Biologics for fracture Healing and PRP application

To improve and expedite repair, various biologic agents, bone grafts, or physical stimulation techniques are used for fracture healing

- Osteoinduction - recruitment and differentiation of pluripotent mesenchymal stem cell into bone forming osteoprogenitor cells
- Osteoconduction - creation of **bone scaffold/matrix** that supports the ingrowth of blood vessels as well as attachment of osteoprogenitor cells
- Osteogenesis- process of bone formation after the differentiation of osteogenic cells into mature osteoblasts

These processes promotes the signals for the phases of fracture healing

- **Autologous Bone Graft**
    - Gold standard to enhance bone healing because it utilizes osteoinductive factors, osteoconductive matrix**,** and osteogenic stem cells

a. Cancellous bone graft

- Effective for fxs that do not require immediate structural support from the graft
- **Provides osteoconductive and osteoinductive functions ; but lacks immediate structural stability and strength**
- Graft is replaced by new bone by process of **Creeping Substitution (see below)** and gains full strength within a year
- Iliac crest, greater troch,distal femur, proximal tibia, calcaneus, olecranon, distal radius, proximal humerus are all possible sites.
- Used for areas of bone loss; Depressed tibial plateau fxs, Nonunions, or revision hip and knee arthroplasty

b. Cortical bone graft

- **Provides good structural support, but much weaker osteoconductive and osteoinductive properties**
- Helpful when immediate structural support is needed but has limited long term healing potential (Thought to be due to the thickness of the matrix limiting diffusion of nutrients, and osteogenesis)
- Usually harvested from ribs, fibula, or crest of the ilium ; Can be transplanted w/wo vascular pedicle
- The blood supply leads to increased biologic activity and regeneration potential
- For defects up to 6cm, nonvascularized cortical graft can be used; Greater than 12cm are good candidates for vascularized grafts.
- Also helpful when environment of host is inadequate; (soft tissue damage, atrophic nonunion, irradiated tissue)

Graft Incorporation (Creeping Substitution)

a. Hematoma formation - release of cytokines and growth factors
b. Inflammation- development of fibrovascular tissue
c. Vascular ingrowth
d. Focal osteoclastic resorption of graft
e. Intramembranous and/or endochondral bone formation on graft surfaces

- **Complications**

Donor site pain, infections, hematomas, neurovasc injuries, iliac wing fxs

Allogenic Bone

- Allograft became popular due to the associated morbidity associated with harvesting autograft
- Harvested from multiple sites including pelvis, ribs, and fibula
- **Preparation of the bone can reduce its osteoinductive potential and its mechanical integrity (Fresh, Fresh Frozen, Freeze dried, irridiated, etc)**
- Incorporates slower than allograft due to lack of progenitor cells; Incorporates better to a well vascularized host bed site

Demineralized Bone Matrix

- Produced by acid extraction of allograft bone; Harvested for cadaveric bone
- Abundance of growth factors gives it more **osteoinductive potential than allografts but little structural support**
- Not regulates so amount of Growth factors can vary
- Helpful when used in conjunction w/ autologous cancellous bone

Bone Graft Substitutes (May Skip this section for sake of time)

Calcium Phosphate

a. Hydroxyapatite
    - **Slowly resorbing compound**
    - Resembles Cancellous bone (pore size)
    - Bone void filler
    - Best in area of low tensile force due to good compressive strength

Calcium Phosphate Cement

- Bone void fillers in treatment of bony defects associated w/ acute fxs
- Maximum compressive strength after 4hrs; **very high compressive strength**
- Designed to be used with internal fixation **due to low torsional and shear strength**
- Often used in depressed tibial plateau fxs

- PRP
    - autologous blood w/ concentrations of platelets above normal.
    - Causes a healing response via growth factors and recruitment of reparative cells
    - Uses include…
- Prep
    - centrifuge to separate RBC
    - Plasma divided into platelet poor and rich portions
    - Surgically: treated w/ Calcium chloride or thrombin b4 application. (activation used before injection which stimulates growth factor release

- Uses
    - Thought to stimulate processes associated with tendon and muscular healing.
    - Laboratory studies have shown increased IGF-1, VEGF, HGF, MMP, and other growth factors when used.
    - Has been used in epicondylitis, patellar tendonitis, achilles tendon tears, and rotator cuff injuries to name few disorders with positive results from PRP treatment
        - There are several PRP prep systems, effectiveness can not be generalized and there are mixed reports in the literature.
        - It is not often reimbursed by third party payers because of this.
        - Costly- can be up to $300 per syringe

Nailed It Ortho podcast episode

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References:

AAOS OKU Review