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 the:

- 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, and
  - tissue ischemia.
- Delay in casualty evacuation.

Diagnosis of a Wound Infection

- The four "-**or**'s": 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 (eg, clostridial gas gangrene or necrotizing fasciitis).
- Systemic effects: 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.

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

- **Orofacial and neck:** Gram-positive cocci and mouth anaerobes are generally responsive to surgery and clindamycin.
- **Thoracic cavity:** Empyema (usually staphylococcal) and pneumonia (*Staphylococcus*, *Streptococcus*, and *Pseudomonas*), especially among those on prolonged mechanical ventilation or those casualties prone to aspiration (polymicrobial).
- **Intraabdominal:** Include posttraumatic or postoperative 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 source control, including debridement and drainage, are the cornerstones of prophylaxis/treatment of all war wound infections.

Treatment

General Principles

- Surgical and antibiotic treatment should begin as early as possible, ideally within 3 hours after injury 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 that all dead material, bacterial contamination, and foreign material have been washed from the wound.

Table 10-1. Recommendations to Prevent Infections Associated With Combat-Related Injuries Based on Level of Care

Level of Care*	Care Category	Recommendations
Role 1 field	Initial care in the field	Bandage wounds with sterile dressings (avoid pressure over eye wounds) Stabilize fractures Transfer to surgical support as soon as feasible
	Postinjury antimicrobials	Provide single-dose point-of-injury antimicrobials if evacuation delayed or expected to be delayed
Role 1 treatment facility/Role 2 without surgical support	Postinjury antimicrobials	Provide IV antimicrobials as soon as possible (within 3 h) Provide tetanus toxoid and immune globulin as appropriate Enhance gram-negative coverage with aminoglycoside or fluoroquinolone not recommended Addition of penicillin to prevent clostridial gangrene or streptococcal infection not recommended Redose antimicrobials if large volume of blood produces resuscitation Use only topical antimicrobials for burns
	Debridement and irrigation	Irrigate wounds to remove gross contamination with normal saline, sterile, or potable water, under low pressure (bulb syringe or equivalent) without additives Do not attempt to remove retained deep soft-tissue fragments if criteria met;† provide Cefazolin 2 g IV × 1 dose
Role 2 with surgical support and Role 3	Postinjury antimicrobials	Provide IV antimicrobials as soon as possible (within 3 h) Provide tetanus toxoid and immune globulin as appropriate Enhance gram-negative coverage with aminoglycoside or fluoroquinolone not recommended Addition of penicillin to prevent clostridial gangrene or streptococcal infection not recommended

(**Table 10-1** *continues*)

Table 10-1 *continued*

Level of Care*	Care Category	Recommendations
		Redose antimicrobials if large volume of blood produces resuscitation Use only topical antimicrobials for burns Antimicrobial beads or pouches may be used Provide postsplenectomy immunizations if indicated
	Debridement and irrigation	Irrigate wounds to remove contamination with normal saline or sterile water, under low pressure (5–10 PSI; eg, bulb syringe or gravity flow) without additives (use 3 L for each type I, 6 L for each type II, and 9 L for each type III extremity fractures) Do not attempt to remove retained deep soft-tissue fragments if criteria met;† provide Cefazolin 2 g IV × 1 dose Do not obtain cultures unless infection suspected
	Surgical wound management	Surgical evaluation as soon as possible Only dural and facial wounds should undergo primary closure NPWT can be used External fixation (temporary spanning) of femur/tibia fractures External fixation (temporary spanning) or splint immobilization of open humerus/forearm fractures
Role 4	Postinjury antimicrobials	Complete course of postinjury antimicrobials Antimicrobial beads or pouches may be used Provide postsplenectomy immunizations if indicated
	Debridement and irrigation	Irrigate wounds to remove contamination with normal saline or sterile water, under low pressure (5–10 PSI; eg, bulb syringe or gravity flow) without additives (use 3 L for each type I, 6 L for each type II, and 9 L for each type III extremity fractures)

(**Table 10-1** *continues*)

Table 10-1 *continued*

Level of Care*	Care Category	Recommendations
		Do not attempt to remove retained deep soft-tissue fragments if criteria met;† provide Cefazolin 2 g IV × 1 dose
		Do not obtain cultures unless infection suspected
		Surgical wound management
		Wounds should not be closed until 3–5 d postinjury
		Only dural and facial wounds should undergo primary closure
		NPWT can be used
		External fixation (temporary spanning) of femur/tibia fractures
		External fixation (temporary spanning) or splint immobilization of open humerus/forearm fractures

IV: intravenous; NPWT: negative pressure wound therapy; PSI: pounds per square inch.

*Role of care, level of care, and echelon of care are considered synonymous with **role**, currently the preferred US military term. **Role 1**—self-aid, buddy aid, combat lifesaver, and combat medic/corpsman care at the point-of-injury; physician/physician assistant care at battalion aid station (US Army) or shock trauma platoon (US Marine Corps [USMC]); no patient holding capacity. **Role 2**—medical company (includes forward support medical company, main support medical company, and area support medical company in US Army) or expeditionary medical support (US Air Force [USAF]); 72-h patient holding capacity, basic blood transfusion, radiography, and laboratory support. May be supplemented with surgical assets (Level 2b) (forward surgical team, US Army; mobile field surgical team, USAF; forward resuscitative surgical system, USMC). **Role 3**—combat support hospital (US Army), Air Force theater hospital (USAF), or casualty receiving ships (US Navy); full inpatient capacity with intensive care units and operating rooms. **Role 4**—regional hospital (Landstuhl Regional Medical Center, Germany) or US naval hospital ships, typically outside of the combat zone; general and specialized inpatient medical and surgical care. **Role 5**—care facilities within the United States, typically tertiary care medical centers.

†Criteria for allowing retained fragments to remain behind: entry/exit wounds <2 cm; no bone, joint, vascular, and body cavity involvement; no high-risk etiology (eg, mine); no obvious infection; and assessible by X-ray.

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Table 10-2. Postinjury Antimicrobial Agent Selection and Duration Based Upon Injury Pattern*

Injury	Preferred Agent(s)	Alternate Agent(s)	Duration
Extremity wounds (include skin, soft tissue, and bone)			
Skin, soft tissue, no open fractures	Cefazolin 2 g IV q6–8h[†,‡]	Clindamycin (300–450 mg PO TID or 600 mg IV q8h)	1–3 d
Skin, soft tissue, with open fractures, exposed bone, or open joints	Cefazolin 2 g IV q6–8h[†,‡,§]	Clindamycin 600 mg IV q8h	1–3 d
Thoracic wounds			
Penetrating chest injury without esophageal disruption	Cefazolin 2 g IV q6–8h[†,‡]	Clindamycin (300–450 mg PO TID or 600 mg IV q8h)	1 d
Penetrating chest injury with esophageal disruption	Cefazolin 2 g IV q6–8h[†,‡] + metronidazole 500 mg IV q8–12h	Ertapenem 1 g IV × 1 dose or moxifloxacin 400 mg IV × 1 dose	1 d after definitive washout
Abdominal wounds			
Penetrating abdominal injury with suspected/known hollow viscus injury and soilage; may apply to rectal/perineal injuries as well	Cefazolin 2 g IV q6–8h[†,‡] + metronidazole 500 mg IV q8–12h	Ertapenem 1 g IV × 1 dose or moxifloxacin 400 mg IV × 1 dose	1 d after definitive washout
Maxillofacial and neck wounds			
Open maxillofacial fractures, or maxillofacial fractures with foreign body or fixation device	Cefazolin 2 g IV q6–8h[†,‡]	Clindamycin 600 mg IV q8h	1 d

(**Table 10-2** *continues*)

Table 10-2 *continued*

Injury	Preferred Agent(s)	Alternate Agent(s)	Duration
Central nervous system wounds			
Penetrating brain injury	Cefazolin 2 g IV q6–8h[†,‡]; consider adding metronidazole 500 mg IV q8–12h if gross contamination with organic debris	Ceftriaxone 2 g IV q24h; consider adding metronidazole 500 mg IV q8–12h if gross contamination with organic debris; for penicillin allergic patients, vancomycin 1 g IV q12h + ciprofloxacin 400 mg IV q8–12h	5 d or until CSF leak is closed, whichever is longer
Penetrating spinal cord injury	Cefazolin 2 g IV q6–8h[†,‡]; **ADD** metronidazole 500 mg IV q8–12h if abdominal cavity is involved	As above; **ADD** metronidazole 500 mg IV q8–12h if abdominal cavity is involved	5 d or until CSF leak is closed, whichever is longer
Eye wounds			
Eye injury, burn, or abrasion	Topical: Erythromycin or Bacitracin ophthalmic ointment QID and PRN for symptomatic relief Systemic: No systemic treatment required	Fluoroquinolone 1 drop QID	Until epithelium healed (no fluorescein staining)
Eye injury, penetrating	Levofloxacin 500 mg IV/PO once daily; before primary repair, no topical agents should be used unless directed by ophthalmology		7 d or until evaluated by a retinal specialist

(**Table 10-2** *continues*)

Table 10-2 *continued*

Injury	Preferred Agent(s)	Alternate Agent(s)	Duration
Burns			
Superficial burns	Topical antimicrobials with twice daily dressing changes (include mafenide acetate[¥] or silver sulfadiazine; may alternate between the two), silver-impregnated dressing changed q3–5d, or Biobrane	Silver nitrate solution applied to dressings	Until healed
Deep partial-thickness burns	Topical antimicrobials with twice daily dressing changes, or silver-impregnated dressing changed q3–5d + excision and grafting	Silver nitrate solution applied to dressings + excision and grafting	Until healed or grafted
Full-thickness burns	Topical antimicrobials with twice daily dressing changes + excision and grafting	Silver nitrate solution applied to dressings + excision and grafting	Until healed or grafted
Point-of-injury/delayed evacuation[¶]			
Expected delay to reach surgical care	Moxifloxacin 400 mg PO ×1 dose; ertapenem 1 g IV or IM if penetrating abdominal injury, shock, or unable to tolerate PO medications	Levofloxacin 500 mg PO × 1 dose; Cefotetan 2 g IV or IM q12h if penetrating abdominal injury, shock, or unable to tolerate PO medications	Single-dose therapy

(**Table 10-2** *continues*)

Table 10-2 *continued*

CSF: cerebrospinal fluid; IM: intramuscular; IV: intravenous; PO: orally; PRN: as needed; QID: four times daily; TID: three times daily.
*Postinjury antimicrobial agents are recommended to prevent early posttraumatic infectious complications, including sepsis, secondary to common bacterial flora. Selection is based on narrowest spectrum and duration required to prevent early infections before adequate surgical wound management. This narrow spectrum is selected to avoid selection of resistant bacteria. The antimicrobials listed are not intended for use in established infections, where multidrug-resistant or other nosocomial pathogens may be causing infection.
†Cefazolin may be dosed based on body mass: 1 g if weight ≤80 kg (176 lbs), 2 g if weight 81–160 kg (177–352 lbs), and 3 g if weight >160 kg (>352 lbs); doses up to 12 g daily are supported by the Food and Drug Administration (FDA)-approved package insert.
‡Pediatric dosing: Cefazolin, 20–30 mg/kg IV q6–8h (maximum: 100 mg/kg/d); metronidazole, 7.5 mg/kg IV q6h; clindamycin, 25–40 mg/kg/d IV divided q6–8 h; ertapenem, 15 mg/kg IV or IM q12h (children up to 12 years) or 20 mg/kg IV or IM once daily (children older than 12 years; maximum: 1 g/d); ceftriaxone, 100 mg/kg/d IV divided q12–24h (dosing for central nervous system injury); levofloxacin, 8 mg/kg IV or PO q12h (levofloxacin is only FDA-approved in children for prophylaxis of inhalational anthrax in children older than 6 months, but this dose is commonly used for other indications); vancomycin, 60 mg/kg/d IV divided q6h (dosing for central nervous system injury); and ciprofloxacin, 10 mg/kg IV (or 10–20 mg/kg PO) q12h.
§These guidelines do not advocate adding enhanced gram-negative bacteria coverage (ie, addition of fluoroquinolone or aminoglycoside antimicrobials) in type III fractures.
¥Mafenide acetate is contraindicated in infants younger than 2 months.
¶Postinjury antimicrobial therapy as suggested by the Tactical Combat Casualty Care Committee.
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- Wounds should be irrigated to minimize gross contamination with saline or sterile water by bulb syringe or gravity flow from irrigant bag.
- The skin is left open, and a lightly moistened sterile gauze dressing is applied.
- For larger wounds, placement of a vacuum-assisted closure device may be indicated.
- Antibiotics should be started as soon as possible after wounding, then continued for 24 hours, depending on the size, extent of destruction, and degree of contamination of the wound.

Table 10-3. Specific Antibiotic Coverage for Theater-Specific Concerns: Culture Specific Recommendations

Culture	Recommendations
Carbapenem-resistant *Acinetobacter*	**1st Line** (if sensitive): Tobramycin 5–7 mg/kg qd × 10–14 days (monitor troughs if capable; goal, 2.0; otherwise, proceed to 2nd-line drug if Cr increases >0.5) **2nd Line:** Colistin 2.5–5.0 mg/kg/d in 2–4 divided doses **3rd Line:** Tigecycline 100 mg load, then 50 mg qd × 10 days
MRSA pneumonia	**1st Line:** Linelozid 600 mg IV/PO BID (literature suggests linelozid offers a treatment advantage over vancomycin) **2nd Line:** Vancomycin 15 mg/kg q12h × 10–14 days (maintain trough level of 15–20 μg/mL)

For SEPSIS (Empiric Treatment):

- Perform empiric cultures. Then initiate antibiotics within 4 hours.
- 1st Line: Carbapenem with antipseudomonal coverage imipenem 1 g q6h or meropenem 1 g q8h **PLUS** Amikacin 15–20 mg/kg/d or gentamicin 5–7 mg/kg/d. Consider adding vancomycin 15 mg/kg q12h if VAP suspected.

CRITICAL: But this should be based on individual site antibiotigram.

BID: twice a day; Cr: creatine; IV: intravenous; MRSA: methicillin-resistant *Staphylococcus aureus*; PO: per os (by mouth); qd: every day; VAP: ventilator-associated pneumonia.
Data source: Reprinted, with minor modifications, from Appendix C, Specific Antibiotic Coverage for Theater-Specific Concerns, Clinical Practice Guidelines (Agency for Healthcare Research and Quality, Rockville, MD).

  - If time from wounding to initiation of antibiotics is >6 hours, or time from wounding to surgery is >12 hours, give an antibiotics-using regimen for established infection.
- The choice of empiric antibiotic is dependent on the part of the body injured (Tables 10-1 to 10-3).
- 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 used in abscess cavities to prevent premature closure and reformation.
- Empiric broad-spectrum antibiotic therapy is initiated against likely pathogens and continued for 7–10 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 1–2 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.
  - **In addition to surgical debridement of war wounds, additional prophylactic measures for tetanus-prone wounds include:**
    - Administration of 0.5 mL IM of **tetanus toxoid** if prior tetanus immunization is uncertain, less than three doses of tetanus vaccine or >5 years since the last dose.
    - Administration of 250–500 U 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.
  - 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.**
  - **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).
  - **Postoperative 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.
  - **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 undertreated cases.

- The diagnosis is made by a 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 is often problematic: treatment must be aimed at all possible organisms.
- **IV antibiotic** therapy.
- **Clindamycin,** 900 mg q8h; **plus penicillin G**, 4 million U q4h; **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: Imipenem, 1 g IV q6h.

- **Intraabdominal infections.**
  - Prevention.
  - Regimens (start as soon as possible and continue x **24 hours** post-op):
    - **Single agent: cefotetan, 1.0 g q12h**; or ampicillin/sulbactam, 3 g q6h; or cefoxitin, 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 7–10 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 cefoxitin, 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 cefoxitin—have been proven effective.
  - **Ventilator-associated pneumonia**: *Staphylococcus*, *Pseudomonas*, and other nosocomial *Enterobacteriaceae*. Broad coverage is best with such agents as imipenem, ceftazidime, or piperacillin/tazobactam plus ciprofloxacin. Vancomycin should also be initiated if concern for methicillin-resistant *Staphylococcus aureus*.

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.
- Administer broad-spectrum intravenous antibiotics for the most likely pathogens.
- Use intensive care unit 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 the following:

- Imipenem, 1 g IV q6h.
- Piperacillin and clavulanate (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 a once-daily dosing strategy and no renal impairment); or ciprofloxacin, 400 mg q12h.
- Addition of vancomycin, 15 mg/kg q12h, if methicillin-resistant *Staphylococcus aureus* is a likely pathogen.
- Addition of linezolid, 600 mg q12h, if vancomycin-resistant enterococcus is a likely pathogen.

Battlefield casualties are at high risk for infection. In particular, war wounds are predisposed to infection due to environmental

Table 10-4. Spectrum and Dosage of Selected Antibiotic Agents

Agent	Antibacterial Spectrum	Dosage
Penicillin G	*Streptococcus pyogenes*, penicillin-sensitive *Streptococcus pneumoniae*, clostridial spp.	4 mU IV q4h
Ampicillin	Enterococcal spp., streptococcal spp., *Proteus*, some *Escherichia coli*, *Klebsiella*	1–2 g IV q6h
Ampicillin/sulbactam	Enterococcal spp., streptococcal spp., *Staphylococcus*,* *E coli*, *Proteus*, *Klebsiella*, clostridial spp., *Bacteroides*/*Prevotella* spp.	3 g IV q6h
Nafcillin	Staphylcoccal spp.,* streptococcal spp.	1 g IV q4h
Piperacillin/clavulanate	Enterococcal spp., streptococcal spp., *Staphylococcus*,* *E coli*, *Pseudomonas*, and other enterobacteriaceae, clostridial spp., *Bacteroides*/*Prevotella* spp.	3.375 g IV q6h
Imipenem	Enterococcal spp., streptococcal spp., *Staphylococcus*,* *E coli*, *Pseudomonas*, and other enterobacteriaceae, clostridial spp., *Bacteroides*/*Prevotella* spp.	1 g IV q6h
Cefazolin	Staphylococcal spp.,* streptococcal spp., *E coli*, *Klebsiella*, *Proteus*	2 g IV q8h
Cefoxitin	Staphylococcal spp.,* streptococcal spp., *E coli* and similar enterobacteriaceae, clostridial spp., *Bacteroides*/*Prevotella* spp.	1–2 g IV q6h
Ceftazidime	Streptococcal spp., *E coli*, *Pseudomonas*, and other enterobacteriaceae	2.0 g IV q8h
Ceftriaxone	Streptococcal spp., staphylococcal spp.,* *Neisseria* spp., *E coli*, and most enterobacteriaceae (**NOT** *Pseudomonas*), clostridial spp.	1 g qd
Ciprofloxacin	*E coli*, *Pseudomonas*, and other enterobacteriaceae	400 mg q12h
Gentamicin	*E coli*, *Pseudomonas*, and other enterobacteriaceae	5–7 mg/kg qd (based on once-daily dosing strategy and no renal impairment)
Vancomycin	Streptococcal, enterococcal, and staphylococcal spp. (including MRSA, not VRE) q12h	15 mg/kg q12h
Erthromycin	Streptococcal spp., clostridial spp.	0.5–1.0 g q6h
Clindamycin	*Streptococcus* spp., *Staphylococcus* spp.,* clostridial spp., *Bacteroides*, and *Prevotella* spp.	900 mg q8h
Metronidazole	Clostridial spp., *Bacteroides*, and *Prevotella* spp.	500 mg q6h

MRSA: methicillin-resistant *Staphylococcus aureus*; spp.: species; VRE: vancomycin-resistant enterococci.

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

*Not MRSA.

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, to include amputations, should have the skin left open. Antibiotics play an adjunctive role in the prophylaxis of wound and other infections in the battlefield medical treatment facility. Knowledge of likely pathogens for particular infections and sites, as well as optimal antibiotics to eradicate those pathogens (Table 10-4), will aid the battlefield clinician in averting and treating infections.

References

Conger NG, Landrum ML, Jenkins DH, et al. Prevention and management of infections associated with combat-related thoracic and abdominal cavity injuries. *J Trauma*. 2008;64(3 Suppl):S257–S264.

Hospenthal DR, Murray CK, Andersen RC, et al. Guidelines for the prevention of infections associated with combat-related injuries: 2011 update (endorsed by the Infectious Diseases Society of America and the Surgical Infection Society). *J Trauma*. 2011;71(2):S210–S234.

Murray CK, Hsu JR, Solomkin JS, et al. Prevention and management of infections associated with combat-related extremity injuries. *J Trauma*. 2008;64(3 Suppl):S239–S251.

Wortmann GW, Valadka AB, Moores LE. Prevention and management of infections associated with combat-related central nervous system injuries. *J Trauma*. 2008;64(3 Suppl):S252–S256.

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