

# Toxic Shock Syndrome

## ***A Health Professional's Guide***



Toxic Shock Syndrome

*information service*

[www.tssis.com](http://www.tssis.com)

The Toxic Shock Syndrome Information Service (TSSIS) was set up in 1993 following a spate of heightened media interest which generated a great deal of alarmist and misleading information about Toxic Shock Syndrome (TSS) focused almost exclusively on menstrual TSS and tampons.

TSSIS has been recognised by both the past and present Governments as an authoritative source of information. The service provides accurate researched information on TSS to interested parties such as the medical profession, health educators, media and the general public. In support of the educational programme it has distributed in excess of 2 million general information leaflets. In addition, there has been wide distribution of additional materials designed for the medical profession.

TSSIS is funded by industry but is run independently on behalf of the medical panel which oversees all activities and literature. The panel consists of specialists in relevant medical disciplines and provides a cross section of expertise including a member who has many years experience in health education.

In addition to a range of leaflets, videos and poster there is a website via which individual UK enquiries can be dealt with and a pre-recorded consumer advice line.

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## Acknowledgement

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This leaflet is based on a chapter by Dr. Deresiewicz entitled, "Staphylococcal Toxic Shock Syndrome," which appears in the Marcel Dekker, Inc. book, Superantigens: Molecular biology, immunology, and relevance to human disease, Leung, DYM, Huber, BT, and Schlievert, PM, eds. (New York: Marcel Dekker, 1997), pp 435-479. Textual material is used with the permission of the publisher (telephone no. 001-800-228-1160).

This leaflet also contains a section from Dr. Colin A. Michie MA FRCPCH FLS, Consultant Senior Lecturer in Paediatrics at Ealing NHS Hospital Trust, London.



## Introduction

Staphylococcal toxic shock syndrome (TSS) is a rare, life-threatening systemic bacterial intoxication. It occurs in diverse clinical settings, often mimicking more common febrile conditions. With early treatment, the serious consequences of TSS (organ failure, limb loss, death) can often be avoided. The diagnosis rests exclusively on clinical grounds and, while often readily established, it must first be considered. Accordingly, health professionals should be familiar with the manifestations of TSS, and should vigilantly consider the diagnosis in appropriate clinical settings.

## What is TSS?

TSS is an acute, noncontagious systemic illness characterised by high fever, hypotension, rash, multi-organ dysfunction, and cutaneous desquamation during the early convalescent period (Table 1). It is caused by any of several related staphylococcal exotoxins. The exotoxins of *S. aureus* are proteinaceous compounds that are secreted at certain times during bacterial growth. The most common TSS toxins are toxic shock syndrome toxin-1 (TSST-1; ~75 percent of cases) and staphylococcal enterotoxin B (SEB; 20-25 percent of cases).

## How Common is TSS?

TSS is a very rare illness - much rarer than one would predict based only on the considerations discussed above. Health Department figures likely understate the true incidence, both because of incomplete reporting and misdiagnosis. Nevertheless, only about 18 “probable” or “confirmed” cases (see Table 1 for definitions) are reported in the UK each year, from a total population of some 58 million [UK Public Health Laboratory Service]. A similar number of cases meeting 4 or fewer criteria are also reported. The mortality rate for confirmed or probable menstrual cases has historically been about 2.5 percent. It is two- to three-fold higher for nonmenstrual cases.

## How Does TSS Occur?

The pathogenesis of TSS proceeds as follows: (1) human colonisation or infection by a strain of *S. aureus* capable of producing a TSS toxin (“toxigenic strain”), (2) toxin production, (3) toxin absorption, and (4) intoxication.

The cross-sectional carriage rate of *S. aureus* is 15-40 percent. The anterior nasopharynx is the principal site of carriage; others include the axillae, vagina, and perineum. Among normal postmenarcheal European women, the rate of vaginal colonisation is 5-20 percent and is greatest during the menses. Tampon use does not influence that rate, nor do tampons enhance vaginal staphylococcal growth. About 25 percent of all *S. aureus* strains are toxigenic. Roughly 4-10 percent of normal people harbour toxigenic strains at any given time.

Although toxigenic strains have the genetic potential to produce toxins, they actually do so only at limited times, times when toxin production serves the bacterium’s survival needs. The exact nature of the environmental signals that cue the bacterium to produce toxin *in vivo* are not fully understood. Even less is known about the requirements and mechanisms for toxin uptake, but circulating toxin can be demonstrated in human TSS patients.

Intoxication by the TSS toxins is a very complex process. The toxins affect the host immune system, causing an exuberant and pathological host inflammatory response. Antibodies directed at the TSS toxins protect against TSS, and develop by early adolescence in the majority of people. Interestingly, TSS is often not immunising; recurrent menstrual TSS is well-described.

## In What Settings Does TSS Occur?

TSS can occur whenever a nonimmune person is exposed to a TSS toxin. Illness is said to be “menstrual” if it occurs during the menstrual period and “nonmenstrual” if at other times. Each category accounts for about half of cases (Table 2). The risk of TSS is greater in younger than in older people, the acquisition of protective antibodies being a function of age.

## What Does TSS Look Like?

The clinical features of full-blown TSS are captured by the case definition (Table 1). A minority of patients report mild prodromal symptoms. The acute illness typically begins precipitously, with high fever, nausea, vomiting, abdominal pain, severe muscle pain and tenderness, and headache, followed shortly by profuse watery diarrhoea. One or another feature of the illness may dominate the early presentation, leading to diagnostic confusion. Orthostasis or hypotension and the characteristic macular erythroderma develop over the next 48 hours. The erythroderma is usually generalised and often intense, but may be locally distributed, and may be mild or fleeting. *The site of staphylococcal colonisation and toxin production may appear entirely benign.*

While not accounted for by the case definition of TSS, mild systemic intoxications by the TSS toxins probably occur. These cases lack two or more of the diagnostic criteria for TSS and should not properly be called TSS. Nevertheless, they have certain features particularly suggestive of that diagnosis. Less exuberant toxin production by some strains, partial immunity in some hosts, or prompt correction of inciting conditions in some patients may explain these mild cases.

## When Should the Diagnosis of TSS be Considered?

The differential diagnosis of the patient acutely ill with fever, rash and hypotension is extensive (Table 3). A careful history with attention to past health, possible infectious exposures, travel, vocation, hobbies, vaccination status, menstrual status and medication usage often narrows the diagnostic possibilities considerably.

### *Consider TSS in*

- 1) Any patient with fever and hypotension, whether exanthem is obvious or inapparent, especially if an alternative diagnosis is not readily apparent.

### **Suggestive epidemiological settings include:**

- Females who are either menstruating or postpartum
- Females using barrier contraceptives
- Postoperative patients
- Patients with varicella or Herpes zoster infection
- Patients with chemical or thermal burns

Laboratory findings consistent with TSS include leukocytosis, elevated prothrombin time, hypoalbuminemia, hypocalcemia, and pyuria. Each is present in greater than 70 percent of patients.

- 2) The less ill patient with suggestive symptoms who fails to meet diagnostic criteria, but who is in an epidemiological risk group. For example, consider the possibility of mild systemic staphylococcal intoxication in young women reporting substantial or recurrent perimenstrual flu-like illness, particularly if that illness is associated with erythroderma or desquamation. Of course, the great majority of women experiencing nonspecific perimenstrual symptoms have syndromes unrelated to TSS or the staphylococcal toxins.

## How Should TSS be Treated?

### *Treatment involves several key components:*

- 1) **Identification and decontamination of the site of toxin production:** Drain or debride the lesion, remove foreign material, and irrigate copiously. Recent surgical wounds should be explored and irrigated even when signs of inflammation are absent.
- 2) **Aggressive fluid resuscitation:** Loss of fluid into the extravascular compartment can be very substantial. Maintenance of cardiac filling pressures is critical in order to prevent end organ damage. Adult patients with TSS have required up to 10 L of fluid in the first 24 hr.
- 3) **Administration of antistaphylococcal antibiotics:** Semisynthetic penicillins have been widely used for TSS. Growing evidence, however, suggests that the protein synthesis inhibitor clindamycin is more efficacious in this illness. Accordingly, the author recommends treating suspected TSS patients with clindamycin (900 mg i.v. every 8 hours for adults, 13 mg/kg i.v. every 8 hours for children), either alone or in combination with a cell wall active agent (semisynthetic penicillin or vancomycin). If the diagnosis of TSS is initially uncertain, broader empiric coverage is appropriate.
- 4) **General supportive care:** Intensive care monitoring is often indicated. Replete calcium and magnesium, provide ventilatory, pressor, and inotropic support, manage rhabdomyolysis, renal dysfunction, and / or coagulopathy.
- 5) **Administration of pooled human immunoglobulin:** This should be reserved for refractory cases or cases associated with an undrainable focus of infection. All commercial immunoglobulin preparations contain high levels of anti-TSST-1 antibody. A single infusion of 400 mg/kg i.v. will generate a protective titre in a nonimmune patient.

## Burns Information

Burns and scalds often damage normal skin defences, allowing bacteria to grow and synthesise toxins. For many years it has been known that children in particular following burns are prone to develop confusion, fever, low blood pressure, diarrhoea and a rash - in other words, toxic shock syndrome. This condition may be seen following very small areas of skin damage; it may be fatal with a similar mortality rate to the tampon-related disease. As menstrually related TSS has become less common, this paediatric problem has become more evident. The early use of antibiotics by mouth may prevent the development of TSS following a burn, but at present it is difficult to identify those most at risk. Various dressings and topical treatments have little effect on the incidence of the illness. Any sick child with a burn or scald must have a blood pressure measurement in order to exclude TSS.

## Biography

Dr. Colin Michie qualified from Oxford in 1983, and has trained as a paediatrician with a special interest in infectious diseases. For some 10 years he has been involved in investigations into the effects of bacterial toxins; he has treated a number of patients with TSS. He currently works in Ealing Hospital NHS Trust and has specialist clinics and laboratory groups in Guys Hospital and Imperial College.

## Table 1: **Toxic Shock Syndrome: Case Definition**<sup>1</sup>

- I. **Fever:** temperature  $\geq 38.9$  C
- II. **Rash:** diffuse macular erythroderma ("sunburn")
- III. **Hypotension:** systolic blood pressure  $\leq 90$  mm Hg (adults) or  $\leq 5$ th percentile for age (children under 16 years of age), or orthostatic hypotension, dizziness or syncope
- IV. **Multisystem dysfunction:** at least three:
  - A. **Gastrointestinal:** vomiting or diarrhoea at onset of illness
  - B. **Muscular:** severe myalgias, or serum creatine phosphokinase level (CPK)  $\geq$  twice the upper limit of normal
  - C. **Mucous membranes:** vaginal, oropharyngeal, or conjunctival hyperemia
  - D. **Renal:** blood urea nitrogen (BUN) or creatinine  $\geq$  twice the upper limit of normal, or pyuria ( $\geq 5$  leucocytes per high-power field), in the absence of urinary tract infection
  - E. **Hepatic:** total serum bilirubin or transaminase level  $\geq$  twice the upper limit of normal
  - F. **Hematologic:** platelets  $\leq 100,000$  per L
  - G. **Central nervous system:** disorientation or alteration in consciousness but no focal neurological signs at a time when fever and hypotension are absent
- V. **Desquamation:** 1 to 2 weeks after the onset of illness (typically palms and soles)
- VI. **Evidence against an alternative diagnosis:** If obtained: negative cultures of blood, throat, or cerebrospinal fluid;<sup>2</sup> absence of a rise in antibody titres to the agents of leptospirosis, measles or Rocky Mountain spotted fever.

Source Reingold AL, Hargrett NT, et al Toxic shock syndrome surveillance in the United States 1980 to 1981, *Ann Intern Med* 1982; 96(Part 2): 875-880

1 "Confirmed" case meets all six criteria, "probable" case meets 5 of the 6

2 Blood culture may be positive for *S. aureus*.

Table 2: **Toxic Shock Syndrome: Clinical Settings<sup>1</sup>**

### **Menstrual TSS**

- I Tampon-associated<sup>2</sup>
- II Not tampon-associated

### **Nonmenstrual TSS**

- I TSS Related to the Female Genitourinary Tract
  - associated with barrier contraceptive use (diaphragm, contraceptive sponge)

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  - occurring in the puerperium

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  - following nonobstetric gynaecological surgery

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  - associated with septic abortion

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- II TSS Related to Skin or Soft Tissue Infections
  - primary staphylococcal infections (folliculitis, cellulitis, carbuncle, muscle abscess)

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  - staphylococcal superinfections of preexisting lesions (burns, insect bites, varicella/zoster infections, surgical wounds)<sup>3</sup>

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- III TSS Related to Respiratory Tract Infections
  - upper respiratory tract focus (sinusitis, pharyngitis, laryngotracheitis, odontogenic infection)

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  - lower respiratory tract focus (staphylococcal pneumonia)

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- IV TSS Related to Skeletal Infections
  - osteomyelitis

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  - septic arthritis

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1 Menstrual and nonmenstrual cases occur with approximately equal frequencies and are clinically identical. The mortality rate of nonmenstrual illness is substantially higher, likely due to delayed diagnosis of nonmenstrual cases.

2 The risk of TSS is particularly high in seronegative women with a prior history of TSS. Such women should avoid use of tampons or barrier contraceptives until such time as seroconversion is documented.

3 The time interval to onset of postoperative TSS ranges from hours to weeks after the surgical procedure. The risk of TSS is particularly great following rhinoplasty or nasal septoplasty, in which settings it has been estimated at 16.5 cases per 100,000 population at risk.

### Table 3: **Illnesses That May Resemble Toxic Shock Syndrome**

- Severe group A streptococcal infections (scarlet fever, necrotising fasciitis, toxic shock-like syndrome)<sup>1</sup>
- Kawasaki syndrome<sup>2</sup>
- Staphylococcal scalded skin syndrome<sup>3</sup>
- Rocky Mountain spotted fever
- Leptospirosis
- Meningococemia
- Gram-negative sepsis
- Exanthematous viral syndromes (e.g., measles, adenoviral infection, certain enteroviral infections, dengue)
- Severe allergic drug reactions

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1 Streptococcal toxic shock-like syndrome may be clinically indistinguishable from TSS. Extensive soft tissue destruction and exudative pharyngitis are suggestive of a streptococcal etiology.

2 Rare above the age of 4 years. Presents subacutely rather than acutely. Thrombocytosis (rather than thrombocytopenia) is common.

3 Rare above the age of 5 years. The skin may be diffusely tender, and sloughs early on. Systemic toxicity is rare.

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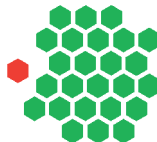
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