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RELIAS MEDIA

Infections and Prophylaxis in Pediatric Trauma Patients

The emergency medicine physician serves a critical role for trauma and surgical patients. Early recognition of infections and understanding the indications for prophylaxis are critical for management of pediatric trauma patients. The authors explore the most common etiologic agents by body system and prophylactic and therapeutic strategies.

—Ann M. Dietrich, MD, FAAP, FACEP

Traumatic injuries can disrupt the body's natural barriers against invasive pathogens, particularly the skin and mucosal surfaces. Depending on the location of the initial trauma, the trajectory of possible ballistic components, the epithelial surfaces disrupted, the pathogenic and opportunistic organisms that colonize such surfaces, and the presence and nature of contaminants accompanying the external insult, a broad spectrum of infections may develop in any given trauma patient.

Fortunately, the practitioner may approach such injuries with a logical framework to anticipate the most likely pathogenic organisms at hand. Although there are no specific guidelines available for post-traumatic infections and prophylaxis in pediatric patients, it is possible to extrapolate the most likely organisms to colonize and infect wounds from a variety of literature, including case series, prospective trials, reviews, the American Academy of Pediatrics (AAP) *Red Book*, as well as some information from the Infectious Diseases Society of America's (IDSA) guidelines for the prevention of infections associated with combat-related injuries.[1,2] With such an approach, prophylactic antibiotics may be selected as appropriate for the patient's injuries and the context of the trauma. (*See Table 1.*) In patients who develop post-traumatic infections, the rational deduction of likely pathogens based on the considerations mentioned earlier will help in selecting empiric therapy until definitive microbiological identification can be provided. This article will summarize such considerations and recommendations for a variety of traumatic injuries in pediatric and adolescent patients.

Epidemiology

Injuries and accidents are among the leading causes of morbidity and mortality for children of all ages, and they predominate especially among children > 1 year of age.[3] The leading causes of accidents and injury-related deaths in each age group vary, but motor vehicle accidents, burns, homicides, suicides, and firearm-related deaths account for the majority, along with drowning deaths. (*See Table 2.*)

The mechanisms associated with these causes of death also may lead to substantial risk of infection among survivors of such injuries. In general, infections are a frequent cause of in-hospital complications among trauma and burn survivors, and are significantly associated with increased length of hospital stay and mortality.[4,5]

Data from the 1990s demonstrated that survivors of pediatric trauma most frequently experienced such infectious complications as abscesses and wound infections, followed by pulmonary infections, bacteremia, as well as peritonitis, osteomyelitis, and

EXECUTIVE SUMMARY

- Survivors of pediatric trauma most frequently experience such infectious complications as abscesses and wound infections, followed by pulmonary infections, bacteremia, as well as peritonitis, osteomyelitis, and sinusitis.
- Patients with HIV and immunocompromising conditions who have grossly contaminated wounds should receive tetanus immunoglobulin regardless of their prior immunization status.
- The timing of antimicrobial prophylaxis in extremity wounds is another important consideration. Studies suggest a higher infection rate when prophylactic antimicrobials are given after three hours following an injury vs. a rate of 4.7% when given within three hours.
- Risk factors for the development of endophthalmitis following eye trauma include metal (rather than glass) as the penetrating material, the retention of intraocular foreign bodies, lens disruption, and delayed closure of an open globe or penetrating injuries greater than 24 hours old. Among both pediatric and adult patients, environmental *Bacillus* species are an important and frequent cause of post-traumatic endophthalmitis, along with coagulase-negative staphylococci, and, among children, streptococcal species.
- Individuals with burns are at significant risk of infections due to the breakdown of the skin, which serves as the body's natural defense and primary immunologic barrier. It is not the toxic effect of thermally injured skin that places patients at risk of significant mortality, but the metabolic and bacterial consequences of a large open wound.
- All burns should undergo thorough cleansing and debridement, estimation of extent and depth, and coverage with appropriate topical antimicrobial agents within eight hours of injury.
- Topical antimicrobials recommended for all depths of burns include mafenide acetate or silver sulfadiazine. Mafenide is a topical sulfonamide with broad-spectrum Gram-positive and Gram-negative activity, including activity against *Pseudomonas* spp. It also has the ability to penetrate through eschar.
- Silver-impregnated dressings are another recommended option for burns and have the advantage of requiring fewer dressing changes, having better patient tolerance, and providing equivalent antimicrobial benefits.
- Cat scratches pose a risk for cat scratch disease from *Bartonella henselae*, symptoms of which include fever, enlarged and tender lymph nodes, and a pustule at the scratch site. Cat scratch disease should be treated with azithromycin.

sinusitis.[6] Isolates from these infections included predominantly *Staphylococcus aureus*, followed by Gram-negative species such as *Escherichia coli*, *Pseudomonas aeruginosa*, and *Klebsiella pneumoniae*, with a smaller number of *Streptococcus pyogenes* isolates as well.[6] Although aerobic pathogens were isolated most frequently, anaerobes were not uncommon, and many infections were polymicrobial in nature.

This article will detail initial management in wound infection prevention, followed by specific considerations for different body sites and situations.

Wound Cleansing, Debridement, and Irrigation

Irrigation is a vital component of any initial wound management. This primarily involves the application of a nontoxic fluid to remove debris and wound exudate to promote wound healing.[7] Normal saline (0.9%) typically is favored, because it is an isotonic solution and does not interfere with normal healing processes, and does not damage tissues or alter the normal bacterial flora of the skin.[8] The choice of tap water vs. sterile saline has been debated, with multiple studies performed to compare infection rates. In terms of acute wounds, animal studies have not found a difference in infection rates in acute soft tissue wounds cleaned with tap water compared with sterile saline.[9,10] Likewise, authors of a study of 530 pediatric patients with simple lacerations did not find a significant difference in infection rates between tap water and sterile saline irrigation,[11] suggesting that tap water may be an effective alternative in the prehospital or emergency department setting.

Pressure lavage is an important component of wound cleansing, and multiple experimental studies consistently have demonstrated its ability to prevent infection.[8] In terms of mechanism, it is thought that a pressurized stream of water may overcome microbial adhesion mechanisms associated with bacteria that are bound to the surface of host tissues on the wound surface. The most effective pressure for removal of bacterial contamination is not precisely known; however, most authors recommend pressures of 5 to 8 PSI.[12] This pressure can be achieved by using a 19-gauge syringe or catheter on a 60-cc syringe.[13] Pressures greater than 15 PSI are likely to lead to both soft tissue and bone injury.[14] The risk of infection has been found to increase with higher lavage pressures, likely secondary to tissue damage.[15] Overall, however, there is a paucity of quality evidence to support the use of pressure irrigation.[8]

There are limited data on the most effective volume of irrigant to use. A frequently cited rule of thumb is 60 mL of irrigant per centimeter of wound length.[16] Others suggest irrigating simple wounds with 250 mL of fluid total.[10] Current IDSA guidelines for removing contamination recommend irrigation of wounds with normal saline or sterile water under low pressures (5 to 10 PSI with a bulb syringe or gravity flow), with additional volume recommendations to use 3 liters for Type I, 6 liters for Type II, and 9 liters for Type III extremity fractures.[1]

Tetanus Toxoid Considerations

Tetanus is a rare but potentially lethal infectious complication of any injury. *Clostridium tetani* is an obligate anaerobe found ubiquitously in soil, as well as in human and animal gastrointestinal tracts.[17] The spores of this organism may contaminate any wound. As the bacillus replicates within the injury site, tetanospasmin toxin is elaborated and produces its effects on the motor end plates of skeletal muscle and

Table 1. General Pathogen Considerations and Recommendations for Antibiotic Prophylaxis for Trauma Related to Regional/System Anatomy

Region/System	Pathogen Considerations	Recommended Prophylaxis
Extremities	*Staphylococcus aureus*, Group A Streptococcus, coagulase-negative staphylococci, Gram-negative bacilli	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours* for duration of 1-3 days following definitive washout • With recommended trauma or orthopedic surgery consultation
Penetrating eye injury	Environmental *Bacillus* species, coagulase-negative staphylococci, streptococcal species	• Systemic levofloxacin IV/PO 16-20 mg/kg/day divided Q12-24 hours (up to adult dose of 750 mg/day)** for duration of 7 days • With mandatory ophthalmology consultation
Maxillofacial	*Staphylococcus aureus*, Gram-negative bacilli, oropharyngeal flora	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours* • If disruption of oral or pharyngeal mucosa: PLUS • Metronidazole IV 15 mg/kg loading dose, followed by 30-40 mg/kg/day divided Q6-8 hours for duration of at least 1 day following definitive washout • With mandatory otolaryngology consultation
Thoracic without esophageal involvement	*Staphylococcus aureus*, alpha- and beta-hemolytic streptococci, Gram-negative bacilli	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours* for duration of at least 1 day following definitive washout • With mandatory trauma surgery consultation
Thoracic with esophageal involvement	*Staphylococcus aureus*, alpha- and beta-hemolytic streptococci, Gram-negative bacilli, oral and enteric anaerobes	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours* PLUS • Metronidazole 15 mg/kg IV loading dose, followed by 30-40 mg/kg/day divided Q6-8 hours for duration of at least 1 day following definitive washout • With mandatory trauma surgery consultation
Abdominal	*Escherichia coli*, other Gram-negative, Gram-positive, and anaerobic polymicrobial components, including *Enterococcus* spp., *Bacteroides* spp., and *Enterobacter cloacae*	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours PLUS • Metronidazole 15 mg/kg IV loading dose, followed by 30-40 mg/kg/day divided Q6-8 hours*** for duration of at least 1 day following definitive washout • With mandatory trauma surgery consultation
Central nervous system	*Staphylococcus aureus*, coagulase-negative staphylococci, beta-hemolytic streptococci, other Gram-negatives and some clostridial species	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours • If hollow viscus injury or presence of organic debris is present: PLUS • Metronidazole 15 mg/kg IV loading dose, followed by 30-40 mg/kg/day divided Q6-8 hours for at least 5 days or longer if cerebrospinal fluid leaks are ongoing • With mandatory neurosurgery consultation
Bite Wounds	See Table 4	• Amoxicillin-clavulanate PO 45 mg/kg/day divided Q12 hours (up to adult dose of 875/125 1 tab PO BID)**** • Consider need for rabies prophylaxis • Consult infectious disease specialist for monkey bites

* If patients have a previous history of anaphylaxis to β-lactam antibiotics, clindamycin is an acceptable alternative. In cases where cefazolin and metronidazole are recommended in combination, clindamycin may replace both agents.
**Moxifloxacin is also an acceptable alternative in adult patients, but is not approved for pediatric use.
***Other regimens include cefoxitin with or without gentamicin; gentamicin plus metronidazole and ampicillin; meropenem monotherapy; other acceptable combinations typically used for perforated appendicitis.
****Other acceptable regimens in allergic patients include oral trimethoprim-sulfamethoxazole plus clindamycin.
IV: intravenous; PO: oral; BID: twice per day

Adapted from: 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 Suppl 2):S210-S234.
Kimberlin DW, Long SS, Brady MT, Jackson MA, eds. *Red Book 2018 Report of the Committee on Infectious Diseases.* 31st ed. American Academy of Pediatrics; 2018.
Gilbert DN, Chambers HF, Eliopoulos GM, et al, eds. *The Sanford Guide to Antimicrobial Therapy 2019.* Antimicrobial Therapy, Inc.; 2019.

synapses of the spinal cord. Deep wounds that may encourage anaerobic respiration, as well as those that are grossly contaminated with soil or feces, often have been considered to be particularly at risk, but past studies have indicated that up to 80% of cases are produced in instances with relatively insignificant wounds.[17,18] As tetanospasmin is produced, the patient begins to experience worsening muscle spasms from inhibition of acetylcholine from nerve terminals in muscle tissue. Sometimes these muscle spasms may occur locally surrounding the infected site, but the toxin usually produces general manifestations,

Table 2. Leading Causes of Injury Deaths by Age Group, United States – 2018

Rank/Age	< 1 year	1-4 years	5-9 years	10-14 years	15-24 years
1	Unintentional suffocation	Unintentional drowning	Motor vehicle accident	Suicide suffocation	Motor vehicle accident
2	Homicide unspecified	Motor vehicle accident	Unintentional drowning	Motor vehicle accident	Unintentional poisoning
3	Motor vehicle accident	Homicide unspecified	Fire/burn	Suicide firearm	Homicide firearm
4	Homicide, other specified	Fire/burn	Homicide firearm	Homicide firearm	Suicide firearm
5	Undetermined suffocation	Unintentional suffocation	Unintentional suffocation	Unintentional drowning	Suicide suffocation

Adapted from Centers for Disease Control and Prevention. Ten Leading Causes of Death and Injury. Updated March 30, 2020. https://www.cdc.gov/injury/wisqars/LeadingCauses.html

Table 3. Tetanus Toxoid Recommendations

Past number of doses of previous tetanus toxoid-containing vaccines	Clean, minor wound		Any other wound, including those contaminated by dirt, feces, as well as frostbite, crush injuries, and burns	
	DTaP, Tdap, or Td	TIG*	DTaP, Tdap, or Td	TIG
Unknown or < 3	Yes	No	Yes	Yes
≥ 3	No**	No	No***	No

*Patients with HIV or severe immunocompromise with grossly contaminated wounds should receive TIG regardless of past immunization status
**Yes, if it has been 10 years or greater since the patient's last tetanus toxoid-containing vaccine
***Yes, if it has been 5 years or greater since the patient's last tetanus toxoid-containing vaccine
Adapted from: Centers for Disease Control and Prevention. Tetanus: For Clinicians. Updated Jan. 23, 2020. https://www.cdc.gov/tetanus/clinicians.html

including trismus (lockjaw); spasms of the neck, back, and abdomen; and rigid posturing (opisthotonos), leading to generalized tonic seizures and eventual death in the absence of medical care.[17]

Tetanus is rare in the United States, largely because of the success of almost universal vaccination of the population. Between 2009 and 2017, the United States experienced only 264 cases of tetanus, and nearly every case was in someone who either never received the tetanus toxoid vaccine or who did not stay up to date on their recommended 10-year booster shots.[19] However, tetanus remains a pertinent concern throughout the developing world, with the World Health Organization reporting more than 15,000 cases globally in 2018 alone.[20]

Tetanus is averted primarily through receipt of the initial vaccination series. The immunization history of the patient is the most important consideration when managing postinjury tetanus prophylaxis. The Centers for Disease Control and Prevention recommends that unvaccinated patients or those with an unknown vaccination history begin a primary series of tetanus-toxoid-containing vaccine. Additionally, they should be assessed for the need for tetanus immunoglobulin (TIG).[19] (*See Table 3.*) Of note, patients with HIV and immunocompromising conditions who have grossly contaminated wounds should receive TIG regardless of their prior immunization status.

Extremity Wounds

Pathogens introduced via traumatic extremity wounds can result in skin, soft tissue, and/or bone infections. The major pathogens associated with trauma-related extremity soft tissue and skin infections are Group A Streptococcus (*S. pyogenes*) and *S. aureus*.[21] Pyomyositis and osteomyelitis may develop in the setting of an extremity trauma via contiguous spread of infection to the bone from adjacent soft tissues. Along with *S. aureus* and *S. pyogenes*, aerobic Gram-negative bacilli also should be considered in deep soft-tissue infections secondary to extremity injuries.[21,22] Additionally, puncture wounds of the plantar aspects of the feet and wounds contaminated with water and soil may be infected with *Pseudomonas* spp. and *Aeromonas* spp.[23,24]

The selection of appropriate antibiotic prophylaxis is an important consideration when managing extremity wounds. Some sources suggest that antibiotic selection should vary based on the extent of injury and the presence and degree of open fracture as defined by the Gustilo-Anderson open fracture grading system.[25] Briefly, Type I open fractures are associated with clean (non-contaminated) wounds less than 1 cm in length; Type II open fractures are associated with lacerations greater than 1 cm in length without extensive soft tissue damage, flaps, or avulsions; and Type III open fractures are associated with either an open segmental fracture, an open fracture with extensive soft tissue damage, or a traumatic amputation. Currently, coverage for Gram-positive skin flora is recommended most frequently for Type I and Type II open fractures.[1]

Studies have demonstrated that broader-spectrum Gram-negative coverage (such as would be achieved with fluoroquinolones

or aminoglycosides) in these types of traumatic extremity wounds does not improve outcomes and actually increases the rates of resistant Gram-negative infections.[26] Cefazolin serves as adequate prophylaxis in trauma-related injuries against Gram-positive skin flora and methicillin-susceptible *S. aureus*.[1,27,28] If patients have a previous history of anaphylaxis to β-lactam antibiotics, clindamycin is an acceptable alternative. Some authors have suggested that Type III open fractures are associated with increased morbidity and risk of infection because of compromised vascularity, wound contamination, and fracture instability.[25] For these injuries, some guidelines recommend Gram-negative coverage with ceftazidime and gentamicin, which is supported by researchers who found a higher rate of infection for Type III fractures treated with ciprofloxacin compared to those treated with ceftazidime/gentamicin.[29] This contrasts with common practice taken from IDSA combat-related trauma guidelines, which support the exclusive use of cefazolin for all types of fractures.[1] For penetrating injuries through the sole of the foot, particularly through the shoe or with concern for soil contamination, fluoroquinolones should be considered for prophylaxis because of the possible introduction of *Pseudomonas* spp.[23,24]

The timing of antimicrobial prophylaxis in extremity wounds is another important consideration. Studies suggest a higher infection rate (7.4%, 49 of 661 patients) when prophylactic antimicrobials are given after three hours following an injury vs. a rate of 4.7% (17 of 364 patients) when given within three hours.[22] The ultimate duration of antimicrobial prophylaxis is not clearly defined, but prospective studies suggest therapies as short as one day may be effective, which is in contrast to the traditionally recommended five days of therapy.[30] Current IDSA guidelines recommend a one- to three-day course of prophylaxis for all extremity wounds, including those with open fractures.[1]

Eye, Maxillofacial, and Neck Wounds

Eye trauma may lead to disruption or penetration of ballistic or foreign material into the globe. This potentially may introduce pathogenic bacteria into the otherwise sterile anatomic planes and spaces of the eye, leading to endophthalmitis or other vision-threatening infections. Prior work with adult patients suggests that in the absence of antibiotics, 3% to 10% of ocular trauma cases may be complicated by endophthalmitis.[31,32] Although this rate is relatively low, endophthalmitis is vision-threatening, and the administration of appropriate prophylactic antibiotics may reduce the rate of post-traumatic infectious endophthalmitis to less than 1%.[32] Risk factors for the development of endophthalmitis include metal (rather than glass) as the penetrating material, the retention of intraocular foreign bodies, lens disruption, and delayed closure of an open globe or penetrating injuries greater than 24 hours old. Among both pediatric and adult patients, environmental *Bacillus* species are an important and frequent cause of post-traumatic endophthalmitis, along with coagulase-negative staphylococci, and, among children, streptococcal species.[31,33,34] Rarely, Gram-negative bacilli and environmental molds have been described as an infectious etiology. Outcomes may be poor with any etiologic organism, but especially in the case of *Bacillus* species.[35] Ophthalmology consultation is critical in any suspected or confirmed case of ocular trauma, penetrating injury, or infectious endophthalmitis.

Systemic levofloxacin or moxifloxacin is the recommended prophylaxis after open-globe ocular trauma, with relatively lower rates of post-traumatic endophthalmitis described after use of these medications.[1,36] Prophylaxis should be continued for at least seven days, or until appropriate ophthalmology evaluation. Empiric treatment of post-traumatic endophthalmitis will require intravitreal antibiotics and possible vitrectomy, and thus ophthalmology consultation is critical. Empiric systemic therapy should include vancomycin or ciprofloxacin.[37]

Maxillofacial and neck injuries may involve a relatively wide variety of pathogens in post-trauma infections. These have not been well-characterized, but studies from combat situations and civilian surgeries have suggested that *S. aureus* predominates, although Gram-negative organisms and oropharyngeal flora also may cause infection.[38,39,40,41]

Current guidelines recommend post-traumatic injury prophylaxis with intravenous (IV) cefazolin for at least one day based on studies centered on head and neck surgical prophylaxis, with the addition of metronidazole if disruption of the oral or pharyngeal mucosa is suspected.[1,28] Clindamycin is an acceptable alternative for those with confirmed allergy or other intolerance to cefazolin. When true post-traumatic infections of the head and neck develop, Gram-negative upper respiratory isolates and anaerobes should be considered alongside Gram-positive flora and *S. aureus* as potential causative agents.[41] Consultation with otolaryngology surgical services is critical in all maxillofacial injuries and post-traumatic infections.

Thoracic Wounds

Penetrating thoracic trauma or thoracic trauma management requiring the use of a chest tube may introduce pathogenic bacteria into typically sterile anatomic compartments, notably the pleural potential space, as well as the mediastinum, pericardial sac, lung parenchyma, etc. The use of prophylactic antibiotics may reduce the rate of empyema and other post-traumatic infections in such situations.[1,42] Surgical consultation is recommended in all situations of penetrating trauma to the chest.

The need for specific antimicrobial regimens in thoracic trauma may be distinguished further based on the flora that may contaminate such wounds — essentially by whether the esophagus has been disrupted or involved in the injuries. Without esophageal involvement, *S. aureus*, alpha- and beta-hemolytic streptococci, and Gram-negative bacilli, among others, are expected pathogens contributing to post-traumatic empyema and other infections, which frequently are polymicrobial in nature.[43,44] IV cefazolin for at least 24 hours is recommended for prophylaxis in chest wounds without esophageal involvement.[1] In the event of post-traumatic empyema or other infection in this context, empiric therapy must take into account the high likelihood of staphylococcal (and potential methicillin-resistant *S. aureus* [MRSA]) involvement, as well as possible contributory Gram-negatives.

In the event of post-traumatic thoracic injuries with disruption or perforation of the esophagus, concern is raised for the possible introduction of oropharyngeal and enteric anaerobes into the pleural, mediastinal, and pericardial spaces. Contamination or superinfection with staphylococci and Gram-negatives still is a pertinent concern. For these reasons, both cefazolin and metronidazole are recommended for prophylaxis for at least one day following definitive washout.[1]

Alternatives to this regimen include ertapenem or moxifloxacin. For infections that develop in patients with esophageal involvement, empiric therapy must include anaerobic coverage, as well as take into account the high likelihood of staphylococcal or Gram-negative involvement.

Abdominal Wounds

Penetrating abdominal injuries are highly concerning for disruption of hollow viscus organs and leakage of their contents into otherwise sterile anatomic compartments. The high burden of potentially pathogenic organisms in these injuries accounts for high rates of post-traumatic infection. In case series of soldiers injured on World War I battlefields (and hence, prior to the antibiotic era), injuries with colonic perforation led to infection in 60% to 75% of cases.[45,46] More recent data from civilian trauma centers suggest that, even with appropriate postoperative antibiotics, penetrating abdominal injuries may lead to infections in 30% of all cases and in 70% of cases with colonic perforation.[47,48] Data from American military operations in Iraq and Afghanistan likewise confirm such high rates of sepsis and infection following penetrating abdominal injuries.[49] Based on a recent Cochrane review of studies regarding antimicrobial prophylaxis following abdominal trauma, the duration and precise regimen of antibiotics remain uncertain and supported by relatively low-quality evidence.[50] Later, this article will discuss likely pathogenic species to be targeted, and regimens supported by surgical prophylaxis and combat-related studies, as well as recommendations from the AAP.

When approaching patients with penetrating abdominal trauma, a high priority must be placed on addressing the microbiological burden of such injuries. Gross fecal contamination must be addressed at the time of primary surgical repair to reduce overall contamination to the sterile compartments of the peritoneum and retroperitoneum. IDSA guidelines recommend against skin closure if colonic perforation or tissue destruction accompanies such injuries to avoid infectious complications.[1] *E. coli* predominates in the microbiological profile of all post-traumatic infections, often alongside other Gram-negative, Gram-positive, and anaerobic polymicrobial components, including *Enterococcus* spp., *Bacteroides* spp., and *Enterobacter cloacae*.[51]

For prophylaxis following penetrating abdominal injuries, IDSA guidelines recommend the use of cefazolin and metronidazole to target such enteric Gram-negative and anaerobic organisms, administered for at least 24 hours following surgery.[1] Alternative regimens suggested by these guidelines include single-dose ertapenem or moxifloxacin. Recommendations from the AAP include cefoxitin with or without gentamicin, or gentamicin, metronidazole, and ampicillin, meropenem alone, or any other regimen deemed appropriate for the congruent situation of perforated appendicitis.[28]

When encountering post-traumatic infections of the abdomen, providers should tailor therapy to target polymicrobial components, including Gram-negative, Gram-positive, and anaerobic commensals and pathogens. Recent data from a civilian trauma center in Southern California suggest that Gram-negatives frequently are susceptible to third-generation cephalosporins, carbapenems, and quinolones, while enterococci frequently are susceptible to penicillins in such cases.[51] Complicated intra-abdominal infections following trauma require surgical and pediatric infectious disease consultation.

Wounds Involving the Central Nervous System

Penetrating injuries to the brain and spine may lead to indriven fragments of bone, debris, and the offending bullet or other material responsible for the injury. This may lead to contamination of the otherwise sterile brain and spinal cord, and, in the case of the latter, the preceding ballistic track may cross through the hollow viscus organs of the peritoneum, introducing Gram-negative and anaerobic organisms. Prior studies based on military casualties with central nervous system injuries and infections from World War II, the Vietnam War, the Lebanese Civil War, and the Iran-Iraq War have suggested a variety of microbial pathogens may contaminate such wounds and cause post-traumatic infection in the central nervous system.[52,53,54,55,56] Chief among these are staphylococcal species, especially *S. aureus*, but coagulase-negative staphylococci, beta-hemolytic streptococci, other Gram-negatives, and some clostridial species may be involved as well. In both military and civilian case series, penetrating trauma to the cranium and central nervous system from any mechanism may cause meningitis, osteomyelitis of the skull, and brain abscesses as infectious sequelae.[57] While superficial infections frequently are caused by *S. aureus*, deep-seated infections, such as brain abscesses, also may be due to Gram-negative bacteria.

Current guidelines from the IDSA, supported by surgical prophylaxis recommendations from the AAP, recommend that patients with penetrating injuries to the central nervous system undergo prophylaxis with intravenous cefazolin, with the addition of metronidazole if the wound is contaminated with organic debris, or if there is suspected association of a hollow viscus injury with a spinal cord injury.[1,28] The ultimate duration of prophylaxis is determined primarily by the time to definitive closure of any cerebrospinal fluid leaks, but five days are recommended as a minimum duration.

Treatment of post-traumatic infection of the central nervous system must involve neurosurgical expertise to determine if debridement of the scalp or drainage/aspiration of deep-seated abscesses is possible. Antibiotic therapy should take into account the high prevalence of staphylococci in such infections, as well as the possible presence of Gram-negative facultatively aerobic bacteria. Treatment of such infections also should ensure adequate dosing and antibiotic selection to achieve central nervous system penetration because of the unique pharmacodynamic characteristics of the blood-brain barrier. Consultation with a pediatric infectious disease specialist is recommended.

Burns

Individuals with burns are at significant risk of infections due to the breakdown of the skin, which serves as the body's natural defense and primary immunologic barrier. It is not the toxic effect of thermally injured skin that places patients at risk of significant mortality, but the metabolic and bacterial consequences of a large open wound.[58] Complications in burn patients arise primarily due to secondary infections; therefore, topical antimicrobial prophylaxis should be initiated at the beginning of burn treatment.[59] Systemic effects of secondary infections (e.g., systemic inflammatory response syndrome) can be difficult to distinguish in burn injuries, since such injuries themselves often lead to a hyperdynamic, hypermetabolic, and proinflammatory state.[60]

Current guidelines emphasize

mechanical cleansing with irrigation as a critical component to all burn injury care.[1,61] International guidelines state that tap water and sterile saline both are appropriate choices, as long as thorough irrigation occurs, especially with low-pressure lavage.[61] All burns should undergo thorough cleansing and debridement, estimation of extent and depth, and coverage with appropriate topical antimicrobial agents within eight hours of injury.[1] More extensive burns — deep partial-thickness and full-thickness — should undergo early (within five days) excision and grafting.

Topical antimicrobials are recommended for burns of all degrees of severity.[1] Topical therapy has the advantage of producing high concentrations of the active agent at the site of injury. This is particularly true after mechanical cleansing via irrigation, which disrupts bacterial biofilms and matrices, thus making infectious agents more "accessible" to any given topical antimicrobial.[61] Practitioners also should bear in mind that systemic absorption and delivery of oral antimicrobial agents may be compromised in deeper burns secondary to disruption of blood vessels, and, thus, topical formulations hypothetically may be more effective in situ.

Topical antimicrobials recommended for all depths of burns include mafenide acetate or silver sulfadiazine.[1] Mafenide is a topical sulfonamide with broad-spectrum Gram-positive and Gram-negative activity, including activity against *Pseudomonas* spp. It also has the ability to penetrate through eschar.[60] Silver is a staple in burn management and is found in numerous topical products, including silver nitrate, silver sulfadiazine, and silver-based dressings. Elemental silver and silver-based compounds have been known to have bactericidal properties as early as 1000 B.C.,when they were used for medicinal purposes and to render water potable.[62] Silver's antimicrobial properties include activity against Gram-positive, Gram-negative, and fungal organisms. The mechanism of this activity is secondary to interactions with thiol groups, release of intracellular potassium, direct cellular membrane disruption, and microbial DNA interaction.[62] Silver-impregnated dressings are another recommended option and have the advantage of requiring fewer dressing changes, having better patient tolerance, and providing equivalent antimicrobial benefits. Silver-impregnated dressings require changes every three to five days. In contrast, topical antimicrobials must be applied twice daily with dressing changes. In all situations, topical antimicrobial therapy should be used until all burn injuries are successfully covered with healed skin.[1]

Systemic antimicrobial prophylaxis for burn injuries generally is discouraged unless there are concomitant injuries for which antibiotics would be indicated.[1,61] A Cochrane systematic review of 36 randomized, controlled trials of systemic and topical antimicrobial prophylaxis in burn injuries failed to demonstrate any evidence that systemic antibiotic prophylaxis reduces the risk of local infection, sepsis, or infection-related mortality.[63] However, IDSA guidelines allow for consideration of systemic antimicrobials for perioperative prophylaxis during excision and grafting procedures.[1] If used, cefazolin 2 g IV every six hours to eight hours is appropriate for skin flora coverage. Pediatric patients should receive the same antimicrobial agents as adults (topical and systemic), with the exception of mafenide acetate, which should not be used in neonatal patients because of a risk of kernicterus with sulfonamides. Dosing of systemic antimicrobial agents should be weight-based in children less than 40 kg.

Burn injury infections occur with less frequency than in the past, given the use of early debridement and topical antimicrobial application as recommended by current guidelines.[1] However, early signs of infection are important to recognize. Specific microorganisms should be considered based on the presence of eschar separation and color change in the wound. *Pseudomonas* colonization may create a yellow/green exudate. Invasive *Pseudomonas* infections often are black. In general, fungal infections are more insidious in nature, and may not be obvious immediately in the acute phase. *Candida* infections typically are more purulent. *Aspergillus* species infections may appear gray-brown, while *Mucor* species infections may appear black.[60] In all cases of infectious complications following burns, burn specialists and infectious disease consultation are recommended.

Wound Contaminants and Retained Foreign Bodies

All penetrating wounds have the potential to introduce environmental microorganisms. Important considerations include wounds contaminated by water (fresh water and salt water) and organic material, such as soil.

Both superficial and deeper invasive infections can occur after contamination of open wounds by fresh water or salt water.[64] Much of the data surrounding the epidemiology and microbiology of aquatic injuries and infections comes from disaster research. Data from the 2004 tsunami in Thailand found that the majority of early-onset soft tissue infections were polymicrobial, with Gram-negative bacteria as the most commonly isolated organisms, including *Aeromonas* species, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *Proteus* species.[65] Further data demonstrated that late-onset infections were caused mostly by rapidly growing marine mycobacteria that required specific antimycobacterial antimicrobials.[66] Of the early-onset infections, *Aeromonas* species are some of the most common.[64] This organism lives in fresh and brackish water, with an increased incidence of infections during warmer months. Commonly, it is seen after near-drowning accidents. Infections caused by *Aeromonas* species include cellulitis, pyoderma furuncles, and necrotizing infections.[64] The majority of isolates are susceptible to aminoglycosides, third- and fourth-generation cephalosporins, fluoroquinolones, and imipenem.[65] *Vibrio vulnificus* is a highly virulent Gram-negative curved bacilli that is found in marine environments, and causes multiple types of infections. It is a known cause of acute gastroenteritis and invasive sepsis, classically following meals of undercooked shellfish, but it also is a known pathogen in necrotizing wound infections following marine injuries.[67] Antibiotic therapy, typically with a third-generation cephalosporin plus doxycycline, should be initiated empirically with any concerns for *V. vulnificus* infections.[68]

Soil may contain varying amounts of bacteria depending on the amount of sunlight, temperature, pH, and nutrients in a given sample. Microorganisms in soil can be indigenous or introduced from animal waste, flooding, or sewage.[69] A classic soil-related infection is wound botulism, caused by the toxin-producing, anaerobic, rod-shaped, spore-forming bacteria, *Clostridium botulinum*. *C. botulinum* and its spores are found ubiquitously in soil, dust, and marine and freshwater sediments.[70] Wound botulism occurs when *C. botulinum* contaminates disrupted tissue planes,

followed by bacterial replication and toxin production.[71] The production of toxin leads to systemic symptoms of botulism, which is a neuroparalytic disorder that manifests with acute, afebrile, symmetric, descending flaccid paralysis. Antimicrobial agents are not prescribed routinely in cases of botulism, and some (such as aminoglycosides) actually may potentiate the paralytic effects of the toxin. Instead, therapy is focused on supportive care and the use of botulism antitoxin.[71]

The botulism antitoxin approved for use in the United States is Botulism Antitoxin Heptavalent, which is a mixture of immune globulin fragments. It is approved for use for the treatment of symptomatic botulism following exposure to botulinum neurotoxin serotypes A, B, C, D, E, F, or G in adult and pediatric patients.[72] The adult dose is one vial, starting at an infusion rate of 0.5 mL/min for the first 30 minutes and doubling the rate every 30 minutes to a maximum of 2 mL/min. The pediatric dose is 20% to 100% of the adult dose, starting at 0.01 mL/kg/min, increasing by 0.01 mL/kg/min every 30 minutes to a maximum dose of 0.03 mL/kg/min. For infants younger than 1 year of age, the dose is 10% of the adult dose, regardless of body weight, with a starting rate of 0.01 mL/kg/min, increasing by 0.01 mL/kg/min to a maximum infusion rate 0.03 mL/kg/min.[72]

Penetrating wounds also may introduce foreign bodies, which can lead to inflammation, delayed healing, damage to surrounding tissues, and infection. Imaging modalities most helpful for detecting foreign bodies include plain film radiographs, computed tomography (CT), magnetic resonance imaging (MRI), and ultrasound.[73] Plain films are the preferred imaging method for detecting foreign bodies, especially when dealing with radiopaque foreign bodies, such as metal, glass, and gravel.[73] Multi-view radiographs are most helpful in identifying the relative positions of foreign bodies in three dimensions. Radiolucent objects, such as wood, plastic, and plant matter, are not visualized easily using plain radiographs.[74] CT is more useful for identifying an object's precise location to aid in removal; however, CT scans are limited by metallic artifacts. MRI cannot be used if an object's composition is unknown due to imaging artifacts and the potential harm to the patient if the object is ferromagnetic in nature. Ultrasound has the advantages of portability and lack of radiation exposure; however, it is mostly useful for detecting only superficial foreign bodies.[74]

Table 4. Important Pathogenic Bacteria in Bite Wounds

Type of Bite	Aerobic Bacteria	Anaerobic Bacteria
Dog	*Pasteurella* spp *Streptococcus* spp *Staphylococcus* spp *Capnocytophaga canimorsus*	*Fusobacterium* spp *Bacteroides* spp *Prevotella* spp *Propionibacterium* spp *Peptostreptococcus* spp
Cat	*Pasteurella* spp *Streptococcus* spp *Staphylococcus* spp *Moraxella* spp	*Fusobacterium* spp *Bacteroides* spp *Porphyromonas* spp *Prevotella* spp *Propionibacterium* spp
Human	*Streptococcus* spp *Staphylococcus* spp *Eikenella corrodens* *Haemophilus* spp	*Fusobacterium* spp *Prevotella* spp *Peptostreptococcus* spp *Veillonella* spp

Adapted from: Bula-Rudas FJ, Olcott JL. Human and animal bites. *Pediatr Rev* 2018;39:490-500.

Human and Animal Bites

Human and animal bites warrant special consideration in post-traumatic prophylaxis and infection. Animal bites may occur from many different species beyond domestic dogs and cats, and the risk for different bites depends on many factors, including living conditions, locally indigenous species, and exposure to animals.[75] In the United States, dog bites account for the majority of all such injuries (80% to 90%), followed by cats (5% to 15%), and rodents (2% to 5%). The remainder of bites are from rabbits, ferrets, farm animals, monkeys, and reptiles.[75] The most common complication from all types of bites is infection, the rates of which vary based on the animal causing the injury. Even with early presentation, the infection rate among all dog bites is much lower (< 20%) when compared to cat bites (> 50%).[76] In addition, the rate of infection seems to rise with increasing time to presentation. Because of this, it is recommended that cultures be obtained from all bites that are older than eight hours and from all human bites.[75]

Animal bites can cause a variety of injuries based on the animal causing the bite. Dog bites typically cause abrasions, puncture wounds, lacerations, and crush injury to tissues. Cat and rodent bites often cause puncture wounds that may penetrate into deep tissues. Human bites typically cause an occlusion-type injury (from upper and lower teeth coming together and sinking into the skin) or a clenched-fist injury (fight bites).[58] Clinical signs and symptoms of bite wound infections can present as soon as several hours to days after the injury. Common signs and symptoms include pain, erythema, swelling, and purulent drainage. Lymphadenitis and fevers are less common. Complications of animal bite infections include cellulitis, osteomyelitis, tenosynovitis, and brain abscesses.[76]

The majority of infections due to animal bites are polymicrobial in nature. Prospective data on the microbiology of animal bites encountered in an emergency department identified an average of five different bacterial isolates per culture in dog and cat bites.[77] Specific pathogenic considerations vary based on the species of animal responsible for the bite. (*See Table 4.*) The most common organism isolated from both dog and cat bites is *Pasteurella* species. *Capnocytophaga canimorsus* has been identified as a cause of severe infection and sepsis in immunocompromised and asplenic children.[76] Human bites typically consist of anaerobic and aerobic microorganisms.[76] *Eikenella corrodens* is a common cause of clenched-fist human bite injuries. Numerous other systemic infections may be caused by human and animal bites, including rabies, *Bartonella*, tularemia, brucellosis, leptospirosis, rat-bite fever, and hepatitis B and C virus infections.[76]

The management of bite wounds varies based on the type of animal bite, time from injury, and evidence of infection.

Table 5. Post-Splenectomy Antimicrobial Recommendations

Patient Characteristics	Antimicrobial Choice
Age < 3 years	Oral penicillin V 125 mg BID
Age > 3 years	Oral penicillin V 250 mg BID
Adults	Penicillin V 250 mg BID or amoxicillin 500 mg BID
Penicillin allergy	Erythromycin 250 mg BID

BID: Twice daily

Adapted from: Rubin LG, Schaffner W. Clinical practice. Care of the asplenic patient. *N Engl J Med* 2014;371:349-356.

Table 6. Post-Splenectomy Vaccination Recommendations for Adults (Age > 19 Years)

Vaccine	Primary Series	Revaccination
Pneumococcal vaccine - PCV13 plus PPSV23	1 dose of PCV13 followed by 1 dose PPSV23 ≥ 8 weeks later	PPSV23 every 5 years
***Haemophilus influenzae* type b vaccine** - Hib	1 dose	None needed
Meningococcal serotype ACWY vaccine - MenACWY	2 doses at least 8 weeks apart	Every 5 years
Meningococcal serotype B - MenB-FHbp or MenB-4C	2 doses of MenB-4C at least 1 month apart or 3 doses of MenB-FHbp at 0, 2, and 6 months	Not applicable

Adapted from: Centers for Disease Control and Prevention. Asplenia and Adult Vaccination. Updated May 2, 2016. https://www.cdc.gov/vaccines/adults/rec-vac/health-conditions/asplenia.html

Prophylactic antibiotics should be administered based on wound severity and host immune competence. Current guidelines demonstrate marginal benefit to prophylactic therapy in dog bites in otherwise immunocompetent individuals who present > 12 hours after injury. High-risk bites or immunocompromised individuals should receive preemptive antimicrobial coverage for three to five days. Examples of high-risk characteristics include puncture wounds or wounds to the face, hands, or feet.[21] Antimicrobial coverage for both aerobic and anaerobic bacteria is imperative in the treatment of animal bites, and amoxicillin-clavulanate is used often in the outpatient and emergency department setting.[21] Trimethoprim-sulfamethoxazole plus clindamycin is an alternative in individuals with serious allergic reactions to penicillins.[78] When parenteral therapy is indicated, ampicillin-sulbactam or piperacillin-tazobactam are appropriate choices; vancomycin also should be added if there are any concerns for MRSA.[76]

Cat scratches pose a risk for cat scratch disease from *Bartonella henselae*, symptoms of which include fever, enlarged and tender lymph nodes, and a pustule at the scratch site.[79] Cat scratch disease should be treated with azithromycin.[21]

Dog bites result in approximately 55,000 deaths globally per year from rabies. In the United States, more than 90% of rabies cases occur from wildlife bites, predominantly bats, followed by raccoons, skunks, and foxes.[76] Prophylaxis for rabies includes the vaccine series and rabies immune globulin (RIG). Individuals who have received prior rabies immunizations who have rabies antibody titers should receive only a vaccine booster in the case of new exposure. Individuals without prior immunization should receive a four-dose series of rabies vaccines along with a dose of human RIG for post-exposure prophylaxis. The four-dose vaccine series is administered on days 0, 3, 7, and 14 following injury. RIG should be infiltrated around the wound.[76] The need for rabies post-exposure prophylaxis varies according to the animal type. Dog, cat, and ferret bites require prophylaxis if the animal develops any signs of rabies in observation or if there is any suspicion of rabies. Rats, skunks, raccoons, foxes, and most other carnivores should be regarded as rabid unless the animal is proven negative, or unless the geographic area is classified as rabies-free.[78]

Primate bites are uncommon in the United States; however, they pose a risk of herpes B virus in research laboratory workers. Herpes B virus (Macacine alphaherpesvirus 1) closely resembles human herpes simplex virus (HSV) types 1 and 2, and is endemic in rhesus monkeys, pigtailed macaques, and cynomolgus monkeys.[80] Herpes B virus is similar to HSV in that it resides in the trigeminal and lumbosacral sensory ganglia and periodically reactivates, causing intermittent asymptomatic shedding. Infections in humans are rare but can cause flu-like symptoms that progress to encephalomyelitis. If the infection is untreated, the death rate can be as high as 70% to 80%. Prompt antiviral post-exposure prophylaxis for monkey bites should be initiated with valacyclovir or acyclovir.[80]

Splenectomy Considerations

The spleen is a critical element of the human immune system. It regulates both the innate and adaptive immune system as both a phagocytic filter and a production center of human antibodies.[81] Its critical importance was first illustrated by studies that reported cases of overwhelming infections caused by encapsulated bacteria in infants younger than 6 months of age who had undergone prior splenectomies.[82] The spleen is particularly effective at protecting the body from encapsulated bacteria through Immunoglobulin M-mediated phagocytosis via memory B cells that are unique to the spleen.[81]

Incidents and conditions leading to splenectomy or functional asplenia include traumatic splenic rupture, anatomic defects, severe hemolytic anemia, immune-mediated cytopenias, metabolic storage diseases, sickle cell anemia, and secondary hypersplenism.[58] The most significant post-splenectomy complications include sepsis, pneumonia, and meningitis. Rates of these infections vary, with prior analyses between 1966 and 1996 identifying a 3.2% prevalence of infections with a 1.4%

Table 7. Post-Splenectomy Vaccination Recommendations for Children

Vaccine	< 2 years old	> 2 years old	Revaccination
Pneumococcus - PCV13 and PPSV23	4-dose series of PCV13 at 2, 4, 6, and 12 to 15 months of age	1 dose PPSV23 ≥ 8 weeks after last dose of PCV13	PPSV23 every 5 years
***Haemophilus influenzae* type b** - Hib	4- or 3-dose series depending on brand at 2, 4, 6 and 12-15 months of age	Only if prior series not completed	None needed
Meningococcus serotype ACWY	4-dose series at 2, 4, 6, and 12 months of age	2 doses ≥ 8 weeks apart	Every 5 years
Meningococcus serotype B	Not until age 10 years	At age 10 years: 2 or 3 doses depending on brand	None needed

Adapted from: Centers for Disease Control and Prevention. Immunization Schedules for Health Care Providers. Updated Feb. 3, 2020. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-indications-compliant.html

mortality rate.[83] The risk of infections is 50 times greater in splenectomized patients than the general population.[84] Mortality can be as high as 50% in patients who develop postsplenectomy sepsis, most commonly from *Streptococcus pneumoniae*.[85] The disease course in post-splenectomy patients can be sudden in onset with fulminant progression, and sepsis should be suspected in any asplenic patient presenting with severe or febrile illness.[85]

Splenectomy places patients at risk for infections and sepsis from encapsulated bacteria, especially *S. pneumoniae*, as highlighted earlier. Other encapsulated bacteria for which such patients are at higher risk include *Haemophilus influenzae* and *Neisseria meningitidis*. More rare pathogens include *C. canimorsus*, *Babesia*, and *Bordetella holmesii*.[85] Preventing post-splenectomy sepsis depends on vaccination and prophylactic antimicrobial therapy and empiric antimicrobial therapy.

Prophylactic antimicrobial therapy is recommended for certain asplenic patients, including children and older individuals who have experienced an episode of post-splenectomy sepsis. The AAP recommends daily oral penicillin in asplenic children younger than 5 years of age and in older children and individuals for at least one year after splenectomy.[86] Prophylactic penicillin should be initiated in infants with sickle cell disease as soon as a diagnosis is made. The duration of prophylactic therapy is not defined, but the AAP currently recommends discontinuation at 5 years of age in fully immunized children with sickle cell disease who have not had a severe pneumococcal infection. For other causes of asplenia, some experts continue prophylaxis throughout childhood and into adulthood.[86] Lifelong prophylaxis is recommended for children and adults with a history of sepsis caused by encapsulated organisms.[85] The antimicrobial agent of choice and doses vary by age. (*See Table 5.*)

Post-splenectomy patients who present with acute illness, including fever, must seek medical attention immediately and should be initiated on empiric antibiotics. Empiric coverage for adult and pediatric patients should include vancomycin and ceftriaxone or cefotaxime.[87]

Immunizations against *S. pneumoniae*, *N. meningitidis*, and *H. influenzae* type B (Hib) should be provided within 14 days of splenectomy.[1] PCV13 followed eight weeks later by PPSV23 is recommended.[88] Immunization recommendations vary based on age. (*See Tables 6 and 7.*)

Conclusion

Injuries and trauma may cause a wide variety of disruptions in the body's natural barriers and anatomic spaces, leading to contamination and infection. By considering the framework discussed earlier, and following applicable guidelines, practitioners may logically provide prophylaxis and treat secondary infections in trauma patients. Burns, animal bites, and grossly contaminated wounds all warrant additional considerations. Finally, practitioners should always consider tetanus prophylaxis, and whether additional immunization or prophylactic antibiotics are warranted in patients who have undergone traumatic or surgical splenectomy.

References

A complete list of references can be found online at https://bit.ly/2WnQDhY.

CME/CE Questions

1. A 5-year-old girl presents to your emergency department after her older brother fired an airsoft rifle inside the house, causing a ricochet that injured the patient. The parents could not locate the plastic airsoft pellet. The child complains of severe left eye pain. On evaluation, you are concerned for a penetrating globe injury. Which of the following is true?
   a. Gram-negative bacilli are a common cause of post-traumatic endophthalmitis.
   b. Systemic vancomycin is recommended for antimicrobial prophylaxis due to frequent infection with environmental *Bacillus* species.
   c. Systemic cefazolin is the recommended empiric treatment for post-traumatic endophthalmitis.
   d. The presence of a retained foreign object in this situation increases the risk of post-traumatic endophthalmitis.
2. A 16-year-old boy is shot during a drug deal. He is stabilized at a regional medical center and transferred to your hospital for definitive management. Based on imaging obtained by the trauma team and radiology, the trajectory of the bullet crossed his right upper chest, the upper lobe of the right lung and associated pleura, the esophagus, and into the T2 vertebral body. All bullet fragments were removed operatively. He initially received vancomycin and ceftriaxone at the outside hospital,

before completing five days of cefazolin prophylaxis at your center. Now, seven days after his injury and operation, he has developed fever and respiratory distress. Repeat computed tomography demonstrates the development of empyema. Which of the following is true?

a. His infection is likely due to Methicillin-resistant *Staphylococcus aureus*; empiric monotherapy with vancomycin is indicated.
b. His infection is likely due to resistant Gram-negative bacteria; empiric monotherapy with cefepime is indicated.
c. His antimicrobial prophylaxis neglected to take into account likely contamination with anaerobic organisms.
d. He received appropriate antimicrobial prophylaxis, but there is likely a retained bullet fragment in the thorax.

3. A 7-day-old girl is under evaluation at your center for concerns of abuse and neglect reported by a neighbor. The parents frequently use intravenous drugs and admit to setting the newborn down near the radiator in their apartment. She has suffered several partial-thickness burns on her extremities. Which of the following is true?

a. The patient should be started on IV cefazolin prophylaxis due to her young age.
b. The patient should not receive systemic antibiotic therapy, but topical mafenide acetate should be applied after thorough irrigation.
c. Systemic antimicrobials may be considered for perioperative prophylaxis during excision and grafting procedures.
d. Burn injuries should undergo thorough irrigation and debridement but do not require antimicrobial prophylaxis.

4. A 7-year-old boy presents to your center. He was sleeping in a rustic cabin with his family over the weekend. The parents discovered a live bat in the room the boy was sleeping in. They did not capture the bat. Your examination reveals a possible bite wound on the boy's hand. Which of the following is the recommended course of action?

a. Initiate immunization with 1.0 mL dose of rabies vaccine in the deltoid intramuscularly (day 0), followed by doses on days 3, 7, and 14 after the first dose. Concomitant with the first dose of vaccine, administer rabies immunoglobulin around the suspected bite.
b. Administer rabies immunoglobulin around the suspected bite. Do not administer rabies vaccine immediately to avoid interaction of immunoglobulin and vaccine.
c. Administer rabies immunoglobulin and vaccine around the suspected bite. Administer subsequent doses of vaccine on days 3, 7, and 14 after the first dose.
d. This situation does not warrant post-exposure prophylaxis because a bite was not witnessed.

5. A 14-year-old girl is trapped under a farm tractor after it rolls off the edge of a raised road. She has numerous superficial wounds that are grossly contaminated with dirt and manure. She undergoes washout and debridement of her wounds. On review of her state immunization records, you note she is up to date on all recommended vaccines, including Tdap at age 11. Which of the following is true regarding tetanus prophylaxis in her situation?

a. Tetanus is only likely in deep wounds when anaerobic conditions prevail, and superficial wounds and scratches do not require evaluation of immunization status and prophylaxis.
b. She was immunized less than 5 years ago and thus does not require any booster vaccine or tetanus immunoglobulin.
c. Regardless of immunization status she warrants a booster dose with Tdap but not tetanus immunoglobulin.
d. The contaminated nature of her wounds warrants tetanus immunoglobulin regardless of immunization status.

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- discuss any discharge or follow-up instructions with patients.

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Practical, Evidence-Based Reviews in Pediatric Emergency Care

Infections and Prophylaxis in Pediatric Trauma Patients

General Pathogen Considerations and Recommendations for Antibiotic Prophylaxis for Trauma Related to Regional/System Anatomy

Region/System	Pathogen Considerations	Recommended Prophylaxis
Extremities	*Staphylococcus aureus*, Group A Streptococcus, coagulase-negative staphylococci, Gram-negative bacilli	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours* for duration of 1-3 days following definitive washout • With recommended trauma or orthopedic surgery consultation
Penetrating eye injury	Environmental *Bacillus* species, coagulase-negative staphylococci, streptococcal species	• Systemic levofloxacin IV/PO 16-20 mg/kg/day divided Q12-24 hours (up to adult dose of 750 mg/day)** for duration of 7 days • With mandatory ophthalmology consultation
Maxillofacial	*Staphylococcus aureus*, Gram-negative bacilli, oropharyngeal flora	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours* • If disruption of oral or pharyngeal mucosa: PLUS • Metronidazole IV 15 mg/kg loading dose, followed by 30-40 mg/kg/day divided Q6-8 hours for duration of at least 1 day following definitive washout • With mandatory otolaryngology consultation
Thoracic without esophageal involvement	*Staphylococcus aureus*, alpha- and beta-hemolytic streptococci, Gram-negative bacilli	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours* for duration of at least 1 day following definitive washout • With mandatory trauma surgery consultation
Thoracic with esophageal involvement	*Staphylococcus aureus*, alpha- and beta-hemolytic streptococci, Gram-negative bacilli, oral and enteric anaerobes	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours* PLUS • Metronidazole 15 mg/kg IV loading dose, followed by 30-40 mg/kg/day divided Q6-8 hours for duration of at least 1 day following definitive washout • With mandatory trauma surgery consultation
Abdominal	*Escherichia coli*, other Gram-negative, Gram-positive, and anaerobic polymicrobial components, including *Enterococcus* spp., *Bacteroides* spp., and *Enterobacter cloacae*	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours PLUS • Metronidazole 15 mg/kg IV loading dose, followed by 30-40 mg/kg/day divided Q6-8 hours*** for duration of at least 1 day following definitive washout • With mandatory trauma surgery consultation
Central nervous system	*Staphylococcus aureus*, coagulase-negative staphylococci, beta-hemolytic streptococci, other Gram-negatives and some clostridial species	• Cefazolin IV 30 mg/kg (up to adult dose of 2 g) dosed Q6-8 hours • If hollow viscus injury or presence of organic debris is present: PLUS • Metronidazole 15 mg/kg IV loading dose, followed by 30-40 mg/kg/day divided Q6-8 hours for at least 5 days or longer if cerebrospinal fluid leaks are ongoing • With mandatory neurosurgery consultation
Bite Wounds	See Table 4	• Amoxicillin-clavulanate PO 45 mg/kg/day divided Q12 hours (up to adult dose of 875/125 1 tab PO BID)**** • Consider need for rabies prophylaxis • Consult infectious disease specialist for monkey bites

* If patients have a previous history of anaphylaxis to β-lactam antibiotics, clindamycin is an acceptable alternative. In cases where cefazolin and metronidazole are recommended in combination, clindamycin may replace both agents.
**Moxifloxacin is also an acceptable alternative in adult patients, but is not approved for pediatric use.
***Other regimens include cefoxitin with or without gentamicin; gentamicin plus metronidazole and ampicillin; meropenem monotherapy; other acceptable combinations typically used for perforated appendicitis.
****Other acceptable regimens in allergic patients include oral trimethoprim-sulfamethoxazole plus clindamycin.
IV: intravenous; PO: oral; BID: twice per day

Adapted from: 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 Suppl 2):S210-S234.
Kimberlin DW, Long SS, Brady MT, Jackson MA, eds. *Red Book 2018 Report of the Committee on Infectious Diseases.* 31st ed. American Academy of Pediatrics; 2018.
Gilbert DN, Chambers HF, Eliopoulos GM, et al, eds. *The Sanford Guide to Antimicrobial Therapy 2019.* Antimicrobial Therapy, Inc.; 2019.

Leading Causes of Injury Deaths by Age Group, United States – 2018

Rank/Age	< 1 year	1-4 years	5-9 years	10-14 years	15-24 years
1	Unintentional suffocation	Unintentional drowning	Motor vehicle accident	Suicide suffocation	Motor vehicle accident
2	Homicide unspecified	Motor vehicle accident	Unintentional drowning	Motor vehicle accident	Unintentional poisoning
3	Motor vehicle accident	Homicide unspecified	Fire/burn	Suicide firearm	Homicide firearm
4	Homicide, other specified	Fire/burn	Homicide firearm	Homicide firearm	Suicide firearm
5	Undetermined suffocation	Unintentional suffocation	Unintentional suffocation	Unintentional drowning	Suicide suffocation

Adapted from Centers for Disease Control and Prevention. Ten Leading Causes of Death and Injury. Updated March 30, 2020. https://www.cdc.gov/injury/wisqars/LeadingCauses.html

Tetanus Toxoid Recommendations

Past number of doses of previous tetanus toxoid-containing vaccines	Clean, minor wound		Any other wound, including those contaminated by dirt, feces, as well as frostbite, crush injuries, and burns	
	DTaP, Tdap, or Td	TIG*	DTaP, Tdap, or Td	TIG
Unknown or < 3	Yes	No	Yes	Yes
≥ 3	No**	No	No***	No

*Patients with HIV or severe immunocompromise with grossly contaminated wounds should receiveTIG regardless of past immunization status
**Yes, if it has been 10 years or greater since the patient's last tetanus toxoid-containing vaccine
***Yes, if it has been 5 years or greater since the patient's last tetanus toxoid-containing vaccine
Adapted from: Centers for Disease Control and Prevention. Tetanus: For Clinicians. Updated Jan. 23, 2020. https://www.cdc.gov/tetanus/clinicians.html

Post-Splenectomy Vaccination Recommendations for Children

Vaccine	< 2 years old	> 2 years old	Revaccination
Pneumococcus - PCV13 and PPSV23	4-dose series of PCV13 at 2, 4, 6, and 12 to 15 months of age	1 dose PPSV23 ≥ 8 weeks after last dose of PCV13	PPSV23 every 5 years
***Haemophilus influenzae* type b** - Hib	4- or 3-dose series depending on brand at 2, 4, 6 and 12-15 months of age	Only if prior series not completed	None needed
Meningococcus serotype ACWY	4-dose series at 2, 4, 6, and 12 months of age	2 doses ≥ 8 weeks apart	Every 5 years
Meningococcus serotype B	Not until age 10 years	At age 10 years: 2 or 3 doses depending on brand	None needed

Adapted from: Centers for Disease Control and Prevention. Immunization Schedules for Health Care Providers. Updated Feb. 3, 2020. https://www.cdc.gov/vaccines/schedules/hcp/imz/child-indications-compliant.html

Post-Splenectomy Antimicrobial Recommendations

Patient Characteristics	Antimicrobial Choice
Age < 3 years	Oral penicillin V 125 mg BID
Age > 3 years	Oral penicillin V 250 mg BID
Adults	Penicillin V 250 mg BID or amoxicillin 500 mg BID
Penicillin allergy	Erythromycin 250 mg BID

BID: Twice daily

Adapted from: Rubin LG, Schaffner W. Clinical practice. Care of the asplenic patient. *N Engl J Med* 2014;371:349-356.

Post-Splenectomy Vaccination Recommendations for Adults (Age > 19 Years)

Vaccine	Primary Series	Revaccination
Pneumococcal vaccine - PCV13 plus PPSV23	1 dose of PCV13 followed by 1 dose PPSV23 ≥ 8 weeks later	PPSV23 every 5 years
***Haemophilus influenzae* type b vaccine** - Hib	1 dose	None needed
Meningococcal serotype ACWY vaccine - MenACWY	2 doses at least 8 weeks apart	Every 5 years
Meningococcal serotype B - MenB-FHbp or MenB-4C	2 doses of MenB-4C at least 1 month apart or 3 doses of MenB-FHbp at 0, 2, and 6 months	Not applicable

Adapted from: Centers for Disease Control and Prevention. Asplenia and Adult Vaccination. Updated May 2, 2016. https://www.cdc.gov/vaccines/adults/rec-vac/health-conditions/asplenia.html

Important Pathogenic Bacteria in Bite Wounds

Type of Bite	Aerobic Bacteria	Anaerobic Bacteria
Dog	*Pasteurella* spp *Streptococcus* spp *Staphylococcus* spp *Capnocytophaga canimorsus*	*Fusobacterium* spp *Bacteroides* spp *Prevotella* spp *Propionobacterium* spp *Peptostreptococcus* spp
Cat	*Pasteurella* spp *Streptococcus* spp *Staphylococcus* spp *Moraxella* spp	*Fusobacterium* spp *Bacteroides* spp *Porphyromonas* spp *Prevotella* spp *Propionobacterium* spp
Human	*Streptococcus* spp *Staphylococcus* spp *Eikenella corrodens* *Haemophilus* spp	*Fusobacterium* spp *Prevotella* spp *Peptostreptococcus* spp *Veillonella* spp

Adapted from: Bula-Rudas FJ, Olcott JL. Human and animal bites. *Pediatr Rev* 2018;39:490-500.

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References

1. 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 Suppl 2):S210-S234.
2. Kimberlin DW, Long SS, Brady MT, Jackson MA, eds. *Red Book 2018-2021 Report of the Committee on Infectious Diseases.* 31st ed. American Academy of Pediatrics; 2018.
3. Centers for Disease Control and Prevention. Ten Leading Causes of Death and Injury. Updated March 30, 2020. https://www.cdc.gov/injury/wisqars/LeadingCauses.html
4. Teixeira Lopes MCB, de Aguiar W Júnior, Yamaguchi Whitaker I. In-hospital complications in trauma patients according to injury severity. *J Trauma Nurs* 2019;26:10-16.
5. Lopes MCBT, de Aguiar Júnior W, Whitaker IY. The association between burn and trauma severity and in-hospital complications. *Burns* 2020;46:83-89.
6. Brook I. Aerobic and anaerobic microbiology of infections after trauma in children. *J Accid Emerg Med* 1998;15:162-167.
7. Fernandez R, Griffiths R. Water for wound cleansing. *Cochrane Database Syst Rev* 2012;(2):CD003861.
8. Fry DE. Pressure irrigation of surgical incisions and traumatic wounds. *Surg Infect* (Larchmt) 2017;18:424-430.
9. Angerås MH, Brandberg A, Falk A, Seeman T. Comparison between sterile saline and tap water for the cleaning of acute traumatic soft tissue wounds. *Eur J Surg* 1992;158:347-350.
10. Moscati RM, Mayrose J, Reardon RF, et al. A multicenter comparison of tap water versus sterile saline for wound irrigation. *Acad Emerg Med* 2007;14:404-409.
11. Valente JH, Forti RJ, Freundlich LF, et al. Wound irrigation in children: Saline solution or tap water? *Ann Emerg Med* 2003;41: 609-616.
12. Edlich RF, Rodeheaver GT, Morgan RF, et al. Principles of emergency wound management. *Ann Emerg Med* 1988;17:1284-1302.
13. Morse JW, Babson T, Camasso C, et al. Wound infection rate and irrigation pressure of two potential new wound irrigation devices: The port and the cap. *Am J Emerg Med* 1998;16:37-42.
14. Dirschl DR, Duff GP, Dahners LE, et al. High pressure pulsatile lavage irrigation of intraarticular fractures: Effects on fracture healing. *J Orthop Trauma* 1998;12:460-463.
15. Wheeler CB, Rodeheaver GT, Thacker JG, et al. Side-effects of high pressure irrigation. *Surg Gynecol Obstet* 1976;143:775-778.
16. Tintinalli JE, Stapczynski J, Ma OJ, et al. *Tintinalli's Emergency Medicine: A Comprehensive Study Guide*. 7th ed. McGraw-Hill Medical; 2012.
17. Cherry JD, Federman M. Tetanus. In: Cherry JD, Harrison GJ, Kaplan SL, et al, eds. *Feigin and Cherry's Textbook of Pediatric Infectious Diseases*. 8th ed. Elsevier; 2019:1304-1312.
18. Pratt EL. Clinical tetanus; a study of 56 cases, with special reference to methods of prevention and a plan for evaluating treatment. *JAMA* 1945;129:1243-1247.
19. Centers for Disease Control and Prevention. Tetanus: For Clinicians. Updated Jan 23, 2020. https://www.cdc.gov/tetanus/clinicians.html
20. World Health Organization. Immunization, Vaccines, and Biologicals: Tetanus. Updated July 25, 2019. https://www.who.int/immunization/monitoring_surveillance/burden/vpd/surveillance_type/passive/tetanus/en/
21. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2014;59:e10-e52.
22. Murray CK, Hsu JR, Solomkin JS, et al. Prevention and management of infections associated with combat-related extremity injuries. *J Trauma* 2008;64(Suppl 3): S239-S251.
23. Cherry JD, Harrison GJ, Kaplan SL, et al. Skin Infections. In: Cherry JD, Harrison GJ, Kaplan SL, et al, eds. *Feigin and Cherry's Textbook of Pediatric Infectious Diseases*. 8th ed. 2019.
24. Eron LJ. Targeting lurking pathogens in acute traumatic and chronic wounds. *J Emerg Med* 1999;17:189-195.
25. Kim PH, Leopold SS. In brief: Gustilo-Anderson classification. [corrected]. *Clin Orthop Rel Res* 2012;470:3270-3274.
26. Lloyd BA, Murray CK, Shaikh F, et al; Infectious Disease Clinical Research Program Trauma Infectious Disease Outcomes Study Group. Antimicrobial prophylaxis with combat-related open soft-tissue injuries. *Mil Med* 2018;183:e260-e265.
27. Cefazolin. In: Gilbert DN, Chambers HF, Eliopoulos GM, et al, eds. *The Sanford Guide to Antimicrobial Therapy 2019*. Antimicrobial Therapy, Inc.; 2019.
28. Table 5.2: Antimicrobial Prophylaxis in Pediatric Surgical Patients. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book 2018 Report of the Committee on Infectious Diseases*. 31st ed. American Academy of Pediatrics; 2018.
29. Patzakis MJ, Bains RS, Lee J, et al. Prospective, randomized, double-blind study comparing single-agent antibiotic therapy, ciprofloxacin, to combination antibiotic therapy in open fracture wounds. *J Orthop Trauma* 2000;14:529-533.
30. Hoff W, Bonadies J, Cachecho R, Dorlac W. East Practice Management Guidelines Work Group: Update to practice management guidelines for prophylactic antibiotics use in open fractures. *J Trauma* 2011;70:751-754.
31. Durand ML. Endophthalmitis. *Clin Microbiol Infect* 2013;19:227-234.
32. Andreoli CM, Andreoli MT, Kloek CE, et al. Low rate of endophthalmitis in a large series of open globe injuries. *Am J Ophthalmol* 2009;147:601-608.e2.
33. Abu el-Asrar AM, al-Amro SA, al-Mosallam AA, al-Obeidan S. Post-traumatic endophthalmitis: Causative organisms and visual outcome. *Eur J Ophthalmol* 1999;9:21-31.
34. Alfaro DV, Roth DB, Laughlin RM, et al. Paediatric post-traumatic endophthalmitis. *Br J Ophthalmol* 1995;79:888-891.
35. Miller JJ, Scott IU, Flynn HW Jr, et al. Endophthalmitis caused by *Bacillus* species. *Am J Ophthalmol* 2008;145:883-888.
36. Colyer MH, Weber ED, Weichel ED, et al. Delayed intraocular foreign body removal without endophthalmitis during Operations Iraqi Freedom and Enduring Freedom. *Ophthalmology* 2007;114:1439-1447.
37. Endophthalmitis, Post-traumatic. In: Gilbert DN, Chambers HF, Eliopoulos GM, et al, eds. *The Sanford Guide to Antimicrobial Therapy 2019.* Antimicrobial Therapy, Inc.; 2019.
38. Akhlaghi F, Aframian-Farnad F. Management of maxillofacial injuries in the Iran-Iraq war. *J Oral Maxillofac Surg* 1997;55:927-930.
39. Zaytoun GM, Shikhani AH, Salman SD. Head and neck war injuries: 10-year experience at the American University of Beirut Medical Center. *Laryngoscope* 1986;96: 899-903.
40. Russell MD, Goldberg AN. What is the evidence for use of antibiotic prophylaxis in clean-contaminated head and neck surgery? *Laryngoscope* 2012;122:945-946.
41. Brook I, Frazier EH. Aerobic and anaerobic microbiology of infection after trauma. *Am J Emerg Med* 1998;16:585-591.
42. Sanabria A, Valdivieso E, Gomez G, Echeverry G. Prophylactic antibiotics in chest trauma: A meta-analysis of high-quality studies. *World J Surg* 2006;30:1843-1847.
43. Eren S, Esme H, Sehitogullari A, Durkan A. The risk factors and management of post-traumatic empyema in trauma patients. *Injury* 2008;39:44-49.

44. O'Connor JV, Chi A, Joshi M, et al. Post-traumatic empyema: Aetiology, surgery and outcome in 125 consecutive patients. *Injury* 2013;44:1153-1158.
45. Wallace C. A study of 1,200 cases of gunshot wounds of the abdomen. *BMJ* 1916;4:679.
46. Fraser J, Drummond H. Three hundred perforating wounds of the abdomen. *BMJ* 1917;1:321.
47. Fullen WD, Hunt J, Altemeier WA, et al. Prophylactic antibiotics in penetrating wounds of the abdomen. *J Trauma* 1972;12:282-289.
48. Thadepalli H, Gorbach SL, Broido PW, et al. Abdominal trauma, anaerobes, and antibiotics. *Surg Gynecol Obstet* 1973;137:270-276.
49. Steele SR, Wolcott KE, Mullenix PS, et al. Colon and rectal injuries during Operation Iraqi Freedom: Are there any changing trends in management outcome? *Dis Colon Rectum* 2007;50:870-877.
50. Herrod PJ, Boyd-Carson H, Doleman B, et al. Prophylactic antibiotics for penetrating abdominal trauma: Duration of use and antibiotic choice. *Cochrane Database Syst Rev* 2019;12:CD010808.
51. Schnuriger B, Inaba K, Eberle BM, et al. Microbiological profile and antimicrobial susceptibility in surgical site infections following hollow viscus injury. *J Gastrointest Surg* 2010;14:1304-1310.
52. Ascroft PB, Pulvertaft RJ. The bacteriology of head wounds. *Br J Surg* 1947;55(Suppl 1): 183-186.
53. Carey ME, Young H, Mathis JL, Forsythe J. A bacteriological study of craniocerebral missile wounds from Vietnam. *J Neurosurg* 1971;34(2 Pt 1):145-154.
54. Hagan RE. Early complications following penetrating wounds of the brain. *J Neurosurg* 1971;34(2 Pt 1):132-141.
55. Taha JM, Saba MI, Brown JA. Missile injuries to the brain treated by simple wound closure: Results of a protocol during the Lebanese conflict. *Neurosurgery* 1991;29: 380-384.
56. Aarabi B. Comparative study of bacterial contamination between primary and secondary exploration of missile head wounds. *Neurosurgery* 1987;20:610-616.
57. Bayston R, de Louvois J, Brown EM, et al. Use of antibiotics in penetrating craniocerebral injuries. "Infection in neurosurgery" working party of British Society for Antimicrobial Chemotherapy. *Lancet* 2000;355:1813-1817.
58. Kliegman RM, St. Geme J. *Nelson Textbook of Pediatrics*. 21st ed. Elsevier; 2020.
59. Glik J, Labus W, Kitala D, et al. A 2000 patient retrospective assessment of a new strategy for burn wound management in view of infection prevention and treatment. *Int Wound J* 2018;15:344-349.
60. Hill DM, Sinclair SE, Hickerson WL. Rational selection and use of antimicrobials in patients with burn injuries. *Clin Plast Surg* 2017;44:521-534.
61. ISBI Practice Guidelines Committee; Steering Subcommittee; Advisory Subcommittee. ISBI Practice Guidelines for Burn Care. *Burns* 2016;42:953-1021.
62. Atiyeh BS, Costagliola M, Hayek SN, Dibo SA. Effect of silver on burn wound infection control and healing: Review of the literature. *Burns* 2007;33:139-148.
63. Barajas-Nava LA, López-Alcalde J, Roqué i Figuls M, et al. Antibiotic prophylaxis for preventing burn wound infection. *Cochrane Database Syst Rev* 2013;(6):CD008738.
64. Diaz JH, Lopez FA. Skin, soft tissue and systemic bacterial infections following aquatic injuries and exposures. *Am J Med Sci* 2015;349:269-275.
65. Hiransuthikul N, Tantisiriwat W, Lertutsahakul K, et al. Skin and soft-tissue infections among tsunami survivors in southern Thailand. *Clin Infect Dis* 2005;41:e93-e96.
66. Appelgren P, Farnebo F, Dotevall L, et al. Late-onset posttraumatic skin and soft-tissue infections caused by rapid-growing mycobacteria in tsunami survivors. *Clin Infect Dis* 2008;47:e11-e16.
67. Oliver JD. Wound infections caused by *Vibrio vulnificus* and other marine bacteria. *Epidemiol Infect* 2005;133:383-391.
68. Centers for Disease Control and Prevention. *Vibrio* Species Causing Vibriosis. Updated March 5, 2019. http://www.cdc.gov/vibrio/index.html
69. Baumgardner DJ. Soil-related bacterial and fungal infections. *J Am Board Fam Med* 2012;25:734-744.
70. Espelund M, Klaveness D. Botulism outbreaks in natural environments – an update. *Front Microbiol* 2014;5:287.
71. American Academy of Pediatrics. Botulism and Infant Botulism. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases.* American Academy of Pediatrics 2018; 283-286.
72. U.S. Food & Drug Administration. BAT (Botulism Antitoxin Heptavalent (A,B,C,D,E,F,G)- (Equine). Updated Dec. 11, 2018. https://www.fda.gov/vaccines-blood-biologics/approved-blood-products/bat-botulism-antitoxin-heptavalent-b-c-d-e-f-g-equine
73. Campbell EA, Wilbert CD. Foreign body imaging. *StatPearls*. Treasure Island (FL): StatPearls Publishing; 2020.
74. Aras MH, Miloglu O, Barutcugil C, et al. Comparison of the sensitivity for detecting foreign bodies among conventional plain radiography, computed tomography and ultrasonography. *Dentomaxillofac Radiol* 2010;39:72-78.
75. Hunstad D. Animal and Human Bites. In: Kliegman RM, St. Geme J. *Nelson Textbook of Pediatrics*. 21st ed. Elsevier; 2020: 3816-3819.
76. Bula-Rudas FJ, Olcott JL. Human and animal bites. *Pediatr Rev* 2018;39:490-500.
77. Talan DA, Citron DM, Abrahamian FM, et al. Bacteriologic analysis of infected dog and cat bites. Emergency Medicine Animal Bite Infection Study Group. *N Engl J Med* 1999;340:85-92.
78. American Academy of Pediatrics. Bite wounds. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2015 Report of the Committee on Infectious Diseases.* 30th ed. American Academy of Pediatrics; 2015:205-210
79. Centers for Disease Control and Prevention. Bartonella Infection: Cat Scratch Disease FAQs. Updated Jan. 11, 2016. https://www.cdc.gov/bartonella/cat-scratch/index.html
80. Barkati S, Taher H, Beauchamp E, et al. Decision tool for Herpes B virus antiviral prophylaxis after macaque-related injuries in research laboratory workers. *Emerg Infect Dis* 2019;25(9). doi: 10.3201/eid2509.190045
81. Di Sabatino A, Carsetti R, Corazza GR. Post-splenectomy and hyposplenic states. *Lancet* 2011;378:86-97.
82. King H, Shumacker HB Jr. Splenic studies. I. Susceptibility to infection after splenectomy performed in infancy. *Ann Surg* 1952;136:239-242.
83. Bisharat N, Omari H, Lavi I, Raz R. Risk of infection and death among post-splenectomy patients. *J Infect* 2001;43:182-186.
84. Hansen K, Singer DB. Asplenic-hyposplenic overwhelming sepsis: Postsplenectomy sepsis revisited. *Pediatr Dev Pathol* 2001;4:105-121.
85. Rubin LG, Schaffner W. Clinical practice. Care of the asplenic patient. *N Engl J Med* 2014;371:349-356.
86. Immunization and Other Considerations in Immunocompromised Children. In: Kimberlin DW, Brady MT, Jackson, MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases.* American Academy of Pediatrics; 2018: 72-91.
87. Morgan TL, Tomich EB. Overwhelming post-splenectomy infection (OPSI): A case report and review of the literature. *J Emerg Med* 2012;43:758-763.
88. Nuorti JP, Whitney CG; Centers for Disease Control and Prevention. Prevention of pneumococcal disease among infants and children - use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine - recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2010;59:1-18.