

Non-Operative Treatment... and when it is time to refer.

- Neck Pain
- Cervical Radiculopathy
- Back Pain
- Lumbar radiculopathy



William R Fitz, MD

Neck Pain

- Etiology: usually DDD or arthritis
- Treatment: Posture education and eliminate aggravating factors, NSAID, PT w exercises.
- If no improvement after 4-6 wks then consider referral for MRI and possible injections or ablations.

C2/3 Arthropathy



Cervical Radiculopathy

- Etiology: Usually discogenic or stenosis.
- Refer immediately with intractable pain and/or severe neurologic loss.
- Treatment with Prednisone, NSAID, Neurontin, posture education, eliminate aggravating factors, PT w traction and exercises.
- If no improvement after 3 wks or progressive neurologic decline then consider referral for MRI and possible surgery.

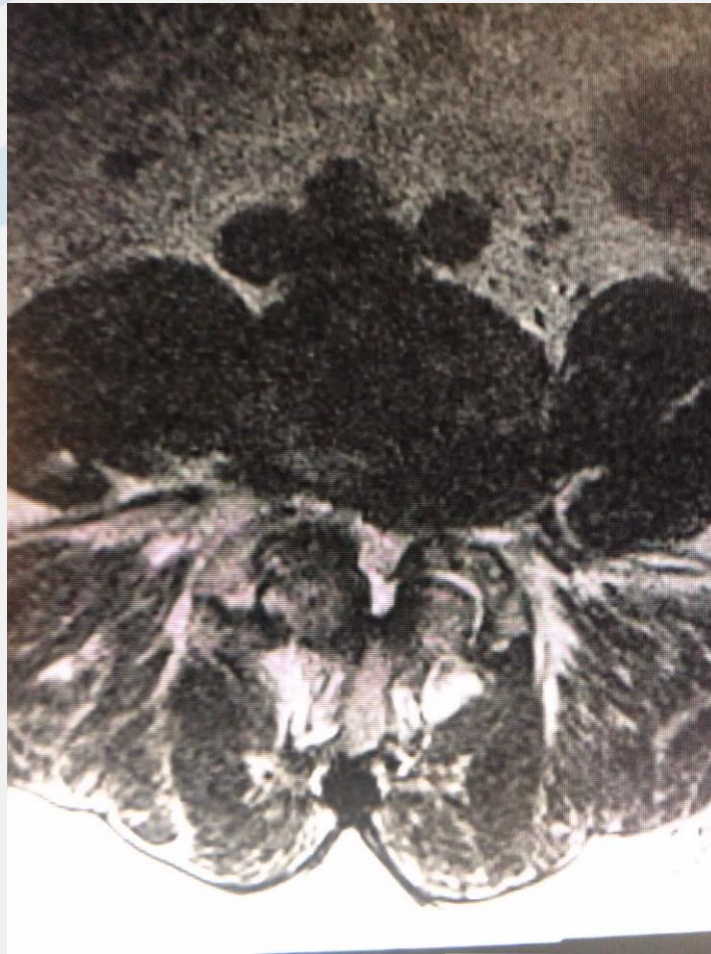
Cervical DDD



Back Pain

- Etiology: Usually DDD or arthritis
- Treatment: w back brace, NSAID, Prednisone for acute flare-up, restrictions, PT for exercises.
- If no improvement after 4-6 wks than consider referral for MRI and possible injections.

Severe arthropathy



Lumbar Radiculopathy

- Etiology: Usually HNP or stenosis
- Refer immediately with Intractable pain, pain at night, progressive neurologic loss, Bowel or bladder dysfunction, fracture, or suspected infection.
- Treatment: Avoid aggravating factors, Prednisone, NSAID, Neurontin, LSO, PT.
- If no improvement after 3-4 wks then consider referral for MRI and possible injections.

Severe Stenosis



OrthoBiologics



Hope vs Hype

William R Fitz, MD

Types of Orthobiologics

- Platelet Rich Plasma (PRP)
 - Growth factors stimulate tissue healing and can stimulate and signal local stem cells.
 - Cost Range from \$400 to \$650 and includes the office visit fee
- Bone Marrow Aspirate Concentrate (BMAC)
 - Autologous bone marrow contains stem and progenitor cells, which under the right conditions have the capacity to generate new tissues.
 - The method of aspiration can be done in the clinic but is most often done in the operating room.
 - Pricing varies based on the site of service and can range up to \$4,000 per injection.
- Amniotic Fluid, Placental Tissue, and Umbilical Cord Tissue
 - A growing number of products are being sold that are composed of these materials
 - These materials thus far appear to be safe but 12 infections were reported last year. However, the viability of cells or the ability to provide predictable and lasting improvement in the treatment of common causes of joint pain has not yet been established.

Orthobiologics

- Cell based therapies, such as PRP, can accelerate healing of these common injuries
 - Mild to moderate osteoarthritis/degenerative arthritis of joints, especially the hip and knee
 - Tendon injuries, including partial tears of the rotator cuff of the hip and lateral epicondylitis (tennis elbow)

Orthobiologics

Looking for quicker healing



Arthritis Today, November 2010:

“Physicians report that the demand for PRP has soared after pro golfer Tiger Woods received injections to accelerate healing after knee surgery.”

“And two Pittsburgh Steelers, Troy Polamalu and Hines Ward,

What are Orthobiologics?

- Biologic substances that help musculoskeletal injuries heal quicker

Platelet-rich plasma therapy: not new, no performance benefit

4:07 PM

Platelet-rich plasma (PRP) therapy made sports headlines even before **Dr. Anthony Galea** brought it back into the news. After suffering a sprained medial collateral ligament in his right knee in the January 2009 AFC Championship Game, Pittsburgh Steelers wide receiver **Hines Ward** received a variation of PRP therapy from a team physician and, two weeks later, caught two passes for 43 yards in a Super Bowl victory over the Arizona Cardinals.

The public revelation of Ward's treatment prompted widespread Internet speculation that the procedure, which involves extracting a patient's blood and then re-injecting a portion of it, was tantamount to blood doping. It isn't. In the most typical form of blood doping, blood is extracted from an athlete and then re-injected after enough time has passed that the athlete's body has replaced the lost blood on its own. The result is an increased number of oxygen-carrying red blood cells in the athlete and a hearty endurance boost.

Platelet-rich plasma therapy provides no such advantage. In PRP, about two tablespoons of a patient's blood are extracted and spun in a centrifuge until the red cells are separated from a concentrated dose of platelets. Platelets, which are responsible for the clotting following a cut, contain substances called growth factors, proteins that promote the growth of soft tissue such as ligaments or tendons. In PRP, the platelets are injected immediately back into the body. No red blood cells are injected and no performance benefit is gained.

Story Highlights

- Platelet-rich plasma therapy (PRP) is a treatment for musculoskeletal injuries.
- Some PRP is banned by WADA.
- A Dutch study found that PRP does not improve performance.



Hines Ward received platelet-rich plasma therapy after a knee injury in the January 2009 AFC Championship Game. He returned for the Super Bowl and caught two passes for 43 yards.

Ronald C. Madra/Sports Imagery/Getty Images

PRP is in the news

The screenshot shows the ESPN website interface. At the top, there are navigation links for NFL, NBA, MLB, Soccer, MMA, and NCAAF. The main navigation bar includes 'Home', 'Scores', 'Schedule', 'Standings', 'Stats', 'Fantasy Football: Sign Up', 'Teams', 'Tickets', 'Power Rankings', 'Free Agency', and 'More'. The featured article is titled 'Bosa injury 'significant'; PRP shot for McKinnon' and is dated 'SAN FRANCISCO 49ERS 3d - Nick Wagoner'. Below the article title is a video player showing a scene from a game with a player in a red jersey and a coach. The video player has a progress bar at 0:39 / 2:42 and a 'SHARE TO WATCH' overlay.

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Bosa injury 'significant'; PRP shot for McKinnon
SAN FRANCISCO 49ERS 3d - Nick Wagoner

Patriots teammates pulling for Josh Gordon beyond football
NEW ENGLAND PATRIOTS 18h - Mike Reiss

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Early signs: Jets GM Joe Douglas has a plan, and Adam Gase likes it
NEW YORK JETS 18h - Rich Cimini

Liam Collins 'trying to change' in

Bosa injury 'significant'; PRP shot for McKinnon

SAN FRANCISCO 49ERS - SAN FRANCISCO 49ERS - SAN FRANCISCO

SHARE TO WATCH
Total Views: 1,234,567
Views: 123,456
Likes: 12,345
Comments: 1,234

0:31

0:39 / 2:42

Biologic Agents in Athletes

- **The Use of Biologic Agents in Athletes with Knee Injuries.**
- **Abstract**
- **Biologic agents are gaining popularity in the management of bony and soft tissue conditions about the knee. They are becoming the mainstay of nonoperative therapy in the high-demand athletic population.** The most well-studied agents include platelet-rich plasma (PRP) and stem cells-both of which have shown promise in the treatment of various conditions. Animal and clinical studies have demonstrated improved outcomes following PRP treatment in early osteoarthritis of the knee, as well as in chronic patellar tendinopathy. Early clinical evidence also lends support for PRP in the augmentation of anterior cruciate ligament (ACL) reconstruction. Research investigating the role of biologic agents in collateral ligament and meniscal injuries is ongoing. Studies assessing the utility of stem cells have shown encouraging results in the setting of osteoarthritis. Unfortunately, strict regulations by the FDA continue to restrict their application in clinical practice. A major limitation in the interpretation of current data is the significant variability in the harvesting and preparation of both PRP and stem cells. As the volume and quality of evidence continue to grow, biologic agents are poised to become an integral component of comprehensive patient care throughout all orthopedic specialties.
- J Knee Surg 2016

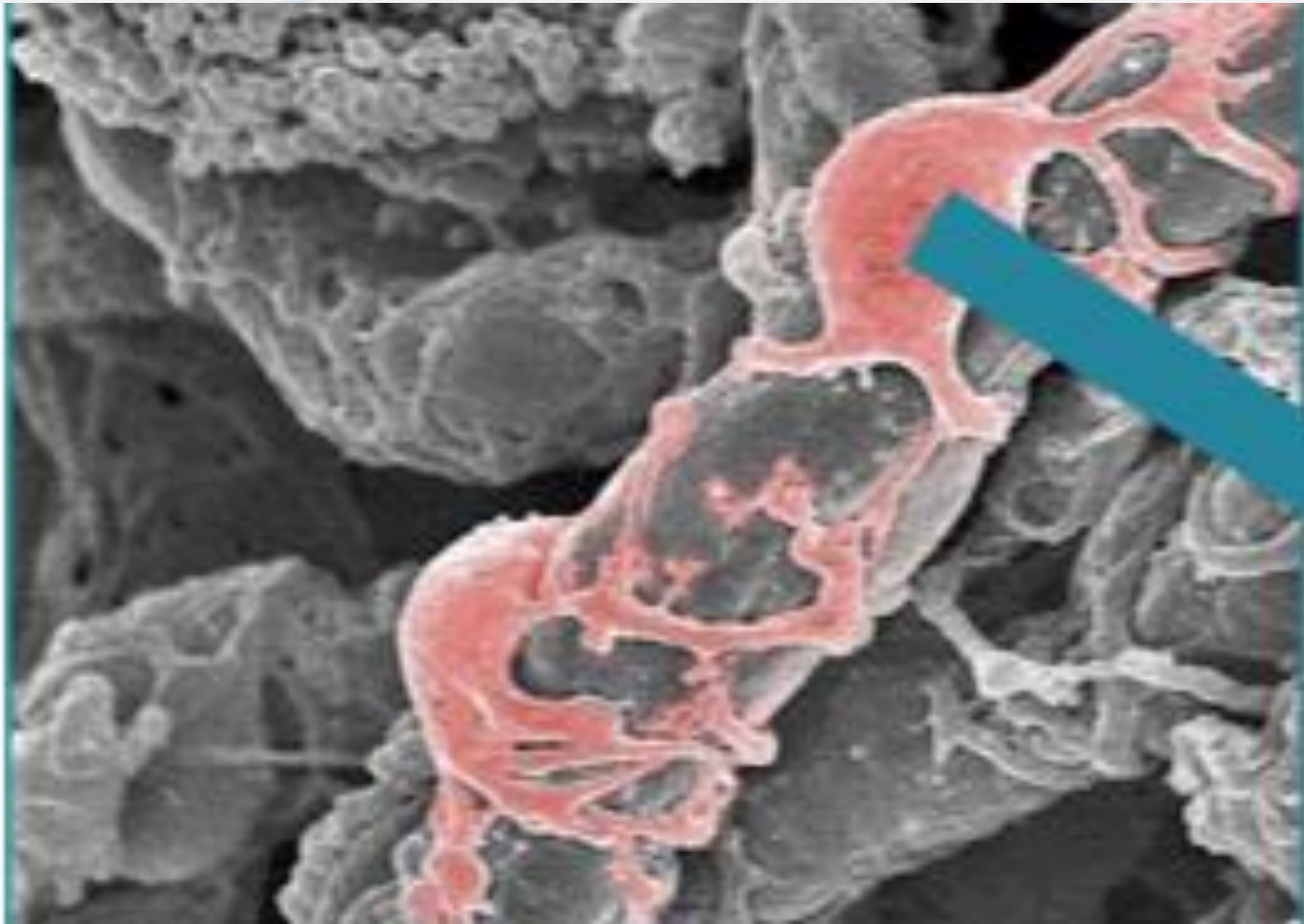
The Hype – Stem Cells

now offers Allografts containing **Stem Cells** as a Regenerative Therapy, based on a 21st-century therapeutic procedures to help alleviate your shoulder, hip, and knee pain without relying on complex surgical procedures or medication.

The How and Why – Allografts Containing Stem Cells

An Allograft containing Stem Cells is one of the most effective treatments available today to help in the regeneration of tendon injuries, ligament damage, and osteoarthritis. This procedure is non-invasive and harnesses your body's natural healing potential to combat shoulder, hip and knee problems. The whole procedure takes approximately one hour and has no known adverse side effects. The new cells will stimulate existing healthy cells and tissues to operate at a higher level of function, boosting the body's repair mechanisms to aid in the healing process. These highly adaptive cells then remain in the body, continually locating and repairing any damage they encounter.

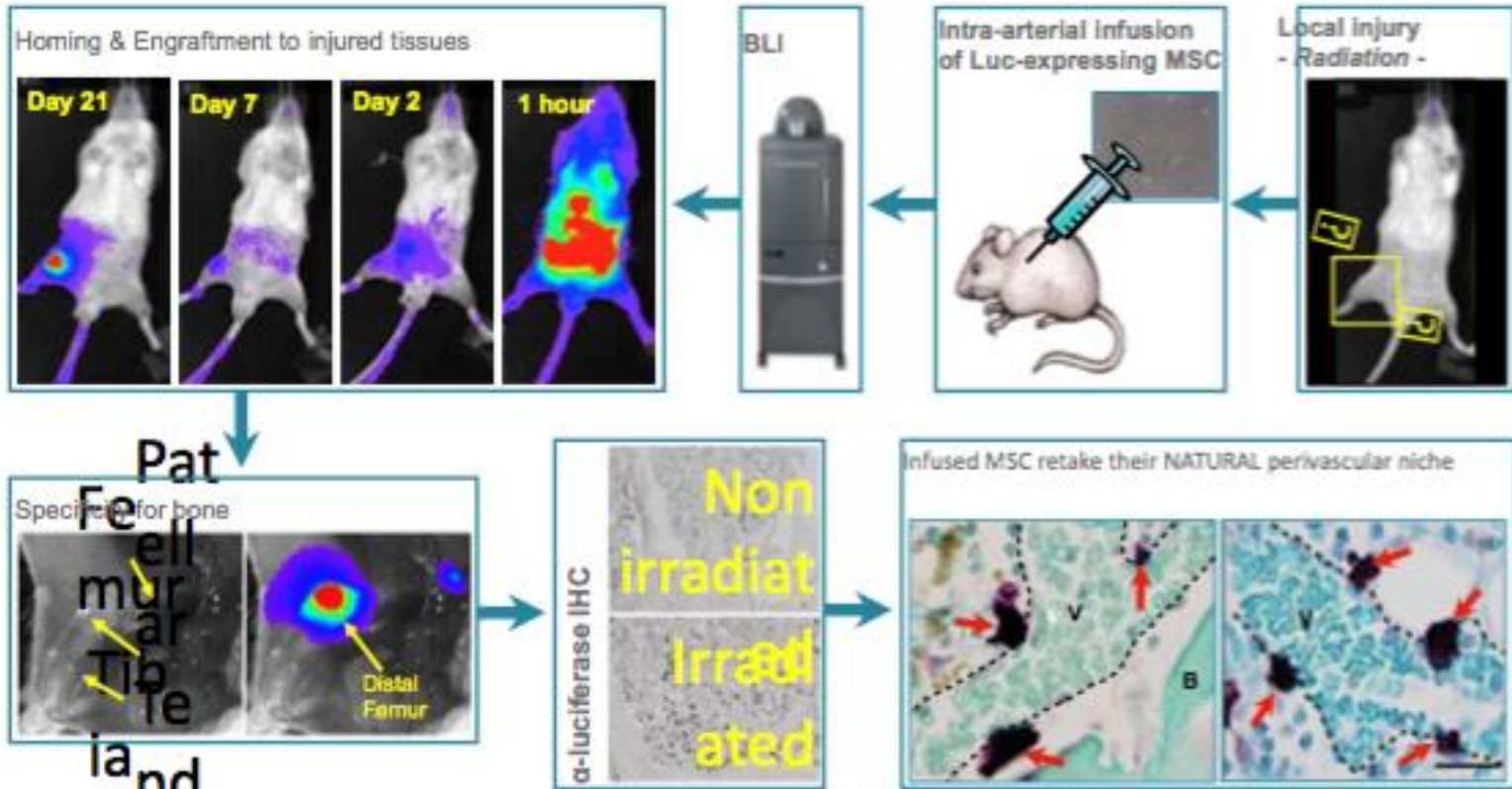
Stem cells are perivascular cells



How stem cells work

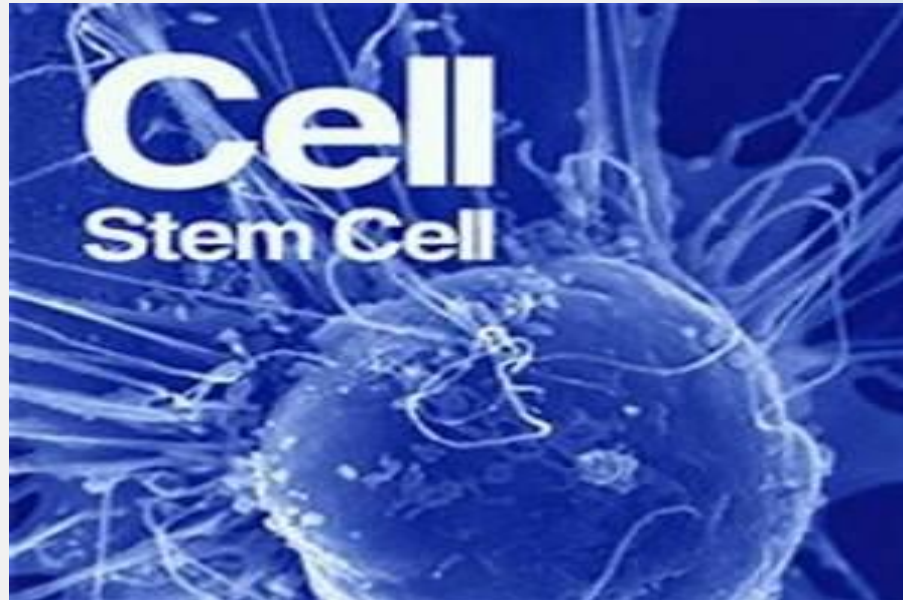
In Vivo – Injury model
- infusion -

(Lin P, Correa D, Caplan AI: Molecular Therapy 2012)



Stem Cells

- Derived from bone marrow (350K)
- Derived from fat (1 million)
- Operate as signaling cells and do not turn into tissue



Stem cells from Amniotic Fluid, Umbilical cord tissue, and placenta



No Viable Stem Cells

Are Amniotic Fluid Products Stem Cell Therapies? A Study of Amniotic Fluid Preparations for Mesenchymal Stem Cells With Bone Marrow Comparison

Alberto J. Panero, DO*, Alan M. Hirahara, MD, FRCSC, Wyatt J. Andersen, ATC, more...

[Show all authors](#) ▾

First Published March 7, 2019 | Research Article



<https://doi.org/10.1177/0363546519829034>

[Article information](#) ▾

Altmetric

29



Results:

MSCs could not be identified in the commercial AFPs or the unprocessed amniotic fluid. MSCs could be cultured from the bone marrow aspirates. Nucleated cells were found in 2 products (PalinGen and FloGraft), but most of these cells were dead. The few living cells did not exhibit established characteristics of MSCs. Growth factors and hyaluronan were present in all groups at varying levels.

No Viable Stem Cells

Note: 12 infections last year

References:

(1) Dustin R. Berger, Nicolette F. Lyons, and Neven J. Steinmetz. In Vitro Evaluation of Injectable, Placental Tissue-Derived Products for Interventional Orthopedics. Interventional Orthopedics Foundation Annual Meeting. Denver, 2015. <https://interventionalorthopedics.org/wp-content/uploads/2017/08/AmnioProducts-Poster.pdf>

(2) Liliya Beckett, Andrea Matuska, PhD, Stephanie Hon, DVM, Michelle L. Delco, DVM, PhD, Brian J. Cole, MD, Lisa A. Fortier, DVM, PhD. Proteomic analysis and cell viability of nine amnion-derived biologics. Orthopedic Research Society Annual Meeting, New Orleans, 2018.
<https://app.box.com/s/vcx7uw17gupg9ki06i57lno1tbjmwaf>

(3) Panero, A. J., Hirahara, A. M., Andersen, W. J., Rothenberg, J., & Fierro, F. (2019). Are Amniotic Fluid Products Stem Cell Therapies? A Study of Amniotic Fluid Preparations for Mesenchymal Stem Cells With Bone Marrow Comparison. *The American Journal of Sports Medicine*, 47(5), 1230–1235.
<https://doi.org/10.1177/0363546519829034>

Cracking down on Stem Cell Clinics

The lead up to and beginning of a likely crackdown

A subset of these clinics are particularly risky and egregious in their behavior. While this subset constitutes maybe “only” one or two hundred such clinics out of maybe a thousand such firms today, they are responsible for a disproportionate share of risk to patients. Thousands of patients are at real health dangers just from these clinics. These clinics also are financially harming vulnerable patients and their families as well. Furthermore, they also pose a threat to the legit stem cell field.

While possible stepped up action by the FDA has been called for and speculated about for years including by me here on this blog and in publications [such as my piece in Cell Stem Cell](#) earlier this year, it seems the FDA under Scott Gottlieb means business this time. My sense is that we are most likely witnessing the beginning of a real crackdown on the narrower subset of the riskiest few dozen stem cell clinic firms out there.

What’s different this time?

We’ve seen Gottlieb’s FDA issue more [warning letters](#) already. Not a flood of them, but more than in past years. Also this FDA has used much bolder language on stem cell clinics. Most importantly, the latest [warning letter](#) to umbilical cord supplier [Genetech](#) related to it and marketer [Liveyon](#) having been involved in documented serious adverse events in many patients was accompanied by a [press release](#) from the FDA that was historic in some ways. For instance, the agency indicated it’s going to be sending out letters potentially to many stem cell firms, focusing on those posing the greatest risks.

These letters, which admittedly are not official warning letters, still by the sound of it should be interpreted by [the 20 or so clinics](#) that get them as warnings of a sort. It makes sense that FDA picked the clinics it was most concerned about to send these letters to rather than sending them to all of the nearly 1,000 clinics in the US.



Dr. Scott Gottlieb, Commissioner of the FDA, has led a pronounced increase in activity on unproven stem cell clinics so far during his tenure.

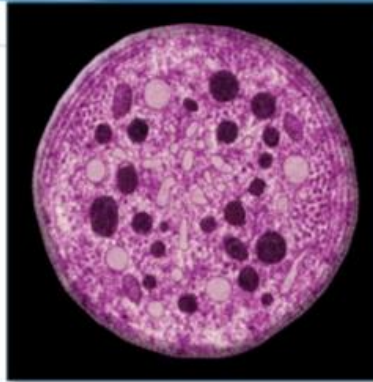
Platelet Rich Plasma - PRP

- Not all PRP is the same
 - ACP
 - LR-PRP
 - LP-PRP
 - Target specific

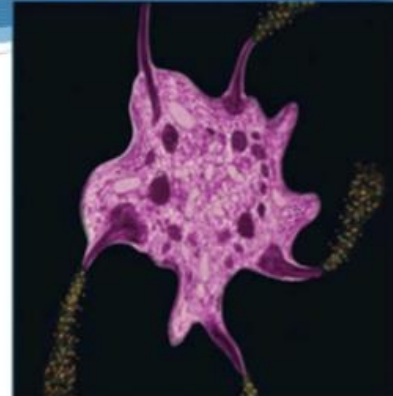


The Platelet does more than clot blood

Platelet as a Regenerative Powerhouse



- Platelet Cytokines
- Growth Factors



- Attract and Recruit Stem Cells
- Cell Proliferation and Tissue Growth



PRP

Growth Factors

Platelet- Rich Plasma

- Insulin-like growth factor (IGF-1)
 - Amplifies platelet response
- Hepatocyte growth factor (HGF)
 - Mitogenic, morphogenic and antiapoptotic functions

Kosai K, Matsumoto K, Fukanoshi H, et al. Hepatocyte growth factor prevents endotoxin-induced lethal hepatic failure in mice. *Hepatology* 1990;30(1):151–159.

Matsumoto K, Nakamura T. Hepatocyte growth factor: molecular structure, roles in liver regeneration and other biological functions. *Crit Ver Oncog* 1992;3(1–2):27–54.

PRP

Growth Factors

Platelet- Rich Plasma

- Vascular endothelial growth factor (VEGF)
 - Powerful angiogenesis stimulator that can help with the healing of chronic wounds and endochondral ossification
- Basic fibroblastic growth factor (bFGF)
 - Involved in angiogenesis
- Epidermal growth factor (EGF)
 - Mitogenic factor for fibroblasts, endothelial cells and keratinocytes

Bennett SP, Griffiths GD, Schor AM, et al. Growth factors in the treatment of diabetic foot ulcers. *Br J Surg* 2003;90(2):133–146.

Maes C, Carmeliet P, Moermans K, et al. Impaired angiogenesis and endochondral bone formation in mice lacking the vascular endothelial growth factor isoforms VEGF164 and VEGF188. *Mach Dev* 2002;111(1–2):61–73.

Platelet Function for tissue repair

- Promotes angiogenesis
- Promotes formation of extracellular collagen rich matrix
- Promotes Chemotaxis of stem cells
- Induces proliferation of tenocytes and tendon stem cells
- Has anti-inflammatory and antibiotic effect
- Steroids decrease tenocyte viability

PRP in Tendinopathies/OA

- Level I Evidence for
 - Lateral Epicondylitis
 - Patellar Tendinopathy
 - OA Symptoms

The 3 best indications for PRP

- Elbow Tendinopathy
- Gluteal Tendinopathy
- Knee osteoarthritis- mild to moderate arthritis. Not likely to work for severe bone on bone arth



PRP mechanism of action

- **Platelet rich plasma (PRP) induces chondroprotection via increasing autophagy, anti-inflammatory markers, and decreasing apoptosis in human osteoarthritic cartilage. 2017**
- **RESULTS:**
- PRP increased significantly the proliferation of chondrocytes, decreased apoptosis and increased autophagy and its markers along with its regulators FOXO1, FOXO3 and HIF-1 in osteoarthritic chondrocytes. Furthermore, PRP caused a dose-dependent significant decrease in MMP3, MMP13, and ADAMTS-5, IL-6 and COX-2 while increasing TGF- β , aggrecan, and collagen type 2, TIMPs and intracellular IL-4, IL-10, IL-13.
- **CONCLUSION:**
- These results suggest that PRP could be a potential therapeutic tool for the treatment of OA.

PRP Effects

- The Positive Effects of Different Platelet-Rich Plasma Methods on Human Muscle, Bone, and Tendon Cells. AJSM 2012
- Addition of PRPLP to osteocytes, myocytes, and tenocytes significantly increased cell proliferation ($P .05$) compared with the controls. Adding PRPDS to osteoblasts and tenocytes increased cell proliferation significantly ($P .05$), but no significance was shown for its addition to myocytes. The addition of PRPHP significantly increased cell proliferation compared with the controls only when added to tenocytes ($P .05$).

Case Report

- 76 yo white female c/o lateral hip pain for 8 years since THR.
- Exam FROM, Neuro intact, tender over lat hip, gait normal
- X-ray without signs of loosening of component.
- US confirmed Gluteus medius tendon tear.
- Pain free after 2 PRP injections

Most Misunderstood

- Lateral hip Pain
 - 90% is not associated with Bursitis
 - Most commonly associated with a chronic tendinopathy of the Gluteus minimus or Gluteus medius as they insert on the Greater Trochanter of the femur
 - The rotator cuff of the hip

Lateral Hip

What causes the pain?

Research shows us that lateral hip pain is caused by wear and tear in the tendons of the muscles around your hip as they insert on the bone.



Normal Gluteus Medius and Minimus



Gluteus Medius Partial Tear



Severe Gluteus Medius and Minimus Atrophy



PRP for Gluteal Tendinopathy

Orthop J Sports Med. 2016 Nov 9;4(11):2325967116671692. eCollection 2016 Nov.

Platelet-Rich Plasma Injections With Needle Tenotomy for Gluteus Medius Tendinopathy: A Registry Study With Prospective Follow-up.

Lee JJ¹, Harrison JR¹, Boachie-Adjei K¹, Vargas E¹, Moley PJ¹.

⊕ Author information

Abstract

BACKGROUND: Gluteal tendinopathy is a prevalent condition that can be associated with significant pain and disability. To date, no studies have prospectively assessed the efficacy of intratendinous platelet-rich plasma (PRP) injections as a minimally invasive treatment for gluteus medius tendinopathy.

PURPOSE: To prospectively assess the efficacy of intratendinous PRP injections as treatment for chronic recalcitrant gluteus medius tendinopathy.

STUDY DESIGN: Case series; Level of evidence, 4.

METHODS: During the study period between July 2011 and November 2015, data were collected from the Hospital for Special Surgery Center for Hip Preservation Outcomes Registry on participants who underwent ultrasound-guided intratendinous PRP injections for recalcitrant gluteus medius tendinosis and/or partial tears of the tendon associated with moderate to severe lateral hip pain for longer than 3 months. All participants were assessed pre- and postinjection with 4 outcome measures: modified Harris Hip Score (mHHS), Hip Outcome Score-Activities of Daily Living subscale (HOS-ADL), Hip Outcome Score-Sport-Specific subscale (HOS-Sport), and the International Hip Outcome Tool-33 (iHOT-33). Demographic data, including age, sex, height, weight, body mass index, and smoking status, were also collected.

RESULTS: A total of 21 patients were included in the study, with a mean follow-up of 19.7 months (range, 12.1-32.3 months). The mean improvements from preinjection to postinjection follow-up were 56.73 to 74.17 for mHHS, 68.93 to 84.14 for HOS-ADL, 45.54 to 66.72 for HOS-Sport, and 34.06 to 66.33 for iHOT-33. All mean outcome measure improvements were clinically and statistically significant ($P < .001$). Length of follow-up was positively correlated with improvements in HOS-ADL ($P = .021$) and HOS-Sport ($P = .004$) scores. No adverse events were observed during or after the procedure.

CONCLUSION: In this registry study with prospective follow-up, we found ultrasound-guided intratendinous PRP injections to be a safe and effective treatment option for chronic recalcitrant gluteus medius tendinopathy due to moderate to severe tendinosis and/or partial tendon tears. Well-powered randomized controlled studies are warranted to confirm our findings and further define the ideal candidates for this treatment.

PRP better than steroid for Gluteal Tendinopathy

Am J Sports Med. 2018 Mar;46(4):933-939. doi: 10.1177/0363546517745525. Epub 2018 Jan 2.

The Effectiveness of Platelet-Rich Plasma Injections in Gluteal Tendinopathy: A Randomized, Double-Blind Controlled Trial Comparing a Single Platelet-Rich Plasma Injection With a Single Corticosteroid Injection.

Fitzpatrick J^{1,2,3}, Bulsara MK⁴, O'Donnell J⁵, McCrory PR⁶, Zheng MH^{1,7}.

Author information

Abstract

BACKGROUND: Gluteus medius/minimus tendinopathy is a common cause of lateral hip pain or greater trochanteric pain syndrome.

HYPOTHESIS: There would be no difference in the modified Harris Hip Score (mHHS) between a single platelet-rich plasma (PRP) injection compared with a corticosteroid injection in the treatment of gluteal tendinopathy.

STUDY DESIGN: Randomized controlled trial; Level of evidence, 1.

METHODS: There were 228 consecutive patients referred with gluteal tendinopathy who were screened to enroll 80 participants; 148 were excluded (refusal: n = 42; previous surgery or sciatica: n = 50; osteoarthritis, n = 17; full-thickness tendon tear, n = 17; other: n = 22). Participants were randomized (1:1) to receive either a blinded glucocorticoid or PRP injection intratendinously under ultrasound guidance. A pain and functional assessment was performed using the mHHS questionnaire at 0, 2, 6, and 12 weeks and the patient acceptable symptom state (PASS) and minimal clinically important difference (MCID) at 12 weeks.

RESULTS: Participants had a mean age of 60 years, a ratio of female to male of 9:1, and mean duration of symptoms of >14 months. Pain and function measured by the mean mHHS showed no difference at 2 weeks (corticosteroid: 66.95 ± 15.14 vs PRP: 65.23 ± 11.60) or 6 weeks (corticosteroid: 69.51 ± 14.78 vs PRP: 68.79 ± 13.33). The mean mHHS was significantly improved at 12 weeks in the PRP group (74.05 ± 13.92) compared with the corticosteroid group (67.13 ± 16.04) (P = .048). The proportion of participants who achieved an outcome score of ≥74 at 12 weeks was 17 of 37 (45.9%) in the corticosteroid group and 25 of 39 (64.1%) in the PRP group. The proportion of participants who achieved the MCID of more than 8 points at 12 weeks was 21 of 37 (56.7%) in the corticosteroid group and 32 of 39 (82%) in the PRP group (P = .016).

CONCLUSION: Patients with chronic gluteal tendinopathy >4 months, diagnosed with both clinical and radiological examinations, achieved greater clinical improvement at 12 weeks when treated with a single PRP injection than those treated with a single corticosteroid injection. Registration: ACTRN12613000677707 (Australian New Zealand Clinical Trials Registry).

KEYWORDS: gluteal tendinopathy; leukocyte; platelet-rich plasma

PRP vs Steroid in Gluteal Tendinopathy

Am J Sports Med. 2018 Mar;46(4):933-939. doi: 10.1177/0363546517745525. Epub 2018 Jan 2.

The Effectiveness of Platelet-Rich Plasma Injections in Gluteal Tendinopathy: A Randomized, Double-Blind Controlled Trial Comparing a Single Platelet-Rich Plasma Injection With a Single Corticosteroid Injection.

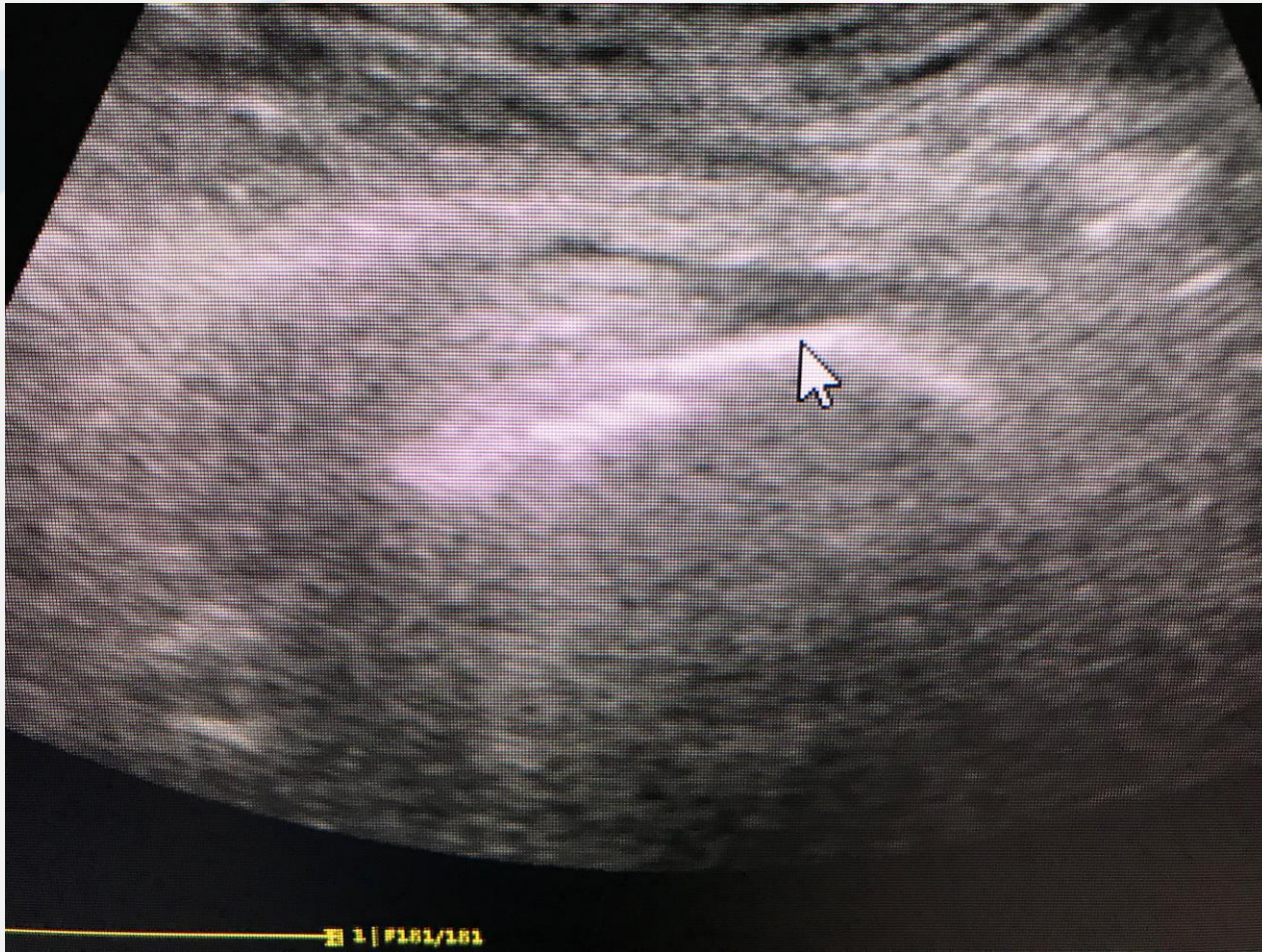
Fitzpatrick J^{1,2,3}, Bulsara MK⁴, O'Donnell J⁵, McCrary PR⁶, Zheng MH^{1,7}.

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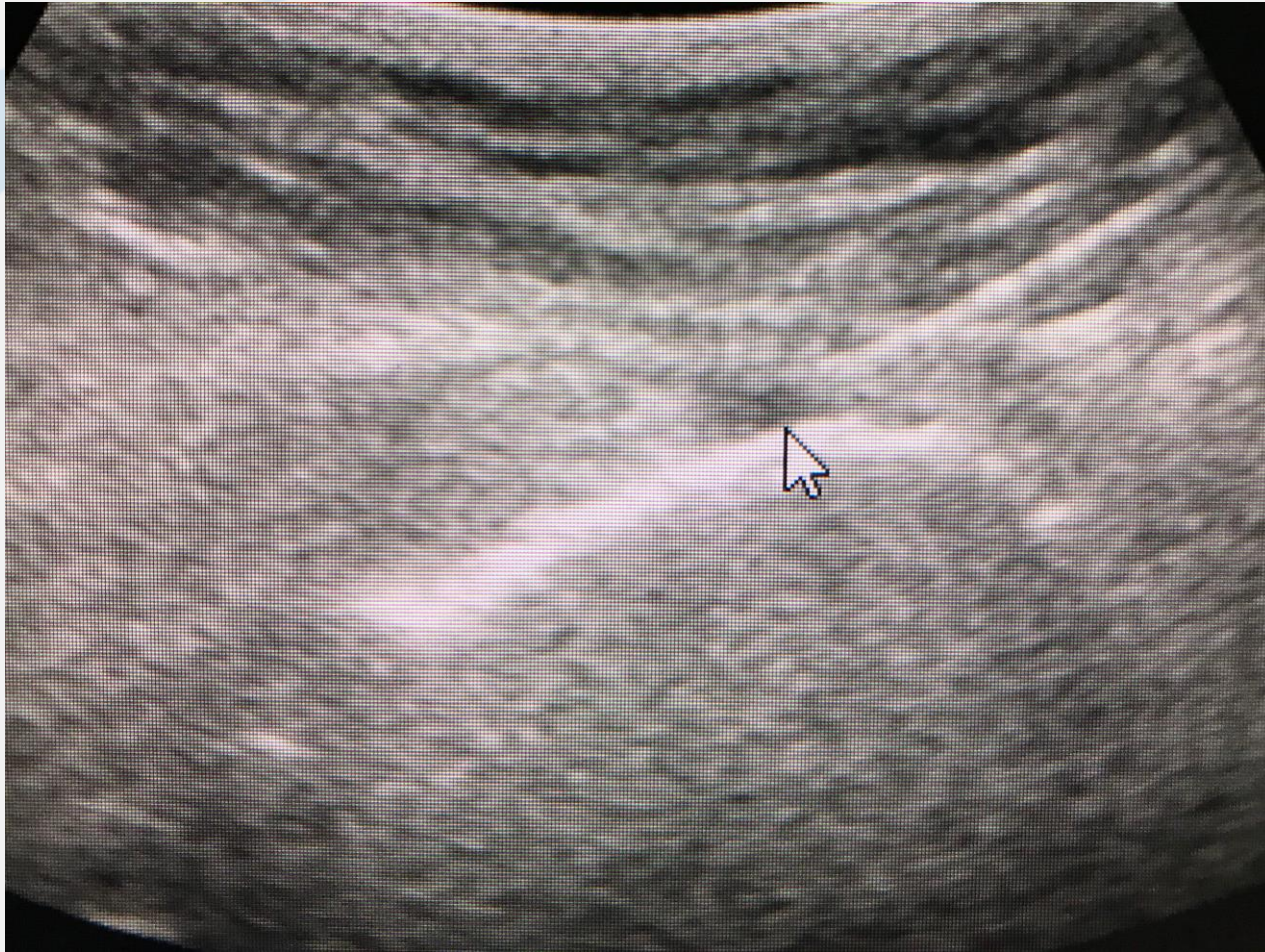
PRP for Chronic Tendinopathy

- **Treatment of Chronic Tendinopathy with Ultrasound-Guided Needle Tenotomy and Platelet-Rich Plasma Injection 2011**
- Conclusions: In this case series, we found US-guided percutaneous needle tenotomy followed by PRP injection to be a safe and effective treatment for chronic, recalcitrant tendinopathy, and this treatment was associated with sonographically apparent improvements in tendon morphology.

Partial Gluteus Medius Tear



Partial Gluteus Medius tear after PRP



Systematic review:PRP works for Tendinopathy

- Efficacy of platelet-rich plasma injections for symptomatic tendinopathy: systematic review and meta-analysis of randomised injection- controlled trials. 2017
- Results A total of 16 randomised controlled trials (18 groups) of PRP versus control were included. Median sample size was 35 patients, a study size that would require an effect size 1.0 to achieve statistical significance. **PRP was more efficacious than control in reducing tendinopathy pain, with an effect size of 0.47 (95% CI 0.22 to 0.72, $p < 0.001$), signifying a moderate treatment effect.**

PRP better than steroid for lateral epicondylitis

- **Positive Effect of an Autologous Concentrate in Lateral Epicondylitis in a Double-Blind Randomized Controlled Trial. (2010)**
- Results: 100 Patients. PRP vs Corticosteroid. 27cc blood to 3cc PRP.
- No cell counts. One injection at point of tenderness and peppering the tendon. No adverse events (pain from injection for 3-4 wks). Steroid group was better 0-8wks out. PRP better @ 12-52 wk w signif improvement in pain and DASH (disabilities of the arm, shoulder, hand) scores. PRP group improved up to 52 wks.

PRP for Lat Epicondylitis

Vol. 39, No. 6, 2011

PRP vs Corticosteroid Injection in Lateral Epicondylitis 1203

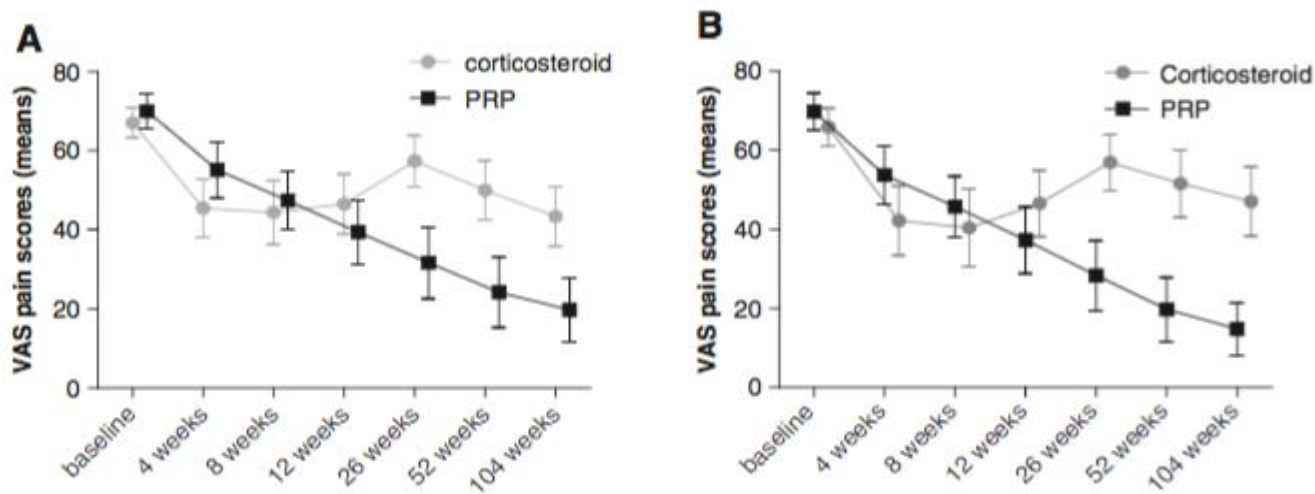


Figure 2. The course of visual analog scale (VAS) pain scores across assessment points. Bars present 95% confidence intervals. Patients with chronic lateral epicondylitis were randomly assigned to the platelet-rich plasma (PRP) group or the corticosteroid group. A, intention to treat; B, reintervention excluded.

PRP safe and effective for Knee OA

- **Intra-articular Autologous Conditioned Plasma Injections Provide Safe and Efficacious Treatment for Knee Osteoarthritis: An FDA-Sanctioned, Randomized, Double-blind, Placebo-controlled Clinical Trial. 2016**
- **RESULTS:**
- No adverse events were reported for ACP administration. Furthermore, the results demonstrated no statistically significant difference in baseline WOMAC scores between the 2 groups. However, in the ACP group, WOMAC scores at 1 week were significantly decreased compared with baseline scores, and the scores for this group remained significantly lower throughout the study duration. At the study conclusion (12 months), subjects in the ACP group had improved their overall WOMAC scores by 78% from their baseline score, compared with 7% for the placebo group.
- **CONCLUSION:**
- **ACP is safe and provides quantifiable benefits for pain relief and functional improvement with regard to knee OA.** No adverse events were reported for ACP administration. After 1 year, WOMAC scores for the ACP subjects had improved by 78% from their baseline score, whereas scores for the placebo control group had improved by only 7%. Other joints affected with OA may also benefit from this treatment.

PRP helps Knee OA

1) Effectiveness of platelet-rich plasma in the treatment of moderate knee osteoarthritis: a randomized prospective study (Phys Ther Sci. 2015)

Results: 102 patients w Gd 3 OA were treated w 1, 2, or 3 injections of PRP at 2 wk intervals. 30-40 cc blood to 4-5 cc PRP (no cell counts). No complications. VAS, WOMAC and TUG scores all significantly improved compared to baseline over 6 months. A single injection showed significant less improvement compared to 2 and 3 injections.

PRP better than Placebo in Knee OA

- **Treatment With Platelet-Rich Plasma Is More Effective Than Placebo for Knee Osteoarthritis. (2013)**
- Results: Randomized, double blind, placebo control. 26 w one PRP injection, 25 w 2 PRP injections, 23 w one normal saline injection. 50cc blood to 8cc PRP per knee w 2.4 billion plts per knee. Signif pain reduction in both PRP groups and worsening pain in saline grp. Signif improvement of WOMAC score in single inj grp but not in double inj group even though scores improved as trends were the same in pain and WOMAC for 6 months although started to show decrease in improvements at 6 months.

PRP better than Steroid

- Effect of single injection of platelet-rich plasma in comparison with corticosteroid on knee osteoarthritis: a double-blind randomized clinical trial. 2016
- **CONCLUSIONS:**
- Our study demonstrated that one shot of PRP injection, decreased joint pain more and longer-term, alleviated the symptoms, and enhanced the activity of daily living and quality of life in short-term duration in comparison with CS.

PRP better than HA for knee OA

- **2) Treatment of Knee Osteoarthritis with Autologous Platelet-Rich Plasma in Comparison with Hyaluronic Acid. (2012)**
- Results: 120 patients. Three injections in one wk intervals. 27cc blood to 3cc PRP w 4.5x concentration w 2 billion total platelet. Safe w no adverse events. Statistically better results in PRP group with both improved pain and WOMAC (assesses pain, stiffness, function) scores.

PRP better than HA for Knee OA

Plasma (PRP) Versus Hyaluronic Acid (A one-year randomized clinical trial). (Clin Med Insights Arthritis Musculoskelet Disord. 2015)

RESULTS:

At the 12-month follow-up, WOMAC pain score and bodily pain significantly improved in both groups; however, better results were determined in the PRP group compared to the HA group ($P < 0.001$). Other WOMAC and SF-36 parameters improved only in the PRP group. More improvement (but not statistically significant) was achieved in patients with grade 2 OA in both the groups.

CONCLUSION:

This study suggests that PRP injection is more efficacious than HA injection in reducing symptoms and improving quality of life and is a therapeutic option in select patients with knee OA who have not responded to conventional treatment.

PRP better than HA and Saline for Knee OA

- **Efficacy of Platelet-Rich Plasma in the Treatment of Knee Osteoarthritis: A Meta-analysis of Randomized Controlled Trials.**
- Current evidence indicates that, compared with HA and saline, intra-articular PRP injection may have more benefit in pain relief and functional improvement in patients with symptomatic knee OA at 1 year postinjection.

PRP better than HA for Hip OA

- **Ultrasound-Guided Injection of Platelet-Rich Plasma and Hyaluronic Acid, Separately and in Combination, for Hip Osteoarthritis: A Randomized Controlled Study. 2016**
- **RESULTS:**
- A total of 111 patients were randomly assigned to 3 groups and received 3 weekly injections of either PRP (44 patients), PRP+HA (31 patients), or HA (36 patients). At all follow-ups, the PRP group had the lowest VAS scores. In particular, at 6-month follow-up, the mean VAS score was 21 (95% CI, 15-28) in the PRP group, 35 (95% CI, 26-45) in the PRP+HA group, and 44 (95% CI, 36-52) in the HA group ($P < .0005$ [PRP vs HA] and $P = .007$ [PRP vs PRP+HA]; $F = 0.663$). The WOMAC score of the PRP group was significantly better at 2-month follow-up (mean, 73; 95% CI, 68-78) and 6-month follow-up (mean, 72; 95% CI, 67-76) but not at 12-month follow-up. A significant, "moderate" correlation was found between interleukin-10 and variations of the VAS score ($r = 0.392$; $P = .040$). Significant improvements were achieved in reducing pain and ameliorating quality of life and functional recovery.
- **CONCLUSION:**
- **Results indicated that intra-articular PRP injections offer a significant clinical improvement in patients with hip OA without relevant side effects. The benefit was significantly more stable up to 12 months as compared with the other tested treatments.** The addition of PRP+HA did not lead to a significant improvement in pain symptoms.

PRP better than HA for Hip OA

- **) Ultrasound-Guided Injection of Platelet-Rich Plasma and Hyaluronic Acid, Separately and in Combination, for Hip Osteoarthritis: A Randomized Controlled Study. (2016)**
- Results: 102 patients treated w PRP, PRP+HA, and HA. PRP signif better at 6 months in VAS and WOMAC.

3) Multiple PRP injections are more effective than single injections and hyaluronic acid in knees with early osteoarthritis: a randomized, double-blind, placebo-controlled trial. (Knee Surg Sports Traumatol Arthrosc. 2017)

RESULTS: There was a statistically significant improvement in the IKDC and EQ-VAS scores in all the treatment groups compared with the control group. The knee scores of patients treated with three PRP injections were significantly better than those patients of the other groups. There was no significant difference in the scores of patients injected with one dose of PRP or HA. In the early OA subgroups, significantly better clinical results were achieved in the patients treated with three PRP injections, but there was no significant difference in the clinical results of patients with advanced OA among the treatment groups.

CONCLUSION:

The clinical results of this study suggest IA PRP and HA treatment for all stages of knee OA. For patients with early OA, multiple (3) PRP injections are useful in achieving better clinical results. For patients with advanced OA, multiple injections do not significantly improve the results of patients in any group.

Systematic review:PRP effective with no increased risk

- **Intra-articular platelet-rich plasma injections for knee osteoarthritis: An overview of systematic reviews and risk of bias considerations. 2017 RESULTS:**
- Ten systematic reviews were eligible for inclusion. The Jadad decision making tool suggested that the reviews with highest AMSTAR score should be selected. According to the ROBIS tool, there were 4 systematic reviews with low risk of bias and 6 with high risk of bias. As a result, two systematic reviews conducted by Dai et al and Meheux et al with highest AMSTAR score and low risk of bias were selected as the best evidence.
- **CONCLUSIONS:**
- **The present overview demonstrates that PRP is an effective intervention in treating knee OA without increased risk of adverse events.** Therefore, the present conclusions may help decision makers interpret and choose PRP with more confidence.

A2M

Rapidly Increasing Awareness of A2M

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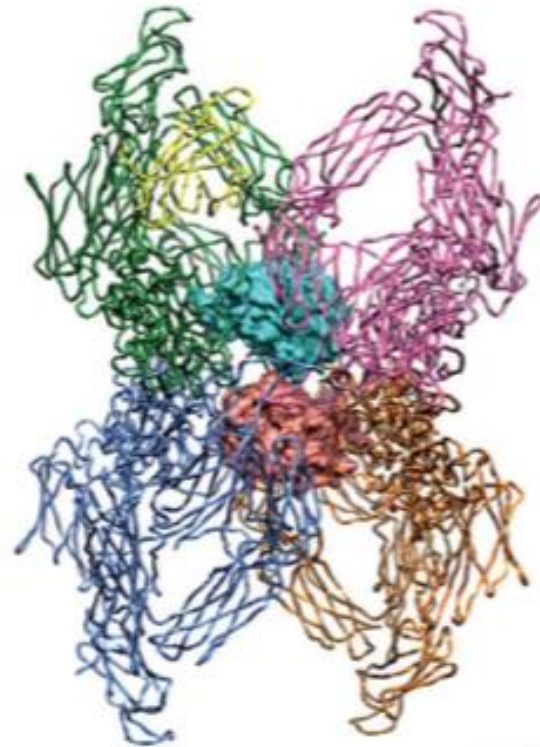
Identification of α_2 -Macroglobulin as a Master Inhibitor of Cartilage-Degrading Factors That Attenuates the Progression of Posttraumatic Osteoarthritis

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Richard Terek,³ Braden C. Fleming,³ Mary B. Goldring,⁶ Michael G. Ehrlich,³
Ge Zhang,⁷ and Lei Wei⁵

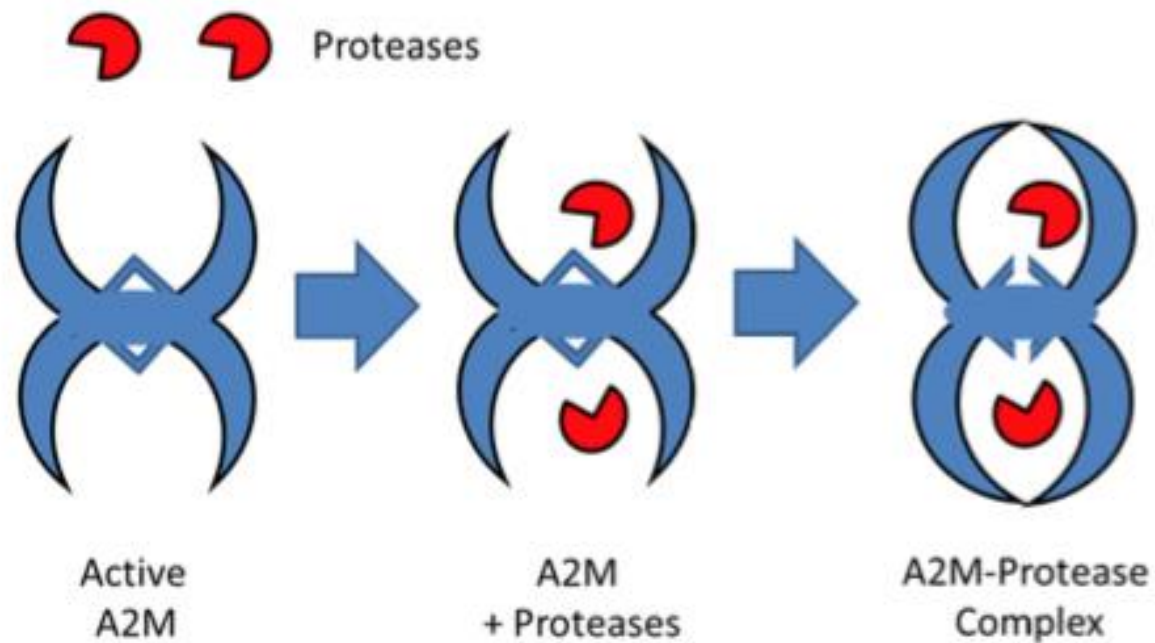
Our Venus Flytrap

α -2-Macroglobulin

1. α -2-Macroglobulin (A2M) is a **tetramer** (720KDa), with monomers connected by disulfide bonds and dimers connected by hydrophobic interactions
1. Its made in the liver (99%), found in relatively high concentration in plasma (~6 mg/mL)
2. Broad Spectrum **protease inhibitor**
 - Inhibits MMPs & ADAMTS
 - Binds to and regulates cytokines and GFs
3. A2M has a **bait region**, that upon cleavage, induces a conformation change trapping the protease



α -2-Macroglobulin Inhibition of Proteases



2) α 2-Macroglobulin: Autologous Protease Inhibition Technology. (Phys Med Rehabil Clin N Am. 2016)

Abstract

α ₂-Macroglobulin (A2M) is a plasma glycoprotein best known for its ability to inhibit a broad spectrum of serine, threonine, and metalloproteases as well as inflammatory cytokines by a unique bait-and-trap method. A2M has emerged as a unique potential treatment of cartilage-based pathology and inflammatory arthritides. This article describes the unique method by which A2M not only inhibits the associated inflammatory cascade but also disrupts the catabolic process of cartilage degeneration. Autologous concentrated A2M from plasma is currently in use to successfully treat various painful arthritides. Future directions will focus on recombinant variants that enhance its anti-inflammatory and disease-modifying potential.

1) Identification of α 2-macroglobulin as a master inhibitor of cartilage-degrading factors that attenuates the progression of posttraumatic osteoarthritis. (Arthritis Rheumatol. 2014)

RESULTS:

In both normal subjects and OA patients, α 2 M levels were lower in SF as compared to serum, and in OA patients, MMP-13 levels were higher in SF than in serum. In vitro, α 2 M inhibited the induction of MMP-13 by IL-1 in a dose-dependent manner in human chondrocytes. In the rat model of ACLT OA, supplemental intraarticular injection of α 2 M reduced the concentration of MMP-13 in SF, had a favorable effect on OA-related gene expression, and attenuated OA progression.

CONCLUSION:

The plasma protease inhibitor α 2 M is not present in sufficient concentrations to inactivate the high concentrations of catabolic factors found in OA SF. **Our findings suggest that supplemental intraarticular α 2 M provides chondral protection in posttraumatic OA.**

The End...Orthobiologics to keep us
going for our grandkids and
doughnuts...

