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***Critical Dermatological Emergencies: A Literature Review of Clinical
Presentation, Diagnosis, and Treatment of Necrotising Fasciitis, Toxic Epidermal
Necrolysis, and Stevens-Johnson Syndrome***

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LIST OF ABBREVIATIONS

Abbreviation	Meaning
CRP	C-reactive protein
CT	Computed tomography
HIV	Human immunodeficiency virus
LRINEC	Laboratory Risk Indicator for Necrotizing Infection
MeSH	Medical Subject Heading
MRI	Magnetic Resonance Imaging
MRSA	Methicillin-Resistant Staphylococcus aureus
NF	Necrotising fasciitis
NSAIDs	Non-steroidal anti-inflammatory drugs
P-NSTI	Polymicrobial Necrotizing Soft Tissue Infection
PTSD	Post traumatic stress disorder
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
SJS	Stevens-Johnson syndrome
SSTI	Skin and soft tissue infections
TBSA	Total body surface area
TEN	Toxic epidermal necrolysis
WSES	World Society of Emergency Surgery
WBC	White blood cell count

ABSTRACT IN LITHUANIAN

Įvadas: kritinės dermatologinės būklės, tokios kaip nekrotizuojantis fascitas (NF), toksinė epiderminė nekrolizė (TEN) ir Stivenso–Džonsono sindromas (SJS), yra sunkios, greitai progresuojančios ligos, reikalaujančios skubaus atpažinimo ir klinikinio valdymo. Vis dėlto, ankstyva diagnozė tebėra iššūkis, nes šios ligos dažnai imituoja labiau paplitusius dermatologinius ar infekcinius simptomus, todėl gali būti vėluojama pradėti tinkamą gydymą. Išsamus šių ligų epidemiologijos, klinikinių požymių, diagnostikos metodų ir gydymo strategijų supratimas yra būtinas siekiant pagerinti pacientų gydymo rezultatus ir padėti gydytojams teikti tiek skubią, tiek stacionarią pagalbą. Tačiau esama literatūra yra labai, fragmentuota ir nevienodos kokybės, todėl būtina apibendrinti esamus įrodymus, kad būtų galima priimti veiksmingus klinikinius sprendimus.

Tikslas: šios sisteminės apžvalgos tikslas – įvertinti ir apibendrinti esamus duomenis apie NF, SJS ir TEN epidemiologiją, klinikinius požymius, diagnostiką, gydymą ir baigtis, siekiant padėti laiku atpažinti šias ligas ir priimti veiksmingus klinikinius sprendimus. Metodai: „PubMed“ duomenų bazėje buvo atlikta sisteminė literatūros paieška, naudojant atitinkamus medicinos temų antraštes (MeSH terminus) ir tekstinius žodžius, apsiribojant anglų kalba parašytais straipsniais, paskelbtais per pastaruosius 15 metų. Pašalinus dubliuojamus įrašus, tyrimai buvo atrinkti dviem etapais pagal PRISMA gaires: pirmiausia atlikta pavadinimų ir santraukų atranka, po kurios sekė viso teksto vertinimas, remiantis iš anksto nustatytais įtraukimo ir išbraukimo kriterijais. Išgauti duomenys apėmė epidemiologiją, klinikinius požymius, diagnostiką ir gydymo rezultatus.

Rezultatai: iš viso atrankos kriterijus atitiko 38 tyrimai. Literatūros duomenimis, NF, SJS ir TEN yra nuolat siejami su greitu ligos progresavimu, diagnostiniais sunkumais bei dideliu sergamumu ir mirtingumu. Ne kartą nustatyta, kad ankstyvas atpažinimas ir laiku taikomos intervencijos, ypač skubus chirurginis gydymas NF atveju ir greitas priežastinių vaistų nutraukimas SJS/TEN atveju, pagerina gydymo rezultatus. Nepaisant vertinimo ir gydymo strategijų įvairovės, daugiadisciplininė ir palaikomoji priežiūra išlieka esminėmis veiksmingo gydymo sudedamosiomis dalimis. Išvada: ši apžvalga rodo, kad NF, SJS ir TEN tebėra sunkūs dermatologiniai skubios pagalbos atvejai, kuriuose pavėluotas diagnozavimas reikšmingai pablogina pacientų ligos baigtį. Nors įtrauktuose tyrimuose buvo pateikti įvairūs diagnostikos ir gydymo metodai, ankstyvas nustatymas, laiku suteikta pagalba ir koordinuota daugiadisciplininė priežiūra nuosekliai buvo siejami su geresne prognoze. Rezultatai pabrėžia nuolatinį poreikį didinti klinikinį sąmoningumą, standartizuoti diagnostikos strategijas ir taikyti įrodymais pagrįstus gydymo protokolus, siekiant paremti veiksmingą sprendimų priėmimą šių greitai progresuojančių ligų atveju. Raktažodžiai: klinikinis valdymas, dermatologinės ekstremalios situacijos, diagnostika nekrotizuojantis fascitas, Stivenso–Džonsono sindromas, sisteminė apžvalga, gydymas, toksinė epiderminė nekrolizė

ABSTRACT

Background/Introduction: Critical dermatological emergencies such as necrotising fasciitis (NF), toxic epidermal necrolysis (TEN), and Stevens–Johnson syndrome (SJS) represent severe, rapidly progressing conditions that require urgent recognition and clinical management. Despite this, early diagnosis remains a challenge, as these disorders often mimic more common dermatological or infectious presentations, leading to delay in appropriate treatment. A thorough understanding of their epidemiology, clinical features, diagnostic approaches, and treatment strategies is essential for improving patient outcomes and guiding clinicians in emergency and inpatient care settings. However, existing literature is widely dispersed and varies in quality, making it necessary to synthesise current evidence to support effective clinical decision-making.

Aim and Objectives: This systematic review aimed to evaluate and summarise the current evidence on the epidemiology, clinical presentation, diagnosis, treatment, and outcomes of NF, SJS, and TEN, in order to support timely recognition and effective clinical decision-making.

Materials and Methods: A systematic literature search was conducted in PubMed using relevant Medical Subject Headings (MeSH terms) and text-words, restricted to English-language articles published within the last 15 years. After duplicate removal, studies underwent a two-phase screening process according to PRISMA guidelines: initial title and abstract screening, followed by full-text evaluation based on predefined inclusion and exclusion criteria. Extracted data included epidemiology, clinical presentation, diagnostics, treatments, and outcomes.

Results: In total, 38 studies have met the eligibility criteria. Across the literature, NF, SJS, and TEN were consistently associated with rapid progression, diagnostic challenges, and high morbidity and also mortality. Early recognition and the timely intervention, particularly prompt surgical management in NF and early withdrawal of causative drugs in SJS/TEN, were repeatedly shown to improve the outcomes. Despite variability in assessment and treatment strategies, multidisciplinary and supportive care remained essential components of effective management.

Conclusion: This review demonstrates that NF, SJS, and TEN remain severe dermatological emergencies in which delayed recognition significantly worsens patient outcomes. Although the included studies have presented varied diagnostic and treatment approaches, early identification, and timely intervention, and the coordinated multidisciplinary care were consistently associated with improved prognosis. The findings highlight the continued need for heightened clinical awareness, standardised diagnostic strategies, and evidence-based management protocols to support effective decision-making in these rapidly progressing conditions.

Keywords: Clinical management, Dermatological emergencies, Diagnosis, Necrotising fasciitis, Stevens–Johnson syndrome, Systematic review, Treatment, Toxic epidermal necrolysis

1. INTRODUCTION

Dermatological emergencies, including necrotising fasciitis (NF), toxic epidermal necrolysis (TEN), and Stevens-Johnson syndrome (SJS), must be recognised because of their fast growth to skin necrosis and the possibility of permanent skin damage. These disorders can manifest very rapidly, often presenting right in front of practitioners, which may lead to an underestimation of their severity in the early stages. Therefore, early detection is very important, since fast medical intervention can significantly decrease the risk of systemic infection, organ failure, and severe patient mortality. Dermatological emergencies require a multidisciplinary approach because of their severity. The medical team should include dermatologists, acute and intensive care doctors, and surgeons. Timely intervention plays a key role in improving patient outcomes, as these disorders can lead to disfiguring scars and longer hospitalizations, which may be associated with psychological effects such as depression, anxiety, and post-traumatic stress disorder (PTSD) (1).

The mortality rates that are linked to these emergencies can be elevated if not addressed quickly and effectively, particularly in those instances such as NF or TEN. Identifying these principal risk factors, which include infections, drugs, trauma, and implementing preventative measures could reduce the incidence of these life-threatening conditions. Early discontinuation of any causative drugs in instances of drug induced TEN may prevent its development and in turn enhance the prognosis. In addition to the immediate threat to life, these disorders may lead to permanent complications that include scarring, contractures, constant pain, and psychological illness (2). These issues can significantly and also heavily impact the patients quality of life, diminishing the ability to work efficiently, engage in social activities, and to maintain their self-esteem.

In addition to the physical complications the patient might endure. Dermatological emergencies frequently impose also considerable financial and social burdens due to the extended time of the treatments, the possibility of disability, and the requirement for specialized care. The healthcare system must prioritize the education and training of clinicians to guarantee quick diagnosis and treatment, while also encouraging awareness of the significance of emergency interventions in these clinical situations. Since these illnesses may first manifest in emergency rooms or primary care settings, it is essential for non-dermatologists to be able to identify these situations and make correct recommendations (3). It is also worth noting that some skin emergencies are rare and very difficult to diagnose. Patient and family education is therefore also crucial for enhancing patient outcomes, since understanding of these conditions will facilitate timely reactions and improved patient quality of care.

2. MATERIALS AND METHODS

2.1 SYSTEMATIC LITERATURE REVIEW

A systematic literature search was conducted using the PubMed database to identify scientific and medical literature relevant to critical dermatological emergencies. Medical Subject Heading (MeSH) terms were identified using the MeSH database on the National Center for Biotechnology Information website (<https://pubmed.ncbi.nlm.nih.gov/>). Entry terms related to the thesis topic such as “Necrotising Fasciitis,” “Toxic Epidermal Necrolysis,” and “Stevens-Johnson Syndrome” were used to identify corresponding MeSH terms. For example, the search term “Necrotising Fasciitis” , “Toxic Epidermal Necrolysis” and “Stevens-Johnson Syndrome” directly matched respective MeSH terms.

The literature search combined identified MeSH terms and text words using the Boolean operators and are as follows:

- ("Necrotizing Fasciitis"[Mesh]) AND ("Epidemiology, Etiology and Pathophysiology "[Mesh]) (58 results)
- ("Necrotizing Fasciitis"[Mesh]) AND ("Clinical presentation and Diagnosis"[Mesh]) (46 results)
- ("Necrotizing Fasciitis"[Mesh]) AND ("Treatment and management"[Mesh]) (39 results)
- ("Stevens-Johnson Syndrome"[Mesh]) AND ("Epidemiology, Etiology and Pathophysiology "[Mesh]) (42 results)
- ("Stevens-Johnson Syndrome"[Mesh]) AND ("Clinical presentation and Diagnosis "[Mesh]) (36 results)
- ("Stevens-Johnson Syndrome"[Mesh]) AND ("Treatment and management "[Mesh]) (31 results)
- ("Toxic Epidermal Necrolysis"[Mesh]) AND ("Epidemiology, Etiology and Pathophysiology "[Mesh]) (28 results)
- ("Toxic Epidermal Necrolysis"[Mesh]) AND ("Clinical presentation and Diagnosis "[Mesh]) (21 results)
- ("Toxic Epidermal Necrolysis"[Mesh]) AND ("Treatment and management "[Mesh]) (11 results)

The search was limited according to the inclusion and exclusion criteria described in section 2.2. The selection process and results are detailed in section 2.3.

2.2 INCLUSION AND EXCLUSION CRITERIA

Studies published within the last 15 years were included if they were clinical studies, clinical trials, controlled clinical trials, comparative studies, or observational studies focusing on clinical presentation, diagnosis, or treatment of necrotising fasciitis, toxic epidermal necrolysis, or Stevens-Johnson syndrome.

Only articles published in English were considered. Excluded were editorials, commentaries, case reports with fewer than five patients, abstracts without full texts, and studies not directly related to the critical dermatological emergencies of interest.

2.3 STUDY SELECTION

The literature search initially retrieved 312 results, which were screened following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. Duplicates (n = 34) were removed, and the remaining 278 articles underwent title and abstract screening based on the inclusion and exclusion criteria. Subsequently, 208 articles were excluded. Full texts of the remaining 70 articles were reviewed thoroughly, leading to the exclusion of 37 further studies. Reference mining of the included articles yielded an additional 5 relevant studies. In total, 38 studies were included in the final review.

2.4 DATA EXTRACTION

The following data were extracted from each included study:

- Authors
- Year of publication
- Aim of the study
- Study design
- Number and characteristics of patients
- Clinical presentation features
- Diagnostic methods used
- Treatment approaches described
- Outcome measures and results
- Conclusions

3. NECROTIZING FASCIITIS

3.1 EPIDEMIOLOGY, AETIOLOGY AND PATHOPHYSIOLOGY

NF is a rare, rapidly advancing, and frequently severe bacterial infection that leads to significant necrosis of subcutaneous tissue and fascia, while comparatively preserving muscle and skin tissues. Necrotising fasciitis indicates a "decaying infection of the fascia." The estimated incidence in the Western world is between 0.24–0.4 cases per 100,000 persons every year, which rendering it one of the most difficult and challenging emergencies encountered by healthcare professionals. In certain regions, NF exhibits an even higher prevalence, with more than one case reported per 100,000 people (4).

NF possesses a complex aetiology, characterised by diverse underlying causes, risk factors, anatomical involvement, and pathogenic processes. The disorder leads to extensive tissue damage and destruction, potentially affecting the epidermis and deep muscles. The infectious process typically advances along fascial planes, which possess a restricted blood supply, possibly complicating diagnosis and surgical intervention, as the superficial tissues may first look unaffected. It can quickly spread, resulting in infection and inflammation of the fascia, peri-fascial areas, and later more involvement of the adjacent and underlying skin, soft tissues and muscles (5).

NF is notably prevalent among individuals with predisposing comorbidities and risk factors, such as diabetes, chronic like conditions, immunosuppression, bad eating habits, old age, non-steroidal anti-inflammatory drug (NSAID) usage, obesity, liver scarring, intravenous drug use, alcoholism, peripheral vascular disease, chronic renal failure, immunological disorders, human immunodeficiency virus (HIV), paraplegia, underlying malignancies, and varicella infection. A case study done by Bingol-Kologlu has described also the onset of NF as subsequent to the use of a menthol-containing lotion to the cervical area (4,5).

The mortality rates linked to NF are extremely high and even those who survive frequently have an extended clinical journey. Timely clinical suspicion and diagnosis are therefore essential for beneficial outcomes; yet a correct diagnosis is achieved in about only 15% to 34% of cases. In 2015, the World Society of Emergency Surgery issued new recommendations for the management of skin and soft tissue infections (SSTIs). These recommendations encompassed a new classification that classified SSTIs into three principal categories: surgical site infections, non-necrotizing SSTIs, and necrotising SSTIs. For necrotizing SSTIs, such as cellulitis, fasciitis, myositis, and Fournier's gangrene, the World Society of Emergency Surgery (WSES) guidelines recommend the surgical interventions, including surgical drainage and the debridement of all necrotic tissue, in addition to antibiotics as an adjunct therapy (6).

NF may also occur subsequent to surgical operations, invasive interventions, or even basic treatments like phlebotomy. The causal agents are often a diverse bacterial community capable of gas production. Hippocrates also has offered a clinical description of NF, attributing it to erysipelas, as early as before 500 BC, this shows that this condition has been acknowledged for ages and aligns with contemporary comprehension of NF.

The classification of NF is complex, including characteristics such as the causative microorganisms, the depth of infection, and the affected anatomical region. NF can be categorised into a lot categories according to the primary bacteria that cause the illness, such groups can include streptococcal NF, clostridial NF, polymicrobial NF, and monomicrobial NF, among others. The extent of infection can also vary with NF impacting either superficial fascia, deep fascia, or both. Anatomically, NF may manifest in several anatomical areas, including the limbs, trunk, or head and neck. This detailed classification system aids in directing suitable care and treatment approaches for this rapidly advancing and severe illness.

The primary bacterial aetiologies of NF are mostly group A *Streptococcus*, *Clostridium perfringens*, and a mixture of aerobic and anaerobic microorganisms. Furthermore, *Staphylococcus aureus* can induce monomicrobial NF. Over the past twenty years, methicillin-resistant *Staphylococcus aureus* (MRSA) has become a notable factor in *S. aureus*-associated NF, despite mortality rates being mostly comparable between MRSA and methicillin-susceptible *S. aureus* infections. The collaborative effect of several bacteria increases tissue damage and complicates therapeutic approaches. As mentioned previously, the infection progresses rapidly along the fascial planes, resulting in incremental fascial damage at a rate of 2–3 cm/h (7).

3.2 CLINICAL PRESENTATION

The clinical manifestation of NF may be misleading in the initial stages, frequently mimicking more prevalent skin infections such as cellulitis. After a few days, the superficial skin, appearing unchanged, will evolve into an erythematous, red purple to blue-grey discolouration. The skin becomes swollen, inflamed, shiny, also increased temperature and tenderness upon palpation. At this stage, the skin is highly sensitive to touch and palpation and may also exhibit discomfort that is disproportionate to the observed symptoms. Skin damage will start within three to five days, accompanied by the formation of primary lesion like bullae, blisters, and also cutaneous gangrene. NF is typically linked with severe pain that is disproportionate to the observed symptoms, as mentioned previously, along with systemic septic manifestations, unlike non-necrotizing infections. Physical examination may reveal pain and tenderness to palpation extending beyond the erythematous margin, crepitus, and cellulitis. The development of bullae, ecchymotic alterations, and dysesthesia

or paraesthesia should be regarded as symptoms indicative of NF. Subcutaneous emphysema and crepitus are frequently seen.

In contrast to cellulitis, NF progresses rapidly, accompanied by intense and disproportionate pain, fever, and subcutaneous crepitus. Nevertheless, it is frequently misdiagnosed as cellulitis or other soft tissue infections in 70-85% of instances. Misdiagnosis results in delayed therapy and worse consequences. When cellulitis patients exhibit worsening or alarming symptoms, physicians should immediately assess the situation, initiate intravenous antibiotics, and consider surgical intervention (Fig. 1 , 2) (8).



Figure 1: Clinical presentation upon admission to the Emergency Department.



Figure 2: Six hours after the first surgical debridement.

3.3 DIAGNOSIS

Because of the difficulties in separating the non-necrotizing from necrotising skin tissue infections, rapidly spreading and progressing infections must be treated quickly and aggressively. The Laboratory Risk Indicator for Necrotizing Infection (LRINEC) Score, established in a 2004 study, tries to distinguish, differentiate, and establish necrotising soft tissue infections from other critical soft tissue infectious diseases, it is considered one of the most widely used diagnostic tools. This score method relies on variations in the following 6 distinct variables: C-reactive protein (CRP), white blood cell count (WBC), hemoglobin, sodium, creatinine, and glucose (Tab. 1).

Table 1: Laboratory Risk Indicator for Necrotizing Infection (LRINEC) scoring system.

Parameter	Range / Threshold	Score
C-reactive protein (mg/L)	< 150	0
	≥ 150	4
Total white cell count, WBC ($\times 10^3/\text{mm}^3$)	< 15	0
	15–25	1
	> 25	2
Hemoglobin (g/dL)	> 13.5	0
	11–13.5	1
	< 11	2
Sodium (mmol/L)	≥ 135	0
	< 135	2
Creatinine (mg/dL)	≤ 1.6	0
	> 1.6	2
Glucose (mg/dL)	≤ 180	0
	> 180	1

A Laboratory Risk Indicator for Necrotizing infection score of 6 will show a high predictive positive value of 92% and a negative predictive value of 96%, suggesting it as a significant chance of necrotising soft tissue infection. A LRINEC score of 8 or above indicates a 75% probability of necrotising infection. Imaging techniques, such as conventional radiography, ultrasound, computed tomography (CT) scan, magnetic resonance imaging (MRI), are essential for the diagnosis and treatment of necrotising soft tissue infections. While the diagnosis is essentially clinical, these imaging modalities can offer corroborative information when the diagnosis is questionable.

Normal radiographs may show increased soft tissue thickness and radioopacity comparable to cellulitis; nevertheless, their diagnostic use is restricted. Soft-tissue gas is specific but lacks high sensitivity, since it appears in only 25% of Type 1 necrotising fasciitis patients after the disease has progressed. Additionally, plain radiographs may reveal non-specific markers of soft tissue swelling, perhaps simulating cellulitis and myositis. Research indicates that non-diagnostic plain radiographs might result in diagnostic errors and lead to interruptions in surgical intervention, hence increasing morbidity and mortality.

Ultrasonography is also an effective modality in NF, as it can recognise subcutaneous emphysema along the fascial planes, swelling, increased echogenicity of adipose tissue with interspersed serous collections, and also abscess and pus development, therefore facilitating timely surgical intervention. A CT scan has around 100 percent sensitivity and 80-98 percent specificity in identifying NF. It reveals soft-tissue attenuation, fat stranding, and the presence of fluid or air inside fascial planes. Nonetheless, CT results in the first stages of NF are only minor. Furthermore, negative findings on an intravenous contrast-enhanced CT scan might effectively eliminate the necessity for surgical intervention in individuals initially suspected of NF.

MRI has emerged as the preferred method for the comprehensive assessment of soft tissue infections. Numerous studies have proven its efficacy in distinguishing non-necrotizing cellulitis, responsive to medical treatment, from severe NF, necessitating aggressive debridement. The combination of MRI and clinical examination may facilitate the evaluation of the necessity and degree of debridement. The principal observation in MRI is the thickening of the deep fasciae that resulting from fluid buildup and reactive hyperaemia (9). MRI is also crucial for evaluating the severity of the condition, facilitating surgical planning, and identifying underlying causes (9).

In instances of strong clinical suspicion of NF, and when imaging results are also negative or imaging facilities are inaccessible, a 'Finger Test' may be utilised for diagnostic confirmation. Following adequate infiltration with local anaesthesia, a 2- to 3-centimeter incision is created in the skin extending to the deep fascia. The lack of haemorrhage and/or the presence of "dishwater-coloured pus" in the lesion strongly indicates NF. Gentle probing of the tissues with the finger, which should separate effortlessly with minimum resistance, indicates a positive Finger Test for NF.

3.4 TREATMENT AND MANAGEMENT

The treatment and management of NF requires a very comprehensive strategy involving immediate surgical intervention, broad-spectrum antibiotic therapy, and also supportive care. Empiric antibiotic therapy should be therefore initiated immediately upon suspicion of NF, even before confirmatory diagnostic tests are completed. The key treatment concepts include effective control and

management of infection sites, such as surgical drainage of abscesses, thorough debridement of necrotic tissue, and pathogen identification via specimen analysis, which guides necessary modifications to the antimicrobial therapy. Timely surgical intervention is crucial for source control and the excision of necrotic tissue, hence enhancing antibiotic penetration and reducing the bacterial load.

The suggested antimicrobial regimens for the treatment of NF encompass the following options: One option is imipenem (1 g every 6 to 8 hours) combined with daptomycin (6 mg/kg 1/t daily) and clindamycin (600 to 900 mg 4/t daily). Another regimen involves piperacillin/tazobactam (either 3.375 g every 6 hours or 4.5 g every 8 hours), also paired with daptomycin and clindamycin at the same dosages. A third alternative consists of meropenem (1 g intravenously every 8 hours), vancomycin (15 to 20 mg/kg per dose every 8 to 12 hours), and clindamycin (600 to 900 mg 4/t daily).

As previously stated, early and quick surgical cleaning of the necrotic tissue is fundamental to management of NF. It alleviates the infection demand, reduces subsequent tissue loss, limits the necessity for amputation, and thus, reduces mortality. Debridement must be thorough, and all necrotic and weakly perfused tissues that can be readily removed from the fascia with little pressure should be removed.

The literature offers varying viewpoints on the amount of tissue that should be first removed, as the skin often appears normal. The authors performed a microscopic examination of presumably normal tissues in NF and identified significant early vascular thrombosis and vasculitis, suggesting that these tissues hold a considerable risk for deterioration and complete thickness loss (10). After the first debridement, the patient could require another surgical debridement, as the overall haemodynamic instability associated with peripheral vasoconstriction might lead to progressive skin necrosis. After debridement of all affected tissues, careful wound management with different dressing materials prepares the wound bed for soft tissue repair. After the complete elimination of necrotic tissue and the presence of granulation tissue, a consultation with a plastic surgeon is advisable. In many instances, initial wound closure is impracticable, requiring the plastic surgeon to reconstruct the soft tissues and primary wound closure using a muscle flap. If sufficient skin is not available for grafting, synthetic skin may be employed.

Hyperbaric oxygen therapy is a viable therapeutic option; however, the difficulties associated with transferring critically sick patients to the hyperbaric facility restrict its practical use. Although hyperbaric oxygen may benefit small wounds, there is little evidence to suggest it enhances healing or survival for profound and big wounds. Hyperbaric oxygen serves as an adjuvant treatment and does not replace surgical debridement. This form of therapy may be advantageous when the patient is haemodynamically stable, and some evidence indicates it can decrease mortality. However still,

hyperbaric oxygen should be regarded as a supplementary method rather than a substitute for surgical intervention and debridement (Tab. 2) (10).

Table 2: Algorithm for Treatment and Management of Necrotizing Fasciitis

Steps	Management Actions
1. Clinical suspicion	Severe pain out of proportion to examination, rapidly progressive swelling/erythema, systemic toxicity, LRINEC score ≥ 6 . Early recognition is essential, as diagnostic delay increases mortality.
2. Immediate action	Begin empiric broad-spectrum IV antibiotics immediately (e.g., imipenem + daptomycin + clindamycin; piperacillin/tazobactam + daptomycin + clindamycin; or meropenem + vancomycin + clindamycin). Start fluid resuscitation, analgesia, vasopressors if required. Obtain blood/tissue cultures if feasible but never delay therapy. Arrange urgent surgical consultation.
3. Surgical management	Early and aggressive debridement of all necrotic/poorly perfused tissue (ideally within 24 hours). Repeat debridement every 24–48h as needed. Intraoperative specimens should be sent for microbiological culture and histopathology. Removal should include seemingly normal tissue if vascular thrombosis/vasculitis is suspected.
4. Adjunctive measures	Admit to ICU for organ support and close monitoring. Hyperbaric oxygen therapy may be used in stable patients, but only as an adjuvant. IVIG may be considered in cases of streptococcal toxic shock syndrome.
5. Wound care and reconstruction	Following infection control, use advanced dressings and negative pressure therapy. Plastic surgery input is required for reconstruction, using muscle flaps, skin grafts, or synthetic skin substitutes if donor sites are limited.
6. Long-term management	Tailor antibiotics to culture results. Provide nutritional support, physiotherapy, and occupational therapy to restore function. Psychological counseling should be offered to address trauma, body image concerns, and quality-of-life issues.

3.5 PROGNOSIS AND COMPLICATION

The research discovered many critical parameters linked to prognosis and complications of NF. Advanced age, chronic renal insufficiency, certain laboratory anomalies, including raised leukocyte count, increased creatinine levels, and diminished platelet count and systolic blood pressure, were associated with increased mortality. Clostridial infection was independently linked to an elevated mortality risk (11).

A study indicated that transfer status independently predicted in-hospital mortality in patients with NF. Patients who went to a tertiary care centre exhibited worse results relative to those treated

initially at the same hospital. The need for haemodialysis and a history of cirrhosis were independently correlated with increased mortality, indicating significant physiological deterioration. Although the date of transfer and preceding debridement did not yield statistical significance, early transfer without debridement was associated with a trend indicating better survival (11). Treatment in a Level 1 trauma centre significantly reduced the risk of in-hospital mortality, indicating that the availability of resources and clinical expertise may affect patient outcomes. For example, smoking status emerged as a protective factor in the multivariate analysis, however the underlying mechanism is still not well understood. Although antibiotic treatment was more suitable in patients with Polymicrobial Necrotizing Soft Tissue Infection (P-NSTI), the antibiotic regimen did not independently correlate with survival rate, highlighting the critical need of fast surgical debridement. These findings show a significance of early identification, adequate triage, and specialized treatment to enhance the prognosis of NF.

Amputation risk factors include advanced age, male gender, non-white ethnicity groups, history of diabetes, presence of a chronic wound as the underlying cause, involvement of the lower extremities, and transfer status. In contrast, infections associated with intravenous drug use were linked to reduced chances of amputation. Another research indicated that individuals with elevated Charlson Comorbidity Index scores had also a higher likelihood of limb amputation or mortality resulting from NF in the upper or lower extremities. On the other hand, individuals exhibiting lower scores were more commonly linked to mono-infection by *Streptococcus pyogenes*. In survivors, advanced age, female gender, perineal involvement, and prior amputation were associated with an increased probability of discharge to a skilled care facility, even after accounting the insurance status and history of drug use (Fig. 3) (13).



Figure 3: Progression of NF following boils, 12-day-old girl, <5% BSA involved. Note healing with very fine, acceptable scar (arrow).

4. TOXIC EPIDERMAL NECROLYSIS AND STEVENS-JOHNSON SYNDROME

4.1 EPIDEMIOLOGY, AETIOLOGY AND PATHOPHYSIOLOGY

SJS and TEN are uncommon yet severe mucocutaneous reactions, primarily triggered by different types of drugs, and comprise dermatological emergencies due to their tendency for considerable morbidity and mortality. These disorders are marked by significant epidermal necrosis and separation, impacting both the skin and mucous membranes. SJS and TEN are both presently recognised as a disease spectrum rather than separate illnesses, sharing a same pathogenesis but varying in severity according to the proportion of total body surface area (TBSA) affected. SJS encompasses less than 10% TBSA, TEN exceeds 30%, and the SJS/TEN overlap ranges from 10% to 30% TBSA (14).

Epidemiological studies have indicated different rates of infection based on where people live and demographic characteristics of the population. A study done in the United Kingdom reported an incidence of 5.76 per million individuals every year from 1995 to 2013 (14). In the United States, another study revealed annual incidence rates of 9.2, 1.6, and 1.9 per million individuals for SJS, SJS/TEN overlap, and TEN, respectively, from 2009 to 2012. Comparable trends have been also noted in Asia; specifically, a study done in South Korea indicated an incidence rate of 3.96–5.03 cases of SJS and 0.94–1.45 cases of TEN per million individuals from 2009 to 2013. The study also reported 5.3 incidence of SJS and 0.4 instances of TEN per million children yearly among paediatric populations (15).

Numerous studies consistently revealed a greater incidence of these disorders in females, with a female-to-male ratio of around 1.5:1. Mortality rates differ markedly by severity: SJS has rates of 4.8% to 9%, SJS/TEN overlap ranges from 19.4% to 29%, and TEN exhibits mortality rates between 14.8% and 48%. Fatality rates are affected by patient age, preexisting comorbidities, time of diagnosis, and the accessibility of available intensive supportive treatment (16).

SJS and TEN are often recognised as delayed-type hypersensitivity (Type IV) reactions, typically induced by medication or, less commonly, infections. The clinical onset is generally sudden, characterised by early symptoms such as fever, malaise, and systemic toxicity, proceeded by fast progressing mucocutaneous blistering and epidermal detachment. The involvement of ocular, oral, and vaginal mucosa is characteristic of the disease. As mentioned previously, medications are the predominant causative agents of SJS/TEN, constituting the majority of cases.

Frequent medication types include Penicillins, cephalosporins, fluoroquinolones, sulfonamides antibiotics, nevirapine, and NSAIDs, such Ibuprofen, diclofenac, and other oxicam derivatives, additionally anticonvulsants such as Carbamazepine, phenytoin, phenobarbital. And other medications such allopurinol, nevirapine, etc where also identified among others among others.

Nonetheless, *Mycoplasma pneumoniae* and other infectious agents, including CMV and HSV, have been identified as possible triggers, especially in paediatric populations. Significantly however, in 15–30% of cases, there is no definitive causal agent, complicating both prevention and diagnosis.

Epidemiological data support these associations, with the most frequent causative categories being antibiotics (34.0%), followed by NSAIDs (16.5%) and anticonvulsants (14.6%), while agents such as allopurinol and nevirapine comprise a smaller but important proportion (Tab. 3).

Table 3: Most common causative drug categories in SJS/TEN.

Drug category	Examples	Proportion of cases (%)
Antibiotics	Penicillins, cephalosporins, fluoroquinolones, sulfonamides	34.0%
NSAIDs	Ibuprofen, diclofenac, oxicam derivatives	16.5%
Anticonvulsants	Carbamazepine, phenytoin, phenobarbital	14.6%
Others miscellaneous	Allopurinol, nevirapine, etc.	Unidentified

The pathophysiological basis of SJS/TEN are complex and therefore complicated, which including genetic susceptibility, immune system dysregulation, and the direct toxic impact of medications or their metabolites on keratinocytes. Specific HLA alleles, including HLA-B*15:02 (highly correlated with carbamazepine hypersensitivity in Han Chinese populations) and HLA-B*58:01 (connected to allopurinol-induced TEN), significantly enhance vulnerability. These connections advocate for genetic screening before beginning high-risk medications in certain ethnic groups.

New data makes it more clear how these interactions between drugs, HLA molecules, and T-cell receptors (TCRs) combine to cause keratinocyte apoptosis. The cytotoxic CD8⁺ T cells and NK cells are rapidly genetically stimulated in predisposed individuals when the culprit medications (or metabolites) either bind directly to HLA/TCR (the p-i concept) or alter the given peptide repertoire. Granulysin, perforin/granzyme B, Fas ligand (FasL), TRAIL, and TNF- α are the cytolytic mixture released by these effector cells, which causes extensive epidermal apoptosis and detachment. Granulysin, among these mediators, is frequently seen in blisters and serum at high concentrations and is thought to be the main cause of widespread keratinocyte damage in SJS/TEN.

In addition to apoptosis, more recent research indicates that necroptosis—a lytic, planned kind of cell death controlled by RIPK3/MLKL also plays a role in inflammation amplification and epidermal loss. Necroptosis-pathway blockage has been suggested as a therapeutic target under

investigation since drug-triggered signalling can push keratinocytes towards necroptosis, helping to explain fulminant development even after drug discontinuation.

The exact sequence of immunological reactions remains under research; nonetheless, it is believed that reactive drug metabolites or drug–HLA complexes trigger T-cell–mediated cytotoxicity. CD8⁺ cytotoxic T lymphocytes and natural killer cells are believed to induce keratinocyte apoptosis via multiple mechanisms, including the secretion of perforin, granzyme B, Fas ligand, TNF- α , and notably granulysin, which is now regarded as a principal mediator of extensive epidermal necrosis in SJS/TEN (5,16).

Over 100 medications have been associated with the onset of SJS/TEN, often exhibiting symptoms 4 to 30 days following the first administration of the drug. The immunological process seems to rely on the ability of specific medications to function as haptens, attaching to endogenous proteins and creating neoantigens, or alternatively engaging directly with immune receptors, such as the T-cell receptor, within a pharmacological interaction (p-i) framework. These immunological responses result in extensive keratinocyte apoptosis, compromised integrity of the skin, and subsequent outcomes including sepsis, fluid loss, and multi-organ failure (17).

4.2 CLINICAL PRESENTATION

The clinical signs and symptoms of SJS and TEN are distinctive, and diagnosis is predominantly determined by clinical features rather than laboratory or histological evidence. The disease usually starts with a prodromal phase lasting 1 to 3 days, characterised by fever, malaise, sore throat, cough, and conjunctivitis, sometimes resembling an upper respiratory tract infection or febrile viral sickness. Subsequent to this nonspecific general symptoms, individuals quickly exhibit painful mucocutaneous lesions, characterised by mucosal involvement at numerous places. The early skin lesions often manifest as dark erythematous macules, unusual target lesions, or purpuric patches, commonly accompanied by a burning sensation and superficial pain in the skin. Typically, the characteristic raised target lesions associated with erythema multiforme are often missing, aiding in the differentiation of SJS/TEN from milder hypersensitivity reactions.

Following this, the dermal eruption advances quickly, spreading symmetrically, predominantly affecting the torso and proximal extremities. Within hours to 2–3 days, lesions combine, resulting in the production of flaccid bullae and extensive epidermal peeling. A positive Nikolsky sign, characterised by epidermal separation under light lateral pressure on erythematous skin, is frequently encountered. Perilesional erythema is a significant indicator of active illness and can function as an effective marker for assessing therapy response (Fig. 4) (18).



Figure 4: Skin lesions in a 14-year-old boy who developed SJS after taking penicillin for pneumonia.

Mucosal involvement is almost universal and generally include oral, ocular, and vaginal mucosa. Erosive mucositis may lead to odynophagia, dysuria, photophobia, respiratory manifestations, and gastrointestinal disturbances. Severe ocular involvement may manifest as conjunctival hyperaemia, ulceration, synechiae, and can advance to keratinization, corneal scarring, or blindness in chronic situations. Furthermore, the desquamation of respiratory epithelium can contribute to oxygen loss and severe respiratory distress, especially in individuals with TEN (Fig. 5).



Figure 5: Mucosal involvement of the eye in a patient with Stevens-Johnson syndrome.

Systemic symptoms are prevalent in the SJS/TEN spectrum and indicate the significant systematic inflammation and metabolic load. These encompass compromised thermoregulation, elevated energy consumption, and vulnerability to hypovolemia and electrolyte imbalance. As the illness advances, re-epithelialization usually starts several days after the end of disease activity, with complete skin healing often occurring within three weeks; however, mucosal recovery, particularly at pressure-sensitive or highly mobile areas, may require a longer period of time.

The consequences of SJS and TEN are significant, encompassing both acute and chronic morbidity. The breakdown of the skin barrier predisposes individuals to subsequent bacterial infections and sepsis, a predominant cause of mortality. Chronic consequences frequently include pigmentary alterations, hypertrophic scarring, and skin weakness. Ocular problems, including sicca syndrome, conjunctival fibrosis, and blindness, can also result in significant disability. Involvement of the gastrointestinal and respiratory tracts may lead to oesophageal strictures, dysphagia, and hypopharyngeal stenosis, frequently necessitating delicate surgical or endoscopic intervention.

Furthermore, the mucosa of the vaginal and urinary tracts may be impaired as mentioned previously, resulting in labial adhesions, urethral strictures, or dyspareunia in survivors. Such consequences may need reconstructive surgeries and lead to enduring impairments in quality of life of the patient. The first erosive and haemorrhagic mucosal involvement influences feeding, hydration, and airway management, demanding a multidisciplinary treatment strategy that often includes dermatologists, ophthalmologists, intensivists, and surgeons.

The two validated scoring systems that are most frequently used to evaluate the severity of SJS and TEN are SCORTEN and ABCD-10. When present on the first day of admission, each of the seven SCORTEN parameters, which are age >40 years, presence of malignancy, heart rate >120/min, initial epidermal detachment >10% of body surface area, serum urea >10 mmol/L, serum glucose >14 mmol/L, and serum bicarbonate <20 mmol/L, contributes to one point. From roughly 3% (scoring 0–1) to over 90% (score 5–7), the final score (0–7) has a substantial correlation with anticipated mortality. Recent data indicates that SCORTEN may overstate mortality in contemporary treatment settings, despite its widespread use, proven discriminatory abilities, and strong calibration across several cohorts (19).

A more recent, streamlined model termed ABCD-10 has five parameters: age ≥ 50 years, serum bicarbonate <20 mmol/L, >10% BSA detachment (each worth 1 point), active cancer (2 points), and dialysis before admission (3 points). The range of its overall score is 0 to 8. When compared to SCORTEN, ABCD-10 gives cancer more weight and includes dialysis as a high-risk variable in a novel way. Despite exhibiting comparable discrimination to SCORTEN, ABCD-10's calibration is often inadequate with a tendency to overestimate mortality at higher scores and underestimate it at lower values.

Both scoring systems have to be calculated within the first day of admission, with predictive accuracy improving when reassessed at 48–72 hours. SCORTEN continues to be the recommended prognostic tool for mortality risk stratification in SJS/TEN, with superior calibration across a variety of populations and clinical situations, according to recent comparative research (20).

4.3 DIAGNOSIS

As mentioned earlier, the diagnosis is predominantly determined by clinical features rather than laboratory or histological evidence. However, numerous dermatological disorders can closely resemble the clinical characteristics of SJS and TEN, especially in their early stages. Precise and early differentiation is therefore crucial, as treatment techniques and prognoses range significantly among these diseases. Clinicians need to rely on a combination of clinical data, patient history, histology and cytopathology, and, where warranted, immunofluorescence tests. The following are the primary differential diagnoses to consider when assessing a patient with suspected SJS/TEN.

- Erythema multiforme major manifests as elevated target lesions spread over the extremities, which can exhibit either typical or atypical characteristics. It is predominantly induced by viruses like the HSV or *Mycoplasma pneumoniae*. In contrast to SJS/TEN, systemic symptoms are often minor or even non-existent, involvement of fewer than two mucosal locations is typical, and the illness often recurs.
- Staphylococcal scalded skin syndrome mostly affects pediatric population and is induced by exfoliative toxins generated by *Staphylococcus aureus*. Clinically, it manifests as superficial epidermal desquamation and pain, local impacting flexural regions, but notably, lack mucosal involvement which is a distinguishing characteristic that differentiates it from SJS/TEN.
- Paraneoplastic pemphigus is a severe autoimmune blistering disease linked to underlying malignancies, especially such as non-Hodgkin lymphoma and Castleman disease. The condition is marked by a polymorphous eruption that show flaccid blisters, erosions, lesions resembling erythema multiforme, frequently associated with significant and painful mucosal involvement.
- Pemphigus vulgaris predominantly impacts middle-aged and elderly adults, which is characterized by the flaccid intraepidermal blisters and erosions. These lesions frequently manifest on the scalp, torso, flexural areas, and mucosal membranes. The condition is often chronic, and histopathological examination shows acantholysis with positive direct immunofluorescence for intercellular IgG.

- Bullous pemphigoid predominantly impacts the elderly and is characterised by a first phase of urticarial plaques, proceeded by the development of tight subepidermal blisters. Mucosal involvement is uncommon, aiding in its differentiation from SJS/TEN. The blisters are often itchy rather than painful.
- Generalised bullous fixed drug eruption is a medication-induced blistering condition that may TEN. It manifests as well-defined, erythematous to violaceous dark patches or plaques that may progress to develop central bullae. In contrast to TEN, the lesions reappear at the same locations with re-exposure to the causative medication and generally exhibit more localised desquamation.
- Acute graft-versus-host disease can clinically resemble SJS/TEN, particularly in individuals who have received bone marrow or allogeneic stem cell transplants. This disease often starts with acral lesions that extend proximally and may include follicular-centric eruptions, diarrhoea, jaundice, and hepatic dysfunction, which are characteristics that are helpful in distinguishing it from classic SJS/TEN.

Skin biopsy and histopathological analysis are not mandatory for the diagnosis of SJS/TEN, but however, they are strongly recommended, particularly in early or atypical cases, this is to support the diagnosis and exclude other clinically similar conditions. Histologically, SJS/TEN is characterised by full-thickness epidermal necrosis that results from widespread keratinocyte apoptosis, leading to subepidermal blister formation. Early lesions may also show scattered apoptotic keratinocytes and vascular interface changes, accompanied by a sparse lymphocytic infiltrate in the dermis. Direct immunofluorescence is generally negative, which helps differentiate SJS/TEN from other autoimmune blistering disorders. For optimal diagnostic yield, a biopsy should be indeed obtained from the edge of a fresh lesion, including both affected and adjacent normal-appearing skin, as fully necrotic areas may provide non-specific findings. If direct immunofluorescence is performed, a separate sample from perilesional skin is recommended (20).

4.4 TREATMENT AND MANAGEMENT

The preliminary treatment of SJS/TEN include the recognition and quick withdrawal of any possible causative medications. Research indicates that early withdrawal of the medication corresponds with improved patient outcomes. Research also indicates that individuals who have TEN as a result of medications with prolonged half-lives encounter an increased mortality risk. Immediate withdrawal of the problematic drug is therefore essential and important, as it can facilitate the reduction of acute skin breakdown and promote accelerated epithelialization. It is important to

highlight that when an underlying reaction is associated with medications that have extended half-lives, the pathological processes can last for an extended duration even after the drug is discontinued.

Determining the responsible drug is quite simple and easy when only one medication is present. However, when many medications or combination drugs are employed, identifying the specific causative drug becomes extremely difficult and very challenging. Due to the critical and potentially fatal characteristics of SJS/TEN, it is often recommended to stop all drugs administered to the patient. However, if the administration of a certain medicine is imperative, it may be replaced with a structurally different alternative. The determination to maintain or replace essential medications has to be conducted via an interdisciplinary strategy in collaboration with the attending physician. Ultimately, it is imperative to limit medication consumption to the essential minimum (21).

Patients diagnosed with SJS/TEN require hospitalisation for proper medical treatment. A thorough patient history must be acquired, with an accurate record of all drugs administered in the two months prior to the start of the disease. Coexisting medical disorders and chronic illnesses must also be acknowledged. Determining the temporal association between drug exposure and the onset of allergic responses, while also taking into account any personal or familial history of drug reactions, is therefore essential for identifying the likely causative agent.

The preliminary examination must include an examination of the patient's airway, respiration, circulation, urinary output, and any indicators of septicemia. The proportion of body surface area impacted, together with the severity, scope, and quantity of mucosal sites involved, must be precisely evaluated and recorded. The degree of erythema and epidermal detachment, encompassing both removable and completely detached epidermis, must be documented and illustrated on a body map within the medical records. Moreover, images captured at the moment of admission and throughout different phases of treatment might act as a crucial protection against any medicolegal complications. Preliminary investigations comprise of a hemogram, liver and renal function assessments, blood electrolyte analysis, blood glucose measurement, blood culture, regular urinalysis with microscopy, skin swab culture, and finally chest xray.

In addition to supportive treatment, careful and regular monitoring of the patient's vital signs, such as pulse rate, blood pressure, respiratory rate, fluid intake, and urine output, is an essential component of the management strategy. Moreover, continuous and regular monitoring should concentrate on blood glucose, serum electrolytes, and serum creatinine concentrations. Acquiring relevant cultures may also be required in some cases. Healthcare personnel must be attentive for possible sources of sepsis and consequences such as septicemia and disseminated intravascular coagulation in patients undergoing immunosuppressive therapy. These complications can be evaluated by specific testing, such as coagulation assays, D-dimer assays, and fibrin degradation products, where applicable (21).

In the care of wound-related conditions it is essential to meticulously monitor the sterilization of the wound region to prevent sepsis and subsequent infections via; Adherence to rigorous hand hygiene measures with chlorhexidine, reduce the use of disruptive medical devices such as catheters and lines, observe for symptoms of sepsis and administer treatment without delay, establish environmental regulations and sepsis protocols, and lastly implement appropriate antibiotic use.

Patients with significant skin involvement require careful management of body fluids and electrolytes to prevent dehydration and imbalances. Individuals with TEN suffer considerable fluid and electrolyte depletion due to blistering and fluid loss, resulting in a state of hypovolemia that necessitates careful fluid and electrolyte management. The initial fluid demand for TEN patients is around two-thirds to three-quarters of that for burn patients with comparable skin involvement and should be administered using macromolecules or saline solutions. Fluid administration is directed by the Parkland formula and should strive to sustain a urine output of 1000 to 1500 ml. Excessive correction of hypovolemia may result in pulmonary oedema. Blood transfusion may also be advantageous in certain instances by diluting medication metabolites, cytokines, and autoantibodies, while also supplying immunoglobulins and nutrients.

Upon admission, patients should get dietary assistance, prioritising oral feeding where possible. In the early stages, when swallowing difficulties are prominent, a fluid or semisolid diet may be easier to digest by the patient. Timely and continuous enteral nourishment is advantageous, since it reduces problems and facilitates the prompt cessation of intravenous lines. The advised caloric consumption is 30–35 kcal/kg/day, and protein supplementation is administered to avert unfavourable nitrogen levels.

It is advisable to leave the unattached or removable skin intact, since it functions as a natural dressing. Consistent wound irrigation with sterile water or normal saline is therefore essential, irrespective of the patient's mobility, to eliminate infected debris and reduce the likelihood of infection. Scientific literature suggests that silver nitrate spray is an accessible and economical topical therapy for wound care, as it reduces close interaction with the wound and the accompanying pain.

In case study utilizing silver nitrate was administered bi-daily until re-epithelialization was accomplished, which typically require 5 to 10 days. The Nikolsky sign test was performed on the damaged skin to assess re-epithelialization progress, therefore averting needless debridement. All four patients demonstrated a full response to the therapy, reporting only slight burning without discomfort during the administration of silver nitrate. No notable adverse effects, including those associated with silver absorption, toxicity, or local irritation, were observed (22).

The combination of systemic treatment with silver nitrate therapy produces an immediate positive clinical response. Topical antiseptics, including 0.5% silver nitrate and 0.05% chlorhexidine, are employed for washing, dressing, or applying to the afflicted skin. Non-adhesive dressings, perhaps

infused with 0.5% silver nitrate, petrolatum, polyvinylpyrrolidone-iodine, or hydrogels, can be utilised on regions of the body exhibiting skin erosion. Topical antibiotics and anti-infectives with sulfa components should be avoided, especially because when a sulfa derivative is suspected as the causal factor. In accordance with recent strategies to enhance systemic outcomes through the management of skin lesions, innovative dressings are being developed and employed to facilitate quicker healing, control sepsis, and mitigate the damaging inflammatory response linked to SJS and TEN. Furthermore, Nano Crystalline Silver is a dressing component that exhibits remarkable antibacterial activities and the ability to reduce the excessive inflammation typical of these illnesses. According to prior findings, these sophisticated treatments seem to be successful in a group of patients in the management of sepsis and beginning the "tipping point" towards recovery (16).

Recent studies have also recognised bacterial cellulose as a viable biomaterial for the treatment of complicated wounds, since it has the advantageous characteristics such as biocompatibility, non-toxicity, and elevated hydrophilicity, allowing it to be sustained an ideal moist wound environment while acting as a barrier to microbial infiltration. Moreover, it has the ability to mitigate pain, facilitate skin regeneration, and be augmented with antimicrobial medicines, indicating its significant potential for use in severe dermatological emergencies (23).

Wet compresses are used bi-daily to eliminate oral and nasal crusts. Antiseptic sprays or mouthwashes are utilised many times daily for treating oral erosions. Mild ointments, like white petroleum or Dex panthenol, are advised for the treatment of mucosal lesions in the oral cavity and on the lips. Patients should conduct standard saline rinses or utilise antiseptic or anaesthetic mouthwashes for oral hygiene. Furthermore, the use of saline compresses followed by lubricants is advisable for the lips, as this aids in softening any haemorrhagic crusts that may form or develop.

Ocular complications are prevalent and serious in SJS and TEN, with the potential to result in blindness. Symptoms in the acute stage do not consistently anticipate future results; hence, even mild cases need specialised treatment. Regular eye examinations are crucial, irrespective of the observable symptoms. Timely, preventive interventions, including preservative-free drops, topical antibiotics/steroids, and amniotic membranes, may avoid late complications.

The ophthalmological care of acute SJS and TEN must prioritize infection prevention and the reduction of any inflammatory damage. Studies have shown that chronic dry eye may emerge as a delayed consequence linked to the use of topical antibiotics. In the acute phase, empiric topical antibiotics such chloramphenicol, occasionally in conjunction with corticosteroids, may be used to prevent subsequent infections. Nonetheless, the additives used in these eye drops may adversely affect the tear glands, potentially resulting in dry eye syndrome. Contemporary topical antibiotics such as moxifloxacin may be advantageous due to their superior permeability and effectiveness against prevalent infections, facilitating diminished dose needs. The use of topical antibiotics must be

judiciously evaluated, since empirical use in the absence of clinical infection indicators is inadvisable. Adhering to proper eye hygiene with regular saline rinses might reduce the likelihood of infection.

Topical cyclosporine may assist in managing ocular signs of SJS and TEN by reducing swelling. Nonetheless, the data substantiating its application is insufficient. Cyclosporine may serve as an efficacious immunosuppressant for several disorders. Topical cyclosporine has demonstrated efficacy in managing inflammatory and immune-mediated eye disorders, indicating possible advantages for TEN. Certain case reports suggest favourable outcomes with the combination of topical moxifloxacin, cyclosporine, and dexamethasone in treating ocular involvement in SJS (24).

Current study demonstrates that high-potency topical steroids can effectively diminish ocular swelling and enhance visual outcomes in patients with SJS and TEN. Patients administered topical glucocorticoid therapy exhibited a higher likelihood of acquiring adequate visual abilities, with over 75% attaining 20/200 or above. Moreover, the use of topical steroids correlated with a substantial reduction in the likelihood of severe vision impairment below 20/2,000. The findings indicate that high-dose topical corticosteroid treatment can reduce the detrimental ocular consequences of severe dermatological disorders, resulting in enhanced visual outcomes for afflicted individuals (16,23).

Genital signs associated with SJS and TEN may encompass erosive and ulcerative vaginitis, vulvar bullae, and vaginal adhesions. Significant scarring during ulceration repair may hinder vaginal normal functions. Uncommon consequences encompass vaginal blockage, metaplastic alterations resulting in dyspareunia and post-coital haemorrhage. Routine genital exams are therefore essential for assessing mucosal involvement. Erosions may lead to adhesions or strictures, which can be treated with moist dressings. Proposed preventative measures including the use of intravaginal steroids, vaginal castings, and hormonal contraception during the acute phase of SJS/TEN.

In SJS and TEN, the necrotic epidermis readily separates from the underlying dermis as mentioned previously, rendering the skin very fragile and susceptible to further damage. Proper handling of patients is therefore essential to prevent unintentional injury, particularly during repositioning or evaluations. Conservative wound treatment often entails retaining detached epidermis as a natural biological dressing, employing bland emollients and nonadherent dressings to uphold the integrity of the barrier, reduce fluid loss, and promote re-epithelialization. Nevertheless, conservative therapy may be inadequate in instances characterised by significant epidermal loss, prolonged healing, signs of infection, or wound conversion (19,20).

Surgical debridement emerges as an appropriate treatment option in such instances. The objective of the surgical intervention is to limit microbial load, facilitate re-epithelialization, and eliminate systemic infection by excising necrotic tissue and debris that act as substrates for colonisation, especially by *Staphylococcus aureus* and *Pseudomonas aeruginosa*.

Debridement promotes the formation of a sterile wound allowing for the efficient use of sophisticated dressings like Biobrane, xenografts, or allografts. Hydro-surgical procedures, such as Versajet, are increasingly favoured for their accuracy, minimised harm to healthy dermis, and suitability for anatomically intricate regions. In contrast to conventional sharp or blunt techniques, hydro-surgery more effectively maintains healthy tissue, facilitating keratinocyte migration and collagen remodelling (25).

In individuals with localised injury or intact dermis, less intrusive approaches such as mechanical washing or enzymatic debridement might be enough. Aggressive surgical surgery is often reserved for those patients who have clinical worsening after conservative treatment. Although several small-scale studies indicate advantages such as accelerated healing, less complications, and enhanced survival, the current data is constrained by the lack of extensive, controlled trials. Prognostic instruments such as SCORTEN, although beneficial, may exaggerate fatality rates in proficient centres with established care protocols (26). Consequently, the choice to do surgical debridement must be personalised, weighing infection management and wound healing against the maintenance of skin function and integrity (Fig. 5).

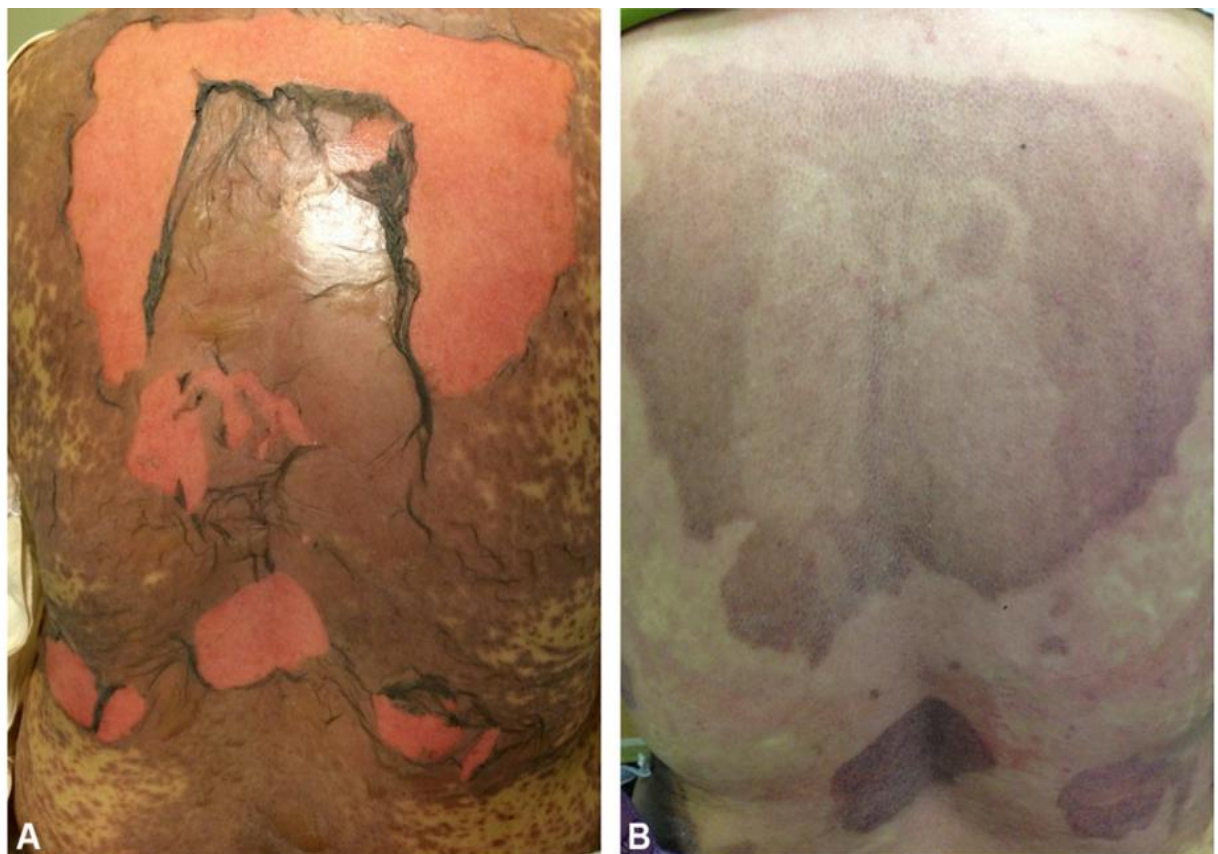


Figure 5: A, Sheet-like detachment, blisters, and raw erosions on back of patient with Stevens-Johnson syndrome/toxic epidermal necrolysis. B, post inflammatory hyperpigmentation accentuated in areas where detached epidermis was not left in situ.

The comprehensive treatment and management of SJS/TEN can be summarized in an algorithmic approach (Tab. 4.), which complements the detailed descriptions above and highlights the stepwise sequence of interventions from recognition to prognosis.

Table 4: Treatment and Management Algorithm for SJS/TEN

STEP	ACTIONS
1. INITIAL RECOGNITION & WITHDRAWAL	• Suspect SJS/TEN (mucocutaneous lesions, epidermal detachment) • Immediate withdrawal of suspected drug(s) • Replace essential meds with non-cross-reactive alternatives
2. ADMISSION & ASSESSMENT	• Admit to ICU or burns unit • Full drug history (past 2 months) • Evaluate airway, breathing, circulation, urinary output, sepsis • Estimate TBSA detachment & mucosal involvement (body map/photos) • Baseline labs: CBC, renal/liver function, electrolytes, glucose, urinalysis, cultures, chest X-ray
3. SUPPORTIVE CARE	• Monitor vitals: HR, BP, RR, O₂, fluid balance • Fluid & electrolyte replacement (2/3–3/4 Parkland formula, aim UO 1000–1500 mL/d) • Nutrition: early enteral feeding (30–35 kcal/kg/d, high protein) • Analgesia, temperature regulation • Sepsis prevention: asepsis, hand hygiene, minimize devices
4. WOUND & SKIN CARE	• Leave detached epidermis intact when possible • Non-adhesive sterile dressings • Topical antiseptics (0.5% silver nitrate, 0.05% chlorhexidine) • Advanced dressings: nanocrystalline silver, bacterial cellulose, Biobrane, xenografts, hydrogels • Irrigate with sterile water/saline
5. SPECIFIC SYSTEMIC THERAPIES	• Cyclosporine (3–5 mg/kg/d, taper) • Corticosteroids (early, high-dose, short course) • IVIG (mixed evidence, consider in select cases) • TNF-α inhibitors (etanercept, infliximab, adalimumab) — increasing evidence of benefit
6. ORGAN/MUCOSA CARE	• Ocular: ophthalmology input, preservative-free tears, topical antibiotics/steroids, amniotic membrane • Oral/genital: saline rinses, lubricants, intravaginal steroids/castings if needed
7. SURGICAL MANAGEMENT	• Conservative preferred; retain necrotic epidermis • Consider hydro-surgical or sharp debridement only if extensive necrosis, worsening infection, or failure of conservative care
8. PROGNOSTIC ASSESSMENT	• Apply SCORTEN or ABCD-10 scoring • Guides prognosis and intensity of monitoring

There is a lack of high-quality data for the treatment of SJS/TEN; the existing research consists of 2-open randomised controlled trials (RCT) and other small observational surveys, case series, or retrospective reviews. The medications claimed to exhibit certain benefits are summarised in (Tab. 6) (27).

Table 6: Systemic treatment options for SJS/TEN.

TREATMENT	RECOMMENDED DOSAGE
CYCLOSPORINE (PO)	3–5 mg/kg/d q12 h for 2 weeks with gradual taper
ETANERCEPT (SC)	25 mg SC injection or 50 mg if > 65 kg twice weekly until re-epithelialization
CORTICOSTEROIDS (IV)	Dexamethasone 1.5 mg/kg/day for three days Prednisolone 60–250 mg/day for 2 to 12 days Methylprednisolone 250–1000 mg/day for three days
INTRAVENOUS IMMUNOGLOBULIN	4 g/kg divided over 3 days OR 0.75 g/kg/d for 4 days OR 1 g/kg/d for 3 days

Abbreviations: PO = oral, IV = intravenous, SC = subcutaneous

Cyclosporine, due to its T alpha cell action, has potential as an autoimmune-regulating agent, having shown favourable effects on hospital duration and the advancement of skin detachments in patients with SJS/TEN in limited observational studies (28). Cyclosporine is nephrotoxic and is thus contraindicated in individuals with renal impairment, as renal function is essential for SCORTEN and ABCD-10 prognostic assessments. Corticosteroids are frequently administered orally and intravenously. Research indicates that the timely use of big dose of steroids within one to two days after symptom start results in enhanced outcomes as well. Nevertheless, additional data indicates that corticosteroid usage correlates with a heightened risk of infection/inflammation. Intravenous immunoglobulin (IVIG), presumably functioning through the suppression of the Fas receptor, has been used and utilized and used in conjunction with steroids. A 2021 systematic review with meta-analysis indicated that corticosteroid/IVIG combination treatment was the sole intervention demonstrating a mortality advantage relative to the control group (29). Numerous studies have then indicated that IVIG offers few advantages and may be detrimental to those with impaired renal function. The time frame for initiating therapies such as IVIG and corticosteroids to attain a favourable impact is likely too brief for practical clinical use (30).

Biologic TNF- α inhibitors, including etanercept, have demonstrated efficacy as a therapy with minimal adverse effects. A study done in 2022 indicated that etanercept used biweekly until healing was the sole therapy that achieved low-certainty evidence, perhaps providing a greater mortality

advantage compared to corticosteroids. Patients using TNF- α inhibitors have attained full skin re-epithelialization more rapidly than those receiving other therapies, including corticosteroids (31). A randomised, controlled open-label experiment comparing the differences between intravenous corticosteroids to etanercept shown a considerable reduction in the time to re-epithelialization as well (32). The combination with other therapies may provide benefits; a multicentre study indicated that etanercept combined with corticosteroids resulted in better mortality rates compared to corticosteroids/IVIG and corticosteroids alone. Special groups, like pregnant patients and children, may necessitate more considerations and adjustments in therapy. For instance, while managing a pregnant patient with SJS/TEN, comprehensive evaluation of foetal condition, mode of delivery, and the potential impact of the illness on the foetus is very essential.

Recent investigations have revealed elevated TNF- α levels as a critical role in the pathogenesis of SJS/TEN, principally through the induction of keratinocyte death. The interaction of TNF- α with TNF receptor 1 initiates divergent cell death mechanisms: cell death occurs upon activation of caspase-8, whereas necroptosis ensues when caspase-8 is inactivated. Cytotoxic CD8⁺ T cells also participate in the pathogenic process by secreting TNF- α and soluble FasL. TNF- α is a multifunctional cytokine that plays a crucial role in regulating inflammatory responses and is associated with the development of several inflammatory and autoimmune disorders. It is crucial for sustaining a proper immunological response by activating and regulating immune system processes. Increased concentrations of TNF- α have been seen in the blood and blister fluid of patients with SJS/TEN, highlighting its critical involvement in disease aetiology (31). TNF- α inhibitors have been identified as prospective therapeutic interventions for SJS/TEN, with data indicating their capacity to impede disease development and enhance survival rates (33).

TNF- α inhibitors have shown considerable efficacy in clinical applications for illnesses such as Crohn's disease and rheumatoid arthritis. They are increasingly utilised in acute graft-versus-host disease with moderate outcomes, particularly in cases resembling SJS/TEN. These therapeutic drugs operate as either antagonists, inhibiting the interaction of TNF- α with its receptors (TNFR1/2), or as agonists, facilitating reverse signalling and triggering death in TNF- α -producing immune cells (31). Authorised TNF- α inhibitors comprise etanercept, infliximab, adalimumab, golimumab, and certolizumab. Adalimumab displays unique molecular attributes, modes of action, and therapeutic administration techniques in contrast to other TNF- α inhibitors. In contrast to etanercept, a soluble recombinant fusion protein that competitively binds soluble TNF- α and blocks TNF receptor activation, adalimumab is a completely human monoclonal antibody. It directly neutralises the particular portion of the released TNF- α molecule while exhibiting diminished immunogenicity. Moreover, adalimumab is delivered subcutaneously as a singular dosage for SJS/TEN, providing a less frequent and presumably safer therapeutic regimen in comparison to other TNF- α inhibitors.

Adalimumab in conjunction with corticosteroids markedly expedited skin lesion healing, diminished hospitalisation length, shortened re-epithelialization time, and decreased corticosteroid exposure, all without elevating the occurrence of serious treatment-related side effects (34).

4.5 PROGNOSIS AND COMPLICATION

The prognosis of SJS and TEN directly related to early recognition, withdrawal of the causative agent, and the quality of supportive care. The SCORTEN score is the most often employed prognostic instrument for assessing mortality risk. The assessment relies on seven clinical parameters: age over 40 years, malignancy, tachycardia, first epidermal detachment above ten percent, excessive urea, high glucose, and low bicarbonate levels. Numerous studies verify the effectiveness of this score; nevertheless, its accuracy could decrease with time due to developments in medical care and supportive care. Although newer versions such as Re-SCORTEN and ABCD-10 have been introduced, SCORTEN still continues to exhibit superior overall performance. Nonetheless, it may exaggerate mortality rates in some cases, especially when utilised in environments with contemporary ICU procedures and immunomodulatory treatments (35).

Comorbidities also significantly influence prognosis. Patients with a higher prevalence of multiple medical disorders, especially the elderly patients, experience an increased risk of death. Receiving care at bigger urban academic medical centres is associated with better results, possibly due to the presence of skilled multidisciplinary teams and greater healthcare resources.

Numerous patients who experience the acute phase of SJS and TEN subsequently suffer a variety of severe long-term effects. Chronic vision issues are among the most common and have catastrophic effects to the patient, including disorders such as dry eye syndrome, conjunctival scarring, symblepharon, and corneal neovascularisation. These ocular symptoms can result in significant vision impairment or blindness, frequently requiring lifetime specialised ophthalmological treatment (36).

Cutaneous sequelae are also common. Individuals affected may encounter lasting pigmentation changes, hypertrophic scar growth, or the production of keloids. Moreover, mucosal regions, including the oral cavity, genitalia, and anus, may heal with strictures, adhesions, and persistent pain, adversely affecting activities such as ingestion, sexual activity, and urine.

Infections remain a significant issue, especially during the first healing phase. The breakdown of the skin's protective barrier increases patients' susceptibility to recurrent dermatological and systemic infections, including sepsis and pneumonia. Organ failure due to sepsis is a major factor in late-stage death (37, 38).

The psychological impact of SJS/TEN must not be disregarded. A significant number of patients have PTSD, anxiety, depression, and substantial declines in their quality of life. The traumatic

experience involving severe illness, bodily deformities, and extended hospitalisation leads to lasting psychological distress. The combination of mental health assistance and social reintegration programs is therefore essential for effective long-term treatment (Fig. 6, 7).

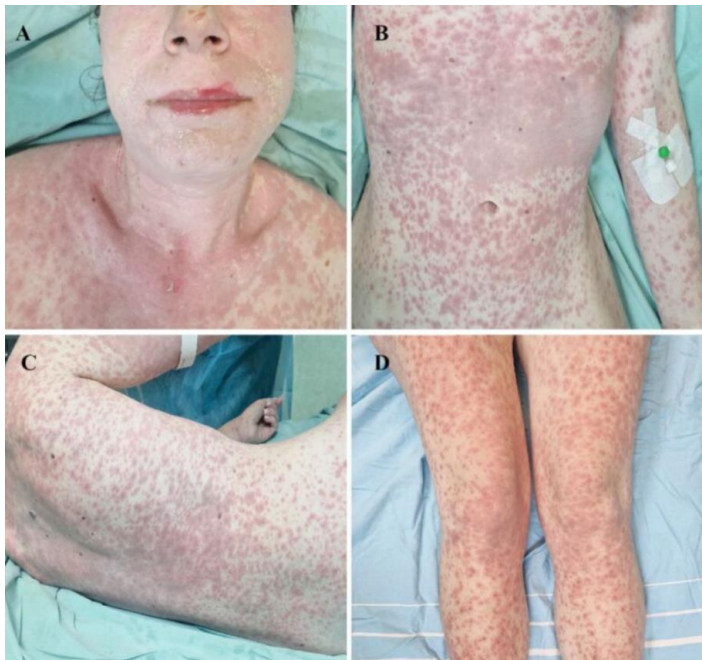


Figure 6: Clinical presentation at admission in the Burn Center, with generalized, erythematous, blistering rash: (A) Face and neck; (B) Anterior torso and left upper limb; (C) Posterior torso; (D) Lower limbs)



Figure 7: Clinical presentation at follow-up one week after discharge: re-epithelization on the (A) face and neck, (B) torso, (C) upper limb and torso, (D) lower limbs)

5. DISCUSSION

5.1 DIAGNOSTIC CHALLENGES IN CLINICAL PRACTICE

A significant challenge that occurs in clinical practice is the rapid and accurate diagnosis of SJS, NF, and TEN (38, 39). In order to implement the correct and appropriate treatment and enhance better patient outcomes, early diagnosis is therefore crucial and essential. However, as mentioned previously, given their varied clinical presentations, manifestations, and resemblance to more prevalent, milder dermatological conditions, therefore, these disorders can be challenging to identify (40, 41). Early symptoms of SJS, TEN, and NF often overlap, making prompt identification indeed difficult (42, 43). Since patients are more likely to initially consult with general care physicians and emergency physicians than to dermatologists, it is imperative and of importance that all practitioners are knowledgeable with frequently occurring symptoms associated with NF, SJS, and TEN (44).

The initial presentation of these disorders is one of the main diagnostic challenges. For example, non-specific symptoms like pain, swelling, and erythema are frequently the first signs of NF and are frequently misinterpreted with cellulitis or other soft tissue infections. In a comparable way, SJS/TEN may also first present with flu-like symptoms before developing a rash that resembles drug outbreaks or viral blisters. However, SJS/TEN can be differentiated from common mimicry conditions including erythema multiforme, drug rash eosinophilia with systemic symptoms, and morbilliform drug reaction due to certain characteristics (45).

Delays in detection and treatment may result as a result of this diagnostic dilemma, which in turn raises the risk of morbidity and death. Additionally, NF can manifest in a variety of ways, from a benign-looking rash to clear skin necrosis with cardiovascular instability. Differentiating early-stage fasciitis from cellulitis may therefore be challenging. As mentioned previously, For NF, early diagnosis and vigorous, timely medical and surgical treatment are very critical. Due to its rarity and the fact that it is a quickly progressive systemic disease with severe cutaneous, mucosal, and systemic signs, SJS/TEN may also present with a clinical issues for physicians treating individuals with this syndrome (46).

Patient outcomes might be considerably worsened by misdiagnosis and treatment delays, which are still widespread. In one case report, the attending physician's lack of competence resulted in a delayed identification and treatment of NF (47). Therefore, clinical alertness and knowledge about differential diagnosis concerns are crucial. Clinicians must also remain vigilant for NF in the initial workup of localized soft tissue infection.

Accurate risk assessment is essential for directing treatment choices and evaluating patient outcomes in the management of NF and SJS/TEN (48). To help with this procedure, a number of rating systems have been created. The likelihood of NF can be determined by the Laboratory Risk Indicator for NF score (LRINEC Score for Necrotising Soft Tissue Infection). As mentioned previously, Patients with a score of more than 6 should be closely examined for any signs of NF (49). Currently, the most popular validated method for predicting fatality rates in SJS/TEN is the (Severity-of-illness Score) for TEN (50). And while both the LRINEC score and SCORTEN are valuable, various studies have questioned their reliability and applicability (51, 52). To assess the severity of the disease in SJS/TEN, other prognostic scoring systems have therefore been developed in addition to SCORTEN. The ABCD-10 score, a new alternative prognostic measure, is one of these scales (53, 54). While one study indicated that SCORTEN is still more effective than ABCD-10 at predicting mortality in epidermal necrolysis, another study showed that ABCD-10 performed similarly and that there was no discernible difference in its capacity to distinguish between in-hospital mortality outcomes (55). However, before ABCD-10 may be widely used in clinical practice, more validation across a variety of patient populations is indeed necessary (56).

Acute renal failure has been identified as a major comorbidity that may have a bigger impact on patient prognosis than is currently taken into consideration in ABCD-10 or SCORTEN (56). likewise, SCORTEN may overstate mortality in facilities with established specialised supportive care pathways and standardised treatment methods. Results have been demonstrated to be far better in these situations than those predicted by SCORTEN alone (57). Despite these drawbacks, SCORTEN is still widely used and also used as a standard treatment for quality in clinical settings all over the world.

It's crucial to remember that even when prediction scores are employed, selecting the best course of action may still be difficult (54). There is disagreement on the validity of component laboratory data, clinical characteristics, and the estimated mortality risk. Practical issues are crucial when using these instruments in emergency and critical care settings. Clinicians should use each rating system in conjunction with their own clinical judgement and be conscious of all its limitations. They should have a high level of suspicion, and they should lower the threshold for additional investigation when necessary, especially when the clinical presentation is ambiguous or the scoring system produces also unclear results.

5.2 DIAGNOSTIC TOOLS IN CRITICAL DERMATOLOGICAL CONDITIONS

The diagnosis of critical dermatological emergencies like NF, TEN, and SJS poses a significant challenge, often relying on clinical assessment, evaluation, and conventional laboratory markers. To enhance early and precise diagnosis, recent research has concentrated on finding new biomarkers and diagnostic instruments (58). Understanding the specific biomarkers and diagnostic instruments for drug eruptions and their clinical utility based on the pathophysiology of these eruptions is therefore crucial, as mentioned previously (59). The relevance of these biomarkers must be interpreted within the clinical context of each disease, rather than as universally applicable indicators.

In the field of burn management, extensive research has focused on identifying reliable biomarkers that can help, aid, and assist in the early detection of infection and sepsis, predict survival rates, monitor tissue damage accurately, wound healing, and organ dysfunction as well. Despite these attempts, there is no one biomarker that has shown enough sensitivity or specificity to be routinely used in clinical practice (60).

This restriction is mostly caused by the complicated inflammatory reactions that the patients experience, which can coexist with both infectious and non-infectious systemic reactions. Therefore, current research indicates that biomarker combinations, as opposed to individual indications, may offer higher diagnosis accuracy (61). For these biomarker panels to be clinically significant, they must show not just efficacy but also stability and reproducibility in a variety of clinical settings. These biomarker panels must also demonstrate stability and reproducibility in a range of clinical contexts in addition to efficacy in order to be clinically significant (62). The creation of validated biomarker profiles has considerable potential to improve burn patient outcomes, guide therapy choices, and improve rapid sepsis recognition as research progresses.

Early diagnosis continues to be the most important factor affecting prognosis in NF, since prompt and aggressive medical and surgical intervention significantly lowers mortality. The use of laboratory and imaging biomarkers has become more crucial in enabling prompt distinction because the early clinical presentation of NF can mimic non-necrotizing soft tissue infections, as previously has been demonstrated. Clinicians can identify patients at risk of NF and stratify the severity of soft tissue infections using the LRINEC score, which is based on regularly obtained laboratory data (49). Furthermore, when combined with LRINEC scoring, procalcitonin has demonstrated use as a marker of severe bacterial infection and systemic inflammation, providing supplementary diagnostic insight (63). By incorporating these diagnostic techniques into everyday practice, clinical decision-making and surgical timing may be greatly improved, leading to better outcomes through early detection and intervention (64).

In order to enable early diagnosis and tailored treatment approaches, biomarker discovery in SJS/TEN has also concentrated on finding indications that correlate with disease activity and severity. Patients with SJS/TEN had significantly higher levels of granulysin, a cytotoxic protein secreted by activated CD8⁺ regulatory T cells and natural killer cells, in their blood and blister fluid. Granulysin has also been identified as a major modulator of keratinocyte apoptosis (65). notably, granulysin levels have been demonstrated to be correlated with clinical severity and could be a useful early indicator that can differentiate between less severe drug eruptions of SJS/TEN prior to complete epidermal detachment (65). likewise, a possible biomarker linked to necroptotic cell death pathways, which is crucial for the extensive epidermal degradation typical of SJS/TEN, is receptor-interacting protein kinase. As a possible target for future therapeutic intervention, elevated levels of this protein expression may thus offer insight into the severity of the disease as well as underlying pathophysiological mechanisms.

5.3 FUTURE PERSPECTIVES AND RECOMMENDATIONS

New efforts to treat critical dermatological skin emergencies such as NF, SJS, and TEN ought to place an emphasis on early detection, more accurate diagnosis, and individualised treatment plans. Improved early detection is still the most essential factor, especially in primary care and emergency situations when these individuals are frequently seen for the first time. To avoid delays in diagnosis, training programs and evidence-based clinical guidelines should highlight the subtle early indications of these illnesses. To address the existing gaps in clinical practice, new precise and sensitive diagnostic indicators must be developed concurrently as well.

For the advancement of early detection, precise risk stratification, and prognosis prediction, biomarker research must continue. In NF, SJS, and TEN, efforts should be focused on finding and confirming new biomarkers that accurately represent disease activity and treatment response. A interesting direction for further research is the integration of multi-omics techniques, such as proteomics, metabolomics, and genomes. These technologies may make it possible to identify complicated molecular signatures, which would facilitate precision-based therapies and a more thorough assessment of disease processes.

Finally, SJS and TEN should receive special attention due to their high fatality rates and quick progression. Initiating prompt treatment and enhancing survival outcomes depend on early detection of clinical course and severity. To improve the overall quality of care for these life-threatening illnesses, collaborative multi-center studies, standardised treatment protocols, and the use of innovative diagnostic tools is highly advised.

6. CONCLUSION

This systematic review aimed to evaluate the available literature on necrotising fasciitis (NF), toxic epidermal necrolysis (TEN), and Stevens–Johnson syndrome (SJS), focusing on their epidemiology, clinical presentation, diagnosis, treatment, and outcomes. Across the included studies, these conditions were consistently described as severe and rapidly progressing dermatological emergencies in which delays in recognition and management significantly increase the risk of morbidity and mortality. The findings of the review do support the importance of early identification, recognition, and timely intervention, which were repeatedly associated with improved patient outcomes.

For NF, the review showed that early clinical suspicion together with timely surgical intervention remain the most important factors influencing the prognosis. Although laboratory-based tools such as the LRINEC score and imaging techniques may assist in supporting the diagnostic process, the literature clearly showed that these methods cannot reliably exclude NF, and that the clinical judgement continues to play the central role. Studies also emphasized that early antibiotic therapy and multidisciplinary involvement contribute to improved outcomes and reduced complications.

For SJS and TEN, the findings highlight that again early recognition and the immediate withdrawal of the causative medication are essential steps that consistently improve prognosis. Supportive management, including careful fluid balance, wound care, infection prevention, and symptom control, formed the basis of treatment across studies. While several pharmacological therapies were discussed, including intravenous immunoglobulin (IVIG), cyclosporine, and systemic corticosteroids, the evidence regarding their effectiveness remains mixed. Similar to NF, multidisciplinary care was frequently associated with better outcomes. It was also highlighted that while certain aspects of management are well supported in the literature, such as early surgical intervention in NF and prompt drug withdrawal in SJS/TEN, many therapeutic approaches still lack strong or consistent evidence.

In conclusion, this review met its objectives by summarising key epidemiological features, clinical presentations, diagnostic approaches, treatment options, and outcomes associated with NF, SJS, and TEN. The findings of this systematic review demonstrate that early recognition, timely intervention, and controlled multidisciplinary care remain central for improving patient outcomes in these rapidly progressing conditions. Future research should focus on developing clearer diagnostic criteria, evaluating treatment strategies in more standardised settings, and establishing evidence-based management protocols that support clinicians in making timely and effective decisions.

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CONFLICT OF INTEREST

The author declares no conflict of interest related to the content or findings presented in this thesis.

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