

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- β 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