

LRI Emergency Department and Children's Hospital

Recognition, Diagnosis and Management of Toxic Shock Syndrome in Children *Including those with Burns*

Staff relevant to:	Emergency Department, Plastic Surgery, Paediatrics, Paediatric Intensive Care Unit and Microbiology
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Introduction and Who Guideline Applies To

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.

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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

Stable

Resuscitation

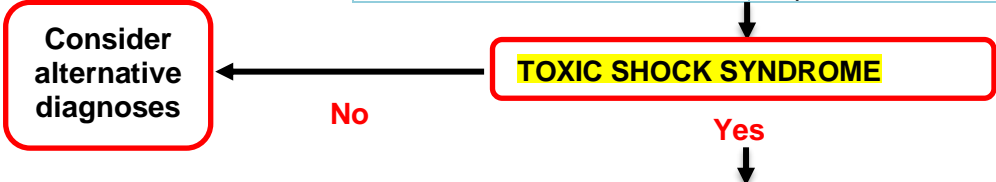
Paediatric Advanced Life Support

Early senior doctor review

Treat as per UHL sepsis guideline

Stabilised

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



Toxic Shock Syndrome Management			
Name	Hospital Number	DOB	Done
1. High flow oxygen			
2. Obtain IV/IO access			
3. Obtain bloods – Blood gas, FBC, U&E, CRP, LFTs, Ca ²⁺ , clotting, glucose, blood cultures, group & save			
4. Give empirical antibiotics – see page 8.			
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 >1 mls/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: <u>body</u> = Urgotul Ag, gauze, bandage / <u>head + neck</u> = soft paraffin			
9. Senior ED doctor, Paediatric, (Plastic Surgery if skin loss), PICU, Microbiology reviews			

RECHECK PATIENT

- If normal physiology not restored after ≥ 40 ml/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 (1g/kg, with a 2nd dose 24hrs later if no improvement)**

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 1. Risk factors for Toxic Shock Syndrome in Children ^(4, 5)

Staphylococcal TSS	Specific to Streptococcal TSS
<ul style="list-style-type: none">• Retained menstrual products• Skin disruption - trauma, burns, surgery• Osteomyelitis, arthritis• Respiratory infections – influenza• Septorhinoplasty, sinusitis• Postpartum infection, mastitis	<ul style="list-style-type: none">• Viral infection - VZV, influenza• Immunosuppression/deficiency e.g. HIV, diabetes, drugs, nephrotic syndrome• Age <1• Malignancy• Intravenous drug use

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- α , 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** ⁽¹⁰⁾

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 2. Adapted from UHL Paediatric Sepsis Screening Tool ⁽¹⁰⁾

Appearance	Appears ill Looks mottled/ashen Cyanosis of skin, lips or tongue Non-blanching rash	Demeanour	Altered behaviour or mental state No response to social cues Unable to rouse, does not stay awake Weak high-pitched/continuous cry
Breathing	Grunting/apnoea Low SpO ₂ or new/increased FiO ₂ Increased respiratory rate	Exposure	High or low temperature
Circulation	Low blood pressure High (or low) heart rate Reduced urine output		

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 ⁽⁷⁾. 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) ⁽²⁾

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

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

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

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 $\geq 39^{\circ}\text{C}$, 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

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

c. Focused Examination

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

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 speciality** 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. This will require a microbiology code.

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

1st Line OR Proven MSSA	IV flucloxacillin 50mg/kg every 6 hours + IV clindamycin 10mg/kg every 8 hours¹
1st Line penicillin-allergic patients² OR Proven/suspected MRSA	IV vancomycin Refer to Medusa IV vancomycin monograph ³ + IV clindamycin 10mg/kg every 8 hours¹
Proven Streptococcal	IV benzylpenicillin 50mg/kg every 4-6 hours + IV clindamycin 10mg/kg every 8 hours¹

¹IV clindamycin dose is higher than routine starting dose, but appropriate for TSS. Requires microbiology code

²Take a thorough history – in non-anaphylactic reactions ³rd generation cephalosporin may be appropriate – discuss with microbiology.

³ 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)

- **Wound swab(s)** to be sent for MC&S
- **Gentle clean** of the wound with antimicrobial solution & gauze
- **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 ≥ 40 ml/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** (1g/kg, with a 2nd dose 24hrs later if no improvement)
- **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. Complete the “**New Patient Request Form**” and send to the **email** address immunoglobulins.mailbox@uhl-tr.nhs.uk Note that prior approval is not required for TSS, however the appropriate documentation must be completed to allow retrospective approval, otherwise the department will be charged for the product, in line with NHSE commissioning guidance.
3. Once form submitted and IVIG prescribed, **contact ward or on-call pharmacist** to arrange supply of IVIG.
4. Complete the “**Immunoglobulin request form**” on the Immunoglobulins webpage
The Pharmacist can help to complete this form
5. Administration information for IVIG is available via [Medusa](#)

Dose is 1g/kg initially with a further dose of 1/kg after 24 hours if no improvement. The same dose applies for 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.

Education and Training

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

Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Review of children discharged or transferred from UHL hospitals with a diagnosis of toxic shock syndrome	Retrospective case note review	Consultant Paediatrician	3 yearly	Local joint Children's & Paed ED clinical practice group

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

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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	
Guideline Lead (Name and Title) Ruth Radcliffe – Consultant Ms R Agarwal - Consultant	Executive Lead Chief Medical Officer
Details of Changes made during review: Changed dose of IVIG from 2g/kg to 1g/kg Added that non-allergic reactions to penicillin treatment with 3 rd generation cephalosporin’s may be appropriate Updated new patient request form, process and immunology email	

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 Guideline¹⁷*

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

