Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis - Full Clinical Guideline

Reference no.: CG-DERM/2023

1. Introduction

Stevens-Johnson Syndrome (SJS) and Toxic Epidermal necrolysis (TEN) are severe mucocutaneous reactions, usually to drugs, characterized by blistering and epithelial sloughing. The two terms describe phenotypes within a severity spectrum, in which SJS is the less extensive and TEN the more extensive form. Although rare (incidence 1-2 cases/million/year), SJS/TEN is a devastating disease; in severe cases the acute phase may be accompanied by a variety of systemic complications, including multi-organ failure. The mortality for SJS is < 10%, with the figure rising to 30% for TEN.

2. Aim and Purpose

These guidelines aim to provide recommendations on the diagnosis and management of SJS/TEN, to inform clinical decision-making and to indicate when referral to a specialist unit should be made.

3. Definitions, Keywords

BSA	Body surface area
CXR	Chest X Ray
FBC	Full blood count
ICU	Intensive Care Unit
IVIG	Intravenous immunoglobulin
LFT	Liver function tests
SCORTEN	Prognostic markers and scoring in toxic epidermal necrolysis
SJS	Stevens Johnson Syndrome
TEN	Toxic Epidermal Necrolysis
UE	Urea and electrolytes

Summary of management

If SJS or TEN is suspected by the receiving team, inform the Dermatology SpR on call immediately via switchboard. In addition make a referral via ExtraMed.

Dermatology on call hours are 0800-2000 Monday-Thursday and 0800-1600 Friday. The receiving team should perform an initial assessment (history, examination and initial investigations), stop potential causative drugs and all non-essential medications, as detailed below.

Initial assessment on presentation **HISTORY, EXAMINATION AND INITIAL INVESTIGATIONS TO BE PERFORMED BY RECEIVING TEAM**	• Take a detailed history from the patient and/or relatives to include: 1. Date of onset of (i) prodrome (fever, malaise, etc.), (ii) rash and (iii) blistering 2. Past medical history - note HIV status and history of malignancy 3. Current medications (not discontinued) 4. Suspected drugs causing TEN with dates of initiation and discontinuation 5. Allergies or history of drug reactions 6. Document all suspected and known allergies on admission; verify accuracy of information and make necessary amendments before the end of the patient's inpatient episode • Perform a full physical examination, including baseline body weight and record the vital signs, including oxygen saturation • Specific clinical examination to include: 1. Percentage of body surface area (BSA, Appendix 1) affected by (i) erythema and (ii) blistering or skin loss - supplement written documentation with clinical photography 2. Presence of (i) ocular involvement - ophthalmology review within 24 hours of presentation at specialist centre, (ii) oral involvement and (iii) urogenital involvement - urology or gynaeology review upon transfer if specialist opinion required 3. Presence of (i) nasogastric tube and (ii) urinary catheter • Order a set of investigations: FBC, U&E, LFT, glucose, magnesium, phosphate, bicarbonate, mycoplasma serology, CXR, and baseline body weight Initiate a primary management plan: 1. establish peripheral venous access 2. if patient cannot maintain adequate nutrition orally, insert a nasogastric tube and institute nasogastric feeding 3. insert a urinary catheter if urogenital involvement is causing significant dysuria/retention 4. **Refer urgently to dermatology on call SpR (the dermatology SpR will liaise with the Dermatology consultant on call ASAP)** 5. Calculate SCORTEN as early as possible (definitely within the first 24 hours) (Appendix 2) **N.B. Dermatology will perform urgent skin biopsy for histology and direct immunofluorescence, see 'Skin biopsy' section**
Determination of drug causality **TO BE PERFORMED BY RECEIVING TEAM**	Identify causative agent and **withdraw immediately** Withdraw any non-essential medications Dermatology will subsequently review medications and coordinate ongoing management

Skin biopsy	• Skin biopsy to be sent for histology and direct immunofluorescence (DIF) will be performed by Dermatology team. Frozen section is acceptable. This should be discussed with the histology and immunology Consultants, and laboratory staff. Frozen section histology should be reported if received before 1pm. DIF should be reported within 7 days. A DIF result is not necessary for the patient to be accepted by the Birmingham Burns Unit. • Patient with suspected SJS/TEN will have a biopsy taken for frozen section as early as possible in working hours (if patient assessed after 1 pm the biopsy will be as early as possible the next day) The biopsy can be performed by any dermatology registrar who is available and does not necessarily have to be the registrar who initially assessed the patient). • Discuss the case with Dr Gandhi, or Dr Hawari in pathology, so the pathologist and laboratory are aware an urgent frozen section biopsy is been sent. Report as quickly as feasible. -If patient has <30% BSA affected and doesn't meet criteria for transfer to Birmingham - DIF could be reported as soon as possible. -If patient has >30% BSA affected and meets criteria for transfer to Birmingham, DIF should be **reported within 7 days**. The immunologist Dr Huissoon reports in Derby on Thursday. The results of DIF are not required for transfer to the Burns Unit, but should be made available within a week.
Care setting	• Multi-disciplinary team should be convened and co-ordinated by a specialist in skin failure, usually dermatology, and including clinicians from intensive care, ophthalmology and skin-care nursing/tissue viability nurses • Patients with **> 30% BSA epidermal loss should be admitted without delay to a Burn Centre or ICU** with experience of treating patients with SJS/TEN and facilities to manage the logistics of extensive skin loss wound care • Patients with **> 10% but < 30% BSA predicted/actual epidermal loss should be admitted to ICU** • Patients must be barrier-nursed in a side room on ICU controlled for humidity, on a pressure-relieving mattress with the ambient temperature raised to between 25° and 28°C
Referral to specialist centre	**Referrals from Derby are made to Birmingham. This will be done by the Dermatology Team.** □ Criteria for referral to Birmingham: 1. Adult patients with a clinical diagnosis and biopsy findings consistent with TEN 2. Actual or predicted skin loss of at least 30% of BSA • Initial contact should be made via telephone to Birmingham's **On-Call Consultant Dermatologist only** during dermatology on-call hours between 0900h and 1900h (daily, including weekends) • Outside dermatology on-call hours, cases can be discussed with Birmingham Burns Consultant On-Call

Skin management regimen 1 **Applicable to all patients in all settings**	**For cases that are not transferred, the following skin management regimen should be followed:** • Employ strict barrier nursing to reduce nosocomial infections • Take swabs for bacterial and candidal culture from three areas of lesional skin, particularly sloughy or crusted areas, on alternate days throughout the acute phase • Administer systemic antibiotics **only** if there are clinical signs of infection
Skin management regimen 2 **This may involve a conservative and / or surgical approach based on the specialist multi- disciplinary team's daily review of the individual needs of the patient**	**Institute a conservative approach in all patients as follows and involve Tissue Viability nurses from an early stage:** • Regularly cleanse wounds and intact skin by irrigating gently using warmed sterile water, saline or an antimicrobial such as chlorhexidine (1/5000) • Apply a greasy emollient, such as 50% white soft paraffin with 50% liquid paraffin (50/50 WSP/LP), over the whole epidermis, including denuded areas • Apply a topical antimicrobial agent to sloughy areas only (choice should be guided by local microbiological advice). Consider Silver-containing products/dressings. • The detached, lesional epidermis may be left ***in situ*** to act as a biological dressing. Blisters should be decompressed by piercing and expression or aspiration of tissue fluid. • Apply non-adherent dressings to denuded dermis (suitable dressings include Atrauman or see wound care formulary). • A secondary foam or burn dressing should be used to collect exudate (suitable dressings include Zetuvit E or see wound care formulary). **Refer to Birmingham if patient develops >30% BSA epidermal loss or shows evidence of the following: clinical deterioration, extension of epidermal detachment, sub-epidermal pus, local sepsis, wound conversion and/or delayed healing.**
Fluid replacement regimen	• Site venous lines through non-lesional skin, whenever possible, and change peripheral venous cannulas every 48 hours • Monitor fluid balance carefully: catheterize if appropriate/necessary • Establish adequate intravenous fluid replacement initially. Fluid replacement can be guided by urine output and other endpoint measurements. Individualized fluid management should be adjusted on a daily basis. • With improvement of SJS/TEN mouth involvement, oral administration of fluids should be progressively increased
Nutrition regimen	• Provide continuous enteral nutrition throughout the acute phase • Deliver up to 20 to 25 kcal/kg/day during the early, catabolic phase and 25 to 30 kcal/kg/day during the anabolic, recovery phase
Analgesia	• Use a patient appropriate validated pain tool to assess pain in all conscious patients at least once a day • Patients should receive adequate analgesia to ensure comfort at rest, with the addition of supplementary opiates, as required • Additional analgesia may be needed to address increased pain associated with patient handling, re-positioning and dressing changes

Supportive Therapeutic Measures	• Immobile patients should receive low molecular weight heparin • Patients in whom enteral nutrition cannot be established should receive a proton pump inhibitor to reduce the risk of stress-related gastro-intestinal ulceration • Neutropenic patients may benefit from recombinant human G-CSF
Treatment of eye involvement	An urgent referral to ophthalmology should be made and ocular care guided by them. Suggested care includes: • Apply an ocular lubricant (e.g. non-preserved hyaluronate or carmellose eye drops) every two hours through the acute illness • Ocular hygiene must be carried out as advised by ophthalmologist • Application of topical corticosteroid drops (e.g. non-preserved dexamethasone 0.1% twice a day) may reduce ocular surface damage • Administer a broad-spectrum topical antibiotic as prophylaxis (e.g. levofloxacin drops four times a day) in the presence of corneal fluorescein staining or frank ulceration • In the unconscious patient, prevention of corneal exposure is essential
Treatment of mouth involvement	• Daily oral review is necessary during the acute illness • Apply white soft paraffin ointment to the lips every two hours through the acute illness • Clean the mouth daily with warm saline mouthwashes or an oral sponge • Use an anti-inflammatory oral rinse or spray containing benzydamine hydrochloride every three hours, particularly before eating • Use an anti-septic oral rinse containing chlorhexidine twice a day • Use a potent topical corticosteroid mouthwash (e.g. betamethasone sodium phosphate) four times a day
Treatment of urogenital involvement	• Daily urogenital review is necessary during the acute illness • Apply white soft paraffin ointment to the urogenital skin and mucosae every four hours through the acute illness • Use a potent topical corticosteroid ointment once a day to the involved, but noneroded, surfaces • Use a silicone dressing (e.g. Mepilex, Silflex or see wound care formulary) to eroded areas
Treatment of airway involvement	□ Respiratory symptoms and hypoxaemia on admission should prompt early discussion with an intensivist and rapid transfer to an ICU or Burn Centre, where fibre-optic bronchoscopy should be undertaken
Active therapy	□ There is insufficient quality or consistency of existing evidence to make specific recommendations either for or against the use of active interventions. There is a lack of consensus even among clinicians with experience in managing SJS/TEN, with, for example, strong advocates for use and avoidance of IVIg.
Discharge and follow-up	• Give the patient written information about drug(s) to avoid • Encourage the patient to wear a MedicAlert bracelet • Drug allergy should be documented in the patient's notes; all doctors involved in the patient's care should be informed • Report the episode to the national pharmacovigilance authorities (Yellow Card online) • Organize an out-patient clinic appointment, and if required an ophthalmology outpatient appointment, within a few weeks of discharge
Diagnostic testing	• Routine drug hypersensitivity testing is not recommended following an episode of SJS/TEN. • Seek specialist advice on hypersensitivity testing where: ○ the culprit drug is not known **or** ○ medication avoidance is detrimental to the individual **or** ○ accidental exposure is possible

A summary of the pathway of care is available in Appendix 3

3. References

Creamer D, Walsh SA , Dziewulski P et al. UK guidelines for the management of StevensJohnson syndrome/toxic epidermal necrolysis 2016. Br J Dermatol 2016; 174: 1194-1227 & J Plast Reconstr Aesthet Surg 2016; 69: e119-e153.

Bastuji-Garin S, Fouchard N, Bertocchi M et al. SCORTEN: a severity-of-illness score for toxic epidermal necrolysis. J Invest Dermatol 2000; 115:149–53.

University Hospitals Birmingham NHS Foundation Trust Clinical guideline: Management of Toxic Epidermal Necrolysis (TEN); August 2015

4. Documentation Controls

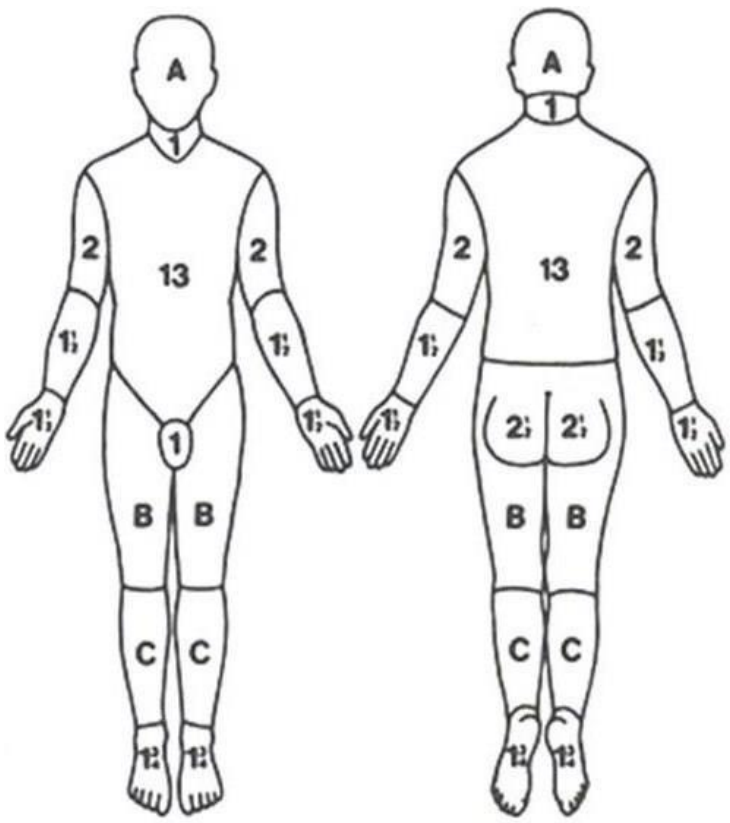
Development of Guideline:	Dr R Simpson; Dr J Mann
Consultation with:	Dr. Kid Wan Shum; Dr. Adam Ferguson Allied specialities (Clinical Leads as point of contact) MAU – Dr Said Din Ophthalmology – Mr M Anandan ICU – Dr James Low Histopathology – Dr Nirav Gandhi Immunology – Dr Aarnoud Huissoon Tissue viability – Karen Gourley
Approved By:	30/10/2018 - Dermatology 25/07/2019 - Medical Division Medicine Division – Dec 2023
Review Date: Reviewed By: New review date:	July 2022 Dr. Aswatha Nambi, Dr. Oluwamayowa Aboluwarin, Dr. Kid Wan Shum 14.12.2023 (no change) December 2026
Key Contact:	Dermatology consultant team

5. Appendices

Appendix 1

PERCENTAGE TOTAL BODY SURFACE AREA LOSS (%TBSA)

MAP AND CALCULATION



REGION	% LOSS
HEAD	
NECK	
ANT. TRUNK	
POST. TRUNK	
RIGHT ARM	
LEFT ARM	
BUTTOCKS	
GENITALIA	
RIGHT LEG	
LEFT LEG	
TOTAL LOSS	

RELATIVE PERCENTAGE BODY SURFACE AREA AFFECTED BY GROWTH

AREA	AGE 0	1	5	10	15	ADULT
A=1/2 OF HEAD	9.5	8.5	6.5	5.5	4.5	3.5
B=1/2 OF ONE THIGH	2.75	3.25	4	4.5	4.5	4.75
C=1/2 OF ONE LEG	2.5	2.5	2.75	3	3.25	3.5

Appendix 2 - SCORTEN

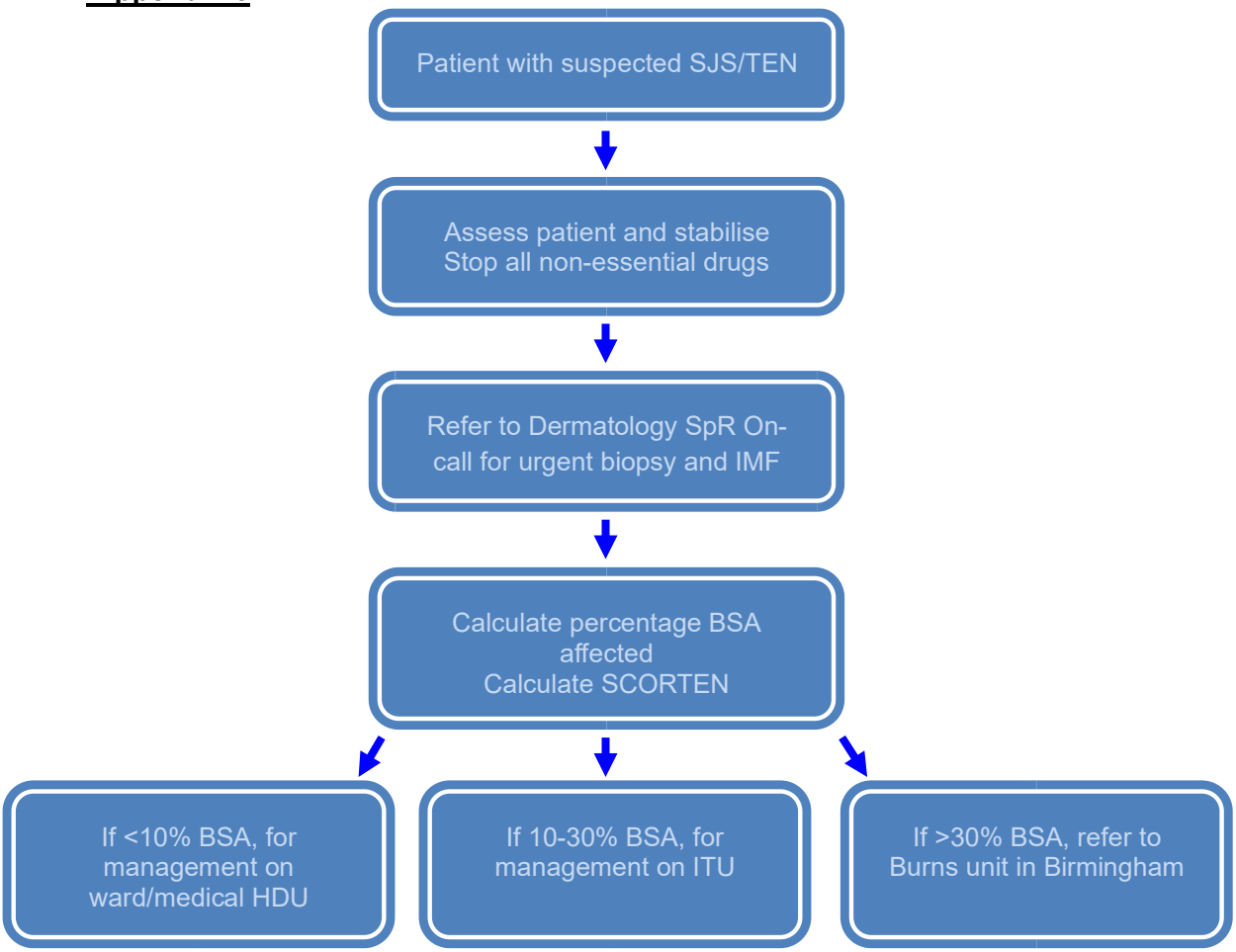
PROGNOSTIC FEATURES AND SCORING MECHANISM IN TEN (SCORTEN)

Uses 7 independent variables each associated with poor prognosis. Score 1 for each variable

1. Age > 40 years
2. Heart rate > 120 per min
3. Malignancy
4. Body surface affected by blistering at day 1 > 10%
5. Urea level > 10mmol/L
6. Bicarbonate level < 20mmol/L
7. Glucose level > 14mmol/L

SCORTEN	PROBABILITY OF DEATH
0-1	0-10%
2	10-19%
3	20-39%
4	40-59%
>5	> 60

Appendix 3



Key Management principles:

- Fluid balance
- Infection
- Thermoregulation
- Analgesia
- Dressing
- Pressure care
- Eye assessment/ care