Surg.* 2014;33(1):10-16. 10.12788/j.sder.0058
- Lin CC, Chen CB, Wang CW, Hung SI, Chung WH. Stevens-Johnson syndrome and toxic epidermal necrolysis: Risk factors, causality assessment and potential prevention strategies. *Expert Rev Clin Immunol.* 2020. [Crossref]
- Seccombe EL, Arden-Jones M, Walker W, et al. Bronchiolitis obliterans as a long-term sequela of Stevens-Johnson syndrome and toxic epidermal necrolysis in children. *Clin Exp Dermatol.* 2019;44(8):897-902. [Crossref]
- Oba U, Yamada H, Suenobu S, et al. Toxic epidermal necrolysis in a child 6 months post-hematopoietic stem cell transplantation. *Pediatr Transplant.* 2017;21(5):4.41. [Crossref]
- Antoon JW, Goldman JL, Lee B, Schwartz A. Incidence, outcomes, and resource use in children with Stevens-Johnson syndrome and toxic epidermal necrolysis. *Pediatr Dermatol.* 2018;35(2):182-187. [Crossref]
- Hsu DY, Brieva J, Silverberg NB, Paller AS, Silverberg JL. Pediatric Stevens-Johnson syndrome and toxic epidermal necrolysis in the United States. *J Am Acad Dermatol.* 2017;76(5):811-817. [Crossref]
- Belver MT, Michavila A, Bobolea I, Feito M, Bellón T, Quirce S. Severe delayed skin reactions related to drugs in the paediatric age group: A review of the subject by way of three cases (Stevens–Johnson syndrome, toxic epidermal necrolysis and DRESS). *Allergol Immunopathol.* 2016;44(1):83-95. [Crossref]
- Techasatian L, Panombualert S, Uppala R, Jetsrisuparb C. Drug-induced Stevens-Johnson syndrome and toxic epidermal necrolysis in children: 20 years study in a tertiary care hospital. *World J Pediatr.* 2017;13(3):255-260. [Crossref]
- Köksal TB, Özbek ÖY, Özmen E, Tepeoğlu M. Stevens johnson sendromu tanisi alan bir çocuk olgu. *Güncel Pediatr.* 2018;16(1):115-124. Available from: <https://dergipark.org.tr/en/pub/pediatri/issue/36190/411400>
- Barea-Jiménez N, Calero J, Molina-Negrón D, López-Del Valle L. Treatment for oral lesions in pediatric patients with Stevens–Johnson syndrome: A case report and literature review. *Int J Clin Pediatr Dent.* 2020;30(4):489-496. [Crossref]
- Liotti L, Caimmi S, Bottau P, et al. Clinical features, outcomes and treatment in children with drug induced Stevens-Johnson syndrome and toxic epidermal necrolysis. *Acta Biomed.* 2019;90(3):52-60. [Crossref]
- Chahal D, Aleshin M, Turegano M, Chiu M, Worswick S. Vaccine-induced toxic epidermal necrolysis: A case and systematic review. *Dermatol Online J.* 2018;24:1. Available from: <https://escholarship.org/uc/item/7qn5268s>
- Maverakis E, Wang EA, Shinkai K, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis standard reporting and evaluation guidelines: Results of a National Institutes of Health Working Group. *JAMA Dermatol.* 2017;153(6):587-592. [Crossref]
- Xu L, Zhu Y, Yu J, Deng M, Zhu X. Nursing care of a boy seriously infected with Steven-Johnson syndrome after treatment with azithromycin. A case report and literature review. *Medicine (Baltimore).* 2018;97(1):e9112. [Crossref]
- Wetter DA, Camilleri MJ. Clinical, etiologic, and histopathologic features of Stevens-Johnson syndrome during an 8-year period at Mayo Clinic. *Mayo Clin Proc.* 2010;85(2):131-138. [Crossref]
- Okubo Y, Nochioka K, Testa MA. Nationwide survey of Stevens-Johnson syndrome and toxic epidermal necrolysis in children in the United States. *Pediatr Dermatol.* 2017;34(2):206-208. [Crossref]
- Ou GJ, Wang J, Ji X, et al. A study of HLA-B*15:02 in 9 different Chinese ethnics: Implications for carbamazepine related SJS/TEN. *HLA.* 2017;89(4):225-229. [Crossref]
- Ramirez E, Bellon T, Tong HY, et al. Significant HLA class I type associations with aromatic antiepileptic drug (AED)-induced SJS/TEN are different from those found for the same AED-induced DRESS in the Spanish population. *Pharmacol Res.* 2017;115:168-178. [Crossref]
- Khor AH, Lim KS, Tan CT, et al. HLA-A*31: 01 and HLA-B*15:02 association with Stevens-Johnson syndrome and toxic epidermal necrolysis to carbamazepine in a multiethnic Malaysian population. *Pharmacogenet Genomics.* 2017;27(7):275-278. [Crossref]
- 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(1):147-176. [Crossref]
- Chafanska L, Saunte DM, Behrendt N, et al. Pediatric toxic epidermal necrolysis treated successfully with infliximab. *Pediatr Dermatol.* 2019;36(3):342-345. [Crossref]
- Brockow K, Arden-Jones M, Mockenhaupt M, et al. EAACI position paper on how to classify cutaneous manifestations of drug hypersensitivity. *Allergy.* 2018;74(1):14-27. [Crossref]
- López-García JS, RivasJara L, García-Lozano CI, Conesa E, de Juan IE, Murube del Castillo J. Ocular features and histopathologic changes during follow-up of toxic epidermal necrolysis. *Ophthalmology.* 2011;118(2):265-271. [Crossref]
- Chatproedprai S, Wutticharoenwong V, Tempark T, Wanankul S. Clinical features and treatment outcomes among children with Stevens-Johnson syndrome and toxic epidermal necrolysis: A 20-year study in a tertiary referral hospital. *Dermatol Res Pract.* 2018;2018:1-9. [Crossref]
- Kaneko Y, Seko Y, Sotozono C, et al. Respiratory complications of Stevens-Johnson syndrome (SJS): 3 cases of SJS-induced obstructive bronchiolitis. *Allergol Int.* 2020;69(3):465-467. [Crossref]
- Sato S, Kanbe T, Tamaki Z, et al. Clinical features of Stevens-Johnson syndrome and toxic epidermal necrolysis. *Pediatr Int.* 2018;60(8):697-702. [Crossref]
- Van Batavia JP, Chu DI, Long CJ, Jen M, Canning DA, Weiss DA. Genitourinary involvement and management in children with Stevens–Johnson syndrome and toxic epidermal necrolysis. *J Pediatr Urol.* 2017;13(5):490.e1490.e7. [Crossref]
- Sorrell J, Anthony L, Rademaker A. Score of toxic epidermal necrosis predicts the outcomes of pediatric epidermal necrolysis. *Pediatr Dermatol.* 2017;34(4):433-437. [Crossref]
- Alerhand S, Casella C, Koymfman A. Stevens-Johnson syndrome and toxic epidermal necrolysis in the pediatric population: a review. *Pediatric Emerg Care.* 2016;32(7):472-476. [Crossref]
- Sibbald C, Putterman E, Micheletti R, Treat J, Castelo-Soccio L. Retrospective review of drug-induced Stevens-Johnson syndrome and toxic epidermal necrolysis cases at a pediatric tertiary care institution. *Pediatr Dermatol.* 2020;37(3):461-466. [Crossref]

31. Wang CW, Lang LY, Chen CB, et al. Randomized, controlled trial of TNF- α antagonist in CTL-mediated severe cutaneous adverse reactions. *J Clin Invest*. 2018;128(3):985-996. [\[Crossref\]](#)
32. Zimmermann S, Sekula P, Venhoffetal M. Systemic immunomodulating therapies for Stevens-Johnson syndrome and toxic epidermal necrolysis: A systematic review and metaanalysis. *JAMA Dermatol*. 2017;53(6):514-522. [\[Crossref\]](#)
33. González-Herrada C, Rodríguez-Martín S, Cachafeiro L, et al. Cyclosporine use in epidermal necrolysis is associated with an important mortality reduction: Evidence from three different approaches. *J Invest Dermatol*. 2017;137(10):2092-2100. [\[Crossref\]](#)
34. Gavian GM, Kanigsberg ND, Ramien M. Pediatric Stevens-Johnson syndrome/toxic epidermal necrolysis halted by Etanercept. *J Cutan Med Surg*. 2018;22(5):514-515. [\[Crossref\]](#)
35. St John J, Ratushny V, Liu KJ, et al. Successful use of cyclosporin A for Stevens-Johnson syndrome and toxic epidermal necrolysis in three children. *Pediatr Dermatol*. 2017;34(5):540-546. [\[Crossref\]](#)
36. Antoon JW, Goldman JL, Shah SS, Lee B. A retrospective cohort study of the management and outcomes of children hospitalized with Stevens-Johnson syndrome or toxic epidermal necrolysis. *J Allergy Clin Immunol Pract*. 2019;7(1):244-250.e1. [\[Crossref\]](#)
37. Trommel N, Hofland HW, vanKomen RS, Dokter J, vanBaar ME. Nursing problems in patients with toxic epidermal necrolysis and Stevens-Johnson syndrome in a Dutch burn centre: A 30-year retrospective study. *Burns*. 2019;45(7):1625-1633. [\[Crossref\]](#)
38. Charlton OA, Harris VR, Phan K, Mewton E, Jackson CJ, Cooper A. Toxic epidermal necrolysis & Steven Johnson syndrome. A comprehensive review. *Adv Wound Care*. 2020;9:426-439. [\[Crossref\]](#)
39. Jaller JA, McLellan BN, Balagula Y. Wound management in Stevens-Johnson syndrome and toxic epidermal necrolysis. *Curr Dermatol Rep*. 2020;9:58-72. Available from: <https://link.springer.com/article/10.1007%2Fs13671-020-00285-3>
40. McCarthy K, Donovan R. Management of a patient with toxic epidermal necrolysis using silicone transfer foam dressings and a secondary absorbent dressing. *J Wound Ostomy Continence Nurs*. 2016;43(6):650-651. [\[Crossref\]](#)
41. Castillo B, Vera N, Ortega-Loayza AG, SeminarioVidal L. Wound care for Stevens-Johnson syndrome and toxic epidermal necrolysis. *J Am Acad Dermatol*. 2018;79(4):764-767. [\[Crossref\]](#)
42. Fu Y, Gregory DG, Sippel KC, Bouchard CS, Tseng SC. The ophthalmologist's role in the management of acute Stevens-Johnson syndrome and toxic epidermal necrolysis. *Ocul Surf*. 2010;8(4):193-203. [\[Crossref\]](#)
43. Xiang Q, Gao X, Fang J, et al. Lacrimal passage irrigation in children with Stevens-Johnson syndrome or toxic epidermal necrolysis: A five-year retrospective study. *BMC Ophthalmol*. 2019;19(1):22. [\[Crossref\]](#)
44. Lee HY. How different is Stevens-Johnson syndrome/toxic epidermal necrolysis in children? *Br J Dermatol*. 2019;181(1):10-11. [\[Crossref\]](#)