

## Chapter 10

# Infections

### Introduction

**All wounds incurred on the battlefield are grossly contaminated with bacteria. Most will become infected unless appropriate treatment is initiated quickly.**

The battlefield environment is conducive to wound infection due to

- Absence of “sterile” wounding agents on the battlefield. All foreign bodies (wounding projectile fragments, clothing, dirt) are contaminated with bacteria.
- High-energy projectile wounding (devitalized tissue, hematoma, tissue ischemia).
- Delay in casualty evacuation.

### Diagnosis of a Wound Infection

- The four “-ors:” dolor, rubor, calor, and tumor—**pain and tenderness, redness, warmth, and swelling.**
- Drainage or discharge, ranging from frank pus to the foul “dishwater” discharge of clostridial infection.
- Crepitus, radiographic evidence of soft-tissue gas, epidermal blistering, and/or epidermal necrosis are the hallmarks of necrotizing soft tissue infection, such as clostridial gas gangrene or necrotizing fasciitis.
- Systemic effects such as fever, leukocytosis, unexplained tachycardia, or hypotension.
- Confirm diagnosis by Gram stain and culture, if available, and/or tissue biopsy.

### Common Microorganisms Causing Battlefield Infections

- Gram-positive cocci: staphylococci, streptococci, and enterococci.
- Gram-negative rods: *Escherichia Coli*, *Proteus*, and *Klebsiella*.
  - *Pseudomonas*, *Enterobacter*, *Acinetobacter*, and *Serratia* are common nosocomial pathogens usually expected among casualties who have been hospitalized for an extended period, not those fresh off the battlefield.
- *Salmonella*, *Shigella*, and *Vibrio* should be suspected in cases of bacterial dysentery.
- Anaerobic Gram-positive and Gram-negative rods: *Clostridia*, *Bacteroides*, and *Prevotella* species.
- Fungal species: *Candida* species should be suspected in casualties hospitalized for prolonged periods, those malnourished or immunosuppressed, or those who have received broad spectrum antibiotics, adrenocortical steroids, or parenteral nutrition. Empiric therapy should be considered in appropriate patients with presumptive evidence of fungal infection.

**The greatest threat of infection to the wounded battlefield casualty is the development of clostridial myonecrosis (gas gangrene), commonly due to *Clostridium perfringens*.**

### Common Patterns of Infection

- **Skin, soft tissue, muscle, and bone:** Primarily due to staphylococcal, streptococcal, and clostridial species. These infections include wound abscess, cellulitis, septic arthritis, osteomyelitis, necrotizing fasciitis, and gas gangrene.

***Clostridium tetani* can enter through any wound—even minor burns and corneal abrasions. Prophylaxis is required to prevent tetanus toxemia.**

- **Intracranial:** Meningitis, encephalitis, and abscess, commonly due to staphylococci and Gram-negative rods, which are difficult to treat due to the impervious nature of the meninges to common antibiotics.

- **Orofacial and neck:** Gram-positive cocci and mouth anaerobes, generally responsive to surgery and clindamycin.
- **Thoracic cavity:** Empyema (usually staphylococcal) and pneumonia (*Staphylococcus*, *Streptococcus*, *Pseudomonas*), especially among those on prolonged mechanical ventilation or those casualties prone to aspiration (polymicrobial).
- **Intraabdominal:** Include posttraumatic or post-operative abscess, and peritonitis due to *Enterococcus*, Gram-negative rods, and anaerobic bacilli. *Clostridium difficile* is often responsible for a potentially severe diarrheal colitis that occurs following the administration of even one dose of antibiotic.
- **Systemic sepsis:** A syndrome caused by a bloodborne or severe regional infection resulting in a global inflammatory response (fever, leukocytosis, tachycardia, tachypnea, and possibly hypotension).
  - A similar inflammatory response without infection can be caused by a focus of retained necrotic tissue, or the mere act of sustaining severe trauma.
  - Culprit microorganisms will not be recovered in all cases of sepsis syndrome.
  - Although typically associated with Gram-negative organisms, any bacterial or fungal agent can cause sepsis.

**Prompt surgical debridement is the cornerstone of prophylaxis/treatment of war wound infections.**

## Treatment

### General Principles

- Surgical and antibiotic treatment should begin early and be repeated in the prophylaxis of war wound infection.
- Optimally, surgical debridement should be achieved within 6 hours of injury.
- Following initial exploration and debridement, the wound should be sufficiently irrigated to ensure all dead material, bacterial contamination, and foreign material has been washed from the wound.

- Excessive irrigation, especially under pressure, should be avoided, because this can dilute the body's natural immune cellular defenses and contribute to bacteremia.
- The skin is left open, and a lightly moistened sterile gauze dressing is applied.
- Antibiotics should be started ASAP after wounding, then continued for 24 hours, depending on the size, extent of destruction, and degree of contamination of the wound.
  - If time from wounding to initiation of antibiotics is > 6 hours, or time from wounding to surgery is > 12 hours, give antibiotics using regimen for established infection.
- The choice of empiric antibiotic is dependent on the part of the body injured (Table 10-1).
- Once a battlefield wound has become infected, treatment is two-fold—surgical and medical.
  - Surgical strategy remains the same: Open the wound, remove infected and necrotic tissue, and inspect for foreign material.
  - Drainage is generally employed in abscess cavities to prevent premature closure and reformation.
  - Empiric broad-spectrum antibiotic therapy is initiated against likely pathogens and continued for 7 to 10 days.
  - Ideally, obtain cultures and tailor therapy to cover the actual pathogens recovered on Gram stain and culture. Routine bacteriology is often not available in forward medical facilities.
  - Because *Bacteroides* and *Clostridia* are difficult to culture, tailor antibiotic therapy to cover these organisms.
  - If the debrided wound still has possibly ischemic tissue or retained foreign material, the patient is returned to the OR every 1 to 2 days for redebridement, until absolute assurance of healthy, clean tissue is achieved.

### Specific Infections

- Tetanus.
  - Battlefield wounds are “tetanus-prone” due to high levels of contamination with *Clostridium tetani*.
  - Bacteria grow anaerobically and release a CNS toxin that results in muscle spasm, trismus, neck rigidity, and back arching.

Table 10-1. Empiric Antibiotic Coverage for War Injuries.

Site of Injury	Empiric Antibiotic	Covered Organisms
<b>Cranium/penetrating injury</b>	Ancef/Vanc + Flagyl	Gram positives + anaerobes
<b>Maxillofacial</b>	brain injury	
<b>Neck</b>	Ancef + clindamycin	Gram positives + anaerobes
<b>Chest</b>	Ancef	Skin flora
<b>Abdomen</b>	Ancef	Skin flora
<b>Liver</b>	Fluoroquinolone/2nd generation cephalosporin	Gram negatives, gram positives, + anaerobes
<b>Gastrointestinal tract</b>	Carbapenam/penicillin (Zosyn) with gross contamination	"
<b>Gastrointestinal tract</b>	2nd generation cephalosporin without gross contamination	"
<b>Genitourinary</b>	Aminoglycoside + 2nd generation cephalosporin	"
<b>Spleen</b>	2nd generation cephalosporin + fluoroquinolone + immunize splenectomy patients later for encapsulated organisms	"
<b>Pelvic</b>		
With gastrointestinal injury	Carbapenam or combo penicillin	Gut flora + anaerobes
No gastrointestinal injury	2nd generation cephalosporin	Skin organisms
<b>Extremity</b>		
Soft tissue only	Ancef or 2nd generation cephalosporin + aminoglycoside	
Bone /vascular involvement	2nd generation cephalosporin + aminoglycoside and fluoroquinolone	

Treat gross contamination of any wound with debris from uniforms and the environment with broad spectrum Gram-negative and anaerobic coverage regardless of area of injury, eg, Ancef + penicillin + gentamicin; or Unasyn alone.



- o **In addition to surgical debridement of war wounds, additional prophylactic measures for tetanus-prone wounds include**
  - ◆ Administration of 0.5m L IM of **tetanus toxoid** if prior tetanus immunization is uncertain, less than three doses, or more than five years since last dose.
  - ◆ Administration of 250–500 units IM of **tetanus immune globulin** in a separate syringe and at a separate site from the toxoid if prior tetanus immunization is uncertain or less than three doses.
- o Treatment for established tetanus includes
  - ◆ IV antibiotics (penicillin G, 24 million U/d; or doxycycline, 100 mg bid; or metronidazole, 500 mg q6h for 7 days).
  - ◆ Tetanus immune globulin.
  - ◆ Wound debridement as needed.
  - ◆ IV diazepam to ameliorate the muscle spasm.
  - ◆ Place patient in a dark, quiet room free of extraneous stimulation.
  - ◆ May warrant endotracheal intubation, mechanical ventilation, and neuromuscular blockade.
- **Soft-tissue infections.**
  - o **Cellulitis** is manifested by localized skin erythema, heat, tenderness, and swelling or induration.
    - ◆ Treatment: IV antibiotics against streptococcal and staphylococcal species (IV nafcillin, cefazolin or, in the penicillin-allergic patient, clindamycin or vancomycin).
  - o **Post-operative wound infections** become evident by wound pain, redness, swelling, warmth, and/or foul or purulent discharge, with fever and/or leukocytosis.
    - ◆ Treatment: **Open the wound**, drain the infected fluid, and debride any necrotic tissue present.
    - ◆ The wound is left open and allowed to close via secondary intention.
  - o **Necrotizing soft tissue infections** are the most dreaded infections resulting from battlefield wounding. These include **clostridial myonecrosis (gas gangrene)** and **polymicrobial infections** caused by *Streptococcus*, *Staphylococcus*, *Enterococcus*, *Enterobacteriaceae*, *Bacteroides*, and *Clostridia*.

- ◆ The organisms create a rapidly advancing infection within the **subcutaneous tissues** and/or **muscle** by producing exotoxins that lead to bacteremia, toxemia, and septic shock.
- ◆ **All layers of soft tissue can be involved**, including skin (blistering and necrosis), subcutaneous tissue (panniculitis), fascia (fasciitis), and muscle.
- ◆ Clinical manifestations begin locally with severe pain, crepitus, and with clostridia, a thin, brown, foul-smelling discharge.
- ◆ The skin may be tense and shiny, showing pallor or a bronze color.
- ◆ Systemic signs include fever, leukocytosis, mental obtundation, hemolytic anemia, and hypotension, progressing rapidly to multiple organ failure and death in untreated or under-treated cases.
- ◆ The diagnosis is made by history of severe unexpected wound pain combined with palpable or radiographic soft tissue gas (air in subcutaneous tissue and/or muscle).
- ◆ Absence of soft-tissue gas does not exclude diagnosis of necrotizing infection.
- ◆ **Treatment is surgical**, including early, comprehensive, and repeated (every 24–48 hours) debridement of all dead and infected tissue, combined with **antibiotics**.
- ◆ **Excision** of affected tissue must be as radical as necessary (including amputation or disarticulation) to remove all muscle that is discolored, noncontractile, nonbleeding, or suspicious.
- ◆ Identification of causative organisms often problematic: Treatment must be aimed at all possible organisms.
- ◆ **IV antibiotic therapy.**
- ◆ **Clindamycin**, 900 mg q8h; **plus penicillin G**, 4 million U q4; **plus gentamicin**, 5–7 mg/kg qd.
  - ◇ As a **substitute for clindamycin**: metronidazole, 500 mg q6h.
  - ◇ As a **substitute for penicillin**: ceftriaxone, 2.0 g q12h, or erythromycin 1.0 g q6h.
  - ◇ As a **substitute for gentamicin**: ciprofloxacin, 400 mg q12h.

- ◆ Alternative regimen: penicillin G, 4 million U q4h **plus** imipenem, 500 mg q6h.
- **Intraabdominal infections.**
  - ◆ **Prevention.**
  - ◆ Regimens (start ASAP, continue x **24 hours** post-op).
    - ◇ Single agent: **cefotetan 1.0 g q12h**, or ampicillin/sulbactam, 3 g q6h, or ceftiofloxacin, 1.0 g q8h.
    - ◇ Triple agent: ampicillin 2 g q6h; **plus** anaerobic coverage (metronidazole, 500 mg q6h; or clindamycin, 900 mg q8h); **plus** gentamicin 5–7 mg/kg qd.
  - ◆ **Established** intraabdominal infection (peritonitis or abscess).
  - ◆ Same regimen as above, except continue for 7 to 10 days.
  - ◆ Drain all abscesses.
- **Pulmonary infections.**
  - ◆ **Empyema** (generally Streptococcal) following penetrating thoracic trauma is typically due to contamination from the projectile, chest tubes, or thoracotomy.
  - ◆ Diagnosis: Loculations, air/fluid levels on radiograph, pleural aspirate.
  - ◆ Treatment.
    - ◇ Chest tube initially, and thoracotomy if unsuccessful.
    - ◇ Cefotaxime, or ceftriaxone, or ceftiofloxacin, or imipenem.
  - ◆ **Pneumonia** is most frequently due to aspiration (eg, patients with head injury) and prolonged mechanical ventilation.
  - ◆ The diagnosis is made through radiograph finding of a new pulmonary infiltrate that does not clear with chest physiotherapy, combined with
    - ◇ Fever or leukocytosis.
    - ◇ Sputum analysis showing copious bacteria and leukocytes.
  - ◆ Empiric therapy is directed toward likely pathogens.
    - ◇ **Aspiration:** Streptococcal pneumonia, coliforms, and oral anaerobes are likely. IV antibiotics such as ampicillin/sulbactam, clindamycin, or ceftiofloxacin have proven effective.
    - ◇ **Ventilator-associated pneumonia:** *staphylococcus*, *Pseudomonas*, and other nosocomial *Enterobacteriaceae*. Broad coverage is best with such agents as imipenem,



ciprofloxacin, vancomycin, and/or ceftazidime, plus an aminoglycoside.

### Systemic Sepsis

Sepsis can be defined as infection combined with a prolonged systemic inflammatory response that includes two or more of the following conditions.

- Tachycardia.
- Fever or hypothermia.
- Tachypnea or hyperventilation.
- Leukocytosis or acute leukopenia.

Progression to septic shock is manifest by systemic hypoperfusion: profound hypotension, mental obtundation, or lactic acidosis. Treatment is a three-pronged approach:

- Identify and eradicate the source.
- Broad-spectrum intravenous antibiotics for the most likely pathogens.
- ICU support for failing organ systems, such as cardiovascular collapse, acute renal failure, and respiratory failure.

It is often difficult to identify the source of sepsis, but it is the **most important factor** in determining the outcome. Potential sources of occult infection include

- An undrained collection of pus such as a wound infection, intraabdominal abscess, sinusitis, or perianal abscess.
- Ventilator-associated pneumonia.
- Urinary tract infection.
- Disseminated fungal infection.
- Central intravenous catheter infection.
- Acalculous cholecystitis.

Intensive care support for sepsis involves vigorous resuscitation to restore perfusion to prevent multiple organ dysfunction. This requires optimization of hemodynamic parameters (pulmonary artery occlusion pressure, cardiac output, and oxygen delivery) to reverse anaerobic metabolism and lactic acidosis. Endpoints of resuscitation, such as urine output, base deficit, and blood lactate levels guide successful treatment. Until the source for sepsis is identified and actual pathogens isolated, empiric therapy with broad-spectrum intravenous antibiotics is warranted. Suitable regimens might include

- Imipenem, 500 mg q6h.
- Piperacillin and tazobactam (Zosyn), 3.375 g q6h; or ceftazidime, 2.0 g q8h; or cefepime, 2.0 g q12h; PLUS gentamicin, 5–7 mg/kg qd (based on once-daily dosing strategy and no renal impairment); or ciprofloxacin, 400 mg q12h.
- Addition of vancomycin, 1.0 g q12h if methicillin-resistant *Staphylococcus aureus* is a likely pathogen.
- Addition of linezolid, 600 mg q12h if vancomycin-resistant enterococcus (VRE) is a likely pathogen.

## Conclusion

Battlefield casualties are at high risk for infection. In particular, war wounds are predisposed to infection due to environmental conditions on the battlefield, devitalized tissue, and foreign bodies in the wound. The key to avoiding wound infection is prompt and adequate wound exploration, removal of all foreign material, and excision of all dead tissue. All battlefield wounds and incisions should have the skin left open. Antibiotics play an adjunctive role in the prophylaxis of wound and other infections in the battlefield MTF. Knowledge of likely pathogens for particular infections and sites, as well as optimal antibiotics to eradicate those pathogens (Table 10-2), will aid the battlefield clinician in averting and treating infections.

Table 10-2. Spectrum and Dosage of Selected Antibiotic Agents.

Agent	Antibacterial Spectrum	Dosage
Penicillin G	<i>Streptococcus pyogenes</i> , penicillin-sensitive <i>Streptococcus pneumoniae</i> , clostridial sp	4 mil U IV q4h
Ampicillin	Enterococcal sp, streptococcal sp, <i>Proteus</i> , some <i>E coli</i> , <i>Klebsiella</i>	2 g IV q6h
Ampicillin/sulbactam	Enterococcal sp, streptococcal sp, <i>Staphylococcus</i> , <i>E coli</i> , <i>Proteus</i> , <i>Klebsiella</i> , <i>Clostridial</i> sp, <i>Bacteroides</i> / <i>Prevotella</i> sp	3 g IV q6h
Nafcillin	<i>Staphylococcal</i> sp,* streptococcal sp	1 g IV q4h
Piperacillin/tazobactam	Enterococcal sp, streptococcal sp, <i>Staphylococcus</i> , <i>E coli</i> , <i>Pseudomonas</i> and other enterobacteriaceae, clostridial sp, <i>Bacteroides</i> / <i>Prevotella</i> sp	3.375 g IV q6h
Imipenem	Enterococcal sp, streptococcal sp, <i>Staphylococcus</i> , <i>E coli</i> , <i>Pseudomonas</i> and other enterobacteriaceae, clostridial sp, <i>Bacteroides</i> / <i>Prevotella</i> sp	500 mg IV q6h
Cefazolin	<i>Staphylococcal</i> sp,* streptococcal sp, <i>E coli</i> , <i>Klebsiella</i> , <i>Proteus</i>	1.0 g IV q8h
Cefoxitin	<i>Staphylococcal</i> sp,* streptococcal sp, <i>E coli</i> and similar enterobacteriaceae, clostridial sp, <i>Bacteroides</i> / <i>Prevotella</i> sp	1.0 g IV q6h
Ceftazidime	Streptococcal sp, <i>E coli</i> , <i>Pseudomonas</i> and other enterobacteriaceae	2.0 g q8h
Ceftriaxone	Streptococcal sp, <i>staphylococcal</i> sp,* <i>Neisseria</i> sp, <i>E coli</i> and most enterobacteriaceae (NOT <i>Pseudomonas</i> ), clostridial sp	2.0 g q12h
Ciprofloxacin	<i>E coli</i> , <i>Pseudomonas</i> and other enterobacteriaceae	400 mg q12h
Gentamycin	<i>E coli</i> , <i>Pseudomonas</i> and other enterobacteriaceae	5–7 mg/kg qd (based on once-daily dosing strategy and no renal impairment)
Vancomycin	Streptococcal, enterococcal, and <i>staphylococcal</i> species (including MRSA; not VRE)	1.0 g q12h
Erythromycin	Streptococcal sp, clostridial sp	0.5–1.0 g q6h
Clindamycin	<i>Streptococcus</i> sp, <i>Staphylococcus</i> sp,* clostridial sp, <i>Bacteroides</i> , and <i>Prevotella</i> sp	900 mg q8h
Metronidazole	Clostridial sp, <i>Bacteroides</i> and <i>Prevotella</i> sp	500 mg q6h

\*Not methicillin resistant *Staphylococcus aureus* (MRSA)

Dosage and dosage intervals are average recommendations. Individual dosing may vary.