What is Needed for Optimal Fusion?

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Bone Healing: A Symphony of Events

Chemotaxis (attracts cells)

Cytokines
Hormones
VEGF
PDGF
FGF
GDFs

BMPs
TGF-β
PDGF
IGFs
FGFs

Stem Cell

BMPs
GDFs

Differentiation
Commitment

Proliferation
Progression

Growth Factors:
PDGF, TGF-β, IGFs

Elaboration of Matrix and Angiogenesis

BMPs, PDGF, TGF-β

Remodeling
Maturation

Functional Tissue
BMPs, Hormones, GFs released during remodeling

Orchestrated Bone Healing
What is the ideal graft?

A composite of the right components

<table>
<thead>
<tr>
<th>Cells</th>
<th>Matrix</th>
<th>Signals</th>
</tr>
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<tbody>
<tr>
<td>Host or</td>
<td>Structure or</td>
<td>DBM or</td>
</tr>
<tr>
<td>Cultured</td>
<td>Void Filler</td>
<td>Growth Factor</td>
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January 10, 2002 – Infuse Panel

- "The Holy Grail"
- Would revolutionize spine surgery
- Solve the previously unsolvable
Bone Morphogenetic Protein

New Study Links Spine Product From Medtronic to Risk of Stability in Men

Bloomberg Studies Failed to Reveal Infuse Risks to Patients

BMP – Cervical Spine

Edema Osteolysis Seroma
What alternatives do we have?

- **Allograft-based**
  - Cancellous
  - Cortical
  - DBM

- **Synthetic**
  - Calcium
  - Collagen
  - Hydroxyapatite
  - PEEK

- **Stem cells**
- **Growth factors**
- **BMP**

**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
Imported 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 ICBGs 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

Carroll RJ, Arnoczky SP, O’Connell 2007

Stem Cell Therapies

Questions?
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.

Embryonic/Amniotic
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**

- Cells are immunoprivileged
- Cells do not stimulate immune response: they lack MHC/HLA class II antigens
- MSCs also secrete cytokines that modulate immune reactions

Cancellous bone prior to processing

MSCs depleted and osteogenic cells remaining after processing
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