Clinical Management of Scarlet Fever and Toxic Shock Syndrome

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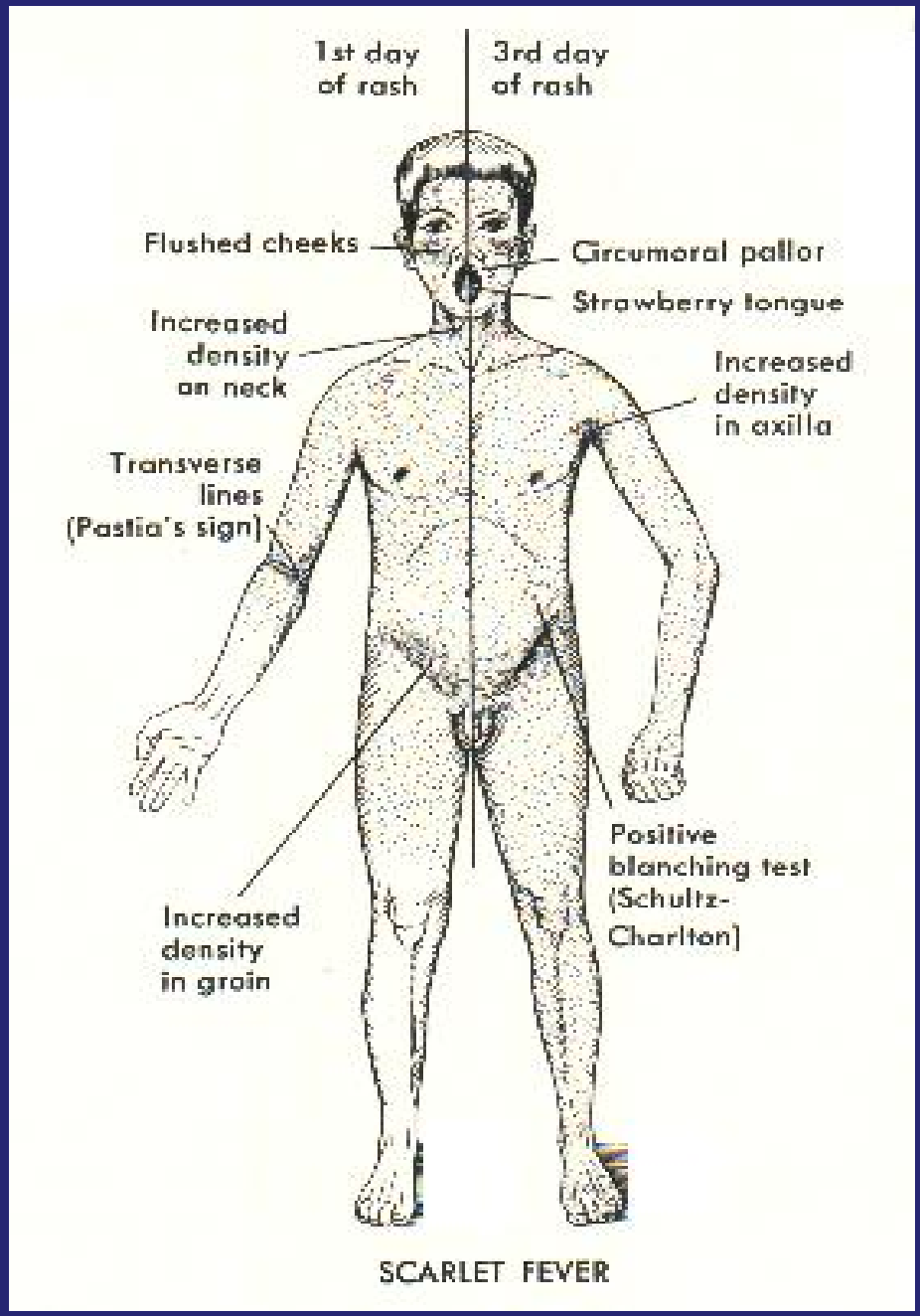
Streptococcus pyogenes - human disease

Causes a spectrum of pyogenic non-invasive and invasive as well as non-pyogenic complications

- **Non-invasive pyogenic infections**
  - pharyngitis, tonsillitis
  - scarlet fever
  - otitis media
  - mastoiditis
  - impetigo
- **Invasive, pyogenic infections**
  - meningitis
  - pneumonia
  - erysipelas
  - lymphangitis
  - celhulitis
  - necrotizing fasciitis
  - endometritis
  - TSLS

Scarlet Fever

- A clinical diagnosis characterized by the presence of:
  - fever,
  - blanchable erythematous macular rash,
  - sandpaper-like skin texture,
  - Pastia's lines,
  - circumoral pallor and
  - strawberry tongue.



- Disease Progression

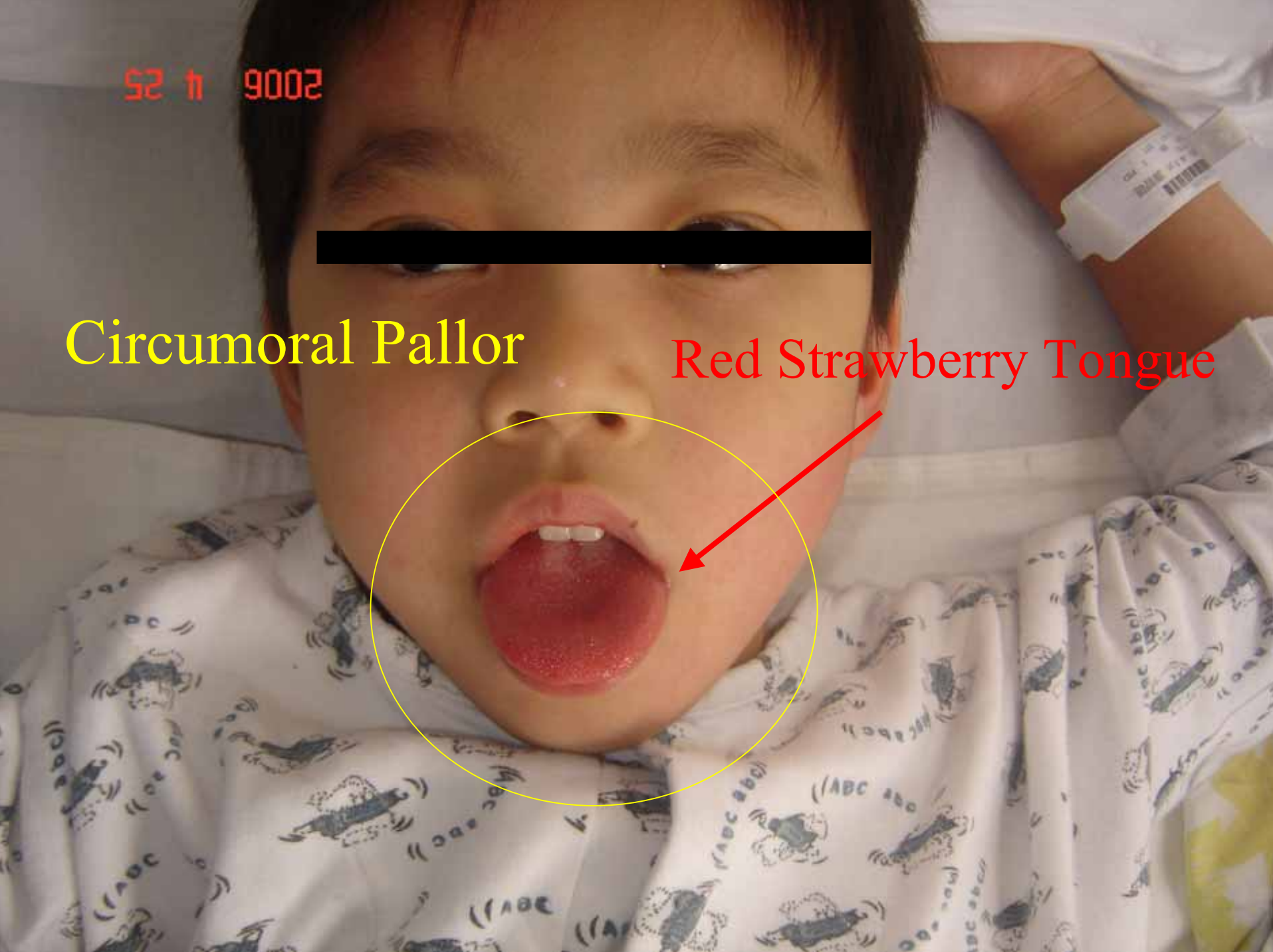
Strawberry Tongue

- 1st day – White strawberry tongue
  - The tongue is heavily coated with a white membrane through which edematous red papillae protrude
- Day 4 or 5 – Red Strawberry tongue
  - the white membrane sloughs off, revealing a shiny red tongue with prominent papillae

White and red strawberry tongue

Circumoral pallor

- The face is usually flushed, and circumoral pallor is observed


Circumoral Pallor
Red Strawberry Tongue

Rash

- The characteristic exanthem consists of a fine erythematous punctate eruption that appears within 1-4 days following the onset of the illness
- It first appears on the upper trunk and axillae and then becomes generalized, although it is usually more prominent in flexural areas, such as the axillae, popliteal fossae, and inguinal folds
- It may also appear more intense at dependent sites and sites of pressure, such as the buttocks.
- It can also appears on the face

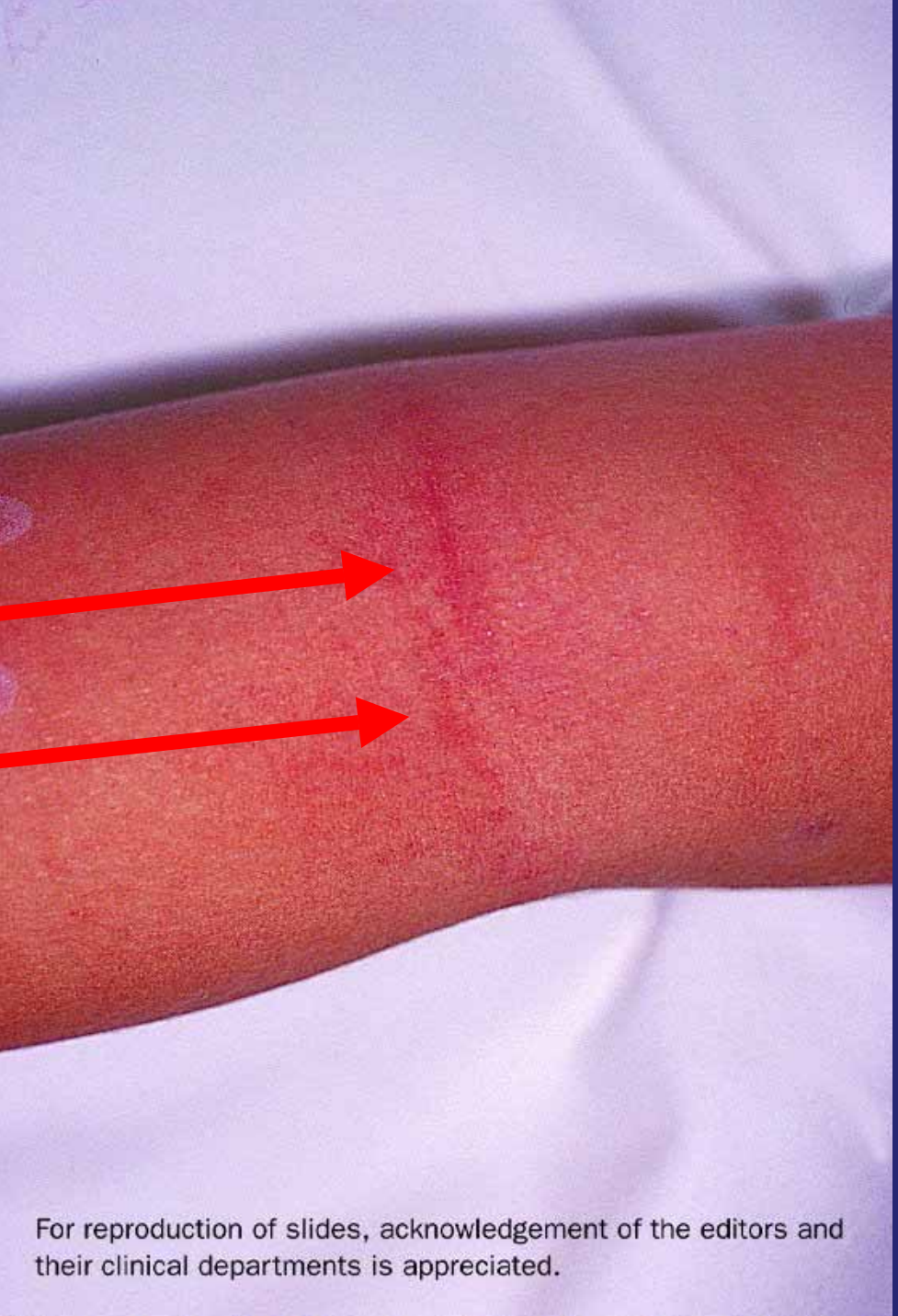

Erythematous rash which blanch on pressure
2006 4 25

Sand Paper like skin

- The eruption imparts a dry rough texture to the skin that is reported to resemble the feel of sandpaper

Pastia lines

- Capillary fragility is increased, and often, transverse areas of hyperpigmentation with petechiae in the axillary, antecubital, and inguinal areas can be observed



- Pastia’s line

Desquamation

- The cutaneous rash lasts for 4-5 days, followed by fine desquamation, the extent and duration of which is directly related to the severity of the eruption
- May not present in some patients

Classification

- It can be classified clinically into 2 categories: ‘Classical’ and ‘Surgical’ scarlet fever.
- A minority of cases may deteriorate rapidly with shock.

‘Classical’ Scarlet Fever

- The primary focus of infection is acute tonsillitis / pharyngitis caused by *Streptococcus pyogenes* (Group A Streptococcus).
- Skin rash usually arises from day 2 of fever.

‘Surgical’ Scarlet Fever

- It arises from wound infection (often trivial) after trauma, burn, scald or recent varicella infection.
- Caused by *Streptococcus pyogenes*, and less commonly, *Staphylococcus aureus*.
- One of the commonest complication of varicella.
- Typically the skin rash occurs 3-4 days after the onset of varicella.
- Risk of developing Toxic Shock Syndrome is higher for ‘Surgical’ scarlet fever when compared with ‘Classical’ scarlet fever.


Infected chickenpox lesions
Rash blanch on pressure
2006 5 21

Management

- Document pulse rate, blood pressure, capillary refill time, hydration status and urine output during clinical assessment. Repeated assessments are required
- Ensure adequate hydration
- Send throat swab and blood for culture
- Actively search for any minor wound if ‘surgical’ scarlet fever is suspected, and send wound swab for culture
- Urgent Gram smear of pus or aspirate from local infected lesions is always helpful to facilitate early diagnosis and guide antibiotic regimen.

For “Classical” Scarlet Fever

- Penicillin for 10 days
  - Alternative regimen if allergic to penicillin:
    - 2nd generation cephalosporins (e.g. cefuroxime) for 10 days
    - cross-hypersensitivity with penicillin is more likely with 1st generation cephalosporins (e.g. cephalexin)
  - Extend treatment to 14 days if blood culture positive
  - Tetracyclines, sulphonamides and fluoroquinolones should not be used
  - Use of macrolides should be discouraged as significant erythromycin resistance is encountered locally (i.e. resistance to other macrolides including clarithromycin and azithromycin as well)

For “Surgical” Scarlet Fever

- Augmentin or Cefuroxime for 10 days (Penicillin alone is not adequate as coverage for Staphylococcus aureus is also required)
- Extend treatment to 14 days if blood culture positive
- Surgical management of local skin and soft tissue infection if indicated

Management

- Anti-pyretics are indicated but the use of NSAIDs should be avoided
- Watch out for warning signs of toxic shock syndrome (see below)
- Look for any complications:
  - Acute suppurative complications: peritonsillar / parapharyngeal / retropharyngeal abscess (risk of airway obstruction)
  - Post-infectious non-suppurative complications: acute rheumatic fever (rare), acute post-streptococcal glomerulonephritis

Toxic Shock Syndrome (TSS)

- It is caused by exotoxin-producing *Staphylococcus aureus* or *Streptococcus pyogenes*.
- The three cardinal features include:
  - profound shock,
  - rapid onset of multi-organ failure and
  - erythroderma.
    - The first two features distinguish toxic shock from septic shock, while the third feature might not be present in some cases of streptococcal TSS.
  - The mortality for Streptococcal TSS is much higher when compared with Staphylococcal TSS.

Warning signs of toxic shock syndrome

- Severe soft tissue infection
  - Rapidly progressive cellulitis
    - Usually associated with diffuse or localized pain that is abrupt and severe
  - Necrotizing fasciitis
    - Characterized by areas of bluish discoloration and anaesthesia
  - Gangrenous myositis (rare)
- Hypotension (rapid onset)
  - At presentation or within 4-8 hours after admission
  - Poor response to fluid challenge

Warning signs of toxic shock syndrome

- Change in mental status, e.g. acute confusion
- Hypothermia (developed after shock)
- Recent varicella infection is a risk factor
- Evidence of multi-organ involvement, such as:
  - Raised creatinine level
  - Deranged liver function (raised ALT/AST)
  - Raised creatine kinase level
  - Coagulopathy
  - Acute respiratory distress syndrome (ARDS)

Management of toxic shock syndrome

- Early identification and intensive care
- Vigorous fluid replacement
  - Up to 3 times circulatory volume may be required to maintain BP (i.e. 240ml/kg/day) due to massive capillary leakage
- Inotropic support is required together with fluid replacement, dopamine and noradrenaline are the preferred agents
- Ventilatory support is often necessary as up to 50% of Streptococcal TSS develop ARDS

Management of toxic shock syndrome

- Early debridement of necrotizing fasciitis, if any
  - Thorough search for infected skin or soft tissue
  - Early liaison with surgical team and arrange urgent imaging to delineate depth and extent of infection

Prompt antibiotic therapy

- Empirical antibiotics should cover both *Staphylococcus aureus* and *Streptococcus pyogenes* before the organism is identified.
  - **Cefotaxime or a carbapenem** is preferred
- **Clindamycin** is effective against serious skin and soft tissue staphylococcal infection.
  - It has an immunomodulatory effect and inhibits toxin production.
  - However, streptococcal resistance to Clindamycin is encountered locally and the use of Clindamycin alone is not recommended.
  - Most experts will include clindamycin in the antibiotic regimen.
  - Linezolid can be considered as an alternative treatment in face of clindamycin resistance.
  - Vancomycin should be considered if MRSA is suspected according to clinical setting (e.g. hospital acquired infection, prolonged ICU admission, etc)

Prompt antibiotic therapy

- Once the culture result is available, a narrower spectrum antibiotic should be selected based on the susceptibility result. Penicillin is the drug of choice for *Streptococcus pyogenes*, and Cloxacillin for MSSA

Intravenous immunoglobulin (IVIG)

- Probably beneficial and is recommended by most experts especially for Streptococcal TSS but the evidence from randomized control trial is lacking
- 1g/kg/dose infused over 4-6 hours (slower if fluid overload from cardiac or renal failure is a concern), total two doses 24 hours apart.

Criteria for diagnosis of Streptococcal TSS

- The Working Group on Severe Streptococcal Infections established the following clinical guideline for diagnosis of GAS TSS:
- Isolation of GAS from a normally sterile site (eg, blood cerebrospinal, pleural, or peritoneal fluid, tissue biopsy, or surgical wound) plus
- Hypotension (systolic blood pressure ≤90 mm Hg in adults or <5th percentile for age in children)

- PLUS two or more of the following:
- Renal impairment (in children, two-times upper limit of normal for age; in patients with pre-existing renal disease ≥ twofold elevation over baseline)
- Coagulopathy (e.g., thrombocytopenia, disseminated intravascular coagulation)
- Liver involvement (e.g., ≥ two-times upper limit of normal for age of transaminases or bilirubin; in patients with pre-existing liver disease ≥ twofold elevation over baseline)
- Adult respiratory distress syndrome
- Erythematous macular rash, may desquamate
- Soft tissue necrosis (e.g., necrotizing fasciitis, myositis, or gangrene)
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- If GAS is isolated from a nonsterile site (e.g., throat, vagina, skin lesion) but the patient fulfills the other criteria noted above, a diagnosis of probable GAS TSS can be made if no other etiology for the illness is identified.

Criteria for the diagnosis of Staphylococcal TSS:

- Five categories of clinical features are needed for the diagnosis, as follows:

- Fever
- Rash - A diffuse macular erythroderma
- Desquamation - Occurs 1-2 weeks after onset of illness, involving palms and soles
- Hypotension (systolic blood pressure < 90 mm Hg, orthostatic drop in diastolic blood pressure < 15 mm Hg, orthostatic syncope, and dizziness)

- Evidence of multisystem involvement in 3 or more of the following systems:
- Gastrointestinal - Vomiting or diarrhea at the onset of illness
- Muscular - Severe myalgia or creatine kinase (CK) elevation (>2 times normal upper limit)
- Mucous membrane - Vaginal, oropharyngeal, or conjunctival erythema
- Renal - BUN or serum creatinine greater than 2 times the upper limit of normal
- Hepatic - Bilirubin or transaminases greater than 2 times the upper limit of normal
- Hematological - Platelets less than 100,000
- Central nervous system - Disorientation or alteration in consciousness without focal signs

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