Clinical Guideline

BURNS SERVICE - CHILDREN WITH ACUTE SEVERE BLISTERING/ SKIN LOSS

SETTING
Bristol Royal Hospital for Children (BRHC)

FOR STAFF
All staff who provide direct patient care

PATIENTS
All children with Exfoliative Disorders such as Staphylococcal Scalded Skin Syndrome, Stevens-Johnson Syndrome and Toxic Epidermal Necrolysis referred to the South West UK Children’s Burn Centre

1. Guideline Statement

Blistering can occur in many skin diseases in children. Certain acute severe conditions (sometimes known as skin loss or exfoliative disorders) (Table 1) can be life threatening.

While e.g. impetigo or erythema multiforme can be safely treated close to home by GPs and local dermatology/paediatric services, the more severe and extensive conditions involving de-epithelialisation of the skin as in toxic epidermal necrolysis (TEN) should be escalated to facilities where appropriate multi-disciplinary (MD) care can be provided [1, 2, 3, 4, 5, 6, 8, 17, 18, 29, 35, 40], as mortality rates are high (Table 2) and mostly due to secondary bacteraemia [23]. This guideline provides an aid-memoire for staff caring for such patients.

2. Purpose of the Guideline

There are no universally formalised guidelines developed to date for the management of the skin loss disorders shown in Table 2. Therefore treatment methods vary widely. These guidelines are evidence based and designed to optimise the referral path as well as management of children with acute-onset severe blistering conditions requiring admission to specialised centres.

The below outlined conditions will be discussed in this document:

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>SJS (Steven-Johnson syndrome)</td>
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<tr>
<td>SJS/TEN overlap</td>
</tr>
<tr>
<td>TEN (Toxic epidermal necrolysis)</td>
</tr>
<tr>
<td>SSSS (Staphylococcal scalded skin syndrome)</td>
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</table>

In terms of their consequences to the patient these disorders can resemble burns injuries resulting in loss/failure of body integument. [14]:
- significant loss of fluids and shifts in the homeostasis resulting in hypovolaemia and electrolyte imbalances
- impaired thermoregulation
- risk of septicaemia
- pain
- specialised wound care requirements

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Therefore severe forms of some acute blistering disorders in children should be treated in burns units and centres, where specialised intensive care is readily available and multidisciplinary team approach can be offered [1, 2, 3, 4, 5, 6, 8, 17, 18, 29, 35, 40].

The specialists involved in these cases include the following:

<table>
<thead>
<tr>
<th>Professional</th>
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<tbody>
<tr>
<td>Paediatric Dermatologist</td>
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<tr>
<td>Paediatrician</td>
</tr>
<tr>
<td>Paediatric Anaesthetist/Intensivist</td>
</tr>
<tr>
<td>Burns surgeon</td>
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<tr>
<td>Specialised nursing staff</td>
</tr>
<tr>
<td>Microbiology and Infection control</td>
</tr>
<tr>
<td>Pain team</td>
</tr>
<tr>
<td>Dietitian</td>
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<tr>
<td>Ophthalmologist</td>
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<tr>
<td>Gynaecologist</td>
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<tr>
<td>Urologist</td>
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<tr>
<td>Occupational Therapist/ Physiotherapist</td>
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<td>Play Specialist</td>
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<td>Paediatric Psychologist</td>
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### 3. Definition of Terms

<table>
<thead>
<tr>
<th>Condition</th>
<th>Definition</th>
<th>Causes</th>
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<tbody>
<tr>
<td>Steven Johnson syndrome</td>
<td>A group of rapidly progressive and potentially life threatening skin loss disorders of varying degrees of severity characterised by confluent subepidermal detachment (epidermal necrolysis) of the skin and mucosal surfaces</td>
<td>Adverse drug reactions in &gt;80%</td>
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<tr>
<td>SJS/TEN overlap</td>
<td></td>
<td></td>
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<tr>
<td>Toxic epidermal necrolysis</td>
<td></td>
<td></td>
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<tr>
<td>Staphylococcal scalded skin syndrome</td>
<td>Rare potentially life threatening blistering skin disease caused by the exfoliative (epidermolytic) exotoxins (A and B) secreted into the circulation from the site of primary infection by the Staphylococcus aureus</td>
<td>Staphylococcus aureus</td>
</tr>
</tbody>
</table>

### Mortality rates associated:

<table>
<thead>
<tr>
<th>Condition</th>
<th>Mortality rates</th>
<th>Annual incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema multiforme [32]</td>
<td>0%</td>
<td>1.2 -6 / 1 000 000</td>
</tr>
<tr>
<td>Steven Johnson syndrome [6, 13, 25 30]</td>
<td>1-5%</td>
<td>6 / 1 000 000</td>
</tr>
<tr>
<td>SJS/TEN overlap</td>
<td>Not reported</td>
<td>Not reported</td>
</tr>
<tr>
<td>Toxic epidermal necrolysis [6, 13, 25, 30, 35]</td>
<td>25-50%</td>
<td>1-2 / 1 000 000</td>
</tr>
<tr>
<td>Staphylococcal scalded skin syndrome [21, 18]</td>
<td>21%:</td>
<td>0.09-0.13 / 1000 000</td>
</tr>
<tr>
<td></td>
<td>- in children – 11% (reduced to &lt;5% with timely and appropriate treatment)</td>
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</table>

### 4. Roles and Responsibilities

The Consultant Burn Surgeon will deliver shared care for these patients in conjunction with the HDU/ PIC Consultant / General Paediatrician and Consultant Dermatologist. The Burn Care multi-disciplinary team will be involved in providing direct treatment/ care to these patients and other support services will be called upon as required.
### Clinical, Diagnostic and Prognostic features

**Table 3.** Clinical and diagnostic features of disorders discussed in the guideline [9, 10, 17, 18, 22, 25, 26, 30, 32, 33, 35, 36, 37, 38, 39]:

<table>
<thead>
<tr>
<th></th>
<th>SJS</th>
<th>SJS/TEN overlap</th>
<th>TEN</th>
<th>SSSS</th>
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</thead>
<tbody>
<tr>
<td><strong>Causative agent</strong></td>
<td>Adverse drug/hypersensitivity reaction in 80% of cases (Usually antibiotics, anticonvulsants, NSAIDs, allopurinol or an anti-retroviral)</td>
<td></td>
<td>Exfoliative (epidermolytic) exotoxins (A and B) secreted into the circulation from the site of primary infection by the Staph. aureus</td>
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</tr>
<tr>
<td><strong>Manifestation and clinical symptoms</strong></td>
<td>Systemic prodromal symptoms (12-72 hours in TEN and 4-5 days in SJS): fever, malaise, sore throat/difficulty swallowing, conjunctivitis; followed by development of cutaneous lesions, starting on the trunk, face, palms and soles.</td>
<td></td>
<td>Short (~48 hours in duration) prodromal period: sore throat, fever, malaise, followed by extremely tender erythematous patches on the face, neck, axillae and perineum.</td>
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<tr>
<td><strong>Bullae</strong></td>
<td>Mostly isolated lesions, some can be confluent (mainly on face/trunk)</td>
<td>Isolated lesions, some can be confluent (mainly on face/trunk)</td>
<td>Confluent lesions (anywhere on the body)</td>
<td>Tender erythematous patches, mostly in flexural areas, later flaccid bullae develop, enlarge, may become more confluent, rupture easily revealing moist erythematous base. Skin desquamation occurs and eventually heals without scarring provided there is no secondary infection, which might lead to full thickness skin loss and hence - permanent scarring.</td>
</tr>
<tr>
<td><strong>Mucosal involvement</strong></td>
<td>Involvement of at least 1 mucosal surface occurs in over 90% of cases, and 70% of patients will have 2 mucosal areas affected. The disease can affect respiratory, gastrointestinal and genital tracts as well as conjunctiva</td>
<td></td>
<td>Mucosae are spared</td>
<td></td>
</tr>
<tr>
<td><strong>Nikolsky's sign</strong></td>
<td>Positive</td>
<td>Positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Detachment area (% of TBSA)</td>
<td>&lt;10 %</td>
<td>10-30%</td>
<td>30%</td>
<td>Mild &lt;10%, Moderate 10-20%, Severe 20%</td>
</tr>
<tr>
<td><strong>Detachment depth</strong></td>
<td>Epidermal necrosis with sub-epidermal bulla formation</td>
<td></td>
<td>Intra-epidermal cleavage through the stratum granulosum without any signs of necrosis</td>
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</tr>
<tr>
<td>(Full thickness skin biopsies (1x for frozen sections and 1x for formalin fixed examination) obtained from the border of intact epidermis) [10, 36, 37, 40]</td>
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<tr>
<td><strong>Laboratory investigations</strong></td>
<td>No specific abnormalities in blood tests, but severe forms may exhibit hyponatraemia and other electrolyte disturbances (mostly iatrogenic), uraemia, hyperglycaemia. A rise of inflammatory markers from the baseline levels taken on admission may indicate a secondary infection</td>
<td></td>
<td>Hyponatraemia, neutropenia/lymphopenia with an unimpressive elevation in inflammatory markers. Rise of inflammatory markers from the baseline levels taken on admission may indicate a secondary infection</td>
<td></td>
</tr>
<tr>
<td><strong>Microbiology</strong></td>
<td>Negative wound swab results, unless secondary infection has occurred</td>
<td></td>
<td>Negative blister swabs, but the primary source of infection should be sought: isolation of exfoliative exotoxins A or B producing Staphylococcus aureus, rarely MRSA can be found.</td>
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</tbody>
</table>

Secondary infection most commonly demonstrates growth of Pseudomonas spp.
Prognosis (TEN and TEN-SJS overlap)

Prognosis, severity of the disease and mortality can be assessed using SCORTEN disease severity score, which has been developed for adults with TEN, but can also be used in children (Table 4 [6, 10]). The assessment should be carried out within the first 24 hours after admission and then 3 days later. The score is a sum of the 6 clinical variables (in children):

- tachycardia
- presence of cancer or haematological condition
- epidermal detachment involving >10% of TBSA on day 1
- blood urea >10mmol/L
- glucose >14mmol/L
- bicarbonate <20 mEq/L

Table 4: SCORTEN level and predicted mortality

<table>
<thead>
<tr>
<th>SCORTEN</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>3.2%</td>
</tr>
<tr>
<td>2</td>
<td>12.1%</td>
</tr>
<tr>
<td>3</td>
<td>35.3%</td>
</tr>
<tr>
<td>4</td>
<td>58.3%</td>
</tr>
<tr>
<td>5 or greater</td>
<td>90%</td>
</tr>
</tbody>
</table>

6. The Referral Pathway

**Referral Criteria and Pathway: Child with blisters**
7. The Management plan

**INITIAL ASSESSMENT:**
- Assessment and management of ABCDEs/secondary survey
- History to include all recent illnesses and drug exposure including over the counter remedies

* For the paediatric burns service at Bristol Royal Hospital for Children please call 0117 923 0000 (switchboard), bleep number 6780

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**Please note**

Assessment of a skin condition is a part of secondary survey.

The general condition of any child with a blistering disorder should first be assessed and managed as outlined in the national Paediatric Life Support guidelines.
INITIAL INVESTIGATIONS:
- Wound swabs
- MRSA surveillance screen
- Blood culture
- FBC, U&E, Coagulation, CRP, Group and save serum, LFTs, Ca, Mg, phosphate

DIAGNOSIS AND ASSESSMENT
- Paediatric dermatology input is essential starting at presentation and especially at making the diagnosis [32]
- Contact BRI switchboard for Specialist Registrar on-call, who will contact consultant
- Clinical assessment of skin appearance – best performed in theatres in severe forms to ensure sterile environment and to decrease pain and distress
- 2x full thickness skin biopsies (1x for frozen sections, 1x for formalin fixation) should be obtained from the border of intact epidermis surrounding bullous lesions
- SCORTEN disease severity score can be used to evaluate prognosis in TEN

FLUIDS / HYDRATION: The Parkland Resuscitation formula should not be used! [14, 18, 19, 25, 28, 34, 35]
- Start with 80% maintenance requirement with isotonic fluids to avoid hyponatraemia: 0.9% Saline / 5% Dextrose (Hartmann’s in children of > 5yrs age).
- Watch for fluid overload and hyponatraemia, check sodium levels regularly
- Further fluid type and regimen should be dictated by frequent evaluations of weight, fluid balance, CVP, U&Es, and assessment of perfusion status by clinical signs and arterial blood gases (base excess, lactate levels)
- Consider small dose of Furosemide early, especially if oxygen requirements are increasing
- Give 5 ml/kg boluses of 0.9% Saline or Gelofusine as required judged on:
  - Urine output (beware ADH response and accept 0.5mls/kg/hr urine output maximum)
  - Base deficit
  - Lactate
  - Capillary refill time and core-peripheral temperature difference (useful but may be difficult to assess because of dressings)
- Urinary catheter is mandatory
- Central venous line for access and blood tests (removed as soon as possible at the start of recovery)

INFECTION CONTROL [14, 18, 19, 23]
- Isolation room
- Strict hygiene observation and barrier nursing
- Dressing change under aseptic precautions
- Regular wound swabs
- Antibiotics only to be started to treat a particular infection or secondary sepsis
- Antibiotics should not to be started as prophylaxis

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SKIN, MUCOSAL AND WOUND CARE [10, 14, 16, 18, 19, 23, 25, 31, 32, 33, 35, 38]

- Cleansing and debridement of de-vitalized tissues in theatre is recommended to ensure sterile environment and to alleviate discomfort.
- Sterile synthetic dressings:
  - Silver-based dressings may be used: Acticoat™, silver impregnated Urgotul™
  - Non-adherent dressings covered by damp gauze
  - Hydrocolloid dressings are useful on small areas
  - Dressings for cannulas and other devices as well as any other adherent dressings should be avoided due to potential shearing of the skin on removal.
- Biological dressings such as skin homografts, cadaver allografts or porcine xenografts can be considered once desquamation is complete.
- Daily theatre changes of dressings may be required until recovery starts.
- Minimal handling, basic hygiene measures and aseptic technique for procedures are essential to decrease the risk of secondary infection.
- In SJS/TEN mucosal surfaces should be cleansed gently with N. Saline dampened gauze several times a day to prevent symblepharon, conjunctival synechia, entropion, ingrowth of eyelashes, phimosis and vaginal synechia.
- Daily dermatology review is essential.
- Consider gynaecology/urology review.
- Air-filled mattresses should be considered to reduce the risk of pressure sores.
- Topical anaesthetic solutions/ointments should be considered for oral and genital ulcerations.

NUTRITION [13, 19, 36]

- NG or ideally NJ feeding should be initiated (NJ tube will allow feeding to continue during daily theatre trips).
- Oral intake should be encouraged.
- Assess and manage any problems of gut motility and absorption.
- Assess and manage need for vitamin and elemental supplementation.
- Avoid parenteral nutrition.

TEMPERATURE [14, 19]

- Monitor core temperature.
- Aim for core temperature of 36.5-37°C.
- Adjust the ambient temperature accordingly (should reach 30-32°C).
- Nurse in a single cubicle and keep warm with radiant heating/bair hugger.
ANALGESIA [18, 25, 38]
- Regular IV/PO Paracetamol
- NSAIDS are contraindicated
- Fentanyl infusion 1mcg/kg/ml at 1-4ml/kg/hr (Refer to HDU protocol)
- Consider low dose Midazolam infusion (50-100mcg/kg/h) (Refer to HDU protocol)
- Consider Ketamine infusion as alternative and if Fentanyl dose increasing rapidly
- Refer to ‘Guideline for management of itching’: Gabapentin is recommended (100mg once to 3x daily for a few months)
- Procedural pain relief is of paramount importance: oral Midazolam with Oramorph, Entonox are recommended

SPECIFIC MANAGEMENT: SJS/TEN [10, 11, 12, 13, 14, 19, 20, 23, 25, 27, 31, 32, 33, 35]
- Stop any potential inciting medications, especially any new drugs started within the past 8 weeks
- Stop any prophylactically started antibiotics, steroids and TPN
- Treat in an isolation room to prevent infection
- Initiate enteral nutrition: due to involvement of mucosal membranes swallowing may be difficult and painful, therefore NJ tube is appropriate
- Intubation and ventilation may be appropriate due to involvement of mucous membranes and potential airway obstruction, BUT every attempt to keep the child extubated is paramount
- In systemically unwell children, consider IV Immunoglobulin at a dose of 2g/kg as per Department of Health recommendations [45]. Ophthalmology review is advised as early as possible and should occur daily (up to 90% patients develop ocular pathology with possible long term disturbances)
- Consider gynaecology/urology review if genitalia are affected

SPECIFIC MANAGEMENT: SSSS [10, 11, 12, 16, 17, 18, 19, 20, 22, 26, 27, 35, 37, 38, 39]
- Treat in an isolation room to prevent cross infection
- Start empirical IV antibiotics: Flucloxacillin and Benzylpenicillin or Cephalosporins, (Clarithromycin and macrolides are appropriate if allergic to Penicillin).
- Discuss with infection control as appropriate and tailor the choice of antibiotics according to swab results
USE OF FFP, IVIG, STEROIDS [24, 25, 31]

- Systemic corticosteroids should not be used for either one of these conditions (it is associated with poorer outcomes and higher mortality in SSSS and has not been shown to improve mortality or progress of the disease in TEN/SJS) [6, 7, 9, 10, 35, 36]
- Topical steroid ointments/drops can be used for eyes in TEN/SJS [42], but supporting evidence is sparse
- Cyclosporine, cyclophosphamide, thalidomide should not be used due to toxicity and even increased mortality (with Thalidomide) [6, 15]
- Granulocyte-colony stimulating factor has been used in TEN with observation of shortening in re-epithelialisation times but further evidence is required to support its effectiveness and safety [32]

FURTHER REFERRALS:
Ophthalmology, Gynaecology, Urology, Clinical psychology, Physiotherapy, Play specialists/ Educationalists

8. Monitoring Effectiveness

Prospective data is collected for these patients and use of this guideline and any complications resulting from its use. The data will be entered into the International Burns Injury Database (iBID) and reports can be formulated and presented from this.

9. References


Extended until September 2020


34. Shiga S, Cartotto R. What are the fluid requirements in toxic epidermal necrolysis? *Journal of Burn Care and Research.* 31(1): January/February 2010


**RELATED DOCUMENTS**

- Burns Fluid guideline
- Use of Biobrane guideline
- TSS-Sepsis Guideline
- Guideline for the management of itch in children’s burns

**SAFETY QUERIES**

In the first instance please contact the Burns Office on Ext 27910 or via the Burns Bleep holder on Bleep : 6780