

# BASICS OF PRP THERAPY

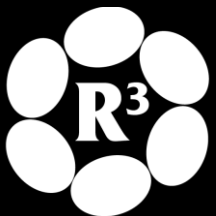
David Greene, MD, MBA  
R3 Medical Training



**MEDICAL TRAINING**

# OUTLINE

- What it is.
- What's in it.
- Single vs. Double Spin.
- Controversy
- Indications/Research

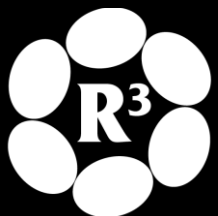


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# DEFINITION

- Autologous blood sample that has a platelet concentration above that contained in normal baseline blood plasma.
- Platelets contain over 30 bioactive proteins, many of which have a fundamental role in tissue healing.



MEDICAL TRAINING



# WHAT DEFINES CLINICAL PRP?

## Normal

- 200,000/microliter

## For Bone/Soft Tissue Enhancement

- 1,000,000 platelets/microliter
- Equals 1 billion platelets per milliliter.
- So typical 5 ml treatment = 5 billion platelets.

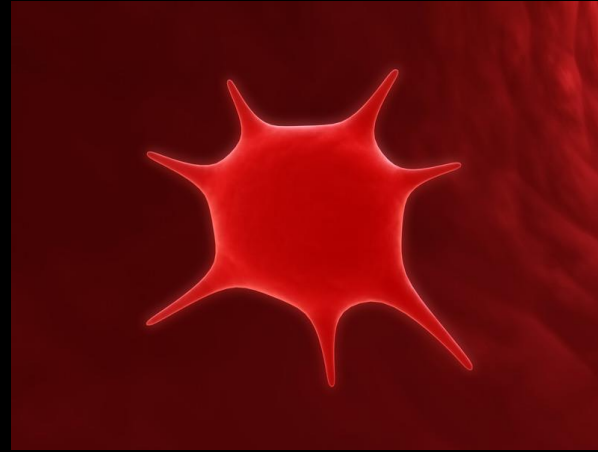


# GROWTH FACTORS IN PRP

Platelet Growth Factor Type	Growth factor Source	Biological Actions
Platelet derived growth factor (a-b )	Platelets, osteoblasts, endothelial cells, macrophages, monocytes, smooth muscle cells	Mitogenic for mesenchymal cells and osteoblasts, stimulates chemotaxis and mitogenesis in fibroblast/glia/smooth muscle cells, regulates collagenase secretion and collagen synthesis, stimulate macrophage and neutrophil chemotaxis
Transforming growth factor TGF(alpha -beta)	Platelets, extracellular matrix of bone, cartilage matrix, activated TH1 cells and natural killer cells, macrophages/monocytes and neutrophils	Stimulates undifferentiated mesenchymal cell proliferation ; regulates endothelial, fibroblastic and osteoblastic mitogenesis ; regulates collagen synthesis and collagenase secretion, regulates mitogenic effects of growth factors, stimulate endothelial chemotaxis and angiogenesis, inhibits macrophage and lymphocyte proliferation
Vascular endothelial growth factor, VEGF	Platelets, endothelial cells	Increases angiogenesis and vessel permeability, stimulates mitogenesis for endothelial cells
Epidermal growth factor, EGF	Platelets, macrophages, monocytes	Stimulates endothelial chemotaxis / angiogenesis, regulates collagenase secretion, stimulates epithelial /mesenchymal mitogenesis
Fibroblast growth factor, FGF	Platelets, macrophages, mesenchymal cells, chondrocytes, osteoblasts	Promotes growth and differentiation of chondrocytes and osteoblasts, mitogenic for mesenchymal cells, chondrocytes and osteoblasts
Connective tissue growth factor CTGF	Platelets through endocytosis from extracellular environment in bone marrow	Promotes angiogenesis, cartilage regeneration, fibrosis and platelet adhesion
Insulin like growth factor – 1 IGF -1	Plasma, epithelial cells, endothelial cells, fibroblasts, smooth muscle cells, osteoblasts, bone matrix	Chemotaxis for fibroblasts and stimulates protein synthesis. enhances bone formation by proliferation and differentiation of osteoblasts

# PRP ACTIVATION

Activation causes granules to fuse to cell membrane (degranulation)



They bind to target cells, like MSC's, osteoblasts, fibroblasts, etc

Proteins/Growth Factors become bioactive (PDGF, TGF-B, et) and secreted. Over 95% are secreted within ONE hour.

This leads to intracellular activation creating gene sequencing to direct cellular proliferation, collagen synthesis, etc to provoke tissue repair and tissue regeneration.

# PRP PREPARATION

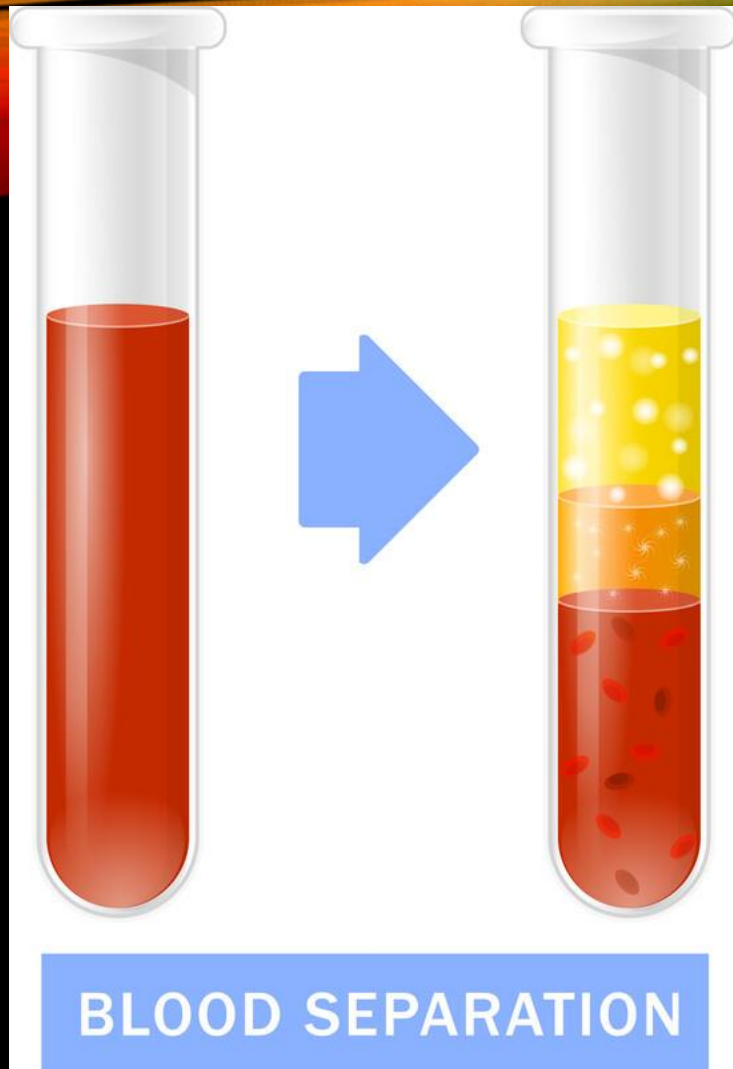
- Blood collection with anticoagulant.
- 1<sup>st</sup> spin separates whole blood into 3 layers.



RBC's at bottom – we don't want these. Studies show blood in joints can lead to degenerative changes. Synovial fluid treated with RBC's results in cell death.



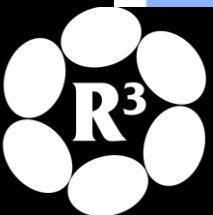
# PRP PREPARATION



Buffy coat is rich in WBC's and platelets.

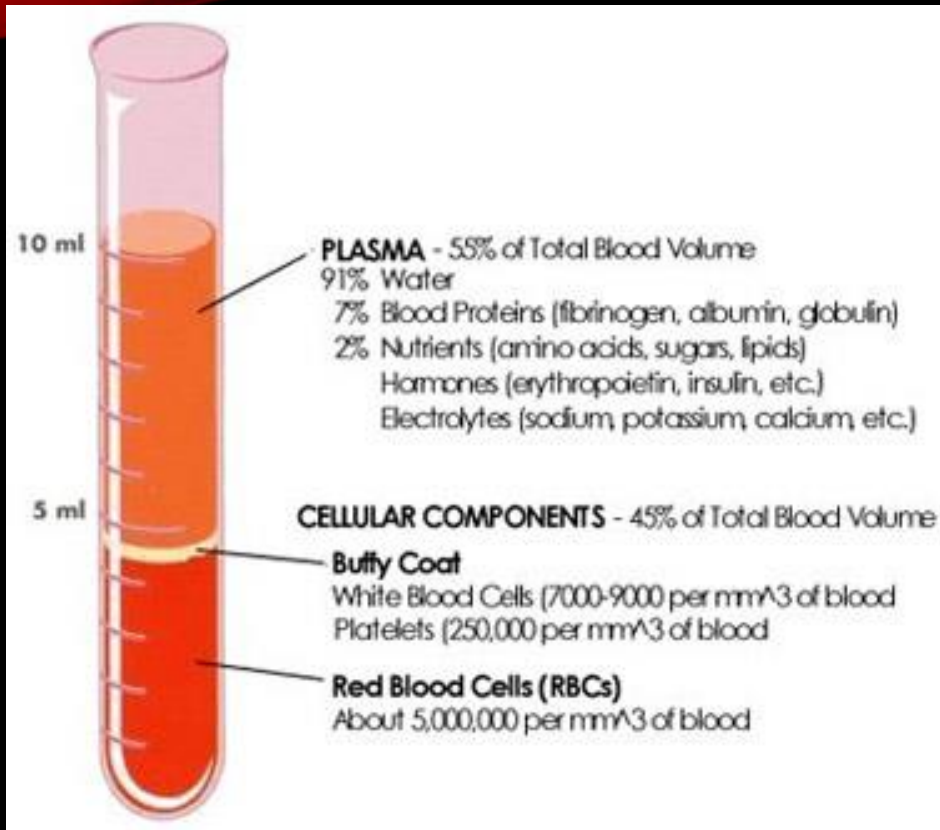
**There are five major types of white blood cells:**

- neutrophils.
- lymphocytes.
- eosinophils.
- monocytes.
- basophils.





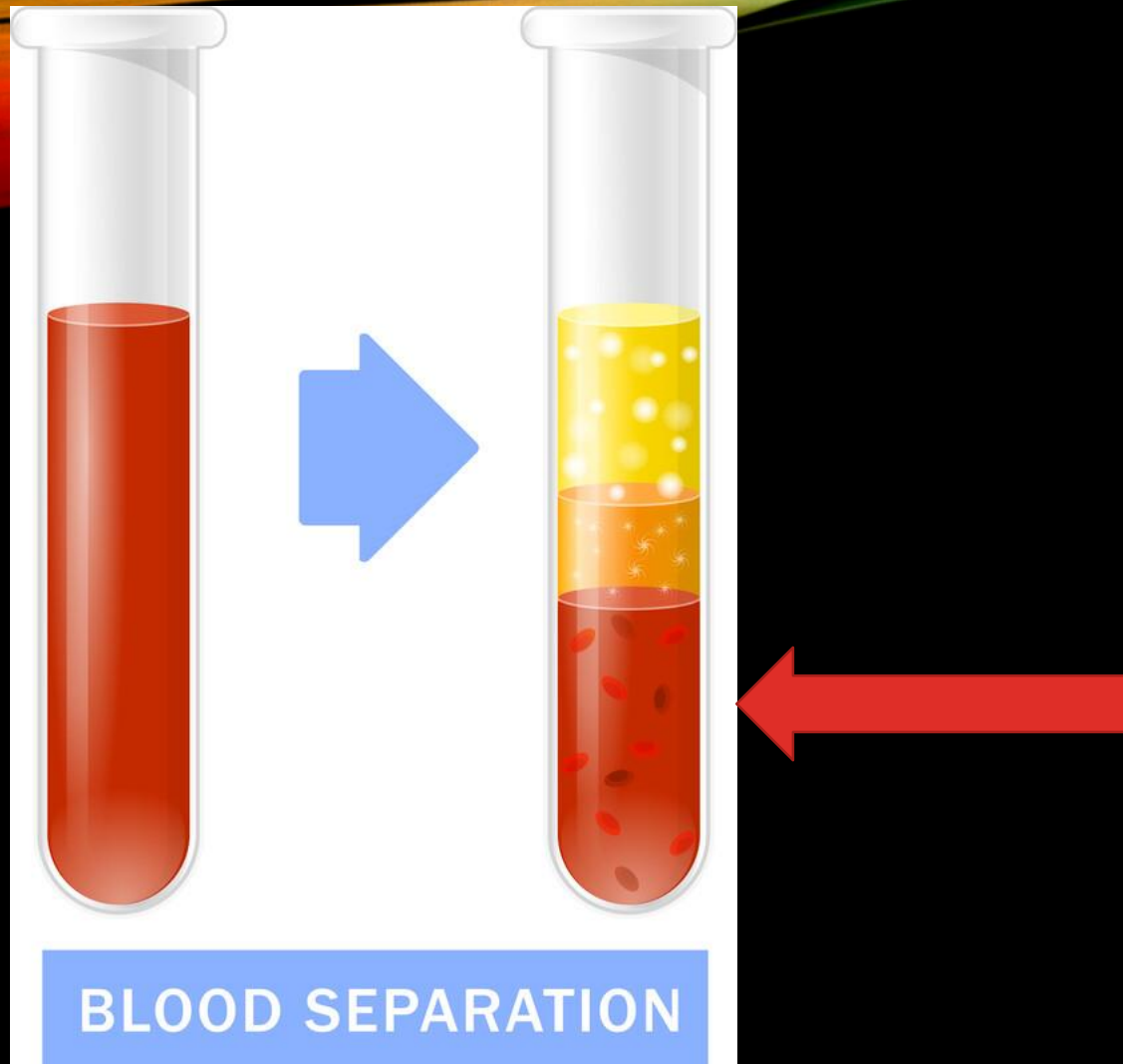
# PRP PREPARATION



Top layer has plasma – water, proteins, electrolyes.



# PRP PREPARATION



If you're just going to do a single spin, you would use the middle layer – buffy coat.

This has a LOT of leucocytes and platelets. So it will be a leucocyte rich (LR) PRP.



## PROCESS OF PRP THERAPY

1



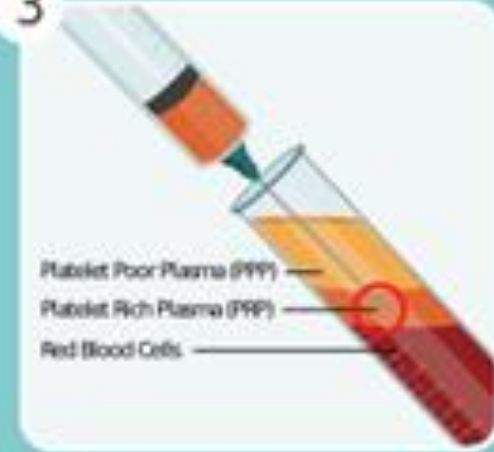
Collect blood

2



Spin down the blood

3



Extract platelet-rich plasma

4

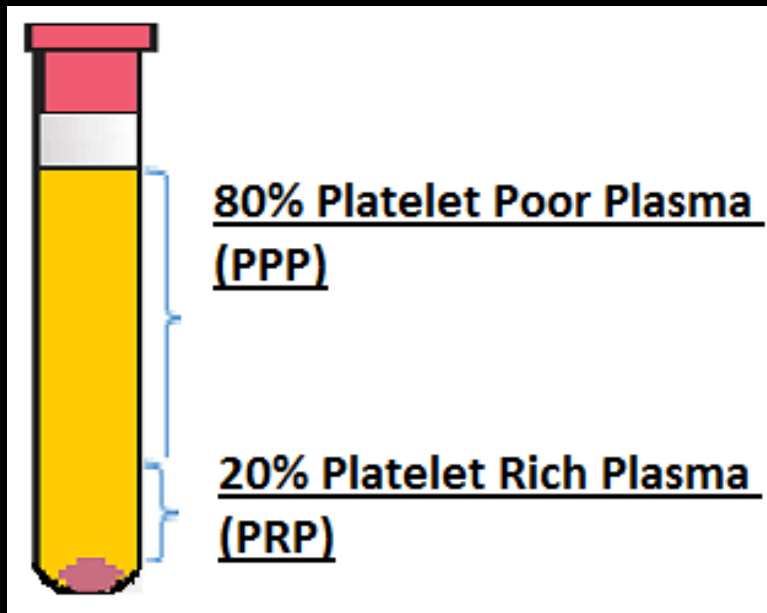


Inject injured area with PRP

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# SECOND SPIN



- The top and middle layers get transferred out.
- Don't want RBC's.
- This creates an upper portion of platelet poor plasma and a bottom layer of platelets with a few RBC's.





**YOU WANT MONOCYTES, NOT GRANULOCYTES**

# UNANSWERED QUESTIONS



- To activate or not?
- Optimal type of PRP to use?
- PRP alone or with stem cells/exosomes?



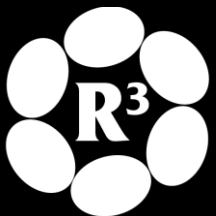
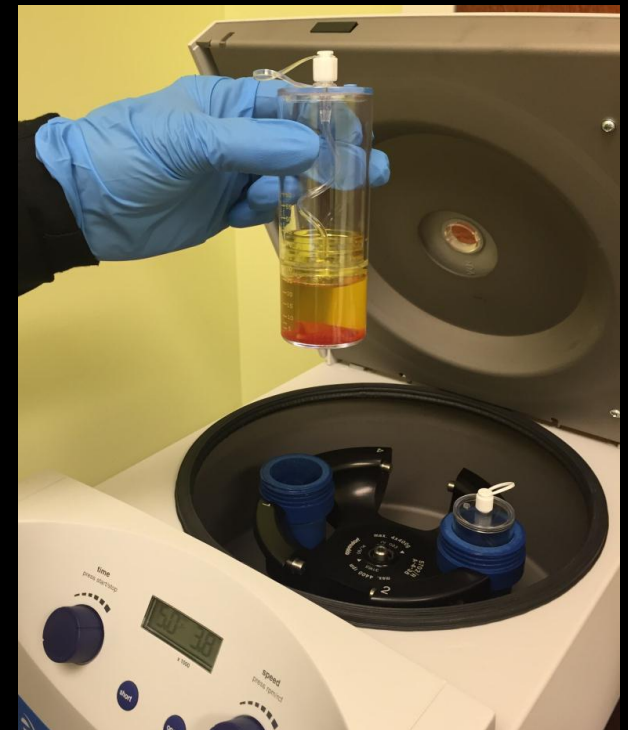
**Table 1** Commercially available PRP systems and their PRP preparations

System	Company	Blood volume required (mL)	Concentrated volume produced (mL)	Processing time (min)	PPP produced?	Increase in [platelets] (times baseline)	Platelet capture efficiency (% yield)
<b>Leukocyte-rich PRP</b>							
Angel	Arthrex	52 [6]	1–20 <sup>a</sup>	17 [6]	+	10 <sup>a</sup>	56–75% [6]
GenesisCS	EmCyte	54 [6]	6 [6]	10 [6]	+	4–7 [6]	61 ± 12% [6]
GPS III	Biomet	54 [6]	6 [6]	15 [6]	+	3–10 [6]	70 ± 30% [6]
Magellan	Isto Biologics/Arteriocyte	52 [6]	3.5–7 [6]	17 [6]	+	3–15 [6]	86 ± 41% [6]
SmartPREP 2	Harvest	54 [6]	7 [6]	14 [6]	+	5–9 [6]	94 ± 12% [6]
<b>Leukocyte-poor PRP</b>							
Autologous conditioned plasma (ACP)	Arthrex	11 [7]	4 [7]	5 [7]	–	1.3 [7]	48 ± 7% [7]
Cascade	MTF	18 [8]	7.5 [8]	6 [8]	–	1.6 [8]	68 ± 4% [8]
Clear PRP	Harvest	54 <sup>a</sup>	6.5 <sup>a</sup>	18 <sup>a</sup>	+	3–6 <sup>a</sup>	62 ± 5% <sup>a</sup>
Pure PRP	EmCyte	50 <sup>a</sup>	6.5 <sup>a</sup>	8.5 <sup>a</sup>	+	4–7 <sup>a</sup>	76 ± 4% <sup>a</sup>

<sup>a</sup>Data obtained from manufacturers' promotional literature or internal studies

# WHY WE OFFER EMCYTE AND PUREPRP

- Offers upwards of 9 billion platelets in a 7ml sample.
- Great control of neutrophils – they are the most abundant leukocyte and show up quickly at injury site. Normally they are cleared quickly by macrophages. If not, they die and release ALL their proinflammatory contents.
- Monocytes – largest of leukocytes and are non-inflammatory. The PurePRP system enhances the immune reponse with monocytes in higher concentrations, while allowing providers to control the neutrophil counts.





# DOES AGE AFFECT PRP QUALITY?

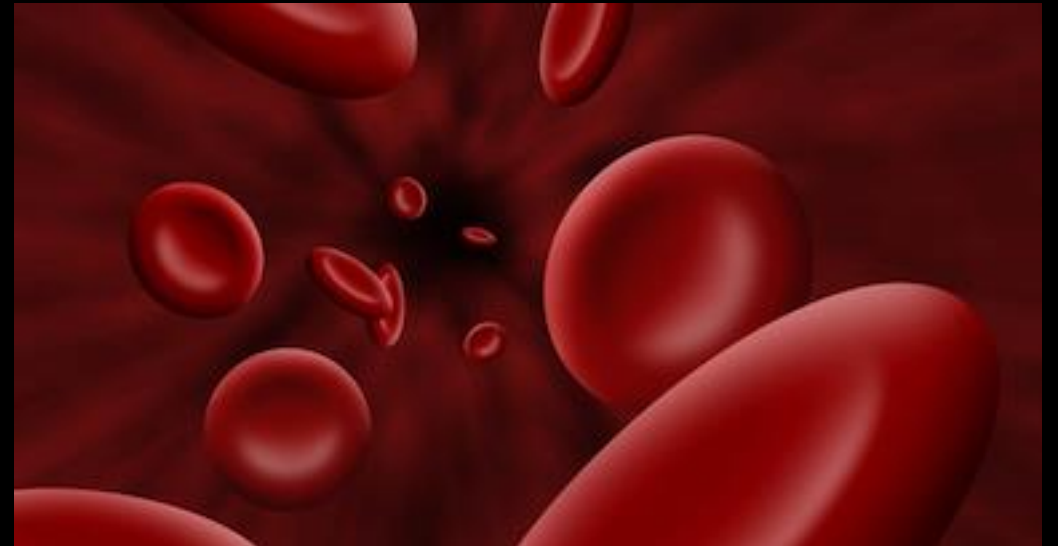


- NO!
- A study by Weibrich et al (2004) showed no significant changes in platelet concentration or growth factors in relation to age or gender.



# INDICATIONS?

- Soft Tissue
  - Achilles
  - Plantar Fasciitis
  - Rotator Cuff
  - Elbow
  - Greater Trochanter
- Joints
  - Knee
  - Hip
  - Spine
  - TMJ



# ACHILLES

- Platelet-Rich Plasma Injection for Chronic Achilles Tendinopathy A Randomized Controlled Trial
- JAMA study. 54 randomized pts age 18-70
- Conclusion Among patients with chronic mid portion Achilles tendinopathy who were treated with eccentric exercises, a PRP injection compared with a saline injection **did not result** in greater improvement in pain and activity.



# PLANTAR FASCITIS

- Is Platelet-rich Plasma Injection more Effective than Steroid Injection in the Treatment of Chronic Plantar Fasciitis in Achieving Long-term Relief?
- Malaysian Orthopedic Journal 2019
- 60 patients, randomized, blinded



Table II: Mean VAS score in both groups

VAS	Group A (PRP)	Group B (Steroid)	P value (at end of 6 months follow-up)
Pre-Treatment	7.137	7.214	
6 Weeks	2.62	1.928	
3 Months	1.931	2.89	
6 Months	1.413	3.785	<0.001

# ROTATOR CUFF

- Nonoperative Treatment of Rotator Cuff Disease With Platelet-Rich Plasma: A Systematic Review of Randomized Controlled Trials
- May 2019 Journal of Arthroscopy
- Looked at 5 studies, over 200 patients.
- The currently limited available evidence on PRP for nonoperative treatment of chronic rotator cuff disease suggests that in the short term, PRP injections **may not be beneficial**. When directly compared with exercisetherapy, PRP **does not result** in superior functional outcomes, pain scores, or range of motion.



# PATELLAR TENDINOPATHY (JUMPER'S KNEE)

- Liddle et al – 81% of patients returned to pre-symptom levels of activity.
- Zayni et al showed better pain relief and function with 2 injections versus one.
- PRP appears to be a viable treatment option for chronic refractory patellar tendinopathy, and leukocyte-rich preparation is recommended. (ONE SPIN)



# LATERAL EPICONDYLITIS (TENNIS ELBOW)

- Meta- analysis showed PRP was better at reducing pain in short and long term versus steroid. Effects lasted up to 2 years. No subcutaneous atrophy.
- One of the best studies (Mishra et al) showed leucocyte rich yielded better long term results than lidocaine or dry needling.



# ELBOW LIGAMENT PARTIAL TEAR

- Podesta et al. followed the progress of 34 throwing athletes being treated for partial thickness tears of the UCL with a single PRP injection [56].
- They found that 30 of the 34 athletes were able to return to the same level of play or higher at an average of 12 weeks





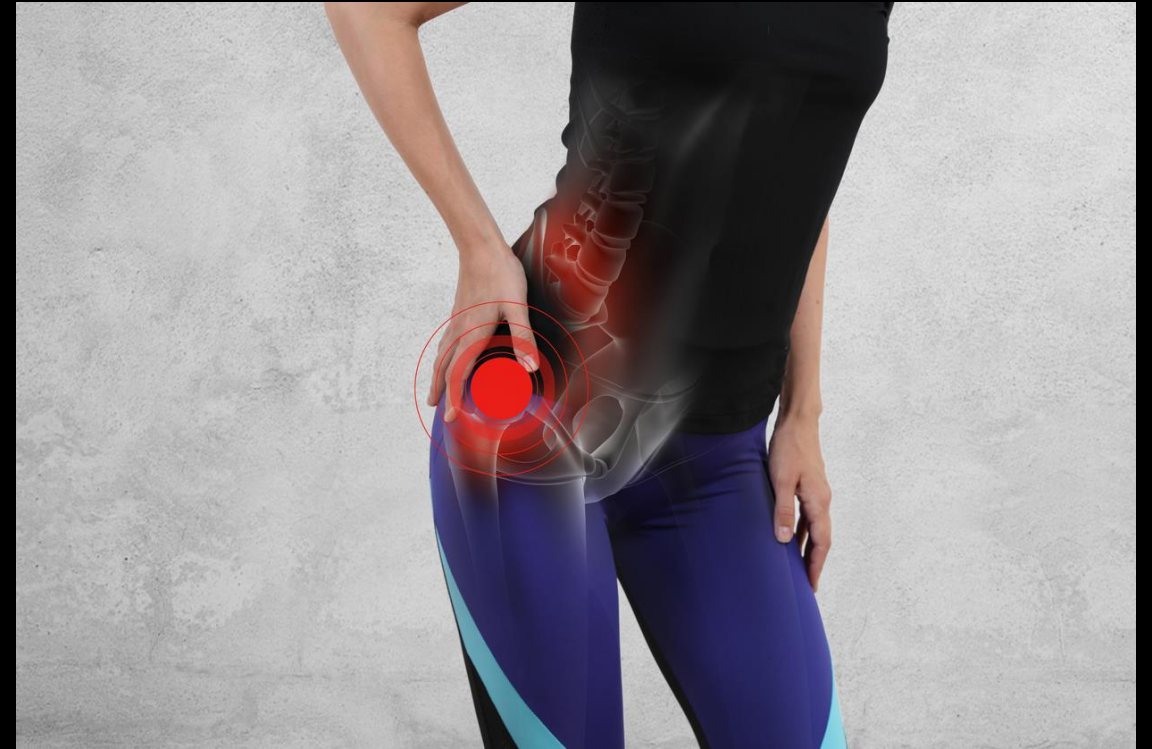
# SHOHEI OHTANI

- While UCL injuries can lead to Tommy John surgery, several pitchers -- including [New York Yankees](#) right-hander [Masahiro Tanaka](#) and [Boston Red Sox](#) left-hander [Chris Sale](#) -- have had PRP injection therapy as a more conservative treatment and continued to pitch without further issues.
- For Ohtani – he still ended up needing the surgery.



# GREATER TROCHANTERIC BURSTITIS

- Platelet-Rich Plasma Versus Surgery for the Management of Recalcitrant Greater Trochanteric Pain Syndrome: A Systematic Review
- March 2020 Journal of Arthroscopy Santiago et al.
- 10 studies evaluated. 210 patients. F/U over 2 years plus.
- PRP outcome was equivalent to surgery (awesome), but quite a few complications with surgery (re-tears, DVT, wound issues, snapping hip).



**Table 3** Study design characteristics for PRP versus control injection for osteoarthritis

Indication	Study	Year of publication	Level of evidence	Sample size		Type of PRP	Number of injections	Intervention/injection volume and contents		Follow-up (months)	Favors PRP?
				PRP	Control			PRP	Control		
Hip osteoarthritis	Battaglia et al. [72]	2013	I	50	50	LR-PRP	3	5 mL PRP	30 mg HA	12	-
Hip osteoarthritis	Dallari et al. [73]	2016	I	44, +HA: 31	36	NR	3	7 mL PRP + HA	30 mg HA	12	+
Hip osteoarthritis	Doria et al. [74]	2017	II	40	40	NR	3	5 mL PRP	15 mg HA	12	-
Hip osteoarthritis	Sante et al. [75]	2016	I	21	22	NR	3	3 mL PRP	30 mg HA	4	+
Knee osteoarthritis	Cole et al. [76]	2017	I	49	50	LP-PRP	3	4 mL PRP	16 mg HA injection	12	+
Knee osteoarthritis	Duymus et al. [77]	2017	I	41	HA: 40, ozone: 39	NR	2	5 mL PRP	40 mg HA, 15 mL ozone	12	+
Knee osteoarthritis	Gormeli et al. [78]	2017	I	PRP (3×): 46, PRP (1×): 45	HA: 46, placebo: 45	NR	3 versus 1	5 mL PRP	30 mg HA, NR saline	6	+
Knee osteoarthritis	Lana et al. [79]	2016	I	36, +HA: 33	36	NR	3	5 mL PRP + 20 mg HA	20 mg HA	12	+
Knee osteoarthritis	Montanez et al. [80]	2016	I	28	27	NR	3	NR	NR HA	6	+
Knee osteoarthritis	Paterson et al. [81]	2016	I	12	11	NR	3	3 mL PRP	3 mL HA	3	-
Knee osteoarthritis	Simental et al. [82]	2016	I	33	32	LP-PRP	3	3 mL PRP	Tylenol 500 mg q8h	4	+
Knee osteoarthritis	Smith et al. [83•]	2016	I	15	15	LP-PRP	3	3–8 mL PRP	3–8 mL saline	12	+

NR not reported, LP-PRP leukocyte-poor PRP, LR-PRP leukocyte-rich PRP, PRGF plasma rich in growth factors, HA hyaluronic acid

Hip = 2/4 positive. Knee = 7/8 positive

# KNEE OA

- The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials
- Journal of Ortho Surgery & Research 2017
- Reviewed 14 studies and 1400 patients.
- Intra-articular PRP injections probably are **more efficacious** in the treatment of knee OA in terms of pain relief and self-reported function improvement at 3, 6 and 12 months follow-up, compared with other injections, including saline placebo, HA, ozone, and corticosteroids.

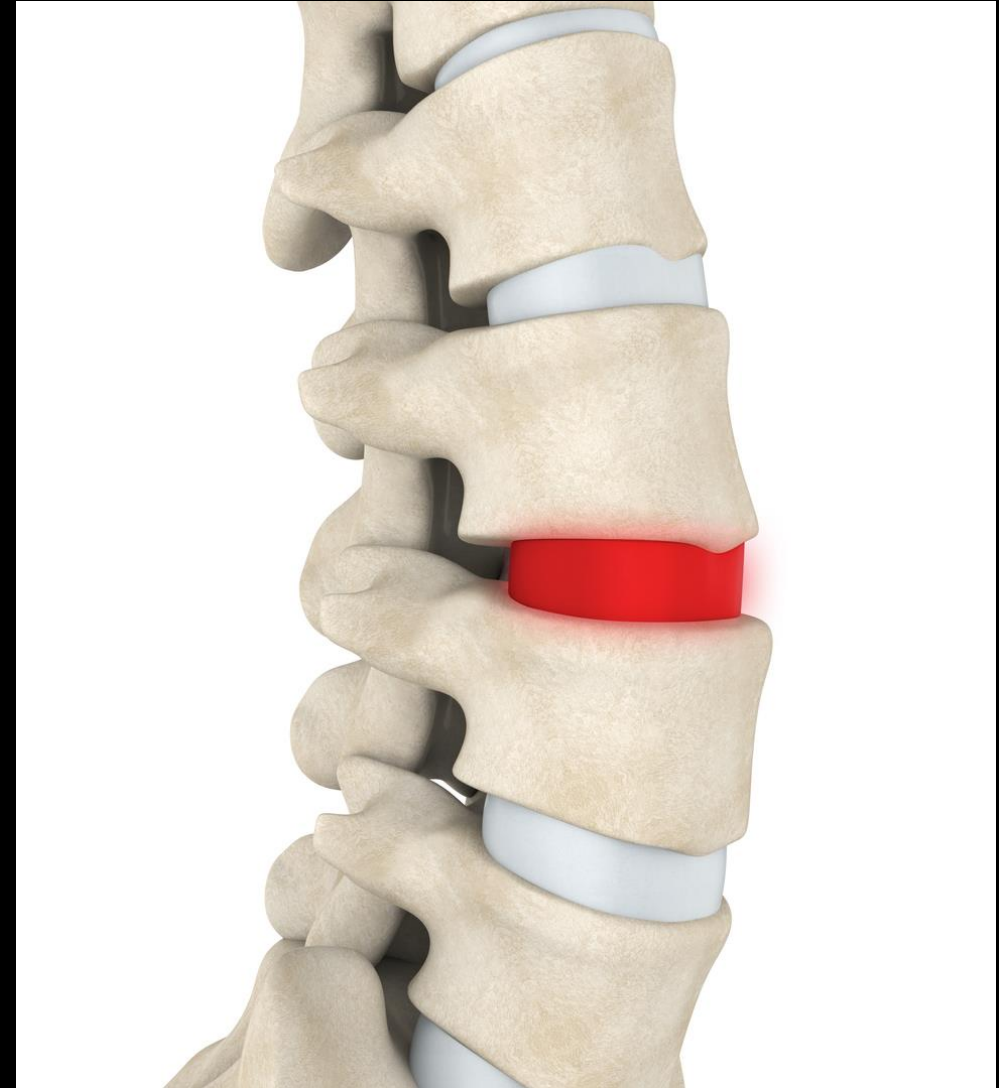
# ONE INJECTION OR MULTIPLE?

- **Single- and double-dose of platelet-rich plasma versus hyaluronic acid for treatment of knee osteoarthritis: A randomized controlled trial.**
- [World J Orthop.](#) 2019
- 95 patients for 4 months.
- Found that the efficacy of PRP increases after multiple injections (3 wks apart).



# DEGENERATIVE DISC DISEASE

- Treatment of symptomatic degenerative intervertebral discs with autologous platelet-rich plasma: follow-up at 5-9 years.
- [Regen Med.](#) 2019
- This subset of patients demonstrated statistically and clinically significant improvements in pain and function at 5-9 years postinjection.



# LUMBAR FACET SYNDROME

- Analysis of the clinical efficacy of platelet-rich plasma therapy in the treatment of patients with isolated facet-syndrome of the lumbar spine
- Russian study – 49 pts followed 18 months.
- Clinical efficacy is confirmed by the persistent significant reduction of pain symptoms and restoration of functional status in the early and late postoperative periods with low risks of adverse outcomes.



# TMJ

- Platelet-rich plasma for the therapeutic management of temporomandibular joint disorders: a systematic review.
- Looked at 6 studies, published 2018 in J Oral Maxillofac Surg.
- Four of the studies found PRP injections to be superior in terms of improvements in mandibular range of motion and pain intensity up to 12 months after treatment, while the remaining two studies found similar results for the different treatments.





# CONCLUSION

- PRP – Very Low Risk and relatively inexpensive.
- Lots of unanswered questions
  - Dosing – we have an idea.
  - Activation
  - LR or LP
- No gold standard.
- Many positive studies despite this!
- Great option, anecdotally great with stem cells/exosomes.

