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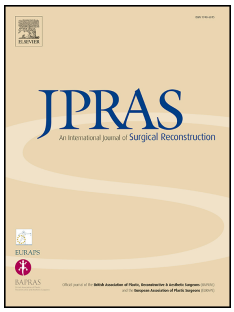

UK guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults 2016

D. Creamer, S.A. Walsh, P. Dziewulski, L.S. Exton, H.Y. Lee, J.K.G. Dart, J. Setterfield, C.B. Bunker, M.R. Ardern-Jones, K.M.T. Watson, G.A.E. Wong, M. Philippidou, A. Vercueil, R.V. Martin, G. Williams, M. Shah, D. Brown, P. Williams, M.F. Mohd Mustapa, C.H. Smith

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UK guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrolysis in adults 2016 (print summary - full guidelines available at http://dx.doi.org/10.1016/j.bjps.2016.01.034)

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Footnote:

This is a new set of guidelines prepared for the British Association of Dermatologists (BAD) Clinical Standards Unit, which includes the Therapy & Guidelines Sub-committee. Members of the Clinical Standards Unit that have been involved are: PM McHenry [Chairman T&G], JR Hughes, M Griffiths, K Gibbon, AJ McDonagh, DA Buckley, I Nasr, VJ Swale, CE Duarte Williamson, NJ Levell, T Leslie, E Mallon, S Wakelin, S Ungureanu, P Hunasehally, M Cork, K Towers [British National Formulary], J Donnelly [British National Formulary], C Saunders [British Dermatological Nursing Group], LS Exton [BAD Information Scientist], AG Brain [BAD Clinical Standards Administrator], MF Mohd Mustapa [BAD Clinical Standards Manager].

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CONFLICTS OF INTEREST:

JKGD (1) grant/research support - Dompe pharmaceuticals, SiFi Pharmaceuticals (non-specific); MA-J (1) commissioned work – Genus Pharmaceuticals (non-specific); (2)

sponsorship to conferences – Abbvie, Janssen-Cilag, Pfizer, Galderma, Steifel (non-specific); (3) clinical trials - Zymogenetics, Pfizer, Genentech, Johnson & Johnson, Centocor, Novartis (non-specific); (4) grant/research support – Emblation (non-specific); (5) developed non-profit website www.drugrash.co.uk to assist clinicians in management of drug allergy (specific). None of the authors have received commercial support from the manufacturers of any medication used in the management of SJS/TEN.

Key words: Stevens-Johnson syndrome, toxic epidermal necrolysis, drug hypersensitivity, management, guidelines

NICE has accredited the process used by the British Association of Dermatologists to produce guidelines. Accreditation is valid for 5 years from May 2010 and has been extended by agreement to May 2016. More information on accreditation can be viewed at *www.nice.org.uk/accreditation*.

For full details of our accreditation visit: *www.nice.org.uk/accreditation*.

Initial assessment on presentation	• Take a detailed history from the patient and/or relatives • Perform a full physical examination, including baseline body weight and record the vital signs, including oxygen saturation • Order a set of investigations: FBC, U&E, LFT, glucose, magnesium, phosphate, bicarbonate, mycoplasma serology, CXR, skin biopsy 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 **(Strength of recommendation D (GPP))**
Determination of drug causality	• Identify causative agent and withdraw immediately **(Strength of recommendation D)**
Prognostic scoring	• Calculate SCORTEN within the first 24 hours **(Strength of recommendation C)**
Care setting	• A multi-disciplinary team should be convened, co-ordinated by a specialist in skin failure, usually dermatology and/or plastic surgery, and including clinicians from intensive care, ophthalmology and skin-care nursing • Patients with greater than 10% 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 must be barrier-nursed in a side room controlled for humidity, on a pressure-relieving mattress with the ambient temperature raised to between 25°and 28℃ **(Strength of recommendation D (GPP))**
Skin management regimen 1 ***Applicable to all patients in all settings***	• 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 **(Strength of recommendation D (GPP))**
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:** • 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 Ag-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 Mepitel™ or Telfa™). • A secondary foam or burn dressing should be used to collect exudate (suitable dressings include Exu-Dry®). **Consider transfer to a Burn Centre in patients with TEN (>30% BSA epidermal loss) and evidence of the following: clinical deterioration, extension of epidermal detachment, sub-epidermal pus, local sepsis, wound conversion and/or delayed healing. In a Burn Centre conservative measures may be supplemented with a surgical approach.**

	• Remove necrotic/loose infected epidermis and clean wounds using a topical antimicrobial agent (e.g. betadine or chlorhexidine) under general anaesthetic • Consider debridment with Versajet™ • Physiological closure with Biobrane/ allograft /xenograft skin in patients with early presentation involving non infected and large confluent areas **(Strength of recommendation D (GPP))**
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 **(Strength of recommendation D)**
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 **(Strength of recommendation C)**
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 **(Strength of recommendation D (GPP))**
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 **(Strength of recommendation C)**
Treatment of eye involvement	• Daily ophthalmological review is necessary during the acute illness • 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 each day by an ophthalmologist or ophthalmic-trained nurse • 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. moxifloxacin 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 **(Strength of recommendation D (GPP))**
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

	(Strength of recommendation D (GPP))
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 non-eroded, surfaces • Use a silicone dressing (e.g. Mepitel^{TM}) to eroded areas **(Strength of recommendation D (GPP))**
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 **(Strength of recommendation D (GPP))**
Active therapy	• If active therapy is instituted it should be given, ideally, under the supervision of a specialist skin failure MDT in the context of clinical research and/or case registry **(Strength of recommendation D)**
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 • Organize an out-patient clinic appointment, and if required an ophthalmology out-patient appointment, within a few weeks of discharge • Refer for review to unit with appropriate sub-speciality interest **(Strength of recommendation D (GPP))**
Diagnostic testing	• Routine drug hypersensitivity testing is not recommended following an episode of SJS/TEN. • Seek specialist advice on hypersensitivity testing where: 1. the culprit drug is not known **or** 2. medication avoidance is detrimental to the individual **or** 3. accidental exposure is possible **(Strength of recommendation D (GPP))**

SUPPORTING INFORMATION

Additional supporting information including the search strategy may be found in the full online version of this article here: http://dx.doi.org/10.1016/j.bjps.2016.01.034.

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