WWW.IJRPR.COM

International Journal of Research Publication and Reviews

Journal homepage: www.ijrpr.com ISSN 2582-7421

Stevens Johnson Syndrome Andtoxic Epidermal Necrolysis : An Overview

Miss. Dhanashri santosh Ghude , Asst.prof.Ms Rajeshree Khandare

Department of pharmaceutics, Pratibhatai Pawar college Of Pharmacy, Shrirampur.
Corresponding E-mail – dhanashrighude24@gmail.com

ABSTRACT:

Stevens Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) are severeadverse cutaneous medication react mucus membranes. Mucocutaneous pain, hemorrhagic erosions, erythema, and more or less severe epidermal detachment manifesting as blisters and regions of denuded skin are allsymptoms. In most cases, drugs are assumed or identified as the primary cause of SJS/TEN, but Mycoplasmapneumoniae and Herpes simplex virus infections are wellknown causes, as are rare cases where the origin is unknown. Allopurinol, Trimethoprimsulfamethoxazole, and other sulfonamide antibiotics, aminopenicillins, cephalosporins, quinolones, carbamazepine, phenytoin, phenobarbital, and oxicamtype NSAIDs are among the medications that have a "high" risk of causing TEN/SJS.Linear IgA dermatosis and paraneoplastic pemphigus, pemphigus vulgaris and bullous pemphigoid, acute generalised exanthematous pustulosis (AGEP), diffused fixed bullous drug eruption, and staphimmunomodulatingnd skin syndrome are among the differential diagnoses (SSSS).Patients with SJS/TEN require prompt diagnosis, identification and interruption of the culprit drug, specialised supportive tretment, ideally in an intensive care unit, and consideration of immunomodulating medicines such as highdose intravenous immunoglobulin therapy, because to the high risk of mortality.

Key words: Stevens johnson syndrome, Toxic epidermal necrolysis, skin and mucus membrane.

Introduction

Stevens_Johnson syndrome was first characterised as an unusual, widespread epidermal eruption in 1922. Fever, inflammation of the buccal mucosa, an d acute purulent conjunctivitis are all symptoms. This disorder's prevalence is unclear, however it is assumed to be quite lowDrugs, infectious agents, a nd idiopathic factors all play a role in this disorder's aetiology.The death rate is largely determined by the patient's age and health, and it can range from 30 to 100 percent. Individuals at the extremes of the age spectrum, such as the very young and the very old, are almost always fatal instances. Infectiou s complications are a common cause of death.

Toxic epidermal necrolysis (TEN) is usually associated with drugs6,7Drugs are Stevens-Johnson's most important cause syndrome, but diseases or a combination of diseases and drugs have also been affected. In the event of reports and studies, more than 100 drugs have been implicated as causes of Stevens-Johnson syndrome or epidermal necrolysis8-13 toxicity.a limited amount of drugs, including sulfonamides, anticonvulsant agents, and allopurinol, are the most common. Conditional conditions; whether non-inflammatory drugs (NSAIDs), analgesic agents, and The nonsulfonamide antibiotic associated with them is controversial. A related risk associated with direct use drugs have never been measured. When there is very wide skin the normal pattern of toxic epidermalnecrolysis. And with bad prognosis (30 to 40 percent mortality rate), this condition is often referred to as toxic epidermal. Necrolysis. The mild forms are known as Stevens-Johnson syndrome A common pattern of Stevens-Johnson Syndrome or Stevens-Johnson syndrome spontaneous and toxic epidermal necrolysis.Stevens-Johnson syndrome (SJS) is a skin condition with a more severe form of toxic epidermal necrolysis syndrome (TEN) or Lyell's syndrome. These two syndromes are said to be present at both ends of the spectrum of adverse skin reactions from severe epidermolysis. They present themselves as severe exfoliative reactions that mainly affect the skin and mucous membranes. erythematous macules, blisters and toothache that occur due to the hard separation of the epidermis and dermis.A limited number of drugs, including sulfonamides, anticonvulsant agents, and allopurinol, are the most common; that non-inflammatory drugs (NSAIDs), analgesic agents, and nonsulfonamide antibiotics are associated with it is controversial. The risk associated with the use of certain drugs has never been calculated. Where there is a very wide skin rash it is a common pattern of toxic epidermalnecrolysis. And with poor prognosis (30 to 40 percent mortality rates), this condition is often referred to as toxic epidermal necrolysis. Soft forms are known as Stevens-Johnson syndrome A common pattern of Stevens Johnson Syndrome or Stevens-Johnson syndrome and toxic epidermal necrolysis. tevens-Johnson Syndrome (SJS) is a life-threateningdrug reaction — mucocutaneous inflammation (SJS, also known as erythema multiforme major, lies in progress between erythema multiformeminor, characterized by targeted skin lesions covering less than 10% of the body surface area, and toxic epidermal necrolysis, characterized by extensive mucocutaneous involvement involving 30 % -100% facial skin. Early diagnosis of SJS is based on clinical presentation, but skin biopsies and specific studies of skin immunofluorescence are important to control other conditions such as autoimmune bullous disease.Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are serious skin conditions that cause your skin to develop rashes, blisters, and then peel. Your mucus membranesincluding your eyes, genitalia and mouth, are also affected. If you get this condition, you'll likely be admitted to a hospital.

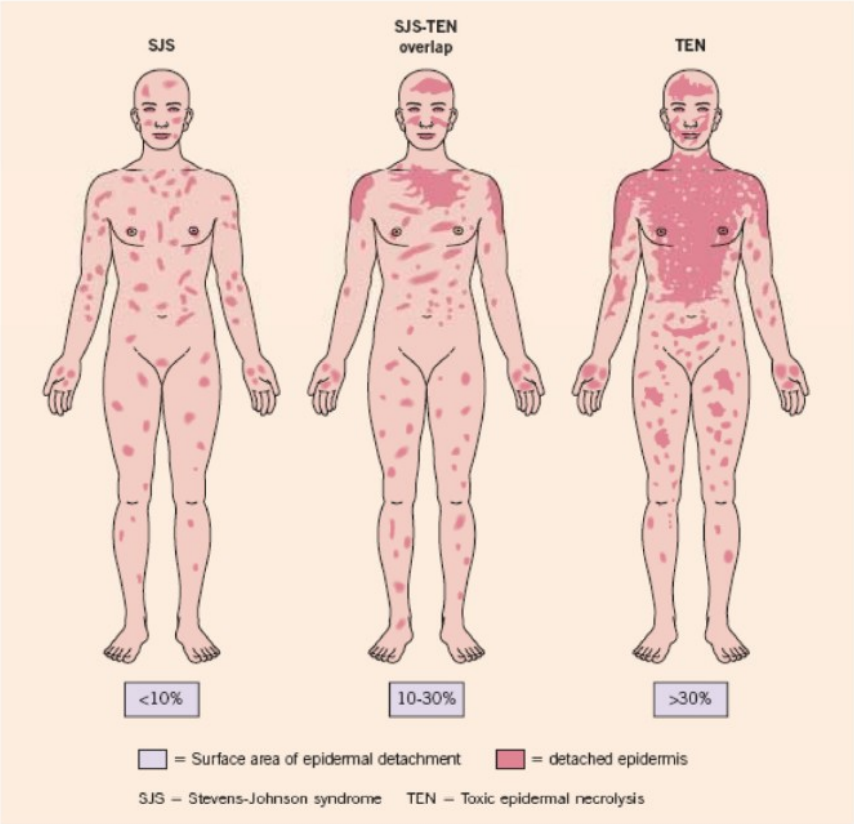

Figure 1. Difference in severity of disease

Table-1: Similarities in clinical presentation

Characteristics	**EM**	**SJS**	**SJS-TEN overlap**	**TEN**
%BSA involved in detachment	<10%	<10%	10-30%	>30%
≥ 1 mucous membrane affected	Up to &)%	>90%	>90%	>905
Spots	No	Yes	Yes	Yes
Atypical targets	Raised	Flat	Flat	Flat
Mortality	Rare	10%	30%	50%
Common cause	Infection	Medication	Medication	Medication
Recurrent	Yes (30%)	No	No	No
Sequelae	Rare	Common	Common	Common

Etiology :

Although a range of etiologies, such as infection sand underlying malignancies, have been implicated as doable motives of SJS, capsules stay the predominant inciting agent. The mostcommonly implicated tablets are sulfa derivatives, nonsteroidal anti-inflammatory agents, penicillin-related and cephalosporin antibiotics, antiepileptics, allopurinol, and terbinafine. There additionally seems tobe an accelerated danger of growing SJS with higher dosages of offending medicines .

Although they have been implicated in uncommon cases, overall, vaccine administration and chemical publicity are hardly ever related with SJS (64–66).Cyclooxygenase-2 inhibitors have additionally been implicated as achievable underlying sources of the disorder. Recreational pills such as cocaine as properly as over-the-counter and choice drugs have also lately been implicated as motives of SJS.According to latest studies, as many as 64% of individuals recognized with SJS have been uncovered to drugs suggesting that in up to one-third of instances nonspecific etiology has been recognized . Althoughmedications are the most frequent causative agent sin adults, comparable developments do no longer follow in the pediatric population. In fact, SJS in pediatric sufferers ismore in many instances brought on with the aid of infectious organisms than damaging drug response. An cognizance of this difference is indispensable to arriving at an correct prognosis and remedy of the condition.

The four etiological categories are as follows:

- Infectious causes
- Drug induced
- Malignancy –related
- Idiopathic

Infectious causes:

Following are the infectious causes:

- Mumps
- Hepatitis
- AIDS
- Influenza
- Herpes simplex virus

In children, Epstein-Barr virus and enteroviruses have been identified. More than half of the patients with Stevens-Johnson syndrome report a recent upperrespiratory tract infection.

Bacterial etiologies include the following:

- Diphtheria.
- Taluremia.
- Maycobacteria.
- Brucellosis.
- Typhoid .
- Mycoplasma pneumonia.
- Lymphogranuloma venereum.

Drug induced :

The most common cause of Stevens Johnson syndrome are antibiotics. Such as analgesics, cough and cold medication, NSAIDs, psychoepileptics, and antigout drugs. Of antibiotics, penicillins and sulfa drugs are prominent; ciprofloxacin has also been reported.

The following anticonvulsants have been implicated:

- Carbamazepine
- Phenytoin
- Lamotrigine
- Valproic acid
- Oxycarbazepine
- Barbiturates

Class of Medication	n (%)
Antibiotics	165 (48.8)
Trimethoprim/sulfamethoxazole	89 (26.3)
β-lactam antibiotics	42 (12.4)
Fluoroquinolones	12 (3.6)
Antiepileptics/mood stabilizers	83 (23.7)
Phenytoin	32 (9.5)
Lamotrigine	30 (8.9)
Carbamazepine	7 (2.1)
Phenobarbital	4 (1.2)
Allopurinol	29 (8.6)
NSAIDs[2]	18 (5.3)

Signs and symptoms :

Typical symptoms of Stevens Johnson syndrome are as follows :

- Headache
- Malaise
- Arthralgia
- Cough

Patients may complain of a burning rash that begins symmetrically on the face and the upper part of the torso. The cutaneous lesions are characterized as follows:

- Urticarial lesions typically are not pruritic.
- Infection may be responsible for the scarring associated with morbidity.
- Although lesions may occur anywhere, the palms, soles, dorsum of the hands, and extensor surfaces are most commonly affected.
- The rash may be confined to any one area of the body, most often the trunk
- The rash can begin as macules that develop into papules, vesicles, bullae, urticarial plaques, or confluent erythema.
- The typical lesion has the appearance of a target; this is considered pathognomonic.
- In contrast to the typical lesions of erythema multiforme, these lesions have only 2 zones of color.
- The lesion's core may be vesicular, purpuric, or necrotic; that zone is surrounded by macular erythema.

Signs of mucosal involvement are as follows :

- Edema
- Ereythemia
- Blistering
- Sloughing
- Necrosis
- Alceration

The following ocular signs may be noted on slit-lamp examination:

- **Conjunctiva:** Papillae, follicles, keratinization, subepithelial fibrosis conjunctival shrinkage, foreshortening of fornices,symblepharon, ankyloblepharon

- **Cornea:** Superficial punctate keratitis, epithelial defect, stromal ulcer, neovascularization, keratinization, limbitis, conjunctivalization, stromal opacity, perforation.
- **Eyelids:** Trichiasis, distichiasis, meibomian gland dysfunction, blepharitis

Figure 2. Sign and symptoms

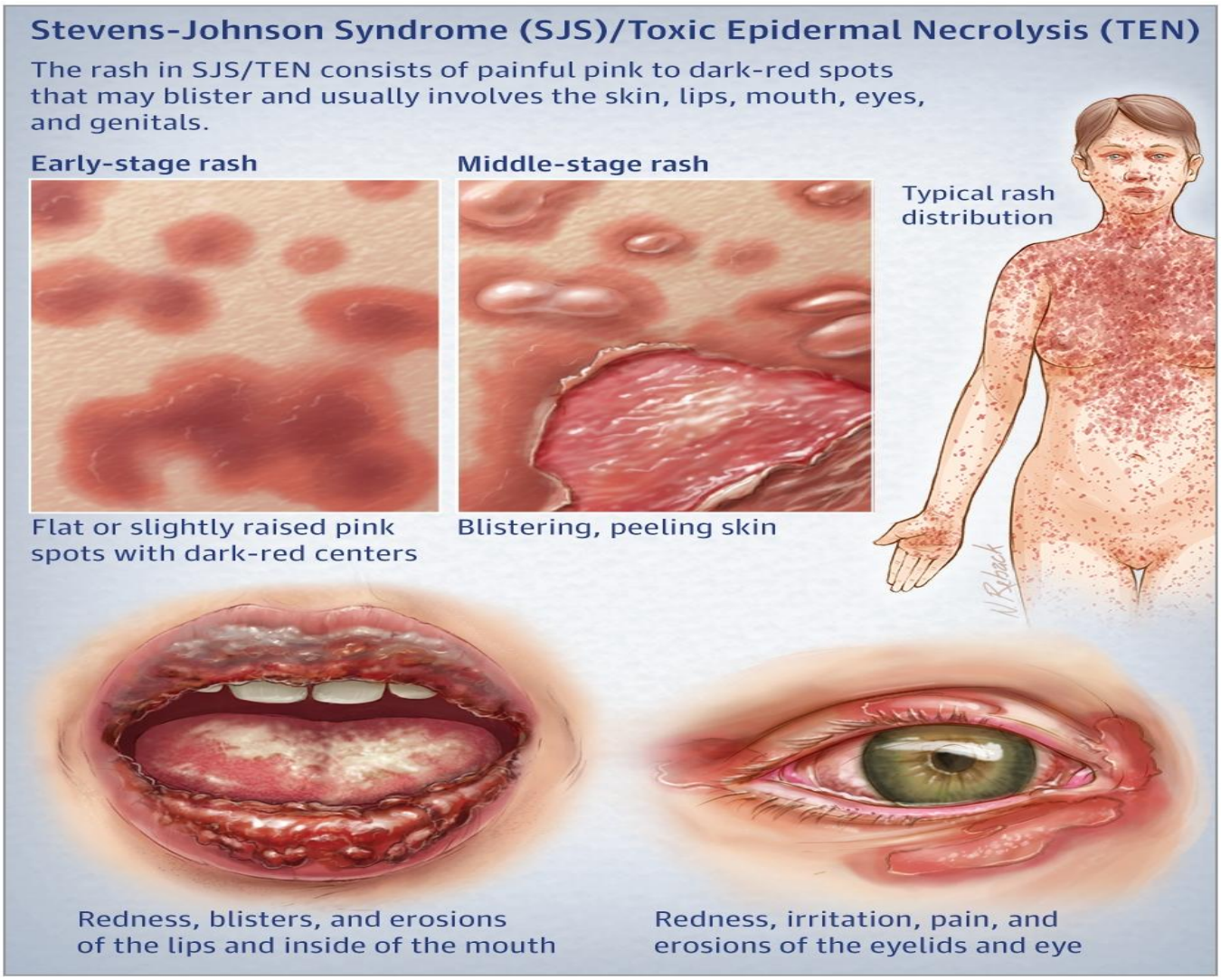

Fig.3 stages of stevens-Johnson syndrome

Clinical manifestation :

SJS usually starts offevolved with indistinct top respiratory tract signs lasting up to two weeks.During this period, sufferers might also whinge of fever,sore throat, chills, headaches, and malaise .Persistent fever lasting longer than four weeks ought to elevate suspicion of a concomitant infection, however research have validated that persevered fever might also happen in up to 85% of instances even in the absence of an related contamination . This is observed by means of the speedy onset of mucocutaneous lesions. Painful erosions of the mucous membranes are frequent and can also have an effect on any aggregate of the lip, oral cavity, conjunctiva, nasal cavity, urethra, vagina,gastrointestinal tract, and respiratory tract throughout the path of the sickness (9–11). Involvement of mucous membranes is evident in about 90% of affected patients, and the absence of mucous membrane involvement ought to solid doubt on the prognosis of SJS. Mucous membrane involvement can end result in each momentary dysfunction and morbidity, as properly as long-term issues due to fibrosis and strictures.

Pathophysiology:

The pathogenesis of SJS/TEN is now not utterly understood however is believed to be immune-mediated, as re-challenging an person with the identical drug can end result in fast recurrence of SJS/TEN.

An idiosyncratic, delayed hypersensitivity response has been implicated in the pathophysiology of Stevens-Johnson syndrome. Certain populace agencies show up greater prone to enhance Stevens-Johnson syndrome than the widely wide-spread population. Slow acetylators, patients who are immunocompromised (especially these contaminated with HIV30,31), and sufferers with Genius tumors present process radiotherapy with concomitant

antiepileptics are amongst these at most risk. Slow acetylators are humans whose liver can't absolutely detoxify reactive drug metabolites. These drug metabolites may also have direct poisonous consequences or can also act as haptens that have interaction with host tissues, rendering them antigenic.
Antigen presentation and manufacturing of tumor necrosis issue (TNF)–alpha through the neighborhood tissue dendrocytes consequences in the recruitment and augmentation of T-lymphocyte proliferation and enhances the cytotoxicity of the different immune effector cells.34A "killer effector molecule" has been recognized that may also play a function in the activation of cytotoxic lymphocytes.35 The activated CD8+ lymphocytes, in turn, can result in epidermal mobilephone apoptosis by using countless mechanisms, which encompass the launch ofgranzyme B and perforin.Both SJS and TEN are characterised with the aid of the detachment of dermis from the papillary dermis at the epidermal-dermal junction, manifesting as a papulomacular rash and bullae as a end result of keratinocyte apoptosis. Keratinocyte apoptosis mediated by way of cytotoxic T-lymphocytes (CD8) in SJS and TENS is modulated via plasma TNF-alpha and interferon-gamma, which are accelerated in sufferers with SJS and TEN. This method is presently hypothesised to take place thru three viable pathways: Fas-Fas ligand interaction; perforin/granzyme B; and granulysin-mediated.

Diagnosis:

The diagnosis depends on the one hand on medical signs and on the different hand on histological features. Typical scientific symptoms at the start consist of areas of erythematous and furious macules on the skin, on which a tremendous Nikolsky signal can be prompted via mechanical stress on the skin, accompanied inside minutes to hours via the onset of epidermal detachment characterised by means of the improvement of blisters. To distinguish SJS, SJS-TEN and TEN the floor place of the detachment is the primary discriminating factor. Histological work up of immediately cryosections or traditional formalin-fixed sections of the pores and skin revealing huge unfold necrotic dermis involving all layers confirms the diagnosis. In order to rule out autoimmune blistering diseases, direct immune fluorescence staining have to be moreover carried out and no immunoglobulin and/or complement deposition in the dermis and/or the epidermal-dermal region ought to be detected.

Differential diagnosis:

Major differential diagnosis of SJS/TEN are autoimmune blistering diseases, consisting of linear IgA dermatosis and paraneoplastic pemphigus however additionally pemphigus vulgaris and bullous pemphigoid, acute generalized exanthematous pustulosism (AGEP), disseminated constant bullous drug eruption and staphyloccocal scalded pores and skin syndrome (SSSS). SSSS used to be one of the most essential differential diagnoses in the past, however the incidence is presently very low with 0.09 and 0.13 instances per one million inhabitants per year.

Treatment :

Topical treatment:

Although the blisters are fragile, they must be left in area or solely be punctured. Erosions can be handled with chlorhexidine, octenisept or polyhexanide options and impregnated no adhesive mesh gauze. The latter is vital if environmental factors, such as excessive room temperature or alternating stress mattress, lead to pores and skin dryness. Silver sulfadiazine ought to be avoided, at least if the causative drug was once cotrimoxazole or every other anti-infective sulfonamide. Some burn care professionals debride the pores and skin beneath regularly occurring anesthesia and follow allografts or different kinds of coverage. However, this instead aggressive method is now not tolerated nicely by way of many aged sufferers with underlying diseases. Furthermore, hypertrophic scars might also appear if debridement is carried out notably and if allografts are constant with staplesdirectly into the skin.
For affected mucosal surfaces, specialised care is critical. The severity of the mucosal involvement is regularly now not inline with the quantity of pores and skin detachment and neglected mucosal lesions can lead to life-long problems. Amultidisciplinary method is wanted and in case of urethral involvement urologists need to be involved. Appropriately placed moist dressings or sitz baths may additionally assist to keep away from adhesions or strictures of genital erosions in women and women. Disinfectant mouth wash must be used to deal with oral erosions and slight ointment, such as dexpanthenol, need to be utilizedon erosions and bloody crusts of the lips.
In the case of eye-involvement, everyday ophthalmologic session is crucial. Specialized lid care is wished on a daily foundation and anti-inflammatory eye drops ought to be given numerous instances per day. Severe blepharitis might also lead toentropion with trichiasis (in developing eye lashes) inflicting similarly corneal damage. Various specialised procedures to ocular involvement have been suggested, such as stem cellphone era of alternative cells, amniotic membrane transplantation and scleral lenses, however are no longer but extensively accepted61,62.Nevertheless, skilled ophthalmologists ought to be concerned inthe care of all sufferers with SJS/TEN, even these that do no longer current with eye-involvement right away, considering that it can also manifest with some lengthen.

Ocular manifestations treatment:

A aggressive lubrication of the ocular surface is usually the first step in treating acute visual symptoms. Most ophthalmologists treat inflammation and cicatricial alterations using topical steroids, antibiotics, and symblepharon.lysis. Tarsorrhaphy may be required in the event of exposure keratopathy. It is possible to maintain ocular integrity. Amniotic membrane grafting, sticky glues, lamellar grafts, and penetrating keratoplasty, either in the anterior or posterior During the acute phase or during follow-up care. Patients with visual impairments may benefit from visual rehabilitation. After at least 3 months of silence in the eye.

Supportive Services:

The control of fluid and electrolyte requirements is an important part of supportive care. With 0.5 percent NaCl mixed with 20 mEq of KCl, intravenous fluid should be given to maintain urine production of 50-80 mL per hour.In the event of hyponatremia, hypokalemia, or hypomagnesemia, prompt and aggressive replacement therapy is essential.Hypophosphataemia is a condition that occurs frequently. Skin debridement should be avoided when treating wounds. This procedure is commonly used in burn units because blistering skin behaves as a natural biological dressing that promotes regrowth.

W**ithdrawal of the offending drug as soon as possible** :

When blisters or erosions form during a medication eruption, it is critical to remove the causative drugs as soon as possible. Garcia-Doval et al. found that the earlier the causative medicine is withdrawn, the better the prognosis, and that the earlier the causative drug is withdrawn, the better the prognosis. Patients who are exposed to causal medications with long half-lives are more likely to die.

Conclusion:

SJS and poisonous epidermal necrolysis (TEN) are viewed as one sickness entity of special severity. SJS/TEN is mainly prompted by using drugs, infections and likely different hazard elements now not but identified. The pathogenesis of SJS/TEN has not been definitely solved, however unique genetic predispositions, which differ amongst ethnic businesses and range between certain inflicting drugs, have been identified. Since to date no therapy has been recognized to be succesful of halting theprogression of pores and skin detachment, supportive administration is imperative to enhance the patient's state, probable greater thanspecific immunomodulating treatments. Despite all therapeutic efforts, mortality is excessive and will increase with sicknessseverity, patients' age and underlying scientific conditions. Survivors can also go through from long-term sequelae such as stricturesof mucous membranes which include extreme eye problems. Therefore, interdisciplinary care and follow-up of sufferers with SJS/TEN is important.

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