BRIGHAM AND
WOMEN'S HOSPITAL

HARVARD
MEDICAL SCHOOL

Clinical Laboratories
75 Francis Street
Boston, Massachusetts 02115

Tel: 617 732-7372, Lab: 617 525-2506, Fax: 617 277-1762
E-mail: onderdonk@aol.com

**Andrew B. Onderdonk, Ph.D.**
*Director*
*Clinical Microbiology Laboratory*

*Professor of Pathology*
*Harvard Medical School*

# Toxic Shock Syndrome Overview

Toxic Shock Syndrome (TSS) was first recognized as a discreet constellation of symptoms in the late 1970's. TSS is caused by strains of *Staphylococcus aureus* producing a specific exotoxin protein called toxic shock syndrome toxin-1 (TSST-1). Epidemiologic studies have shown that TSS can occur during menstruation in women using various forms of catamenial protection, or as non-menstrually related cases in both males and females. The incidence of TSS, according to epidemiologic surveys, is 5-10 cases/100,000 per year for women using tampons. At the present time there is an approximately equal incidence of menstrual and non-menstrual cases of TSS reported in the United States. The number of reported cases of TSS to the CDC has been decreasing since 1982. Non-menstrual cases of TSS can be associated with virtually any infectious process caused by *S. aureus*, including pharyngitis, wound infection, bacteremia and pneumonia. More recent studies have also shown that some strains of *Streptococcus*, notably strains of Lancefield Group A, produce an exotoxin protein with similar activity to TSST-1. Such strains have been reported to cause a TSS-like syndrome both during menstruation and in non-menstruating women, as well as men.

*S. aureus* is a normal member of the host microflora and is commonly isolated from mucosal surfaces, skin and feces. Approximately 30% of adults carry *S. aureus* at one or more body sites, with the anterior nares being the most common source for isolation. Based on recent studies, it has been determined that about 1/3 of *S. aureus* strains isolated carry the genetic information to produce TSST-1. With respect to vaginal microflora, studies have indicated that

5-15% of overtly healthy women carry *S. aureus* as part of their vaginal microflora and that approximately 20% of strains are capable of producing TSST-1. Therefore, only about 1-4% of all women carry the bacteria responsible for TSS disease. Of these women, 85% have high titers of antibody against TSST-1. It is for these reasons that the disease is relatively rare.

By all measures, *S. aureus*, as well as strains that can produce TSST-1 are common members of the human microflora. In addition to being common members of the human microflora, *S. aureus* can also cause a variety of infectious processes, ranging from superficial wound infections to life-threatening bacteremias.

Based on the association of early cases of TSS with the use of a specific tampon product during menstruation, the role of catamenial products as contributing factors in the development of TSS was explored. Extensive research has shown that currently manufactured tampons, regardless of composition, do not alter vaginal microflora. Moreover, tampons do not serve as a nidus for growth of *S. aureus* during menstruation. In vitro studies by a number of investigators have shown that tampons do not promote increased toxin production by TSST-1 producing strains of *S. aureus*. A number of environmental conditions have been cited as possible triggers for production of TSST-1, including low magnesium levels, increased pH and increased oxygen levels. To date, no single environmental factor has been shown to be the exclusive signal for increased production of TSST-1. Epidemiologic data has related tampon absorbency with increased risk for TSS. The relationship between absorbency and increased risk for TSST-1 is not understood, although it has been postulated that higher absorbency tampons allow a larger quantity of oxygen to enter the vaginal vault during use. Commercially available tampon products include package insert information explaining TSS, the symptoms associated with TSS, and what to do if symptoms occur.

Barrier contraceptive devices including diaphragms and contraceptive sponges have also been evaluated for their association with development of TSS. There is no evidence that any of these devices increases the risk for development of TSS as compared to the use of tampons. In vitro studies of spermicidal agents, such as nonoxynol 9, suggest that such agents do not contribute to the risk for development of TSS. The incidence of TSS in women using contraceptive sponges (as typically employed) is similar to that for women using tampons during menstrual flow. Both products provide substantial benefits to the consumer. It would seem prudent for package insert information for such products to include similar cautionary information regarding TSS. The warning included in the package insert for the Today™ contraceptive Sponge as sold in 1995 meets the need to adequately warn consumers regarding TSS disease and to offer adequate advice in the event that symptoms appear.

Andrew B. Onderdonk

Andrew B. Onderdonk

5/31/00

Date

## References


Rheingold AL, et al, Ann Intern Med 1982; 96:875-880

Davis JO, et al, N Engl J Med 1980; 303:1429-35

Todd JK, et al, Lancet 1978; 2:1116-1118

Davis JP, et al, J, Infect Dis 1982; 151:883-889

Kain KC, et al, Clin Infect Dis 1993; 16: 100-106

Onderdonk AB, et al Appl Environ Microbiol 1986; 51:333-339
Appl Environ Microbiol 1987; 53: 2774-2778 and 2779-2784

Onderdonk AB, et al, 1989 Rev Infect Dis 1989 (suppl 1): S61-67

Schlievert P, European Conference on Toxic Shock syndrome 1998, Royal Society of Medicine Press Ltd, pgs 128-130

Centers for Disease Control, '98 summary data for all cases TSS

Total cases of TSS and outcome*

| Year | CASES Definite | CASES Probable | DEATHS* Definite | DEATHS* Probable |
|---|---|---|---|---|
| 1979 | 180 | 47 | 16 | 4 |
| 1980 | 892 | 273 | 42 | 15 |
| 1981 | 586 | 213 | 19 | 6 |
| 1982 | 400 | 192 | 11 | 4 |
| 1983 | 321 | 185 | 9 | 11 |
| 1984 | 267 | 165 | 7 | 5 |
| 1985 | 155 | 134 | 8 | 5 |
| 1986 | 116 | 101 | 7 | 3 |
| 1987 | 88 | 108 | 5 | 4 |
| 1988 | 98 | 90 | 0 | 2 |
| 1989 | 69 | 79 | 1 | 2 |
| 1990 | 51 | 65 | 2 | 3 |
| 1991 | 58 | 57 | 1 | 1 |
| 1992 | 44 | 51 | 1 | 2 |
| 1993 | 29 | 34 | 1 | 1 |
| 1994 | 24 | 30 | 5 | 1 |
| 1995 | 19 | 18 | 1 | 1 |
| 1996 | 4 | 23 | 0 | 0 |
| 1997 | 11 | 13 | 1 | 1 |

* Outcome information not available for all cases. Deaths are for those where outcome information was known.

---

Cases of TSS known to occur during menstrual period and outcome*

| Year | CASES Definite | CASES Probable | DEATHS* Definite | DEATHS* Probable |
|---|---|---|---|---|
| 1979 | 161 | 38 | 14 | 2 |
| 1980 | 814 | 252 | 38 | 13 |
| 1981 | 470 | 183 | 13 | 3 |
| 1982 | 287 | 139 | 4 | 2 |
| 1983 | 225 | 123 | 7 | 6 |
| 1984 | 185 | 115 | 5 | 2 |
| 1985 | 103 | 87 | 5 | 2 |
| 1986 | 67 | 53 | 5 | 0 |
| 1987 | 41 | 69 | 1 | 1 |
| 1988 | 60 | 63 | 0 | 0 |
| 1989 | 53 | 52 | 0 | 0 |
| 1990 | 34 | 40 | 1 | 0 |
| 1991 | 29 | 25 | 1 | 0 |
| 1992 | 20 | 34 | 1 | 1 |
| 1993 | 16 | 25 | 0 | 1 |
| 1994 | 14 | 16 | 4 | 0 |
| 1995 | 9 | 7 | 0 | 0 |
| 1996 | 4 | 10 | 0 | 0 |
| 1997 | 5 | 4 | 0 | 1 |

* Outcome information not available for all cases. Deaths are for those where outcome information was known.