Injectable Collectables: An Overview of Integrative Injectable Treatments

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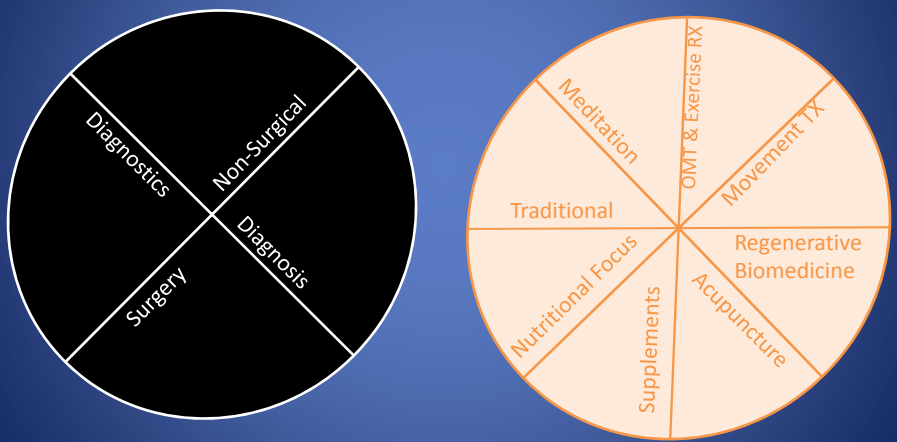
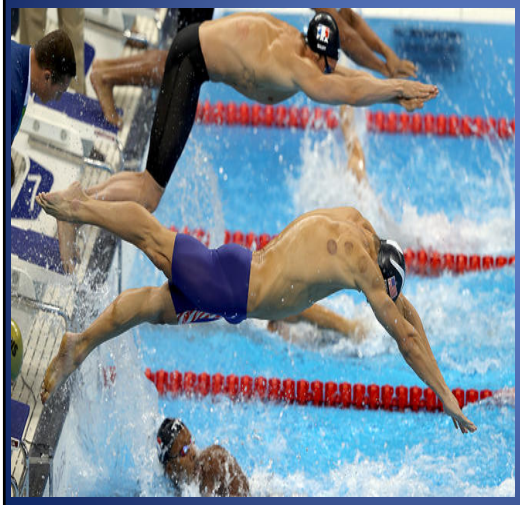
Expanding Therapeutic Options



Traditional Medicine

Integrative Medicine

LECOM Lifestyle and Integrative Medicine



- Osteopathic Manual Medicine
- Cupping/ Gua Sha
- Medical Acupuncture
- **Injection Therapies**
- Movement Therapies
- Nutrition/Dietary Supplements

The principles of integrative medicine:

- A partnership between patient and practitioner in the healing process.
- Appropriate use of conventional and alternative methods to facilitate the body's innate healing response.
- A philosophy that neither rejects conventional medicine nor accepts alternative therapies uncritically.

The Pain Epidemic

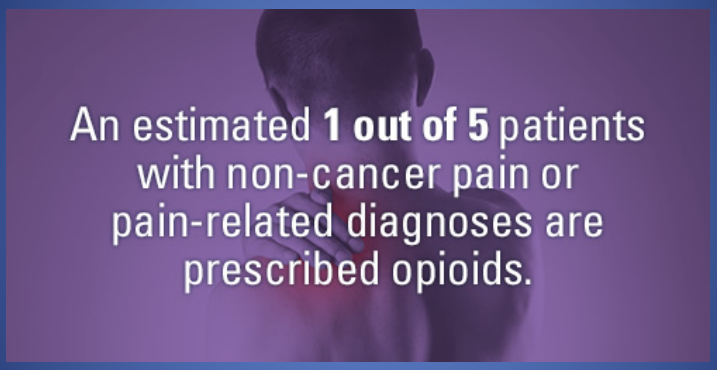
- According to the World Health Organization (WHO), over one-fifth of the world population has experienced some type of chronic pain.
- It is estimated that nearly 35 percent of the U.S. general population has persistent or chronic pain symptoms.

(The National Center for Health Statistics)

The Pain Epidemic

- **Of patients diagnosed with chronic pain and treated by a family physician, 64 percent report persistent pain two years after treatment initiation.**
- **More than 40 Americans die daily from pain killer overdoses.**
- **50% of patients who took pain killers for 3 months still took them 5 years later.**

Realities of Pain Management



Centers for Disease Control and Prevention National Center for Injury Prevention and Control Division of Unintentional Injury Prevention March 2016

Painful Realities

- Centers for Disease Control and Prevention National Center for Injury Prevention and Control Division of Unintentional Injury Prevention March 2016

Realities of Pain Medicine

Nearly **2 million** Americans abused or were dependent on prescription opioids in 2014.

CDC Guideline's Aim:

- Start low and go slow
- When opioids are used, prescribe the lowest possible effective dosage. Only provide the quantity needed for the expected duration of pain.
- **Follow-up**
- Regularly monitor patients to make sure opioids are improving pain and function without causing harm.

CDC Guideline's Aim:

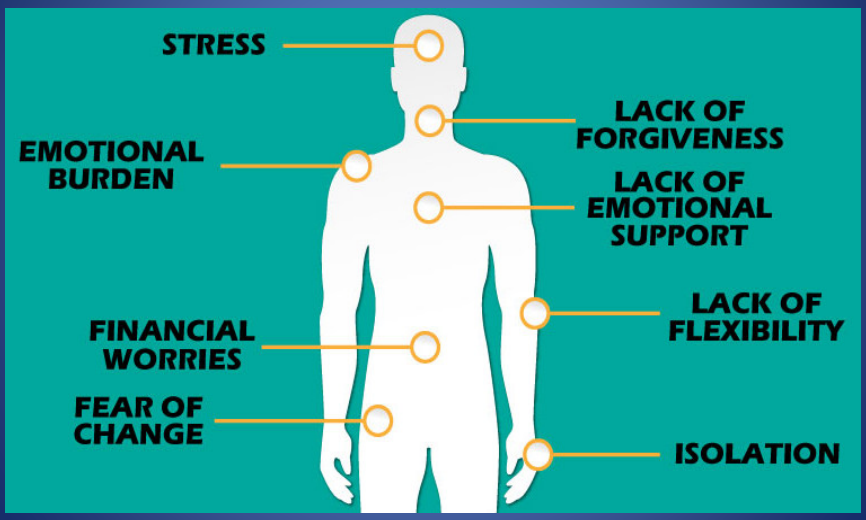
- Use **nonpharmacological** therapies and **non-opioid** pharmacologic therapies (such as anti-inflammatories) for chronic pain.
- Don't use opioids routinely for chronic pain.
- When opioids are used, combine them with nonpharmacological or non-opioid pharmacologic therapy, as appropriate, to provide greater benefits.

Tiers of Non-Surgical Treatment

Conservative management:

- Lifestyle Modifications
- Osteopathic Manual Medicine/Physical Therapy/Home Exercises
- Nutrition/Supplements
- Acupuncture
- **Injection Therapies**
- Psychological Counseling …huh????

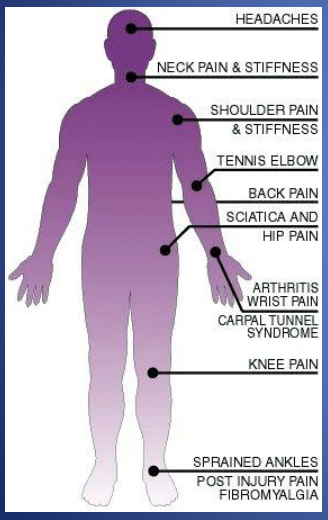
Pain beyond the physical…….

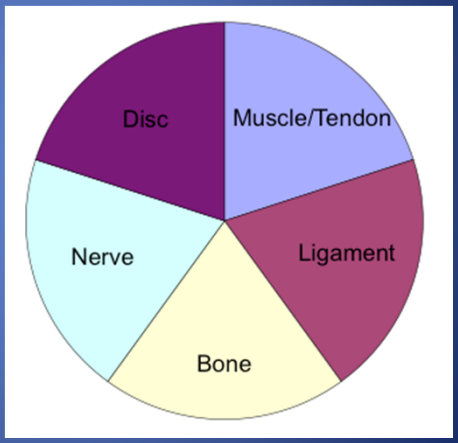


Our "Injectable Collectables":

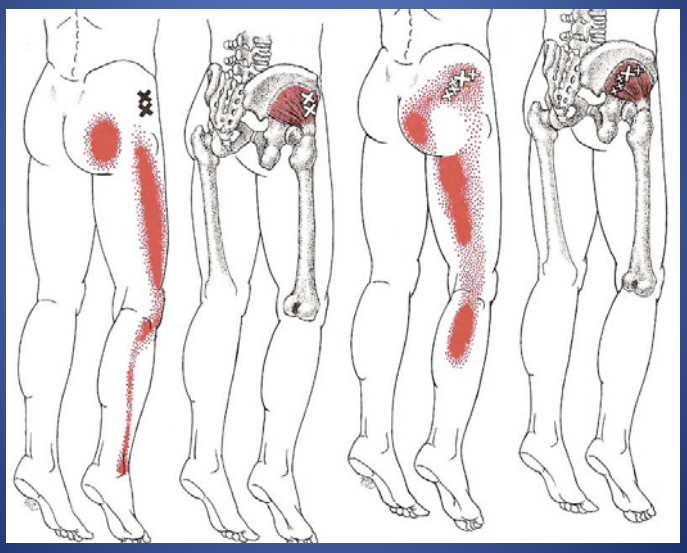
- Viscosupplementation (Hyaluronic Acid)
- Prolotherapy
- Peri-neural Subcutaneous Injections (PSI)
- Platelet rich plasma (PRP)
- Alkalinizing solutions
- Adipocytes

Pain Generators

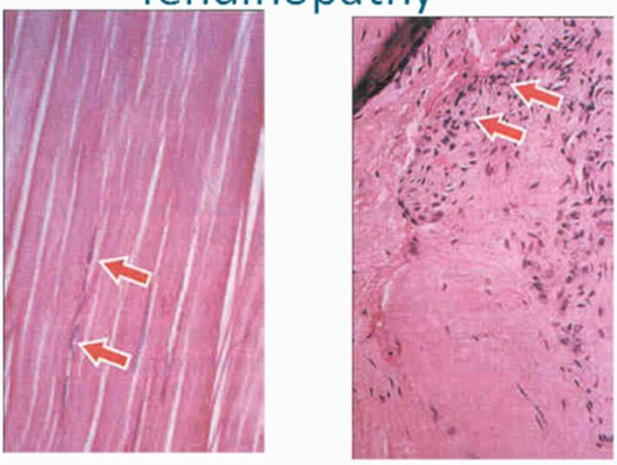




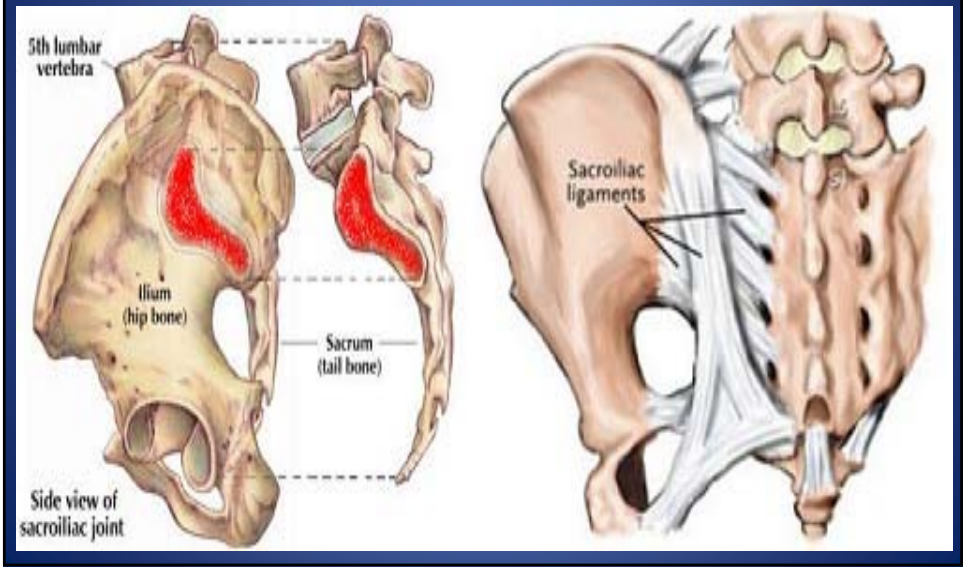
Gluteus Minimus Trigger Points



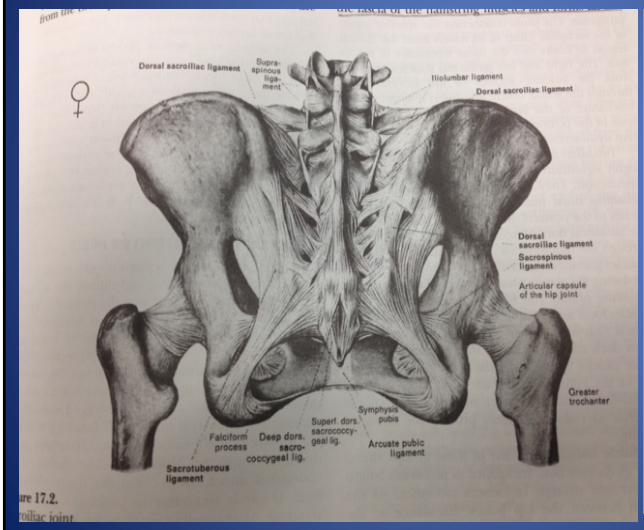
Tendinopathy

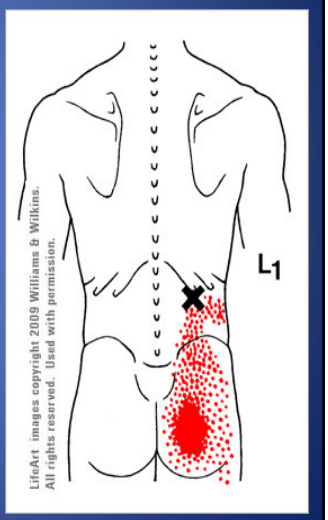


Lumbosacral Pain

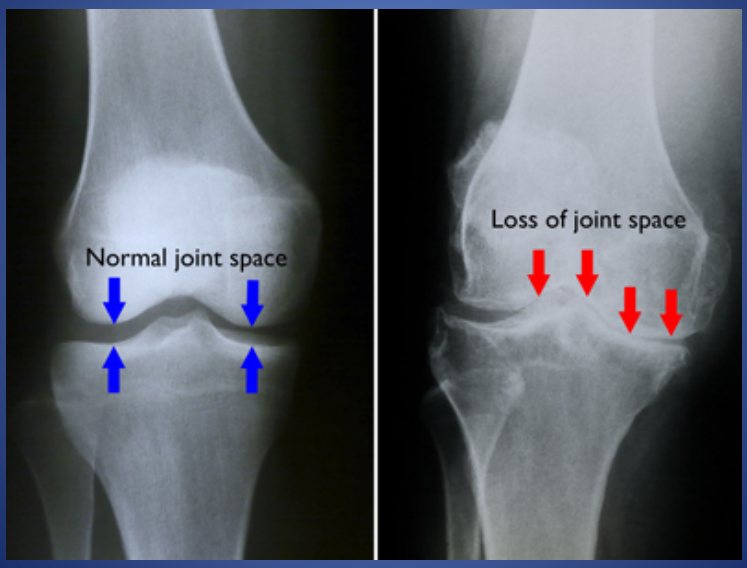


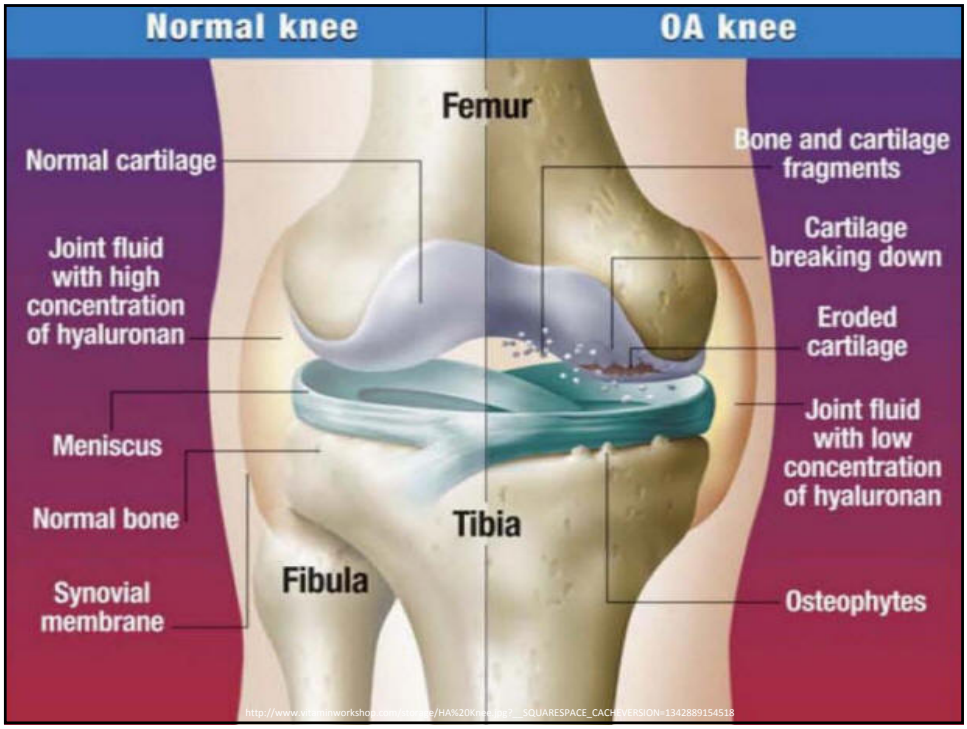
Common Pain Patterns





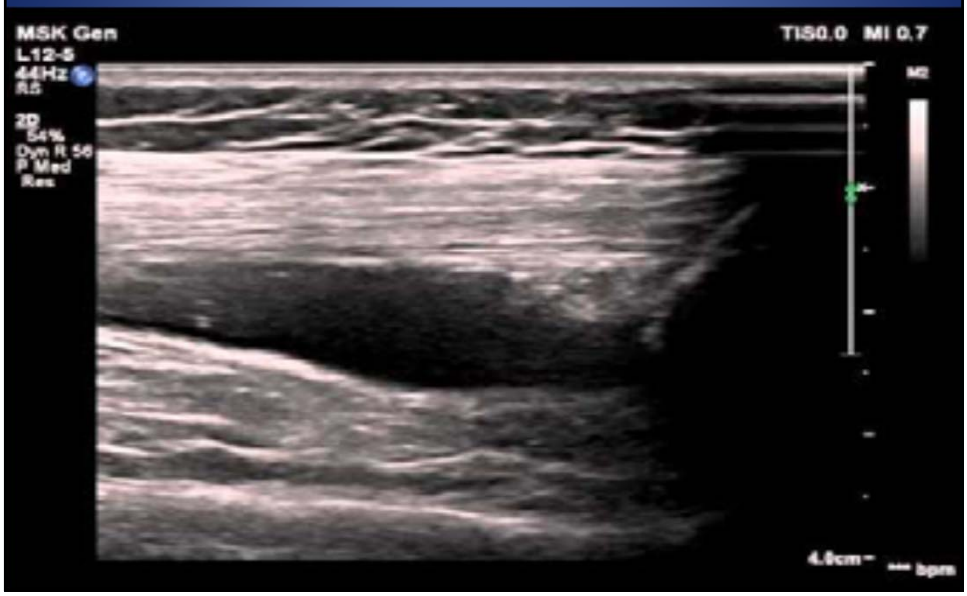
Knee Pain





MSK Ultrasound

Knee Effusion:



Viscosupplementation for the Treatment of Osteoarthritis of the Knee

- **Hyaluronic acid (HA)**: a major component of the synovial fluid.
- Increases the viscosity of the fluid and is one of the main lubricating components.
- Is an important component of articular cartilage.

Viscosupplementation for Osteoarthritis of the Knee: A Systematic Review and Meta-analysis

(*Ann Intern Med.* 2012;157(3):180-191.2012):

- Meta-analysis of large trials with blinded outcome assessment, found a small, clinically irrelevant effect of viscosupplementation on pain.
- For function, no effect remained.

Viscosupplementation for Osteoarthritis of the Knee: A Systematic Review and Meta-analysis (*Ann Intern Med.* 2012;157(3):180-191.2012):

- There are increased risks in adverse events associated with viscosupplementation, but causal mechanisms are unclear
- "We conclude that the benefit of visco supplementation on pain and function in patients with symptomatic osteoarthritis of the knee is minimal or nonexistent. Because of increased risks for serious adverse events and local adverse events, the administration of these preparations should be discouraged."

The Cochrane Collaboration (2006):

- The analyses support the contention that the HA class of products is superior to placebo.
- There is considerable "between-product" variability in the clinical response.
- The clinical effect for some products against placebo on some variables at some time points is in the moderate to large effect size range.

http://www.cochrane.org/CD005321/MUSKEL_viscosupplementation-for-the-treatment-of-osteoarthritis-of-the-knee

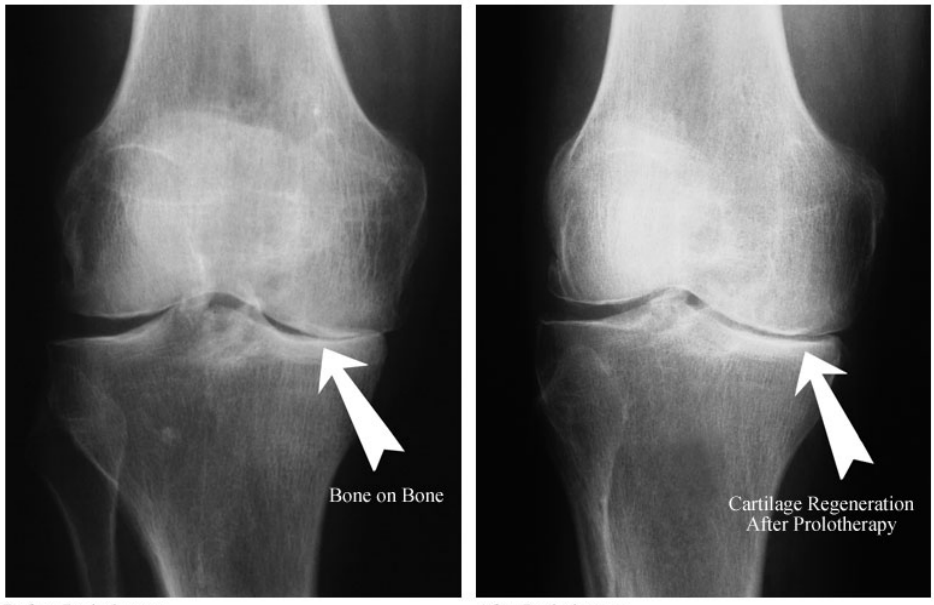
"BOTTOM LINE: There is a lack of quality evidence to support or refute the use of HA intra-articular injections in the treatment of osteoarthritis." While most organizations do not recommend the routine use of injectable hyaluronic acid, it is an option for patients not obtaining relief from other therapies.

https://medsask.usask.ca/documents/newsletters/35.1%20Viscosupplementation.pdf

Prolotherapy

- Injection into degenerated body regions.
- Typically use hyperosmolar dextrose and lidocaine for local anesthesia.
- Administered at joints or at tendons where they connect to bone.
- Treatments are typically given every six weeks for several months for 3 to 6 treatments.

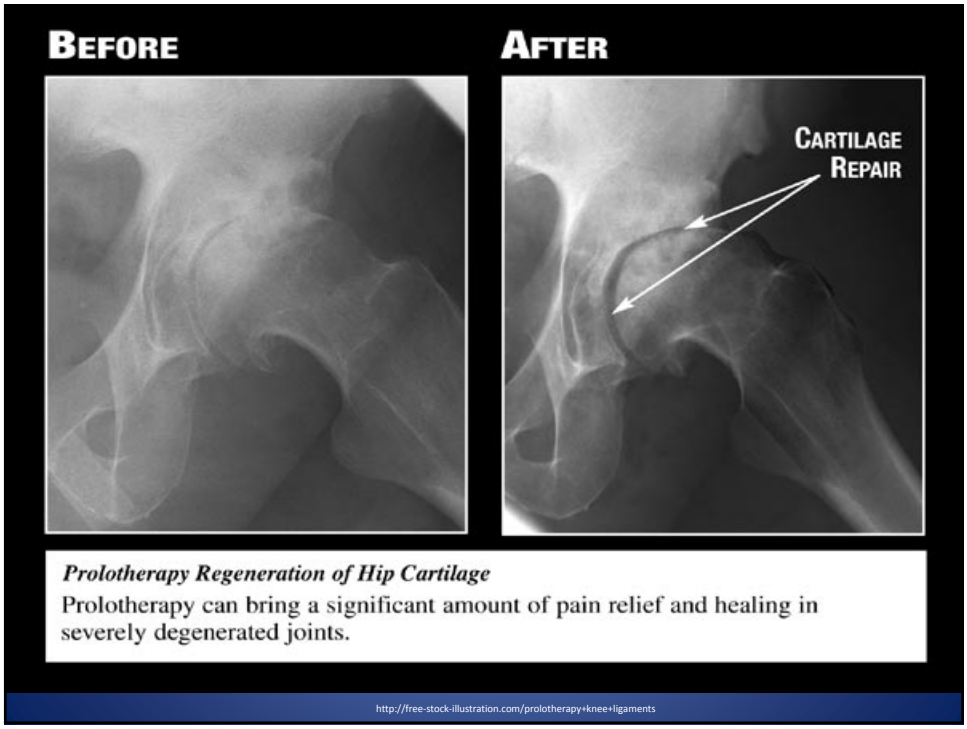
PROLOTHERAPY REGENERATES CARTILAGE



Before Prolotherapy
Knee X-ray Showing Bone on Bone

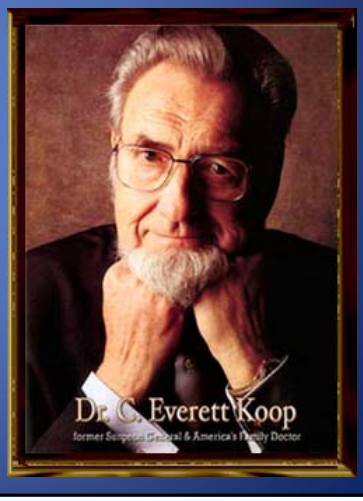
After Prolotherapy
Knee X-ray Showing Cartilage Regeneration After Prolotherapy

http://www.drshaunriddle.com/wp-content/uploads/2013/02/Prolo-Knee.jpg



Former U.S. Surgeon General, C. Everett Koop, on Prolotherapy treatment:

"My intractable pain was not intractable, and I was remarkably improved to the point where my pain ceased to be a problem."



American Journal of Sports Medicine:

In 2012, a systematic review and meta-analysis of seventeen trials studying various injection therapies found that prolotherapy and hyaluronic acid injection therapies were **more** effective than placebo when treating lateral epicondylosis.

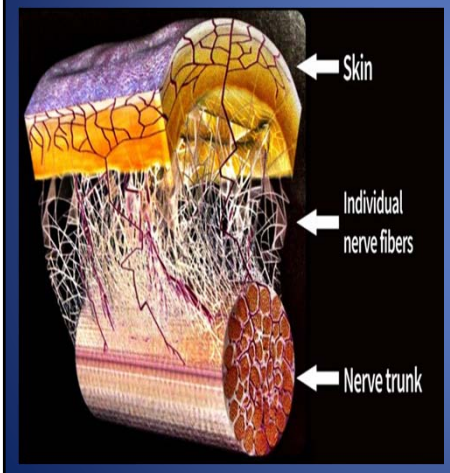
American Journal of Sports Medicine (7). doi:10.1177/0363546512458237. PMID 22972856.

Perineural Injection Technique:

- A technique in which subcutaneous tissue is injected with a 5% dextrose solution using approximately 0.5mL of D5W at each point at a 45degree angle 1-2cm apart.

- The cutaneous nerve is targeted to decrease nerve inflammation. The needle is inserted 0.5-1cm deep and the solution injected while withdrawing the needle to create a skin bleb.

Perineural Injection:

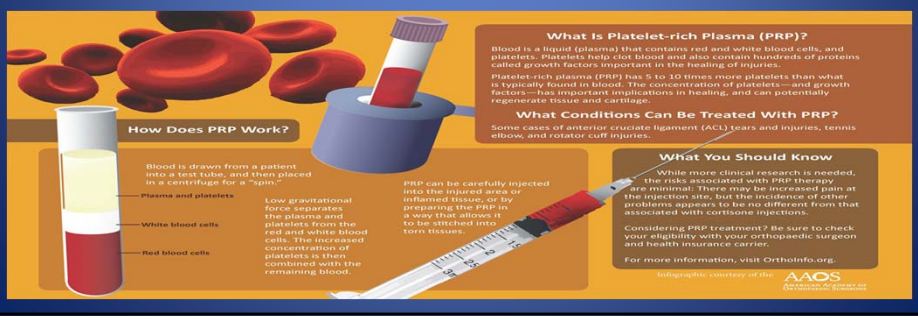


- Nerves sends hundreds of tiny nerve endings that reach just below the skin.
- For the treatment to be effective, the needle only needs to get below the skin to reach the individual nerve fibers.
- This allows the use of a very short small needle.

https://www.beaconortho.com/blog/perineural-injection-therapy-lyftogt-technique-henry-stiene-m-d/

Platelet-rich plasma (PRP)

- Blood plasma enriched with autologous platelets.
- PRP releases growth factors which stimulate healing of bone and soft tissues.



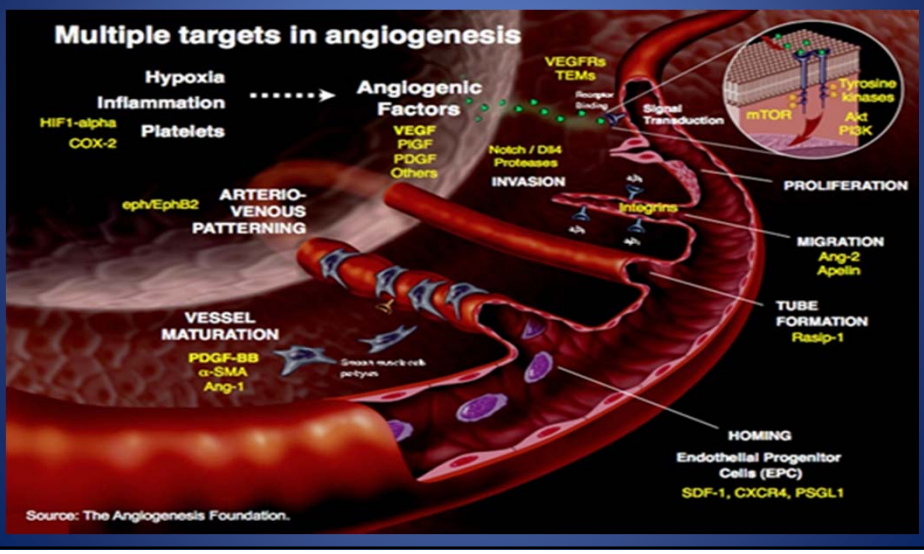
Growth factors

- PRP stimulates tissue recovery by increasing collagen synthesis, enhancing tendon stem cell proliferation, and protein expression.
- **PRP** increases **hyaluronic acid secretion** and caused proliferation of chondrocytes and mesenchymal stem cells in several studies.

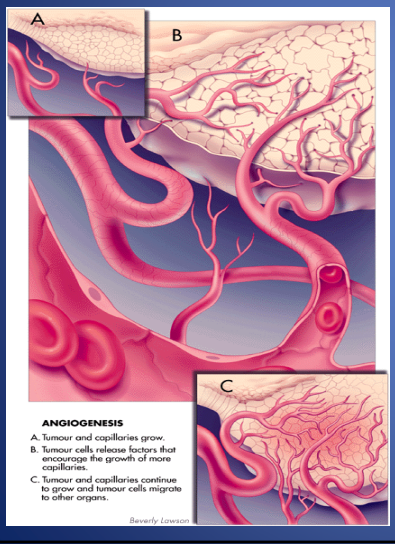
Important Growth Factors in PRP

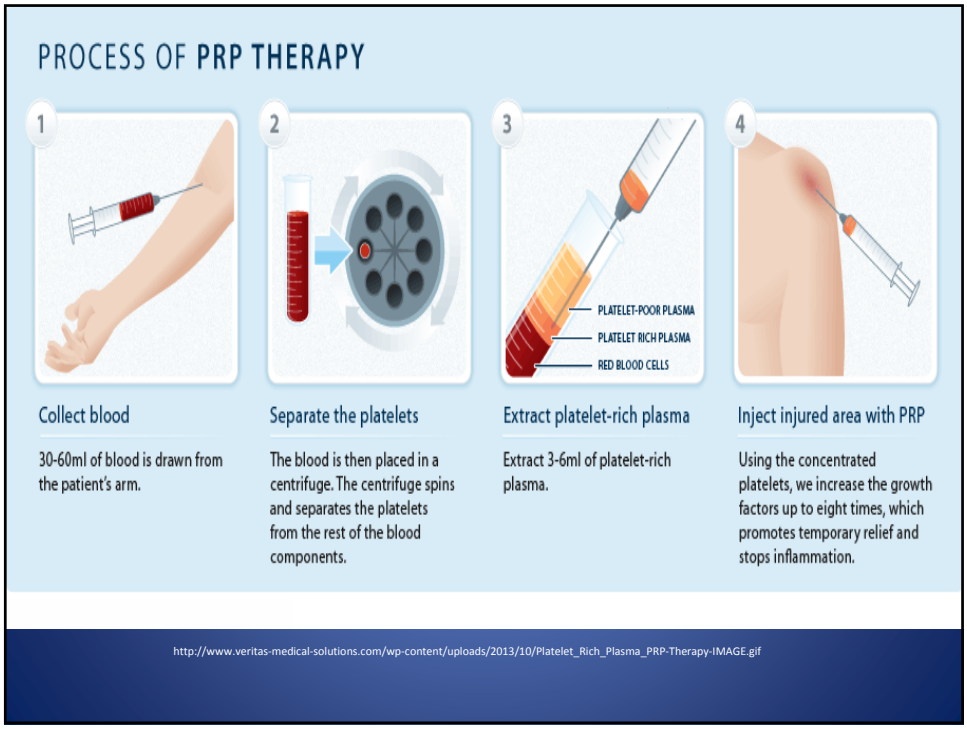
Growth Factor	Phase in Which Most Active	Functions
IGF-1	Inflammation, proliferation	Promotes proliferation and migration of cells, stimulates matrix production
TGF-β	Inflammation	Regulates cell migration, proteinase expression, fibronectin binding interactions, termination of cell proliferation, stimulation of collagen production
VEGF	Proliferation, remodeling	Promotes angiogenesis
PDGF	Proliferation, remodeling	Regulates protein and DNA synthesis at injury site, regulates expression of other growth factors
bFGF	Proliferation, remodeling	Promotes cellular migration, angiogenesis
EGF	Proliferation, remodeling	Stimulates proliferation and differentiation of epidermal cells, stimulates angiogenesis

Does This Look Familiar?



Remember, Angiogenesis: Not Always a "Bad" Thing!





http://www.veritas-medical-solutions.com/wp-content/uploads/2013/10/Platelet_Rich_Plasma_PRP-Therapy-IMAGE.gif

Efficacy of PRP in Knee OA

- Meta analysis performed by Zhang et. al
- 10 randomized trials consisting of 1069 pts.
- Conclusions:
  - PRP and HA are similar in terms of pain relief at 6 months post injection
  - PRP associated with greater, significantly better pain relief and functional improvement over 12 months post injection

Prolo vs PRP & other Proliferants:

- No head-head trials between Proliferants
- Some experts believe that PRP is stronger than Prolotherapy , but there is no evidence that PRP is more effective than Prolotherapy
- Its 3-4 times more expensive.

Hall M, et al. Platelet-rich Plasma: Current Concepts and Application in Sports Medicine. J Am Acad Orthopd Surg 2009; Oct; 17 (10): 602-608. Rabago D, et al. A systematic review of four injection therapies for lateral epicondylosis: prolotherapy, polidocanol, whole blood and platelet-rich plasma. BJSM 2009; 43:471-481. https://lecom.edu/content/uploads/2016/03/Prolotherapy_2016-Edited-for-PNP.pdf

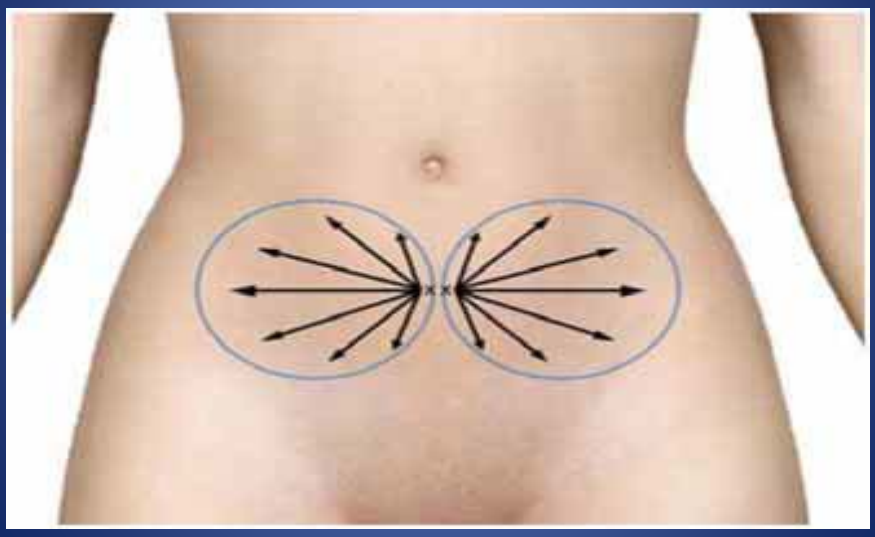
Effectiveness of Intra-articular Injections of Sodium Bicarbonate and Calcium Gluconate

- 74 pts. with knee OA, studied by Rosado et. Al (2015)
- Goal:
  - Evaluate efficacy of single vs. double doses of calcium gluconate when given with sodium bicarbonate
- Outcomes:
  - Solution of sodium bicarbonate and calcium gluconate is effective in reducing symptoms associated with OA
  - Results suggest that beneficial effect is maintained for one year **when given monthly**
    - Lasts for more than 6 months after discontinuation
  - An increase in Calcium gluconate dose is associated with further prevention of joint space narrowing

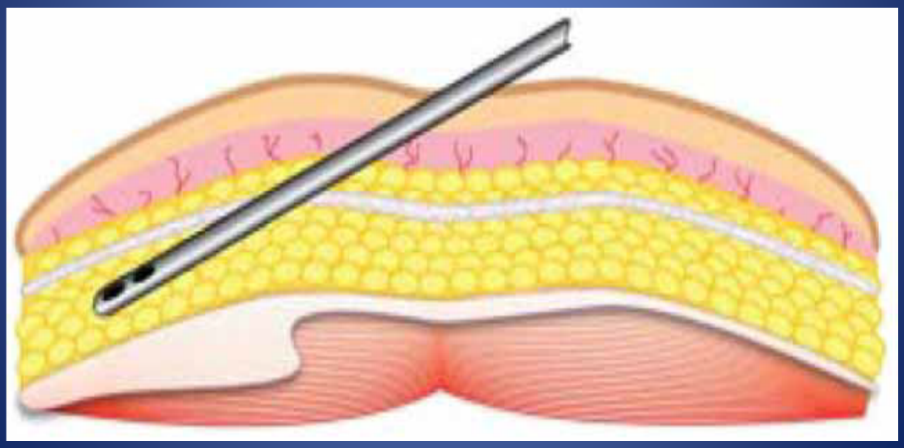
Comparison of Intra-articular Sodium Bicarbonate and Methylpredisolone

- 111 pts. with OA studied by Rosado et. Al (2017)
- Goal:
  - Evaluate effects of sodium bicarbonate and calcium gluconate solution compared to MP in treatment of OA in the knee
- Results:
  - After 3 months, all treatments significantly improved pain scores
- Conclusions:
  - Sodium bicarbonate and calcium gluconate are both effective in symptomatic treatment of OA in the knee
  - **Both are <u>more</u> effective than MP injections in reduction of knee OA symptoms**

Autologous Adipose-derived Stem Cell Injections:



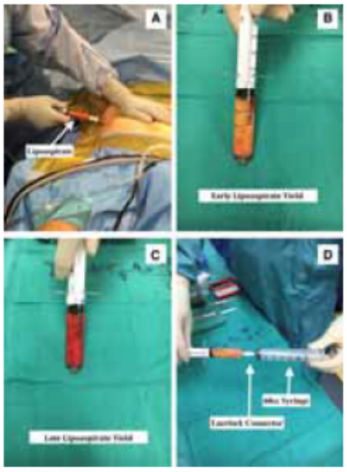
Microcannula below Scarpa's fascia in the adipose tissue plane. Centrifuge



Disposable microcannula cannulas for closed-syringe lipoaspiration of small-volume autologous adipose grafting

Autologous Adipose-Derived Stem/Stromal Cells (AD-SC)

- Historically mesenchymal stem cells (MSC's) have been studied from bone marrow aspiration.
- Adipose is easier to harvest.
- Offers higher nucleated, undifferentiated stem cell counts versus bone marrow.



AD-SC & BM Stem Cells:

Uysai AC et al. Differentiation of adipose derived stem cells for tendon repair. Methods Mol.Bio 2011: 702

- Studies reveal improved wound healing, fibroblast proliferation, migration and collagen secretion, increasing connective tissue strength and healing.
- Differentiation potential to become cartilage, tendon, ligament, bone and skeletal or smooth muscle and are also capable of expressing multiple growth factors that influence, control and manage damaged neighboring cells.

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