Toxic Shock Syndrome (TSS)

November 15, 2020 by Josh Farkas

CONTENTS

- Pathophysiology (#pathophysiology)
- Epidemiology (#epidemiology)
- Clinical presentation (#clinical_presentation)
- Lab tests (#lab_tests)
- Diagnosis
  - Differential diagnosis (#differential_diagnosis)
  - Overall approach to diagnosis (#overall_approach_to_diagnosis)
  - CDC diagnostic criteria (#Centers_for_Disease_Control_diagnostic_criteria)
- Treatment
  - Basic sepsis resuscitation (#basic_sepsis_resuscitation)
  - Antibiotics (#antibiotics)
  - Source control (#source_control)
  - Intravenous immunoglobulin (IVIG) (#intravenous_immunoglobulin)
  - DIC & purpura fulminans (#DIC_&_purpura_fulminans)
  - Preventing nosocomial transmission (#preventing_nosocomial_transmission)
- Algorithm (#summary)
- Podcast (#podcast)
- Questions & discussion (#questions_&_discussion)
- Pitfalls (#pitfalls)
Some Streptococcus and Staphylococcus species secrete superantigens that cause widespread activation of T-lymphocytes (figure above). This triggers a cascade of inflammatory cytokines (similar to septic shock), leading to multiorgan failure.

Most people acquire antibodies that neutralize these toxins. A minority of people lack these antibodies, rendering them vulnerable to toxic shock syndrome.

Streptococcal toxic shock vs. staphylococcal toxic shock

- Streptococcal toxic shock is much more common, potentially affecting patients of all ages.
  - This occurs in the context of an invasive streptococcal infection. The most common source is a soft-tissue infection (e.g., cellulitis, myositis, or necrotizing fasciitis), but any invasive streptococcal infection can cause toxic shock.
  - Toxic shock may be more common than generally recognized (affecting ~20% of patients with invasive group A streptococcal infection).

- Toxic shock syndrome is most closely associated with group A Streptococcus (Streptococcus pyogenes) and Streptococcus dysgalactiae subspecies equisimilis (SDSE). SDSE may be identified in microbiology laboratories as either "Group C" or "Group G" streptococcus. Overall, SDSE is closely related to group A streptococcus and has similar clinical manifestations. Group B streptococcus (Streptococcus agalactiae) is less commonly associated with toxic shock, but several reports suggest that it might cause toxic shock syndrome.

- Staphylococcal toxic shock is less common, affecting mostly younger patients. It often occurs due to mucosal colonization, without invasive infection. This may result from methicillin-sensitive Staphylococcus aureus (MSSA) or methicillin-resistant Staphylococcus aureus (MRSA).

In an adult population, streptococcal toxic shock appears to be considerably more common than staphylococcal toxic shock syndrome. Staphylococcal toxic shock syndrome occurs predominantly among younger patients, because the vast majority of people develop antibodies to staphylococcal toxins by mid-adulthood. Consequently, in an adult ICU population the considerable majority of toxic shock presentations will result from streptococci.
The prevalence has increased over the last few decades, due to shifts in the circulating strains of group A streptococcus. (23830657)

Streptococcal toxic shock always occurs in combination with invasive streptococcal infection. It occurs in ~20% of invasive streptococcal infections due to groups A, C, or G streptococcus.

- The possibility of toxic shock syndrome should be considered in any patient with invasive streptococcal infection.
- The most common focus of infection is soft tissue (e.g., cellulitis, necrotizing fasciitis, myositis, pharyngitis, skin abscess, surgical wound infection).

Toxic shock may result from any invasive infection, for example:

- Pneumonia and empyema (Group A streptococcal pneumonia tends to cause empyema). (31068344)
  
- Septic arthritis (Group A streptococcus may spread hematogenously, affecting several joints simultaneously).
- Peritonitis (Group A Streptococcus may cause a primary peritonitis, without underlying visceral organ pathology).
- Gynecological infections (especially among pregnant or postpartum women):
  - Chorioamnionitis, endometritis.
  - Postoperative obstetric infections (often leading to necrotizing fasciitis).
  - Mastitis.
  - Following minor gynecological procedures (e.g., intrauterine device insertion).

**Staphylococcal toxic shock syndrome**

- This occurs mostly in younger patients (e.g., below ~40 years old). Staphylococcal toxic shock syndrome often results from colonization, without invasive infection.
  
  1. Menstrual-related (~50%)
     - Often with colonization of tampons.
  2. Non-menstrual
     - Colonization of nasal packing or intrauterine device placement.
     - Invasive staphylococcal infections:
       - Soft tissue infections – including burn infection, post-surgical, or postpartum wound infection.
       - Pneumonia.
recurrent episodes of toxic shock syndrome

- This may occur in individuals who lack neutralizing antibodies.
- Common examples:
  - (1) Repeated episodes of menstrual-related staphylococcal toxic shock syndrome.
  - (2) Repeated episodes of cellulitis-related streptococcal toxic shock syndrome.

clinical presentation

There are potentially two components of presentation: the primary site of infection and systemic effects from toxin production. In some cases, clinical manifestations are dominated by toxin secretion, whereas in other cases the primary focus of infection may be more obvious.

primary focus of infection

- In staphylococcal toxic shock, the focus of infection is often clinically silent (e.g., colonized tampon or nasal packing) or unimpressive (e.g., surgical site infection, skin abscess). Staphylococcal toxin suppresses neutrophil function, which may decrease the local signs and symptoms of infection!
- In streptococcal toxic shock, most patients will have an evident focus of infection (often cellulitis or necrotizing fasciitis).
  - In some cases, the primary focus may be subtle (e.g., a small skin abscess or patch of cellulitis).
  - Pain out of proportion to examination may signal necrotizing fasciitis.
- A red flag suggesting toxic shock is a patient with an unimpressive focus of infection (e.g., a small patch of cellulitis) who is in septic shock. Most patients should not develop septic shock due to cellulitis.

systemic features from toxin production

- (1) “Flu-like syndrome” (~25% of patients)
  - Fevers, chills, headache, myalgia, and/or sore throat.
  - Vomiting, diarrhea, and abdominal pain are common (in the context of unexplained septic shock, diarrhea should prompt consideration of toxic shock syndrome).
  - Patients may be incorrectly diagnosed as having influenza or gastroenteritis. Patients may look OK and thereby elude initial diagnosis. Don’t expect patients to appear “toxic” initially!
- (2) Skin findings (~10% of patients)
  - A diffuse erythematous rash is most characteristic. This may be subtle, resembling a sunburn.
  - Erythema may involve the mucous membranes (including conjunctiva and “strawberry tongue”). In patients with darker skin, mucosal changes may be the most noticeable signs (see figure below).
  - A diffuse maculopapular rash may occur as well, which can be pruritic. ([28299216](https://pubmed.ncbi.nlm.nih.gov/28299216/))
  - Desquamation can occur, but this is a delayed finding – it will be absent initially.
- (3) Multisystem organ failure
  - Hypotension, tachycardia, and systolic heart failure (septic myocardial dysfunction) are common.
  - Acute renal failure is common (often disproportionately severe compared to hemodynamic abnormalities).
  - Delirium may occur.
Complete blood cell count and differential showing a left shift

- White blood cell count may be normal, but there is generally a left shift.
  - Increased levels of immature cells (e.g., bands or immature granulocytes – depending on your assay).
  - The neutrophil/lymphocyte ratio is usually quite elevated.

Acute kidney injury

- Acute kidney injury often is the first sign of organ injury. This frequently occurs at an earlier stage than in most types of septic shock, typically preceding hypotension. Consequently, patients may present with advanced acute kidney injury.\(^{(30225523)}\)
- Urine sediment may show pyuria, in the absence of urinary tract infection.

Coagulation studies

- Thrombocytopenia is characteristic. However, this is often a later and ominous sign.
• Full-blown disseminated intravascular coagulation may be seen late in the course of illness.

**Creatinine kinase**

• Creatinine kinase more than twice normal is a component of some definitions of toxic shock syndrome. Profound cytokine elevation may cause release of creatinine kinase from muscle tissue. However, another possibility to consider is necrotizing fasciitis.

**Liver function tests**

• Elevation of bilirubin, AST, and ALT are components of the diagnostic criteria. However, mild abnormalities in liver function tests are commonly seen in septic patients, rendering them wholly nonspecific.

**Cultures**

• Staphylococcal toxic shock syndrome
  - Culture of sterile sites are generally negative (with blood culture yield below <5%).
  - Cultures are used to exclude alternative diagnoses.
  - Swabs of mucosal surfaces or wounds may reveal Staphylococcus (however, this is nonspecific).
• Streptococcal toxic shock syndrome
  - Blood cultures have a yield of ~60%.
  - Other sterile sites may yield cultures depending on the site of infection (e.g., Group A streptococcus has a tendency to cause empyema or peritoneal infection). If necrotizing fasciitis is present with bullae, fluid from bullae may be steriley sampled using a syringe, and sent for analysis.

**Differential diagnosis**

The differential diagnosis will vary depending on specific presentations. Some closer mimics may include:

• Adrenal crisis
• Septic shock due to any other pathogen (e.g., gram-negative organisms)
• Meningococcemia and/or meningococcal meningitis
• Rocky Mountain Spotted Fever
• Leptospirosis
• Kawasaki disease
• Scarlet fever
• Streptococcal scalded skin syndrome
• Toxic shock syndrome due to Clostridium sordellii (often following obstetric procedures)
• Other forms of necrotizing soft tissue infection:
  - Polymicrobial necrotizing fasciitis
  - Clostridial myonecrosis and/or necrotizing fasciitis

**Overall approach to diagnosis**

**Red flags that may allow for early diagnosis**

• (1) **Skin findings** (e.g., diffuse erythroderma, strawberry tongue, conjunctival injection) – these may occur if you’re lucky.
• (2) Any patient with known streptococcal infection plus sepsis syndrome.
• (3) A patient with soft tissue infection plus septic shock (especially the combination of cellulitis plus septic shock). Most patients with cellulitis don't develop septic shock – so this is unusual and suggests streptococcal cellulitis causing toxic shock syndrome.
  - 🍀 A key clue is shock out of proportion to the infectious focus.
• (4) "Gastroenteritis" or "flu-like" illness plus one of the following:
- **Hemodynamic instability** that doesn't respond to fluid resuscitation (gastroenteritis patients should improve dramatically with fluid resuscitation).
- **Dramatic left shift** (e.g., marked bandemia, extremely elevated neutrophil/lymphocyte ratio).
- **(5) Pregnancy** increases the risk of group A streptococcal infection by twenty-fold. Common sites of infection include endometritis, urinary tract, surgical sites, or breast. (24785617) Consider toxic shock in any pregnant patient with sepsis.

**overall diagnostic strategy**

- Consider the diagnosis early and often (e.g., especially in patients displaying red flags as above).
- Consider and evaluate for alternative diagnoses (e.g., meningococcal meningitis).
- When in doubt, initiate treatment for toxic shock (below).
  - The treatment for toxic shock syndrome is fairly benign (and similar to the treatment for septic shock).
  - If you're wrong and the patient doesn't have toxic shock syndrome (e.g., they simply have septic shock), you'll still probably be doing an excellent job of caring for them.

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### Centers for Disease Control diagnostic criteria

#### limitations of formal diagnostic criteria

- Diagnostic criteria were designed for research studies, rather than for everyday clinical practice.
  - Diagnostic criteria describe how well the patients fit the typical description of toxic shock syndrome.
  - Clinical diagnosis, however, is an integrative process which accounts for how well the patient fits features of toxic shock syndrome — as well as the likelihood of having an alternative diagnosis.

- Achieving a good outcome often depends on initiating therapy before the full-blown syndrome develops. This may prevent patients from reaching definitive diagnostic criteria.

- The sensitivity and specificity of these criteria have not been validated in actual clinical practice.

- Diagnostic criteria were designed for light-skinned patients. Among patients with darker skin, it is generally impossible to discern the presence of erythroderma, so these criteria may not perform optimally.

- The diagnostic criteria are included here because they may come up when debating with other services about whether the patient deserves advanced treatment for toxic shock syndrome (e.g., IVIG). Otherwise, these criteria aren't very useful for everyday clinical use.

" Once the full range of symptoms become manifest, the diagnosis is usually straightforward. However, the patient may have developed irreversible organ failure by the time this occurs. – Murray 2005

#### diagnostic criteria for staphylococcal toxic shock syndrome

- **Clinical Criteria**
  1. Fever > 38.9 (102 F)
  2. Rash with diffuse macular erythroderma
  3. Desquamation 1-2 weeks after rash onset
  4. Hypotension (Systolic Bp <90 mm)
  5. Multiorgan involvement, defined as at least three of the following:
     - Gastrointestinal (vomiting or diarrhea)
     - Muscular (severe myalgias or creatinine kinase >2 times the upper limit of normal)
     - Mucous membrane involvement (conjunctival, oropharyngeal, or vaginal hyperemia)
     - Renal (BUN or Cr more than twice the upper limit of normal or urinary sediment with pyuria in the absence of urinary tract infection)
     - Hepatic (total bilirubin, ALT, or AST more than twice the upper limit of normal)
     - Hematologic (platelets <100,000/mm3)
     - Neurologic (alteration in consciousness without focal neurologic signs when fever and hypotension are absent)
  - Laboratory criteria
    - If obtained, blood or cerebrospinal fluid cultures are negative (other than possibly for Staphylococcus aureus bacteremia).
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If obtained, serologies for Rocky Mountain spotted fever, leptospirosis, or measles should be negative.

Classification
- Probable: 4 clinical criteria met, plus laboratory criteria
- Confirmed: 5 clinical criteria met, plus laboratory criteria

**diagnostic criteria for streptococcal toxic shock syndrome**

Clinical criteria
- (1) Hypotension with Systolic Bp <90 mm
- (2) Multiorgan involvement with at least three systems:
  - Gastrointestinal (vomiting / diarrhea)
  - Muscular (severe myalgias or creatinine kinase above twice the upper limit of normal)
  - Mucous membrane involvement (conjunctival, oropharyngeal, or vaginal hyperemia)
  - Renal
    - Creatinine >2 mg/dL (>177 uM/L), or,
    - In patients with chronic kidney disease: a creatinine increase by more than two-fold over baseline.
  - Hepatic
    - Total bilirubin, AST, or ALT above twice the upper limit of normal, or,
    - In patients with chronic liver disease: elevation by more than two-fold over baseline.
  - Hematologic
    - Platelets < 100,000/mm3, or,
    - Disseminated intravascular coagulation (defined by prolonged clotting times, low fibrinogen level, and markedly elevated D-dimer)
    - Acute respiratory distress syndrome (ARDS)
    - Skin: Generalized erythematous, macular rash that can eventually desquamate.
    - Soft tissue necrosis (gangrene, myositis, or necrotizing fasciitis).

Laboratory criteria
- Group A Streptococcus isolation from culture

Classification
- Probable:
  - Both clinical criteria met
  - No alternative etiology for illness
  - No isolation of group A streptococcus from a sterile site.
- Confirmed
  - Both clinical criteria met
  - Isolation of group A streptococcus from a sterile site (e.g., blood, cerebrospinal fluid, synovial fluid, pleural/pericardial/ascitic fluid)

**basic sepsis resuscitation**

**vasopressor and fluid resuscitation**
- Most patients will require immediate vasopressor support, beginning with peripheral pressors and usually progressing to a central line.
- Consider a conservative fluid strategy, because patients often have leaky capillaries and won't respond well to fluids.

**stress-dose steroid**
- Early use of stress-dose steroid may be a rational therapy (e.g., hydrocortisone 50 mg IV q6hr), given the tendency of these patients to develop refractory shock and their underlying immune dysregulation.
- Some patients with advanced toxic shock and disseminated intravascular coagulation may develop acute adrenal insufficiency due to adrenal gland infarction (Waterhouse-Friderichsen syndrome). Although rare, this is important to recognize, as it may lead to a chronic steroid requirement.
- Further discussion of stress-dose steroid in septic shock is found [here](https://emcrit.org/ibcc/sepsis/#steroid).
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**septic myocardial dysfunction**

- Patients with toxic shock seem to exhibit a particular tendency towards the development of myocardial dysfunction, possibly related to exuberant cytokine release and direct effects of bacterial toxins on the myocardium. ([16271055](https://pubmed.ncbi.nlm.nih.gov/16271055/), [32099700](https://pubmed.ncbi.nlm.nih.gov/32099700/)).
- Serial echocardiography should be utilized in patients who aren’t responding well to vasopressors. Myocardial dysfunction may emerge some days after initial admission to critical care.
- Supportive care may include inotropes (e.g., epinephrine).
- With resolution of the toxic shock, myocardial recovery should occur.

*More on sepsis resuscitation here* ([https://emcrit.org/ibcc/sepsis/#top](https://emcrit.org/ibcc/sepsis/#top)).

**antibiotics**

*back to contents* ([#top](#top))

**toxin-suppressive antibiotics**

- Two antibiotics may be used to suppress toxin production: **clindamycin** ([https://emcrit.org/ibcc/antibiotics/#clindamycin](https://emcrit.org/ibcc/antibiotics/#clindamycin)) 900mg IV Q8 and **linezolid** ([https://emcrit.org/ibcc/antibiotics/#linezolid](https://emcrit.org/ibcc/antibiotics/#linezolid)) 600 mg IVq12.
- Clindamycin is most widely recommended.
  - Clindamycin has activity against nearly all Streptococcus and most Staphylococcus (including many strains of MRSA).
  - Clindamycin is supported by more robust data in the treatment of severe group A streptococcal infections.
  - However, clindamycin resistance is increasing, so it cannot be relied upon to cover all strains of Streptococcus. For this reason, clindamycin should be combined with a beta-lactam.
- Linezolid has the advantages of both suppressing toxin secretion and covering all Streptococcus and Staphylococcus (including all MRSA). ([16447124](https://pubmed.ncbi.nlm.nih.gov/16447124/)) Some evidence suggests that the combination of linezolid plus clindamycin is superior to either alone. ([12709354](https://pubmed.ncbi.nlm.nih.gov/12709354/), [29366615](https://pubmed.ncbi.nlm.nih.gov/29366615/)) The combination of linezolid plus clindamycin may be reasonable initially, until it has been clarified whether the patient has staphylococcal or streptococcal infection.

**beta-lactam backbone**

- Beta-lactam antibiotics have the following advantages:
  - (a) Uniform effectiveness against streptococcal species (with no resistance issues).
  - (b) Low toxicity, which allows for prolonged antibiotic courses.
- Beta-lactams are generally combined with clindamycin for the treatment of toxigenic streptococcal infections. Clindamycin suppresses toxin synthesis, while the beta-lactam provides some coverage against clindamycin-resistant strains.
- Selection of the beta-lactam will depend on how sure you are about the focus of infection and the bacterial species. For example:
  - In necrotizing fasciitis, if the bacteria involved is unclear then broad-spectrum coverage is safest (e.g., piperacillin-tazobactam or meropenem).
  - If the patient is known to have a group A streptococcal infection, then penicillin G is the definitive therapy.

**empiric regimen for undifferentiated toxic shock syndrome (possibly staphylococcal or streptococcal)**

- For suspected toxic shock syndrome due to Staphylococcus or Streptococcus, a reasonable initial regimen is triple therapy. This will cover all potential organisms and also provide dual toxin suppression.
  - (1) **Linezolid** ([https://emcrit.org/ibcc/antibiotics/#linezolid](https://emcrit.org/ibcc/antibiotics/#linezolid)) 600 mg IV q6hr.
  - (2) **Clindamycin** ([https://emcrit.org/ibcc/antibiotics/#clindamycin](https://emcrit.org/ibcc/antibiotics/#clindamycin)) 900 mg IV q8hr.
  - (3) A beta-lactam selection may depend on the clinical context:
    - In patients with uncomplicated cellulitis, cefazolin may be adequate.
    - In patients with possible or definite necrotizing fasciitis, piperacillin-tazobactam may be a reasonable initial choice (pending culture results).
    - In patients with possible meningitis, an agent with meningeal penetration may be rational (e.g., ceftriaxone 2 grams IV q12 hours or high-dose meropenem).
Don't be fooled by patients with "beta-lactam allergy" or "penicillin allergy" – it will always be possible to find a beta-lactam antibiotic which is safe to use. Further discussion of beta-lactam allergy here.

Over time, these antibiotics may be de-escalated as follows:

1. **Linezolid**
   - Linezolid may usually be discontinued after MRSA is excluded. Alternatively, if MRSA is the causative agent, then linezolid may be continued (with discontinuation of other agents).
   - Ongoing exposure to linezolid may eventually cause thrombocytopenia (as a cumulative, dose-related adverse effect). A few days of linezolid are probably fine, even in patients with mild thrombocytopenia (as is often the case in toxic shock). For patients with profound or worsening thrombocytopenia, exposure to more than a couple days of linezolid should probably be avoided.

2. **Clindamycin**
   - Clindamycin may be continued until ~1-2 days after the resolution of sepsis syndrome.

3. **Beta-lactam backbone**
   - Beta-lactam therapy is generally continued to cover the duration of therapy (which may vary depending on the site of infection).
   - Following availability of official speciation and sensitivities, the beta-lactam may be narrowed appropriately.
   - In group A/B/C/G streptococcal infections, the optimal beta-lactam is IV *penicillin G*. However, penicillin G requires frequent infusions, so for the sake of convenience it may be easier to use other agents, such as IV *cefazolin* or IV *ceftriaxone*.

**Empiric regimen for suspected streptococcal toxic shock syndrome**

Examples of where this may be appropriate:

- Toxic shock syndrome with blood cultures revealing gram-positive cocci in chains.
- Uncomplicated cellulitis with systemic toxicity (with no risk factors or evidence of MRSA), clinically suggestive for streptococcal cellulitis causing toxic shock.

For patients with severe streptococcal infection, the initial gold-standard antibiotic regimen is a combination of clindamycin plus a beta-lactam. Clindamycin causes toxin suppression, while the beta-lactam facilitates complete eradication of the infection.

Initial regimen

1. **Clindamycin** (900 mg IV q8hr)
2. **Beta-lactam** – selection may depend on the clinical context:
   - In cellulitis, a typical choice would be IV *cefazolin* (as this may provide some coverage for Methicillin-sensitive Staphylococcus aureus (MSSA), just in case that organism is involved)

Over time, these antibiotics may be de-escalated similarly to the strategy described above.

**Source control**

Any focus of infection which is potentially secreting toxin must be aggressively drained or debrided. This may be challenging, because such foci may not be impressive (e.g., a small abscess may cause profound systemic illness). Thus, there should be a low threshold to obtain definitive imaging to thoroughly evaluate for a focus of infection. The presence of a retained tampon/diaphragm/intrauterine device, sinus packing, or infected foreign material must be excluded.

- Surgical wounds should be considered potentially infected, even if they appear benign.
- Particularly with staphylococcal toxic shock syndrome, infected wounds may appear misleadingly benign.

Necrotizing fasciitis

- Patients with septic shock, no obvious focus, and soft tissue pain out of proportion to exam have necrotizing fasciitis until proven otherwise.
- Among patients with necrotizing fasciitis due to group A streptococcal infection, immediate radical excision of involved tissue might not always be advisable. One case series described seven patients who were treated with high-dose IVIG (2 grams/kg/day on day one, and again on days 2-3, as needed), while debridement was delayed. Medical management seemed to reduce the amount of skin involved, allowing for less extensive debridement afterwards. This remains...
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intravenous immunoglobulin (IVIG) basics

- The general concept is that IVIG will often contain toxin-neutralizing antibodies (although there are other potential mechanisms of action as well). ([30225523](https://pubmed.ncbi.nlm.nih.gov/30225523/))
- IVIG is generally safe. Numerous RCTs have been performed investigating the utility of IVIG in septic shock, with analyses of these studies not detecting any safety concerns regarding IVIG. ([24043371](https://pubmed.ncbi.nlm.nih.gov/24043371/)) Despite concerns regarding anaphylaxis in patients with IgA deficiency, this risk appears to be exceptionally low (IgA levels do not need to be checked prior to giving IVIG).
- The main drawback to IVIG is cost (which may run on the order of ~$5,000).

IVIG in streptococcal toxic shock syndrome

![IVIG in streptococcal toxic shock syndrome](https://emcrit.org/?attachment_id=479076)

- Definitive evidence will probably never exist (given the difficulty of performing a trial on a disease this rare). The following is the best available evidence.
- Darenberg et al. 2004 ([14999628](https://pubmed.ncbi.nlm.nih.gov/14999628/))
  - This is the best and only prospective RCT investigating IVIG in streptococcal toxic shock syndrome.
  - The study was terminated early after enrolling 21 patients, due to poor recruitment.
  - Patients treated with IVIG experienced an improvement in organ function, whereas control patients did not (figure above).
  - There was a nonsignificant trend towards mortality reduction in patients treated with IVIG.
- Parks et al. meta-analysis, 2018 ([29788397](https://pubmed.ncbi.nlm.nih.gov/29788397/))
• This study involved a combination of Darenberg plus nonrandomized, observational studies. The analysis included only patients treated with clindamycin, thereby avoiding confounding effects due to variable clindamycin use.

• The authors found a potential mortality benefit (figure below). However, as a meta-analysis involving nonrandomized trials, the result remains inconclusive.

• The most commonly utilized regimen for IVIG is **1 gram/kg on day #1, followed by 0.5 grams/kg daily on days 2-3**. For patients who are failing to respond to 1 g/kg, it is reasonable to use higher dose IVIG (2 grams/kg/day).

• In the absence of conclusive evidence, my usual practice is as follows:
  - Initiate IVIG for patients with known or highly suspected streptococcal toxic shock syndrome with persistent vasopressor requirements or high predicted mortality.
  - Stop IVIG once patients are clearly recovering (e.g., liberation from vasopressors). Most patients will require only one or two doses of IVIG (for a total cumulative dose of 1 or 1.5 grams/kg).
  - Discuss IVIG use with infectious disease consultants.

![Figure 1](https://emcrit.org/ibcc/tss/attachment/parks/)

**IVIG in staphylococcal toxic shock syndrome**

• There is less evidence supporting the use of IVIG in staphylococcal toxic shock syndrome. Staphylococcal toxic shock syndrome may be less responsive to IVIG than streptococcal toxic shock syndrome.

• This has led some to recommend against the use of IVIG in staphylococcal toxic shock syndrome. Meanwhile, others have recommended the use of higher doses of IVIG. **The optimal approach is unclear at this point in time.**

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**DIC & purpura fulminans**

**purpura fulminans**

• Patients with sepsis and toxic shock syndrome are at high risk for sepsis-associated DIC. Some patients will develop purpura fulminans, which is an extreme form of disseminated intravascular coagulation involving necrosis of the dermal blood vessels. In severe cases, purpura fulminans causes ischemia and autoamputation of digits or entire extremities.

• Purpura fulminans may require specific and aggressive therapy to avoid limb loss – described further [here](https://emcrit.org/ibcc/pf/).

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**preventing nosocomial transmission**

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The Centers for Disease Control (CDC) recommends contact and droplet precautions for the first day of effective antimicrobial therapy in patients with severe group A streptococcal infection.\(^{30225523}\)

Recommendations to isolate patients are not based on high-level evidence. However, some strains of Streptococcus are definitely more toxigenic than others. Case clusters and outbreaks have been reported.

- (So yeah, we've used 21st century technology to verify what Semmelweis figured out in the 1800s.)

**summary**

[Back to content](https://emcrit.org/?attachment_id=479077)
**Diagnostic Studies**
- Basic labs (CBC with differential, electrolytes, liver function tests)
- DIC labs (PT, INR, fibrinogen, D-dimer)
- Creatinine Kinase
- Blood cultures, Urinalysis & urine culture
- Culture & analysis of any ascitic, pleural, or blister fluid
- Lumbar puncture if necessary to exclude meningitis
- CT scan and/or ultrasound of any potential focus of infection (seemingly unimportant foul of infection may secrete toxin!)

**Hemodynamic stabilization**
- Moderate fluid resuscitation (go easy, it won’t stay in vasculature)
- Early vasopressor support (e.g. norepinephrine).
- Inotropic support if septic myocardial dysfunction (e.g. epinephrine).

**Antibiotics**
- Clindamycin 900 mg IV q8hrs first dose STAT
- Linezolid 600 mg IV q12hr first dose STAT (if MRSA possible)
- Beta-lactam depending on suspected source, for example:
  - Cellulitis or known group A strep: Cefazolin 2g IV q8 may be fine.
  - Necrotizing fasciitis: Piperacillin-tazobactam or meropenem.
  - Meningitis possible: Ceftriaxone 2g IV q12 or meropenem high dose.

**Source Control**
- Debride and/or drain any possible focus of infection.
- Remove potentially involved foreign bodies (e.g. tampon, IUD).
- Explore any potentially infected wound (even if it seems OK).
- When in doubt, consult surgeons early (e.g. gen surg, OB/GYN).

**Intravenous immunoglobulin (IVIG)**
- Most evidence in streptococcal toxic shock syndrome.
- For patients at higher risk of death, consider 1 gram/kg IV x1.

**Stress dose steroid**
- Low threshold for initiation in patients on vasopressor.
- Hydrocortisone 50 mg IV q6hr.

**Prevent nosocomial transmission**
- Droplet & contact precautions for first 24 hours of treatment.

To keep this page small and fast, questions & discussion about this post can be found on another page [here](https://emcrit.org/pulmcrit/tss/).


Podcast

Toxic Shock Syndrome (TSS) - EMCrit Project
Failure to recognize toxic shock syndrome as an entity distinct from septic shock, which requires unique management strategies.

Failure to use IVIG in patients with streptococcal toxic shock and high risk of morbidity and mortality (e.g., persistent vasopressor requirement with failure to respond to conventional therapy).

Failure to aggressively investigate and drain foci of infection (even small abscesses or benign-appearing skin incisions – which may not seem to be clinically relevant).

References


