The Assessment and Treatment of Nonunions

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Objectives

- Definition
- Classification
- Etiologies (systemic, mechanical, biologic)
- History and physical exam, radiographic criteria
- Nonoperative management
- Operative management
- Bone grafting options
- Distraction Histiogenesis
Fracture healing sequence

1. Impact
2. Hematoma
3. Inflammation
4. Soft Callus
5. Hard Callus
6. Remodelling
Fracture Healing

4 distinct processes:
1. Bone marrow
2. Cortex
3. Periosteum
4. External soft tissues

May or may not occur simultaneously
Prerequisites for sequence completion

• Adequate vascularity
  – Inflammatory cells, IL-1, IL-6, platelets, TGFβ, PDGF
  – Angiogenesis, mitogenesis, cell migration, proliferation and synthesis

• Appropriate mechanical stability/strains
  – Influence cell differentiation and bone induction process
Role of mechanical load in skeletal tissue regeneration
Role of mechanical load in skeletal tissue regeneration
Fracture Union

Process of *structural reconstitution* of the broken bone by means of bone regeneration
Union as an endpoint

- Regained structural strength
- Predicted confidently when bending stiffness reaches 7 N-m per degree
- Reached when stiffness reaches 15 N-m per degree

Marsh, CORR 1998
Delayed Union

Failure of a fracture to unite or show progressive healing in the average or usual time for similar fractures (Different for different bones) (4-6 months)
Nonunion

Arrest of the bony fracture repair process and the formation instead of fibrous or cartilagenous interposition tissue

(6-8 months)
Nonunion

No change or progression of radiographic healing over a 3 month period.
Synovial pseudoarthrosis

Nonunion that develops a neoarthrosis with a synovial lining and joint fluid
Etiology of Nonunion

- Systemic status of host
- Nature of traumatic injury
- Orthopaedic fracture care
- Pharmacologic factors
Systemic status of patient

- Age
- Malnutrition: protein and mineral deficiencies
- Anemia: changes in oxygen tension
- IDDM: nutritional, neuropathic, vascular
- Hormone deficiencies: GH, estrogen
Nature of the traumatic injury

- Location of the fracture (nutrient vessel)
- High energy fracture: extensive soft-tissue envelope destruction, vascular injury
- Bone loss
- Infection: intense inflammatory reaction
- Nerve disruption
Orthopaedic fracture care

- Iatrogenic vascular compromise
- Fracture gap (>2 mm)
- Motion at the fracture site
- Cement
- Allograft infection
- Radiation
- Necrotic bone left in wound
Pharmacologic factors

• Corticosteroids
  – Inhibit differentiation of mesenchymal cells into osteoblasts

• Anticoagulants
  – Inhibit clot formation at fracture site
  – Diminish number of cells at fracture site and their normal metabolic response
Pharmacologic factors

- **NSAIDS**
  - Delay ossification by diminishing region blood flow or hindering primitive osteoblasts

- **Antibiotics**
  - Fluoroquinolones cause decreased collagen production and cell membrane disruption

- **Chemotherapeutic Cytotoxics**
  - Doxorubicin and methotrexate delay cartilage matrix production.
Pharmacologic factors

• Smoking
  – Inhibits cellular proliferation during wound healings
  – Promotes vasoconstriction
History and physical exam

- History may be long and complicated
- How did fracture occur: high or low velocity?
- Open or closed?
- Infection or antibiotic allergies?
- Operations
- Complications
History

- Drainage?
- Implants removed? Why and when?
- Skin grafts or muscle transfers?
- Other organ injuries?
- Other fractures? Did they heal?
- Residual disabilities?
Physical exam

- Motion at the nonunion site (gross or patient perception)
- Pain and tenderness
- Status of the skin
- Previous scars or active sinuses
Physical exam

- Vascularity of limb and skin flaps
- Limp: LLD, pain, contracture, weakness
- Malrotation
- Operative goals feasible
- Other sources of pain in the limb
Laboratory tests

- WBC
- ESR
- CRP
- Consider aspiration and culture of nonunion site
Radiographs

- Likely to be numerous
- Radiograph the normal limb for comparison
Classification: Time or degree

1. Delayed union
2. Nonunion
   A. Mobile (gap)
   B. Nonmobile
3. Synovial pseudoarthrosis
Classification:
Site and displacement

1. Diaphyseal
   A. Nondisplaced
   B. Displaced

2. Metaphyseal
   A. Intra-articular
   B. Extra-articular
Weber and Cech’s classification

Strontium radioisotope studies:
1. Nonunions with vital bone ends (i.e. vascularity)
2. Nonunions with poor or no blood supply
Classification: Callus

1. Hypertrophic (vascular-reactive)

2. Atrophic (hypovascular-nonreactive)
Vital nonunions

- ‘Elephant’s foot’ (hypertrophic)
- ‘Horse’s foot’ (less hypertrophic)
- Oligotrophic: no callus but bone ends are vital and vascular
Avascular nonion

No callus

1. Dystrophic
2. Necrotic (comminuted fragments)
3. Defect (gap)
4. Atrophic
Classification:
Infection

1. Noninfected
2. Infected
   A. Nondraining (3 months)
   B. Draining
Nonoperative management: Rationale

• Asymptomatic
• Elderly, osteoporotic
• Sarmiento: functional bracing
• Electrical stimulation: very specific indications
History of electrical stimulation

- 1841 John Birch, surgeon general at St. Thomas Hospital in London
- Electricity for the treatment of a tibial nonunion
- “…shocks of electric fluid passed daily through the space between the ends of the bone for six weeks.”
Indications

- Good position and alignment
- No large gap (> one width of bone at that level)
- No synovial pseudoarthrosis
Physiology

- Increased bone cell proliferation
- Matrix calcification stimulated
- Chemical reaction:
  \[2H_2O + O_2 + 4e^- \rightarrow 4 OH^-\]

Low oxygen tension and high pH favor environment for bone formation
Invasive

- titanium cathode implanted into bony defect
- Generator implanted in soft tissue
Noninvasive

- Electrodes are placed percutaneously or on skin surface
- Limb is immobilized
Results

Brighton 1991:
- 2400 nonunions worldwide
- 74-79% union rate with capacitive or inductive coupling

Sharrard, JBJS 1990:
- Double-blind trial PEMF for delayed union of tibia fractures
- Statistically significant increased healing rate.
Ultrasound

- Low intensity pulsed ultrasound transmitted transcutaneously
- Localized to fracture gap
- Direct deformation of cells
- Acoustic streaming of fluids
Cellular response

- Change in K+ and Ca++ influx into cells
- Affects second messenger systems
- Modulate activity of TGF-β
- Upregulate gene expression of aggrecan
- BMPs, IGF, thrombin
- Increased vascularity
Clinical efficacy: Double-blind prospective studies

Heckman, JBJS 1994:

- 67 closed or Grade I open tibia fx
- All managed nonoperatively
- Ultrasound 20 minutes/day significantly decreased time to union
- 98 days vs 154 days (P=0.0001)
Clinical efficacy: Double-blind prospective studies

Kristiansen et al, JBJS 1997:

- 61 dorsally angulated fractures of the distal radius
- Significantly decreased time to union and loss of reduction (61 vs 98 days).
However…

- Keep in mind stringent indications
- ?Clinical importance of FASTER healing
- No evidence for increased union RATE
Operative management: Rationale

Reverse the causative factors

- **Excess motion** → stable internal or external fixation
- **Gap** → obliterate or diminish space by compression or bone grafting
- **Poor blood supply** → cancellous bone grafting, drilling or petalling of cortices
Preop planning: radiographs

- Nonunion and contralateral side
- Lower extremity: full-length
- CT scan for rotational deformities and joint incongruities
- All available previous radiographs
Tracing and Templates
Trace fragments

Rearrange anatomically and in normal alignment
Determine size and type of implant needed
Other preoperative considerations

- Arthrography or arthoscopy
- Arteriogram
- Gallium and Indium-labeled WBC scan
- Plastic surgery consultation
- Physical therapy consultation
- Infectious disease
Hypertrophic vital nonunions

- Compression and stability
- Bone graft is not necessary
- Shingling to increase surface area
- Correct angular malalignment
Atrophic nonunions

- Stable internal fixation
- Bone graft, shingling and decortication
- Reactivate “bone healing switch”
- Osteoporotic bone:
  - Avoid too much shingling or reaming
  - Screw fixation augmented with PMMA
Metaphyseal/Articular nonunions

• Liberal arthrotomy
• Realign fragments, release adhesions
• Stabilize with interfrag screws
• Attach reconstructed joint to diaphysis with plates under compression
• Adequate fixation to allow early motion
Synovial pseudoarthrosis

- Diagnose by cold cleft on bone scan
- Excise pseudoarthrosis tissue
- Open medullary canals
- Stabilization and bone grafting similar to atrophic nonunions
Infected nondraining nonunions

- At least 3 months nondraining (hardware okay)
- Treated like noninfected nonunions
- Remove all potentially infected fibrous or granulation tissue
- Intraoperative triple Abx irrigation
- Post-op antibiotics
Infected draining nonunions

- If hardware is stable, leave it in
- If hardware is loose, take it out
- I+D of infected tissue, Abx cement
- 1-3 weeks: by-pass with structural graft and/or external fixation
- Malalignment and shortening must be corrected
Bone grafting techniques

- Distraction osteogenesis (bone transport)
- Cancellous bone grafting
- Free fibular grafting
Distraction histogenesis

- Tension at the fracture gap stimulates intramembranous bone formation
Bone transport

Regeneration of intercalary bone defects with combined distraction and transformation osteogenesis
Distraction osteogenesis

Transformation osteogenesis
Histology

- Initial distraction: fibrous bundles
- Vascular sinuses develop
- Osteoblasts appear and osteoid is made
Histology

- ‘Primary mineralization front’ advances from each end across gap
- Ends with mature lamellar bone and marrow
Bone grafting

- **Osteogenesis**
  - Osteoblasts make new bone
- **Osteoconduction**
  - Scaffold for bone formation
- **Osteoinduction**
  - Induce differentiation of mesenchymal cells into bone-forming cells
Cancellous autograft incorporation

1. Hemorrhage and inflammation
2. Vascular invasion
3. New bone formed on dead trabeculae
4. Remodelling

Process is completed between 6 months and one year.
Cancellous autograft: advantages

- Osteogenic
- Oseoconductive
- Osteoinductive
- Rapidly produces and stimulates new bone formation
Cancellous autograft: disadvantages

- Donor site morbidity
- Lack of structural support
Vascularized cortical autograft

- More than 90% of osteocytes survive transplant
- Graft host union occurs quickly
Vascularized Cortical Autograft

- Graft is not resorbed
- Hypertrophy and remodel in response to mechanical stresses similar to normal bone
Advantages

• Immediate structural support
• Vascularity independent of host bed
• May be used in large intercalary defects
Disadvantages

• Donor site morbidity
• Technical expertise required
Newer perspectives

- Bone graft substitutes: must have all 3 properties (osteogenesis, osteoconduction, osteoinduction).
- Include demineralized bone matrix, stem cells and BMP
- Topic for another lecture
Nonunion results

- Application of concepts of stable fixation and regeneration of blood supply
- Over 90% will heal with one procedure

Chapman, Operative Orthopaedics, 1993
Summary

- Bone healing is a complex process
- Mechanical **stability** and adequate vascularity required
- Host factors as well as injury pattern and management contribute to risk for nonunion
- Delayed union: failure to completely heal in 4-6 months (depends on bone)
- Nonunion: 6-8 months or no change in 3
Summary

• Classification system based on vascularity
• Nonoperative management for well-aligned fractures without a large gap or synovial pseuoarthrosis.
• Operative rationale: reverse causative factors
• Bone grafting techniques include cancellous autograft, vascularized cortical graft and distraction osteogenesis.
During the healing of a fracture, which of the following tissue types can accommodate the greatest interfragmentary strain?

1. Granulation tissue
2. Fibrocartilage
3. Cartilage
4. Calcified cartilage
5. Woven bone
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1. Granulation tissue
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A 35-year-old man who sustained a grade II open fracture of the right tibia 9 months ago underwent reamed intramedullary nailing. The patient continues to have pain with weight bearing. Laboratory studies show a normal WBC and ESR, and there has been no change in the radiographs in the past 3 months. Current radiographs are shown.
What is the most likely diagnosis?
1. Delayed union
2. Aseptic nonunion
3. Infected nonunion
4. Synovial pseudoarthrosis
5. Failure of the internal fixation device
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OITE 2001

Which of the following is considered the most important factor in fracture healing in adults?

1. Age of the patient
2. Gender of the patient
3. Neurologic status of the extremity
4. Blood supply
5. Fracture pattern
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