

HOSPITAL FOR SPECIAL SURGERY

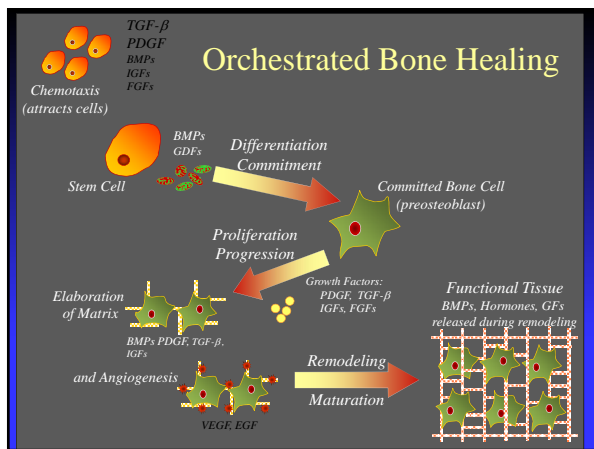
What is Needed for Optimal Fusion ?

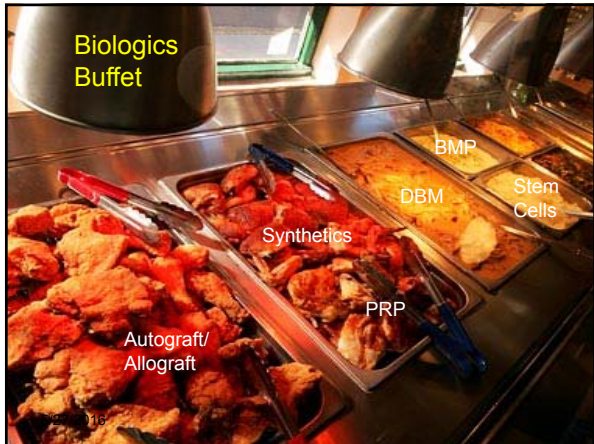
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Bone Healing: A Symphony of Events

A conductor in a tuxedo stands on a green hill, conducting a symphony of bone healing factors represented by colorful text floating in the air. The factors include: Cytokines, Hormones, VEGF, PDGF, FGF, IGF, IGF1/II, Extracellular Matrix Proteins, BMPs 2,4,6,7, and TGFbeta.





What is the ideal graft?

A composite of the right components

Cells	+	Matrix	+	Signals
Host or Cultured		Structure or Void Filler		DBM or Growth Factor

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January 10, 2002 – Infuse Panel



- “The Holy Grail”
- Would revolutionize spine surgery
- Solve the previously unsolvable

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YODA Studies

REVIEWAnnals of Internal Medicine

Effectiveness and Harms of Recombinant Human Bone Morphogenetic Protein-2 in Spine Fusion

A Systematic Review and Meta-analysis

Rongwei Fu, PhD; Shelley Selph, MD; Martan McDonagh, PharmD; Kimberly Peterson, MS; Arpita Tiwari, MHS; Roger Chou, MD; and Mark Helfand, MD, MS

Data Synthesis: Thirteen RCTs and 31 cohort studies were included. For lumbar spine fusion, rhBMP-2 and iliac crest bone graft were similar in overall success, fusion, and other effectiveness measures and in risk for any adverse event, although rates were high across interventions (77% to 93% at 24 months from surgery). For anterior lumbar interbody fusion, rhBMP-2 was associated with nonsignificantly increased risk for retrograde ejaculation and urogenital problems. For anterior cervical spine fusion, rhBMP-2 was associated with increased risk for wound complications and dysphagia. At 24 months, the cancer risk was increased with rhBMP-2 (risk ratio, 3.45 [95% CI, 1.98 to 6.00]), but event rates were low and cancer was heterogeneous. Early journal publications misrepresented the effectiveness and harms through selective reporting, duplicate publication, and underreporting.

Conclusion
reduces pain postsurgically

rates, reduces early cancer incidence

What alternatives do we have?

Allograft-based

- Cancellous
- Cortical
- DBM



Synthetic

- Calcium
- Collagen
- Hydroxyapatite
- PEEK

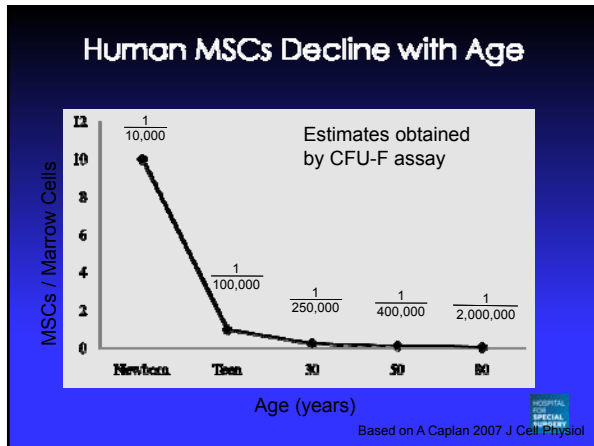
- Stem cells
- Growth factors
- BMP

5/27/2016

Graft Option: Osteogenic Agents

- **PRP Systems**
 - Spin whole venous blood for "buffy coat" which contains platelets, etc.
 - Idea is to get enough PDGF to help bone formation
 - Studies in Europe show exact opposite suspecting high levels of TGF-β

- **Bone Marrow Aspirate**
 - contains real bone forming cells
 - proven to form bone
 - physiologically relevant amounts of all factors
 - the true "cocktail" of factors



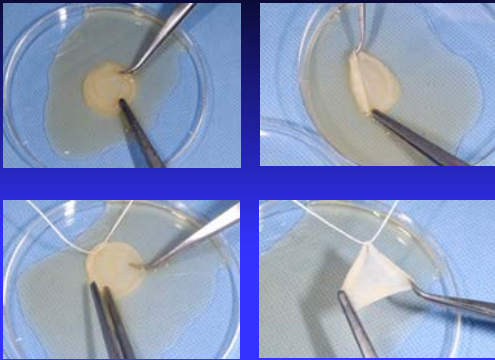
Important PRP papers

- Carreon *et al.* clinical retrospective comparing ICBG vs. ICBG + PRP in posterolateral lumbar fusion
 - 76 patients received 1-level (74%), 2-level (20%) or 3-level (6%) ICBG + PRP
 - 76 age control match ICBG
 - @ 2 years, 25% non-union ICBG + PRP vs. 17% non-union ICBG (not stat sig)
- Weiner *et al.* clinical retrospective comparing ICBG vs. ICBG + PRP in posterolateral lumbar fusion
 - 91% fusion with ICBG vs. 62% fusion with ICBG + PRP

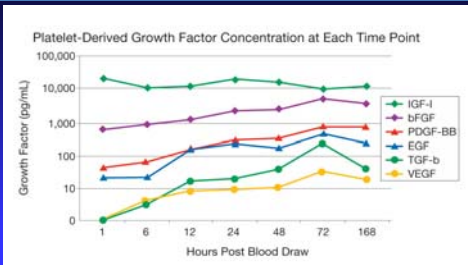
Why are PRP systems not working???

- Platelet gels may dissolve relatively rapidly through fibrinolysis
- The growth factors in platelet gels may be too low to have any osteogenic effect
- Possible presence of growth factors that inhibit bone formation
- Platelets might not survive centrifuge techniques
- Huge difference between systems

Platelet Rich Fibrin Membrane



PRFM: Provides Sustained Release of Growth Factors



Sustained growth factor release over time (7+ Days) to replicate the normal healing process

³Carroll RJ, Arnoczky SP, O'Connell SM 2007

Stem Cell Therapies



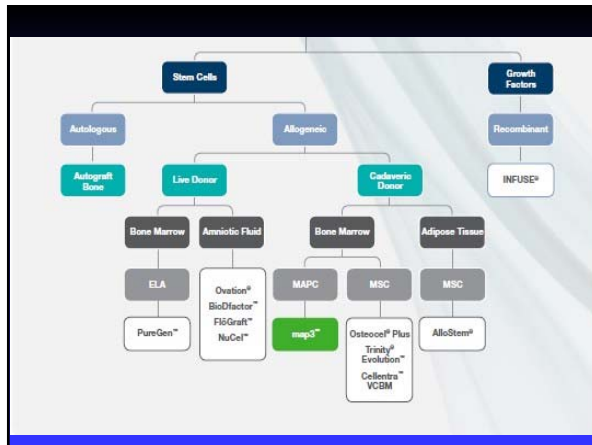
Homologous Use

- 21 CFR 1271.3(c):

"Homologous use means the repair, reconstruction, replacement, or supplementation of a recipient's cells or tissues with an HCT/P (Human Cellular or Tissue Product) that performs the same basic function or functions in the recipient as in the donor."

Essentially, the HCT/P must be used in a manner similar to its natural endogenous function or it is termed a Biological Drug.





Amniotic Fluid Derived Stem cells

- Amniotic derived fluid contains various growth factors and amniotic stem cells
- Collected from live donors

Concerns:

- Number of cells is unknown
 - hAFSC (Amniotic Fluid Stem Cells)
 - Which tissue did they come from?
- Cell viability testing- Unknown
- Same controversy as embryonic stem cells
 - Not allowed in all health systems
- Not Homologous Use**



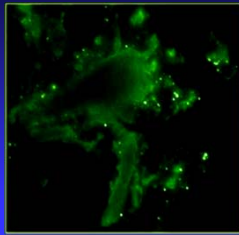
What is a Stem Cell Allograft?

- Cryopreserved allograft bone matrix that contains viable bone-forming cells and demineralized bone matrix
- HCT/P
- Autograft substitute with reliable number of living cells and osteoinductive potential
- **Possesses necessary healing components**
 - **Osteogenic:** contains MSCs and OPCs
 - **Osteoinductive:** DBM component & MSCs
 - **Osteoconductive:** cancellous bone component



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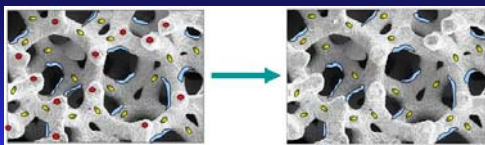
Cells Are Alive After Cryopreservation & Thawing of Stem Cell Allograft



Viable cells confirmed after processing using live/dead staining

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Stem Cell Allografts Do Not Elicit an Immune Response



Cancellous bone prior to processing

HSCs depleted and osteogenic cells remaining after processing

Cells are immunoprivileged
Cells do not stimulate immune response: they **lack MHC/HLA class II antigens** (Major Histocompatibility complex: MHC/Human Leukocyte antigen: HLA)
MSCs also secrete cytokines that modulate immune reactions

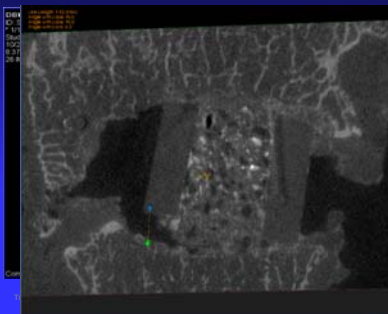
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What is Needed to Optimize Fusion ???

- Support or enhance repair according to the functional needs of the site
- Biocompatible
- Replaced by host bone
- Tailored to the procedure



...just because you use it in the gutters doesn't make it a good choice for your interbody



Spacer w/ DBM
Minimal Endplate
Contact)

Spacer w/ Sponge
Intimate Endplate
Contact)



Thank You