Emerging Topics
Regenerative Medicine in PT

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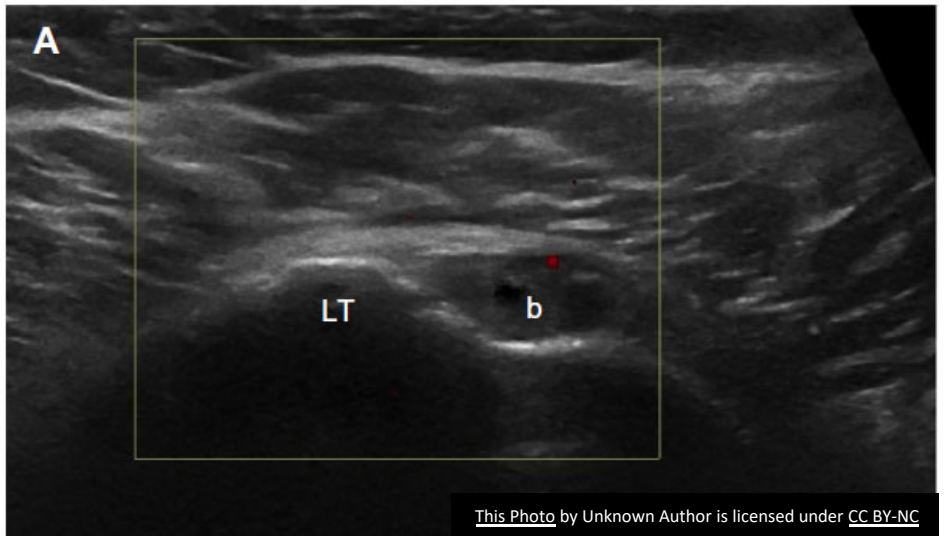
What is Regenerative Medicine

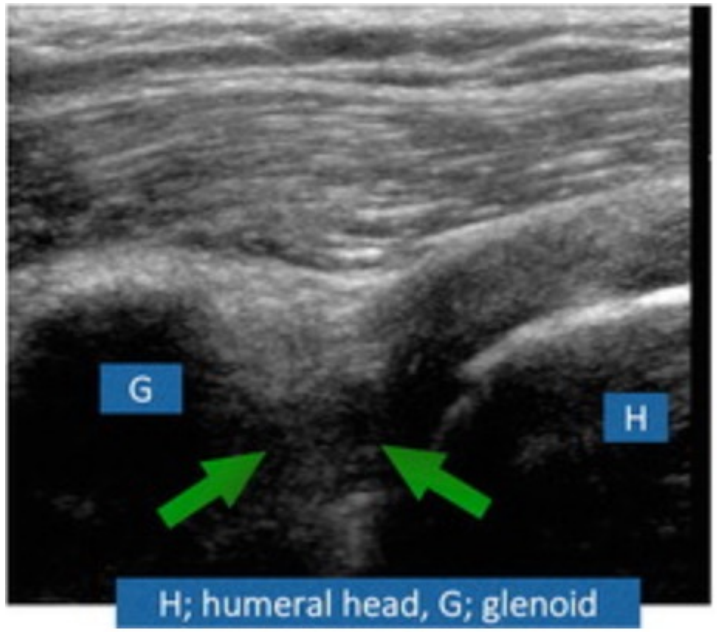
- Regenerative medicine is the branch of medicine that develops methods to regrow, repair or replace damaged or diseased cells, organs or tissues.
- Regenerative medicine includes the generation and use of prolotherapy.
- MSK Ultrasound is used to identify dysfunction in the tissue

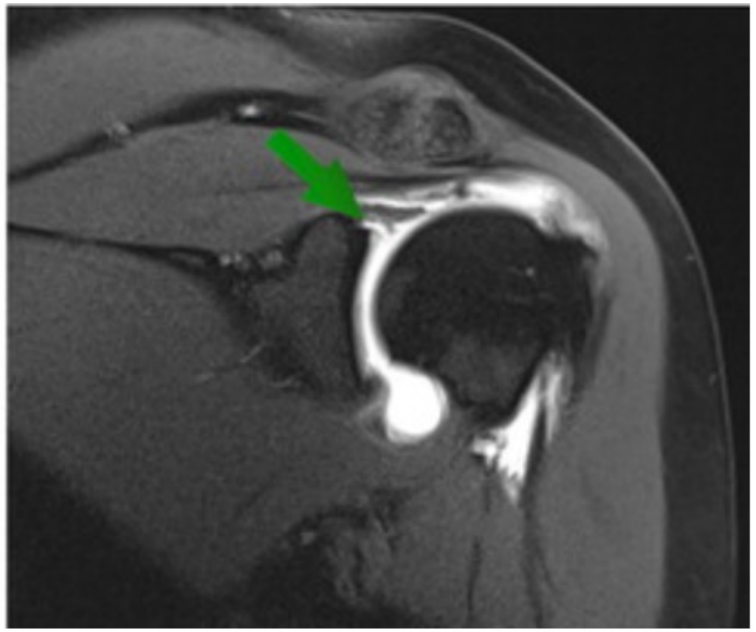


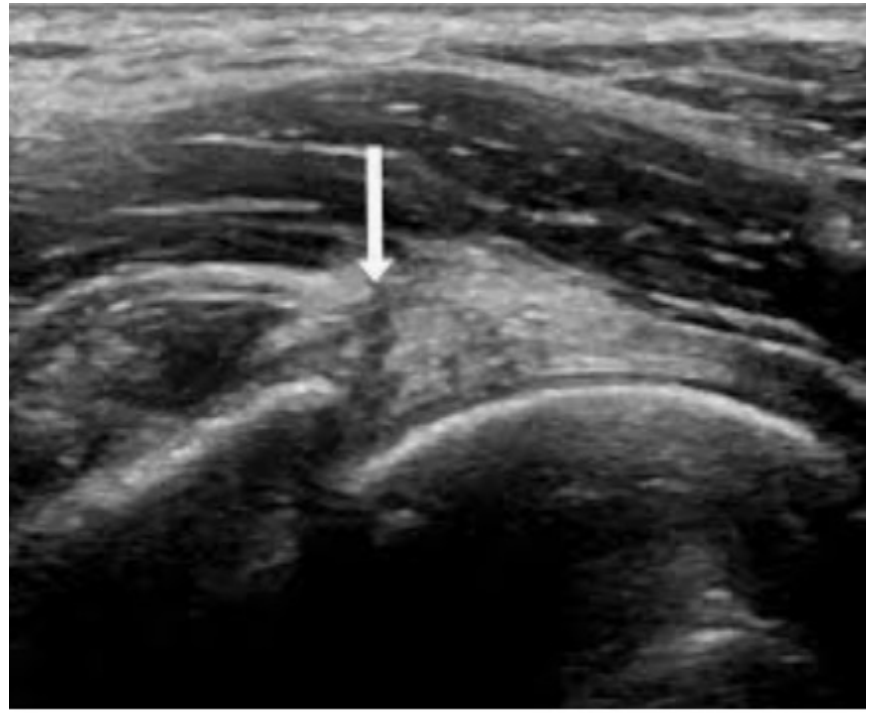
Diagnostic Ultrasound

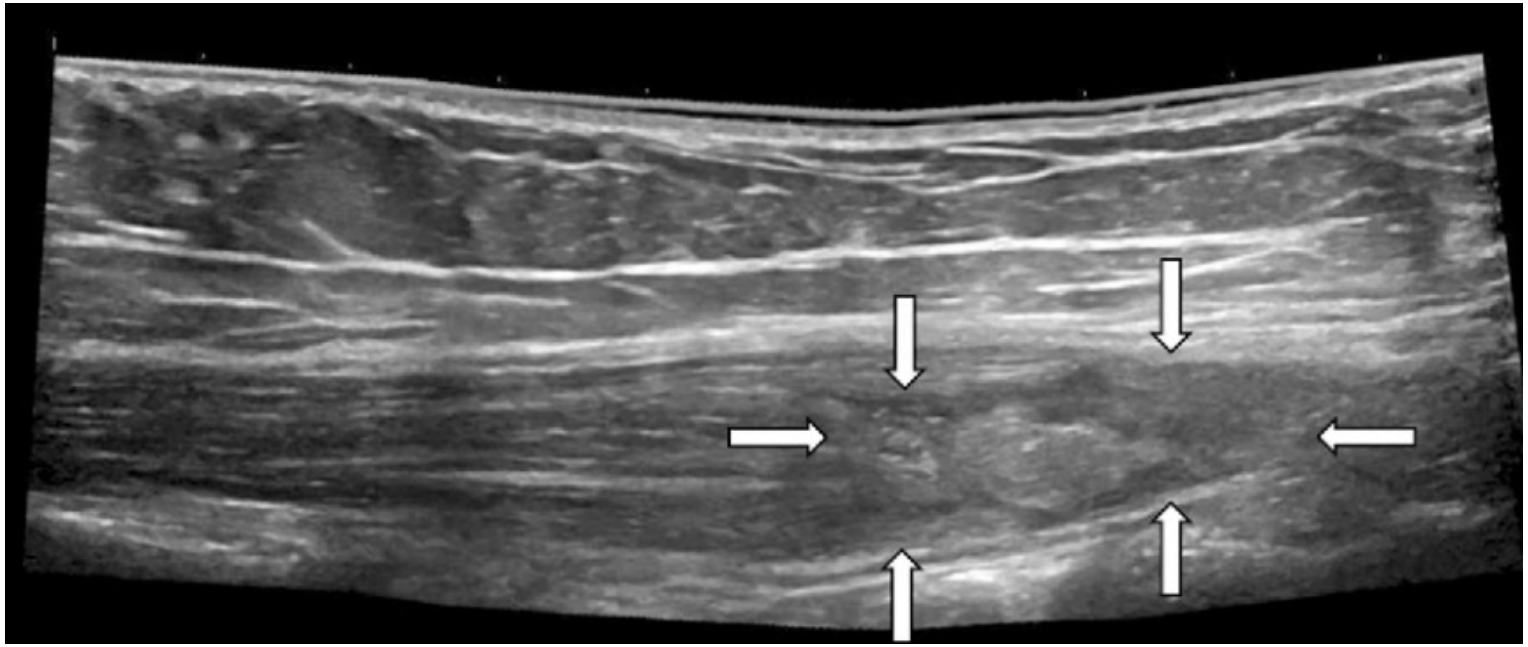
- Also called sonography or diagnostic medical sonography, is an imaging method that uses high-frequency sound waves to produce images of structures within your body.
- Many uses in medicine
  - Musculoskeletal
  - Cardiac
  - Organs – breast, gallbladder, kidneys
  - Veins/arteries

Ultrasound Pictures of Tissue Disruptions







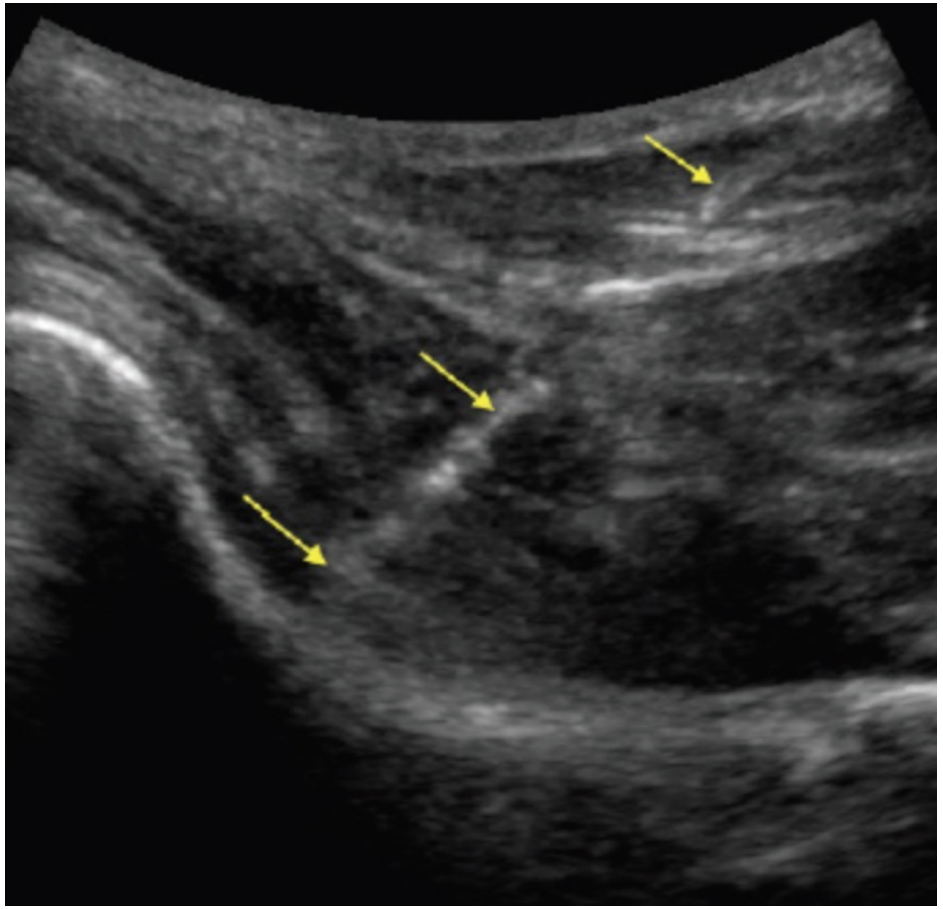


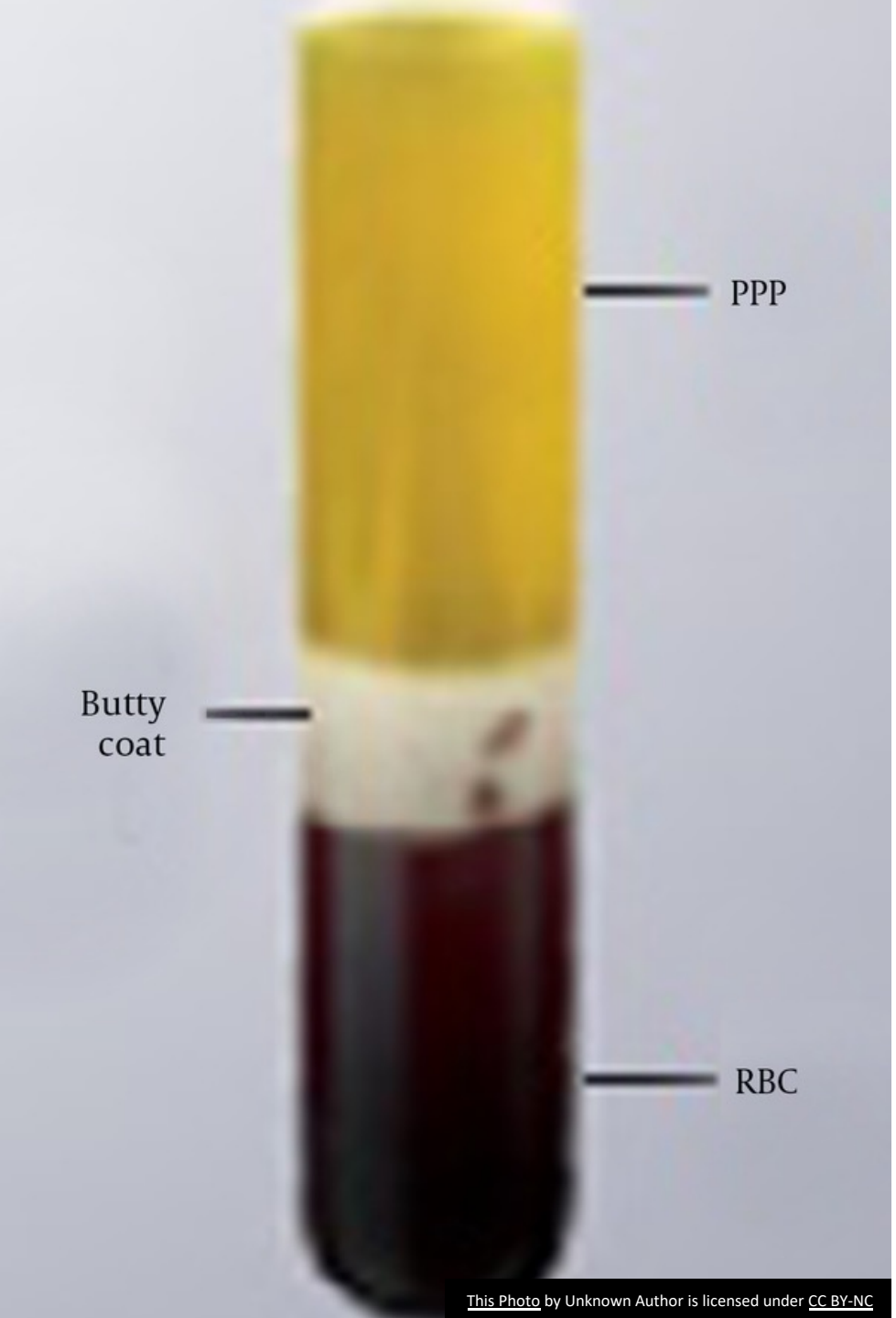
Prolotherapy

- Prolotherapy is defined as the rehabilitation of an incompetent structure by the induced proliferation of new cells.
- It’s the injection of a small volume of solution to painful ligament or tendon sites and adjacent joint spaces over the course of several treatments
- It is designed to stimulate healing and can be used at multiple painful sites such as muscle, ligament/tendon insertions, trigger points, and adjacent joint spaces
- The injection stimulates growth factor production to grow normal cells or tissue.

How Does Prolotherapy Work….

- Prolotherapy causes a temporary inflammatory reaction at the site of injury and tricking the body into initiating repair into tissue that has forgotten that there still is an injury. The irritation and needle microtrauma can influence the tissue to start an inflammatory reaction. This will activate fibroblasts and in turn synthesize collagen and connective tissue.
- Dextrose specifically increases cell protein synthesis, DNA synthesis, cell volume, and proliferation. This leads to increased ligament size and mass, tendon hypertrophy, bone junction strength, and repair of articular cartilage defects.



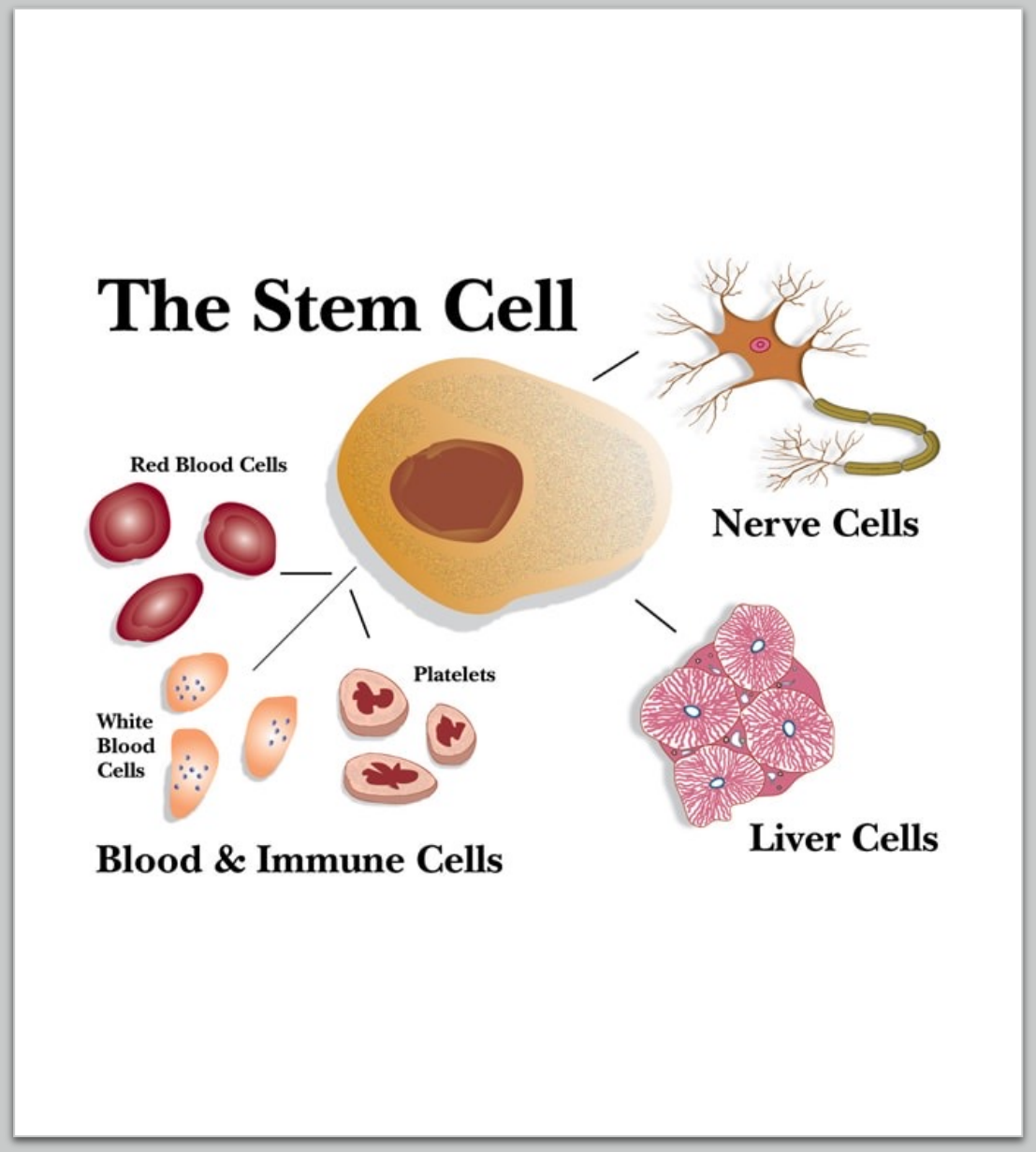


PRP: Platelet Rich Plasma

- Form of Prolotherapy
- Injection of a concentration of plasma into a target tissue
- The plasma contains proteins, cytokines, and other bioactive molecules that initiate and regulate basic aspect of wound healing
- PRP promotes the enhancement of bone remodeling, proliferation, vessel remodeling, angiogenesis, inflammation, coagulation, and cell differentiation. The cytokines and other bioactive factors released from PRP are also known to affect metabolic processes such as cell proliferation, cell chemotaxis, cellular differentiation, gene expression, and extracellular matrix production.

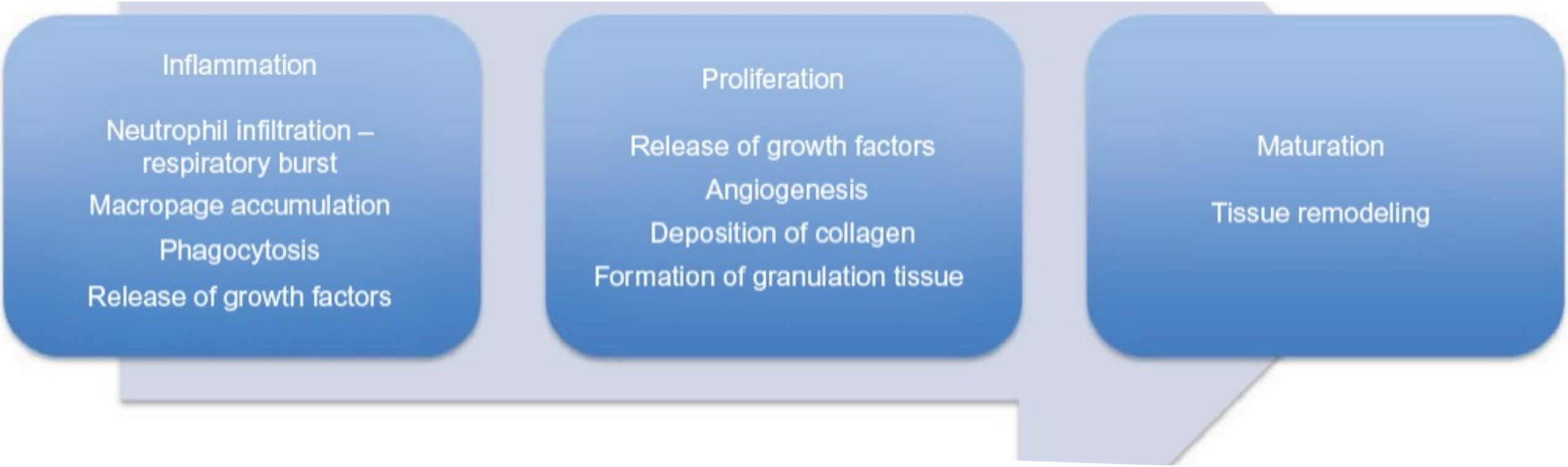
Stem Cell Therapy

- Mesenchymal stem cells (MSCs), can be used as a proliferating solution.
- MSC can be found throughout the body and exist to replenish dying cells and regenerate damaged tissues.
- They can be found in bone marrow and adipose tissue.
- MSCs have the potential to differentiate into a variety of tissues such as bone, cartilage, fat, tendon, muscle, and adipose tissue



Prolotherapy in Sports Medicine

- PRP in sports medicine has been widely used with variable outcomes.
- It has most commonly been used in chronic tendinopathies.
- It has been tried in acute injuries, such as muscle strains, ligament sprains, and partial tears.
- Several studies have noted improved knee stability via revascularization at the osteo- ligamentous interface zone, while other studies have suggested no benefit due to the presence of intraarticular plasmin in a posttraumatic joint

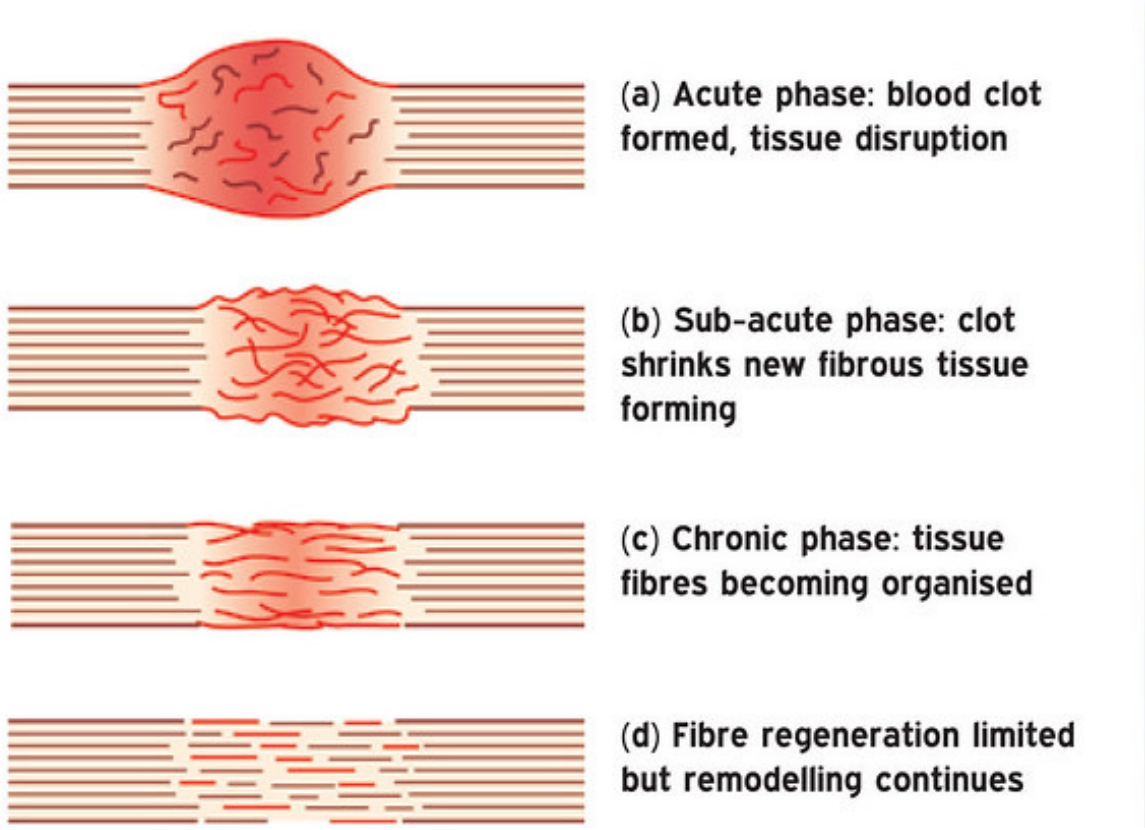


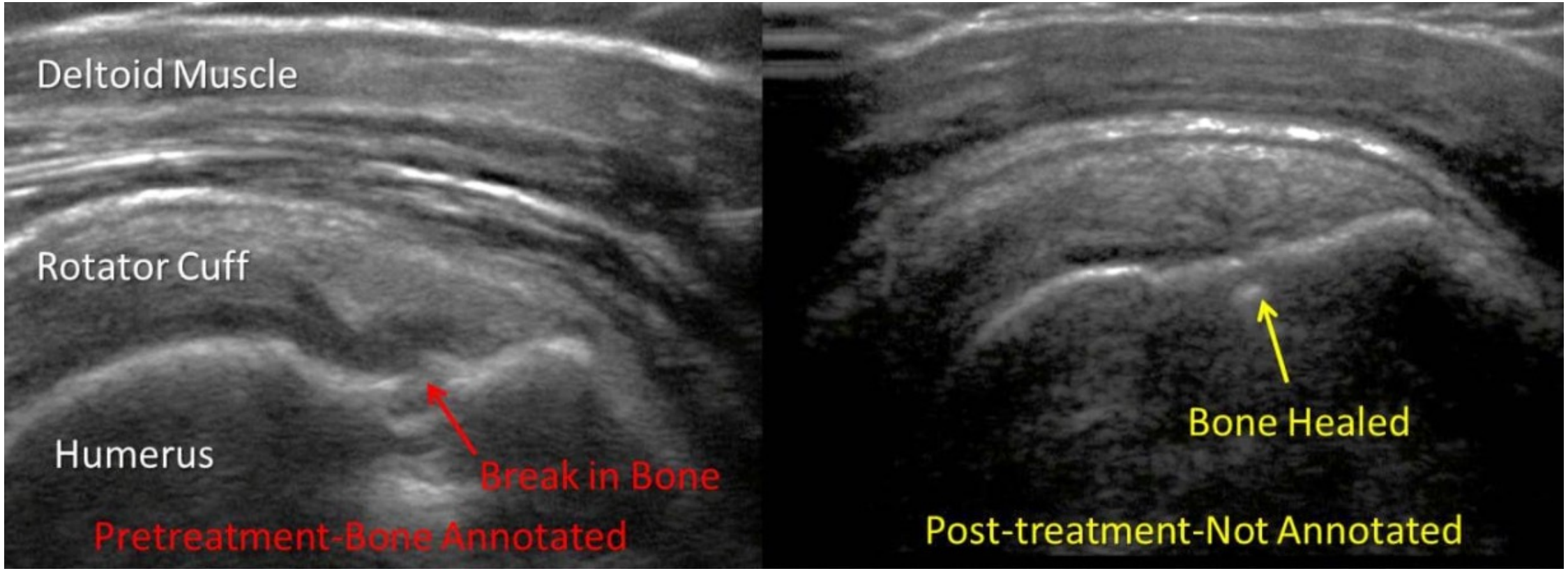
What PT's need to know...

- Rehabilitation post prolotherpy follows the healing process
- 3 phases of healing
  - Phase I Inflammatory/destructive phase
  - Phase II Proliferation/repair phase
  - Phase III Matrix formation/remodeling/maturation

What PT's need to know…

- Prolotherapy induces an inflammatory reaction to tell the body to heal the area
- Lays down new tissue to repair
- Absolute rest is no longer a standard of care
- We need to apply force to the area at the right phase of healing to assist the collagen in lying down appropriately then to strengthen the fibers
- Overloading produces an increased expression of proinflammatory cytokines; physiologic loading creates matrix homeostasis with tenocyte proliferation and matrix production.





Components of Healing

- Tendon – Tendocytes
- Ligament – Fibrocyte
- Muscle – myoblast
- Cartilage – Chondrocyte
- Bone– Chondrocytes/ Osteoblasts

Tendons

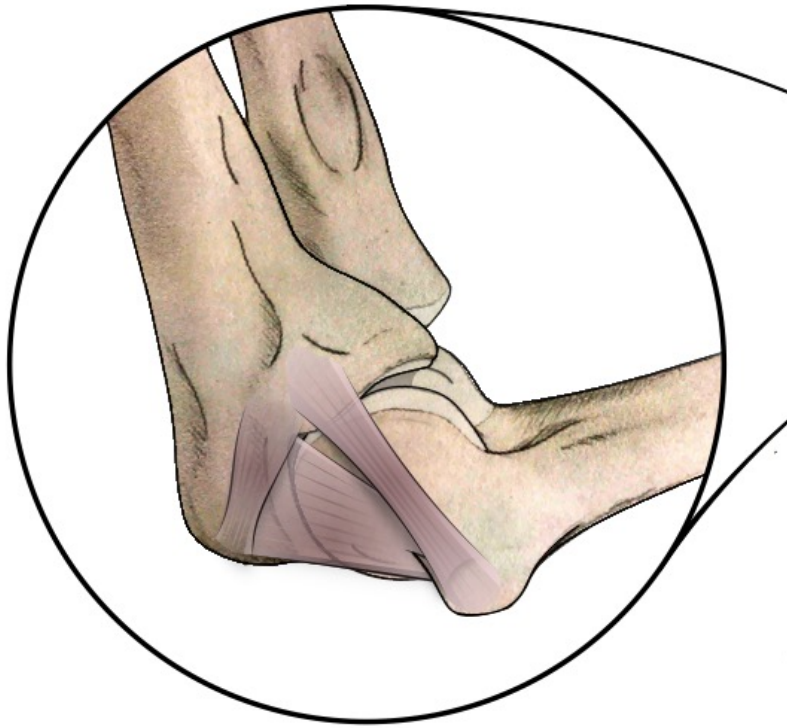
- “Tendonitis” to “tendinosis” and now to chronic tendinopathy
- Many different attempts have been explored to treat chronic tendinopathy and induce a healing response to the tissue.
- Other factors to consider when addressing the cause of pain in patients with chronic tendinopathy include the findings of neural sprouting or neoinnervation
- Tenoblasts and tenocytes constitute 90% to 95% of the cellular elements of tendons and are cells that are able to proliferate and become metabolically active in response to cytokines and growth factors during the inflammatory phase.

Tendons Cont….

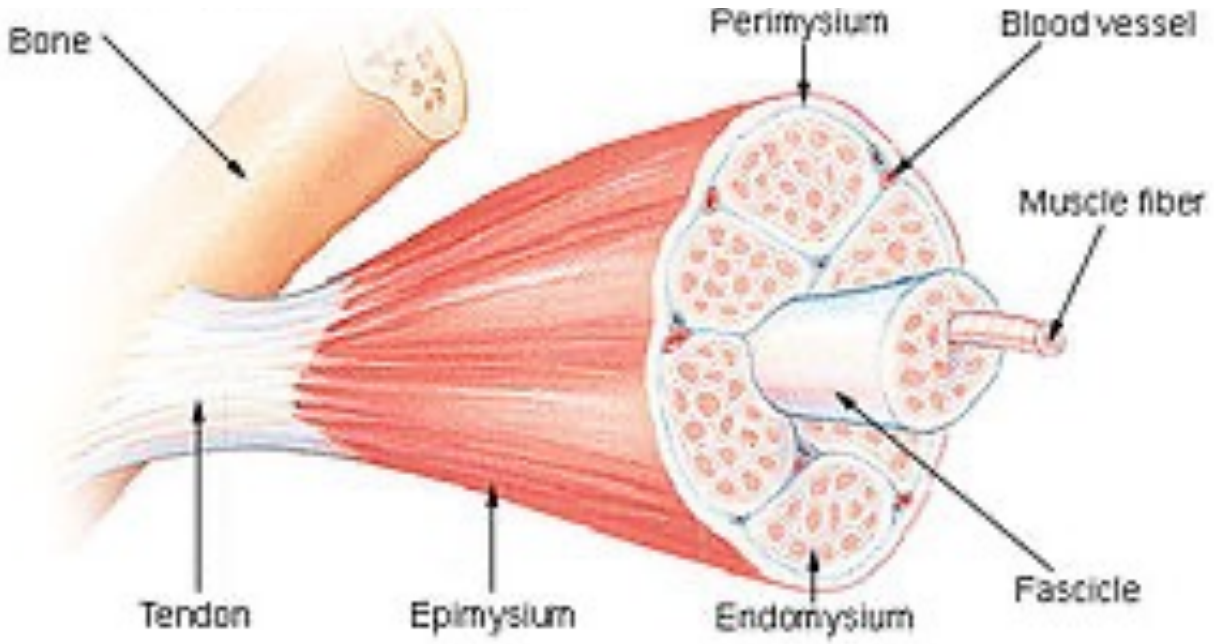
- Tendons transmit forces from muscle to bone
- Failure to adapt to excessive load results in the release of cytokines, high levels of cytokines induces MMP release which leads to degradation of extracellular matrix = tendinopathy
- “Mechanotransduction” refers to the process by which the body converts mechanical loading into cellular responses.
  - No immobilization after tendon injury for prolonged time
  - Mechanical stimulus aides in necessary cellular responses for tissue healing
- Overloading, physiologic loading, and underloading = frequency duration and magnitude of load creates cellular responses needed to restore tissue homeostasis and repair.

Ligaments

- Water, collagen and amino acids
- Collagen type 1 = 75% of dry weight of ligaments
- Proteoglycans, elastin and glycoproteins = 25%
- With tension ligaments deform in a non-linear manner but fibers will eventually become linear as tension is applied
- Ligament injury can take months to heal – remodeled ligament tissue is morphologically and biomechanically inferior = laxity
- Prolotherapy has been shown to enhance ligament healing = increased fibroblast and capillary proliferation, growth factor stimulation = increased strength mass and extracellular matrix



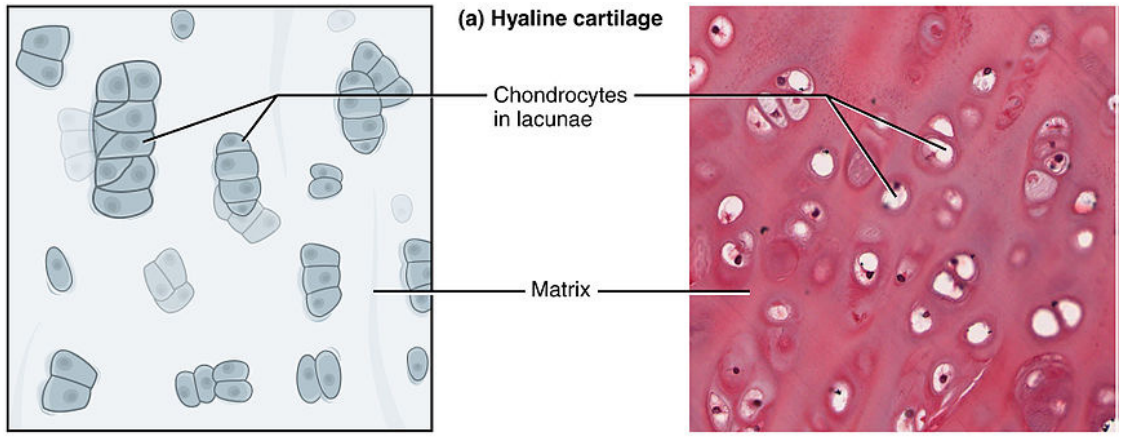
Muscle



- The proliferation and differentiation of muscle cells and the activation of muscle satellite cells characterize skeletal muscle healing.
- Many growth factors play a role in muscle regeneration. PDGF is known for regulating myoblast proliferation and increasing myoblasts during muscle regeneration.

Cartilage

- The degeneration of the cartilage is due mainly to changes in activity of the chondrocytes to catabolic activity. This change in activity causes sclerosis and edema to the subchondral bone and inflammation of the synovium.
- This leads to cartilage loss and increased loads on the subchondral bone
- PRP plays a role in chondrocyte upregulation and cartilage matrix synthesis by the release of growth factors, in particular TFG - β.
- This growth factor helps promote migration of bone-marrow stromal cells toward the site of injury. TGF β - 1 also stimulates proliferation and chondrogenic differentiation.
- This is necessary in the process of differentiation into cartilage.



Rehabilitation Protocol

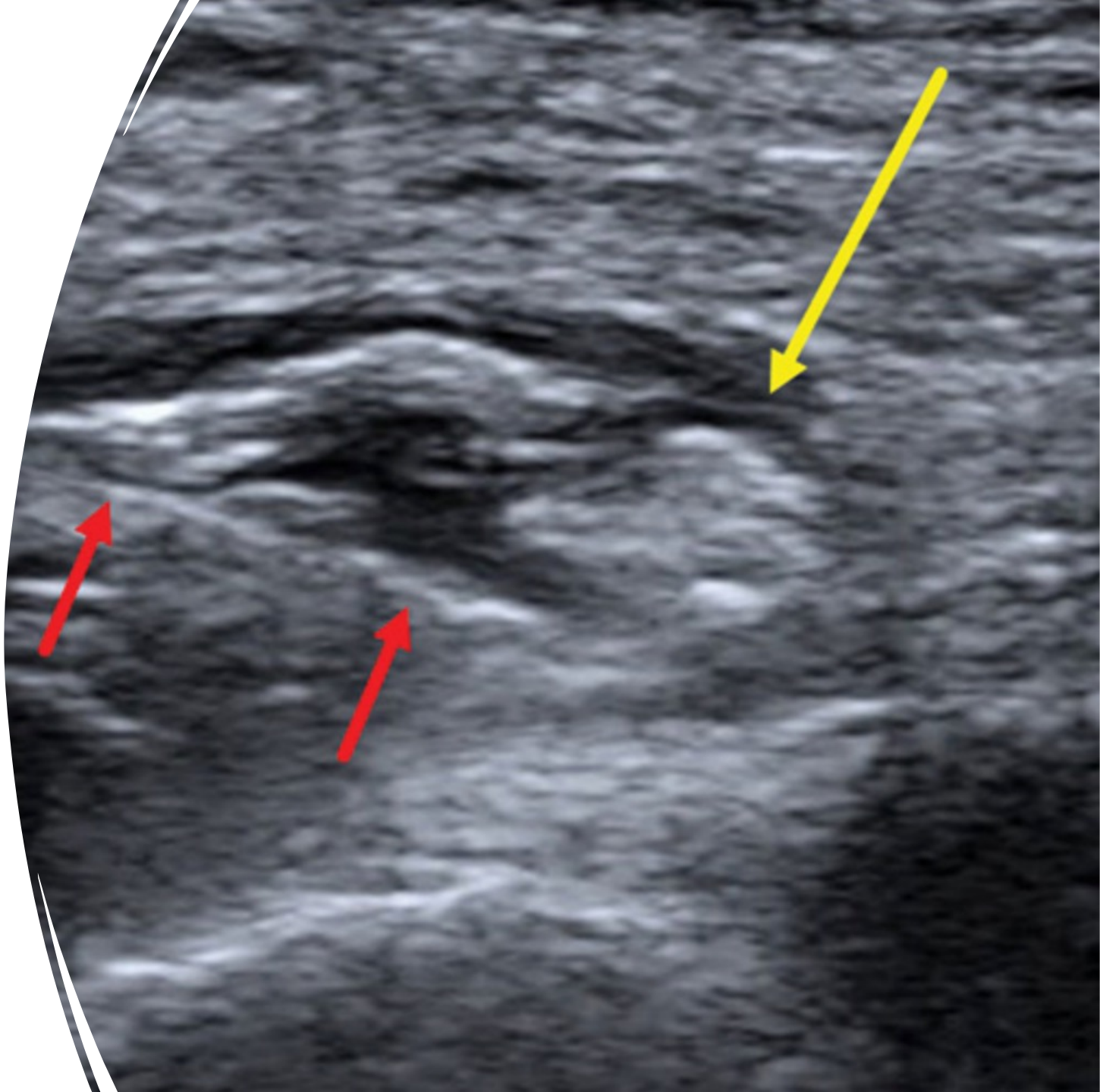
- 3 to 5 day rest and protection
- Davis's Law principle – low load mechanical stress is applied
- Initial protection phase 0 to 7 days
- Initial strength phase isometrics 3 to 7 days
- Concentric strength phase 7 days to 2-4 weeks (will vary depending on procedure and physician)
- Eccentric phase 2 - 4 weeks to 6 weeks (will vary depending on procedure and patient tolerance)
- Plyometric/ return to sport phase 6 to 8 weeks

Soft tissue considerations

- Ligament bracing is recommended post injection but should not restrict ROM
- Muscle length should be fully restored prior to beginning eccentric exercises
- Post stem cells, physical therapy is not initiated until week 2 as to not interrupt the scaffold links to the target tissue

Nerve Hydrodissection

- The unique nerve hydrodissection treatment is done by injecting a volume of fluids around the nerves to release its adhesions from the neighboring structures.
- Nerve Hydrodissection consists of injecting either platelet-rich plasma (PRP) or a 5% dextrose solution (D5W) around the painful nerve. The solution releases the healthy tissue from the scar tissue that formed as a result of an injury or a musculoskeletal lesion.
- Scar tissue Hydrodissection: procedure to release scar tissue along a tendon, muscle, fascia or joint capsule. Can be performed with just saline, saline/prolotherapy, or with PRP.



Scar tissue Hydrodissection

- Technique used with needle hydrodissection to release scar tissue in various tissues:
  - Tendinosis
  - Nerve
  - Fascia
  - Muscle adhesions
  - Joint capsule

Thank You….

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