NECROTIZING SOFT TISSUE INFECTIONS (NSTI)

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Case #1:
• A 47 year female presented to the ER with redness and pain on the left thigh. She had previous colostomy and PEG due to GI problems (dismobility). Ten days prior to presenting to our emergency room, she was seen in the ER in a peripheral hospital where she was given Demerol and Gravol in the left thigh.
• Seventy two hours before arriving in our ER, she noticed discolouration which has been worsening especially in the last 24 hours and she has been febrile. On examination, she presented with a 17 x 10 cm. area of mottled skin; it was painful and had swelling of the left leg. She had difficulty extending the knee. The patient was treated with Clindamycin, Cephalosporin and Gentamycin as soon as seen in the ER.
At surgery, there was necrotic skin and fascia and some of the underlying muscle (vastus lateralis). Thrombosed vessels were found in the necrotic skin.
Case #2:

- A 66 year old hemodialysis female patient was seen in the ICU because of septic shock syndrome.
Case #2

- At surgery, volar fasciotomy was performed necrotic muscles and lots of pus was found. A posterior fasciotomy was performed, same findings. Pus was found all the way to the deltopectoral groove and pectoralis major. During disarticulation of the shoulder joint, the patient arrested and died.
Necrotizing Fasciitis

- **Definition:** It is a rare but potentially fatal infection involving the subcutaneous tissue and fascia. It is commonly known as *flesh-eating disease.*
Necrotizing Fasciitis

History:

Hippocrates circa 500 BC, “Many were attacked by the erysipelas all over the body when the exciting cause was a trivial accident...flesh, sinews, and bones fell away in large quantities...there were many deaths.”

Necrotizing Fasciitis

History:

Dr. Joseph Jones (1871), a Confederate Army surgeon, was the first person to describe this disorder in a large group of patients. He reported 2,642 cases and found a mortality rate of 46%.
Necrotizing Fasciitis

History:

Jean Alfred Fournier (1883) described a similar necrotizing soft-tissue infection of the perineum in five male patients. The condition that bears his name is now described in both male and female patients.
Necrotizing Fasciitis

History:

In the ensuing years many other terms have been used: *necrotizing erysipelas, streptococcal gangrene, and suppurative fasciitis*
Necrotizing Fasciitis

History:

Dr. Wilson (1951) proposed the term *necrotizing fasciitis* to include gas-forming and non-gas-forming necrotizing infection and stated that fascial necrosis is the sine qua non of this process.
Necrotizing Fasciitis

**History:**
Recently, the term *necrotizing soft tissue infection* has been adopted.
ANATOMY

EPIDERMIS ➔ Erysipelas, impetigo, eczthyma

DERMIS ➔ Folliculitis, furunculosis, carbunculosis

SUPERFICIAL FASCIA ➔ Cellulitis

SUBCUTANEOUS TISSUE ➔ Necrotizing fasciitis

DEEP FASCIA ➔ Myonecrosis, pyomyositis

MUSCLE ➔ Myonecrosis, pyomyositis
SKIN AND SOFT TISSUE INFECTIONS (SSTI)

SSTIs are classified as **uncomplicated** or **complicated**

**UNCOMPLICATED SSTIs:**
- Includes cellulitis, erysipelas, simple abscesses, impetigo, eczema, folliculitis, furuncle, carbuncle
- Superficial infections

**TREATMENT:**
- Empiric antibiotic therapy according to likely pathogen and local resistance patterns
- Surgical drainage of abscess

**RISK:**
- Low risk for life- or limb-threatening infection
SKIN AND SOFT TISSUE INFECTIONS

COMPLICATED SSTIs:
- Includes NSTIs, complicated abscesses, infected burn wound, infected ulcers, infection with significant underlying disease state that complicates response to treatment (e.g. DM)
- Deep infections

TREATMENT:
- Broad-spectrum empiric antibiotic therapy
- Surgical drainage of abscess or debridement
- Hospitalization

RISK:
- High risk for life- or limb-threatening infections
SKIN AND SOFT TISSUE INFECTIONS

- Infected Ulcer
- Hand NSTI
- Diabetic Ulcer
- Burn Wound
NECROTIZING SOFT TISSUE INFECTIONS

- Term encompassing all forms of necrotizing infection of skin and soft tissues\(^4\)
  - Necrotizing cellulitis = involvement of dermal + SC layers
  - Necrotizing fasciitis = involvement of fascia
  - Pyomyositis, myonecrosis = involvement of muscle
  - Any combination of the above

All NSTIs involve a similar approach to diagnosis & treatment\(^{13}\)

NSTIs *by definition* include the presence of necrotic/devitalized tissue as part of the pathophysiology\(^9\)

Necrotic tissue provides a growth medium for bacteria and precludes delivery of host defence mechanisms and antimicrobial agents\(^9\)
NECROTIZING FASCIITIS

- Necrotizing infection involving the...
  - Superficial fascia + subcutaneous tissue + deep fascia

- Necrotizing fasciitis is far more common than other NSTIs

Infection can spread widely across the fascial planes with minimal involvement of surrounding skin or muscle.

Blood supply to the fascia is typically more tenuous than that of muscle or healthy skin.
EPIDEMIOLOGY AND CLASSIFICATION

EPIDEMIOLOGY:
- Incidence = 0.04/1000 person-years\textsuperscript{13}
- Affects persons of all ages, of all health status

CLASSIFICATION:
- NSTIs can be classified based on\textsuperscript{13}:
  - **Anatomy** (e.g. perineum and scrotum)
  - **Depth of infection** (e.g. to deep fascia)
  - **Microbial source of infection** (e.g. Type I)
- Classification by anatomy and depth is more useful for research purposes\textsuperscript{13}
- Classification by microbial source may be useful for assessing risk
CLASSIFICATION: TYPE 1

- **Polymicrobial infections**

- **Most common** (55-75% of all NTSIs)

- Average of 4.4 different organisms in wounds
  - Mix of gram-positive cocci, gram-negative rods, and anaerobes
  - Uncommon = bacteroides, clostridium
  - Rare = *C. perfringens, C. septicum*

- Tend to occur in the **perineal** and **trunk** areas
  - Reflects normal flora of those areas

- Often diagnosed in patients who are **immunocompromised** or have chronic disease
CLASSIFICATION: TYPE 2

- **Monomicrobial** infections\(^1\)
- Incidence: Type 2 << Type 1 infections
- Common organisms involved = *S. pyogenes* (GAS) *S. aureus* (including CA-MRSA)
- Severity: Type 2 > Type 1\(^9\)
- Might be associated with **toxic shock syndrome**
- Tends to occur in the **extremities**
- Often diagnosed in otherwise healthy, young, **immunocompetent** hosts
CLASSIFICATION: TYPE 3

- Infection caused by *Vibrio vulnificus*\textsuperscript{13}
- Least common type
- Due to a break in the skin barrier and exposure to sea water, shell fish, or oysters
- Often diagnosed in patients who are immunocompromised or have hepatic disease, DM\textsuperscript{10}
- Associated with a fulminant course, multi-system organ failure will develop within 24h
ETIOLOGY

RISK FACTORS ²,¹¹

- Diabetes mellitus
- Peripheral vascular disease
- Intravenous drug use
- Smoking
- Immunocompromised state
- Chronic illness
- Varicella infection
- Renal failure
- Malnutrition

INITIATING FACTORS ³,¹¹

- Minor trauma
- Operative wound
- Intravenous drug use
- Penetrating injuries
- Decubitus ulcer
- Burns
- Childbirth

NECROTIZING SOFT TISSUE INFECTION
Infection spreads rapidly in tissues (e.g. along fascia in NF)

Bacterial toxins cause inflammation of the walls of the regional blood vessels, resulting in vascular thrombosis

Ischemic environment promotes further spread of bacterial growth

Ischemia and necrosis develops in tissues supplied by the thromboosed vessels

Initial monomicrobial or polymicrobial invasion
CLINICAL PRESENTATION

EARLIER FINDINGS

- Erythema
- Pain/tenderness beyond erythema
- Swelling/edema
- Warmth
- Induration
- Fluctuance
- Fever, chills
- Lack of lymphangitis

Table 3. Symptoms/Signs Associated with Necrotizing Soft-Tissue Infection at the Time of Admission

<table>
<thead>
<tr>
<th>Finding</th>
<th>Percent of patients (n = 89)</th>
<th>Percent of patients (n = 192)</th>
<th>Percent of patients (n = 22)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythema</td>
<td>100</td>
<td>66</td>
<td>95</td>
</tr>
<tr>
<td>Pain or tenderness beyond margins of erythema</td>
<td>98</td>
<td>73</td>
<td>95</td>
</tr>
<tr>
<td>Swelling</td>
<td>92</td>
<td>75</td>
<td>86</td>
</tr>
</tbody>
</table>
Tend to be more specific for NSTIs, but may be present in < 50% of patients

- Skin ecchymosis/ necrosis\(^4\) (skin appears brown-to-bluish)
- Vesicles/bullae serosanguineous foul-smelling exudate
- Gas in the tissues (usually suggests clostridial involvement)
  - Crepitus or on radiographs
- Cutaneous anesthesia\(^4\)
- Shock/tachycardia/hypoTN <90mmHg\(^{10}\)
- Altered mental status
- Pain out of proportion to physical examination\(^6\)
Radiographic testing may help with diagnosis in cases of uncertainty.

Evidence to date\textsuperscript{13}:
- No studies comparing the various modalities
- All modalities either have a:
  - Low sensitivity to detect NSTI early or
  - Low specificity to diagnose it reliably

In reality, clinical judgement is MOST important
- Radiographic testing may actually delay diagnosis & treatment\textsuperscript{15}
**X-RAYS:**\textsuperscript{11,13}
- Can show subcutaneous gas (SC emphysema) or soft-tissue swelling, but cannot show deeper fascial gas
  - SC emphysema: specific, but not sensitive

**CT SCAN:**\textsuperscript{11,13}
- Can reveal deep fascial edema or abscesses as well as gas formation
  - More sensitive, but less specific
DIAGNOSTIC TESTS
RADIOGRAPHIC TESTING

**MRI**:\(^{11,13}\)
- Can show soft tissue or fascial edema
  - High sensitivity, but low specificity

**U/S**:\(^{11,13}\)
- Can be used to detect superficial abscesses
  - Neither sufficiently sensitive or specific
DIAGNOSTIC TESTS
LABORATORY TESTING

STANDARD TESTS:
- CBC + differential, electrolytes, LFTs, coagulation studies, ABG

TISSUE BIOPSY:
- Bedside biopsies (extending down to the deep fascial layer) sent for rapid frozen section
  - Do not biopsy blister or skin surface cultures

SCORING SYSTEMS:
- Recently, two scoring systems based on laboratory studies have been described to help with NSTI diagnosis
DIAGNOSTIC TESTS
LABORATORY TESTING

- Wall et al. (2000)\textsuperscript{16}
  - On hospital admission:
    1. WBC count > 15,400 cells/mm$^3$ or
    2. Na$^+$ level < 135 mmol/L
  - 80% PPV and NPV for NSTI

- Wong et al. (2004)\textsuperscript{17}
  - Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score
    1. 92% PPV and 96% NPV for NSTI (score $\geq$ 6)
    2. Has been validated by several cohort studies

Table 4. Laboratory risk indicator for NF: A score of $\leq$ 5 points indicates a low risk ($<50\%$ probability) of NF; 6-7 points indicate an intermediate risk ($50\%$-$75\%$ probability) of NF; 8 points or more indicate a high risk ($>75\%$ probability) of NF.

<table>
<thead>
<tr>
<th>INVESTIGATION</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum C-reactive protein $\geq$ 150 mg/L</td>
<td>4 points</td>
</tr>
<tr>
<td>White blood cell count</td>
<td></td>
</tr>
<tr>
<td>• 15,000/µL-25,000/µL</td>
<td>1 point</td>
</tr>
<tr>
<td>• $&gt;25,000/µL</td>
<td>2 points</td>
</tr>
<tr>
<td>Hemoglobin</td>
<td></td>
</tr>
<tr>
<td>• 11.0-13.5 g/dL</td>
<td>1 point</td>
</tr>
<tr>
<td>• $&lt;11$ g/dL</td>
<td>2 points</td>
</tr>
<tr>
<td>Serum sodium $&lt;135$ mEq/L</td>
<td>2 points</td>
</tr>
<tr>
<td>Serum creatinine $&gt;1.6$ mg/dL (141 mmol/L)</td>
<td>2 points</td>
</tr>
<tr>
<td>Serum glucose $&gt;180$ mg/dL (10 mmol/L)</td>
<td>1 point</td>
</tr>
</tbody>
</table>

NF—necrotizing fasciitis.
Data from Anaya and Dellinger\textsuperscript{8} and Wong et al.\textsuperscript{22}
DIAGNOSTIC TESTS
OPERATIVE EXAMINATION

- Gold standard for diagnosis

- A small, exploratory incision is made in an area of maximum suspicion\(^1\)

- Can obtain intra-operative biopsy with Gram stain

- C+S of blood and tissue specimens establishes definitive bacteriologic diagnosis\(^1\)

Operative findings suggestive of NSTI:
- “dishwater” brownish exudate or foul-smelling discharge
- Necrosis or lack of bleeding
- Swollen fascia that is dull grey in appearance
- Positive finger test\(^6\)
DIAGNOSTIC TESTS
THE FINGER TEST

A finger is placed superior to the deep fascia and pushed superiorly

Positive test:
Soft tissue **dissects** from the fascia without difficulty

Negative test:
Subcutaneous fat **adheres** strongly to the deep fascia
MANAGEMENT
GENERAL SUPPORTIVE MEASURES

- Fluid and blood resuscitation
- Placement of a central venous catheter
- Maintain adequate oxygenation
- Treatment of any underlying diseases
- Attention to patient’s nutritional needs
  - TPN/EN is required postoperatively to meet the dramatically ↑ nitrogen requirement associated with tissue repair, hyperthermia, sepsis, and vital organ requirements⁴
MANAGEMENT
ANTIBIOTIC THERAPY

- Important to initiate **early and appropriate** empiric antimicrobial therapy\(^{10}\)

- **Evidence to date:**\(^{4,13}\)
  - Inadequate data to support the use of any one antimicrobial regimen over another

**General principles of antibiotic therapy:**
- Blood cultures should be obtained *before* starting antimicrobial therapy\(^{10}\)
- Patients generally require a 10-14 day course
- De-escalation of antimicrobial therapy should occur as early as possible\(^{10}\)
# Management

## Empiric Antibiotic Therapy

<table>
<thead>
<tr>
<th>Type</th>
<th>Traditional</th>
<th>Currently Recommended</th>
<th>For MRSA coverage:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive</td>
<td>Penicillin G</td>
<td>Vancomycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cefalexin</td>
<td>Linezolid</td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>If allergic to penicillin:</em></td>
<td>Daptomycin</td>
<td>Quinupristin/daptomycin</td>
</tr>
<tr>
<td></td>
<td>Vancomycin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ciprofloxacin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gram-negative</td>
<td>Gentamycin</td>
<td>Gentamycin</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ceftriaxone</td>
<td>Ceftriaxone</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Ciprofloxacin</td>
<td>Tetracycline</td>
</tr>
<tr>
<td>Anaerobic</td>
<td>Clindamycin</td>
<td>Clindamycin</td>
<td>Metronidazole</td>
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</tbody>
</table>
TOXIC SHOCK SYNDROME

- Skin rash, shock, hypotension, coagulopathy, organ failure, and NSTI\textsuperscript{10}
- Commonly affects patients with streptococcal staphylococcal infections
- Due to the substantial release of both bacterial-derived toxin and endogenous cytokines, which results in a massive systemic inflammatory response
- Requires aggressive antimicrobial therapy
- Usually requires hospitalization
MANAGEMENT
IV IMMUNE GLOBULIN THERAPY

- IV IG = concentrated pooled product containing IgG isotypes from human donors

- Proposed mechanism -> IG binds staphylococcal- and streptococcal-derived exotoxin, thereby limiting the systemic cytokine surge associated with SIRS

- Suggested dose: 0.2-2g/kg/d for 1-5d
- May be useful in streptococcal/staphylococcal TSS

- **Evidence to date:**
  - Use and efficacy remain controversial
  - Clinical studies (not RCTs however) show evidence of improved outcomes with treatment
Best method of prompt reduction of bacterial inoculum at the infection site

Surgical debridement should be considered if:
- There is no response to abx after a reasonable trial
- Operative findings are positive

There are no established definitions to describe what constitutes delayed or inadequate initial debridement

Evidence to date:
- Timing & adequacy of initial debridement is the most important determinant of mortality
  - Delay of >24 hrs after admission is associated with ↑↑ in mortality
SURGICAL DEBRIDEMENT

TECHNICAL ISSUES

(I) EXTENT OF RESECTION:
- Based on clinical judgement and gross appearance of tissues
- Debride nonviable tissue back to bleeding wound margins
- May require full-thickness excisions

(II) SERIAL DEBRIDEMENTS:
- The infection is rarely eradicated after a single debridement
- Recommended to return to the OR within 24h to ensure adequacy of debridement and lack of progression
- Average number of operative procedures is 3-4/patient
SURGICAL DEBRIDEMENT
TECHNICAL ISSUES

(III) PERINEAL/PERIANAL/PERISCROTAL DEBRIDEMENTS:
- May require temporary diverting colostomy⁴ to facilitate wound hygiene, and protect any reconstructive skin graft/flap
- After scrotal resection, the testes can be placed in pockets in the medial aspect of the thighs, where they can be kept indefinitely
  - Surgical castration is rarely needed

(IV) AMPUTATION:
- Consider if the infection is rapidly spreading towards the torso despite aggressive intervention, or has rendered most muscle groups necrotic
MANAGEMENT
HYPERBARIC OXYGEN THERAPY

- Delivery of 100% O₂ at 2-3x atmospheric pressure resulting in ↑ PₐO₂ and P₇O₂ relative to normal inhalation of 10% O₂¹³

- Suggested doses: 30-90 minutes TID/QID
- No consensus on end point of therapy

**Evidence to date:**¹³
- Role in NSTI remains controversial
- No RCTs have been performed¹⁰
- George et al. (2009)⁸:
  - HBO did NOT ↓ mortality rate, # of debridements, hospital LOS, or duration of antibiotic use
MANAGEMENT
DRESSINGS

- The wound should be left open and treated with wet-to-dry dressings initially.

- Silver sulfadiazine cream is excellent for local antibiotic effect and to keep exposed tendons from desiccating.

- Frequent dressing changes are continued until healthy granulation tissue appears.

- Careful and regular inspection of the wound is necessary.
Vacuum-assisted wound-closure therapy (VAC) may be useful in patients with large wounds, in which wound dressing changes are difficult\textsuperscript{10}.

**Evidence to date:**\textsuperscript{13}
- ↓ time for wound care and closure\textsuperscript{10}
- ↓ drainage\textsuperscript{10}
- ↑ patient comfort, greater mobility\textsuperscript{10}
- No RCTs comparing VAC therapy with traditional wet dressing techniques
PROGNOSIS

- Mortality associated with NTSI is 25-35%\textsuperscript{13}
- Overall mortality in 67 studies of NSTI (3302 patients) was 23.5%\textsuperscript{9}
- Mortality α increases with time to intervention\textsuperscript{13} and depth of infection
- Patients not succumbing to NSTI have a very high morbidity:
  - Elliot et al. (1996)\textsuperscript{5} reported 82% morbidity among 198 patients
- Anaya et al. (2005)\textsuperscript{2} reported amputation rate of approximately 15%\textsuperscript{13}
VARIABLES ASSOCIATED WITH MORTALITY IN NECROTIZING SOFT TISSUE INFECTION

Timing to operative intervention
Age older than 60 years
Number of comorbidities
Diabetes mellitus
Shock of admission
Acute renal failure
Coagulopathy or acidosis on admission
Clostridial or group A streptococcal infection
*Vibrio vulnificus* infection
Admission white blood cell count >30 cells/mm³
Admission serum creatinine > mg/dL

REFERENCES


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