Guidelines for the Treatment of Necrotizing Fasciitis (NF) and Streptococcal Toxic Shock Syndrome (STSS)

DEFINTIONS

Streptococcal toxic shock syndrome is the most severe manifestation of group A streptococcal (GAS) infection with a mortality rate of up to 80%[1]. STSS may be seen in patients with or without necrotizing fasciitis, a presentation of the disease that results in rapidly progressive destruction of the subcutaneous tissue and fascia . Necrotizing fasciitis occurring alone generally has lower associated rates of mortality (around 30%) than when seen with STSS.

The clinical diagnosis of STSS includes[3]:

A. Isolation of GAS from a clinically significant specimen in a patient who is hypotensive (systolic BP ≤ 90 mmHG).

AND

B. Has two or more of the following:
   - i. renal impairment
   - ii. coagulopathy
   - iii. liver dysfunction
   - iv. acute respiratory distress syndrome (ARDS)
   - v. a generalized erythematous macular rash
   - vi. soft-tissue necrosis (including Necrotizing fasciitis or myositis or gangrene)

Patients not meeting these criteria are classified as having invasive or non-invasive infection depending on whether GAS is isolated from a normally sterile or a non-sterile site.

TREATMENT OF STSS

Penicillin G 3 million units IV q6h + Clindamycin 600 mg IV q8h

- Duration of treatment is based upon clinical improvement. Usually, clindamycin is administered for a minimum of 72 hours or until patient is haemodynamically stable for 24 hours. Penicillin is continued for a total of 10-14 days.

Intravenous Immune Globulin

- used as an adjunct to standard medical and surgical treatment for treatment of STSS (13)
- use in necrotizing fasciitis is currently under study

Contraindications:

- known IgA-deficiency or hypogammaglobulinemia
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Dosing Regimen:

- Initial dose of IVIG is 2 g/kg in a single dose (administered as quickly as is feasible for the large volume required (approx. 2.5 L) – usually 3-4 hours).
- A repeat dose of 1-2 g/kg 2-5 days after the initial dose may be considered if patient continues to be hemodynamically unstable or disease is progressing.

Administration of IVIG:

Maximum infusion rates vary depending on manufacturer. The Canadian Red Cross Society is presently obtaining IVIG from Bayer Inc. (IGIV®) which is a 5% human globulin in maltose[9].

IVIG must be ordered through the Blood Bank. Clinicians should verify with the Blood Bank which product is currently available, and its recommended infusion rates.

The recommended rate of infusion for the Bayer product is as follows:

Infusion Protocol for IGIV®

- 0.01 to 0.02 ml/kg body weight per minute for first 30 minutes.
- Gradually increase as tolerated by patient.
- Maximum rate of 0.08 ml/kg/min.

Example:
For a 75 kg patient receiving a total dose of 150 g (2g/kg) of IGIV® (3000 ml), the starting infusion rate would be 0.75 to 1.5 ml/min. After 30 mins, the rate may be increased to the maximum of 6 ml/min if the patient can tolerate the infusion volume. The entire dose will infuse over 9 hours.

IVIG is compatible with dextrose 5% in water (D5W) only; it **is not** compatible with saline. It is recommended that IVIG be infused by a separate line from other medications.

Immune Globulin Suppliers

Product/Manufacturer	Volume/Unit
IGIV (Bayer, Inc.)	1g/20mL
	2.5g/50mL
	5g/100mL
	12.5g/250mL
Iveegam (Immuno)	5g/50mL
Gammagard-SD (Baxter)	2.5g
	5g
	10g
Gammaimune N (Bayer, Inc.) (High titre CMV)	2.5g/50mL

Adverse Effects of IVIG:

- Pallor, flushing, sweating, headache, dizziness
- Nausea, vomiting
- Chills, muscle aches, pains, back discomfort
- Changes in blood pressure, tachycardia
- Low grade fever

- Dyspnea, chest tightening

More Severe Reactions (uncommon)

- Anaphylaxis
- Erythema multiform
- Transmission of infections (e.g. Hepatitis C, or et unidentified blood bourne pathogens)
- Aseptic meningitis
- Leukocytoclastic vasculitis

Adverse effects are rare (<5% of patients); generally infusion rate related.
Usually resolve within 15-30 minutes with temporary slowing or stopping of the infusion.
Pre-medication with diphenhydramine (25-50 mg), acetaminophen (650 mg) or acetylsalicylic acid (650 mg) may be helpful.

ADDITIONAL MANAGEMENT

- Supportive care and surgical debridement where blistering or necrotizing fasciitis are present
- Contact isolation procedures until the patient has received 24 hours of appropriate antibiotic therapy
- Prophylaxis in health care workers is not recommended unless there has been direct contact between secretions of the patient and skin/mucous membrane of the health care worker
- Offer prophylactic antibiotics to household contacts if:
  - They have lived in the same household as the case within the 7 days prior to the case patient becoming ill

  OR
  - They have had direct mucous membrane contact with the oral or nasal secretions of a cases within 7 days prior to the case becoming ill

  - If contact occurred more than 2 weeks prior to the patient becoming ill, it is advisable to swab the contacts and treat only those with positive cultures.

- Suggested Oral Prophylaxis Regimens:
  - Adults:
    - Cephalexin (Keflex) 250 mg PO qid or 500 mg q12h for adults X 10 days
    - Erythromycin 250 mg q6h X 10 days
    - Penicillin VK 300 mg q6h X 10 days
  - Children
    - Cephalexin (Keflex) 25-30 mg/kg/day in divided doses (max.500mg/dose) X 10 days
    - Erythromycin 25-30 mg/kg/day in divided doses (max. 500 mg/dose) X 10 days
    - Penicillin VK 25-30 mg/kg/day in divided doses (max 500 mg/dose) X 10 days

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Adapted from guideline developed by Donna McCracken, BScPharm, January 1998 for Antibiotic Subcommittee at Mount Sinai Hospital.