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Toxic Shock Syndrome in Children

Introduction and Who Guideline Applies To

Key Points

To facilitate best practice in the identification and treatment of children presenting with suspected toxic shock syndrome, including those presenting after burns: from initial presentation in the Emergency Department to definitive management.

Don’t Miss

- An unwell child with a recent burn or other risk factors has toxic shock syndrome until proven otherwise.
- Diagnosis of toxic shock syndrome is clinical.
- If a child appears seriously unwell, proceed straight to Paediatric Advanced Life Support.
- Start the management of toxic shock syndrome in the Emergency Department: do not wait for specialty review.

Related Documents:

1. University Hospitals of Leicester Paediatric Sepsis Screening & Action Tool (hyperlink)
2. The UK Sepsis Trust (hyperlink)
3. MEDUSA – injectable medicines guide (login required) (hyperlink)
TOXIC SHOCK SYNDROME TREATMENT ALGORITHM
TO BE USED IN CONJUNCTION WITH UHL PAEDIATRIC SEPSIS GUIDELINE

UNWELL CHILD

RECENT BURN OR OTHER RISK FACTORS
(SEE PAGE 4)

Observations
- Fever ≥38.9 C, tachycardia, low SpO2, tachypnoea, cap refill >3, hypotension
- See age-specific parameters on UHL paediatric sepsis guideline

Unstable
- Paediatric Advanced Life Support
- Early senior doctor review
- Treat as per UHL sepsis guideline

Stable
- History
- General - Lethargy, irritable
- Symptoms of TSS - Vomiting, diarrhoea, rash, altered mental state, fever

Examination
- General - Lethargy, irritable
- Signs of TSS - Diffuse macular blanching rash, mucosal hyperaemia
- History - Mechanism (e.g. burn ≥2 days), first aid, treatment
- Examine other infection sources - Resp, CVS, GI, neuro, GU, ENT, skin
- Safeguarding - Delayed presentation, unusual story
- Examination of burn/ open wound - Infected burn? Size, depth, location

Consider alternative diagnoses

TOXIC SHOCK SYNDROME

Stabilised

Resuscitation

No

Yes

TOXIC SHOCK SYNDROME TREATMENT ALGORITHM

Name ___________________________ Hospital Number ______________ DOB ____________ Done

1. High flow oxygen

2. Obtain IV/IO access

3. Obtain bloods – Blood gas, FBC, U&E, CRP, LFTs, Ca2+, clotting, glucose, blood cultures, group & save


5. Consider fluid resuscitation +/- catheterisation
   - Fluid bolus: 10-20ml/kg saline over 5-10mins, repeat as needed. Contact PICU after 40ml/kg.
   - Maintain normal HR/BP for age. Maintain urine output >1mls/kg/hr.

6. Give analgesia (e.g. intravenous/intranasal opiate)

7. Monitor observations & fluid balance – Minimum every 15-30 mins

8. Burn/other wound care as needed (with Plastic Surgery input)
   - Gentle clean with saline-soaked gauze. Wound swab MC&S.
   - Dressings: body = Urgotul Ag, gauze, bandage / head + neck = soft paraffin

9. Senior ED doctor, Paediatric, (Plastic Surgery if skin loss), PICU, Microbiology reviews

IF normal physiology not restored after ≥40ml/kg fluid
- consider inotropes/vasopressors with PICU input

IF patient not demonstrating signs of improvement with antibiotics
- consider use of fresh frozen plasma (FFP)

IF patient is not demonstrating signs of improvement after FFP transfusion
- consider use of IVIG (2g/kg)

RECHECK PATIENT
Background

a. Definition

Toxic Shock Syndrome (TSS) is an acute, multi-system inflammatory response to an exotoxin-mediated bacterial infection. It is a rare but life-threatening condition, with rapid progression to septic shock and multi-organ failure \(^{(1,2)}\).

b. Epidemiology

The most common risk factor for TSS in the UK is a small surface area burn in a child \(^{(3)}\). It is typically associated with children aged 1-4 years, two days after a small burn. Other risk factors of TSS in children include:

<table>
<thead>
<tr>
<th>Table 1. Risk factors for Toxic Shock Syndrome in Children (^{(4,6)})</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcal TSS</td>
</tr>
<tr>
<td>Retained menstrual products</td>
</tr>
<tr>
<td>Skin disruption - trauma, burns, surgery</td>
</tr>
<tr>
<td>Osteomyelitis, arthritis</td>
</tr>
<tr>
<td>Respiratory infections – influenza</td>
</tr>
<tr>
<td>Septorhinoplasty, sinusitis</td>
</tr>
<tr>
<td>Postpartum infection, mastitis</td>
</tr>
</tbody>
</table>

The most common pathogens are Gram-positive skin commensals: Staphylococcus aureus and Group A Streptococcus (GAS; S pyogenes) \(^{(6)}\). Methicillin-resistant S aureus (MRSA) strains are also known to cause TSS. The most common exotoxin is TSST-1, released by toxin-producing strains of S aureus \(^{(4)}\).

Streptococcal TSS often occurs at deeper sites than staphylococcal TSS, and is associated with a greater incidence of bacteraemia and mortality in children (5-10% vs 3-5%) \(^{(6)}\). There is 15-50% mortality in untreated TSS \(^{(8)}\).

c. Pathogenesis

Children are susceptible to toxic shock syndrome due to their immature immune systems. Less than 30% of children under 5 have demonstrated antitoxin antibodies; this rises to 80% by adolescence and 90-95% by adulthood \(^{(7,9)}\). Infants under 1 are protected by passive immunity at birth and in breast milk.

The higher incidence of TSS in small burns is thought to be related to their less aggressive management. With larger burns, surgical debridement removes the site of contamination and the transfusion of blood products confers passive immunity \(^{(3)}\).

Pathogenesis starts with colonisation of a burn/wound with toxin-producing strains of S aureus or GAS. Toxins involved in TSS are classed as "superantigens", which bypass the usual antigen-mediated immune pathways. By direct interaction with T-cell receptors, superantigen-MHC complexes stimulate vast numbers of T cells.

The result is a massive, dysregulated cytokine-mediated systemic inflammatory response, involving TNF-a, IL-1 and IL-6. Shock and end-organ injury rapidly follow \(^{(3,7)}\).
Investigations

An unwell child with a recent burn or other risk factors has toxic shock syndrome until proven otherwise

TSS must be suspected in a child with a recent history of a burn or other risk factors, who is systemically unwell, with or without a rash.

Early symptoms and signs of TSS are highly non-specific and may be indistinguishable from a range of childhood illnesses. It is therefore important to treat any unwell child with a burn or other risk factors as TSS unless another definitive diagnosis is made.

Streptococcal TSS is suspected if there is also a history of sore throat or florid cellulitis

a. Recognition of Sepsis

The UHL paediatric sepsis screening & action tool guideline provides an algorithm to screen for and manage paediatric sepsis, and includes the “Sepsis 6” bundle. The general screening criteria are outlined in Table 2, but please review the UHL Paediatric Sepsis Guideline (hyperlink to INsite) to access detailed, age-specific parameters for sepsis.

<table>
<thead>
<tr>
<th>Appearance</th>
<th>Demeanour</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appears ill</td>
<td>Altered behaviour or mental state</td>
</tr>
<tr>
<td>Looks mottled/ashen</td>
<td>No response to social cues</td>
</tr>
<tr>
<td>Cyanosis of skin, lips or tongue</td>
<td>Unable to rouse, does not stay awake</td>
</tr>
<tr>
<td>Non-blanching rash</td>
<td>Weak high-pitched/continuous cry</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Breathing</th>
<th>Exposure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grunting/apnoea</td>
<td>High or low temperature</td>
</tr>
<tr>
<td>Low SpO₂ or new/increased FiO₂</td>
<td></td>
</tr>
<tr>
<td>Increased respiratory rate</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Circulation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Low blood pressure</td>
<td></td>
</tr>
<tr>
<td>High (or low) heart rate</td>
<td></td>
</tr>
<tr>
<td>Reduced urine output</td>
<td></td>
</tr>
</tbody>
</table>

b. Recognition of Toxic Shock Syndrome

Diagnosis of toxic shock syndrome is clinical

There are scoring systems available to help aid diagnosis. However, these do not supersede clinical judgement, and TSS should never be excluded in a highly suspicious case based on these criteria. Please see Appendix 1. (Pages 12 – 13) for flowchart on triaging patients referred from the community with risk factors for toxic shock syndrome.

United States Centre for Disease Control and Prevention

A well-known diagnostic scoring system for TSS has been set out by the United States Centre for Disease Control and Prevention (Table 3)

In the immediate setting, it describes fever, hypotension and a rash in the setting of multisystem organ failure. Desquamation often occurs 1-2 weeks after onset of illness. These criteria can help aid diagnosis in the acute clinical setting.
Investigations (continued)

Table 3 Adapted from CDC guidelines for Toxic Shock Syndrome (other than streptococcal) (2)

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Detail</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Temperature ≥ 38.9°C</td>
</tr>
<tr>
<td>Hypotension</td>
<td>Systolic BP: Adults ≤90mmHg, children &lt;5(^{th}) percentile for age</td>
</tr>
<tr>
<td>Rash</td>
<td>Diffuse macular erythroderma</td>
</tr>
<tr>
<td>Desquamation</td>
<td>1-2 weeks after onset of illness: palms &amp; soles</td>
</tr>
<tr>
<td><strong>Multi-organ failure ≥3 systems:</strong></td>
<td></td>
</tr>
<tr>
<td>- GI</td>
<td>Vomiting or diarrhoea at onset</td>
</tr>
<tr>
<td>- Muscle</td>
<td>Severe myalgia or CK ≥ 2 x upper limit of normal</td>
</tr>
<tr>
<td>- Mucous membranes</td>
<td>Hyperaemia (conjunctival, oropharyngeal)</td>
</tr>
<tr>
<td>- Renal</td>
<td>Urea or creatinine &gt;2 x upper limit of normal</td>
</tr>
<tr>
<td></td>
<td>Positive urinary leucocytes (in absence of UTI)</td>
</tr>
<tr>
<td>- Hepatic</td>
<td>Bilirubin or transaminases &gt;2 x upper limit of normal</td>
</tr>
<tr>
<td>- Haematologic</td>
<td>Platelets &lt;100</td>
</tr>
<tr>
<td>- CNS</td>
<td>Disorientation, altered consciousness (no focal neurological signs)</td>
</tr>
</tbody>
</table>

For streptococcal TSS, the CDC guideline outlines additional clinical features (2, 4):
- Soft tissue necrosis: necrotising fasciitis, myositis, gangrene
- Acute respiratory distress syndrome
- Coagulopathy: low platelets, disseminated intravascular coagulation

**Cole & Shakespeare Abbreviated Criteria**

Cole & Shakespeare (1990) describe an abbreviated set of criteria to identify probable TSS, specifically for use in the paediatric population (8). The criteria are: pyrexia ≥39\(^{o}\)C, rash, diarrhoea +/- vomiting, irritability and lymphopenia. As these are non-specific signs in the unwell child, they are likely to be of limited use in confirming or excluding TSS in the clinical setting.

c. Laboratory Investigations

**Staphylococcal**

Isolation of S aureus supports the diagnosis of Staphylococcal TSS, but negative cultures do not exclude it. S aureus is isolated in:
- 5% of blood cultures (12)
- 80-90% of wound/mucosal swab cultures (13)

**Streptococcal**

Isolation of Group A Streptococcus from a wound swab or a normally sterile site can be diagnostic (14):
- blood cultures, CSF, pleural fluid, peritoneal fluid.
Management

See Toxic Shock Syndrome Treatment Algorithm (Page 3).

a. Observations

Perform vital signs on arrival to the Emergency Department. High fever ≥38.9 degrees, tachycardia, tachypnoea and capillary refill >3 seconds are non-specific signs of toxic shock syndrome.

If a child appears seriously unwell, proceed straight to paediatric ALS

b. Detailed History

<table>
<thead>
<tr>
<th>General</th>
<th>Unwell?</th>
<th>Playing, smiling, feeding / irritable, lethargic, floppy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxic Shock Symptoms</td>
<td>Red flags: vomiting, diarrhoea, high fever, rash, altered mental state</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exclude other sources: respiratory, urine, GI, neurology, ENT, CVS, skin</td>
<td></td>
</tr>
<tr>
<td>History of Illness/Injury</td>
<td>Time: Date, time</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Event: Mechanism, first aid, subsequent treatment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Any safeguarding concerns: Delayed presentation, unusual story or mechanism, pattern of burn/wound</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Past medical: Recent trauma / illnesses, long-term conditions</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Drug history: Regular medications, allergies, vaccinations</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Social history: Family circumstances, social worker</td>
<td></td>
</tr>
</tbody>
</table>

c. Focused Examination

<table>
<thead>
<tr>
<th>General inspection</th>
<th>Does the child look unwell, irritable, lethargic?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Signs of TSS</td>
<td>Diffuse macular blanching rash, mucosal hyperaemia</td>
</tr>
<tr>
<td>Other infection sources</td>
<td>Respiratory, urine, GI, neurology, ENT, cardiovascular, skin</td>
</tr>
<tr>
<td>Examination of burn/wound</td>
<td>Remove dressing. Signs of infected burn/wound? Surrounding cellulitis? Total body surface area, depth, location</td>
</tr>
</tbody>
</table>

d. Management of Toxic Shock Syndrome

Start the management of toxic shock syndrome in the Emergency Department

Do not wait for specialty review

Early identification and management of sepsis is critical to a good outcome.

Implement the Management of Toxic Shock Syndrome (pages 8-9) until results of cultures are received \(^{(10, 15)}\).

Inform the Paediatric team as soon as possible. Best practice for burns/skin loss involves contacting the Plastic Surgery registrar in addition to the Paediatric registrar, and admission under joint care between Paediatrics and Plastic Surgery. If there is an open wound/history of surgical procedure, also contact the relevant surgical specialty according to anatomy.
1. High flow oxygen

2. Obtain IV/IO access

3. Obtain bloods
- Blood gas
  1. High lactate >2 indicates need for fluid resuscitation
  2. Lactate remaining >2 despite fluid resuscitation, or >4 may require early senior review/PICU input
- FBC: Lymphopenia
- U&E: Raised urea/creatinine >2 x upper limit of normal; hyponatraemia
- CRP: May be raised
- LFTs: Raised bilirubin/ALT/AST >2 x upper limit of normal. Albumin may be low.
- Calcium: May be low
- Clotting screen: Coagulopathy in streptococcal TSS
- Blood cultures: May isolate S pyogenes or S aureus
- Blood glucose
- Group & Save: May require fresh frozen plasma transfusion (see page 8)

4. Give empirical antibiotics

Manage all unwell children with suspected sepsis in the Emergency Department with empirical sepsis antibiotics according to the UHL paediatric sepsis guidelines. Add IV clindamycin if TSS is suspected.

If all other sources of infection have been excluded and TSS is strongly suspected, an early switch from empirical sepsis antibiotics to empirical TSS antibiotics (Table 4) can be considered on a case-by-case basis. This requires discussion between the Paediatric team, Plastic Surgery for burns/skin loss, Microbiology and other relevant specialties.

Please re-discuss the empirical antibiotics in Table 4 with Microbiology at 72 hours, to see if antibiotic therapy can be focused based on culture results and clinical response.

**Table 4. Antibiotics for use in toxic shock syndrome**

<table>
<thead>
<tr>
<th>1st Line</th>
<th>OR Proven MSSA</th>
<th>1st Line penicillin-allergic patients OR Proven/suspected MRSA</th>
<th>Proven Streptococcal</th>
</tr>
</thead>
<tbody>
<tr>
<td>IV flucloxacillin 50mg/kg every 6 hours</td>
<td>IV vancomycin Refer to Medusa IV vancomycin monograph*</td>
<td>IV benzylpenicillin 50mg/kg every 4-6 hours</td>
<td></td>
</tr>
<tr>
<td>+ IV clindamycin 10mg/kg every 8 hours*</td>
<td>+ IV clindamycin 10mg/kg every 8 hours*</td>
<td>+ IV clindamycin 10mg/kg every 8 hours*</td>
<td></td>
</tr>
</tbody>
</table>

* Please use the UHL Children's Hospital vancomycin chart to dose and prescribe (available in Paediatric ED and on the wards)

Antibiotics act to reduce the bacterial load and inhibit further colonisation. However, TSS is a toxin-mediated disease. If the clinical course does not show an improvement then consideration must be given to fresh frozen plasma +/- IV immunoglobulin G (IVIG) (10) – please see page 10 for IVIG procedure and administration.
5. **Consider fluid resuscitation**  
Maintain normal heart rate/blood pressure for age, and urine output >1mls/kg/hr  
- **Fluid bolus:** 10-20ml/kg saline over 5-10 mins  
- **Repeat** fluid bolus as needed  
- Beware fluid overload (crepitations, gallop rhythm, hepatomegaly)  
- Consider **catheterisation**

6. **Give analgesia (e.g. intravenous/intranasal opiate)**

7. **Monitor observations and urine output**  
- Minimum every 15-30 minutes

8. **Burn/other wound care as needed (with Plastic Surgery input)**  
- **Gentle clean** of the wound with antimicrobial solution & gauze  
- **Wound swab(s)** to be sent for MC&S  
- **Dressings:**  
  1. **Limbs/trunk:** Urgotul Ag, gauze, bandage  
  2. **Face/neck:** soft paraffin  
  3. **Transfer to another hospital:** cling film as a temporary dressing

9. **Ensure multidisciplinary review**  
- ED doctor, Paediatrics, (Plastic Surgery if burns/skin loss), PICU, Microbiology

**RECHECK PATIENT**

**Unstable – Contact PICU**

**If normal physiology not restored after ≥40ml/kg fluid:**  
- Consider inotropes/vasopressors  
- Liaise with PICU and consider PICU admission

**If patient not demonstrating signs of improvement with antibiotics:**  
- Consider fresh frozen plasma (FFP)  
- ONLY with liaison with **Paediatric** (and **Plastic Surgery** if burn/skin loss) teams  
- FFP transfused at rate of 10-20mls/kg/hr  
- Transfusion should be completed within a maximum of 4 hours

**If patient is not demonstrating signs of improvement after FFP:**  
- Consider IVIG 2g/kg  
- **Lower mortality rates** have been reported with streptococcal TSS and severe cases of staphylococcal TSS\(^9\)  
- There is a risk of **allergic reaction** therefore the patient must be monitored frequently  
- Patient can be in **ED**, on **PICU** or on the **paediatric ward** for administration
Procedure for IVIG infusion and administration:

1. Refer to the InSite webpage on Immunoglobulins by clicking on this hyperlink or by searching “Immunoglobulins” on InSite
2. Look at the “UHL Flow Chart for Requesting Immunoglobulins”
   - Toxic shock syndrome is in the “Blue” category, but one where it can be given out-of-hours in an emergency situation if awaiting panel decision is not appropriate
3. Complete the “New Patient Request Form” and send to the email listed
4. Contact the on-call immunologist via switchboard to approve request
   - This may not be possible out-of-hours or emergency situations, in which case proceed to next step
5. Once form submitted, contact on-call pharmacy who will arrange supply of IVIG
6. Complete the “Immunoglobulin request form” on the Immunoglobulins webpage
   - Pharmacy can help to complete this form
   - Administration information for IVIG is available via Medusa

If out-of-hours, please refer to the “Procedure for out of hours Ig” document and review the criteria for administration.

Dose is 2g/kg across all brands of IVIG in toxic shock syndrome.

**Stable**

If patient is stable:
- Continue empirical TSS IV antibiotics until an organism is isolated
- Re-discuss with microbiology to focus antibiotic therapy and eventually to switch from IV to oral, based on the clinical status and culture results.

Discharge Advice

- Safety netting must be provided to caregivers of all children with burns on discharge.
- Advice should be given to seek urgent medical attention if they suspect their child is becoming unwell after a burn. A useful burns leaflet is available in the Children’s ED and on UHL InSite.
Appendix 1. Triage Pathway for Community Referrals

CHILDREN WITH RISK FACTORS FOR TOXIC SHOCK SYNDROME E.G. RECENT BURN

Adapted from Nottingham Children’s Hospital Guideline

Please circle the relevant boxes outlining your pathway and management plan.

Is your child UNCONSCIOUS?

No

Has your child been sleepier, not eating/drinking, fewer wet nappies than usual, not him/herself?

No

Does your child have a TEMPERATURE >38°C?

No

Does your child have a RASH?

No

Does your child have any DIARRHEA OR VOMITING?

No

Is the parent concerned?

“Dial 999”

Yes

“You need to seek medical attention immediately; please take your child to nearest Emergency Department or DIAL 999”

Yes

Does your child have A NON-BLANCHING RASH?

Yes

“You need to seek medical attention at GP surgery or walk-in centre on the same day, unless something changes.”

No

No

USE YOUR CLINICAL JUDGEMENT

GREEN BOX or ask parent to monitor at home if there is low-grade temperature, small blanching rash or one episode of diarrhoea/vomiting.

YELLOW BOX – if there is one or more “Yes” answers

RED BOX – if any red flags present

PATIENT STICKER
Name:

D.O.B:

Hospital No.:

PATIENT STICKER

ACTIONS

YES  N/A

NURSE-IN-CHARGE:

REGISTRAR INFORMED:

ED INFORMED:

PATIENT NOTES:

OTHERS: ___________________________
**Education and Training**

Training and awareness amongst the relevant specialty departments is required to implement this guideline.

**Monitoring Compliance**

<table>
<thead>
<tr>
<th>What will be measured to monitor compliance</th>
<th>How will compliance be monitored</th>
<th>Monitoring Lead</th>
<th>Frequency</th>
<th>Reporting arrangements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Review of children discharged or transferred from UHL hospitals with a diagnosis of toxic shock syndrome</td>
<td>Retrospective case note review</td>
<td>Consultant Paediatrician</td>
<td>3 yearly</td>
<td>Local joint Children’s &amp; Paed ED clinical practice group</td>
</tr>
</tbody>
</table>

The next version of this guideline should incorporate the upcoming National Toxic Shock Syndrome Guidelines.

**Supporting References**


Key Words
Burns, Inflammatory response, Toxic Shock Syndrome

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.

As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.
### CONTACT AND REVIEW DETAILS

<table>
<thead>
<tr>
<th>Guideline Lead (Name and Title)</th>
<th>Executive Lead</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ms R Vyas - Core Surgical Trainee, Department of Plastic Surgery</td>
<td>Chief Medical Officer</td>
</tr>
</tbody>
</table>

**Details of Changes made during review:**
- **Update February 2020:**
  - New document.
  - Added **dose of IVIG 2g/kg** (pg.’s 3 & 10)
  - Added statement – **IVIG can be given out of hours in an emergency situation** (pg. 10)