

## TOXIC SHOCK SYNDROME

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**Abstract:** Toxic shock syndrome (TSS) is a rare toxin related disease with potentially fatal or catastrophic consequences. This aggressive disease is triggered by staphylococcal or streptococcal toxin release. Immune mediated superantigen responses to toxin result in sustained shock followed by multisystem illness. This may manifest as diarrhoea, thrombocytopenia, coagulopathy, renal failure, hepatic impairment, soft tissue necrosis or acute respiratory distress syndrome (ARDS). There is little data on the incidence of TSS in children in the UK or indeed significant case series commenting on presentation or outcome. This BPSU study will inform paediatricians about incidence and management of this potentially fatal condition.

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**Background:** Toxic Shock Syndrome (TSS) refers to a group of disorders caused by toxin secreting bacteria. TSS was originally described in seven children with fever, rash and shock with sustained hypotension associated with staphylococcal isolation by Todd *et al* in 1978 (1). Various multisystem features were described concurrently including coagulopathy and disseminated intravascular coagulation (DIC), thrombocytopenia, impaired consciousness and mucous membrane involvement. Subsequently a similar syndrome has been reported in association with streptococcal isolation. Various case reports chart other rare bacterial toxin sources (2) which may be explained by phage transfer. The exact mechanism of action is poorly understood but generally agreed to be superantigen related response to toxins. Throughout the 1980s cases were documented associated with minor burns and tampon use. It may be clinically challenging to distinguish between septic and toxin mediated shock, however the development of accurate diagnostic criteria have helped provide clarity. Many cases involve multisystem effects as diverse as diarrhoea and ARDS. Rash is a common feature varying from diffuse macular erythroderma to desquamating generalised erythematous macular rash, sometimes with subcutaneous oedema. Fever is frequent but not always essential as the infection may be quite minor; just enough bacteria to produce significant toxin. Renal failure, coagulopathy, thrombocytopenic, hepatic or neurological features may present.

Based on past studies and current knowledge we estimate there will be maximally 150 cases of TSS annually in the UK (4-7). Predicting the expected numbers of this condition is difficult given the limited availability of data.

We have liaised with the HPA staphylococcal reference laboratories (in London and Edinburgh) and the HPA streptococcal reference laboratories in order to cross reference cases with those reported on a monthly basis. We will mail local paediatricians about the case asking them to report it. We hope to obtain data on toxins secreted by cases in this way.

**Coverage:** UK and Ireland

**Duration:** October 2008 – October 2009 (13 months).

**Research Questions.** The specific aims of the project are, within the UK, to:

- Define the incidence of TSS due to staphylococcal or streptococcal organisms and identify any geographic variation.
- Identify the presence of previously described associated factors with the development of toxic shock syndrome
- Identify the different forms of clinical presentation of TSS due to staphylococcal or streptococcal organisms, including relevant laboratory parameters.
- Identify the key features of clinical management of TSS due to staphylococcal or streptococcal organisms.

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- Identify toxins and bacterial type causing TSS due to staphylococcal or streptococcal organisms
- Identify mortality and morbidity rates caused by TSS due to staphylococcal or streptococcal organisms

### Case Definition:

Any child under 16 years of age whom the attending paediatrician believes has toxic shock syndrome according to the following criteria:

- Fever
- Hypotension- systolic BP less than the 5th centile for age according to the following chart :

Age (Years)	5 <sup>th</sup> Centile Systolic Blood Pressure (mmHg)
0-2	70
2-4	76
4-6	82
6-8	85
8-10	90
10-12	92
12-14	95
14-16	97

(derived from :- Update on the 1987 Task Force Report on High Blood Pressure in Children and Adolescents ([Pediatrics](#). 1996 Oct;98(4 Pt 1):649-58 BP centiles in Great Britain.Jackson LV, Nandu KS Thalange and Tim J Cole *Arch. Dis. Child.* published online 11 Aug 2006.)

- Involvement of at least 2 other systems  
**And either**
- Rash (with or without desquamation)  
**Or**
- No rash **BUT** isolation of Group A streptococcus

This will be the criteria present on the orange card distributed to potential responders.

**Analytic Case Definitions:** The definitions used for staphylococcal toxic shock syndrome will be those adopted by the Centre for Disease Control and Prevention in the United States and streptococcal toxic shock syndrome will be defined by the American Academy of Paediatrics definition (derived from the American working group on Streptococcal Toxic Shock Syndrome). This can be viewed at [http://bpsu.inopsu.com/studies/Toxic\\_Shock\\_Syndrome/protocol.html](http://bpsu.inopsu.com/studies/Toxic_Shock_Syndrome/protocol.html)

### Reporting Instructions:

Please report any child, aged less than 16 years of age, with suspected or confirmed TSS seen by a paediatrician or consultant burns surgeon for the first time in the last month. If a clinician is uncertain or awaiting confirmation, the child should still be reported.

**Methods:** Paediatricians or surgeons reporting a case through the orange card system will be asked to complete a questionnaire seeking information on diagnosis, laboratory results, management and outcomes. Notifications will also be sought through the HPA staphylococcal and streptococcal laboratories concurrently reporting cases directly to the investigators.

**Ethics Approval:** This study has been approved by the Lewisham MREC (Ref: 08/H0810/16) and has been granted PIAG Section 251 Support (Ref: PIAG/BPSU 5-07 (FT2)/2008).

**Funding:** Sir Peter Tizard Bursary, BPSU.

**Reference(s):** Can be viewed at [http://bpsu.inopsu.com/studies/Toxic\\_Shock\\_Syndrome/reference.html](http://bpsu.inopsu.com/studies/Toxic_Shock_Syndrome/reference.html)