# TOXIC SHOCK SYNDROMES IN AUSTRALIA AND NEW ZEALAND 1990-1994

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## Abstract

Following a request for information from the Victorian Minister for Health, two surveys were undertaken to identify cases of 'toxic shock syndrome'. Case definitions of toxic shock syndrome (TSS) and streptococcal toxic shock syndrome (STSS) are presented, and the problems inherent in the identification of these syndromes are discussed. A telephone survey identified 12 Victorian cases for 1994. A mailout questionnaire requesting minimal line data for cases that occurred in 1990 to 1994 (with a response rate of 34%) identified 20 cases for this period in Australia and New Zealand. These cases occurred in 11 males and nine females, with an age range of 12 to 82 years. Of these, nine were apparently due to *Staphylococcus aureus* (and thus were classified as TSS) and nine were due to *Streptococcus pyogenes* (and were classified as STSS). Of the nine cases of TSS, six were female, five of whom were menstruating at the time of admission to hospital. Support is provided for the addition of TSS and STSS to appropriate registers to improve the identification of cases and thus the local and national epidemiology of these rare illnesses.

## Background

Toxic shock syndrome (TSS) is an uncommon, severe, systemic disease of acute onset, caused by bacterial exotoxins produced by *Staphylococcus aureus*. Both menstrual and nonmenstrual TSS occur, with the majority of menstrual cases being associated with the wearing of tampons. Strains of *S. aureus*, producing toxic shock syndrome toxin-1 (TSST-1), cause almost all of the cases of menstrual TSS, whereas strains producing either TSST-1 or enterotoxin B or C may cause nonmenstrual TSS. Only about 20 per cent of strains of *S. aureus* are capable of producing TSST-1. Nevertheless, most adults have developed protective antibodies to TSST-1. Nonmenstrual TSS occurs in males and females of all age groups, usually in association with localised infections such as surgical wound infections and abscesses. The Centers for Disease Control and Prevention (CDC) case definition for TSS requires the presence of five clinical criteria:

1) temperature equal to or greater than 38.9$^{o}$C;

2) hypotension (including syncope or orthostatic dizziness);

3) rash;

4) desquamation of the rash one to two weeks later (except in fatal cases); and

5) abnormalities in three or more organ systems, such as gastrointestinal, muscular, hepatic, renal, haematological, and the central nervous system.

A definite case fulfills all five criteria and a probable case fulfills four of the five criteria[1,2]. Bacteraemia is usually absent but its presence does not exclude a diagnosis of TSS.

In Britain, the Public Health Laboratory Service (PHLS) Staphylococcus Reference Unit conducts local surveys of TSS cases. For these surveys, cases that fulfill the CDC case definition are classified in the United Kingdom as confirmed, those missing one criterion as probable, those missing two criteria as possible and those lacking more than two criteria are classified as unconfirmed. The majority of confirmed and probable cases have been associated with menstruation, whereas the majority of possible and unconfirmed cases are nonmenstrual[3].

*Streptococcus pyogenes* (group A streptococcus) may also cause a toxic shock syndrome, sometimes referred to as toxic shock-like syndrome but usually as streptococcal toxic shock syndrome (STSS). STSS due to *S. pyogenes* was first described in 1987[4]. Like nonmenstrual TSS, STSS occurs in males and females of all age groups and is associated with localised or systemic infection.

The CDC case definition for STSS requires the isolation of group A streptococci and hypotension with two or more of the following:

1) renal impairment;

2) coagulopathy;

3) liver involvement;

4) adult respiratory distress syndrome;

5) rash that may desquamate;

6) soft-tissue necrosis including necrotising fasciitis, myositis and gangrene.

If the group A streptococci are isolated from a normally sterile site, then the illness is considered a definite case of STSS. If isolated from a nonsterile site, the case is classed

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as probable, provided that no other aetiology for the illness is identified[5].

Epidemiological studies on menstrual TSS in the early 1980s in the United States of America, when 95% of all TSS cases were seen in young women, showed that tampon use during menstruation was a significant risk factor. Data analyses also demonstrated that cases were more likely than control subjects to use tampons of high absorbency[1]. One particular brand of tampon used had a unique composition consisting of highly absorbent polyester foam chips and carboxymethyl cellulose. Its removal from the American market resulted in a significant decrease in notifications of menstrual TSS in American women[6]. It was never marketed in the United Kingdom or in Australia. Since then, the absorbency of all brands of tampons has been reduced. Information on the absorbency levels is now provided on the consumer packs of tampons, and users are advised to use tampons of lowest absorbency consistent with their requirements and to handle tampons hygienically[7].

The epidemiological data indicate that the risk of menstrual TSS depends on tampon absorbency rather than tampon composition. In particular, the findings of two independent, recently published studies confirm that tampons made solely of cotton support production of the same or more TSST-1 from *S. aureus* in vitro, when compared with those made of cotton / rayon blends or rayon alone[8,9]. These findings indicated that cotton tampons offer no advantage over cotton / rayon or rayon tampons in preventing menstrual TSS.

Towards the end of 1994 and the beginning of 1995, menstrual TSS was the subject of media attention in Australia, with the death of a teenage girl in Queensland. Investigations into her death are continuing. One case of menstrual TSS in Victoria came to the attention of the then Victorian Minister for Health, Marie Tehan, who requested further information on the incidence of cases in Victoria for 1994.

As well as describing the Victorian cases for 1994, it was decided that a wider survey which reviewed the Australian experience of toxic shock syndrome from 1990 to 1994 would be timely. However, there are several problems with determining the incidence of toxic shock syndrome in Victoria and in the rest of Australia. Firstly, there is no ICD9 (International Classification of Diseases) or Victorian Inpatient Minimum Dataset (VIMD) code as they are syndromes rather than specific diseases. Furthermore, because the causative strains are rarely cultured from blood, they are not reported to the Victorian Hospital Pathogen Surveillance System (VHPSS) at the Microbiological Diagnostic Unit. A comprehensive search produced only one possible case of TSS in which *S. aureus* was isolated from blood in half a million submissions to VHPSS. In addition, no codes presently exist on the independent intensive care unit (ICU) database. It is therefore impossible to find cases through any of the current computerised databases.

## Methods

Health and Community Services (now the Department of Human Services) Victoria decided to investigate the incidence of toxic shock syndrome in two ways: (a) by actively undertaking case-finding retrospectively for the immediately preceding year of 1994 by means of a telephone survey; and (b) by contacting all intensive care physicians through their own society, the Australian and New Zealand Intensive Care Society (ANZICS), and requesting minimal information on cases from 1990 to 1994 by a mailout survey.

For the telephone survey, all hospitals with an ICU in Victoria (private as well as public) were included, and all ICU and infectious disease physicians whom we contacted responded. In this survey, we did not request details of the causative agent.

After a small pilot study, the 350 members on the national ANZICS mailing list were contacted. Line information only, which included gender, approximate month of onset of illness, organism if known, and if the disease was related to tampon use, was sought to encourage the reporting of cases, thus details such as the onset of menstruation, onset of symptoms, brand and type of tampon and length of time since surgery, were not requested in this survey. About one-third of the 350 members are not currently practising in ICUs so were excluded from the survey, leaving a survey sample of 220 ICU physicians.

Because of the difficulty of identifying less severe cases of toxic shock, a decision was made to restrict the survey to cases known to ANZICS members for two reasons: firstly, the diagnosis was likely to be clearly established, and secondly, the severity of the syndrome was likely to make it more memorable. The CDC case definition was included on the data collection form.

## Results

### (a) Telephone survey

The results of the telephone survey, which identified 12 cases of toxic shock syndrome in Victoria for 1994, are summarised in Table 1.

**Table 1. Results of a telephone survey of hospital intensive care units on the incidence of TSS in Victoria in 1994**

| | |
|---|---|
| Number of cases | 12 |
| Gender distribution | 8 female; 4 male |
| Age | 10 adults; 2 children |
| Number tampon associated | 4 |
| Main sequelae | Loss of digits in one woman |

**Table 2. Responses and results of a mailout survey of intensive care unit physicians on TSS and STSS in Australia and New Zealand, 1990 - 31 March 1995**

| Responses and results of ICU survey | ACT | NSW | NT | Qld | SA | Tas | Vic | WA | NZ | Unknown | Totals |
|---|---|---|---|---|---|---|---|---|---|---|---|
| No. of surveys mailed | 3 | 72 | 3 | 34 | 25 | 2 | 55 | 25 | 1 | | 220 |
| No. responded with zero cases | 1 | 12 | 3 | 8 | 7 | 2 | 16 | 4 | 0 | 6 | 59 |
| No. responded with cases reported | 0 | 5 | 0 | 2 | 2 | 0 | 4* | 0 | 1 | 1 | 15 |
| Response rate (per cent) | 33.3 | 23.6 | 100 | 29.4 | 36 | 100 | 36.4 | 16 | 100 | | 34 |
| No. of cases reported | 0 | 8 | 0 | 6 | 2 | 0 | 3* | 0 | 3 | 1 | 23 |

* One case was notified by two ANZICS members.

**(b) ANZICS mailout survey**

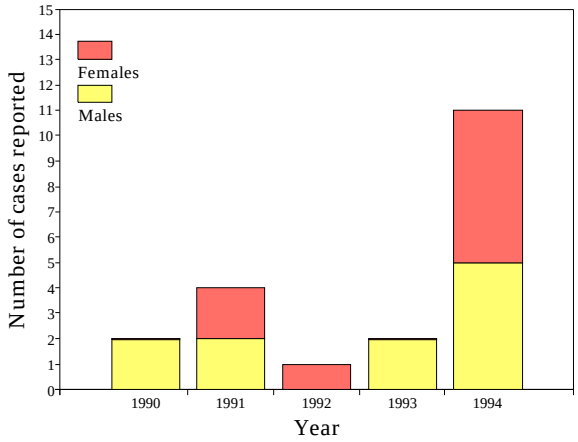
From this survey, 59 ICU physicians replied that they had not seen a case of TSS during the past five years, while 15 sent details on 23 cases, a response rate of 34% (range 16% to 100%). All the reported cases occurred in the eastern States.

Table 2 shows the responses and results of the mailout survey. The ICU physicians also supplied the date of onset for most of the reported cases. An additional three cases were reported for the period 1 January to 31 March 1995 (one from New South Wales and two from Queensland). These are included in the data presented in Table 2 but were excluded from the analyses, as details of 1995 cases had not been sought in the questionnaire. Two other cases were not included in the final data set as they did not fulfill the case definition. One of these was an 18-year-old man with meningococcal disease, and the other was a 30-year-old woman with pneumococcal infection. No deaths were reported among the cases over the period of the survey. One case was notified twice.

The mean age of the cases was 31 years and nine months for females (n = 9) and 31 years and three months for males (n = 10); the age of one male patient was not provided. This difference is not significant (p = 0.96). The age range was 12 to 74 years for females and 7 to 82 years for males.

Cases of TSS and STSS were reported in both males and females in New South Wales, Queensland and Victoria; in females only in South Australia and in males only in New Zealand over the period of the survey. Nine of the 20 cases occurred in females. Figure 1 shows the occurrence of cases in males and females over the years 1990 to 1994 and that most cases in both sexes were reported in 1994. As shown in Table 3, the bacterial species implicated as the source of toxin was *S. aureus* in nine cases (TSS), *S. pyogenes* in nine cases (STSS) and was unspecified in two cases. Of these,

**Figure 1. Sex distribution of TSS and STSS cases for Australia and New Zealand, 1990-1994, by year**




14 cases were classified as definite (seven TSS, six STSS and one unspecified) and six cases were classified as probable (two TSS, three STSS and one unspecified) by the participating ICU physicians. Five of the six females with TSS were menstruating and all of these were using tampons at the time of admission.

**Table 3. Sex distribution of TSS and STSS cases for Australia and New Zealand, 1990-1994, by causative agent**

| | Females (menstruating) | Females (non-menstruating) | Males |
|---|---|---|---|
| *Staphylococcus aureus* | 5 | 1 | 3 |
| *Streptococcus pyogenes* | 0 | 3 | 6 |
| Unknown | 0 | 0 | 2 |
| Total | 5 | 4 | 11 |

## Discussion

A comparison of the results of the telephone survey of hospital ICUs for cases of toxic shock syndrome in Victoria for 1994 (12 cases) with those resulting from the ANZICS mailout survey of ICU physicians for the same State and year (three cases) indicates that the number of notifications obtained through the mailout survey is significantly lower than the actual number of cases. Furthermore, only one-third of the ANZICS members who are currently practising as ICU physicians responded to the postal survey. While it is possible that the Victorian ICU physicians did not give details of cases by postal questionnaire that had already been notified by telephone, this would mean that Victoria had more cases than any other State, approaching half of all Australian cases. It seems much more likely that the postal survey greatly underestimated the number of TSS and STSS cases for all States. Indeed, extrapolation from the Victorian figures suggests that only about a quarter of the total number of cases were notified by the postal survey. Nonetheless, the apparent increase in cases in 1994 is intriguing, although it is possible that recent recall bias may have resulted in more of the cases being reported for that year and media interest in TSS during 1994 may have made cases more memorable.

Several respondents did not use the CDC case definition for TSS which was supplied in the mailout. Instead, they applied more stringent criteria for their case definition. Some commented that our definition was too inclusive. We also received one comment that clearly indicated that the respondent thought we had targetted our questionnaire wrongly - 'This is a paediatric ICU!'

## Conclusions

The apparent quandary regarding the TSS case definition was unexpected, as the CDC definition has been generally widely accepted for many years. It would be timely for intensive care and infectious disease physicians in Australia to collaborate to agree to the case definitions for TSS and STSS and on the classification of those cases that do not fulfill all the criteria of the CDC case definition, such as that used in the United Kingdom for TSS[3]. In Victoria, this has already been attempted with the development of a strategy for TSS case management, under the guidance of the Public Health Branch of the Department of Human Services.

A decision has been made by ANZICS to add toxic shock syndrome to its own computerised register. There is also a need for these toxic shock syndromes to be assigned an ICD9 code and, in Victoria, a VIMD code, so that all cases, whether admitted to an ICU or not, can be identified. A standardised data collection method for TSS and STSS would provide a valuable epidemiological tool.

The advent of absorbency labelling of tampons and the provision of more details about TSS in tampon package inserts go part of the way towards disseminating information about TSS to the group at risk of menstrual TSS[7]. Men, children and post-menopausal women do not use menstrual tampons, however menstruating women accounted for just over half of the cases of TSS and only a quarter of the cases of TSS and STSS in Australia and New Zealand from 1990 to 1994. Information about the age and gender breakdown of cases of TSS and STSS needs to be circulated regularly to health care professionals and to the general public to remind both groups that the toxic shock syndromes are not confined to menstruating women.

Notwithstanding their relative rarity and a degree of confusion about the case definitions and risk groups, TSS and STSS are still with us and need to be borne in mind in the differential diagnosis of severe, multisystem diseases of acute onset in males and females of all age groups.

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**Toxic Shock Syndrome Information Service**

**An independent body, the Toxic Shock Syndrome Information Service, which is comprised of expert medical and pharmaceutical personnel, acts as an educational resource and information service on TSS for both the medical and lay community. The phone number of the service is 1800 634 250.**