

Regenerative Techniques in Orthopedics



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Overview

- What is Regenerative Medicine?
- What does it help?
- What are the main types of treatments?

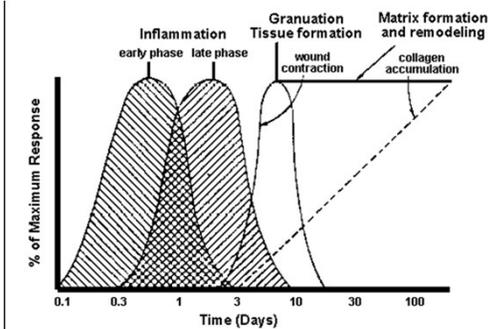
Regenerative Medicine

- Using treatments and biological substances to help a non-healing structure to heal
- Stimulates our innate healing response
- Changes the biology of the structure treated by bringing blood flow to and activating the body's healing system (pericytes & platelets)

3 Phases of Wound Healing

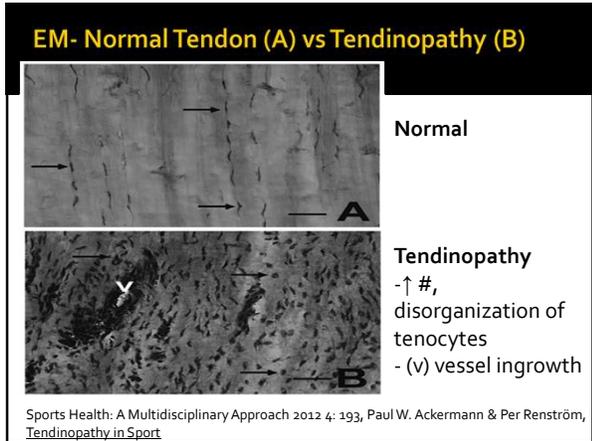
- Inflammatory phase (100 Hours)
 - Platelet aggregation and activation of the classical intrinsic coagulation cascade
- Granulation phase (4-5 Weeks)
 - Laying down scar tissue and early collagen formation
- Remodeling phase (4-5 Months)
 - Removing scar tissue and laying down more collagen

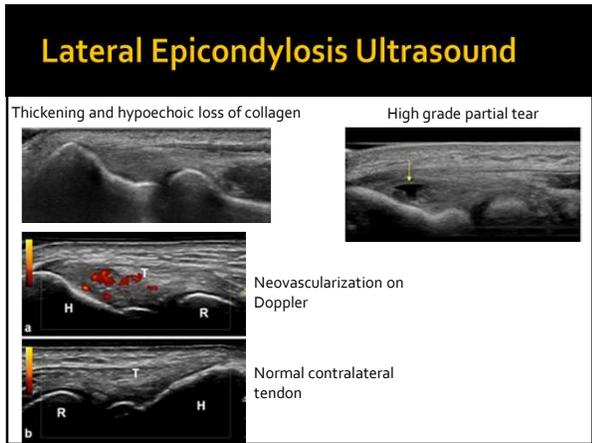
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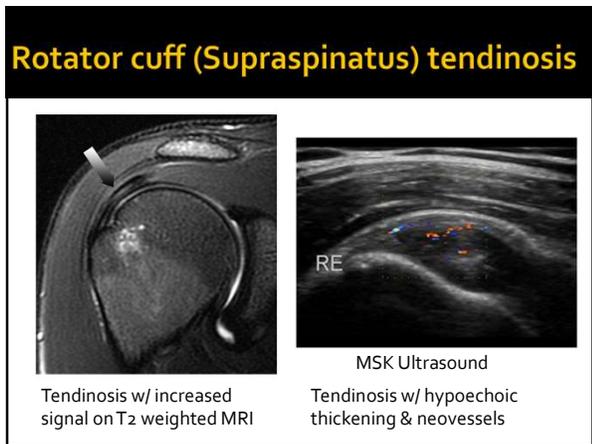


What do Regenerative Treatments help?

- Chronic tendinosis/tendonitis
 - Lateral epicondylitis, patellar or Achilles tendonitis
- Osteoarthritis
 - Improves joint biology, decreasing inflammatory cytokines, stimulates cartilage synthesis
- Ligament, fascia and muscle injuries
 - Partially torn soft tissue injuries and muscle tears

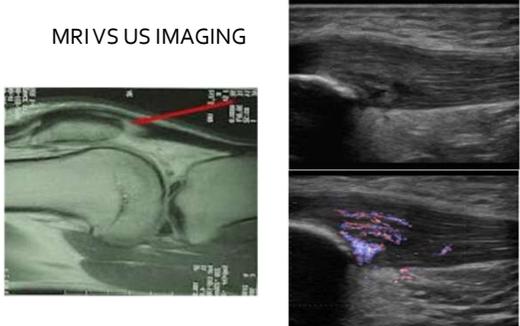






Patellar Tendonitis (Tendinosis) Jumper's Knee

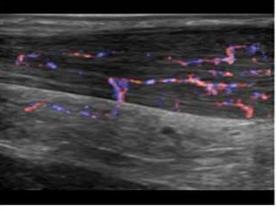
MRI VS US IMAGING



The image shows two side-by-side medical scans. On the left is an MRI scan of a knee joint, with a red arrow pointing to the patellar tendon. On the right are two ultrasound images of the same tendon, showing a thickened and hypoechoic appearance with some internal echogenicity.

Achilles Tendonitis (Tendinosis)

Hypoechoic fusiform thickening w/
Neovascularization



Long Axis view

Hypoechoic thickening w/
vertical Interstitial Split
Tear



Short Axis view

The image contains two ultrasound views of an Achilles tendon. The left view is a long-axis view showing a thickened, fusiform tendon with some internal vascularity. The right view is a short-axis view showing a thickened tendon with a vertical split or tear, indicated by a yellow arrow.

Superiority of Ultrasound vs Landmark Based Injections

- Multiple studies demonstrate significantly improved accuracy of injection
- Many studies demonstrate significantly improved clinical outcomes
- Studies show improved patient satisfaction with Ultrasound compared to blind/fluoro guided injections

-AMSSM Position Paper on Interventional Ultrasound -2014

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OA Definition

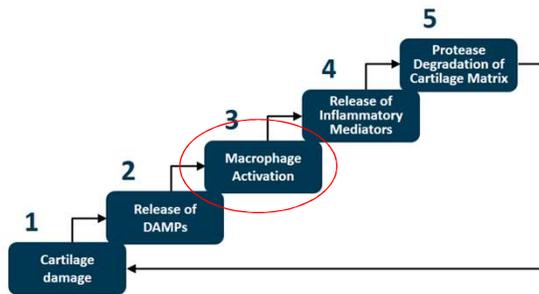
-per Osteoarthritis Research Society International (OARS)

"Osteoarthritis is a disorder involving movable joints characterized by cell stress and extracellular matrix degradation, initiated by micro- and macro-injury that activates maladaptive repair responses including pro-inflammatory pathways of innate immunity. The disease manifests first as a molecular derangement (abnormal joint tissue metabolism) followed by anatomic, and/or physiologic derangements (characterized by cartilage degradation, bone remodeling, osteophyte formation, joint inflammation and loss of normal joint function) that can culminate in illness."

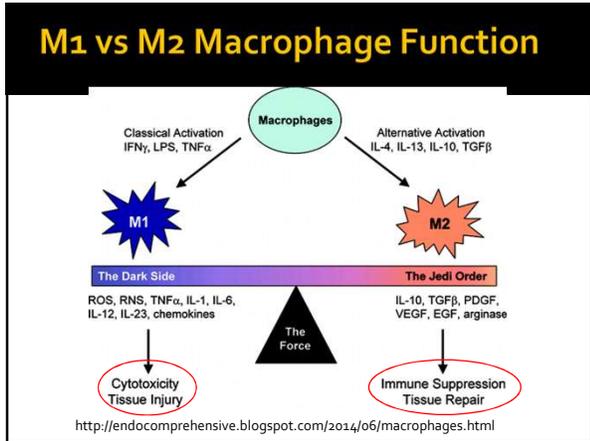
Kraus V, et al. *Osteoarthritis Cartilage*. 2015. doi: 10.1016/j.joca.2015.03.036.^[8]

Biologic Process

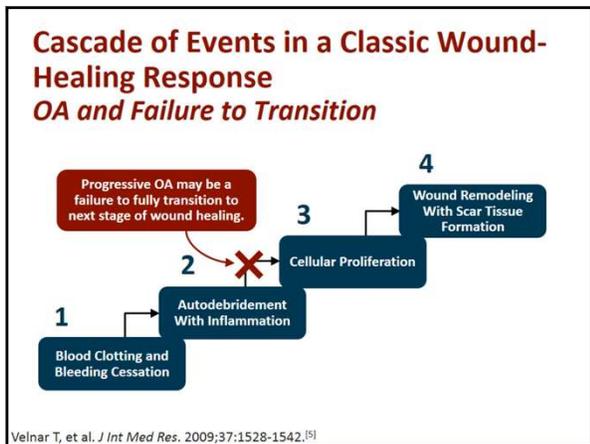
Role of Inflammation in OA



Orlowsky EW, et al. *J Rheumatol*. 2015;42:363-371.^[1]







What techniques/substances are used?

- Physical medicine, strengthening, eccentrics
- Needle tenotomy/fenestrations

- Dextrose Prolotherapy
- Platelet Rich Plasma
- Amniotic Membrane and Cells
- Autologous Stem Cells
 - Bone marrow, lipoaspirate

Biologic Tx	ECM/Scaffold	Growth Factors	Pluripotent cells	Limitations
Dextrose Prolo	None	↑↑	No, may recruit	-Conc ≤ 25% -No ECM/stem cells
PRP	Single layer fibrinogen scaffold	↑↑-↑↑↑	Few, and recruits them to site of healing	-Variability -Thin scaffold -Low stem cells
Bone Marrow Aspirate	Single layer fibrinogen scaffold	↑↑	↑↑	-? scaffold -↑ time -invasive
Lipoaspirate	Complex adipose ECM structure	↑↑	↑↑↑	-↑ time -↑ training -min. invasive
Amniotic Tissues (cryopreserved)	Complex ECM structure	↑↑-↑↑↑	?-↑	-Cost -Variability -Small volumes
Amniotic Tissues (dehydrated)	Complex ECM structure	↑↑-↑↑↑	No, may recruit them	-Cost/variability -Small volumes -No stem cells

Dextrose Prolotherapy

- 10-25% dextrose solution
- Effects:
 - Hyperosmolar/irritative effect
 - Nerve calming effect
 - Increases Growth Factors involved in healing of **cartilage, tendon & ligament (alters DNA)**
 - PDGF, TGFβ, bFGF, IGF

Level I Evidence for Prolotherapy

- Rotator Cuff tendinopathy (Bertrand 2015)
- Knee OA (Rabago 2013, Dumais 2012)
- Osgood Schlatter Disease (Patellar tendinosis) (Topol 2011)
- Thumb and Finger OA (Jahangiri 2014, Reeves 2000)
- Lateral Epicondylitis (Scarpone 2008)

Level II Evidence for Prolotherapy

- Rotator Cuff Tendinopathy (Lee 2015)
- SI joint dysfunction (Kim 2010)
- Lateral epicondylitis (Rabago 2013)
- Low back pain (Yelland 2004)
- Achilles tendinosis (Yelland 2011)
- Adductor/abdominal tendinosis (Topol 2008)
- Knee osteoarthritis (Reeves 2000)
- Chronic ACL Laxity (Reeves 2003)

Platelet Rich Plasma-Why platelets?

- Platelets contain many clotting and **growth factors** that stimulate the healing process
- Once activated, platelets change shape and develop branches that spread over injury
- Growth factors are released which initiate cellular healing and recruit stem cells
- PRP shown to be effective when platelets are concentrated at least 2-3x baseline

Platelets -Activated by Thrombin & Collagen

Inactivated Platelets Activated Platelets

How do you get PRP?

- Various systems (1 or 2 spin systems)
- 30-60 cc venous blood draw from patient
- Centrifuge patient's blood 5-10 minutes

-Images c/o Emycte Corporation

Regenerative Injections -Can use Ultrasound or Fluoroscopy

Subacromial Bursa Deltoid Muscle
Supraspinatus Tendon
Humeral Head

Needle
Supraspinatus tendon

Mesenchymal Stem Cells -Lipoaspirate and Bone Marrow derived

- **Orchestrate healing response**
 - Heal bone, cartilage, ligament, tendon tissues
 - via GF's and cell signaling after macrophage ingestion
- **Anti-inflammatory/immunomodulatory effects**
 - Respond to catabolic inflammatory environment, release cytokines, proteins to ↓ inflammation
 - Restore TH₁/TH₂ and M₁/M₂ ratios
- **Anti-apoptotic effects**
 - Rescues apoptic cells via growth factors & cytokines
- **Anti-microbial effects**

MSCs from Pericytes: "vessel huggers" -in response to environment, cell signaling following trauma

Mesenchymal stem cells: environmentally responsive therapeutics for regenerative medicine.
Murphy MB, Moncivais K, Caplan AI - *Exp. Mol. Med.* (2013)

-After re-establishing a "healed" micro-environment, MSC returns to pericyte form, attached to local vessels

Evidence for Bone Marrow Aspirate in Knee OA

- Bone Marrow + Platelet Products vs PT for knee OA
- 48 pts, KSS, VAS, LEAS scores
- BMA + Platelet Products superior to PT
 - Centeno et al, JTrans Med. 2018 Dec 13;16(1):355
- Bone Marrow + PPP vs Saline in pts w/ bilat knee OA
- 25 pts, OARSI and VAS scores
- 6 and 12 month f/u scores showed no sig diff b/w knees. Both knees were doing very well.
 - Shapiro et al, AJSM. 2017 Jan 45(1):82-90.
 - Shapiro et al, Cartilage. 2018 Aug 30:1947603518796142

Regenerative Techniques in Orthopedics -Take Home Points

- Orthopedic injuries can heal in 3-4 months
- If failing after 3-4 months, consider Regen Med

- HAM and MSC's have a limited but growing body of evidence
- Dextrose Prolotherapy and PRP have Level 1 and Level 2 evidence for OA & tendinopathy
- Ultrasound guidance is key to accurate diagnosis, treatment & optimal outcomes

Questions?

