



2009 OTA Annual Meeting
Manchester Grand Hyatt
San Diego, CA

(#S9): Mini Symposium:
Treatment of Orthopaedic Infections

Elizabeth H, Level II

1:15pm – 2:45pm
Saturday, October 10, 2009

Moderator: William T. Obrebsky, MD

Faculty: Jeffrey O. Anglen, MD
Andrew H. Schmidt, MD

The material presented at this course has been made available by the Orthopaedic Trauma Association for educational purposes only. This material is not intended to represent the only, nor necessarily best, methods or procedures appropriate for the medical situations discussed, but rather is intended to present an approach, view statement or opinion of the faculty which may be helpful to others who face similar situations.

Disclosure: Faculty disclosure can be found starting on page 67 of the 2009 OTA Annual Meeting program.

**OTA Symposium 2009
Postop Wound Infections**

**Jeff Anglen MD
Andrew Schmidt MD
William Obrebskey MD MPH**

Predictors and Diagnosis of Early and Late Post-op Infections

Andrew Schmidt, MD

Predictors of infection after internal fixation

It is generally accepted that infection rates are increased in the following circumstances:

- Open fractures
- Malnourished patients
($<WBC$, $< \text{albumin}$, $< \text{Pre-albumin}$)
- Diabetics
- Peripheral vascular disease
- Immunocompromised patients, incl HIV.
- Transfusion
- EtOH abuse
- Medical co-morbidities

Thanni et al (2004): Evaluated SSI in 90 consecutive patients. Predictors of infection were:

- Duration of operation longer than 120 minutes (OR 2.25, 95% CL 0.48-10.16),
- Male gender (OR 2.01, 95% CL 0.44-10.45),
- Injury-operation interval less than six months (OR 2.00, 95% CL 0.22-46.08),
- Fracture fixation with plates and screws (OR 1.51, 95% CL 0.36-6.40),
- WBC $< 5,000/\text{mm}^3$ (OR 1.50, 95% CL 0.15-16.37),
- Preoperative urinary catheterization (OR 1.48, 95% CL 0.00-16.19),
- Postoperative urinary catheterization (OR 1.24, 95% CL 0.29-5.00).

Diagnosis of Implant – associated infection

- An infected fracture should be considered in anyone with persistent pain or delayed union of a fracture treated with internal fixation.

Tibial Infections After IM Nailing

Three presentations:

- 1) Fever with localized pain, swelling, and erythema at the fracture site without

abscess formation.

- 2) Obvious purulence at the fracture site.
- 3) Delayed presentation with purulent drainage from the fracture site.

Laboratory studies

- Elevations in total leukocyte count, ESR, or C-reactive protein.
- A rising CRP after 48 hours is predictive of a septic complication.

C-Reactive Protein in Patients Undergoing Surgery for Fractures

Two studies: Scherer et al 2001, Neumaier and Scherer 2008

Scherer et al 2001:

- 330 trauma patients undergoing fracture repair had pre-op and at least 3 postop CRP levels done.
- Peak value occurred on POD # 2. Magnitude proportional to surgical trauma.
- Patients with complications had a second rise in CRP, 7/9 infections had increasing CRP before onset of sx.
- A cut-off level of 14 mg/dL on the fourth day after surgery was recorded for the patients with deep wound infection.

Neumaier and Scherer 2008

- 787 patients
- Similar findings to earlier study, except that for deep wound infection, a cutoff level of 96 mg/L (sensitivity 92%, specificity 93%) after the fourth day of surgery was recorded.

Imaging studies are generally nonspecific

- Periosteal new bone, demineralization, or a sequestrum may be seen in chronic infections.
- Indium scans and MRI may also be useful, but are infrequently diagnostic.

There are no specific confirmatory tests other than the finding of bacteria on gram stain or culture.

Methods to Improve Diagnosis

- Sonication of surface dislodges adherent bacteria and improves increased yield 5X
- Examination of sonicated samples by immunofluorescence microscopy and PCR increased yield 10X

Detection of Biomaterial-Associated Infections...

- 22 cases of suspected infected prostheses
- Routine cultures of swabs or pieces of tissue + 41%

- Prolonged culturing + 64%
- Extensive culturing of scrapings from implant surface + 86%

References

- J.L. Carson, D.G. Altman, A. Duff, et al. Risk of bacterial infection associated with allogeneic blood transfusion among patients undergoing hip fracture repair. *Transfusion* 1999;39:694-700.
- Katona P; Katona-Apte J. The interaction between nutrition and infection. *Clin Infect Dis* 2008;15;46(10):1582-1588
- Neumaier M, Scherer MA. C-reactive protein levels for early detection of post-operative infection after fracture surgery in 787 patients. *Acta Orthop* 2008;79:428-432.
- Scherer MA, Neumaier M, von Gumpfenberg S. C-reactive protein in patients who had operative fracture treatment. *CORR* 393: 287-293, 2001.
- Thanni LO, Aigoro NO. Surgical site infection complicating internal fixation of fractures: incidence and risk factors. *J Natl Med Assoc* 2004 Aug;96(8):1070-1072.
- Trampuz A, Zimmerli W. Diagnosis and treatment of infections associated with fracture-fixation devices. *Injury* 2006;37 Suppl:S59-S66.

Treatment of Early Post op Wound Infections

William T Obrebskey MD MPH

- I. Treatment of early post operative wound infection
 - a. Incidence 1% to 20%.
 - b. Fractures - open continuation, multiple operations, soft tissue damage or loss, foreign bodies, malnutrition, dead space, and blood supply.
 - c. Quandary -
 - a. Stability – Union
 - b. Debridement – Eradication,
 - c. To remove or not remove implants. That is the question

- II. Options
 - a. PO antibiotics
 - b. Debride, leave implants, and Antibiotics, time – 2, 4, 6, 12 weeks
Remove all implants.
 - c. Debride and Exchange Implants
 - d. Debride, remove Implants, Antibiotic until infection eradicated, replace Implants

- III. Morbidity
 - a. Time

- b. Pain (Unstable Fracture)
- c. Multiple Operations
- d. Amputation

IV. Data

- A. Trebse R, J Bone Joint Surg Br; 2005.
 - 24 patients with infection of stable implant present < 1 year
 - All culture positive and OR debridement in 71%
 - Antibiotic 2-4 weeks and total IV/PO 3 months
 - Implants: Prostheses – 20, hip 17, knee- 3, ankle- 1, fx orif -4
 - Outcomes – 20/24 no recurrence -83%, all failures- prostheses
- B. Infections associated with orthopedic implants. Trampuz A. Widmer AF. Current Opinion in Infectious Diseases. 19(4):349-56, 2006 Aug.
 - Debride, retain and suppression – 60 % success at 2 years, no rifampin used (21, 22)
 - Debride, single stage exchange – 85% success (23-26)
 - Debride and 2 stage revision - > 90% success (27-29)
- C. Rightmire E, Zurakowski D, Vrahas M. Acute infections after fracture repair: management with hardware in place. Clin Orthop Relat Res. 2008 Feb;466(2):466-72.
 - 69 Pts s/p ORIF w/in 4 months, 17 did **not** have OR debridement
 - 68% (47/69) successful suppression til union
 - 36% (18-47) had late deep infx
 - 32% (22/69) Failed: 8 nonunions, 6 casted, 2 bone graft, 3 ex fix, 2 girdlestones
 - Smoking predicted failure: 79% vs 52%
- Berkes, M Obremsky, WT et al. Treatment of Early Post op Wound Infections. OTA 2008.
 - 123 pts s/p ORIF < 6 weeks with OR debridement and culture positive bacteria
 - IV/po antibiotics 6-12 weeks
 - 72% fractured healed w/o other surgery
 - 30% required HW removal late due to recurrence
 - 64% total no further surgery
 - 6% amputation
 - Failure predicted by IMN, pseudomonas, open fx, lower extremity fx
- Trampuz A. Zimmerli W. Diagnosis and treatment of infections associated with fracture-fixation devices. Injury. 37 Suppl 2:S59-66, 2006 May.
- Trampuz A. Widmer AF. Infections associated with orthopedic implants. Current Opinion in Infectious Diseases. 19(4):349-56, 2006 Aug.

- Debridement and antibiotics – approx 85% “success”
 - Exchange implants – 91%
 - Remove implants if “loose” or resistant organisms: MRSA, enterocci, pseudomonas, fungi
 - Antibiotics for 3 mos if metal retained
 - Consider removal of implants after union, stop antibiotics for 2 weeks prior
- Zimmerli W, et.al.. JAMA 1998; 279:1537–1541
 - RCT of infected prostheses s/p debridement and 2 weeks IV
 - Cipro and placebo 58% retention
 - Cipro and rifampin 100% retention

REFERENCES

1. Struijs PA, Poolman RW, Bhandari M. Infected nonunion of the long bones. *J Orthop Trauma*. 2007 Aug;21(7):507-11. Review.
2. Crowley DJ, Kanakaris NK, Giannoudis PV. Debridement and wound closure of open fractures: the impact of the time factor on infection rates. *Injury*. 2007 Aug;38(8):879-89. Epub 2007 May 29. Review.
3. Trampuz A, Zimmerli W. Diagnosis and treatment of infections associated with fracture-fixation devices. *Injury*. 2006 May;37 Suppl 2:S59-66. Review.
4. Murray CK. Infectious disease complications of combat-related injuries. *Crit Care Med*. 2008 Jul;36(7 Suppl):S358-64.
5. Darouiche RO. Treatment of infections associated with surgical implants. 2004. *N Engl J Med*; 350(14):1422-1429
6. Petty W, Spanier S, Shuster JJ, et al. The influence of skeletal implants on incidence of infection: experiments in a canine model. *J Bone Joint Surg Am*. 1985;67:1236-1244.
7. Schmidt AH, Swiontkowski MF: Pathophysiology of infections after internal fixation of fractures. *Am Acad Orthop Surg*. 2000 Sep-Oct;8(5):285-91. Review.
8. Merritt K, Dowd JD. Role of internal fixation in infection of open fractures: studies with *Staphylococcus aureus* and *Proteus mirabilis*. *J Orthop Res*. 1987;5(1):23-8.
9. Phillips AM. Overview of the fracture healing cascade. *Injury*. 2005 Nov;36 Suppl 3:S5-7.
10. Patzakis MJ, Zalavras CG. Chronic posttraumatic osteomyelitis and infected nonunion of the tibia: current management concepts. *J Am Acad Orthop Surg*. 2005 Oct;13(6):417-27. Review.
11. Trebse R, Pisot V, Trampuz A. Treatment of infected retained implants. *J Bone Joint Surg Br*; 2005. 87(2):249-256.

12. Zimmerli W, Widmer AF, Blatter M et al. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. Foreign-Body Infection (FBI) Study Group. *JAMA*. 1998 May 20;279(19):1537-41.
13. Rightmire E, Zurakowski D, Vrahas M. Acute infections after fracture repair: management with hardware in place. *Clin Orthop Relat Res*. 2008 Feb;466(2):466-72. Epub 2008 Jan 10.
14. Castillo RC, Bosse MJ, MacKenzie EJ, Patterson BM. Impact of smoking on fracture healing and risk of complications in limb-threatening open tibia fractures. *J Orthop Trauma*. 2005 Mar;19(3):151-7.
15. Gaston MS, Simpson AH. Inhibition of fracture healing. *J Bone Joint Surg Br*. 2007 Dec;89(12):1553-60. Review.
16. Gustilo RB, Anderson JT. 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 Am*. 1976 Jun;58(4):453-8.
17. Olsen et al. Risk factors for surgical site infection following orthopaedic spinal operations. *J Bone Joint Surg Am*. 2008 Jan;90(1):62-9.
18. Green E, Lubahn JD, Evans J. Risk factors, treatment, and outcomes associated with nonunion of the midshaft humerus fracture. *J Surg Orthop Adv*. 2005 Summer;14(2):64-72.
19. Lynch JR, Taitsman LA, Barei DP, Nork SE. Femoral nonunion: risk factors and treatment options. *J Am Acad Orthop Surg*. 2008 Feb;16(2):88-97.
20. Infections associated with orthopedic implants. Trampuz A, Widmer AF. *Current Opinion in Infectious Diseases*. 19(4):349-56, 2006 Aug.
21. Zimmerli W, Trampuz A, Ochsner PE. Prosthetic-joint infections. *N Engl J Med* 2004; 351:1645–1654.
22. Zimmerli W, Widmer AF, Blatter M, et al. Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. Foreign-Body Infection (FBI) Study Group. *JAMA* 1998; 279:1537–1541.
23. Ure KJ, Amstutz HC, Nasser S, et al. Direct-exchange arthroplasty for the treatment of infection after total hip replacement: an average ten-year followup. *J Bone Joint Surg Am* 1998; 80:961–968.
24. Hope PG, Kristinsson KG, Norman P, et al. Deep infection of cemented total hip arthroplasties caused by coagulase-negative staphylococci. *J Bone Joint Surg Br* 1989; 71:851–855.
25. Raut VV, Siney PD, Wroblewski BM. One-stage revision of infected total hip replacements with discharging sinuses. *J Bone Joint Surg Br* 1994; 76:721–
26. Callaghan JJ, Katz RP, Johnston RC. One-stage revision surgery of the infected hip: a minimum 10-year followup study. *Clin Orthop* 1999; 369:139–143.
27. Langlais F. Can we improve the results of revision arthroplasty for infected total hip replacement? *J Bone Joint Surg Br* 2003; 85:637–640.
28. Westrich GH, Salvati EA, Brause B. Postoperative infection. In: Bono JV, McCarty JC, Thornhill TS, et al. , editors. *Revision total hip arthroplasty*. 1st ed. New York: Springer; 1999. pp. 371–390.
29. Windsor RE, Insall JN, Urs WK, et al. Two-stage reimplantation for the salvage of total knee arthroplasty complicated by infection: further followup and refinement of indications. *J Bone Joint Surg Am* 1990; 72:272–298

30. Zimmerli W. Widmer AF. Blatter M. Frei R. Ochsner PE.
 Role of rifampin for treatment of orthopedic implant-related staphylococcal infections: a randomized controlled trial. Foreign-Body Infection (FBI) Study Group.JAMA. 279(19):1537-41, 1998 May 20.
31. Diagnosis and treatment of infections associated with fracture-fixation devices.
 Trampuz A. Zimmerli W. Injury. 37 Suppl 2:S59-66, 2006 May

Treatment of Post-fracture Osteomyelitis

Jeff Anglen, MD

- I. Definition
- II. Diagnosis
 - a. Clinical
 - i. Typical signs of infection: drainage, erythema, recurrent swelling
 - ii. More subtle signs: skin changes
 - iii. Pain
 - iv. Stable (healed bone) vs. Unstable (Nonunion)
 - b. Imaging
 - i. Initial Radiographs
 - ii. Nuclear
 - 1. Technetium Polyphosphate
 - 2. Indium labeled leukocytes
 - iii. MRI
 - iv. Fluorodeoxyglucose positron scanning (FDG-PET)

Modality	Sensitivity	Specificity
PET	96% (88-99)	91% (81-95)
Bone Scan	82% (70-89)	25% (16-36)
Leukocyte Scan	61% (43-76)*	77% (63-87)
Combined scan	78% (72-83)	84% (75-90)
MRI	84% (69-92)	60% (38-78)

* LS – periph	84% (72-91)	80% (61-91)
Radiography	60% (28-86)	67% (36-89)
Gallium	80% (44-96)	42% (17-71)
CT	67% (24-94)	50% (3-97)

- c. Laboratory
 - i. C-reactive protein – best indicator for treatment monitoring
 - ii. ESR, WBC
- III. Treatment Plan
 - a. Goals
 - Define success: healed wound, functional limb
 - b. Staging
 - Eliminate infection first, restore live covered wound, reconstruction of function
 - c. Expectations
 - i. 44/46 patients healed at 5 years, with 38/42 returning to work after Rx for tibial osteomyelitic (Siegel et al.)
 - ii. Success rate varies with Host condition
 - Ciorny: 1,966 pts overall success rate 84%
 - A-host: 96% B-host: 73%
- IV. Surgical
 - a. Drain the pus
 - b. Debride
 - i. Remove foreign material completely
 - ii. Resect bone and soft tissues to live margins
 - iii. Dead space management – spacers and Masquelet membranes
 - c. Cover
 - i. Within a week
 - 1. Bead pouch
 - 2. VAC
 - ii. DPC
 - iii. Local flaps
 - iv. Distant flaps
 - d. Manage Defects
 - i. Grafts
 - ii. Ilizarov: transport or shortening/lengthening
 - e. Chop
- V. Antibiotics
 - a. Systemic
 - i. Choice of drug
 - 1. based on culture results from good samples

2. Some initial regimens:

Organism	First Choice	Alternatives
Staphylococcus aureus (meth sens)	Oxacillin or Clindamycin	1 st gen cephalosporin or vancomycin
MRSA	Vancomycin plus rifampin	Linezolid, Bactrim, Minocycline plus rifampin
Streptococci (Pcn sensitive)	Penicillin G	Clindamycin, Erythromycin, vancomycin or ceftriaxone
Strept pneumoniae (Pcn intermediate)	Ceftriaxone	Erythromycin, Clindamycin or Levofloxacin
S pneumoniae (PCN resistant)	Vancomycin	Levofloxacin
Enterococcus sp.	Ampicillin or Vanc	Amp-sulbactam, Linezolid
Enteric Gram neg rods	Fluoroquinolone	3 rd gen cephalosporin
Serratia or Pseudomonas aeruginosa	Levofloxacinin, cefepime plus fluoroquinolone	Ertapenem
Anaerobes	Clindamycin	Amoxicillin-clavulanate, or Metronidazole
Mixed aerobes and anaerobes	Amoxacillin-clavulanate	Etrtapenem

Table from OKU Traum 3

ii. Duration/route of treatment

1. IV at least 2 weeks.
2. total duration controversial 2-6 weeks?
3. longer for suppression
4. agents with good bioavailability by oral route:
Fluoroquinolones, Metronidazole, Linezolid, rifampin, Trimethoprim-Sulfamethoxazole
5. Fluoroquinolones vs. Beta-Lactams: 7 studies suggest no difference (Karamanis et al, 2008)

b. Local

- i. Antibiotic bead and rods
- ii. Absorbable drug delivery systems

c. Do you need an ID consultant?

- i. Is she part of a dedicated osteomyelitis team?
- ii. Does she have a particular interest in Orthopaedic infection?

VI. Supportive Therapies

- a. Tobacco cessation

- b. Nutritional Support
- c. Supplements and Immune boosters
- d. Hyperbaric Oxygen
- e. Electromagnetic

VII. References:

Anglen JO, Watson JT. Chapter 2: Musculoskeletal infection associated with skeletal trauma. In: Surgical Treatment of Orthopaedic Trauma, edited by James P. Stannard, Andrew H. Schmidt, and Philip J. Kregor, Theime, New York, 2007

Calhoun JH, Manring MM: Adult Osteomyelitis. Infect Dis Clin North Am 2005;19:765-786

Ciorny G, DiPasquale D. Treatment of Chronic Infection, J Am Acad Orthop Surg, Vol 14, No 10, September 2006, S105-S110.

Davis JC, Heckman JD, DeLee JC, Buckwold FJ: Chronic non-hematogenous osteomyelitic treated with adjuvant Hyperbaric Oxygen. JBJS Am 1986;68:1210-1217

Karamanis EM, Matthaiou DK, Moraitis LI, and Falagas ME. Flouroquinolones versus B-Lactam based regimens for the treatment of osteomyelitic. A meta-analysis of randomized controlled trials. Spine 33(10): E297-304, 2008

Kent ME, Rapp RP, Smith KM. Antibiotic Beads and Osteomyelitis: Here today, What's coming tomorrow? Orthopedics 29(7): 599-603

McKee MD. Wild LM. Schemitsch EH. Waddell JP. The use of an antibiotic-impregnated, osteoconductive, bioabsorbable bone substitute in the treatment of infected long bone defects: early results of a prospective trial. Journal of Orthopaedic Trauma. 16(9):622-7, 2002

Motsitsi NS. Management of infected nonunion of long bones: The last decade (1996-2006). Injury 39:155-160, 2008

Osmon DR. Berbari EF. Outpatient intravenous antimicrobial therapy for the practicing orthopaedic surgeon. Clinical Orthopaedics & Related Research. (403):80-6, 2002 Oct.

Patzakis MJ, Zalavras CG. Chronic Post-traumatic osteomyelitic and infected nonunion of the tibia: Curren management concepts. JAAOS 13:417-427, 2005

Rao N. Ziran BH. Hall RA. Santa ER. Successful treatment of chronic bone and joint infections with oral linezolid. Clinical Orthopaedics & Related Research. (427):67-71, 2004

Siegel HJ, Patzakis MJ, Holtom PD, Sherman R, ShepherdL: Limb salvage for chronic tibial osteomyelitic: An outcomes study. J. Trauma 2000;48:484-489

Termaat M.F., Raijmakers P.G.H.M., Scholten H.J., Bakker F.C., Patka P., and. Haarman H.J.T.M The Accuracy of Diagnostic Imaging for the Assessment of Chronic Osteomyelitis: A Systematic Review and Meta-Analysis J. Bone Joint Surg. Am., Nov 2005; 87: 2464 - 2471.

Wang J. Li F. Calhoun JH. Mader JT. The role and effectiveness of adjunctive hyperbaric oxygen therapy in the management of musculoskeletal disorders. Journal of Postgraduate Medicine. 48(3):226-31, 2002

Zalavras CG, Marcus RE, Levin LS and Patzakis MJ. Chapter 6: Management of open fractures and subsequent complications. In: Instructional Course Lectures 57, edited by Paul Duwelius and Frederick Azar, AAOS, Rosemont, IL 2009

Zalavras CG, Patzakis MJ, Holtom P. Local antibiotic therapy in the treatment of open fractures and osteomyelitic. Clin Orthop 427:86-93, 2004

Ziran BH and Rao N. Chapter 14: Infections. In: Orthopaedic Knowledge Update Trauma 3, edited by Michael Baumgaertner and Paul Tornetta III, AAOS and OTA, Rosemont IL 2005

Ziran BH. Rao N. Hall RA. A dedicated team approach enhances outcomes of osteomyelitis treatment. Clinical Orthopaedics & Related Research. (414):31-6, 2003 Sep.