CLINICAL ORTHOPAEDICS AND RELATED RESEARCH
Number 360, pp 97–105

Infected Tibial Nonunions (1981–1995)

The Evolution of Change

George Cierny, III, MD

Between 1981 and 1995, 150 consecutive cases of middiaphyseal, infected nonunions of the tibia were treated prospectively on the author's osteomyelitis service. Thirty-nine (78%) of the 49 patients seen between 1981 and 1986 and 94 (93%) of the 101 patients seen 1986 through 1994 underwent successful salvage protocols with a minimum followup of 5 years. The difference in outcomes seen in the two groups eloquently reflects the emergence of specific pharmaceutic, technical, and biologic advances earmarking these two, distinct eras of care.

During the last 2 decades, the treatment of musculoskeletal sepsis, and in particular, osteomyelitis, has changed radically. There is a new understanding of the disease itself, [12,18,30,32,44,45,55,56,67] protocols have evolved articulating its natural history and therapy, [14,15,41,42,51,53] and the resources needed to bring treatment back into the community are understood. [29,50] Before 1978, the principles of orthopaedic care [9,23,38,57,58,66] emphasized sequential debridements, healing by secondary intention, bypass bone grafting, [11,31,33] prolonged antibiotic therapy,[63] and long term orthotic support. Patient selection for treatment, however, was highly restricted. Composite saucerizations of hard and soft tissue were without equally complex reconstruction options for coverage, wound access, and bony reconstitution. Complete excisions were limited to small foci for the proximal limb or both where the ratio of soft tissue to bone favors closure. When the debridement was inside the zone of injury, residual fibrosis and ischemia crippled the host's defenses against an inherent, bacterial persistence. Thus, in situ reconstructions often were limited to open sky grafts (Papineau)[54] because surgeons could not otherwise enhance the wound bed to support the metabolic demands of salvage surgery.

The milestones of change began with the introduction of rigid external fixation frames,[3,37,62] new techniques in tissue transference,[47,52,59] and local antibiotic depots.[8,17,40,64] By 1986, the reconstruction potential of thoroughly debrided wounds reached new heights. Orthopaedists began to use internal hardware,[4,21,27] total joint prostheses,[69] allografts[5,65] and the methods of Ilizarov[34,35] in protocols to salvage previously infected limbs. To show the impact of these advances on treatment and patient selection, the author reports a sequential series of 150 infected tibial nonunions evaluated during two, distinct eras of change.

From Resurgens Orthopaedics, Atlanta, GA, Department of Orthopaedics, Emory University School of Medicine, Atlanta, GA.

Reprints requests to George Cierny III, MD, Resurgens Orthopaedics, 5671 Peachtree Sunwoody Road NE, Suite 900, Atlanta, GA 30342.

THE ERA OF WOUND REVITALIZATION (1981–1986)

In the 1970s, a focus on external fixation enhanced the care of traumatic and debrided wounds by curtailing wound trauma, facilitating wound care, and embracing fracture union. At the same time, surgeons around the world were striving to modify the compromised wound bed with tissue transpositions and microvascular transfers. [26,28,60,61] Within a decade, muscle, skin, bone, organs such as omentum, [48] and entire motor units [24] were used. The concept of wound revitalization [13,15,18,20] became the foundation on which an entire rational for limb salvage developed. With the introduction of antibiotic impregnated methylmethacrylate beads, [17,40,64] the morbidity of treatment declined: Immediate closures were performed after excision, obviating the need for sequential debridements and an open wound interval [7]; the high antibiotic levels within the bead bed sterilized the dead space, thereby sparing marginal tissues and decreasing the incidence of opportunistic infections. [14,16,17,53] Wounds were reconstructed in weeks rather than months, heralding an early, functional rehabilitation. These new methods of stabilization, tissue transference, and antibiotic delivery eliminated the fear of performing a complete excision and established a responsive wound bed to set the stage for an in situ reconstruction (Fig 1).

MATERIALS AND METHODS

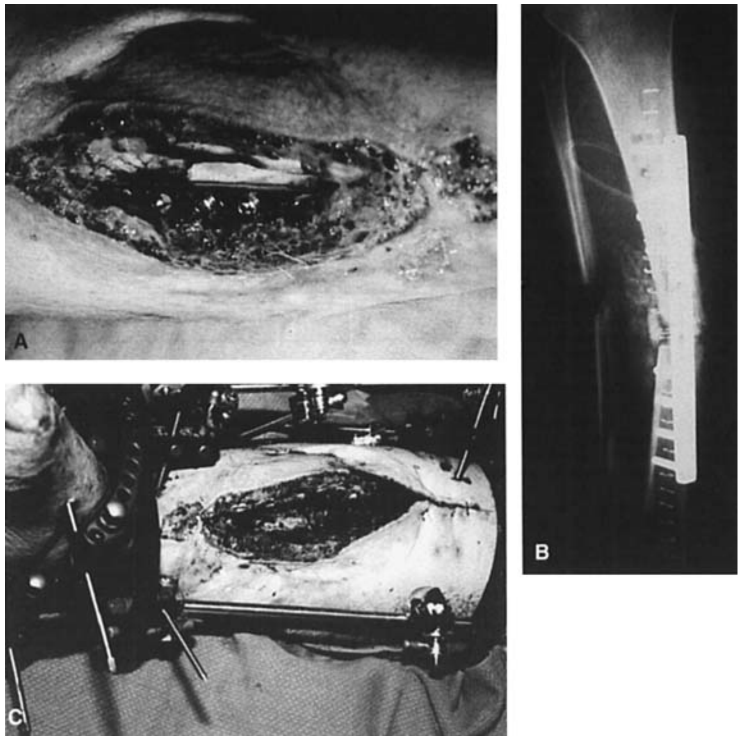
Between 1981 and 1995, 865 cases of tibial osteomyelitis sequentially entered the author's prospective treatment protocols (Galveston, TX: 1981–1985; Atlanta, GA: 1985–1994). Of the 335 infected nonunions in this series, 150 anatomically were confined to the middiaphysis and suitable for comparative review. Limb salvage was attempted in 135 patients (89%). Preoperative cultures, from deep wound margins, [18,55,56] guided antibiotic coverage. All isolates were considered pathogens and received coverage for 6 weeks; adjustments were based on intraoperative cultures and sensitivities using quantitative testing and tube dilutional techniques. The ideal coverage was an oral antibiotic, or antibiotic combination, with a mean inhibitory concentration equal to its mean bactericidal concentration and six times its expected serum concentration. Parenteral coverage was used for the first 4 days and thereafter if oral agents were unavailable or contraindicated. Patients with staged reconstructions received a course of perioperative antibiotics (4 days) at any subsequent procedure from the index debridement; a new isolate, at that time, instigated a new treatment protocol. When the debridement cultures were negative, histologic sections of the cultured specimens confirmed the presence of infection; coverage was changed from the routine of parental Vancomycin (Lilly, Indianapolis, IN) and Cephtazidime (Glaxo Wellcome, Research Triangle Park, NC) to oral Ciprofloxicin (Bayer, West Haven, CT) and Rifampin (Hoechst Marion Roussel, Kansas City, MO) for the duration of the protocol.

All necrotic and ischemic tissues were excised. An immediate wound closure was performed over antibiotic beads. Delayed coverage took place no later than Day 7. The dead space was obliterated completely with cancellous grafts, [46] beads, a flap, or combinations thereof. In staged procedures, beads were exchanged for grafts, free osseous transfers, hardware, or composite reconstructions. Success was defined as a functional, drainage free limb with fracture union.

PATIENTS (1981–1986)

Between 1981 and 1986, 49 patients with infected, diaphyseal nonunions of the tibia were evaluated. Nine (19%) were offered primary ablation because of a poor prognosis in six, morbidity of treatment in two, and prosthetic advantage in one. Of the 40 limb salvage attempts (Table 1), three (8%) were initial treatment failures. The success rate at 2 years was 95% (Fig 1). Antibiotic beads were used in 60%, tissue transfers in 44%, and cancellous grafts in 86% of the reconstructions.

Although external fixation was the preferred method of stabilization (75%), eight nonunions underwent internal fixation with the bead exchange (Fig 2). Sterile fields were documented at the time of these recon-



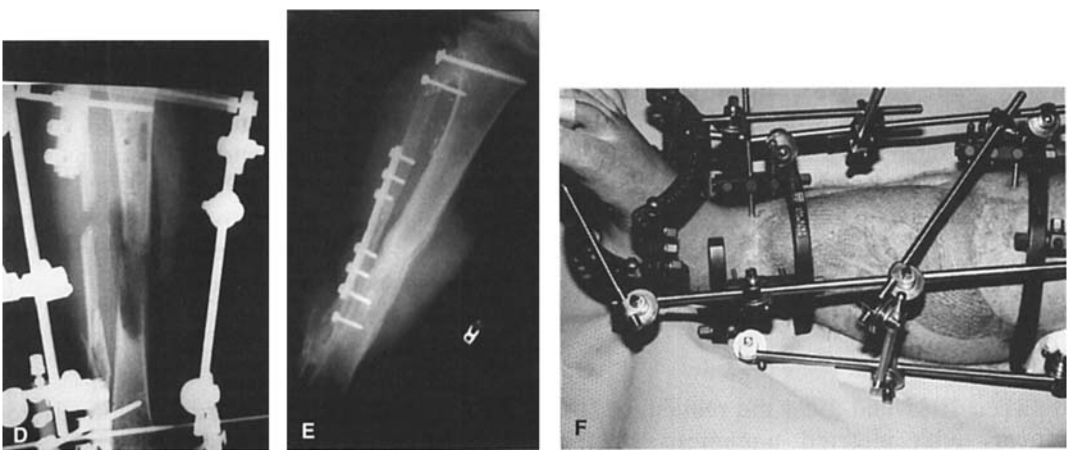


Fig 1A–F. (A) Infected nonunion with unstable fixation, (B) soft tissue loss and sequestered cortex, allograft and hardware. (C,D) The debridement was tangential and exspansile, requiring 30 weeks of multiplanar, external fixation to achieve union. (E,F) The revitalization and reconstruction involved a 50 cc cancellous bone graft with free latissimus dorsi coverage (Day 5) followed by transposition of the ipsilateral fibula (Campanacci) at 6 weeks.

structions.[2,14,36,39,53] No infections occurred in this smaller group.

The ability to consistently sterilize debrided wounds had a great impact on the process of patient selection.[68] Indications for limb salvage broadened further with the introduction of distraction methodologies (Ilizarov[34,35]) to the West. During bone transport, osseous segments and their adjacent soft tissues are moved into an adjoining, debridement defect. Thus, pedicled flaps of nearby bone, muscle, skin, and fat are created and moved within the affected limb itself. Because the vitality of transported tissue persists once docked into its new position, there are no differences in success

TABLE 1. Adult Osteomyelitis Tibial Nonunions (1981–1986)

40 Salvage Attempts

Method	*Percentage*	*Initial Success (%)*
External fixation	75	93
Hardware	20	88
Cast	5	100

Treatment Failures

Method	*Sepsis*	*Nonunion*	*Outcome (Number)*
External fixation[30]	1	1	Amputation (1) Nonunion (1)
Hardware[8]	0	1	Union
Cast[2]	0	0	
Overall success = 95%			

when comparing open and closed methods. Revitalization is not necessary when the debridement extends outside the zone of injury. Closed methods still are used when an otherwise exposed structure is at risk for secondary infection (tendons, vessels, hardware, reamed canals). Bead sterilization, distraction techniques, and internal fixation strategies changed the indications for primary amputation and earmarked the current era of treatment.

THE ERA OF OPEN RECONSTRUCTION (1986–1994)

Patients

Between 1987 and 1994 the remaining 101 patients with infected nonunions of the midtibia received treatment. There were six primary amputations for poor prognosis in four and/or functional advantage in two. Internal fixation, distraction methodologies, and conventional external frames were used, but not interchangeably (Table 2). All infectious sequelae involved new pathogens, were irradicated with one intervention, and did not affect outcome as the initial success rate (91%) rose to 99% at 2-year followup. Thirty-eight percent of these cases used a free flap, 32% a cancellous bone graft, and in 82%, antibiotic beads were implanted before the final reconstruction. The need for tissue transfers diminished as the author's experience with Ilizarov methodologies increased (Fig 3). Marrow composites and bone graft substitutes replaced the standard use of cancellous bone grafts. Antibiotic beads, originally intended for removal, often were left in place, thereby curtailing the need for secondary dead space management.

DISCUSSION

The microbiologic spectrum (Table 3) remained relatively constant throughout this series. There was a decrease in Gram negative rods and an increase in fungal and negative cultures in the last 50 cases; an apparent increase in methicillin resistant Staphylococcus aureus was not statistically significant.

In both eras, the ratio of normal to compromised hosts [18] remained constant at 40% to 60%. The era of open reconstruction brought about a decrease in the primary amputation rate (19% versus 6%) without a

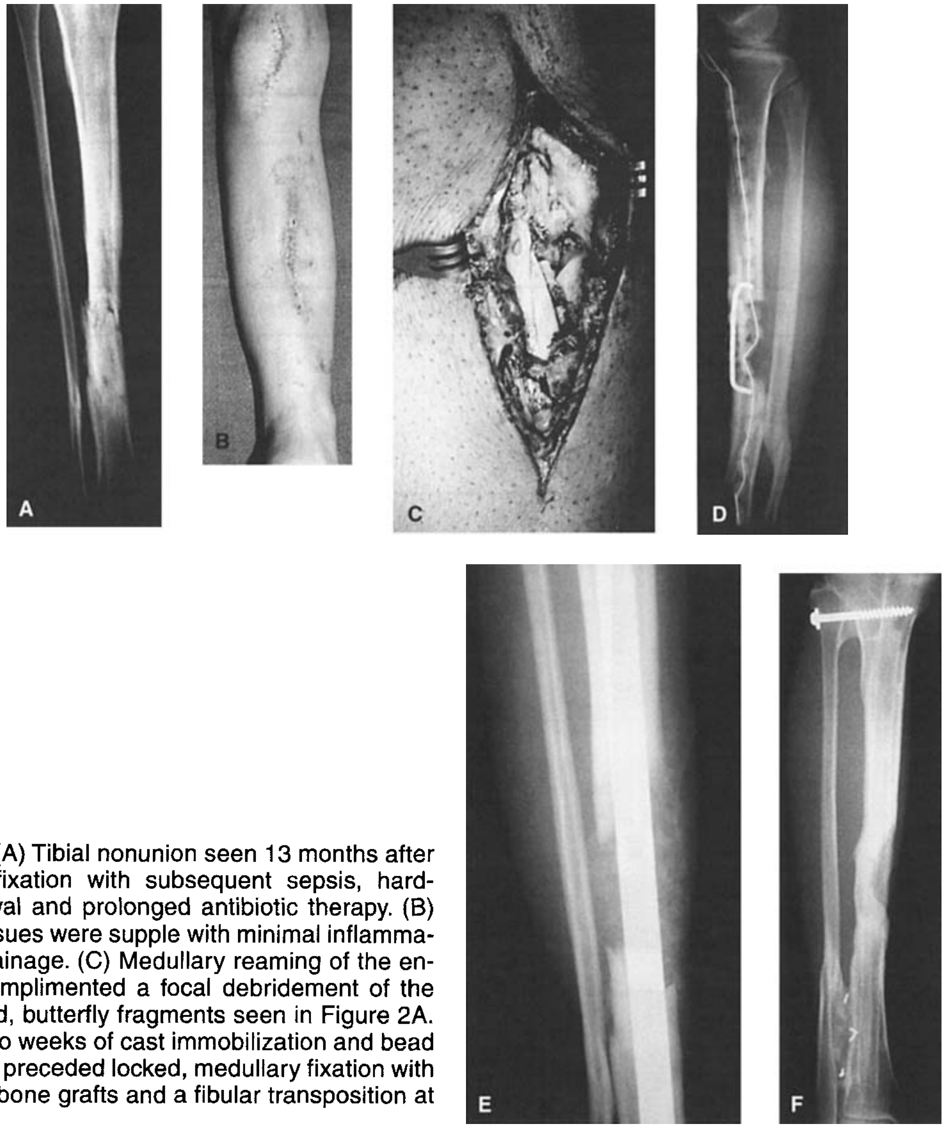


Fig 2A–F. (A) Tibial nonunion seen 13 months after medullary fixation with subsequent sepsis, hardware removal and prolonged antibiotic therapy. (B) The soft tissues were supple with minimal inflammation and drainage. (C) Medullary reaming of the entire tibia complimented a focal debridement of the sequestered, butterfly fragments seen in Figure 2A. (D, E, F) Two weeks of cast immobilization and bead sterilization preceded locked, medullary fixation with cancellous bone grafts and a fibular transposition at 6 weeks.

compromise in outcome or success. The hypothesis that previously infected wounds could be reconstructed as clean [1] wounds has proven true at the author's institutions. In 1994 the authors' reconstruction of 32 segmental, long bone defects saw a 42% incidence of internal fixation and used nine vascularized fibular transfers, nine bone transports, nine allografts, and five prosthetic joints; the success rates were 100%, 89%, 89%, and 100% respectively.

The factors affecting prognosis and treatment include residual foreign materials and/or ischemic and necrotic tissues, host compro-

TABLE 2. Adult Osteomyelitis Tibial Nonunions (1986–1994)

95 Salvage Attempts

Method	*Percentage*	*Initial Success (%)*
External fixation	24	91
Hardware	42	92
Ilizarov	34	87

Treatment Failures

Method (Number)	*Sepsis*	*Nonunion*	*Outcome (Number)*
External fixation (23)	0	2	Union (2)
Hardware (40)	3 (7.5%)	0	Arrest (3)
Ilizarov (32)	1	3 (9%)	Amputation (1)
			Union (3)
Overall success = 99%			

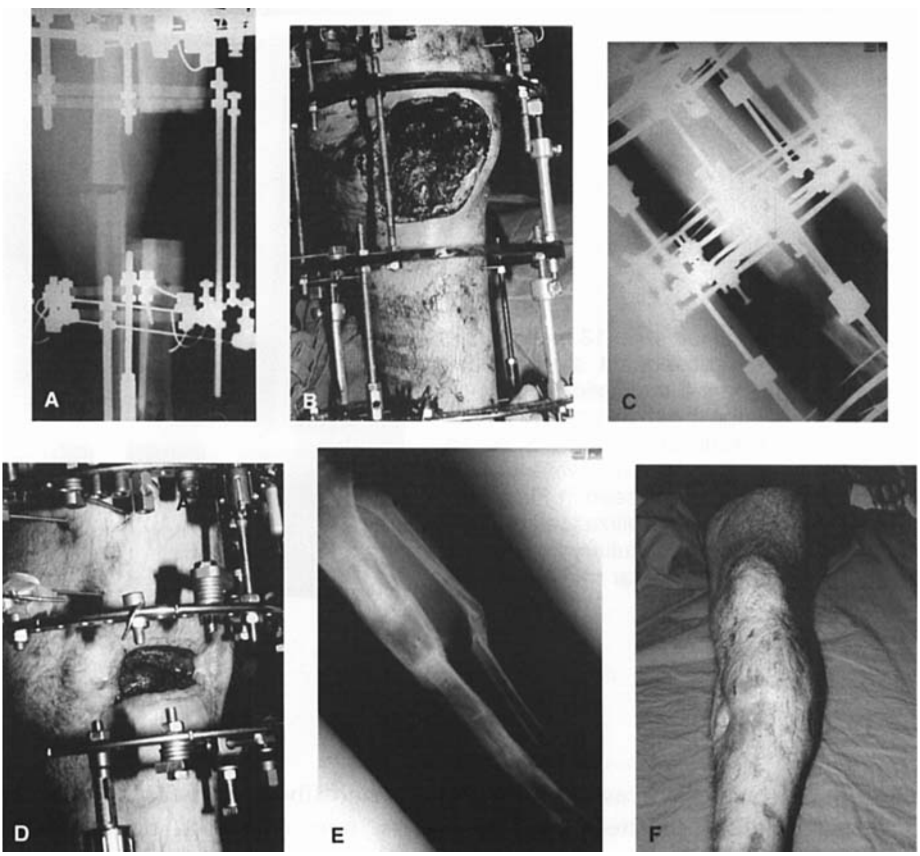
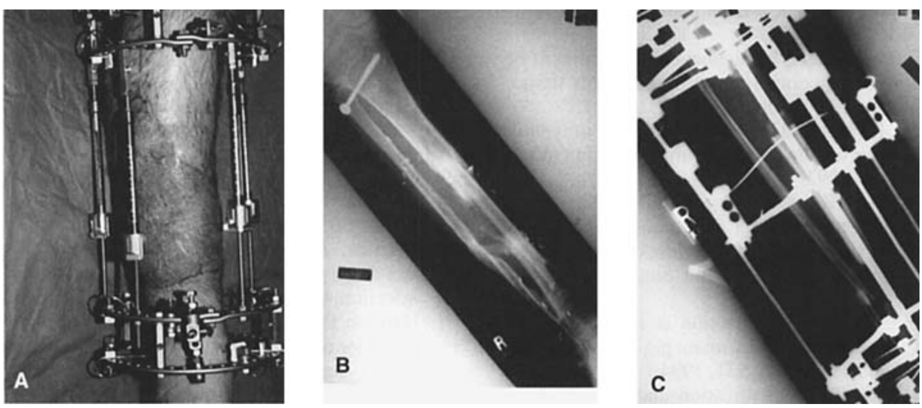


Fig 3A–F. (A,D) A 12–cm hard and soft tissue deficit stabilized with the Ilizarov device after complete excision and a realignment osteotomy of the fibula. Revitalization was not necessary. (C, B) Reconstruction consisted of an open, bifocal transport. Wound approximation coincided with the osseus docking. (E,F) Consolidation of the regenerates, union, complete soft tissue healing and full functional return were documented at 12 months.

mise, [18,32] inappropriate antibiotic coverage, and the lack of patient cooperation or desire. With a complete wound revitalization, the type and/or number of pathogens, the method of stabilization, and early reconstruction have not been detrimental in the author's series. [19] With this knowledge and the confidence inspired by using antibiotic depots, patients now enter a refined selection process wherein they are matched with procedures coinciding with individual preferences and demands, physician experience, host capabilities, and personal levels of comfort. [6,25,43] When vascularized tissue transfers are not available in a community setting, treatment outcomes using open transport methods have proven interchangeable. [22] The combination of the Ilizarov and conventional techniques has streamlined strategies to maximize performance and function (Fig 4).

TABLE 3. Microbiology (150 Consecutive Cases)

Organism	1981	1986	1994
Staphylococci	40	35	38
Gram negative rods	36	35	12
Anaerobes	12	35	15
Enterococcus	11	6	6
Fungus	0	0	4
No growth	2	1	9
Methicillin resistant Staphylococcus aureus	0	6	8



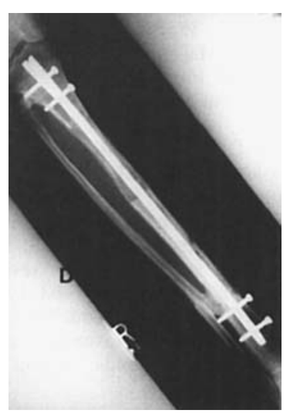


Fig 4A–D. (A) Ilizarov frames used in conjunction with a complex revitalization, (B) free muscle coverage and vascularized fibular transfer and (C,D) closed, unifocal bone transport over a nonreamed nail.

References

1. Ad Hoc Committee of the Committee on Trauma, Division of Medical Sciences, National Academy of Sciences—National Research Council: Post operative wound infections: The influence of ultraviolet irradiation of the operating room and various other factors. Ann Surg 160 (Suppl):1, 1964.
2. Adams K, Couch L, Cierny III G, Calhoun J, Mader JT: In vitro and in vivo evaluation of antibiotic diffusion from antibiotic-impregnated polymethylmethacrylate beads. Clin Orthop 278: 244–252, 1992.
3. Anderson R: An automatic method of treatment for fractures of the tibia and fibula. Surg Gynecol Obstet 58:639–648, 1934.
4. Ballantyne G, Mader JT, Cierny III G: Infected malunion of the femur. Orthop Consult 7: 4–8, 1986.
5. Berry DJ, Chandler HP, Reilly DT: The use of bone allografts in two-stage reconstruction after failure of hip replacements due to infection. J Bone Joint Surg 73A: 1460–1468, 1991.
6. Bowen CVA, Botsford DJ, Hudak PL, Evans PJ: Microsurgical treatment of septic nonunion of the tibia. Clin Orthop 332: 52–61, 1996.
7. Brown P: The prevention of infection on open wounds. Clin Orthop 96:254, 1973.
8. Buchholz HW, Gartmann HD: Infektions prophylaxe und operative behandlung der schleichenden tiden infektion bei der totalen endoprothese. Chirugia 43: 446–453, 1972.
9. Burri C, Passler HH, Henkemeyer H: Treatment of posttraumatic osteomyelitis with bone, soft tissue, and skin defects. J Trauma 13:799–810, 1973.
10. Calhoun JH, Mader JT: Treatment of osteomyelitis with a biodegradable antibiotic implant. Clin Orthop 341:206–214, 1997.
11. Campanacci M, Zaanoli S: Double tibiofibular synostosis (fibula pro tibia) for non-union and delayed union of the tibia: End result review of one hundred seventy-one cases. J Bone Joint Surg 48A: 44–56, 1966.
12. Chang CC, Merritt K: Infection at the site of implanted materials with and without pre-adhered bacteria. J Orthop Res 12: 526–531, 1994.
13. Cierny III G: The Classification and Treatment of Adult Osteomyelitis. In Evarts CM (ed). Surgery of the Musculoskeletal System. New York, Churchill Livingstone 15–35, 1983.
14. Cierny III G: Managing the Debridement Defect. In Coombs RRH, Fitzgerald RH (eds). Infection in the Orthopaedic Patient. London, Butterworth Publishers 45–52, 1987.
15. Cierny III G: The Classification and Treatment of Adult Osteomyelitis. In Evarts CM (ed). Surgery of the Musculoskeletal System. Ed 2. New York, Churchill Livingstone 4337–4380, 1989.
16. Cierny III G, Byrd HS, Jones RE: Primary versus delayed soft tissue coverage for severe open tibial fractures. Clin Orthop 178: 54–63, 1983.
17. Cierny III G, Mader JT, Couch L: Adjunctive local antibiotics in the management of contaminated orthopaedic wounds. Orthop Trans 10:465, 1983.
18. Cierny G, Mader JT, Pennincx JJ: A clinical staging for adult osteomyelitis. Cont Orthop 10:17–37, 1985.
19. Cierny III G, Matava M, Zorn KE: Cancellous bone grafting in the presence of bacterial contamination: Indications, methods, long-term Results. Orthop Trans 14:633, 1990.
20. Cierny III G, Nahai F: Dialogue: Lower extremity reconstruction: Part II. Persp Plast Surg 2:109–121, 1988.
21. Cierny III G, Tetsworth K, Zorn KE: Arthodesis for sepsis at the knee: external vs. medullary fixation. Orthop Trans 18:1128, 1994–1995.
22. Cierny III G, Zorn KE: Segmental tibial defects: Comparing conventional and Ilizarov methodologies. Clin Orthop 301:118–123, 1994.
23. Clawson DK, Dunn AW: Management of common bacterial infections of bones and joints. J Bone Joint Surg 49A:164–182, 1967.
24. Cobbett JR: Free digital transfer: Report of a case of transfer of a great toe to replace an amputated thumb. J Bone Joint Surg 51B: 677–679, 1969.
25. Duwelius PJ, Swiontkowski MF, Schmidt AH: Laser doppler flowmetry in the assessment of osteomyelitis. Compl Orthop: Summer 44, 1994.
26. Fitzgerald Jr. RH, Irons GB, Ruttle PE, et al: Local muscle flaps in the treatment of chronic osteomyelitis. J Bone Joint Surg 67A:175–185, 1985.
27. Friedrich B, Klaue P: Mechanical stability and posttraumatic osteitis: An experimental evaluation of the relation between infection of bone and internal fixation. Injury 9:23–29, 1982.
28. Ger R: Muscle transposition for treatment and prevention of chronic posttraumatic osteomyelitis of the tibia. J Bone Joint Surg 59A: 784–791, 1977.
29. Greene WB (ed): Musculoskeletal Sepsis. AAOS Instructional Course Lectures. Vol 39. St Louis, CV Mosby 495–508, 1990.
30. Gristina, AG, Costerton JW: Bacterial adherence and the glycocalyx and their role in musculoskeletal infection. Orthop Clin North Am 15:517–535, 1984.
31. Harmon PH: A simplified surgical approach to the posterior tibia for bone grafting and fibular transference. J Bone Joint Surg 27A: 496–501, 1945.
32. Heppenstall RB, Goodwin CW, Brighton CT: Fracture healing in the presence of chronic hypoxia. J Bone Joint Surg 58A:1153–1156, 1997.
33. Huntington TW: Case of bone transference. Ann Surg 41:249–252, 1905.
34. Ilizarov GA: The tension-stress effect of the genesis and growth of tissues: Part 1. The influence of stability of fixation and soft tissue preservation. Clin Orthop 238: 249–281, 1989.
35. Ilizarov GA: The tension-stress effect on the genesis and growth of tissues: Part II. The influence of the rate and frequency of distraction. Clin Orthop 239: 236–285, 1989.
36. Jabob EJ, Cierny III G, Fallon MT, McNeill JF, Siderys GS; Evaluation of biodegradable Cefazolin sodium microspheres for the prevention of infection in rabbits with experimental open tibial fractures stabilized with internal fixation. J Orthop Res 11:404–411, 1993

37. Karlstrom G, Olerud S: Percutaneous pin fixation of open tibial fractures. J Bone Joint Surg 57A: 915–924, 1975.
38. Kelly PJ, Wilkowske CJ, Washington II JA: Chronic osteomyelitis in the adult. Curr Pract Orthop Surg 6:120–127, 1975.
39. Kendall RW, Duncan CP, Beauchamp CP: Bacterial growth on antibiotic-loaded acrylic cement. J Arthroplasty 10:817–820, 1995.
40. Klemm K: Die Behandlung Chronischer Knowcken Infektionen Mit Gentamicin PMMA Ketten und Kulgen. In Contzen HE (ed). Gentamicin-PMMA-Kette. Symposium Muchen. Germany, Verlag fur Lehrmittel, Munich, Wissenschaft und Forschung 20–22, 1976.
41. Klemm K, Henry SL, Seligson D: The treatment of infection after interlocking nailing. Tech Orthop 3:54–60, 1988.
42. Levin SL, Maynor ML, Moon RE, et al: Chronic osteomyelitis of the tibia: Treatment with hyperbaric oxygen and autogenous microsurgical muscle transplantation. J South Orthop Assoc 7:43–48, 1998.
43. Lortat-Jacob A, Guiziou B, Ramadier JO: Fractures infectees de jambe. Revue de Chirurgie Orthop 71: 515–526, 1985.
44. Mathes SJ, Alpert BS, Chang N: Use of the muscle flap in chronic osteomyelitis: Experimental and clinical correlation. Plast Reconstr Surg 69: 815–829, 1982
45. Matthew SJ, Feng LJ, Hunt TK: Coverage of the infected wound. Ann Surg 198: 420–429, 1983.
46. Matti H; Uber freie transplantation von knochenspongiosa. Arch Klin Chir 168: 236–245, 1932.
47. McCraw JB, Dibbell DG, Carraway JH: Clinical definition of independent myocutaneous vascular territories. Plast Reconstr Surg 53: 526–535, 1976.
48. McLean DH, Buncke HJ: Autotransplant of omentum to a large scalp defect, with microsurgical revascularization. Plast Reconstr Surg 49:268–270, 1972.
49. Moussa FW, Anglen JO, Gehrke JC, Christenssen G, Simpson WA: The significance of cultures from orthopaedic fixation devices in the absence of clinical infection. Am J Orthop 617–620, 1997.
50. Musculoskeletal Sepsis Society: Eighth Annual Scientific Meeting. St Louis, CO. Denver, (CME) Education Design 1998.
51. Nahai F: Soft tissue reconstruction of the lower extremity. Persp Plast Surg 1: 76–88, 1987.
52. O'Brien BM, Henderson PN, Bennett RC, Crock GW: Microvascular surgical techniques. Med J Aust 1:722–728, 1970.
53. Ostermann PAW, Seligson D, Henry SL: Local antibiotic therapy for severe open fractures: A review of 1085 consecutive cases. Joint Bone J Surg 77B: 93–97, 1995.
54. Papineau LJ: Osteocutaneous resection-reconstruction in diaphyseal osteomyelitis. Clin Orthop 101: 306, 1974.
55. Patzakis MJ, Wilkins J, Kumar J, et al: Comparison of the results of bacterial cultures from multiple sites in chronic osteomyelitis of long bones. J Bone Joint Surg 76A:664–666, 1994.
56. Perry CR, Pearson RL, Miller GA: Accuracy of cultures of material from swabbing of the superficial aspect of the wound and needle biopsy in preoperative assessment of osteomyelitis: J Bone Joint Surg 73A:745–749, 1991.
57. Shannon JG, Woolhouse FM, Eisinger PJ: The treatment of chronic osteomyelitis by saucerization and immediate skin grafting. Clin Orthop 96: 98–107, 1973.
58. Taylor AR, Maudsley RH: Instillation-suction technique in chronic osteomyelitis. J Bone Joint Surg 52B:88–91, 1970.
59. Taylor GI, Miller GDH, Ham FJ; The free vascularized bone graft: A clinical extension of microvascular techniques. Plast Reconstr Surg 55:533–539, 1973.
60. Tonnesen PA, Heerfordt J, Pers M: 150 open fractures of the tibial shaft—The relation between necrosis of the skin and delayed union. Acta Orthop Scand 46: 823–835, 1975.
61. Vasconez LO, Bostwick J, McCraw J: Coverage of exposed bone by muscle transposition and skin grafting. Plast Reconstr Surg 53:526–531, 1974.
62. Vidal J, Rabischong P, Bonnel F, Adrey J: Etude biomechanique de fixateur externe d'Hoffmann dans les fractures de jambe. Montpellier Chir 43–52, 1970.
63. Wadvogel FA, Vasey H: Osteomyelitis: The last decade. N Engl J Med 303:360–366, 1980.
64. Walenkkamp GH: Gentamicin PMMA Beads—A Clinical, Pharmacokinetic and Toxicologic Study. Darmstadt, Germany-Drukkeri, Cliteur, Amsterdam. E Merck 1983.
65. Wang JW, Chen CE: Reimplantation of infected hip arthroplasties using bone allografts. Clin Orthop 335:202–210, 1997.
66. West FW, Kelly PJ, Martin WJ: Chronic osteomyelitis: Factors affecting the results of treatment in 186 patients. JAMA. 213: 11–16, 1970.
67. Whiteside LA, Lesker PA: The effects of extraperiosteal and subperiosteal dissection. J Bone Joint Surg 60A:23–30, 1978.
68. Wiess DA, Stetson WB: Tibial nonunion: Treatment options. J Am Acad Orthop Surg 4:249–257, 1996.
69. Younger ASE, Duncan CP, Masri BA: Treatment of infection associated with segmental bone loss in the proximal part of the femur in two stages with use of an antibiotic loaded interval prosthesis. J Bone Joint Surg 80A:60–69, 1998.