Objectives
- Discuss orthobiologics: popular treatment options available
- Musculoskeletal Ultrasound
  - Diagnostic and therapeutic uses in sports medicine

Orthobiologic options
- Platelet Rich Plasma (PRP)
- Bone Marrow derived stem cells
- Adipose derived stem cells
- Placental derived growth factors and stem cells

Regenerative Medicine
- Engineering of tissue in vitro for subsequent implantation in vivo
  - OR
- Regeneration of tissue directly in vivo.

Aging population + increasingly active lifestyle
- Problem: One of the main issues with tissue healing is that the tissue heals via reactive scar formation instead of truly regenerating new tissue
- Goal: improve the biological environment around the defect to create the best possible healing situations and improve healing response
- Action: biologic manipulation of the healing milieu will play a critical role in the improvement of the healing rate

A Glance at the Regenerative Space in Orthopaedics
What is PRP?

- Type of injection therapy used for various chronic sports injuries to promote healing.
- PRP = abbreviation for Platelet-Rich Plasma.
- Over 6,000 PRP journal articles have been published between 2013–15 (between 2012–13 was about 400).

**Platelet Rich Plasma (PRP) Injection**

The "modern" version of dextrose prolotherapy: Injections of autologous centrifuged blood with platelets concentrated is used as the injectate.

**History of PRP**

- First human application was described in mandibular reconstruction in oromaxillary surgery in 1998 (Robert Marx, Prof. of Surgery and Chief of Oromaxillary Surgery Division at Univ. of Miami).
- Since then, PRP has experienced a surge in clinical uses and research.
- Endorsement from athletes.
  - Tiger Woods
  - Alex Rodriguez (NY Yankees)
  - Masahiro Tanaka (NY Yankees)
  - Kobe Bryant (LA Lakers)
  - Troy Polamalu (Pitts Steelers)
  - Hines Ward (Pitts Steelers, 2009)

**How Is PRP Prepared? Various systems but basics are:**

- Think of:
  - PRP as “Fertilizer”
  - Stem Cells as “Seeds”

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**Normal Blood**

**Platelet Rich Plasma**


“Stem Cell Injection”

- From web. Charlottesville Orthopedic Center PLC
Cell Sources

**ADIPOSE TISSUE**  
(Zuk et al. 2001)

and

**BONE MARROW**  
(Caplan et al. 1991)

and

**Peripheral Blood**  
(Saw et al.)

Mesenchymal Stem Cells

- First identified in **bone marrow** by Caplan in 1991 and, subsequently, in **adipose tissues** by Zuk et al at UCLA in 2001. *Mesenchymal Adult Stem Cells* now know as Medicinal Secreting Cells can differentiate into:
  - Ligament
  - Tendon
  - Cartilage
  - Muscle
  - Bone
  - Adipose tissue

How Does MSCs Help Arthritis?

- Not entirely understood.
- 1) **Regeneration** of cartilage has been demonstrated in vitro and in animal models.

How Does MSCs Help Arthritis?

- 2) **Paracrine mechanism** (cell-to-cell talk) via cytokines and growth factors.

Many Ways to Prepare MSCs...

- In US, however, **FDA does not allow culturing of the stem cells** in clinics.
  (FDA does not allow these cells to be “more than minimally manipulated” or be outside of the patient for over 24 hrs.)
So what we do instead:

Obtaining BM derived MSC’s:

Stem Cells from Adipose Tissue
- Minimally invasive harvest
- Adipose tissue is known to contain properties that may aid in healing and tissue repair
- High concentrations of reparative elements found within adipose tissue
  - 100 to 500 times more reparative cells than from an equivalent amount of bone marrow (these cells in adipose tissue are unlikely to decrease with age, as with bone marrow)
- Almost everyone is happy to donate fat

Adipose Derived Stem Cells
Collect lipoaspirate: approximately 3-4x final desired volume of Lipogems

Micro-vessels are the key
Perivascular cells reside on very tiny blood vessels. These micro-sized blood vessels are HIGHLY concentrated in fat

Perivascular Cells
- Perivascular cells are a type of cell that is wrapped around small blood vessels within adipose tissue.
- It is known to react to a site of injury and promote a reparative environment.
- The natural repair mechanism occurs by communicating with local tissues to aid in healing.
### Injury Response of a Perivascular Cell

**Proposed Sequence of**

- Injury
- Pericyte
- MSC
- Activated MSC
- Medicinal MSC

Arnold Caplan, PhD (2013)

### Perivascular Cells: “Emergency Repair Cells”

**TROPHIC EFFECTS = secreted bioactive**

- Anti-apoptotic
- Anti-scarring
- Angiogenic
- Mitotic

Arnold Caplan, PhD (2013)

### Allograft placental derived products

- Many proprietary companies
- Most are derived from allograft placental tissue typically amniotic layer
- Logistically a prepackaged simple allograft tissue injection

### Allograft Amniotic Tissue

- Release of growth factors
- Stimulation of growth factor production
- Promote mesenchymal stem cell migration
- Recruits circulating hematopoietic stem cells
- Contains angiogenic growth factors

### Potential Orthobiologics Use in Sports Medicine

- AC joint separation
- Achilles tendonitis
- Achilles tendinosis
- Achilles tendon rupture
- ACL repair – BTJ healing
- Ankle sprain (high)
- Bone-Tendon junction (BTJ) healing diseases
- Concussion
- Chronic traumatic encephalopathy (CTE)
- Chronic bursitis
- Dislocated (shoulder) Epicondylitis
- Fracture
- Hamstring
- Hip labral
- Low back strain
- Meniscal injury (knee)
- MCL injuries
- Nerve injuries
- Osteoarthritis
- Plantar fasciitis
- Rotator cuff tears
- Side stitch
- Shin splints
- Spinal cord injury
- Stress Fractures
- Tendinitis
- Tennis elbow
- Turf toe

### Therapeutics/Ultrasound guided injections

- Small or large peripheral joints
- Insures precision
- No “fishing around”
- Ability to document procedures
Therapeutic Applications of MSK U/S?

- **Therapeutic Interventions**
  - aspiration cyst / bursal / hematoma / soft calcification
  - Difficult joint injections
  - Small joints, hip injections
  - Tendon sheath injections
  - Biceps, paratenon of achilles, deQuervain’s
  - Regenerative tendon injections
  - Prolotherapy
  - PRP injections
  - Stem cell injections
  - Nerve entrapments associated with soft tissue injury
  - hydrodissection
  - Releases / Tenotomy with Tenex FAST procedure
  - Lateral elbow
  - Plantar fascia
  - Trigger digit

Why Musculoskeletal Ultrasound?

Ideal for diagnostics & therapeutic injections

- Dynamic Real time patient interaction
- Soft tissue
- Better spatial resolution
- No radiation
- No contraindications
- Low cost

Hypoechoic Defect full thickness rotator cuff tear

- Short Axis
- Long Axis

FLUID AROUND THE LONG BICEPS TENDON

Intra-articular

Does Ultrasound Guidance improve safety and efficacy

41 patients with painful shoulder

**Group 1** blind subacromial injection of 20 mg triamcinolone (n = 20)

**Group 2** US guided injection of 20 mg triamcinolone (n = 21)

assessed within 5 days before injection & 6 weeks after injection

Six weeks after injection, the VAS and the SFA score showed a significantly greater improvement in Group 2 compared with Group 1 (mean VAS score change 34.9 for Group 2 vs 7.1 for Group 1, p < 0.001).

CMC Joint Injection

CMC Osteoarthritis

CMC Osteoarthritis thumb

Naredo et al J Rheumatol ‘04

Subacromial Subdeltoid Bursa Injection
Glenohumeral arthritis

ORTHOPEDICS El Attrache ‘06

- 40 cadaver shoulders injected, 20 anteriorly and 20 posteriorly, to assess the accuracy of injections placed in the glenohumeral joint
- 1 mL gadolinium injected into the joint to determine accuracy of position
- The anterior approach had an 80% accuracy rate and .75 positive predictive value
- The posterior approach had a 50% accuracy rate and .67 positive predictive value.
- Anterior injections produced higher rate of accuracy than posterior injections.

Glenohumeral Joint Injection
- Joint space is often collapsed and indistinguishable
- *Arthroscopy: The Journal of Arthroscopic & Related Surgery*, El Attrache ‘05
  (41 live awake patients injected anteriorly)
- Only 26.8% (11 of 41) of injections placed anteriorly were actually intra-articular

Glenohumeral joint injection using lateral to medial approach
Smith et al, ‘08
Accuracy of Sonographically Guided
Intra-articular Injections in the Native
Adult Hip

Twenty-eight consecutive patients

Overall, 97% of US guided needles were accurate.
1 Inaccurate placement from inadvertent needle withdrawal during connection of the extension tubing for contrast agent injection

Conclusions: US guidance can be used to inject the native adult hip joint with acceptable accuracy.

Finnoff et al PM&R ’10
Accuracy of ultrasound-guided versus unguided pes anserinus bursa injections

- 12 US-guided and 12 unguided pes anserinus bursa injections
- 92% (11 of 12 specimens) in the US-guided
- 17% (2 of 12 specimens) in the unguided
- US-guided injection technique was significantly more accurate than the unguided technique (Williams-corrected chi(2) = 12.528, P < .01).

Peck et al, PM&R ‘10

Accuracy of ultrasound-guided versus palpation-guided acromioclavicular joint injections: a cadaveric study

All 10 US guided (100%) injected into ACJ
10 US guided and 10 palpation-guided ACJ injections

4 of 10 (40%) palpation-guided injections within the ACJ (P = .0054)

Steroid injection for hip osteoarthritis: efficacy under ultrasound guidance
Micu et al, Rheumatology 2010

- 40 patients with hip OA and synovitis detected by US
- 40 IA steroid injection under US guidance compared to age matched controls
- Walking pain VAS reduced vs baseline P<0.001 at 1 & 3 months
- Synovial hypertrophy reduced in 75% at 1 & 3 months vs baseline

Conclusion: efficacious, safe therapeutic approach for pain control and reducing synovial hypertrophy avoiding use of X-ray guidance

Is bigger better???
Conclusion

- Regenerative Medicine for MSK application is still in its infancy as a therapeutic agent yet will likely be a prominent part of the future orthopaedic landscape.
- It appears promising and safe, offering an exciting alternative to chronic injuries unresponsive to conventional treatments as well as acute partial tears and chondral injuries.

Conclusions

- U/S is a useful tool in guiding minimally invasive orthobiologic procedures.
- New and exciting modality that will assist in better diagnosing and treating sports medicine conditions in the training room, sideline, or in your clinic.
- The field is still emerging and expertise takes time and practice.

Hands-On Diagnostic and Interventional MSK US Course
June 8-11, 2017

Go to our website
Andrewsref.org

Thank You!

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References