OPEN

Antibiotic prophylaxis in trauma: Global Alliance for Infection in Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and World Society of Emergency Surgery guidelines

Federico Coccolini, MD, Massimo Sartelli, MD, Robert Sawyer, MD, Kemal Rasa, MD, Marco Ceresoli, MD, Bruno Viaggi, MD, Fausto Catena, MD, PhD, Dimitrios Damaskos, MSc, MBBS, Enrico Cicuttin, MD, Camilla Cremonini, MD, Ernest E. Moore, MD, Walter L. Biffl, MD, *and* **Raul Coimbra, MD, PhD**,
San Diego, California

ABSTRACT: Trauma is a complex disease, and the use of antibiotic prophylaxis (AP) in trauma patients is common practice. However, considering the increasing rates of antibiotic resistance, AP use should be questioned and limited only to specific cases. Antibiotic stewardship is of paramount importance in fighting resistance spread. Definitive rules or precise indications about AP in trauma remain unclear. The present article describes the indications of AP in traumatic lesions to the head, brain, torso, maxillofacial, extremities, skin, and soft tissues endorsed by the Global Alliance for Infection in Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and World Society of Emergency Surgery. (*J Trauma Acute Care Surg.* 2024;96: 674–682. Copyright © 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.)

KEY WORDS: Antibiotic; prophylaxis; therapy; trauma; guidelines.

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

Antibiotic prophylaxis (AP) in surgery is critical to prevent surgical site infections (SSIs). It is defined as the prevention of infectious complications by administering an effective antimicrobial agent before exposure to contamination during surgery.[1] As suggested by Bratzler et al.,[2] AP may also be defined as "the rational, safe, and effective use of antimicrobial agents for the prevention of (initial) SSIs."

The World Health Organization provides strong recommendations on the administration of AP before surgical incision when indicated, depending on the type of operation and its timing and duration.[3] However, AP is often used inappropriately around the globe. Antibiotic misuse reduces patient safety and increases the rate of antimicrobial resistance. Physicians worldwide generally apply wrong criteria when prescribing AP because of errors associated with the following factors: drug, dosage, duration, timing, and/or means of administration. In polytrauma patients, the presence of multiple associated injuries may lead to multiple potential risks of infections. For this reason, antibiotics used for treatment or prophylaxis are commonly applied worldwide without a clear and defined rationale following recommended guidelines. Clinical research reflects this heterogeneous practice associated with the difficulty of standardizing definitions and approaches.[4]

The very liberal use of antibiotics and often their misuse trigger several severe problems.[5] Increased antibiotic resistance, the issues linked to infection by *Clostridioides* spp., and the urgent need to rationalize resources create a need to standardize and control AP prescription.[6] Ideally, AP in trauma should be targeted specifically for each patient, accounting for their individual characteristics. In addition, it should decrease the risk of infection due to single or multiple injuries, reduce the selection of multiresistant species, and have no adverse effects.[7] Liberal and premature administration of antimicrobials should be avoided.[8] Infections must be treated only when present, and their prevention must occur based on specific rules and precise circumstances. The fear of infections must not drive AP prescription. Specific evidence-based indications and antimicrobial stewardship programs must be implemented locally, nationally, and internationally.[9]

Submitted: November 6, 2023, Revised: November 16, 2023, Accepted: November 17, 2023, Published online: December 18, 2023.

From the General, Emergency and Trauma Surgery Department (F.C., C.C.), Pisa University Hospital, Pisa; General and Emergency Surgery (M.S.), Macerata Hospital, Macerata, Italy; Department of Surgery (R.S.), Western Michigan University Homer Stryker MD School of Medicine Kalamazoo, Michigan; Department of Surgery (K.R.), Anadolu Medical Center, Kocaali, Turkey; General, Emergency and Trauma Surgery Department (M.C.), Monza University Hospital, Monza; ICU Department (B.V.), Careggi Hospital, Firenze; Emergency and Trauma Surgery (F.C.), Maggiore Hospital, Parma, Italy; General and Emergency Surgery (D.D.), NHS Lothian, Edinburgh, United Kingdom; General, Emergency and Trauma Surgery Department (E.C.), Pavia University Hospital, Pavia, Italy; Ernest E Moore Shock Trauma Center at Denver Health (E.E.M.), Denver, Colorado; Trauma Surgery Department (W.L.B), Scripps Memorial Hospital, La Jolla, California; and Division of Trauma and Acute Care Surgery (R.C.) and Comparative Effectiveness and Clinical Outcomes Research Center (R.C.), Riverside University Health System, Moreno Valley, California.

Address for correspondence: Raul Coimbra, MD, PhD, Division of Trauma and Acute Care Surgery, Riverside University Health System, 10793 Carillon Court, San Diego, CA 92131; email: rcoimbra@aast.org.

This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/TA.0000000000004233

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

The present article reports on the recommendations proposed and endorsed by the Global Alliance for Infection in Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and the World Society of Emergency Surgery regarding AP in head, brain, torso, maxillofacial, extremities, skin, and soft tissue injuries. We aimed to provide the indications of AP in managing trauma patients.

Notes on the Use of the Guidelines

The guidelines are evidence based, with the grade of recommendation based on the evidence. The guidelines present the methods for optimal management of AP in trauma patients. The practice guidelines promulgated in this work do not represent a standard of practice. They are suggested plans of care based on the best available evidence and the consensus of experts, but they do not exclude other approaches as being within the standard of practice. For example, they should not be used to compel adherence to a given medical management method, which should be finally determined after considering the conditions at the relevant medical institution (staff levels, experience, equipment, etc.) and the characteristics of the individual patient. However, responsibility for treatment results rests with those directly engaged therein and not with the consensus group.

PATIENTS AND METHODS

A computerized search was done by a bibliographer in different databases (MEDLINE, Scopus, EMBASE), and citations published between January 2000 to May 2023 were included when satisfying the primary search strategy: "antibiotic prophylaxis," "trauma," "antibiotic," "heat trauma," "brain trauma," "burns," "skin," "maxillofacial," "thoracic trauma," "abdominal trauma," "facial trauma," "bites," and "guidelines" combined with AND/OR. No search restrictions were imposed. Expert opinion reviews, narrative reviews, case reports, and case series based on less than 30 patients were not considered relevant. The dates were selected to allow comprehensive published abstracts of clinical trials, consensus conferences, comparative studies, congresses, guidelines, government publications, multicenter studies, systematic reviews, meta-analyses, large case series, original articles, and randomized controlled trials (RCTs). Narrative review articles were only used to determine if other cited studies should be included.

The level of evidence was graded as high, moderate, low, and very low. The grade of recommendation, defined as strong, moderate, and weak, was established, considering the Oxford model.[10]

A group of experts from the involved Societies (Global Alliance for Infection in Surgery, Surgical Infection Society Europe, World Surgical Infection Society, American Association for the Surgery of Trauma, and World Society of Emergency Surgery) led by a central coordinator was contacted to express their evidence-based position on the topic. Through the Delphi process, different issues were discussed in several rounds. The central coordinator assembled the different answers derived from each round. Each version was then revised and improved. After three rounds, the process led to 100% agreement on all statements. The final version upon which the agreement was reached resulted in the present article. Statements are summarized in Table 1.

DEFINITIONS

Antibiotic prophylaxis, defined as the use of antibiotics to prevent infections at the site of injury and/or surgical site, must be administered close to the time of procedure initiation or time of injury and according to its pharmacodynamics and pharmacokinetics.

Prolonged AP is defined as AP extending beyond the first 24 hours after an invasive procedure or injury.

Antibiotic therapy is defined as the use of antibiotics aiming to provide adequate drug activity (bacteriostatic or bactericidal) at the site of infection against defined/undefined bacteria. It should exceed the amount needed to inhibit the growth of the microorganism involved and/or kill it.

Head and Brain Trauma

- Antibiotic prophylaxis in blunt head and brain trauma is not indicated in patients treated nonoperatively (moderate recommendation, intermediate-quality evidence).
- Prolonged AP (24 hours) in penetrating head and brain trauma is indicated (moderate recommendation, intermediate-quality evidence).

Blunt head and brain traumas are the most frequent mechanisms of injury, although penetrating injury is prevalent in some regions of the world. The literature on antibiotic therapy in those injuries is generally scarce, and the quality of evidence is low. However, based on the published studies, some indications are clear. No significant differences in infection rates exist between patients who received AP and those who did not.[11–21] No differences were observed between basilar or skull close and open fractures.[22] Data showed heterogeneity in terms of inclusion criteria, duration of antibiotic therapy, and dosages.[13,14] It must be emphasized that differences exist regarding the definition of AP and the timing of administration among different studies published during the last decades. These differences may impair the possibility of obtaining definitive data. Prolonged AP was administered with different drugs (5-day ceftriaxone, 3-day ceftriaxone or ampicillin-sulbactam, and 8-day average course of penicillin, respectively), but the existence of antibiotic-resistant bacteria was not investigated.[23–25]

Maxillofacial Trauma

- Antibiotic prophylaxis in blunt maxillofacial trauma is indicated in patients undergoing open reduction of the fracture (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis in penetrating maxillofacial trauma is indicated (moderate recommendation, intermediate-quality evidence).
- Prolonged AP (24 hours) may be considered in cases of open reduction of contaminated wounds (moderate recommendation, low-quality evidence)

Infection is the most common complication in open mandibular fractures (10–15%).[26] A possible source of contamination is the colonization of the oral cavity. Fractures involving this site could be considered contaminated.[27] No consensus in AP administration for operative and nonoperative facial fractures

© 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

TABLE 1. Summary Statements

	Summary Statements
Head and brain trauma	– Antibiotic prophylaxis in blunt head and brain trauma is not indicated in patients treated nonoperatively (moderate recommendation, intermediate-quality evidence). – Prolonged AP (24 hours) in penetrating head and brain trauma is indicated (moderate recommendation, intermediate-quality evidence).
Maxillofacial trauma	– Antibiotic prophylaxis in blunt maxillofacial trauma is indicated in patients undergoing open reduction of the fracture (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis in penetrating maxillofacial trauma is indicated (moderate recommendation, intermediate-quality evidence). – Prolonged AP (24 h) may be considered in cases of open reduction of contaminated wounds (moderate recommendation, low-quality evidence).
Thoracic trauma	– Antibiotic prophylaxis in healthy patients sustaining blunt thoracic trauma is not indicated (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is not indicated in blunt thoracic trauma patients undergoing chest tube placement (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is indicated in penetrating thoracic trauma patients undergoing chest tube placement (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is indicated in all cases of delayed drainage of retained hemothorax (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is indicated in blunt and penetrating thoracic trauma cases undergoing surgical exploration (thoracotomy/thoracoscopy) (moderate recommendation, intermediate-quality evidence).
Abdominal trauma	– Antibiotic prophylaxis is not indicated in blunt abdominal trauma treated nonoperatively (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis is indicated in penetrating abdominal trauma, especially in patients undergoing surgical exploration (laparotomy/laparoscopy) (moderate recommendation, intermediate-quality evidence). – Prolonged AP (24 h) and/or antibiotic therapy should be considered in patients with hollow viscus injury (moderate recommendation, intermediate-quality evidence).
Open fractures	– Antibiotic prophylaxis effectively reduces wound infections in open fractures, and it should be administered as soon as possible (moderate recommendation, intermediate-quality evidence). – Long-term antibiotic treatment (7–10 d) is ineffective in reducing open fracture wound infection rate (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis longer than 24 h is not indicated in gunshot-related fractures (moderate recommendation, intermediate-quality evidence).
Burns	– Routine AP in burns patients is not indicated (moderate recommendation, intermediate-quality evidence). – Routine source control with extensive irrigation for the removal of contaminated material is part of infection prevention in burn patients (moderate recommendation, intermediate-quality evidence). – No differences exist between systemic and topical AP in preventing infections in burn patients (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis in severe burn patients is indicated in those undergoing endotracheal intubation and mechanical ventilation; it should be ideally administered before the intubation and according to the pharmacokinetics of the chosen antibiotic when possible (moderate recommendation, intermediate-quality evidence). – Antibiotic prophylaxis in severe burn patients may be indicated to prevent split-thickness skin graft infection (moderate recommendation, intermediate-quality evidence). – There is no indication for routine AP following the debridement of devitalized tissues (moderate recommendation, intermediate-quality evidence).
Skin wounds and bites	– Routine AP in skin and soft-tissue injuries is not strictly indicated and should be considered case by case (moderate recommendation, intermediate-quality evidence). – Routine AP in mammalian bites is not strictly indicated and should be considered case by case (moderate recommendation, intermediate-quality evidence). – Accurate prevention of viral infectious disease in animal bites must be performed (i.e., rabies virus) (moderate recommendation, intermediate-quality evidence). – Attention to tetanus immunization must be given (moderate recommendation, intermediate-quality evidence). – Accurate source control should be accomplished by cleaning, irrigating, and disinfecting wounds in all skin and soft tissue injuries, including all mammalian bites (moderate recommendation, intermediate-quality evidence).

exists.[28] In general, no differences exist related to the location of the fracture (condylar, maxillary, zygoma) or among different classes of antibiotics in terms of infectious complications due to AP use. Antibiotic therapy in maxillofacial fractures reduced the incidence of SSIs in four RCTs.[29–31] This is especially true for open fracture reductions. Single-shot regimens or short protocols (maximum of 24 hours) seemed to have the same, if not better, effect than longer treatments. The studies included fractures related to the dental area of the mandible and not the condylar region. Postoperative continuation of antibiotic therapy was investigated.[32] No reduction in SSI was observed with the addition of postoperative antibiotics to the standard perioperative prophylaxis after surgery for maxillofacial trauma (relative risk [RR], 1.11; 95% confidence interval [CI], 0.86–1.44).[30,33–42]

The subgroup of patients with mandibular fractures (RR, 1.00; 95% CI, 0.62–1.67) or whenever open reduction was needed (RR, 1.21; 95% CI, 0.89–1.63) did not show an increase in SSI if antibiotics were continued beyond the prophylactic dose.[30,34,39,40]

No differences in the reduction of SSI were observed with prolonged antibiotic regimens beyond prophylaxis in a recent systematic review and meta-analysis of 27 studies (<24 hours antibiotic regimen was compared with 24–72 hours and >72 hours) by Habib et al.[43] Overall, 16 studies focused on mandible fractures, four studies on midface fractures, and six studies on orbital fractures.

Another systematic review and meta-analysis by Dawoud et al.[44] compared patients who received AP with those without

© 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

antibiotics. No clear advantages of AP in reducing adverse events were found (RR, 1.38; 95% CI, 0.47–4.03). A prolonged (>1 day) antibiotic regimen and preoperative versus postoperative administration of antibiotics showed no benefit (RR, 0.84 [95% CI, 0.54–1.31] and RR, 1.47 [95% CI, 0.74–2.89], respectively).

Thoracic Trauma

- Antibiotic prophylaxis in healthy patients sustaining blunt thoracic trauma is not indicated (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is not indicated in blunt thoracic trauma patients undergoing chest tube placement (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is indicated in penetrating thoracic trauma patients undergoing chest tube placement (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is indicated in all cases of delayed drainage of retained hemothorax (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is indicated in blunt and penetrating thoracic trauma cases undergoing surgical exploration (thoracotomy/thoracoscopy) (moderate recommendation, intermediate-quality evidence).

Overall, 70% to 90% of patients who suffer from moderate-severe thoracic trauma will need tube thoracostomy.[45] Retained hemothorax and penetrating thoracic trauma are risk factors for the development of pneumonia and empyema.[46,47] The posttraumatic empyema rate is 2% to 25% (*Staphylococcus aureus* is responsible for 35–75% of infections).[9] The rate of infections is not different between prehospital and in-hospital chest tube placement.[48] The role of AP in tube thoracostomy after blunt and penetrating thoracic trauma has been widely investigated. An RCT by Heydari et al.,[49] including 104 patients undergoing tube thoracostomy after blunt trauma, showed no significant impact of AP in preventing empyema and pneumonia. Eleven studies with a total of 1,234 patients showed that AP is effective in reducing overall empyema rates (odds ratio [OR], 0.32; 95% CI, 0.17–0.61) and in penetrating trauma patients (OR, 0.28; 95% CI, 0.14–0.57), although it is less effective in blunt trauma (OR, 1.30; 95% CI, 0.46–3.67). When considering the rates of wound infections and pneumonia, AP is effective in reducing infectious complications (OR, 0.24; 95% CI, 0.12–0.49)[45,47,50–58]

A prospective study analyzed 328 patients with retained hemothorax after blunt trauma. In those who had a chest tube placed, the absence of periprocedural antibiotics associated with Injury Severity Score of >25 and blunt mechanism of trauma were independent predictors of pneumonia (OR, 2.6; 95% CI, 1.3–5.4).[46]

A multicenter prospective observational study analyzing 1,887 patients who underwent chest tube placement after traumatic hemopneumothorax showed no differences in the rate of infectious events between the antibiotic versus the nonantibiotic group (2.2% vs. 1.5% respectively, $p = 0.75$).[59] Antibiotics were not associated with the risk of pneumonia (OR, 1.61; 95%, CI, 0.86–3.03; $p = 0.14$) and empyema (OR, 1.51; 95% CI, 0.42–5.42; $p = 0.53$).[12]

In a low-resource setting, a retrospective study analyzed 1,002 patients with penetrating and blunt trauma regarding the use of AP. There was no statistically significant difference in the incidence of empyema between the two groups.[60]

Abdominal Trauma

- Antibiotic prophylaxis is not indicated in blunt abdominal trauma treated non-operatively (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis is indicated in penetrating abdominal trauma, especially in patients undergoing surgical exploration (laparotomy/laparoscopy) (moderate recommendation, intermediate-quality evidence).
- Prolonged AP (24 hours) and/or antibiotic therapy should be considered in patients with hollow viscus injury (moderate recommendation, intermediate-quality evidence).

In abdominal trauma, it is necessary to consider the high risk of contamination and the necessity to clearly define AP and therapy in the case of penetrating trauma and hollow viscus injuries. Before the antibiotic era, the mortality rate of colonic penetrating trauma was 60% to 70%.[61] Several attempts to standardize the indications of AP in abdominal trauma failed[62–64] because of the unclear distinction between AP and antibiotic therapy and the lack of literature on the topic. Many studies underscored the need for anaerobic coverage.[65] In general, no AP should be given to blunt trauma patients unless a hollow viscus injury is suspected. Antibiotic prophylaxis should be given in penetrating trauma, but it should not last more than 24 hours in the absence of hollow viscus injuries; broad-spectrum antibiotics with aerobic and anaerobic bacteria coverage should be preferred, while aminoglycosides should be avoided whenever possible. In the case of hemorrhagic shock and associated acute kidney injury, the dose of antibiotics should be adjusted.[66–95] Hollow viscus injury with contamination should be considered an indication for antibiotic therapy rather than AP. No evidence exists regarding the need for AP in patients with renal injury associated with urine leak without indication of surgery or invasive procedures.[63,65–68]

Important is the golden rule that antibiotic therapy should last for the minimum possible duration that is safe and benefits the patient. In damage-control laparotomy, postoperative antibiotic administration and the presence of hollow viscus injuries were positive predictors of infection (OR, 6.7%; 95% CI, 1.33–33.8 [$p = 0.044$] and OR, 3.45; 95% CI, 1.03–11.5 [$p = 0.02$], respectively), while preoperative administration of antibiotic was a negative predictor of infection (OR, 0.20; 95% CI, 0.05–0.91; $p = 0.037$).[96] Interestingly, neither Injury Severity Score nor damage-control laparotomy were independent predictors of infection. The study, however, did not discriminate between antibiotic therapy and AP, and the heterogeneity of the injuries was significant. A comparative analysis was done between penetrating and blunt trauma patients who underwent trauma laparotomy and followed the prophylaxis guidelines proposed by the Surgical Care Improvement Project or not.[64,97] Results adjusted for confounding factors showed that the group treated according to the Surgical Care Improvement Project guidelines had a lower risk of SSI (OR, 0.43; 95% CI, 0.2–0.94; $p = 0.035$). However, it is unclear which patients received prophylaxis alone and which received antibiotic therapy. The average duration of in-hospital antibiotic therapy (4 vs. 9 days, $p < 0.001$) was considered one of the differences between the

© 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

two groups. This shows the confusion related to the definition of AP and its indications in the trauma literature.

The relationship between the duration of antibiotic therapy for more than 24 hours in penetrating trauma patients in preventing SSI (RR, 1.00; 95% CI, 0.81–1.23), reducing mortality (OR, 1.67; 95% CI, 0.73–3.82), or intra-abdominal infection (RR, 1.23; 95% CI, 0.84–1.80) could not be demonstrated.[24]

Open Fractures

- Antibiotic prophylaxis effectively reduces wound infections in open fractures, and it should be administered as soon as possible (moderate recommendation, intermediate-quality evidence).
- Long-term antibiotic treatment (7–10 days) is ineffective in reducing open fracture wound infection rate (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis longer than 24 hours is not indicated in gunshot-related fractures (moderate recommendation, intermediate-quality evidence).

Long bone open fractures may be the source of acute and chronic infections. Few recommendations about their management exist in international guidelines.[20] Heterogeneity in indications, management, and diagnostic criteria are common issues in the published studies.[23,98–104] Reports showed that several drugs were tested and administered, including penicillin, its derivatives cephalosporines (dicloxacillin, benzylpenicillin, and cloxacillin), and aminoglycosides. No clear definition of prophylaxis exists, and the ideal timing to start AP has also not been clearly determined. Antibiotic administration ranged from 48 hours to 10 days. No investigation of the prophylaxis effects on drug-induced bacterial resistance was performed. Wound infection rates were reported between 13.3% and 22.6% in those receiving AP, which were significantly lower than in those not receiving AP.[23,98–104] However, in some studies, infections occurring within 6 weeks after a surgical intervention were considered early infections. Antibiotic prophylaxis is effective in reducing wound infections (not specifically osteomyelitis), and no benefit seems associated with the duration of prophylaxis for more than 24 hours in gunshot-related fractures. Long-course (7–10 days) antibiotic therapy is not effective in preventing wound infections (not specifically osteomyelitis). Figure 1 shows the decisional algorithm for the use of AP prescription in open fractures.

Burns

- Routine AP in burns patients is not indicated (moderate recommendation, intermediate-quality evidence).
- Routine source control with extensive irrigation for the removal of contaminated material is part of infection prevention in burn patients (moderate recommendation, intermediate-quality evidence).
- No differences exist between systemic and topical AP in preventing infections in burn patients (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis in severe burn patients is indicated in those undergoing endotracheal intubation and mechanical ventilation; it should be ideally administered before the intubation and according to the pharmacokinetics of the chosen antibiotic when possible (moderate recommendation, intermediate-quality evidence).
- Antibiotic prophylaxis in severe burn patients may be indicated to prevent split-thickness skin graft infection (moderate recommendation, intermediate-quality evidence).
- There is no indication for routine AP following the debridement of devitalized tissues (moderate recommendation, intermediate-quality evidence).

In burn patients, infections are of paramount importance, as it is a frequent cause of death or skin graft loss (51z). Infections in these patients are often due to multiresistant species. Primary adequate source control (extensive irrigation, temporary coverage of the burned area, and removal of contaminated material) is critical in reducing the risk of infection. Systemic AP in burn patients reduced all-cause mortality (OR, 0.54; 95% CI, 0.34–0.87).[105] Moreover, systemic prophylaxis seems to be related to reducing pneumonia rates (OR, 0.55; 95% CI, 0.36–0.84).[105] Concerning wound infection, a positive effect

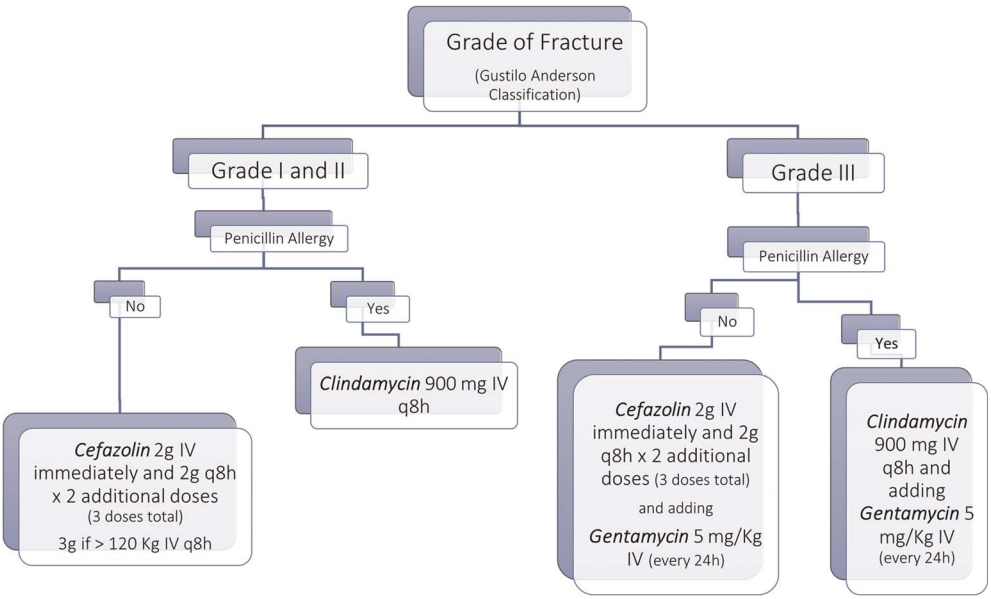


Figure 1. Antibiotic prophylaxis decision algorithm in open fractures.

© 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

of perioperative AP exists (OR, 0.72; 95% CI, 0.52–1.01).[30] Bacteriemia was not affected by any intervention. Antibiotic prophylaxis seems to have a greater effect in reducing gram-positive infections (OR, 0.58; 95% CI, 0.43–0.76) but not those caused by gram-negative species. Great heterogeneity of patients within the different studies exists, making it difficult to consider all these results as definitive. The role of prophylactic topical and systemic antibiotics, nonabsorbable antibiotic regimens, and local prophylactic antibiotics administered via the airway to prevent burn wound infection was investigated by several studies.[106–117] No definitive benefit in systemic or topical AP was found related to sepsis, antibiotic resistance, wound healing, hospital length of stay, or infectious-related mortality. These results apply to both severe (>20% of the body surface area) and less severe (<20% of total body surface area) burn injuries.[118] Topical antibiotic studies evaluated placebo versus neomycin, bacitracin, and polymyxin B. A significant increase in wound infection rate (OR, 1.87; 95% CI, 1.09–3.19) and total length of hospital stay (median, 2.11 days; 95% CI, 1.93–2.28) was observed with silver sulfadiazine. Trimethoprim-sulfamethoxazole alone was associated with a significant decrease in the risk of pneumonia, according to one trial (RR, 0.18; 95% CI, 0.05–0.72), and in general, it seemed beneficial in mechanically ventilated patients as well.[118,119] Nonabsorbable antibiotics seemed to correlate with higher methicillin-resistant *Staphylococcus aureus* rates when associated with cefotaxime (RR, 2.22; 95% CI, 1.21–4.07). No benefits on sepsis or mortality were observed with intratracheally administered antibiotics.

Some benefits in terms of pneumonia-related mortality seemed to be associated with AP in patients with inhalation injury.[120]

Routine use of systemic AP in pediatric burn injury has no beneficial effects.[121] Local or systemic infection rates were similar in the AP and no-antibiotic groups. The same results were observed when the analysis was adjusted for confounding factors (total burn surface area, age, and country income level).[121]

Wound microbiology modifies its components with AP and antibiotic therapy depending on the type of antibiotics used and treatment duration.[122] Multidrug-resistant organisms were found in 39% of patients 1 month from admission. The risk of infection with multidrug-resistant bacteria was very high in patients with <40% of the body surface area burn (OR, 41.7; 95% CI, 2.1–810.7; $p = 0.01$) and in those who received two or more antibiotics (OR, 9.9; 95% CI, 1–92.7; $p = 0.04$).

Skin Wounds and Skin Bites

- Routine AP in skin and soft-tissue injuries is not strictly indicated and should be considered case by case (moderate recommendation, intermediate-quality evidence).
- Routine AP in mammalian bites is not strictly indicated and should be considered case by case (moderate recommendation, intermediate-quality evidence).
- Accurate prevention of viral infectious disease in animal bites must be performed (i.e., rabies virus) (moderate recommendation, intermediate-quality evidence).
- Attention to tetanus immunization must be given (moderate recommendation, intermediate-quality evidence).
- Accurate source control should be accomplished by cleaning, irrigating, and disinfecting wounds in all skin and soft tissue injuries, including all mammalian bites (moderate recommendation, intermediate-quality evidence).

Almost 12 million skin wounds are treated annually in the United States, adding to the count another 1.5 million animal bites.[123] Not administering AP in noncomplicated skin wounds is a well-established practice.[124] Much of the data come from military settings and must be cautiously applied to the civilian environment.[125] Soft tissue injuries are frequently treated in emergency departments. The need for AP, often suggested and used by physicians, needs to be assessed. Broad spectrum AP in open skin and soft tissue combat-related injuries is necessary and beneficial to decrease infection rates and length of hospital stay.[126,127] Data on skin and soft tissue injuries reported a synergistic effect of extensive wound irrigation and AP in decreasing the incidence of infection in moderately and severely contaminated skin and soft tissue injuries.[128] The reported different rates of infections in different management strategies include 17% in irrigation/no AP, 40% in AP/no irrigation, and 75% in no AP/no irrigation group ($p < 0.0005$).

In mammalian bites, clinical results regarding AP are conflicting. It seems that overall AP usage has no significant benefit in mammalian bites. Antibiotic prophylaxis effectively reduces infectious complications in human bites (OR, 0.02; 95% CI, 0–0.33), but no definitive benefits were demonstrated in dog and cat bites. Hand injuries showed a higher complication rate if not treated with AP (2% rate in antibiotic group versus 28% in control (OR, 0.1; 95% CI, 0.01–0.86).[129,130]

CONCLUSION

Antibiotic prophylaxis must be used only when it is indicated. Its overuse has no beneficial effects on patients but has a potential drawback in increasing bacterial resistance. Tailored infection risk calculation for each patient must be performed, with correct source control playing a major role in infection prevention.

AUTHORSHIP

F.C. contributed in the manuscript conception and draft. All authors critically revised the manuscript and contributed with important scientific knowledge, giving the final approval.

DISCLOSURE

Conflicts of Interest: Author Disclosure forms have been supplied and are provided as Supplemental Digital Content (http://links.lww.com/TA/D469).

REFERENCES

1. Global Guidelines for the Prevention of Surgical Site Infection. Geneva, Switzerland: World Health Organization; 2016. Available at: https://www.who.int/gpsc/ssi-prevention-guidelines/en/. Accessed January 15, 2019.
2. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm*. 2013;70:195–283.
3. *Global Guidelines for the Prevention of Surgical Site Infection*. 2nd ed. Geneva, Switzerland: World Health Organization; 2018. Available at: https://apps.who.int/iris/handle/10665/277399. Accessed August 30, 2022.
4. Coccolini F, Kluger Y, Moore EE, Maier RV, Coimbra R, Ordoñez C, et al, the WSES Trauma Quality Indicators Expert Panel. Trauma quality indicators: internationally approved core factors for trauma management quality evaluation. *World J Emerg Surg*. 2021;16(1):6.
5. Ierano C, Thursky K, Peel T, Rajkhowa A, Marshall C, Ayton D. Influences on surgical antimicrobial prophylaxis decision making by surgical craft

© 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

groups, anaesthetists, pharmacists and nurses in public and private hospitals. *PloS One*. 2019;14(11):e0225011.
6. Sartelli M, Ansaloni L, Biffl WA, Coccolini F, De Simone B, Leppaniemi A, et al. World Society of Emergency Surgery—American Association for the Surgery of Trauma Guidelines for management of *Clostridioides* (*Clostridium*) *difficile* infection in surgical patients: an executive summary. *J Trauma Acute Care Surg*. 2021;91(2):422–426.
7. Sartelli M, Coccolini F, Carrieri A, Labricciosa FM, Cicuttin E, Catena F. The "torment" of surgical antibiotic prophylaxis among surgeons. *Antibiotics (Basel)*. 2021;10(11):1357.
8. Dhingra S, Rahman NAA, Peile E, Rahman M, Sartelli M, Hassali MA, et al. Microbial resistance movements: an overview of global public health threats posed by antimicrobial resistance, and how best to counter. *Front Public Health*. 2020;8:535668.
9. Sartelli M, Duane TM, Catena F, Tessier JM, Coccolini F, Kao LS, et al. Antimicrobial stewardship: a call to action for surgeons. *Surg Infect (Larchmt)*. 2016;17(6):625–631.
10. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence. Available at: https://www.cebm.net/wp-content/uploads/2014/06/CEBM-Levels-of-Evidence-2.1.pdf
11. Ignelzi RJ, VanderArk GD. Analysis of the treatment of basilar skull fractures with and without antibiotics. *J Neurosurg*. 1975;43(6):721–726.
12. Klastersky J, Sadeghi M, Brihaye J. Antimicrobial prophylaxis in patients with rhinorrhea or otorrhea: a double-blind study. *Surg Neurol*. 1976; 6(2):111–114.
13. Demetriades D, Charalambides D, Lakhoo M, Pantanowitz D. Role of prophylactic antibiotics in open and basilar fractures of the skull: a randomized study. *Injury*. 1992;23(6):377–380.
14. Eftekhar B, Ghodsi M, Nejat F, Ketabchi E, Esmaeeli B. Prophylactic administration of ceftriaxone for the prevention of meningitis after traumatic pneumocephalus: results of a clinical trial. *J Neurosurg*. 2004;101(5): 757–761.
15. Brodie HA. Prophylactic antibiotics for posttraumatic cerebrospinal fluid fistulae. A meta-analysis. *Arch Otolaryngol Head Neck Surg*. 1997; 123(7):749–752.
16. Villalobos T, Arango C, Kubilis P, Rathore M. Antibiotic prophylaxis after basilar skull fractures: a meta-analysis. *Clin Infect Dis*. 1998;27(2):364–369.
17. Dagi TF, Meyer FB, Poletti CA. The incidence and prevention of meningitis after basilar skull fracture. *Am J Emerg Med*. 1983;1(3):295–298.
18. Zrebeet HA, Huang PS. Prophylactic antibiotics in the treatment of fractures at the base of the skull. *Del Med J*. 1986;58(11):741–748.
19. Frazee RC, Mucha P Jr., Farnell MB, Ebersold MJ. Meningitis after basilar skull fracture. Does antibiotic prophylaxis help? *Postgrad Med*. 1988;83(5): 267–274.
20. Harmon LA, Haase DJ, Kufera JA, Adnan S, Cabral D, Lottenberg L, et al. Infection after penetrating brain injury—an Eastern Association for the Surgery of Trauma multicenter study oral presentation at the 32nd annual meeting of the Eastern Association for the Surgery of Trauma, January 15–19, 2019, in Austin, Texas. *J Trauma Acute Care Surg*. 2019;87(1):61–67.
21. Ganga A, Leary OP, Sastry RA, Asaad WF, Svokos KA, Oyelese AA, Mermel LA. Antibiotic prophylaxis in penetrating traumatic brain injury: analysis of a single-center series and systematic review of the literature. *Acta Neurochir*. 2023;165(2):303–313.
22. Assmann SF, Pocock SJ, Enos LE, Kasten LE. Subgroup analysis and other (mis)uses of baseline data in clinical trials. *Lancet*. 2000;355(9209):1064–1069.
23. Poole D, Chieregato A, Langer M, Viaggi B, Cingolani E, Malacarne P, et al. Systematic review of the literature and evidence-based recommendations for antibiotic prophylaxis in trauma: results from an Italian consensus of experts. *PloS One*. 2014;9(11):e113676.
24. Ratilal BO, Costa J, Sampaio C, Pappamikail L. Antibiotic prophylaxis for preventing meningitis in patients with basilar skull fractures. *Cochrane Database Syst Rev*. 2011;(8):CD004884.
25. Hoff JT, Brewin A, U HS. Letter: antibiotics for basilar skull fracture. *J Neurosurg*. 1976;44(5):649.
26. Hindawi YH, Oakley GM, Kinsella CR Jr., Cray JJ, Lindsay K, Scifres AM. Antibiotic duration and postoperative infection rates in mandibular fractures. *J Craniofac Surg*. 2011;22(4):1375–1377.
27. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Surg Infect (Larchmt)*. 2013;14(1):73–156.
28. Brooke SM, Goyal N, Michelotti BF, Guedez HM, Fedok FG, Mackay DR, Samson TD. A multidisciplinary evaluation of prescribing practices for prophylactic antibiotics in operative and nonoperative facial fractures. *J Craniofac Surg*. 2015;26(8):2299–2303.
29. Andreasen JO, Jensen SS, Schwartz O, Hillerup Y. A systematic review of prophylactic antibiotics in the surgical treatment of maxillofacial fractures. *J Oral Maxillofac Surg*. 2006;64(11):1664–1668.
30. Abubaker AO, Rollert MK. Postoperative antibiotic prophylaxis in mandibular fractures: a preliminary randomized, double-blind, and placebo-controlled clinical study. *J Oral Maxillofac Surg*. 2001;59:1415–1419.
31. Heit JM, Stevens MR, Jeffords K. Comparison of ceftriaxone with penicillin for antibiotic prophylaxis for compound mandible fractures. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 1997;83(4):423–426.
32. Habib AM, Wong AD, Schreiner GC, Satti KF, Riblet NB, Johnson HA, Ossoff JP. Postoperative prophylactic antibiotics for facial fractures: a systematic review and meta-analysis. *Laryngoscope*. 2019;129(1):82–95.
33. Miles BA, Potter JK, Ellis E III. The efficacy of postoperative antibiotic regimens in the open treatment of mandibular fractures: a prospective randomized trial. *J Oral Maxillofac Surg*. 2006;64:576–582.
34. Schaller B, Soong PL, Zix J, Iizuka T, Lieger O. The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomized, double-blind, placebo-controlled pilot clinical study. Part 2: mandibular fractures in 59 patients. *Br J Oral Maxillofac Surg*. 2013;51:803–807.
35. Gaal A, Bailey B, Patel Y, Smiley N, Dodson T, Kim D, Dillon J. Limiting antibiotics when managing mandible fractures may not increase infection risk. *J Oral Maxillofac Surg*. 2016;74:2008–2018.
36. Domingo F, Dale E, Gao C, Groves C, Stanley D, Maxwell RA, Waldrop JL. A single-center retrospective review of postoperative infectious complications in the surgical management of mandibular fractures: postoperative antibiotics add no benefit. *J Trauma Acute Care Surg*. 2016;81:1109–1114.
37. Lovato C, Wagner JD. Infection rates following perioperative prophylactic antibiotics versus postoperative extended regimen prophylactic antibiotics in surgical management of mandibular fractures. *J Oral Maxillofac Surg*. 2009;67:827–832.
38. Gerlach KL, Pape HD. Studies on preventive antibiotics in the surgical treatment of mandibular fractures (in German). *Dtsch Z Mund Kiefer Gesichtschir*. 1988;12:497–500.
39. Zix J, Schaller B, Iizuka T, Lieger O. The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomised, double-blind, placebo-controlled pilot clinical study. Part 1: orbital fractures in 62 patients. *Br J Oral Maxillofac Surg*. 2012;51:332–336.
40. Soong PL, Schaller B, Zix J, Iizuka T, Mottini M, Lieger O. The role of postoperative prophylactic antibiotics in the treatment of facial fractures: a randomised, double-blind, placebo-controlled pilot clinical study. Part 3: Le fort and zygomatic fractures in 94 patients. *Br J Oral Maxillofac Surg*. 2014;52:329–333.
41. Knepil GJ, Loukota RA. Outcomes of prophylactic antibiotics following surgery for zygomatic bone fractures. *J Craniomaxillofac Surg*. 2010;38: 131–133.
42. Zijderveld SA, Smeele LE, Kostense PJ, Tuinzing DB. Preoperative antibiotic prophylaxis in orthognathic surgery: a randomized, double-blind, and placebo-controlled clinical study. *J Oral Maxillofac Surg*. 1999;57(12): 1403–1406.
43. Delaplain PT, Phillips JL, Lundeberg M, Nahmias J, Kuza CM, Sheehan BM. No reduction in surgical site infection obtained with post-operative antibiotics in facial fractures, regardless of duration or anatomic location: a systematic review and meta-analysis. *Surg Infect (Larchmt)*. 2020;21(2): 112–121.
44. Dawoud BES, Kent S, Henry A, Wareing J, Chaudry H, Kyzas P. Use of antibiotics in traumatic mandibular fractures: a systematic review and meta-analysis. *Br J Oral Maxillofac Surg*. 2021;59(10):1140–1147.
45. Bosman A, de Jong MB, Debeij J, van den Broek PJ, Schipper IB. Systematic review and meta-analysis of antibiotic prophylaxis to prevent infections from chest drains in blunt and penetrating thoracic injuries. *Br J Surg*. 2012; 99(4):506–513.
46. Bradley M, Okoye O, DuBose J, Inaba K, Demetriades D, Scalea T, et al. Risk factors for post-traumatic pneumonia in patients with retained haemothorax: results of a prospective, observational AAST study. *Injury*. 2013; 44(9):1159–1164.
47. Maxwell RA, Campbell DJ, Fabian TC, Croce MA, Luchette FA, Kerwin AJ, et al. Use of presumptive antibiotics following tube thoracostomy for traumatic hemopneumothorax in the prevention of empyema and pneumonia–a multi-center trial. *J Trauma*. 2004;57(4):742–748.

© 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

48. Spanjersberg WR, Ringburg AN, Bergs EA, Krijen P, Schipper IB. Prehospital chest tube thoracostomy: effective treatment or additional trauma? *J Trauma*. 2005;59(1):96–101.
49. Heydari MB, Hessami MA, Setayeshi K, Sajadifar F. Use of prophylactic antibiotics following tube thoracostomy for blunt chest trauma in the prevention of empyema and pneumonia. *J Inj Violence Res*. 2014;6(2):91–92.
50. Nichols RL, Smith JW, Muzik AC, Love EJ, McSwain NE, Timberlake G, Flint LM. Preventive antibiotic usage in traumatic thoracic injuries requiring closed tube thoracostomy. *Chest*. 1994;106(5):1493–1498.
51. Gonzalez RP, Holevar MR. Role of prophylactic antibiotics for tube thoracostomy in chest trauma. *Am Surg*. 1998;64(7):617–620.
52. Grover FL, Richardson JD, Fewel JG, Arom KV, Webb GE, Trinkle JK. Prophylactic antibiotics in the treatment of penetrating chest wounds. A prospective double-blind study. *J Thorac Cardiovasc Surg*. 1977;74(4):528–536.
53. Stone HH, Symbas PN, Hooper CA. Cefamandole for prophylaxis against infection in closed tube thoracostomy. *J Trauma*. 1981;21(11):975–977.
54. LeBlanc KA, Tucker WY. Prophylactic antibiotics and closed tube thoracostomy. *Surg Gynecol Obstet*. 1985;160(3):259–263.
55. LoCurto JJ Jr., Tischler CD, Swan KG, Rocko JM, Blackwood JM, Griffin CC, et al. Tube thoracostomy and trauma—antibiotics or not? *J Trauma*. 1986;26(12):1067–1072.
56. Villegas-Carlos F, Vazquez-Martinez AM, Pinedo-Onofre JA, Guevara-Torres L, Belmares-Taboada JA, Sanchez-Aguilar M. Are antimicrobials useful in closed thoracostomy due to trauma? *Cir Cir*. 2009;77(1):29–32.
57. Mandal AK, Montano J, Thadepalli H. Prophylactic antibiotics and no antibiotics compared in penetrating chest trauma. *J Trauma*. 1985;25(7):639–643.
58. Brunner RG, Vinsant GO, Alexander RH, Laneve L, Fallon WF. The role of antibiotic therapy in the prevention of empyema in patients with an isolated chest injury (ISS 9-10): a prospective study. *J Trauma*. 1990;30(9):1148–1153.
59. Cook A, Hu C, Ward J, Schultz S, Moore Iii FO, Funk G, et al, AAST Antibiotics in Tube Thoracostomy Study Group. Presumptive antibiotics in tube thoracostomy for traumatic hemopneumothorax: a prospective, multicenter American Association for the Surgery of Trauma study. *Trauma Surg Acute Care Open*. 2019;4(1):e000356.
60. Kong VY, Sartorius B, Oosthuizen GV, Clarke DL. Prophylactic antibiotics for tube thoracostomy may not be appropriate in the developing world setting. *Injury*. 2015;46(5):814–816.
61. Petersen K, Waterman P. Prophylaxis and treatment of infections associated with penetrating traumatic injury. *Expert Rev Anti Infect Ther*. 2011;9(1):81–96.
62. Brand M, Goosen J, Grieve A. Prophylactic antibiotics for penetrating abdominal trauma. *Cochrane Database Syst Rev*. 2009;(4):CD007370.
63. Herrod PJ, Boyd-Carson H, Doleman B, Blackwell J, Williams JP, Bhalla A, et al. Prophylactic antibiotics for penetrating abdominal trauma: duration of use and antibiotic choice. *Cochrane Database Syst Rev*. 2019;12(12):CD010808.
64. Smith BP, Fox N, Fakhro A, LaChant M, Pathak AS, Ross SE, Seamon MJ. "SCIP"ping antibiotic prophylaxis guidelines in trauma: the consequences of noncompliance. *J Trauma Acute Care Surg*. 2012;73(2):452–456.
65. Thadepalli H, Gorbach SL, Broido PW, Norsen J, Nyhus L. Abdominal trauma, anaerobes, and antibiotics. *Surg Gynecol Obstet*. 1973;137(2):270–276.
66. Bivins BA, Crots L, Obeid FN, Sorensen VJ, Horst HM, Fath JJ. Antibiotics for penetrating abdominal trauma: a prospective comparative trial of single agent cephalosporin therapy versus combination therapy. *Diagn Microbiol Infect Dis*. 1989;12(1):113–118.
67. Bivins BA, Crots L, Sorensen VJ, Obeid FN, Horst HM. Preventative antibiotics for penetrating abdominal trauma—single agent or combination therapy. *Drugs*. 1988;35(Suppl 2):100–105.
68. Bozorgzadeh A, Pizzi WF, Barie PS, Khaneja SC, LaMaute HR, Mandava N, et al. The duration of antibiotic administration in penetrating abdominal trauma. *Am J Surg*. 1999;177(2):125–131.
69. Cornwell EE 3rd, Dougherty WR, Berne TV, Velmahos G, Murray JA, Chahwan S, et al. Duration of antibiotic prophylaxis in high-risk patients with penetrating abdominal trauma: a prospective randomized trial. *J Gastrointest Surg*. 1999;3(6):648–653.
70. Crenshaw C, Glanges E, Webber C, McReynolds DB. A prospective random study of a single agent versus combination antibiotics as therapy in penetrating injuries of the abdomen. *Surg Gynecol Obstet*. 1983;156(3):289–294.
71. Crots LD, Obeid FN, Horst HM, Bivins BA. Twice-daily moxalactam versus gentamicin and clindamycin in patients with penetrating abdominal trauma. *Clin Pharm*. 1985;4(3):316–320.
72. Dellinger EP, Wertz MJ, Lennard ES, Oreskovich MR. Efficacy of short-course antibiotic prophylaxis after penetrating intestinal injury. A prospective randomized trial. *Arch Surg*. 1986;121(1):23–30.
73. Demetriades D, Lakhoo M, Pezikis A, Charalambides D, Pantanowitz D, Sofianos C. Short-course antibiotic prophylaxis in penetrating abdominal injuries: ceftriaxone versus cefoxitin. *Injury*. 1991;22(1):20–24.
74. Ericsson CD, Fischer RP, Rowlands BJ, Hunt C, Miller-Crotchett P, Reed L 2nd. Prophylactic antibiotics in trauma: the hazards of underdosing. *J Trauma*. 1989;29(10):1356–1361.
75. Fabian TC, Hoefling SJ, Strom PR, Stone HH. Use of antibiotic prophylaxis in penetrating abdominal trauma. *Clin Ther*. 1982;5(Suppl A):38–47.
76. Fabian TC, Boldreghini SJ. Antibiotics in penetrating abdominal trauma. Comparison of ticarcillin plus clavulanic acid with gentamicin plus clindamycin. *Am J Med*. 1985;79(5B):157–160.
77. Fabian TC, Croce MA, Payne LW, Minard G, Pritchard FE, Kudsk KA. Duration of antibiotic therapy for penetrating abdominal trauma: a prospective trial. *Surgery*. 1992;112(4):788–795.
78. Fabian TC, Hess MM, Croce MA, Wilson RS, Wilson SE, Charland SL, et al. Superiority of aztreonam/clindamycin compared with gentamicin/clindamycin in patients with penetrating abdominal trauma. *Am J Surg*. 1994;167(3):291–296.
79. Griswold JA, Muakkassa FF, Betcher E, Poole GV. Injury severity dictates individualized antibiotic therapy in penetrating abdominal trauma. *Am Surg*. 1993;59(1):34–39.
80. Heseltine PN, Berne TV, Yellin AE, Gill MA, Appleman MD. The efficacy of cefoxitin vs. clindamycin/gentamicin in surgically treated stab wounds of the bowel. *J Trauma*. 1986;26(3):241–245.
81. Hofstetter SR, Pachter HL, Bailey AA, Coppa GF. A prospective comparison of two regimens of prophylactic antibiotics in abdominal trauma: cefoxitin versus triple drug. *J Trauma*. 1984;24(4):307–310.
82. Jones RC, Thal ER, Johnson NA, Gollihar LN. Evaluation of antibiotic therapy following penetrating abdominal trauma. *Ann Surg*. 1985;201(5):576–585.
83. Kirton OC, O'Neill PA, Kestner M, Tortella BJ. Perioperative antibiotic use in high-risk penetrating hollow viscus injury: a prospective randomized, double-blind, placebo-control trial of 24 hours versus 5 days. *J Trauma*. 2000;49(5):822–832.
84. Kreis DJ Jr., Augenstein D, Martinez O, Echenique M, Plasencia G, Vopal JJ, et al. A prospective randomized study of moxalactam versus gentamicin and clindamycin in penetrating abdominal trauma. *Surg Gynecol Obstet*. 1986;163(1):1–4.
85. Lou MA, Thadepalli H, Mandal AK. Safety and efficacy of mezlocillin: a single-drug therapy for penetrating abdominal trauma. *J Trauma*. 1988;28(11):1541–1547.
86. Moore FA, Moore EE, Mill MR. Preoperative antibiotics for abdominal gunshot wounds. A prospective, randomized study. *Am J Surg*. 1983;146(6):762–765.
87. Moore FA, Moore EE, Ammons LA, McCroskey BL. Presumptive antibiotics for penetrating abdominal wounds. *Surg Gynecol Obstet*. 1987;165(1):29–32.
88. Nelson RM, Benitez PR, Newell MA, Wilson RF. Single-antibiotic use for penetrating abdominal trauma. *Arch Surg*. 1986;121(2):153–156.
89. Nichols RL, Smith JW, Robertson GD, Muzik AC, Pearce P, Ozmen V, et al. Prospective alterations in therapy for penetrating abdominal trauma. *Arch Surg*. 1993;128(1):55–63.
90. Okamoto MP, Gill MA, Nakahiro RK, Chin A, Yellin AE, Berne TV, et al. Cost analysis of cefmetazole versus cefoxitin in the treatment of penetrating abdominal trauma. *Current Therapeutic Research*. 1993;53(2):159–166.
91. Oreskovich MR, Dellinger EP, Lennard ES, Wertz M, Carrico CJ, Minshew BH. Duration of preventive antibiotic administration for penetrating abdominal trauma. *Arch Surg*. 1982;117(2):200–205.
92. Rowlands BJ, Ericsson CD. Comparative studies of antibiotic therapy after penetrating abdominal trauma. *Am J Surg*. 1984;148(6):791–795.
93. Sims EH, Thadepalli H, Ganesan K, Mandal AK. How many antibiotics are necessary to treat abdominal trauma victims? *Am Surg*. 1997;63(6):525–535.
94. Tyburski JG, Wilson RF, Warsow KM, McCreadie S. A trial of ciprofloxacin and metronidazole vs gentamicin and metronidazole for penetrating abdominal trauma. *Arch Surg*. 1998;133(12):1289–1296.

© 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.

Downloaded from http://journals.lww.com/jtrauma by BhDMf5ePHKav1zEoum1tQfN4a+kJLhEZgbsIHo4XMi0hCywCX1AWnYQp/IlQrHD3i3D0OdRyi7TvSFl4Cf3VC4/OAVpDDa8KKGKV0Ymy+78= on 07/25/2024

95. Mazuski JE, Symons WJ, Jarman S, Sato B, Carroll W, Bochicchio G, et al. Reduction of surgical site infection after trauma laparotomy through use of a specific protocol for antibiotic prophylaxis. *Surg Infect (Larchmt)*. 2023; 24(2):141–157.
96. Goldberg SR, Henning J, Wolfe LG, Duane TM. Practice patterns for the use of antibiotic agents in damage control laparotomy and it's impact on outcomes. *Surg Infect (Larchmt)*. 2017;18(3):282–286.
97. Rosenberger LH, Politano AD, Sawyer RG. The surgical care improvement project and prevention of post-operative infection, including surgical site infection. *Surg Infect (Larchmt)*. 2011;12(3):163–168.
98. Berner JE, Ali SR, Will PA, Tejos R, Nanchahal J, Jain A. Standardising the management of open extremity fractures: a scoping review of national guidelines. *Eur J Orthop Surg Traumatol*. 2023;33(5):1463–1471.
99. Braun R, Enzler MA, Rittmann WW. A double-blind clinical trial of prophylactic cloxacillin in open fractures. *J Orthop Trauma*. 1987;1(1):12–17.
100. Dickey RL, Barnes BC, Kearns RJ, Tullos HS. Efficacy of antibiotics in low-velocity gunshot fractures. *J Orthop Trauma*. 1989;3(1):6–10.
101. Patzakis MJ, Wilkins J, Moore TM. Use of antibiotics in open tibial fractures. *Clin Orthop Relat Res*. 1983;178:31–35.
102. Gosselin RA, Roberts I, Gillespie WJ. Antibiotics for preventing infection in open limb fractures. *Cochrane Database Syst Rev.* 2004;2004(1):CD003764.
103. Rojczyk M. Treatment results in open fractures, aspects of antibiotic therapy. *Hefte Unfallheilkd*. 1983;162:33–38.
104. Patzakis MJ, Harvey JP Jr., Ivler D. The role of antibiotics in the management of open fractures. *J Bone Joint Surg Am*. 1974;56(3):532–541.
105. Avni T, Levcovich A, Ad-El DD, Leibovici L, Paul M. Prophylactic antibiotics for burns patients: systematic review and meta-analysis. *BMJ*. 2010; 340:c241.
106. Barajas-Nava LA, López-Alcalde J, Roqué i Figuls M, Solà I, Bonfill Cosp X. Antibiotic prophylaxis for preventing burn wound infection. *Cochrane Database Syst Rev.* 2013;(6):CD008738.
107. Sheridan RL, Weber JM, Pasternack MS, Tompkins RG. Antibiotic prophylaxis for group a streptococcal burn wound infection is not necessary. *J Trauma*. 2001;51(2):352–355.
108. Timmons MJ. Are systemic prophylactic antibiotics necessary for burns? *Ann R Coll Surg Engl*. 1983;65(5):348.
109. Mulgrew S, Khoo A, Cartwright R, Reynolds N. Morbidity in pediatric burns, toxic shock syndrome, and antibiotic prophylaxis: a retrospective comparative study. *Ann Plast Surg*. 2014;72(1):34–37.
110. Ergün O, Celik A, Ergün G, Ozok G. Prophylactic antibiotic use in pediatric burn units. *Eur J Pediatr Surg*. 2004;14(6):422–426.
111. Chahed J, Ksia A, Selmi W, Hidouri S, Sahnoun L, Krichene I, et al. Burns injury in children: is antibiotic prophylaxis recommended? *Afr J Paediatr Surg*. 2014;11(4):323–325.
112. Lyons JM, Davis C, Rieman MT, Kopcha R, Phan H, Greenhalgh D, et al. Prophylactic intravenous immune globulin and polymixin B decrease the incidence of septic episodes and hospital length of stay in severely burned children. *J Burn Care Res*. 2006;27(6):813–818.
113. Munster AM, Xiao GX, Guo Y, Wong LA, Winchurch RA. Control of endotoxemia in burn patients by use of polymyxin B. *J Burn Care Rehabil*. 1989;10(4):327–330.
114. Durtschi MB, Orgain C, Counts GW, Heimbach DM. A prospective study of prophylactic penicillin in acutely burned hospitalized patients. *J Trauma*. 1982;22(1):11–14.
115. Ugburo AO, Atoyebi OA, Oyeneyin JO, Sowemimo GO. An evaluation of the role of systemic antibiotic prophylaxis in the control of burn wound infection at the Lagos University teaching hospital. *Burns*. 2004;30(1):43–48.
116. Deutsch DH, Miller SF, Finley RK Jr. The use of intestinal antibiotics to delay or prevent infections in patients with burns. *J Burn Care Rehabil*. 1990; 11(5):436–442.
117. de La Cal MA, Cerda E, Garcia-Hierro P, van Saene HK, Gomez-Santos D, Negro E, Lorente JA. Survival benefit in critically ill burned patients receiving selective decontamination of the digestive tract: a randomized, placebo-controlled, double-blind trial. *Ann Surg*. 2005;241(3):424–430.
118. Ramos G, Cornistein W, Cerino GT, Nacif G. Systemic antimicrobial prophylaxis in burn patients: systematic review. *J Hosp Infect*. 2017;97(2): 105–114.
119. Kimura A, Mochizuki T, Nishizawa K, Mashiko K, Yamamoto Y, Otsuka T. Trimethoprim-sulfamethoxazole for the prevention of methicillin-resistant *Staphylococcus aureus* pneumonia in severely burned patients. *J Trauma*. 1998;45(2):383–387.
120. Muthukumar V, Arumugam PK, Bamal R. Role of systemic antibiotic prophylaxis in acute burns: a retrospective analysis from a tertiary care center. *Burns*. 2020;46(5):1060–1065.
121. Csenkey A, Jozsa G, Gede N, Pakai E, Tinusz B, Rumbus Z, et al. Systemic antibiotic prophylaxis does not affect infectious complications in pediatric burn injury: a meta-analysis. *PloS One*. 2019;14(9):e0223063.
122. Yeong EK, Sheng WH, Hsueh PR, Hsieh SM, Huang HF, Ko AT, et al. The wound microbiology and the outcomes of the systemic antibiotic prophylaxis in a mass burn casualty incident. *J Burn Care Res*. 2020;41(1):95–103.
123. Singer AJ, Dagum AB. Current management of acute cutaneous wounds. *N Engl J Med*. 2008;359(10):1037–1046.
124. Cummings P, Del Beccaro MA. Antibiotics to prevent infection of simple wounds: a meta-analysis of randomized studies. *Am J Emerg Med*. 1995; 13(4):396–400.
125. Givens M, Muck AE, Goolsby C. Battlefield to bedside: translating wartime innovations to civilian emergency medicine. *Am J Emerg Med*. 2017;35(11):1746–1749.
126. Lloyd BA, Murray CK, Shaikh F, Carson ML, Blyth DM, Schnaubelt ER, 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(9–10):e260–e265.
127. Weintrob AC, Murray CK, Xu J, Krauss M, Bradley W, Warkentien TE, et al. Early infections complicating the Care of Combat Casualties from Iraq and Afghanistan. *Surg Infect (Larchmt)*. 2018;19(3):286–297.
128. Gerhardt RT, Matthews JM, Sullivan SG. The effect of systemic antibiotic prophylaxis and wound irrigation on penetrating combat wounds in a return-to-duty population. *Prehosp Emerg Care*. 2009;13(4):500–504.
129. Medeiros I, Saconato H. Antibiotic prophylaxis for mammalian bites. *Cochrane Database Syst Rev.* 2001;(2):CD001738.
130. Looke D, Dendle C. Bites (mammalian). *BMJ Clin Evid*. 2010;2010:0914.

© 2023 The Author(s). Published by Wolters Kluwer Health, Inc. on behalf of the American Association for the Surgery of Trauma.