EAST PRACTICE MANAGEMENT GUIDELINES WORK GROUP: PRACTICE MANAGEMENT GUIDELINES FOR PROPHYLACTIC ANTIBIOTIC USE IN OPEN FRACTURES

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I. Statement of the Problem

Extremity fractures are caused by either low or high energy forces and may be isolated or combined with other injuries. When the underlying fracture is associated with a cutaneous wound, prevention of wound sepsis remains the primary objective in the management of the soft tissue. There is universal agreement that these wounds require emergency treatment as soon as possible to minimize infectious complications. To help standardize care and comparison of similar injuries in studies, Gustilo et al.[1] classified open fractures into three categories:

Grade (Type) I: Open fracture with a skin wound less than 1 cm long and clean.

Grade (Type) II: Open fracture with a laceration more than 1 cm long without extensive soft tissue damage, flaps, or avulsions.

Grade (Type) III: Either an open segmental fracture, an open fracture with extensive soft tissue damage, or a traumatic amputation.

In their review, the infection rate for type III open fractures was a major problem with an incidence of 24%. Grade III fractures encompassed a wide range of soft tissue wounds and was felt to be too imprecise for standardizing care and comparison. Thus, Gustilo further stratified these wounds according to worsening prognosis with a wound sepsis rate as follows: IIIa - 4%; IIIb - 52%; IIIc - 42%.[2]

IIIa: Adequate soft tissue coverage of a fractured bone despite extensive soft tissue laceration or flaps, or high energy trauma irrespective of the size of the wound.

IIIb: Extensive soft tissue injury loss with periosteal stripping and bone exposure, usually associated with massive contamination.

IIIc: Open fractures associated with arterial injury requiring repair.

The importance of describing type III open fractures with this more accurate classification scheme cannot be overstated. This A/B/C stratification also allows for subsequent upward revision for a wound which evidences progressive soft tissue necrosis following initial evaluation. Although this scoring system is the one most widely used for management decisions and comparison of results of treatment among different series, a recent report has claimed that interobserver agreement is moderate to poor and is case dependent.[3]

An appropriate management plan for open extremity fractures would include coverage with a sterile dressing with gentle pressure applied as necessary to control bleeding. Splinting is carried out, the patient is prophylaxed for tetanus and parenteral antibiotics are administered. Operative wound care should be done under general or regional anesthesia as soon as the patient has been stabilized and cleared for the operating room. Whenever possible, delays of more than six hours should be avoided because of the increased risk of infection. Wound care should involve a thorough debridement of devascularized muscle, fascia, subcutaneous tissue, skin, bone and all foreign material. The importance of adequate surgical debridement can not be overemphasized in controlling wound sepsis since antibiotics are only adjunctive therapy. Determination of the fracture grade should be made at this time. The margins of the wound of compounding are extended as required for debridement and appropriate stabilization of the fracture is effected. The wound is left open under a sterile moisture retaining dressing. A "second-look" may be advisable at 24-48 hours with further debridement if necessary. Ultimately, wound closure may be accomplished by delayed primary closure, split thickness skin graft, local muscle flap rotation, or free tissue transfer with microvascular anastomosis.

Various factors have been recognized as increasing the risk for infection: (1) failure to utilize prophylactic antibiotics; (2) resistance of wound organisms to wound antibiotics; (3) increased time from injury to initiation of antimicrobial agent and operative debridement; (4) extent of soft tissue damage; (5) open tibial fractures; (6) positive post debridement-irrigation cultures; and (7) wound closure in the presence of *Clostridium perfringens.* Other factors shown to have no effect include the length of antibiotic treatment (3 versus 5 to 10 days) and type of wound closure. Stabilization is now usually obtained by unreamed nailing or external fixation.[4] Low infection rates have been reported after severe open fractures treated by reamed intramedullary nailing.[5] Dellinger et al. performed a multivariate logistic regression analysis and identified local factors at the fracture site as more significant risk factors for subsequent infection than Injury Severity Score (ISS), the requirement for blood transfusion, the amount of blood transfused, or the presence of more than one fracture.[6]

Norden found convincing evidence that antibiotics administered before incision reduced the risk of infection after surgical stabilization of closed hip fractures or proximal femoral endoprosthetic replacement.[7] The group receiving antibiotics had a 78% lower rate of infection compared with controls. This study was included in this review to demonstrate the role of prophylactic antibiotics following orthopedic procedures for closed fractures. However, Norden did not address the role of prophylactic antibiotics with regard to open fractures in which bacterial contamination is present preoperatively in 48% to 60% of all wounds and 100% of severe wounds.

Dellinger provided an in depth report of prophylactic antibiotics in open fractures in 1991.[8] He performed a detailed analysis of controlled trials in open fractures and the various studies evaluating choices of antibiotics as well as duration of therapy for these extremity injuries. Subsequent investigations have been carried out to analyze the impact of various antibiotic regimens and the appropriate length of time for continuing therapy.[15-17,22]

II. Process

A. Identification of references

These recommended guidelines for prophylactic antibiotic usage for open fractures are evidence-based. Articles were identified from the literature by independent searches performed by two of the reviewers. One search was performed using OVID MEDLINE and covered the literature from 1985 to 1997. Key words used in this search were “open fracture, antibiotics, prophylaxis, and management”. References from 1975 to 1985 were identified through a MEDLINE search using the following key words: “antibiotic prophylaxis; human; open fractures; bacterial infections - prevention and control; fracture healing; fracture-complications; and surgical wound infections”. These combined searches identified 313 articles. The bibliography of each article was reviewed for additional references which were not identified in the two original searches. Letters to the editors, case reports, and review articles were excluded from further evaluation. This identified 56 studies for evidentiary review. The articles were reviewed by 3 orthopedic trauma surgeons, 2 general surgeons, and two pharmaceutical outcome researchers with interest in pharmacokinetics and health care economics. These individuals then collaborated to produce the guidelines.

1. Quality of the references

The references were classified in the methodology established by the Agency for Health Care Policy and Research (AHCPR) of the U.S. Department of Health and Human Services. Additional criteria and use for Class I articles were taken from a tool described by Oxman et al.[9] Thus, the classifications were:

Class I: Prospective, Randomized, Double-Blinded Study

Class II: Prospective, Randomized, Non-Blinded Trial

Class III: Retrospective Analysis of Patient Series

III. Recommendations

A. Level I

There are sufficient Class I and II data to recommend preoperative dosing with prophylactic antibiotics (as soon as possible after injury) for coverage of gram positive organisms as optimum care for trauma patients with open fractures. For Grade III fractures, additional coverage for gram negative organisms should be given. High-dose penicillin should be added to the antibiotic regimen when there is a concern for fecal/Clostridial contamination such as in farm related injuries.

B. Level II

There are sufficient Class I and Class II data to recommend antibiotics be discontinued 24 hours after wound closure for Grade I and II fractures. For Grade III wounds, the antibiotics should be continued for only 72 hours after the time of injury or not more than 24 hours after soft tissue coverage of the wound is achieved, whichever occurs first (See page 10, paragraph C for discussion).

Definition of Level I recommendation: This recommendation is convincingly justifiable based on the available scientific information alone. It is usually based on Class I data, however, strong Class II evidence may form the basis for a level 1 recommendation, especially if the issue does not lend itself to testing in a randomized format. Conversely, weak or contradictory Class I data may not be able to support a level 1 recommendation.

Definition of Level II recommendation: This recommendation is reasonably justifiable by available scientific evidence and strongly supported by expert critical care opinion. It is usually supported by Class II data or a preponderance of Class III evidence.

IV. Scientific Foundation

A. Historical background

An open fracture was for many thousands of years a sentence of death. Amputation was often considered as the only viable alternative to death. The mortality rate of all kinds of open fractures in the Franco Prussian War was 41%; it was 50% for the lower leg, 66% for the thigh, and 77% for open fractures of the knee joint. Other reports claimed a mortality rate ranging from 54 to 99% for open femur fractures.[10]

In War World I, the mortality rate for an open fracture of the femur remained approximately 80%. The immediate use of the Thomas splint for femur fractures was introduced in 1916, and the mortality rate for open fractures of the femur fell promptly to 16%. Karpmen later recognized that restoration of the bone length reduced the volume of the fascial compartments and therefore the magnitude of blood loss associated with the open fracture, which explained the reduction in mortality observed with the Thomas splint. Also in World War I, Orr evolved a policy of wound excision and debridement, reduction of the fracture, stabilization with plaster, and leaving the traumatic wound open.[11] During the Spanish Civil War, Truetta confirmed Orr's experience with a reported 0.6% septic mortality rate in 1069 open fractures.[12] Thus, World War I was the first time that the role of wound debridement was correlated with a reduction in septic mortality for open fractures. This reduction occurred prior to antibiotics, blood transfusions, intravenous fluids, and modern anesthesia.

During World War II, there was initial enthusiasm for the use of chemotherapeutic agents primarily in the form of sulfonamides in the immediate care of open fractures. The importance of wound excision with debridement and healing by secondary intention was once again appreciated when antibiotics failed to reduce infectious complications when wounds were primarily closed. The role of delayed primary wound closure was evaluated in 25,000 wounds without antibiotic coverage.

There was a 95% success rate in wounds left open for 4 to 10 days despite positive bacterial cultures from the wound.[13]

Patzakis et al. were the first to perform a prospective, randomized study comparing the infectious rates for penicillin with streptomycin, cephalothin, and placebo.[14] The rates were 13.9% for controls, 9.7% for penicillin, and 2.3% for cephalothin. Unfortunately, the study was not double-blinded and did not grade for severity of open fractures. Nonetheless, it was the first report showing a benefit of prophylactic antibiotics in these severe extremity injuries. Since the Patzakis study, there have been multiple reports[14,15,20,26,27,32,35,37,44,61,63] comparing various antibiotic regimens for efficacy in reducing infections and durations of therapy. These articles did stratify for grade of open fracture and form the basis for this evidence-based outcome review.

B. Choice of antibiotic

The majority of studies contain populations of patients with various mechanisms of injury. Hansraj et al.[15] performed a non-blinded comparison of ceftriaxone to cefazolin in extra-articular bony injuries due to gunshot wounds. The mean time between injury and the initial antibiotic dose was 4 hours. All admission cultures were negative, and none of the patients subsequently developed clinical signs of infection. They concluded that the cost of therapy was significantly less with ceftriaxone and resulted in a 1-day reduction in length of stay.[15] This study questions whether low velocity missile injury to extra-articular cortical bone requires any antibiotic prophylaxis.[15] If one feels compelled to use a prophylactic antibiotic in this low-risk group, the authors suggest a single-dose, long-acting antimicrobial is cost effective in this patient population compared with a shorter-acting, first generation cephalosporin which requires multiple dosing.

The benefit of antibiotic coverage in gunshot wounds producing skeletal fractures has also been evaluated in children.[16] Most of these wounds were caused by low velocity missiles. Forty-five patients (59%) received a first generation cephalosporin for 48 hours. None of these patients developed an infectious complication. The authors concluded that children with Grade I and II open fractures produced by low velocity missiles require antibiotics for only 48 hours.

Hope and Cole evaluated the role of antibiotics in children with open tibial fractures.[17] Despite broad-spectrum antibiotics for at least 48 hours, the wound infection rate was 11%. However, the most important variable in these infections was felt to be the severity of the soft tissue injury rather than the antibiotic coverage.[17] In a similar review of open tibial fractures in children, Buckley et al. reported a wound infection rate of 7.3%, osteomyelitis was 4.9%, and pin track infection was 20%.[18] Antibiotics were administered for 48-hour intervals and were repeated with subsequent wound debridement. They concluded the most important variable in reducing wound infection was utilizing delayed wound closure rather than primary closure.[18] Patzakis and Wilkins retrospectively reviewed their experience with various antibiotic regimens including penicillin, cephalothin, and cefamandole as well as a control arm with no antibiotics.[19] They also looked at the infection rate for adults (7.2%) and pediatric patients (1.8%). The various infectious complication rates were 13.9% for placebo, 10% for penicillin plus streptomycin, 5.6% for cephalothin, and 4.5% for cefamandole plus tobramycin. The duration of antibiotic therapy was not correlated with the reduction in infection rate. Thus, they concluded that, for severely contaminated wounds, broad-spectrum antibiotics should be administered as soon as possible after injury and be continued for no more than 72 hours.[19]

Other investigators have relied on wound cultures to direct antibiotic therapy. In a prospective study of open fractures, Robinson et al. reported 83% of the initial cultures as being positive.[20] More importantly, over 90% of the organisms identified in these cultures were sensitive to routine antibiotics (1^{st} generation cephalosporins). Four patients had persistent positive cultures at the time of a second debridement 24 hours after admission, and all developed a deep wound infection. They concluded that sequential wound cultures facilitated antibiotic therapy in the management of open extremity fractures. More recent investigations have shown no correlation of wound cultures at the time of presentation or obtained during the initial debridement and subsequent infection.[21,22,61]

The importance of prophylactic antibiotics for open fractures of the knee, ankle, hand, digits, and skull has also been evaluated and found to be beneficial.[23-33] Benson et al. compared clindamycin against cefazolin and saw no difference in the infection rates.[34] This study suggested that any antimicrobial agent with *Staphylococcus aureus* coverage is adequate effective prophylaxis for open fractures. Thus, there is adequate Class I and II data to document the benefit of prophylactic antibiotics in open extremity fractures. Agents effective against *Staphylococcus aureus* would appear to be adequate for Grade I and II fractures.[1,14,34-38] Since various gram negative organisms are cultured from Grade III wounds after the initial debridement, broader gram negative coverage through the addition of an aminoglycoside is beneficial.[17-20,26,39-53]

C. Duration of therapy

Multiple studies have demonstrated the interaction between antibiotic therapy and wound management.[1,17-20,39,42,44,45,53-62] When Grade I or II wounds are closed primarily, an additional 24 hours of antibiotic coverage is adequate independent of time of initiation after injury.[19,37,39,42,44,45,63] Dellinger et al. observed no relationship between the duration of antibiotic administration (1 day versus 5 days) and the risk of infection, independent of the grade of the fracture.[8,63] Other reports have identified tibial fracture as being the most significant predictor of subsequent infection.[2,6,19,63]

D. Route of antibiotic delivery

Most studies report discussed above use intravenous antibiotics for prophylaxis. An alternative technique, the antibiotic bead pouch, was developed in the late 1980's . Several investigators have utilized aminoglycoside-polymethyl methacrylate (PMMA) beads alone or in addition to parenteral antimicrobials. It has been reported in several series as being useful in the management of traumatic open wounds associated with fracture,[57,68] particularly in cases of Gustilo types IIIB and IIIC injuries with acute infection and types II and IIIB with chronic osteomyelitis (3.7% versus 12%).[56,69] This technique promotes high local tissue levels of antibiotic concentration in the target area with a significantly decreased risk of potentially toxic systemic effects as seen with high dose parenteral delivery. In the acute setting, PMMA beads, which have been impregnated with an aminoglycoside antibiotic, are used in conjunction with 5 days of tradition systemic tobramycin, cefazolin and penicillin prophylaxis.[67] This is combined with a regimen of thorough, serial wound debridements every 48 to 72 hours and bead exchanges with sterile self-adherent porous polyethylene drapes used to seal the wound. Systemic aminoglycoside levels are monitored with "peak" and "trough" levels with the doses being adjusted to maintain a therapeutic range. Soft tissue coverage techniques are carried out based on the immediate needs of the injury, and can include delayed primary closure, split-thickness skin grafting, local flaps or free-tissue transfers, as warranted. Skeletal stabilization is generally managed with intramedullary nailing or external fixation, the latter sometimes being converted to an intramedullary nail after soft tissue coverage has been achieved.[64] The determinants of wound closure/soft tissue coverage include the viability of the local soft tissue envelope after adequate time for demarcation has been allowed, but generally should be done in under 10 days.[66] It is not clear whether local therapy provides adequate tissue levels of antibiotic without systemic administration.

E. Evidentiary table

The evidentiary table contains 54 articles that were utilized to formulate these guidelines. The data are listed alphabetically by Class and include 10 Class I articles, 8 Class II, and 36 Class III references. The following data were retrieved and recorded from each article and are listed under the conclusion sections: (1) protocol design; (2) antibiotics utilized; (3) infectious complications; and (4) conclusions.

V. Summary

Multiple studies have documented the reduction in wound infections with the use of prophylactic antibiotics in the care of patients with open fractures. Although studies with various therapeutic agents have suggested an improved outcome with prolonged (> 24 hours) therapy, none have been done with appropriate controls. The most difficult open fracture wound to care for is the Grade IIIb tibial fracture. Although some authors advocate application of antibiotic impregnated beads for local control of infection in addition to parenteral administration, supportive Class I and II data are not available. These wounds (type III) should receive coverage for gram negative organisms in addition to gram positive coverage.

VI. Future Investigation

There is a need to re-evaluate the current infection rate for long bone open fractures. Studies should specifically focus on high-risk injuries, ie. the Grade IIIb tibial injury. The study design should evaluate the effect of wound debridement, systemic and local antibiotics, duration, and specific agents as well as cost analysis. Because of the relatively low rate of infection, a multi-institutional effort would allow a meaningful study to be completed in a short time period.

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PROPHYLACTIC ANTIBIOTIC USE IN OPEN FRACTURES: EVIDENTIARY TABLE

First Author	Year	Reference	Class	Conclusions
Patzakis MJ	1974	The role of antibiotics in the management of open fractures. *J Bone Joint Surg 56A:532-541*	I	· 310 pts. Randomized Abx regimens (10-day course): 1) Gp 1 + placebo; 2) Gp II + penicillin + streptomycin; 3) Gp III + cephalothin. · Infection rates: Gp I (13.95); Gp II (9.7%); Gp III (2.3%) · Recommend: 1) Abx effective for gram pos., gram neg., staph; 2) wound C&S before debridement most likely to isolate potentially infectious organisms; 3) modify Abx based on C&S results.
Bergman BR	1982	Antibiotic prophylaxis in open and closed fractures: A controlled trial. *Acta Orthop Scand 53:57-62*	I	· Open fractures(n=90): Grade I, N= 55; Grade II & III, N=35. · Abx included: 1) dicloxacillin; 2) benzyl penicillin; 3) placebo. All Abx discontinued after 48 hrs. · No statistical difference in superficial infections for either Abx or by subset analysis for stab wound or lacerations, or Grade I, II, or III fractures. · Gp 3 developed significantly more deep infections. · No difference between dicloxacillin and benzyl penicillin. · Confirms short duration prophylactic Abx reduce deep infections for open fractures.
Benson DR	1983	Treatment of open fractures: A prospective study. *J Trauma 23:25-30*	I	· Compared the effect of clindamycin vs cefazolin. · Quantitative cultures were obtained on admission. · Results: 46% of wounds were contaminated at time of debridement. Infection rate=6.5% · Gram neg. org. resistant to prophylactic agents recovered only 8 times: 4 (50%) became infected. · No difference in infection rate with either agent.
Sloan JP	1987	Antibiotics in open fractures of the distal phalanx. *J Hand Surg 12B:123-124*	I	· 85 open distal phalanx fractures. · Randomized groups: 1) No Abx; 2) cephradine 500 mg po QID x 5 days; 3) cephradine 1 gm IV pre-op, then 500 mg po QID x 5 days; 4) cephradine 1 gm IV pre-op, then 1 gm po postop. · 4.7% infection rate (n=4); 3 infections occurred in "No Abx" group. · No significant difference between 3 Abx regimens. · Recommend:1) Abx prophylaxis nec. for open fractures of distal phalanx; 2) Administration mode does not influence infection rate; 3) Regimen #4 most cost-effective/efficacious.
Dellinger EP	1988	Duration of preventive antibiotic administration for open extremity fractures. *Arch Surg 123:1320-1327*	I	· 248 open fractures-randomized: 1) cefonicid 2 gms x 1 day; 2) cefonicid 2 gms x 1 day, then 1 gm q 24 hrs x 5 days; 3) cefamandole 2 gms, then 1 gm q 6 hrs x 5 days. · 13% infection rate-no significant difference among 3 Abx groups. · Equivalent efficacy for 1-day Abx administration compared to 5 days. · Recommend brief Abx course followed by close observation for postop infection.

First Author	Year	Reference	Class	Conclusions
Peacock KC	1988	Efficacy of perioperative cefamandole with postoperative cephalexin in the primary outpatient treatment of open wounds of the hand. *J Hand Surg 13A:960-964*	I	· 87 pts: 1) Study group: cefamandole 1 gm IV q 4 hrs, then cephalexin 500 mg QID x 3 days @ discharge; 2) control: placebo IV, then placebo po @ discharge. · Infection rate= 0% study group vs 2.1% control (NS). · Abx not routinely indicated; use Abx for serious injuries/specifically identified infections.
Swiontkowski MF	1989	Criteria for bone debridement in massive lower limb trauma. *Clin Orthop 243:41-47*	I	· 60 pts with open extremity fractures. · Abx regimen: cephalosporins + aminoglycosides (type II). · 9.2% deep infection.
Robinson D	1989	Microbiologic flora contaminating open fractures: Its significance in the choice of primary antibiotic agents and the likelihood of deep wound infection. *J Orthop Trauma 3:283-286*	I	· 89 open extremity fractures. · Management protocol: 1) wound culture on admission; 2) repeat culture @ day 1; 3) cefoxitin 1 gm TID x 24 hrs; 4) Garamycin 80 mgs TID x 24 hrs (Grade III). · 83% initial cultures pos.; >90% organisms isolated sensitive to routine Abx. · 1-day pos. culture (n=4) - 100% developed deep wound infection. · Importance of wound cleansing and appropriate Abx. · Sequential wound cultures predict likelihood of infection.
Hansraj KK	1995	Efficacy of ceftriaxone versus cefazolin in the prophylactic management of extra-articular cortical violation of bone due to low-velocity gunshot wounds. *Orthop Clin North Am 26:9-17*	I	· No infectious complications in 100 pts randomized to 1 of 2 Abx protocols (skin wound <1cm): 1) ceftriaxone 1 gm, then repeat 1 gm @ 24 hrs; 2) cefazolin 1 gm, then 1 gm q 8 hrs x 7 doses. · Ceftriaxone/cefazolin both effective prophylactic agents. · Ceftriaxone regimen dec. LOS by 1 day & lowers costs approx. $2300/patient.
Sangha KS	1995	Pharmacokinetics of once-daily dosing of gentamicin in surgical intensive care unit patients with open fractures. *Ann Pharmacother 29:117-119*	I	· 11 pts. with type II/III open extremity fractures: 1) gentamicin 6 mg/kg q 24 hrs x 48 hrs (n=7); 2) gentamicin 2 mg/kg q 8 hrs x 48 hrs (n=4); 3) cefazolin 1 gm q 8 hrs x 48 hrs (n=11). · Increased Cmax, Cpk and AUC once-daily regimen. · No relationship to clinical outcome.
Gustilo RB	1976	Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: Retrospective and prospective analyses. *J Bone Joint Surg 58A:453-458*	II	· 352 pts. Standard protocol: 1) debridement + copious irrigation; 2) primary closure for type I/II fractures; 3) secondary closure for type III fractures; 4) all wounds cultured on admission; 5) oxacillin or ampicillin pre-op, then x 72 hrs. · 158 pts (70.3%) had wound cultures with infection rate of 2.5%. From sensitivity studies on initial wound cultures, cephalosporin would be prophylactic Abx of choice for type III open fractures. Infection rate was 9% & significantly lower than retrospective control.

First Author	Year	Reference	Class	Conclusions
Patzakis MJ	1983	Use of antibiotics in open tibial fractures. *Clin Orthop 178:31-35*	II	· 363 consecutive open tibial fractures. · 4 treatment groups during 10-year period: 1) no Abx; 2) penicillin+streptomycin x 10 days; 3) cephalothin-most received 5-day course of IV therapy followed by oral cephalexin x 5 days; 4) cefamandole+tobramycin x 3 days if initial cultures neg. and 5 days if cultures pos. · Infection rates highest with no Abx (24%). Lowest in Gp 4 (4.5%). · Conclude: no benefit to continuing Abx beyond 3 days.
Merritt K	1988	Factors increasing the risk of infection in patients with open fractures. *J Trauma 28:823-827*	II	· 70 pts-tissue cultures @ debridement; follow-up re: development of clinical infection. · All received combination cephalosporin/aminoglycoside. · Infection rate = 19%. · Infection rate lower in patients treated 24-48 hrs vs 3-7 days.
Ostermann PA	1993	The role of antibiotic therapy in the management of compound frac tures. *Clin Orthop 295:102-111*	II	· 704 consecutive open fractures: 1) Gp A (n=157) - cefazolin/tobra/PCN; 2) Gp B (n=547) - cefazolin/tobra/PCN + tobra-PMMA. · Lower incidence of infection in Gp B vs Gp A (4% vs 17%). · Addition of tobra-PMMA to parenteral Abx dec. infection in highly contaminated wounds and dec. incidence of polymicrobial infection. · Routine use of prophylactic tobra-PMMA deserves prospective multicenter trial.
Ostermann PA	1994	Timing of wound closure in severe compound fractures. *Orthopedics 17:397-399*	II	· 381 open fractures: 1) IV cefazolin/tobra/PCN x 5 days; 2) Abx bead pouch tech. · Overall infection rate=Grade 1(0%); Grade II (2.6%); Grade III (8.4%). · No definitive conclusions due to design of study (ie. no randomization, no control group).
Ostermann PA	1995	Local antibiotic therapy for severe open fractures. A review of 1085 consecutive cases. *J Bone Joint Surg 77B:93-97*	II	· 1085 consecutive open fractures. Gp 1 (n=845): IV cefazolin/tobra/PCN+tobra-PMMA; Gp 2 (n=240): IV cefazolin/tobra/PCN. · Dec. overall infection rate Gp 1 (3.7% vs. 12%); statistical significance only in type III. · Adjuvant local Abx therapy decreases incidence of late infection.
Keating JF	1996	Reamed nailing of open tibial fractures: Does the antibiotic bead pouch reduce the deep infection rate? *J Orthop Trauma 10:298-303*	II	· Parenteral regimen: Cefazolin + Gentamicin x 72 hrs. · Decreased deep infection rate in type II fractures with Abx bead pouch: 4% vs 20% (NS). · Decreased deep infection rate in type III fractures with Abx bead pouch: 8% vs. 20% (NS).
Wisniewski TF	1996	Gunshot fractures of the humeral shaft treated with external fixation. *J Orthop Trauma 10:273-278*	II	· First generation cephalosporin x 72 hrs. · Incidence of infection (21%): deep wound sepsis (2); pin track infection (5); osteomyelitis (1).
First Author	**Year**	**Reference**	**Class**	**Conclusions**
Kennedy T	1975	Management of tibial fractures. *Minn Med 58:525-528*	III	· 109 pts with 118 open and closed tibial fractures. · Closed methods + early weight-bearing union in 98%. · Pins and plaster 62.5% delayed union rate. · All type I/II closed primarily. No infection supporting use of prophylactic Abx.

				· Infection rate 3.8% type III wounds. · Type I/II wounds can be closed primarily provided adequate debridement and high doses or pre and postoperative Abx are used. · Weaknesses: no mention of Abx or durations.
Clancey GJ	1978	Open fractures of the tibia: A review of one hundred and two cases. *J Bone Joint Surg 60B:118-122*	III	· 102 open tibial fractures. · Protocol defined by grade of soft tissue injury: I, II, or III. All wounds left open regardless of type of fixation employed. · IV methicillin+IM kanamycin x 72 hrs. · Superficial & deep infection rate similar (15%) for casting & internal fixation.
Gustilo RB	1979	Use of antimicrobials in the management of open fractures. *Arch Surg 114:805-808*	III	· 520 open fractures; 50.7% pos. cultures on admission; various Abx regimens. · 2.4% infection rate with cephalothin. · Recommend: 1) Abx effective against Staph aureus-infective org. 6-70%; 2) cephalothin effective in all open fractures; 3) aminoglycosides-add for severely contaminated wounds; 4) Abx duration $\leq$ 3 days.
Pinckney LE	1981	The stubbed great toe: A cause of occult compound fracture and infection. *Radiology 138:375-377*	III	· 6 children with open fractures of distal phalanx of great toe caused by stubbing. · Anatomic relationship distal phalanx and nail make recognition ofoccult compound fracture difficult by physical exam. · History of small amount of bleeding from the nail fold or laceration proximal to nail fold significant for open phalangeal fracture. · 1st 4 cases were delayed presentation with obvious infection. Last 2 cases presented within 2 days of injury. Treated with 2 wks of Abx. None dev. infection. · Conclude: stubbed toes in children at great risk of open compound fracture and should be treated promptly with Abx to avoid development of osteomyelitis.
Christensen J	1982	Fractures of the shaft of the tibia treated with AO-compression osteosynthesis. *Injury 13:307-314*	III	· 40% of pts had open fractures. 93% received prophylactic Abx on admission. None with open fractures developed infections. · Abx included methicillin+gentamicin x 5 days, then dicloxacillin x 7 days. · Rigid internal fixation advocated for all displaced fractures of tibial shaft, esp. open fractures.
First Author	**Year**	**Reference**	**Class**	**Conclusions**
Mendelow AD	1983	Prophylactic antimicrobial management of compound depressed skull fracture. *J Royal Coll Surg Edinb 28:80-83*	III	· 223 pts with depressed skull fractures - 176 cases were open. · 107 pts treated prophylactically with ampicillin or a sulfonamide. · Infection rate of 1.9% significantly lower than rate of infection in pts receiving no Abx or any combination Abx.
Franklin JL	1984	Immediate internal fixation of open ankle fractures. Report of thirty-eight cases treated with a standard protocol.	III	· Open ankle fractures (n=38). · Standard protocol IV broad-spectrum cephalosporin in ED x 48 hrs. · 1 deep infection, 5 superficial infections.

		J Bone Joint Surg 66A:1349-1356		
Rosenwasser RH	1984	Compound frontobasal skull fractures: Surgical management of the acute phase. *South Med J 77:347-350*	III	· Open skull fractures (n=5). · Recommended Abx coverage: nafcillin 2 gms IV q 6 hrs, ticarcillin 2 gms IV q 6 hrs and tobramycin dosed according to body weight. · 4 of 5 pts had no infection.
Johnson KD	1986	Orthopedic experience with methicillin-resistant Staphylococcus aureus during a hospital epidemic. *Clin Orthop 212:281-288*	III	· 23 pts with open fractures which cultured for MRSA. · 97% received 1st gen. cephalosporin; 40% received tobramycin. · 22% required amputation; 13% healed with chronic drainage. · MRSA infections related to author's hospital+prior Abx use consideration for all Ortho services in large hospitals. · Prophylaxis involves prevention of crossinfection, personal hygiene, and controlled short-term use of broad-spectrum Abx.
Burgess AR	1987	Pedestrian tibial injuries. *J Trauma 27:596-601*	III	· 70 pts with high-energy (> 65% Grade III) tibial fractures. · Received IV cephalosporin-variable regimens. · Prophylactic Abx important factor in reduction of morbidity.
Gustilo RB	1987	Classification of type III (severe) open fractures relative to treatment and results. *Orthopedics 10:1781-1788*	III	· 303 open fractures; established treatment regimen. · 4.4% wound sepsis: type I (0%); type II (2.5%); type III (13.7%). · Type III open fractures: cephalosporin (29%); cephalosporin+aminoglycoside (8.8%). · Continue Abx x 3 days. · Wound cultures: 83% pos. initially; 30% pos. post-debridement. No correlation between wound culture and clinical infection. · Recommend: 1) type I/II: cefamandole 2 gms @ admission, 1 gm q 8 hrs x 3 days; 2) type III: cefamandole (as above) + aminoglycoside 3-5 mg/kg/24 hrs x 3 days; 3) farm injuries: penicillin 10-12 million U; 4) repeat Abx: wound closure, internal fixation, bone grafting.
First Author	**Year**	**Reference**	**Class**	**Conclusions**
Wilson NI	1987	A survey, in Scotland, of measures to prevent infection following orthopaedic surgery. *J Hosp Infect 9:235-242*	III	· Questionnaire study of orthopedic surgeons re: details of Abx prophylaxis. · 75% routinely use Abx in open fractures: penicillinase-resistant penicillin (60%); cephalosporin (36%); gentamicin (4%). · Duration of Abx > 48 hrs (79%); 24-48 hrs (15%); < 24 hrs (6%). · Most select appropriate Abx. · Regimens could be more cost-effective by more accurate timing & duration of therapy.
Patzakis MJ	1989	Factors influencing infection rate in open fracture wounds. *Clin Orthop 243:36-40*	III	· 77 infections in 1104 open fractures (7%). · Wound cultured @ admission, @ debridement, and after irrigation. · Abx regimens: 1) no Abx; 2) penicillin (IV)+streptomycin (IM) x 10 days; 3) IV cephalothin x 10 days; 4) IV cephalothin x 5 days, then cephalexin (po) x 5 days; 5) IV cefamandole + tobramycin (IM) x 3-5 days (based on results of initial wound cult.). · 7.2% infection (adults); 1.8% infection (peds).

				· Effectiveness of Abx: no Abx-13.9% infection; penicillin/streptomycin-10%; cephalothin-5.6%; cefamandole/tobramycin-4.5%. · Time to initiation of Abx: < 3 hrs-4.7% infection; > 3hrs-7.4% infection. · No correlation with duration of Abx therapy. · Recommend: 1) early surgical debridement; 2) broad-spectrum Abx ASAP after injury; 3) continue Abx for 3 days; 4) type I/II-partial wound closure; 5) type III-delayed wound closure, tissue transfer (7 days).
Buckley SL	1990	Open fractures of the tibia in children. *J Bone Joint Surg 72A:1462-1469*	III	· Wound cultures in ED. · Routine tetanus prophylaxis. · Protocol: 1) min. 48 hrs Abx coverage; 2) 1st gen. cephalosporin; 3) aminoglycoside (type III); 4) penicillin (farm-related injury); 5) Abx repeated for subsequent procedures (48-72 hrs). · Wound infection rate=7.3%; osteomyelitis = 4.9%; pin-track infection = 20%. · Infection rates lower in children vs adults; no infection with delayed wound closure.
Henry SL	1990	The prophylactic use of antibiotic impregnated beads in open fractures. *J Trauma 30:1231-1238*	III	· 404 open fractures/339 pts.: Grade I (31.4%); Grade II (38.9%); Grade III (30.7%). Gp A (n=70) systemic Abx (cefazolin/tobra/PCN); Gp B (n=334) systemic Abx + tobra beads. · Overall infection rate = 21.4% Gp A vs 4.2% Gp B. · Polymicrobial infection=87.5% Gp A vs 55.6% Gp B. · Recommend prospective multicenter trial to establish efficacy of routine prophylactic use.
Kaltenecker G	1990	Lower infection rate after interlocking nailing in open fractures of femur and tibia. *J Trauma 30:474-479*	III	· Grade I/II open fractures: 23 femur/56 tibia. · Protocol: 1) wound covered in ED/no cultures; 2) penicillin. · 96.2% infection-free rate. · Abx required when interlocking nails used for stabilization.
First Author	**Year**	**Reference**	**Class**	**Conclusions**
Russell GG	1990	Primary or delayed closure for open tibial fractures. *J Bone Joint Surg 72B:125-128*	III	· 90 consecutive pts. · Compared primary with delayed closure for deep infection. · All pts received Abx (PCN, cloxacillin, or 1st gen. cephalosporin). · Gustilo classification: I (37); II (35); IIIa (4); IIIb (1); IIIc (4). · Primary closure 20% deep infection rate; 3% delayed closure. · Conclude - avoid primary closure.
Suprock MD	1990	Role of antibiotics in open fractures of the finger. *J Hand Surg 15A:761-764*	III	· 91 finger fractures: 1) +Abx=po 1st gen. cephalosporin/dcloxacillin/erythromycin x 3 days (n=45); 2) -Abx=no Abx (n=45). · No difference infection rate between groups (8.7% vs 8.9%). · Routine Abx not indicated for open finger fractures.
Hoffer MM	1992	Shrapnel wounds in children. *J Bone Joint Surg 74A:766-769*	III	· 19 children with open extremity fracture. · All wounds managed open/closure by secondary intention. · Abx choice based on availability.
Hope PG	1992	Open fractures of the tibia in children.	III	· 95 open tibia fractures: type I (24%); type II (55%); type III (21%)- broad-spectrum Abx at

		J Bone Joint Surg 74B:546-553		least 48 hrs. · 11% wound infection - infection rate correlated with degree of soft tissue injury. · Most type I, some type II wounds suitable for primary closure after debridement, irrigation, & use of systemic Abx for at least 48 hrs: 1) cephalosporins q 4 hrs x 3 days; 2) gentamicin + penicillin due to gross contamination @ time of presentation (3 pts). · 2 documented infections (10%)/ Complications correlated with wound severity.
Sanders R	1992	The salvage of open grade IIIb ankle and talus fractures. *J Orthop Trauma 6:201-208*	III	· 11 open, Grade IIIb ankle fractures. · Management protocol: 1) multiple debridements devitalized bone & soft tissue; 2) osseus defects filled x/Abx impregnated beads (tobra); 3) temporary external fixation; 4) delayed closure, bone grafting, dynamic compression plating. · Antibiotic protocol: 1) cephalothin+tobramycin+penicillin; 2) Abx discontinued @ discharge if serial bone cultures neg; 3) specific Abx initiated for pos. bone cultures x 6 wks. · 9.1% acute infection. · Protocol obtains wound coverage, ankle/subtalar fusion, & eradicates osteomyelitis.
Bednar DA	1993	Effect of time delay from injury to primary management on the incidence of deep infection after open fractures of the lower extremities caused by blunt trauma in adults. *J Orthop Trauma 7:532-5*	III	· 82 open fractures of the lower extremity. · Management protocol: 1) tetanus prophylaxis; 2) Grade I/II/IIIa- cefazolin; 3) Grade IIIb/IIIc- cefazolin + gent/tobra; 4) Abx continued x 48 hrs, repeat with any subsequent surg. procedure. · Deep infection = 4.9%. · Short delay to definitive primary surgical management not prognostically important.
First Author	**Year**	**Reference**	**Class**	**Conclusions**
Henry SL	1993	The antibiotic bead pouch technique. The management of severe compound fractures. *Clin Orthop 295:54-62*	III	· 704 consecutive open fractures. · 227 managed with Abx bead pouch tech. for temp. coverage of wounds with and without soft tissue defects + cefazolin/tobra/PCN IV. · Wound infection = 5.3%; osteomyelitis = 3.9%. · Most useful for severe Grade III wounds-bead pouch serves as substitute for soft tissue. · Recommend prospective randomized study to determine if only local Abx delivery by beads is sufficient and may replace parenteral Abx.
Seligson D	1994	The management of open fractures associated with arterial injury requiring vascular repair. *J Trauma 37:938-940*	III	· Methods (n=72): 1) cefazolin/tobra/PCN x 5 days (100%); 2) Abx bead pouch (43%)-non-randomized. · 10 wound infections (14%); 3 osteomyelitis (4%). · Recommend: mandatory parenteral broad-spectrum Abx and adjuvant use of aminoglycoside-PMMA beads.
Victoroff BN	1994	Extremity gunshot injuries treated in an urban children's hospital. *Pediatr Emerg Care 10:1-5*	III	· 76 wounds: 23 fractures (30%)/53 soft tissue wounds (70%); most low-velocity. · 45 pts received Abx: 1st gen. cephalosporin (45/45); cephalosporin =+ aminoglycoside (2/45). · 19/24 pts with fractures (79%) received Abx x 48 hrs. · No infections in 45 pts receiving Abx. · Recommend Grade I/II fractures - Abx for 48 hrs.

Acello AN	1995	Treatment of open fractures of the foot and ankle: A preliminary report. *J Foot Ankle Surg 34:329-346*	III	· Initiation of appropriate Abx ASAP is important variable in reducing rate of infection. · 60-70% open fracture wounds contaminated @ time of initial inspection (aerobic GPC/GPR). · Increasing trend toward gram neg. infections has reduced clinical relevance of predebridement wound cultures. · No studies document superiority of long-term vs. perioperative Abx coverage. · Recommended regimen (Gustilo): 1) Type 1: cefazolin; 2) Type II/III: cefazolin + amino-glycosides; 3) 3-day course, additional 3-day course when wound in surgically manipulated; 4) 1st generation cephalosporin adequate after 3 days if wound is not clinically infected. · Retrospective study: comparison of cefazolin/gent (n=19) vs cefazolin/Cipro (n=6) in open fractures of the foot and ankle. · C/G = 10.5% infection; C/C = 0% infection rate.
First Author	**Year**	**Reference Title**	**Class**	**Conclusions**
Cole JD	1995	A sequential protocol for management of severe open tibial fractures. *Clin Orthop 315:84-103*	III	· Protocol: 1) Cefazolin initiated in ED, continued x 36 hrs; 2) Aminoglycoside added for highly contaminated wounds by clinical examination. · Infection rate = 2%, majority of published studies. · Importance of re-establishing physiologic wound barrier (i.e. early wound closure) prevents dessication/contamination of wounds. · IM nailing safe in open tibial fractures.
Geissler WB	1995	Compression plating of acute femoral shaft fractures. *Orthopedics 18:655-660*	III	· 71 femur fractures: 58 closed / 13 open. · Parenteral Abx. · Infection rate = 0%. · Compression plating (non-standard) requires prophylactic Abx, bone grafting, meticulous technique.
Kreder HJ	1995	A review of open tibia fractures in children. *J Pediatr Orthop 15:482-488*	III	· Protocol: 1)Tetanus prophy. when appropriate; 2) Wound cultures/Abx in ED, continue min. 48 hrs or until definitive wound coverage; 3) Type I/II: broad-spectrum gram pos. coverage; 4) Type III: aminoglycoside; 5) Anaerobic coverage-contaminated playground/barnyard. · Infection rate = 14%. · Incidence of infection function of time to injury (> 6 hrs) & presence of neurovascular injury.
Marsh JL	1995	Major open injuries of the talus. *J Orthop Trauma 9:371-376*	III	· 17 open talar fractures - received perioperative Abx. · Infection rate = 38% > other open fractures. · Recommended primary talar body excision in select cases.
Buckley SL	1996	Severe (type III) open fractures of the tibia in children. *J Pediatr Orthop 16:627-634*	III	· Protocol: 1) Cephalosporin + aminoglycoside initiated in ED; 2) Penicillin- farm -related injuries; 3) Minimal duration Abx = 48 hrs; 4) Abx repeated for subsequent debridements. · Osteomyelitis (15%). · Wound irrigation & debridement, parenteral Abx, and early soft tissue coverage decrease incidence of osteomyelitis. · Incidence of complications similar in pediatric and adult type II fractures; children more

				successfully treated for complications.
Cullen MC	1996	Open fracture of the tibia in children. *J Bone Joint Surg 78A:1039-1047*	III	· 2% superficial wound infection / 0% osteomyelitis. · Prevalence of infection lower in children vs. adults. · Prevention depends on 1) thorough debridement, 2) irrigation, 3) fracture stabilization, and 4) parental Abx.
First Author	**Year**	**Reference Title**	**Class**	**Conclusions**
Grimard G	1996	Open fractures of the tibia in children. *Clin Orthop 332:62-70*	III	· Broad-spectrum Abx. · Average duration Abx = 5 days. · 7.1% infection rate: Grade I (3); Grade II (2); GradeIII (1). · No correlation between rate of infection and grade of injury. · No relationship between rate of infection and time to debridement. · No significant effect on infection as a function of type of wound closure.
Steiner AK	1996	Open fractures and internal fixation in a major African hospital. *Injury 27:625-630*	III	· Ampicillin = most commonly used Abx. · Postoperative infections (18.5%). · Infectious complications not related to Abx use.
Song KM	1996	Open fractures of the tibia in children. *J Pediatr Orthop 16:635-639*	III	· Protocol: 1) Tetanus prophylaxis; 2) 1st gen. cephalosporin x 24 hrs; 3) Repeat Abx with subsequent procedures. · 3 deep infections (8%): Staph aureus; type II (2) type III (1). · Infectious complications related to choice of fixation (i.e. internal vs. external) and time external fixator left in place.
Torchia ME	1996	Open fractures of the patella. *J Orthop Trauma 10:403-409*	III	· 10.7% deep wound infection - type II (3) / type IIIB(3). · Infection rate correlates with degree of soft tissue damage. · Cultures at the time of initial debridement of no value in predicting subsequent infection; infection frequently nosocomial: Pseudomonas (3), Group D strep. (2), Enterobacter (1), Enteropeptococcus (1), Staph aureus (1).