

Antibiotic Considerations in the Management of Pediatric Open Fractures

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Abstract: Standard treatment for pediatric open fractures in the Emergency Department (ED) includes prompt administration of intravenous antibiotics and tetanus prophylaxis, bedside irrigation, and reduction or immobilization based on the fracture pattern. Recommendations for management of open fractures in the pediatric population are mostly based on a 1989 landmark study by Patzakis et al., which analyzed factors influencing infection rates in adults. To our knowledge, there is no consensus regarding optimal antibiotic treatment protocols for pediatric open fractures. To that end, we set out to review the literature for current trends in antibiotic management of open pediatric fractures. We specifically reviewed antibiotic choice, length of treatment, and subsequent infection rates.

Key Concepts:

- The Gustilo-Anderson classification system provides a framework to discuss pediatric open fractures.
- There is a paucity of high-quality literature that helps direct care of open fractures in pediatric and adolescent patients.
- Most recommend urgent administration of 1st generation cephalosporins for all open fractures with additional antibiotics for grade III injuries or those contaminated with soil or dirty water (i.e., freshwater or marine injuries).
- Prospective multicenter trials are needed to generate enough power to provide high-quality antibiotic regimen recommendations and the role of surgery in these injuries.

Introduction

The incidence of open pediatric fractures varies from center to center, but most authors agree that they account for 2–9% of all fractures in children.^{1–4} Pediatric open fractures are caused by a variety of mechanisms, including motor vehicle accidents, pedestrians struck, and falls from a height.^{2,3} The most common locations of open fractures are the tibia (34%) and the radius (32%), followed by the hand (10%), femur (6.7%), humerus (6.5%), and foot (4.3%).^{1,4} In pediatric patients with

open fractures, the rate of post-injury infection is 2-10%. Bacterial contamination based on the environment of the antecedent trauma (farm injury, bowel injury, salt, or freshwater) can be present with any of the open fracture types, but the degree of contamination tends to increase with higher Gustilo-Anderson Grade. In a series of 552 fractures, Skaggs et al. reported a 3% infection rate overall, and higher rates with increasing Gustilo-Anderson classification type (Type I – 2%, Type II – 2%, and Type III – 8%).^{1,5}

The modified Gustilo-Anderson classification system is used clinically to characterize open fractures in both adults and children.⁶ Type I open fractures are typically caused by low energy mechanisms and are characterized by simple fracture patterns with a wound no larger than one centimeter, minimal soft tissue damage, and a clean wound bed. Type II fractures are caused by moderate energy mechanisms with wound sizes typically between 1 to 10 centimeters, often with moderate soft tissue damage and comminution. Type III fractures are the result of high-energy injuries with wounds greater than 10 centimeters, extensive soft tissue damage, and severe comminution. Type III fractures are further divided into three sub-types: Type IIIA fractures have soft tissues amenable to either primary closure or skin grafting and do not require any form of vascular repair. Type IIIB fractures require free flap or rotational flap coverage. Type IIIC fractures are characterized by arterial damage requiring vascular repair.

Although the Gustilo-Anderson classification is the most commonly used classification scheme for open fractures, it does have poor interobserver reliability (60%), possibly as a result of characteristic overlap between types.^{7,8} In this review, we focus on the Gustilo-Anderson classification system as it is most commonly used in the pediatrics literature. The OTA Open Fracture Classification has better interobserver reliability but is not commonly used because of its complexity.⁹ Another scheme, the Mangled Extremity Severity Score (MESS), is used to identify patients that might benefit from amputation.¹⁰

Recommendations for the management of open fractures in the pediatric population are mostly based on a 1989 landmark study by Patzakis et al. which looked at factors that affect infection rates.¹¹ The management of open fractures in children has been primarily adopted from this paper and later publications from the adult literature:

1. Antibiotic administration within 3 hours of the injury, specifically a first-generation cephalosporin, has been shown to reduce infection rates in adults.¹¹ In severely contaminated Type II and Type III injuries in adult

patients, most authors recommend adding gentamicin; however, there is no high-level evidence to support this practice.^{2,12,13} Penicillin is often added to cover Clostridium species and anaerobes in patients with farm injuries and broader coverage in open fractures contaminated by freshwater (*Aeromonas* and *Pseudomonas* species) and saltwater (*Vibrio* species).^{2,12-14} Clindamycin may be substituted when a penicillin allergy is suspected. The duration of antibiotic treatment is less clear; however, the adult literature has shown that longer courses of antibiotics are not superior to shorter courses.^{11,15}

2. Tetanus prophylaxis with tetanus toxoid is indicated for all adult patients who have had fewer than three immunizations, have not received a booster within 5 years, or who have uncertain immunization histories.¹⁶

3. Operative irrigation and debridement with fracture stabilization is usually indicated in the adult literature; however, new management protocols have challenged the need for operative management of Type I open fractures.¹⁷⁻²⁰

Subsequent studies regarding antibiotic administration in the pediatric population have been less evidence-based and have relied on protocols based on physician discretion and institutional practice patterns. Surveys of orthopaedic residency programs and of Pediatric Orthopaedic Society of North America (POSNA) members revealed no consensus regarding optimal treatment protocols for pediatric open fractures, highlighting the need for further research on this important subject.^{22,23} We reviewed the literature on pediatric open fractures to identify common antibiotic and operative management protocols with the goal of producing a comprehensive, evidence-based protocol to be implemented at our institution.

Literature Review

While this report is not designed as a meta-analysis study intended for peer-reviewed publication, we performed a very extensive literature review and focused on those studies that provide adequate data for children and adolescents with open fractures. We feel the following

is an excellent summary to drive discussion on the optimal antibiotic use in open fractures in children and adolescents.

In November 2020, we searched MEDLINE and Web of Science electronic databases for all relevant studies regardless of publication date. A total of 298 potentially relevant publications were identified (Figure 1).

Title, abstract, and article screening allowed for exclusion of 288 studies and content. This left 10 studies (nine retrospective, one prospective) published from 1997-2017 for final analysis. Data was extracted and compiled into tables for each Gustilo-Anderson Type (Type I – Table 1; Type II – Table 2; Type III – Table 3). There was a combined patient total of 1,197 (Type I – 833, Type II – 197, Type III – 167 patients), with age ranging between 1 and 18 years old, 73% male and 27% female. Follow-up ranged from 1 to 56 months.

Antibiotic management of Type I open fractures varied among studies. Each protocol included administration of a first-generation cephalosporin, typically Cefazolin, while one study used Amoxicillin/Clavulanic Acid (Table 1).^{1,5,17–20,24–26} Only two studies documented the time to administration of antibiotics (i.e., 292 minutes from injury²⁰ and less than 3 hours from presentation²⁶), while the remaining authors simply documented that antibiotics were administered promptly.^{1,5,17–19,24,25} Antibiotics were usually administered for 24 hours; however, two studies administered antibiotics for 48 hours^{25,26} and three other studies had a proportion of patients (57% in Godfrey et al.) who only received one dose.^{18,20,25} Three studies provided a 1 to 7-day course of antibiotics at discharge^{19,25,26} while two studies did not prescribe oral antibiotics at discharge.^{17,20} Nine studies reported a 0-4% infection rate (Table 1). In six of the studies, administration of antibiotics was typically followed by irrigation and debridement (I&D) as well as closed reduction in the emergency room.^{17–20,24,25} Two studies, including 377

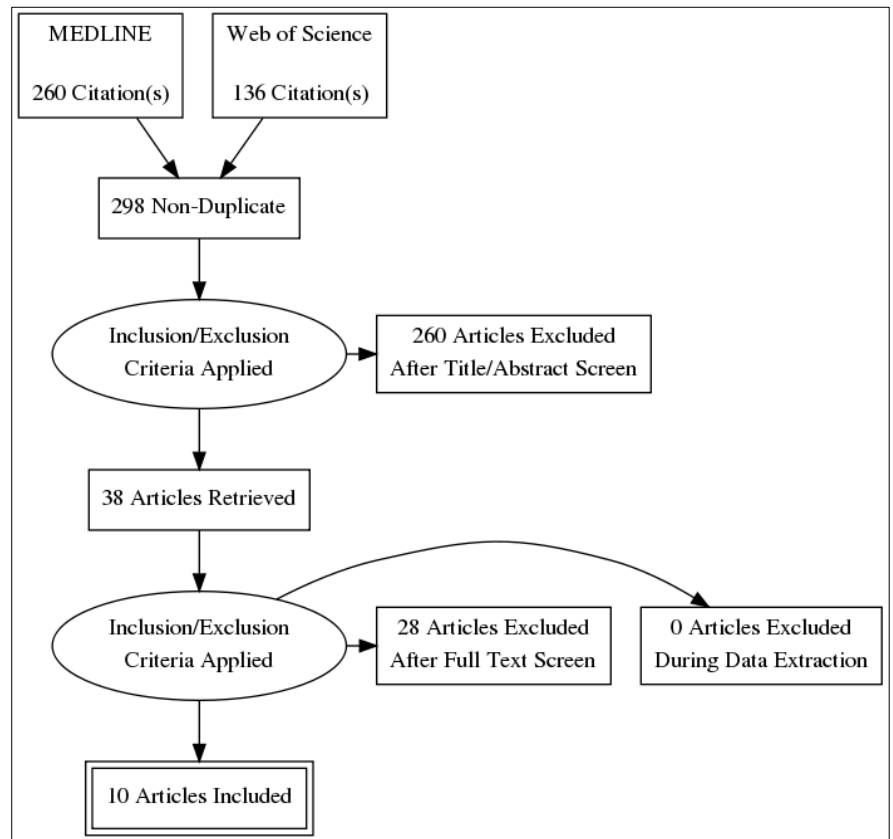


Figure 1. Study selection flow chart. A flow chart describing the process by which studies were identified, screened, and included.

patients, compared operative and nonoperative irrigation and debridement for open tibia and forearm fractures.^{18,25} They found no difference in infection rates in the forearm (3% for operative vs. 0% for nonoperative) and tibia (0% for operative and 2% for nonoperative).^{18,25}

Studies on the management of Type II and Type III fractures were limited, with only five included in this review (Tables 2 and 3).^{1,5,21,26,27} Pandya et al.²⁷ administered antibiotics within 131 minutes from injury and Nandra et al.²⁶ within 3 hours of presentation while the remaining authors documented prompt administration without citing specific timelines. The authors noted that antibiotic choice was at the discretion of the attending, and there was substantial variability in the antibiotics administered.^{1,5,27} For example, Hutchins et al. used a first-generation cephalosporin for Type II femur fractures, and for Type III fractures they advocated for additional

Table 1. Literature Review/Type I Fracture Management

Year	Title	Author	Design	Patients	Anatomic Location	Treatment Protocol	Outcome
2000	Open Femur Fractures in Children: Treatment, Complications, and Results	Hutchins et al.	Multicenter retrospective cohort	25	Femur	Intravenous antibiotics upon presentation, operative irrigation and debridement	0% infection rate
2005	The effect of surgical delay on acute infection following 554 open fractures in children	Skaggs et al.	Multicenter retrospective cohort	302	Forearm and tibia	Intravenous antibiotics upon presentation, operative irrigation and debridement	2% infection rate <6hr to surgery, 2% in 7-24 hour to surgery, no significant difference
2009	Nonoperative management of pediatric grade 1 open fractures with less than a 24-hour admission	Doak and Ferrick	Single-center retrospective cohort	25	Forearm	Intravenous Cefazolin upon presentation, nonsurgical management with bedside irrigation, fracture reduction and stabilization, 1- to 7-day course of oral antibiotics	4.0% infection rate
2014	Results of the treatment of the open femoral shaft fractures in children	Tomaszekski et al.	Single-center retrospective cohort	12	Femur	Intravenous Cefazolin upon presentation, nonsurgical debridement, and intramedullary nailing	0% infection rate
2014	A protocol for the management of pediatric Type I open fractures	Lobst et al.	Single-center prospective cohort	45	Forearm	Intravenous Cefazolin upon presentation and over 24hr hospital admission, nonsurgical management with bedside irrigation, fracture reduction and stabilization, no oral antibiotics	0% infection rate
2014	Is nonoperative treatment of pediatric Type 1 open fractures safe and effective?	Bazzi et al.	Single-center retrospective cohort	40	Forearm and tibia	Intravenous Cephalexin upon presentation, nonsurgical management with bedside irrigation, fracture reduction and stabilization, no oral antibiotics	0% infection rate
2017	Operative versus nonoperative management of pediatric Type 1 open forearm fractures.	Goss et al.	Single-center retrospective cohort	155	Forearm	23% fractures treated operatively and 48hrs of postop antibiotics, 77% of fractures treated with bedside irrigation, intravenous antibiotics for 24-48 hours and 5-7 days of oral antibiotics	3% infection rate with surgery, 0% without surgery, no significant difference

Table 2. Literature Review/Type II Fracture Management

Year	Title	Author	Design	Patients	Anatomic Location	Treatment Protocol	Outcome
2000	Open Femur Fractures in Children: Treatment, Complications, and Results	Hutchins et al.	Multicenter retrospective cohort	9	Femur	Intravenous first-generation cephalosporin upon presentation >48hrs, operative irrigation and debridement, and fixation	0% infection rate
2005	The effect of surgical delay on acute infection following 554 open fractures in children	Skaggs et al.	Multicenter retrospective cohort	154	Forearm and tibia	Intravenous antibiotics upon presentation continued for >24hrs, operative irrigation and debridement, fixation method determined by surgeon preference	3% infection rate in <6hr to surgery group and 0% in 7-24hr group, no significant difference
2012	Immediate Intramedullary Flexible Nailing of Open Pediatric Tibial Shaft Fractures	Pandya et al.	Single-center retrospective cohort	26	Tibia	14 open and 12 closed fractures treated with intravenous antibiotics for >48hrs and flexible nailing	7% infection rate in open, 0% in closed, no significant difference
2017	The management of open tibial fractures in children	Nandra et al.	Single-center retrospective cohort	8	Tibia	Intravenous Amoxicillin/Clavulanic acid upon presentation, operative irrigation and debridement, combined treatment of skeletal and soft-tissue injuries	0% infection rate

Table 3. Literature Review/Type III Fracture Management

Year	Title	Author	Design	Patients	Anatomic Location	Treatment Protocol	Outcome
1997	Treatment of Type II and Type III Open Tibia Fractures in Children	Bartlett et al.	Single-center retrospective cohort	17	Tibia	Operative irrigation and debridement, external fixation, and postoperative 3-day course of Cefazolin	40% infection rate; 0% deep infections
2000	Open Femur Fractures in Children: Treatment, Complications, and Results	Hutchins et al.	Multicenter retrospective cohort	9	Femur	Intravenous first-generation Cephalosporin and Gentamycin for >48hrs, irrigation and debridement, external fixation, IM nail or ORIF	50% deep infection rate
2005	The effect of surgical delay on acute infection following 554 open fractures in children	Skaggs et al.	Multicenter retrospective cohort	98	Forearm and tibia	Intravenous antibiotics upon presentation continued for >24hrs, operative irrigation and debridement, fixation method determined by surgeon preference	10% infection rate <6hr to surgery, 2% in 7-24hr group, no significant difference
2017	The management of open tibial fractures in children	Nandra et al.	Single-center retrospective cohort	43	Tibia	Intravenous Amoxicillin/Clavulanic acid upon presentation continued for >48hrs, operative irrigation and debridement, combined treatment of skeletal and soft-tissue injuries	26% superficial and 7% deep infection rate

gram-negative (e.g., Gentamicin) and anaerobic (e.g., penicillin) coverage, resulting in a deep infection rate of 0% and 50%, respectively.⁵ Nandra et al. used Amoxicillin/Clavulanic Acid for the management of Type II and Type III tibia fractures with a 0% and 26% superficial infection rate, respectively.⁵ Antibiotics were typically continued for greater than 48 hours and up to 7 days.^{1,5,21,26,27} Antibiotic administration was followed by operative irrigation and debridement with fixation method determined by the fracture pattern and surgeon preference.^{1,5,21,26,27} Skaggs et al. found that the time to surgery did not affect infection rates for Type II and Type III fractures.¹ There was no consensus on the continuation of antibiotics postoperatively.^{1,5,21,26,27} Bartlett et al., for the management of Type III tibia fractures, provided a postoperative 3-day course of Cefazolin resulting in a 40% superficial infection rate and a 0% deep infection rate.²¹

We reviewed the literature for trends in antibiotic administration and perioperative management of pediatric open fractures. Based on our review, prompt administration of antibiotics is advised in order to decrease infection rates.^{1,5,17-21,24-27} Specifically, administration of antibiotics within 3 hours of injury has been shown to decrease infection rates.^{11,26,27} The choice of antibiotic was variable based on Gustilo-Anderson fracture type, with a strong consensus that a first-generation cephalosporin can reduce infection rates for Type I and Type II fractures. There was no high-level evidence to suggest that the addition of gram-negative coverage is necessary in Type III fractures, as is common practice in many institutions.^{2,13} In addition, it is important to remember that Gentamicin can cause renal toxicity as well as ototoxicity.²⁸ Nandra et al. suggested that Amoxicillin/Clavulanic Acid may have of role in reducing infection rates with Type III fractures.²⁶ Duration of antibiotics was 24 hours for Type I.^{1,5,17-19,24} For Type II and Type III fractures, antibiotics were given for more than 48 hours with the addition of a post-discharge course of oral antibiotics.^{1,5,21,26,27} In the literature, there has been a shift to bedside irrigation and debridement in the Emergency Department followed by closed reduction

for Type I fractures, as opposed to management in the operating room.^{17-20,24,25} Type II and Type III fractures require operative irrigation and debridement in addition to fixation.²

These findings are consistent with a study that surveyed academic orthopaedic residency programs for antibiotic treatment patterns for open pediatric fractures.²³ Type I fractures were most commonly treated with a cephalosporin alone (97%) for less than 48 hours (87%). Type II fractures were treated by most programs with a cephalosporin alone with no aminoglycoside (84%) for less than 48 hours (80%). Type III fractures were treated by most programs with a cephalosporin and an aminoglycoside (IIIa – 50%, IIIb – 54%, IIIc – 53%) for less than 48 hours (IIIa – 60%, IIIb – 53%, IIIc – 51%). A prospective, double-blind, randomized controlled trial by Dellinger et al. compared a 1-day versus 5-day course of postoperative antibiotics in 248 patients with open fractures.¹⁵ No significant difference in infection rates was found between the 1-day course (13%) and the 5-day course (12%), and these findings were consistent across all Gustilo-Anderson types.¹⁵ However, it is important to note that patients less than the age of 14 were excluded from this study, and so the generalizability of these findings to patients under 14 years old is unclear.

Antibiotic management continues to be guided by the foundational Patzakis et al. randomized prospective study, which analyzed factors that influenced infection in 1,100 adults and children with open fractures.¹¹ The infection rate was 2% for patients treated with a cephalosporin, 10% for those treated with penicillin and streptomycin, and 14% for those who had not been given antibiotics. When antibiotics were administered within 3 hours after injury, there was an infection rate of 4.7% (17/364), and when antibiotics were delayed >3 hours, the infection rate was 7.2% (49/661). Notably, the duration of antibiotic treatment, the type of wound closure, and time from injury to debridement had no effect on infection rate, findings which were supported by Skaggs et al.^{1,11}

Table 4. Authors' Current Management Protocol Based on Literature

	Type I	Type II	Type III
Antibiotic (within 3hrs)	Cefazolin	Cefazolin	Cefazolin + Gentamicin OR Amoxicillin/Clavulanic Acid
Length	24-48 hours	48 hours	48 hours
OP/Non-Op	OP/Non-Op* *faculty discretion	OP (within 24 hours)	OP (within 24 hours)

Retrospective case series have shown no difference in infection rates with nonoperative versus operative management of Type I fractures.¹⁷⁻²⁰ However, concern regarding serious and even life-threatening infection continues to limit the universal adoption of nonoperative treatment protocols.^{5,26} Type III fractures continue to have high infection rates, for example, osteomyelitis (50%) in open femur fractures.⁵ Of the studies surveyed on the management of pediatric Type III fractures, Nandra et al. had the lowest infection rate (26% superficial and 7% deep) with the use of Amoxicillin/Clavulanic Acid.²⁶ While only documented in this study, the use of Amoxicillin/Clavulanic Acid may have a role in decreasing open fracture infections.

In general, low-energy gunshot wounds are not classified as open fractures and may be safely treated nonoperatively if not grossly contaminated.^{21,28-30} Dickey et al. reported similar rates of infection in patients treated with Cefazolin for 24 hours compared to those treated without antibiotics.³⁰ However, some authors argue that gross contamination may not always be apparent, and therefore, they recommend Cefazolin for 48 hours or Ceftriaxone for 24 hours after injury.^{11,30-32} High-energy gunshot wounds with extensive contamination mandate immediate treatment that follows an open fracture protocol with antibiotics for 48-72 hours. For these open fractures, a first-generation cephalosporin with the possible addition of an aminoglycoside, penicillin, or a broad-spectrum antibiotic for at least 48 to 72 hours should be instituted. Fracture fixation, neurovascular injury, and soft tissue compromise should also be addressed.

To our knowledge, there are no consensus guidelines for antibiotic administration for pediatric open fractures. However, in 2006, the Surgical Infection Society released evidence-based guidelines for prophylactic antibiotic use in *adult* open fractures.¹³ Hauser et al. recommended the use of a first-generation cephalosporin for 24-48 hours in patients with Type I fractures and a first-generation cephalosporin for 48 hours in patients with Type II and III fractures. The Society determined that there is insufficient data to conclude that 1) prophylactic antibiotics directed against gram-negative bacteria are beneficial in any open fracture, 2) prolongation of prophylactic antibiotic use past the initial perioperative period is beneficial in any open fracture, and 3) penicillin should be administered routinely to patients receiving other indicated antibiotic prophylaxis for open fractures in the setting of Clostridium-prone injuries. While well-studied in the adult population, it is still unknown whether these practices produce similar outcomes in the pediatric population. Therefore, there is a need for more high-quality, prospective studies looking at open fractures in the pediatric population in order to produce a comprehensive set of antibiotic administration guidelines. Unfortunately, it is logistically difficult to develop prospective studies of this nature, which is why we set out to review the current literature in order to provide a standardized algorithm based on the best available current evidence.

Our Institution's Protocol

At our Level 1 trauma center, we start all pediatric patients with open fractures on a first-generation cephalo-

sporin (i.e., Cefazolin) as soon as possible from the time of injury. Our providers add Gentamycin for all Type III fractures of the lower extremity; however, two of our three providers defer Gentamycin for Type III fractures of the upper extremity. Fluroquinolones are added for marine injuries, Doxycycline for freshwater injuries, penicillin for farm injuries, and Zosyn (Piperacillin-Tazobactam) for concurrent bowel injuries. Duration of antibiotics was highly variable, varying from 24 hours to 48 hours of IV antibiotics to 5-7 days of oral antibiotics.

Next, a bedside irrigation is performed with saline and an anti-septic solution (usually povidone-iodine or hydrogen peroxide), and meticulous debridement of any visible debris is performed. The wound is left open and dressed with Xeroform (Covidien, Mansfield, MA) and soft-tissue dressings. Subsequently, closed reduction of the fracture with application of a splint is performed, all under conscious sedation provided by the ED staff. Many Type I open fractures are managed operatively at our institution based on the individual treatment preferences of the pediatric orthopaedic attendings. Type II and III fractures are taken to the operating room for formal irrigation and debridement with appropriate surgical stabilization.

Conclusion

In this review, we described the current trends in antibiotic management of open pediatric fractures. Our study did not focus on the role of surgery in open fractures, but it is likely that the final infection rate, antibiotic choice, and surgical management are intimately related. Based on our review of the literature we found that Gustilo and Anderson Type I pediatric open fractures are generally managed with the administration of a first-generation cephalosporin (e.g., Cefazolin) within 3 hours of injury and fracture stabilization in the emergency department.

It remains controversial whether all Type I open fractures should be treated with formal operative irrigation

and debridement (I&D) or whether ED irrigation and debridement is safe and effective. Surgeon bias and personal experience factor into these decisions. Is a pin-prick, open ulna fracture in a child who falls down carpeted stairs in pajamas the same as the child who falls off a swing set into the dirt with the same fracture and a 5mm opening? While multicenter efforts are currently being made to provide clarity on this issue, it will require a very large study with enough power to help define the parameters for these two types of treatment. Provider experience, as well as patient compliance and follow-up, are critical for success. If concerns exist, no one can be faulted to perform an operative I&D. For Types II & III fractures, these may be similarly managed with a first-generation cephalosporin and provisional bedside irrigation, and fracture stabilization; however, these fracture types require further debridement and fracture stabilization in the operating room. Additional gram-negative coverage (e.g., Gentamicin) is frequently added for Type 3 fractures, and in cases of farm injuries, anti-clostridial drugs such as penicillin may be added; the evidence supporting these practices, however, is lacking.

Overall, we found a paucity of high-quality evidence regarding antibiotic management of open pediatric fractures. There is insufficient evidence to support the use of additional postoperative oral antibiotics. There exists significant variability in institutional protocols, especially for Type III open fractures. In our own institution, we found significant variability amongst attendings in antibiotic choice and duration of treatment. There is a need for appropriately powered prospective studies that analyze antibiotic appropriateness and infection rates in order to develop a universally accepted protocol. This will likely require large scale prospective multicenter trials from dedicated POSNA members.

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