

## Biologic Therapies for Nonunions

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Substances that *stimulate osteoinductivity* at a site of bone healing:

- Demineralized bone matrix
- Recombinant BMP
- Parathyroid hormone
- Bone marrow aspirate concentrate

### **DBM**

- Prepared from cadaveric human bone
- Acid extraction of bone leaving
  - Collagen, Noncollagenous proteins, Bone growth factors
- BMP quantity extremely low and variable
- Sterilization may further decrease the availability of BMP

### **DBM vs BMP**

- How does this amount in DBM compare to pure rhBMP-2 or rhBMP-7?
  - BMP-2 (Infuse): 12 mg
  - BMP-7 (OP-1): 3.5 mg
- *A million times less, Weakly osteogenic*
  - Bone graft expander, defect filler

### **rhBMP**

- Recombinant human bone morphogenetic protein
- Isolated by Marshall Urist in 1965
- TGF- $\beta$  superfamily

### **BMP-2 in open tibial fx**

- BESST: Prospective, randomized study, 450 patients
- 44% reduction in risk of nonunion/delayed union with high dose BMP-2
- Significantly faster fracture healing
- Significantly fewer invasive interventions, hardware failures, infections

### **BMP controversy**

- 2011 Allegations:
  - Underreported complications
  - 85% off-label use; mainly in spine
  - Retrograde ejaculation, excessive HO formation, cancer concerns
- Highly conflicted investigators

### **Parathyroid hormone**

- Recombinant PTH (1-34); Teriparatide (Forteo)
  - Anabolic osteogenic agent, SubQ daily injection, approved for osteoporosis

### **PTH - data**

- Much small animal data: Very effective
- Clinical data
  - 65 geriatric pelvic fx
  - 102 distal rad fx
  - Both reduced healing time
- Drawbacks: cost

### **Bone Marrow Aspirate**

- Animal studies
  - Numerous; Increased torsional rigidity; faster healing; Results consistent and conclusive
- Clinical data
  - Perc injection of 60 tibial NU: **88% healed**
  - 11 distal tibial NU (no infection, deformity, instability), no concentrate: **82% healed**
  - 51 pts with NU, >2 mm defect (26 BMAC, 25 ICBG): 75% BMAC healed, 78% ICBG healed, BMAC faster

### **Summary**

- First and foremost, identify what nonunion needs
- Many drawbacks to autograft
- Numerous options available “off the shelf”
- Familiarize with mechanisms, efficacy, handling characteristics, and COSTS of each