

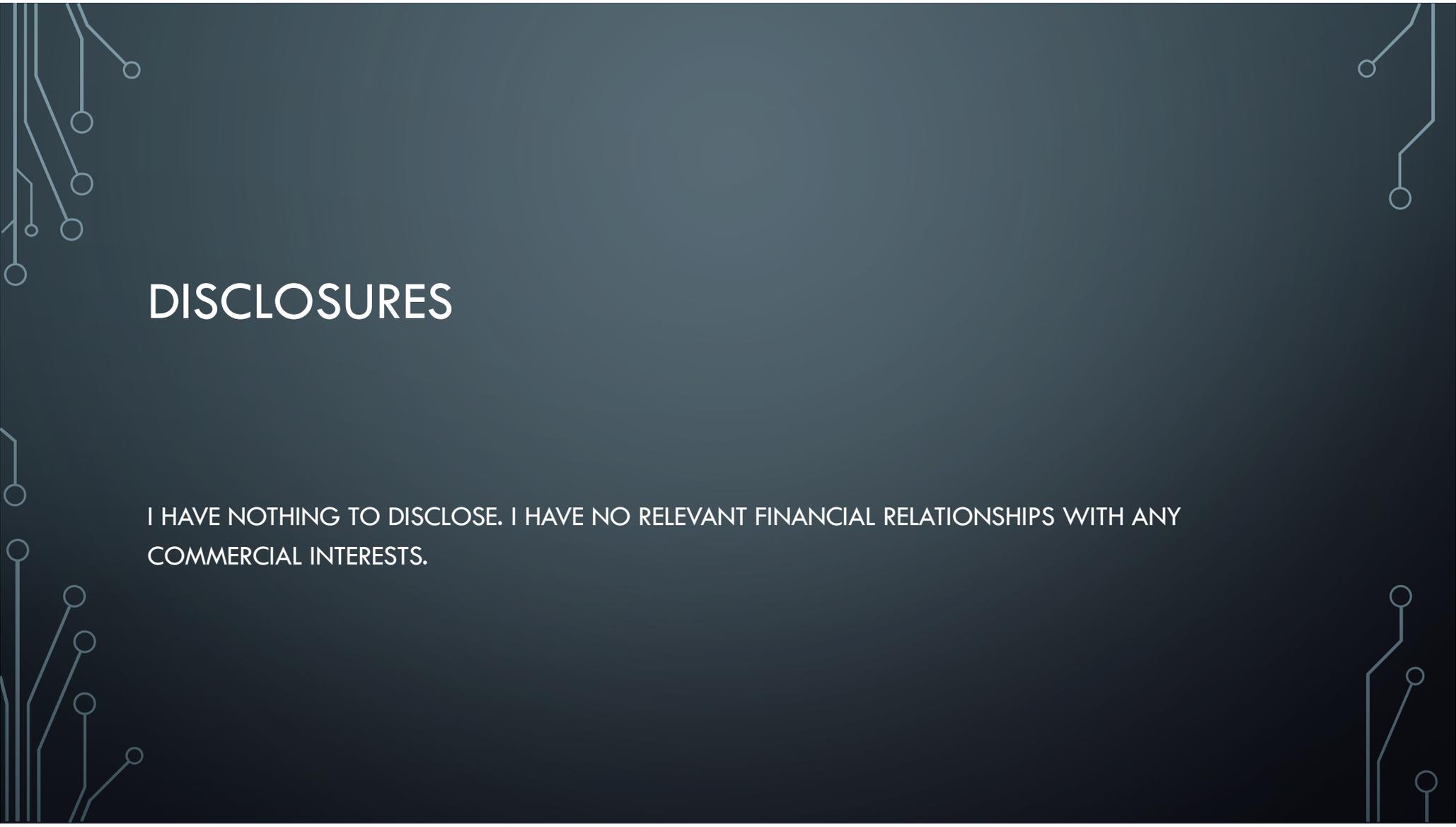


# BIOLOGICS IN ORTHOPEDICS

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# DISCLOSURES

I HAVE NOTHING TO DISCLOSE. I HAVE NO RELEVANT FINANCIAL RELATIONSHIPS WITH ANY COMMERCIAL INTERESTS.

# WHAT ARE BIOLOGICS?

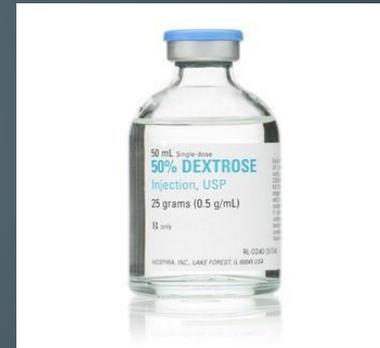
- A class of nonpharmacologic treatments being used for a variety of conditions in many areas of medicine.
- In orthopedics, these biologic therapies are used to improve healing of musculoskeletal injuries and chronic conditions
- The FDA defines them as “sugars, proteins, nucleic acids or complex combinations of these substances, or may be living entities such as cells and tissues.”

# TYPES OF BIOLOGICS

- Prolotherapy
- Blood derived therapies
- Cellular therapies

# PROLOTHERAPY

- Also sometimes called proliferation therapy
- Prolotherapy is an injection-based treatment used in chronic musculoskeletal conditions
- A small amount of solution, often dextrose, saline or lidocaine, in a sterile water mixture is injected near a painful or damaged ligament, tendon, or joint. This solution acts as an irritant to induce an inflammatory response



# PROLOTHERAPY

- This irritant is thought to stimulate the body's inflammatory process leading to first an acute inflammatory phase for the first 1-3 days then to the proliferative phase for about 2-3 weeks and then eventually to remodeling of the tissue.
- During this proliferative phase there is an increase in fibroblast, endothelial cell and myofibroblast activity.

# PROLOTHERAPY

- Multiple injection sites may be needed. In most cases the area is anesthetized with lidocaine or ethyl chloride. The solution is then injected into the treatment area. Depending on the injury or condition, a series of two or three injections may be performed 4 weeks apart.
- No special equipment required (ultrasound)

# PROLOTHERAPY

- Post-prolotherapy, there can be injection site soreness. This usually resolves over 24 to 72 hours. Is it recommended that ice be used at the site of the injection.
- Patients are told to refrain from using any steroids or NSAIDs for about seven days after the procedure.
- Side effects can include hyperglycemia, weight gain, skin discoloration and hypertension.

# PROLOTHERAPY

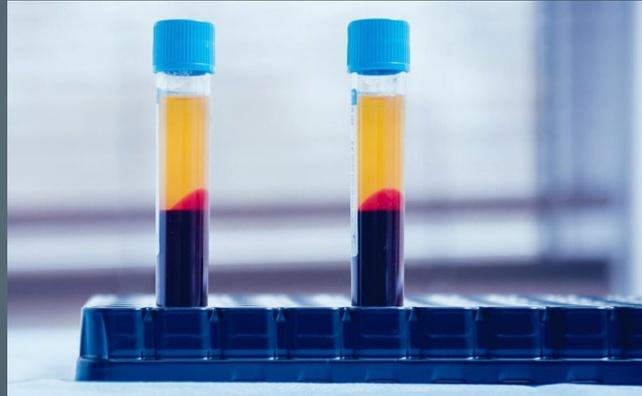
- Tendonitis
- Sprains and ligament injuries, including ligamentous laxity
- Arthritis
- Plantar fasciitis
- Morton's neuroma
- Medial and lateral epicondylitis
- Chronic low back pain
- Fibromyalgia

# PROLOTHERAPY

- Although dextrose, saline and lidocaine are FDA approved, the FDA does not approve of prolotherapy
- Multiple injections usually required
- Not covered by insurance
- Effectiveness is lacking evidence
- Poorly understood mechanism, placebo effect

# PRP

- Platelet rich plasma
- A blood derived biologic therapy (also autologous whole blood)
- Blood derived therapies involve the local administration of blood or blood constituents treated to produce supra-physiologic concentrations of cytokines to promote the growth and division of host repair cells and mediate the inflammatory process.



# PRP

- Activated platelets release granules that contain inflammatory and growth factors, including platelet derived growth factor, transforming growth factor beta, fibroblast growth factor, vascular endothelial growth factor and epidermal growth factor.
- PRP is defined as a concentrate with platelet levels greater than the baseline count in whole blood, sometimes up to 9 times higher

# PRP

- Produced by centrifugation of the patient's blood, which separates the denser red cells from the plasma. The plasma components are divided into a fine buffy coat and an adjacent layer of plasma.
- There are different techniques to get the separated layers, including a “double spin” technique
- Biotech companies will provide the centrifuge, phlebotomy and injection kits

# PRP

- After blood is drawn and processed, the PRP layer is extracted and is injected into the affected tendon, ligament, or joint and sometimes at multiple sites
- Lidocaine is thought to interfere with platelet activation
- One to 4 injections over a two week period can be done
- Recommended that the patient refrain from steroids and NSAIDs two weeks after the PRP injection

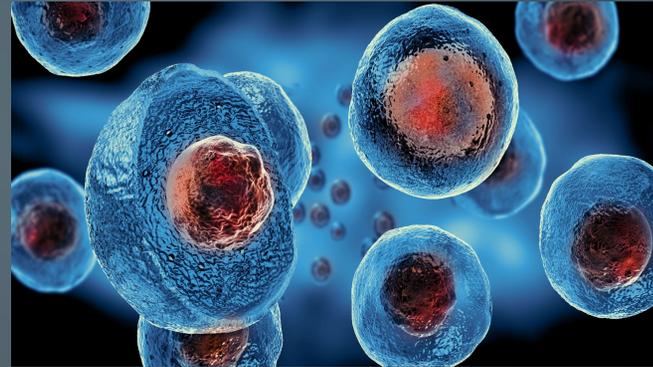
# PRP

- Osteoarthritis
- Tendinopathies
- Muscle strains and tears
- Rotator cuff injuries
- Achilles injuries
- Ligamentous injuries

# PRP

- Treatment preparation and return-to-sport protocols not standardized
- Costly and not covered by insurance
- Requires special equipment
- Clinical trials are limited
- Contraindicated in patients with blood dyscrasias like thrombocytopenia
- Not FDA approved, but World Anti-Doping Agency does not prohibit autologous PRP local injections, only systemic injection of blood products

# STEM CELLS



- Cell based biologic therapy
- Involves introducing cells directly into local tissue and can include mesenchymal stem or stromal cells (MSC's) autologous tenocytes and dermal fibroblasts.
- Supposed to produce a regenerative effect by incorporation into the injured tissue and the adjacent tissues
- They can also remain unengrafted and produce cytokines in the local tissues

# STEM CELLS

- There are several different types of stem cells, but they all possess the properties of proliferation and differentiation into adult cell lines. The mesenchymal stem cell is a rare undifferentiated multipotent stem cell considered to be the body's repair cell. MSC's are capable of differentiation into muscle, tendon, ligament, fat, bone, and cartilage.
- MSC's do not initiate host rejection, so allogenic cells can be used. MSC's are found in bone marrow, adipose tissue and amniotic tissue

# STEM CELLS

- Harvested by bone marrow aspirate from the pelvis or lipoaspirate from the abdomen, usually under local anesthetic. MSCs are isolated and then can be proliferated in a culture medium
- Also mesenchymal stem cells from the amniotic sac of newborn babies can be used
- The stem cells are then injected into the affected tissue. There is also a graft matrix version that can be used in surgical procedures

# STEM CELLS

- Also recommended that the patient not take NSAIDs or steroids for 1-2 weeks after the stem cell injection
- It may take 1 to 6 months before noticing an improvement in condition
- Not a clear return-to-sport protocol
- Requires downtime and could have pain especially with bone marrow aspiration

# STEM CELLS

- Chronic tendon injuries
- Chronic ligament injuries
- Degenerative conditions
- Osteoarthritis
- Meniscus tears
- Labrum tears
- May not be indicated in muscle tears because of skeletal satellite cells

# STEM CELLS

- A lot of time and money invested and regulatory oversight with stem cell harvesting and preparation
- WADA allows stem cell treatments as long as they return the functioning of the affected area to normal
- FDA recently took the amniotic stem cells off the market and is treating it as a “drug”
- Not recommended in pregnant patients or a history of cancer or recent remission of cancer
- Still considered rather controversial
- Limited human studies on effectiveness
- Most expensive of the treatments

## BIOLOGICS SUMMARY

- Prolotherapy, PRP and stem cells can be used for chronic or refractory MSK injuries and conditions to help promote healing
- Considered minimally invasive
- More research is needed on all of these techniques to further determine efficacy of the treatments
- Cost can be an issue

# THANK YOU

- Questions?

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