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Abstract

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Keywords

Staphylococcal, Toxic shock syndrome

Conflict of Interest Statement

To the best of my knowledge, none of the authors has any conflict of interest, financial or otherwise.

CASE REPORT

A Rare Presentation of Fulminant Toxic Shock Syndrome in a Healthy 10-Year-Old Male Patient

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Abstract

Staphylococcal toxic shock syndrome (STSS) is characterized by acute, progressive illness with fever, rapid-onset hypotension, and multisystem organ failure. The clinical course of STSS is attributable to host response to exotoxins with superantigenic properties. Fulminant staphylococcal infection is often associated with a deep focus of infection. In this report, we present a 10-year-old boy with multisystem organ failure as a result of STSS, a rare fatal complication following soft tissue injury. The rapid and fulminant progression of the disease in our patient precluded early timely diagnosis of STSS that may have allowed for the initiation of life-saving supportive intervention. Furthermore, the rapidly developing STSS occurred without an identifiable infectious source. The diagnosis of STSS was made upon the sum total of the clinical presentation, laboratory and autopsy findings, and antemortem and postmortem microbiology studies. It is crucial for health care providers to be aware of the possibility of STSS, even in the absence of overt focal infections and risk factors. A high index of suspicion for STSS should be present in critically ill patients presenting with a precipitous course of sepsis, septic shock, or systemic inflammatory response syndrome (SIRS).

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1. Introduction

Toxic shock syndrome is a superantigen-mediated disease caused by *Staphylococcus aureus* (*S. aureus*) and *Streptococcus pyogenes*. The characteristics of toxic shock syndrome include an acute, progressive illness associated with fever, rapid-onset hypotension, and precipitous multisystem failure. Staphylococcal toxic shock syndrome (STSS) may result from any staphylococcal infection, mucosal colonization, in association with abscesses or burns, and following surgical procedures.[1] Risk factors for STTS include absence of protective antitoxin antibodies, aplastic anemia, diabetes, chronic hepatitis C, cancer, human immunodeficiency virus infection or the acquired immunodeficiency syndrome, and injection-drug use.[2–4]

The Center for Disease Control provides several criteria for the diagnosis of STSS, that divide the diagnosis of STSS into probable and confirmed by using a multimodal approach (Table 1).[5]

The early diagnosis of STSS is important to target the treatment for *S. aureus* toxin-mediated disease, including supportive management, antimicrobial therapy, intravenous immunoglobulins (IVIG), and corticosteroids.[6] We describe the case of an otherwise healthy patient without a known source of infection or predisposing risk factors who succumbed to fulminant STSS.

2. Case Presentation

A 10-year-old Caucasian male with a known history of congenital left-sided ureterovesical obstruction was transported to a community hospital in cardiac arrest. The patient began to complain of left hip and groin pain following football practice, two days prior to admission. On the day before admission, he stayed home from school secondary to continued hip pain,

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Table 1. Staphylococcal toxic shock syndrome.

Clinical Criteria

An illness with the following clinical manifestations:

- Fever: temperature greater than or equal to 102.0 °F (greater than or equal to 38.9 °C)
- Rash: diffuse macular erythroderma
- Desquamation: 1−2 weeks after onset of rash
- Hypotension: systolic blood pressure less than or equal to 90 mm Hg for adults or less than fifth percentile by age for children aged less than 16 years
- Multisystem involvement (three or more of the following organ systems):
  - Gastrointestinal: vomiting or diarrhea at onset of illness
  - Muscular: severe myalgia or creatine phosphokinase level at least twice the upper limit of normal
  - Mucous membrane: vaginal, oropharyngeal, or conjunctival hyperemia
  - Renal: blood urea nitrogen or creatinine at least twice the upper limit of normal for laboratory or urinary sediment with pyuria (greater than or equal to 5 leukocytes per high-power field) in the absence of urinary tract infection
  - Hepatic: total bilirubin, alanine aminotransferase enzyme, or asparate aminotransferase enzyme levels at least twice the upper limit of normal for laboratory
  - Hematologic: platelets less than 100,000/mm3
  - Central nervous system: disorientation or alterations in consciousness without focal neurologic signs when fever and hypotension are absent

Laboratory Criteria for Diagnosis

Negative results on the following tests, if obtained:

- Blood or cerebrospinal fluid cultures (blood culture may be positive for *Staphylococcus aureus*)
- Negative serologies for Rocky Mountain spotted fever, leptospirosis, or measles

Case Classification

Probable

A case which meets the laboratory criteria and in which four of the five clinical criteria described above are present

Confirmed

A case which meets the laboratory criteria and in which all five of the clinical criteria described above are present, including desquamation, unless the patient dies before desquamation occurs

The table has been adapted from Toxic Shock Syndrome (Other Than Streptococcal) (TSS) 2011 Case Definition.[5]

which was treated with ibuprofen. On the day of admission, the patient began to experience vomiting, diarrhea, and fever to 39.4 °C, followed by disorientation and abnormal movements suggestive of seizure activity. Shortly after, he collapsed, followed by apnea and pulselessness, ventricular fibrillation, evolving to pulseless electrical activity (PEA), which was treated with Pediatric Advanced Life Support (PALS) protocol, with return of spontaneous circulation (ROSC). The total time of cardiopulmonary resuscitation (CPR) was estimated at 20−30 min. In the Emergency Department of the community hospital he was started on vancomycin and ceftriaxone for a suspected possible infectious etiology, and intravenous fluids were administered for volume support. Norepinephrine and bicarbonate drips were given for profound hypotension and metabolic acidosis. On admission, his recorded vital signs included a blood pressure in the 60s/20s (mmHg) and a rectal temperature of 39.9 °C. Pertinent findings on physical examination included cool extremities with faint central and peripheral pulses, a distinctly prolonged capillary refill time of ~10 s, and mottled skin surfaces, signs all indicative of poor perfusion. Cardiac and pulmonary examinations revealed normal S1 and S2 heart sounds without murmurs and lungs that were clear to auscultation bilaterally, although pitting edema was noted in the lower legs. EKG showed normal sinus rhythm with a rate of 94 bpm. The patient's chest x-ray did not show focal consolidation or a pleural effusion. Arterial blood gas (ABG) analysis was performed and revealed a pH of 6.83, HCO3- of 7 mmol/L, pCO2 of 41 mmHg, and base excess of −28.2 mmol/L, indicative of a pronounced metabolic acidosis. He was then transferred to the PICU for further management. He developed renal failure with laboratory features of azotemia (BUN: 37 mg/dL; reference range [RR]: 7−17 mg/dL and creatinine: 4.11 mg/dL [RR: 0.23−0.61 mg/dL]). That deteriorated to anuria with no urine output. Additional noteworthy metabolic derangements included marked hypocalcemia and hyperphosphatemia (serum calcium: 4.7 mg/dL [RR: 8.9−10.1 mg/dL] and phosphorous: 11.4 mg/dL [RR: 3.78−6.47 mg/dL]). As the patient exhibited combined features of refractory hypotension, signs of poor perfusion concerning for poor cardiac output, and absence of urine output on presentation, he was deemed to be in critical condition with a grave prognosis. Over the next several hours, despite increasing doses of epinephrine and norepinephrine, as well as crystalloid and colloid infusions, the patient's blood pressure continued to

Table 2. Laboratory workup.

Blood Test	Result	Reference Value
pH, Arterial	<6.827	7.38–7.46
pCO2	41 mmHg	32–46 mmHg
pO2	402 mmHg	74–108 mmHg
HCO3, Arterial	4.2 mmol/L	21.0–29.0 mmol/L
Base Excess, Arterial	−28.2 mmol/L	-2-+2 mmol/L
O2 Sat, Arterial	97.3%	92–96%
Sodium	133 mmol/L	134–143 mmol/L
Potassium	5.9 mmol/L	3.4–4.7 mmol/L
Chloride	102 mmol/L	96–109 mmol/L
Bicarbonate	7 mmol/L	21–31 mmol/L
Glucose	180 mg/dL	74–118 mg/dL
BUN	37 mg/dL	7–17 mg/dL
Creatinine	4.11 mg/dL	0.23–0.61 mg/dL
Anion Gap	24 mmol/L	9–16 mmol/L
Calcium	4.7 mg/dL	8.9–10.1 mg/dL
Phosphorus	11.4 mg/dL	3.78–6.47 mg/dL
Magnesium	3.0 mg/dL	1.6–2.2 mg/dL
WBC	4.78 K/uL	5.7–10.5 K/uL
Neutrophils, Absolute	1.39 K/uL	1.8–5.4 K/uL
RBC	3.80 M/uL	3.9–5.0 M/uL
Hemoglobin	10.9 g/dL	11.1–14.5 g/dL
Hematocrit	33.4%	32.9–21.5
Platelets	57 K/uL	150–400 K/uL
Prothrombin Time	40.1 s	11.5–13.5 s
Prothrombin Time, INR	3.5	0.8–1.2
aPTT	68.5 s	27–38 s

fall. Because the patient's clinical presentation prompted the consideration of an infectious etiology with resultant septic shock, a workup including blood culture and parameters for disseminated intravascular coagulation (DIC) was initiated, with elevated prothrombin time (PT: 40.1 s; RR: 11.5–13.5 s; INR: 3.5) and activated partial thromboplastin time (aPTT: 68.5 s; RR: 27–38 s) and thrombocytopenia (platelet count: 57 K/uL: RR: 150–400 K/uL). Various laboratory parameters are summarized in Table 2. Blood cultures and PCR assay were submitted for microbial culture and viral respiratory pathogen panel, including SARS-CoV-2 (Table 3). Approximately 9 hours after admission, in light of the patient's poor prognosis, all medications were discontinued and the patient was pronounced dead. The death was reported to and accepted for jurisdiction by the County Medical Examiner's Office, based upon criteria of both a sudden unexplained death and the consideration of a transmissible communicable infection that carried potential public health implications.

At autopsy, no source of infection, including the site of the initial trauma, was identified. Autopsy revealed widespread mucosal and serosal hemorrhages (Figs. 1 and 2), as well as petechiae of the skin, palpebral conjunctivae, and epicardial and visceral pleural surfaces; these findings are characteristic of the hemorrhagic diathesis of disseminated intravascular coagulation (DIC) that manifests following the consumption of platelets and therefore reflect profound derangements in primary hemostasis. Other gross autopsy findings included swelling of the face and scalp, bilateral serosanguineous pleural effusions, serous ascites, slight brain swelling, pulmonary edema, and congestive splenomegaly. The presence of the left megaureter (left ureter width: ~1 cm and right ureter width: ~0.4 cm) with slight calyceal dilatation of the left kidney (left hydronephrosis; Fig. 3) confirmed the clinically documented congenital obstruction of left ureterovesical junction. The most notable microscopic autopsy findings were intracapillary fibrin thrombi, which were seen within the adrenal glands, kidneys, skin, and mesenteric lymph nodes. Additional distinctive microscopic findings consisted of adrenal cortical hemorrhages, marked hemophagocytosis within vertebral bone marrow, and acute cholangitis with mixed inflammation and edema of portal tracts. These findings were similar to those described in sepsis-related death.[7] Postmortem toxicology was negative for illicit drugs.

In an attempt to elucidate an infectious etiology and source for the child's abrupt downward clinical course, additional microbiologic investigations were pursued and samples submitted, including PCR for identification of *S. aureus* virulence factors and respiratory pathogen panel, aerobic and stool cultures. Confirmatory antemortem and postmortem microbiology laboratory findings are summarized in Table 2 and include the following: a) isolation of *S. aureus* from antemortem blood, b) postmortem isolation of *S. aureus* from multiple organs and cerebrospinal fluid, c) detection of *S. aureus* virulence factors, including toxic shock syndrome toxin-1 (TSST-1) and *S. aureus* enterotoxin A (SEA) DNA by real-time polymerase chain reaction (PCR).

Based upon the sum total of the decedent's clinical presentation, and laboratory findings, autopsy findings, and antemortem and postmortem microbiology studies, including cultures and molecular methods for *S. aureus* virulence factors and toxins, the cause of death in this 10-year-old boy was certified as multisystem organ failure as a result of a rare fatal complication *S. aureus* infection, namely STSS.

3. Discussion

STSS is caused by a host response to superantigens from *S. aureus*, which are proteins capable of directly activating T-lymphocytes by bypassing certain steps of the antigen-mediated immune response sequence, namely, the normal

Table 3. Antemortem and postmortem microbiology findings.

Antemortem Microbiology Laboratory Findings	Result	Reference value
SARS-CoV-2 PCR	Not Detected	Negative
Blood Culture	Growth of *S. aureus*[a]	No growth
Postmortem Microbiology Laboratory Findings	**Result**	**Reference value**
S. aureus Virulence Factors DNA PCR [b]:		
S. aureus DNA	Detected	Not Detected
mecA gene DNA	Not Detected	Not Detected
Panton-Valentine leukocidin (PVL) DNA	Not Detected	Not Detected
Toxic shock syndrome toxin-1 DNA	Detected	Not Detected
Exfoliative toxin A DNA	Not Detected	Not Detected
Exfoliative toxin B DNA	Not Detected	Not Detected
S. aureus enterotoxin A DNA	Detected	Not Detected
S. aureus enterotoxin B DNA	Not Detected	Not Detected
S. aureus enterotoxin C DNA	Not Detected	Not Detected
S. aureus enterotoxin D DNA	Not Detected	Not Detected
S. aureus enterotoxin E DNA	Not Detected	Not Detected
S. aureus Toxic Shock Syndrome Toxin	Not Detected	Not Detected
Postmortem Microbiology Laboratory Findings	**Result**	**Reference Value**
Blood Culture (heart blood)	No growth	No growth
Respiratory Pathogen Panel RNA PCR[c]:		
Influenza Type A	Negative	Negative
Influenza Type B	Negative	Negative
Respiratory Syncytial Virus	Negative	Negative
Human Metapneumovirus	Negative	Negative
Aerobic Cultures:		
CSF	*S. aureus*	No growth
Right and left lungs	*S. aureus*	No growth
Liver	*S. aureus*	No growth
Spleen	*S. aureus*	No growth
Fascia Lata	No growth	No growth
Stool Culture:		
Colon	No growth	Normal enteric flora

[a] *Staphylococcus aureus*.
[b] Blood.
[c] Nasopharyngeal.

histocompatibility complex (MHC)-restricted antigen specificity. When this process occurs, it can activate up to 30% of total T-lymphocytes, thereby precipitating an explosive release of cell mediators known as cytokines, which amplify the immune response by recruiting and further activating additional T- and B-lymphocytes.[8] The majority of cases of STSS are due to the four exotoxins with superantigenic properties: TSST-1, SEA, SEC, and SEB.[9] SEA has been specifically associated with septic shock in the course of bacteremia.[10]

In the present case, despite presumptive treatment for bacterial infections with broad-spectrum antibiotics, the child was not able to overcome the effects of the *S. aureus*-produced exotoxins with superantigenic properties. This is a rare case of fulminant STSS without an identifiable source of infection. TSS can occasionally occur without an established source of infection; however, fulminant staphylococcal infection is often associated with a deep focus of infection, including necrotizing pneumonia, necrotizing fasciitis, and infective endocarditis.[1,11]

In the present case, the most likely source of infection appears to be a soft tissue injury, given the temporal relationship of the onset of left lower extremity pain with a recent football practice, although this cannot be proven with certainty. It is also possible that obstruction of ureterovesical junction facilitated the subclinical mucosal colonization of *S. aureus* within the left megaureter, and that soft tissue injury caused mucous membrane breakdown in the susceptible host (i.e., insufficient antibody to *S. aureus* produced exotoxins). In our patient, a urine sample could not be obtained for microbiological culture due to anuria following acute kidney failure. An additional consideration was that the patient was

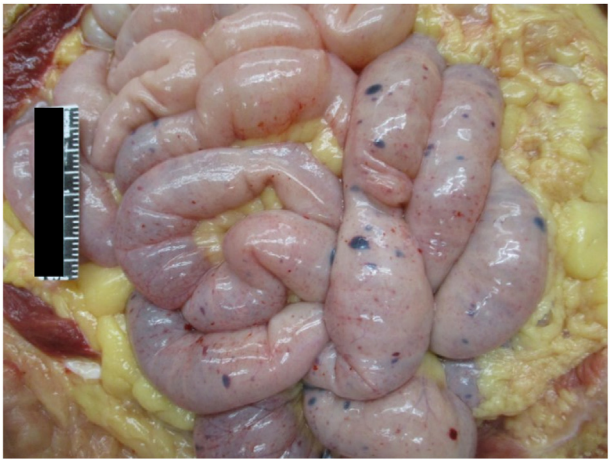

Fig. 1. The serosal surfaces of loops of small intestine are studded with numerous fine petechiae, some of which are focally confluent and appear "purpuric".

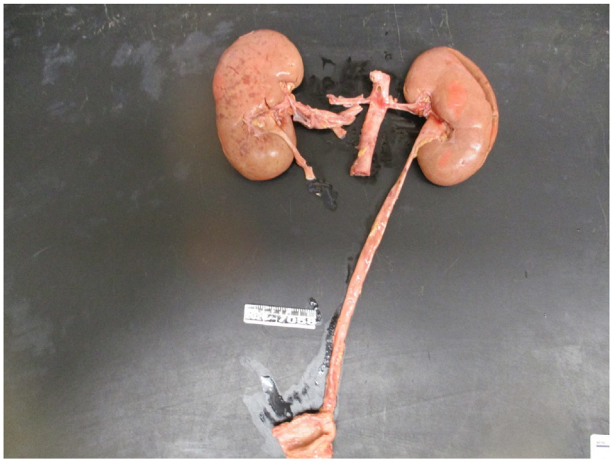

Fig. 3. Both kidneys are displayed in their in situ configuration to highlight asymmetrical dilatation of the left ureter (megaureter; left ureter width: ~1 cm; right ureter width: ~0.4 cm) due to congenital left ureteropelvic obstruction.

treated with ibuprofen at home. The link between the use of nonsteroidal anti-inflammatory drugs (NSAID) and the development of STSS has been reported.[12] Specifically, NSAIDs can enhance production of cytokines and impair granulocytes production.

It was suggested that the toxigenic strain of *S. aureus* may originate from the patient's own site of colonization rather than infection, especially, after disruption of the skin or mucous membrane or after surgery.[2,13] Asymptomatic carriage of TSST-1-producing *S. aureus* was demonstrated in genital and nasal mucosa.[14,15] Factors that trigger the transformation of asymptomatic colonization or infection with a toxin-producing strain of *S. aureus* into TSS are poorly understood. One possible explanation for the development of TSS is the inability of the host to acquire antibodies to TSST-1 due to genetic predisposition or age-related differences.[8] Individuals aged <20 years were shown to have lower titers or absence of antibodies to TSST-1 as compared with older individuals.[8,15,16]

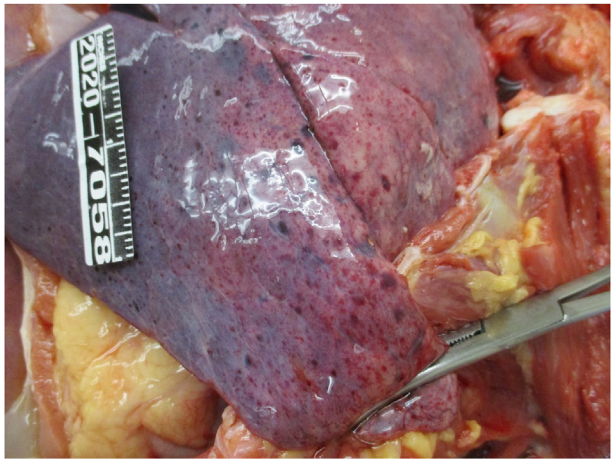

Fig. 2. Numerous petechiae, some of which are focally confluent, decorate the costal visceral pleural surface of the left lung.

The present case presented several challenges. Firstly, the rapid progression of the disease in our patient precluded early diagnosis of STSS. Our patient did not exhibit all of the signs and symptoms required to satisfy the complete clinical criteria established by the Centers for Disease Control and Prevention (CDC) for the probable or confirmed diagnosis of STSS. This patient met only four out of six criteria, including fever >39.9 °C, hypotension with SBP ≤5th percentile in <16 years old, multi-organ involvement, and blood cultures positive for *S. aureus*.[11] However, many of these criteria develop later in the course of the disease and should not be used for diagnosis in the acute settings.[6] For example, skin desquamation occurs within 1–2 weeks after the appearance of the generalized cutaneous rash. In addition, the presence of *S. aureus* DNA and *S. aureus* secreted toxins (TSST-1 and SEA) DNA by real-time PCR in an isolate obtained from the decedent's blood was not confirmed until day 15 postmortem. Secondly, the rapid development and fulminant course of STSS occurred without an identifiable infectious source.

4. Conclusion

It is crucial for health care providers to be aware of the possibility of STSS, even in the absence of overt focal infections and risk factors. In critically ill patients with a fulminant course of sepsis or septic shock, there should be a high index of suspicion for

STSS, Moreover, further research into discovering new diagnostic techniques for earlier detection of *S. aureus* virulence factors is urgently needed in order to optimize patient outcomes.

Conflict of interest

The authors declare there are no conflicts of interest.

References

1. Murray RJ. Recognition and management of Staphylococcus aureus toxin-mediated disease. *Intern Med J*. 2005;35 Suppl 2: S106−S119. https://doi.org/10.1111/j.1444-0903.2005.00984.x.
2. Chuang YY, Huang YC, Lin TY. Toxic shock syndrome in children: epidemiology, pathogenesis, and management. *Paediatr Drugs*. 2005;7(1):11−25. https://doi.org/10.2165/00148581-200507010-00002.
3. Hon KL, Fung RCM, Leung KKY, Leung AKC, Hui WF, Cheung WL. Case rep pediatr. 2021" title="Staphylococcus aureus infections in the paediatric intensive care unit: illustrated cases. Case rep pediatr. 2021">Staphylococcus aureus infections in the paediatric intensive care unit: illustrated cases. *Case Rep Pediatr*. 2021;2021:6661932. https://doi.org/10.1155/2021/6661932. Published 2021 Jun 4.
4. Miller LG, Perdreau-Remington F, Rieg G, et al. Necrotizing fasciitis caused by community-associated methicillin-resistant Staphylococcus aureus in Los Angeles. *N Engl J Med*. 2005; 352(14):1445−1453. https://doi.org/10.1056/NEJMoa042683.
5. Center for Disease Control and Prevention. *Toxic shock syndrome (other than streptococcal) (TSS) 2011*; 2011. Available at: https://ndc.services.cdc.gov/case-definitions/toxic-shock-syndrome-2011.
6. Gottlieb M, Long B, Koyfman AJ. The evaluation and management of toxic shock syndrome in the emergency department: a review of the literature. *J Emerg Med*. 2018;54(6): 807−814. https://doi.org/10.1016/j.jemermed.2017.12.048.
7. Lucas S. The autopsy pathology of sepsis-related death. In: Fernandez R, ed. *Severe sepsis and septic shock-understanding a serious killer*. InTech; 2012:71−100.
8. Lappin E, Ferguson AJ. Gram-positive toxic shock syndromes. *Lancet Infect Dis*. 2009;9(5):281−290. https://doi.org/10.1016/S1473-3099(09)70066-0.
9. DeVries ES, Lesher L, Schlievert PM, et al. Staphylococcal toxic shock syndrome 2000-2006: epidemiology, clinical features, and molecular characteristics. *PLoS One*. 2011;6(8), e22997. https://doi.org/10.1371/journal.pone.0022997.
10. Ferry T, Thomas D, Genestier AL, et al. Comparative prevalence of superantigen genes in Staphylococcus aureus isolates causing sepsis with and without septic shock. *Clin Infect Dis*. 2005;41(6):771−777. https://doi.org/10.1086/432798.
11. Gillet Y, Henry T, Vandenesch F. Fulminant staphylococcal infections. *Microbiol Spectr*. 2018;6(5). https://doi.org/10.1128/microbiolspec.GPP3-0036-2018.
12. Huang YC, Hsueh PR, Lin TY, Yan DC, Hsia SH. A family cluster of streptococcal toxic shock syndrome in children: clinical implication and epidemiological investigation. *Pediatrics*. 2001;107(5):1181−1183. https://doi.org/10.1542/peds.107.5.1181.
13. Chesney PJ. Clinical aspects and spectrum of illness of toxic shock syndrome: overview. *Rev Infect Dis*. 1989;11(Suppl 1): S1−S7.
14. Lansdell LW, Taplin D, Aldrich TE. Recovery of Staphylococcus aureus from multiple body sites in menstruating women. *J Clin Microbiol*. 1984;20(3):307−310. https://doi.org/10.1128/jcm.20.3.307-310.1984.
15. Jacobson JA, Kasworm EM, Crass BA, Bergdoll MS. Nasal carriage of toxigenic Staphylococcus aureus and prevalence of serum antibody to toxic-shock-syndrome toxin 1 in Utah. *J Infect Dis*. 1986;153(2):356−359. https://doi.org/10.1093/infdis/153.2.356.
16. Vergeront JM, Stolz SJ, Crass BA, Nelson DB, Davis JP, Bergdoll MS. Prevalence of serum antibody to staphylococcal enterotoxin F among Wisconsin residents: implications for toxic-shock syndrome. *J Infect Dis*. 1983;148(4):692−698. https://doi.org/10.1093/infdis/148.4.692.