CLINICAL SYMPOSIUM 2017:
WHAT’S NEW IN SPORTS & SHOULDER

California Orthopedic Association
Annual Meeting 2017
Biologics in Sports Medicine

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Disclosures:

- **Arthrex Inc**: Product Royalties / Paid Consultant
- **SLACK Inc**: Publication Royalty
- **AAOS**: Sports Medicine Program Committee
- **AOSSM**: Committee of Delegates
Sometimes the Solution isn’t a Mechanical One…

- **Degeneration** of tendon or cartilage
- “Unsolvable” b/c there is NO biologic stimulus
- It likely isn’t Repairable…you would have to ask it to **REGENERATE**
Biologics

Offers the allure of the Holy Grail
Can we effect *de*-generation?
Can we stimulate *re*-generation?
Our generation’s solution to find…

➢ Mesenchymal Stem Cells

➢ Platelet-Rich Plasma

➢ Growth Factors/Cytokines

Qs: Sources, Concentrations and Applications
Regulators are not comfortable with the rise of Biologics
FDA & Regulatory Environment:

• Minimal manipulation of cell tissue
• Homologous use
• Cannot be combined with drug or device
• Autologous use
• Point-of-care (no lab use)
Mesechymal Stem Cells (MSC)

WHAT?

Bone Marrow:
- Microfracture
- Bone Marrow Aspirate Concentration (BMAC)

Adipose:
- Liposuction
- Fat Pad
**MSC Definition:**
Int’l Society for Cellular Therapy (ISCT)

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Mesechymal Stem Cells (MSC)

HOW?

Directly:
- Differentiating into damaged cell types

Indirectly:
- Stimulate angiogenesis
- Limiting Inflammation
- Recruiting Progenitors
About MSCs:

What we Know:

✓ Cultured in monolayer (plastic-adherent)
✓ Can differentiate into: Osteoblasts, Adipocytes, Chondroblasts

What we Don’t Know:

✓ Specifics of lineage induction
✓ Whether the desired lineage is induced before MSC delivery
Clinical Applications:

Is It Safe?

Does It Work (RCT)?
Is It Safe?

- A Prospective, Single-Blind, Placebo-Controlled Trial of BMAC for knee OA (Level 2)

- Clinical Outcomes of autologous BMAC injection in degenerative arthritis of the knee

- Multi-center study: 3012 procedures
Is It Safe?

• A Prospective, Single-Blind, Placebo-Controlled Trial of BMAC for knee OA (Level 2)

• Clinical Outcomes of autologous BMAC injection in degenerative arthritis of the knee

• Multi-center study: 3012 procedures
Does It Work?

Knee OA

Concentrated Bone Marrow Aspirate for the Treatment of Chondral Injuries and OA of the knee: A Systematic Review of Outcomes


- 11 studies (3 for OA; 8 for focal chondral injury)
- All reported “good/excellent outcomes” but marginal quality studies (Level 4)
Does It Work?
For Mild-Mod Knee OA

A Prospective, Single-Blind, Placebo-Controlled Trial of BMAC for knee OA

• N=25 with knee pain
• BMAC (52ml spun to 6cc) v. Saline (6cc)

Similar relief of pain in both BAC and saline tx’ed knees
Does It Work?
For Tendinopathy (RC)

Biologic augmentation of RC repair with MSC during arthroscopy improves healing and prevents further tears: a case-controlled study


- N= 90 pts. (45 RCR + BMAC / 45 RCR - BMAC)
- Minimum 10 year F/U
- @ 6 months: 100% RCR+BMAC healed (v. 67%)
- @ 10 years: 87% v. 44%
Platelet-Rich Plasma (PRP)

WHAT?

Sample of autologous blood with platelet concentrations above baseline

- Platelets
- Plasma
- Leukocytes
Platelet-Rich Plasma (PRP)

**HOW?**

**Differentiation:**

**Indirectly:**

- Growth Factors
  - Chemoattractants
  - Stimulate cell proliferation
Platelet-Rich Plasma (PRP)

What else does PRP contain?

- **Inflammatory Cytokines**
  - TNFα
  - IL-1

- **Matrix MetalloProteinases**
  - MMP2
  - MMP9

Known to increase tissue damage
Clinical Applications:

Is It Safe?

Does It Work?
Is It Safe?

PRP versus saline for knee osteoarthritis


- Level 1 study
- 12 month follow-up
- No adverse events
Is It Safe?

PRP versus saline for knee osteoarthritis


- Level 1 study
- 12 month follow-up
- No adverse events

YES
Does It Work?

Knee OA

Efficacy of Intra-articular Platelet-Rich Plasma Injections in Knee Osteoarthritis: A Systematic Review


- 6 articles reviewed (Level 1) / 739 patients
- Mean age 59.9 y / 38 week avg. follow-up

PRP injection results in significant clinical improvements up to 12 months post-injection
Does It Work?
Knee OA (Advanced)

Platelet-Rich Plasma Injections for Advanced Knee Osteoarthritis: A Prospective, Randomized, Double-Blinded Clinical Trial

- 75 patients with symptomatic K-L grade 3-4 randomized to a single LP-PRP or corticosteroid IA injection
- VAS, KOOS, SF-36 @ 1,3 and 6 months
Does It Work?

Knee OA (Advanced)

• All variables improved in both groups
• Magnitude of improvements tended to be greater in PRP group

For late stage OA, a single PRP IA injection has similar results to a single shot of corticosteroid
Does It Work?

PRP v HA

A Prospective, Double-Blind, Randomized Controlled Trial Comparing Clinical Outcomes and Effects of IA Biology for the Treatment of Knee Osteoarthritis


- Level 1
- N=99 pts randomized to 3 consecutive IA injections
- VAS, WOMAC, IKDC
- Pre- and Post- treatment synovial fluid collected
Does It Work?

PRP v HA

- Higher IKDC and lower VAS @ 24 weeks and 52 weeks in PRP cohort.
- Mild OA and lower BMI had better outcomes
- Trend toward a decrease in 2 pro-inflammatory cytokines (IL-1β and TNFα) in the PRP cohort
Does It Work?

Hip OA

Ultrasound-Guided Injection of PRP and HA Separately and in Combination for Hip OA: A Randomized Controlled Trial


- N=111
- Randomized into 3 groups: 3 weekly injections
- VAS, WOMAC, Harris Hip Score @ 2, 6 & 12 months
3 Randomized Groups:

- **PRP**
  - VAS 21* (p<0.05)
  - WOMAC better at 2 and 6 months (p<0.05)

- **PRP + HA**
  - VAS 35*

- **HA**
  - VAS 44*

* At all follow-up timelines
Results:

- IA PRP injections offered **significant clinical improvement** in patients with **hip OA** without relevant side effects
What about PRP for Tendinopathy?

“The Sweet Spot”
The Effectiveness of PRP in the Treatment of Tendinopathy: A Meta-analysis of RCT


• 18 Studies (1066 participants)

Most significant outcomes in the PRP groups were seen in those treated with LR-PRP preparations
Recomendations:

• Peppering technique
• Intra-tendinous injection
• Ultrasound guidance
Patellar Tendinopathy

PRP as a Treatment for Patellar Tendinopathy: a double-blind, randomized controlled trial


- 23 patients randomized to LR-PRP or Dry Needling
- @ 12 weeks the PRP group had no failures *(p<0.05)*
- Results dissipate over time (>26 weeks)
Lateral Epicondylitis

Efficacy of PRP for Chronic Tennis Elbow: a double-blind, prospective, multi-center, randomized controlled trial of 230 patients


• No significant differences @ 12 weeks
• LR-PRP group had better improvement @ 24 weeks
Human Amniotic-Derived Products

- Amnion is separated from maternal Chorion
- 3 layers:
  - Epithelial cells – actively produce growth factors
  - Basement membrane
  - Avascular mesenchymal tissue
Human Amniotic-Derived Products

- Dehydrated or Cryopreserved
- Decellularized
- Tissue falls under FDA Section 361 product
  - Low safety risk “Allograft”
Clinical Applications:

Is It Safe?
Does It Work?
The Placenta: Applications in Orthopaedic Sports Medicine

Human Amniotic Membrane-Derived Products in Sports Medicine
The Placenta: Applications in Orthopaedic Sports Medicine

PROBABLY

Human Amniotic Membrane-Derived Products in Sports Medicine
Does It Work?

- Provide a matrix for cellular migration
- Enhance wound healing
- Reduce inflammation
- Antibacterial
- Reduce pain at application site

*361 product only as a wound covering*

*o/w considered “off label” use*
Does It Work?

- There are currently 6 human studies reported
- 5 of 6 applicable to Foot/Ankle pathology
- No RCT available
Conclusions:

- Research in Biologics for Sports Medicine is starting to bear fruit.
- The role of PRP in OA and tendinopathies is becoming more clear.
- Knowledge gaps still exist with respect to MSC.
- Amniotic cells and tissue need RCT study.
“It’s nothing a few stem cells and another 75 years of research can’t fix.”