The Japanese National Institute of Infectious Diseases reports a rise in the number of patients diagnosed with toxic shock syndrome (TSS) in Japan. TSS is a rare, life-threatening, toxin-mediated infectious disease linked to the toxin-producing strains of *Staphylococcus aureus* or *Streptococcus pyogenes* (group A streptococcus) in the majority of cases. TSS leads to rapid and severe shock, multiple organ failure, and death. Clinical cases of TSS involving other bacteria have also been reported.

The number of Streptococcal TSS cases in Japan reached 1019 by June 9, much higher than the 941 registered cases in 2023. Ken Kikuchi, a professor of infectious diseases at Tokyo Women's Medical University stated in an interview with The Japan Times that "At the current rate of infections, the number of cases in Japan could reach 2,500 this year, with a mortality rate of 30%".

A rise of toxic shock syndrome in Japan

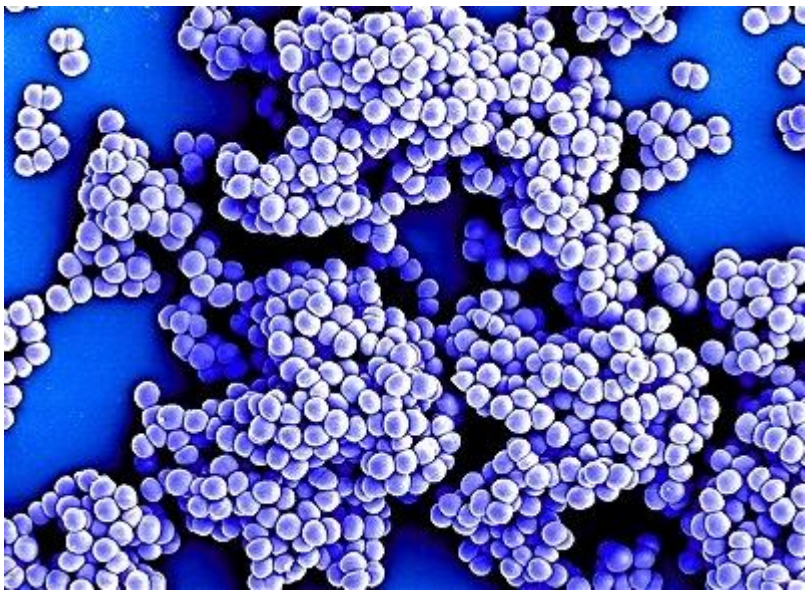
Year	Case numbers
2019	894
2020	718
2021	622
2022	708
2023	941
2024 to June 9	1019

About TSS

Todd et al. published 1978 the first description of Staphylococcal toxic shock syndrome in a case series of seven pediatric patients. TSS started with high fever, cephalalgia, confusion, cutaneous rash, conjunctival hyperemia, and digestive signs and progressed to severe shock, renal and hepatic failure, and disseminated intravascular coagulation. Exotoxin-producing *Staphylococcus aureus* was isolated from the foci of infection (empyema and abscess) of two patients and nasopharyngeal, vaginal, and tracheal swabs of four patients, but not from blood, cerebrospinal fluid, or urine. In six patients who survived, desquamation of the palm of the hands or sole of the feet was seen during recovery. In 1987, Cone et al.

described “Streptococcal toxic shock-like syndrome” in two patients infected with severe group A *Streptococcus* with a clinical presentation similar to Staphylococcal TSS.

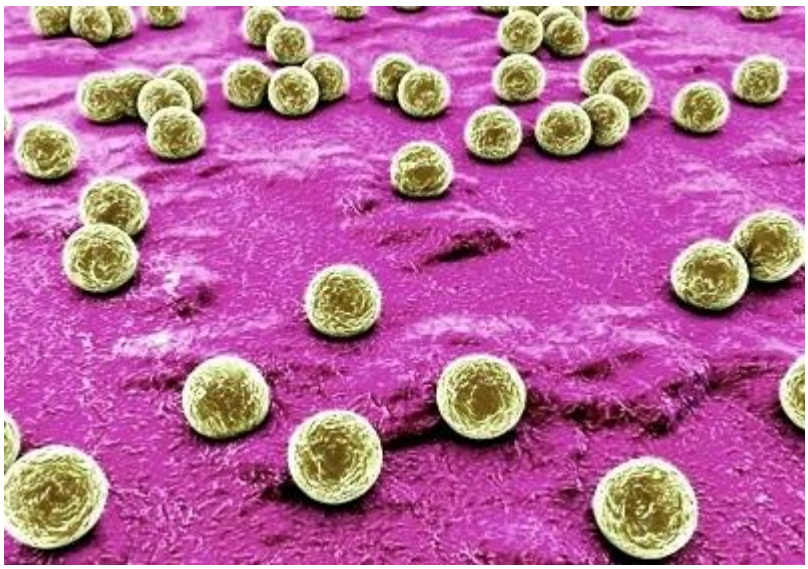
Numerous studies have analyzed the pathophysiology, epidemiology, clinical presentation, microbiological features, and outcome of TSS, including this review article by French authors.



Epidemiology of TSS

The annual prevalence of Staphylococcal TSS is estimated to be between 0.03 and 0.07 per 100,000 people. As Staphylococcal TSS is categorized into menstrual and non-menstrual TSS, the estimated incidence of menstrual TSS in the United Kingdom is 0.09 per 100,000 women and that of non-menstrual TSS is 0.04 per 100,000 persons. The highest incidence of menstrual TSS is found in women aged 13 to 24 years (1.41 per 100,000 women). Streptococcal TSS is a rare disease, occurring in 8-22% of patients with severe Streptococcus pyogenes infection, or 40-50% of patients with necrotizing soft tissue infection. Most commonly, TSS occurs in the pharyngeal mucosa, skin, and vagina, although pneumonia, septic arthritis, burns, or a minor trauma could be the site of TSS. It can also

occur in the postpartum period in young women. Notably, in 50% of cases, the source of the Streptococcal TSS remains unknown.



The pathophysiology of TSS

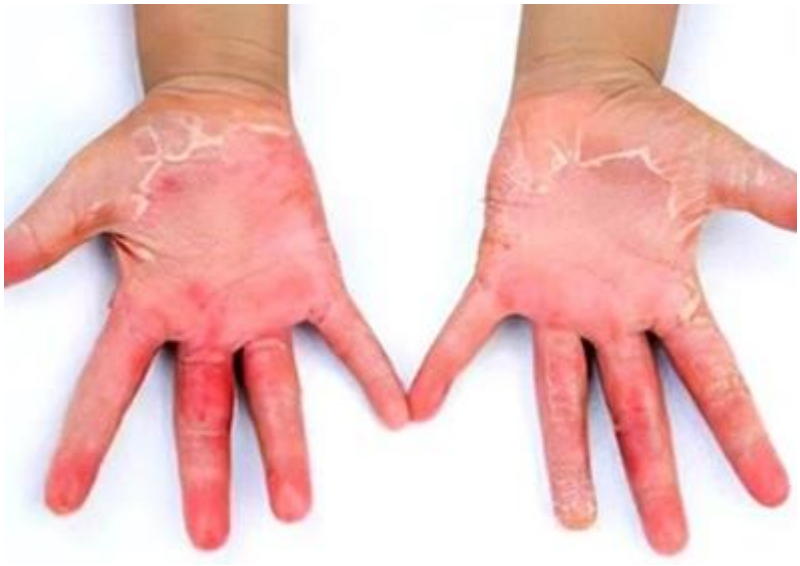
The pathophysiological mechanism of TSS is linked to the bacterial superantigenic exotoxins, which are bacterial virulence factors genetically encoded and secreted. The main superantigenic exotoxins of *Staphylococcus aureus* are the toxic shock syndrome toxin—1 (TSST-1) and enterotoxins (about thirty have been described). The TSST-1 protein is responsible for 89-95% of menstrual and 50% of nonmenstrual TSS. The remaining 50% of non-menstrual TSS is related to Staphylococcal enterotoxins A, B, and C.

The main superantigenic exotoxins of *Streptococcus pyogenes* are Streptococcal pyrogenic exotoxins (SpE) A, B, and C and streptococcal superantigen A (SsA). The majority of streptococcal isolates causing TSS are the emm1 (41.1% of cases), emm3 (8.4% of the cases), emm28 (8.9% of the cases), and emm89 (9.8% of the cases) strains.

Bacterial superantigenic exotoxins can induce nonspecific, polyclonal activation of 5 to 30% of the total population of T cells, a massive release of proinflammatory cytokines, and the expansion of the inflammatory response.

Clinical presentation of TSS

Staphylococcal non-menstrual TSS is most commonly postoperative, but it can also occur postpartum, after abortion, or in nonsurgical cutaneous lesions. Menstrual TSS in healthy young menstruating women without neutralizing antibodies is associated with vaginal colonization of TSST-1-producing *Staphylococcus aureus*. There is no statistically significant difference between non-menstrual and menstrual TSS in the occurrence of clinical signs, such as fever, rash, desquamation, hypotension, renal, hepatic, or hematologic failure, and shock. The Centers for Disease Control and Prevention have proposed diagnostic criteria for Staphylococcal TSS, which allow only a retrospective diagnosis, as they include the desquamation of the palms of the hands and soles of the feet, which occurs 8 to 21 days after the onset of the illness. However, a French multicentric retrospective study described staphylococcal menstrual TSS in patients who did not meet the CDC criteria for a confirmed TSS, and only half of them met the criteria for a probable TSS. Staphylococcal TSS has a mortality rate of approximately 5%.



Streptococcal TSS most commonly occurs in elderly patients between the ages of 50 and 69 with comorbidities (diabetes, malignancy, hepatic disease, chronic renal impairment, and heart disease). Streptococcal TSS clinical presentation includes hypotension, acute kidney failure, liver failure, multiorgan failure syndrome, and disseminated intravascular

coagulation. Streptococcal TSS mortality rate is high and estimated at 14-64% in different published series.

Previous publications have reported clinical cases of TSS involving other bacteria, such as groups B, C, and G streptococci, *Yersinia pseudotuberculosis, Pseudomonas fluorescens, Mycoplasma arthritidis,* and *Clostridium.*

Conclusion

The Japanese National Institute of Infectious Diseases reports a rise in the number of patients with toxic shock syndrome in Japan in 2024. TSS does not represent a novel infectious disease *per se*, as its diagnosis, treatment, and prevention are already well-established. However, due to signs of increasing incidence, further research is needed.

This article was published in Antibiotics.

Journal Reference

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