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PRP: What happens after the injection?

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Disclosures - NONE

 UCSF Sports Medicine uses the RegenKit THT Autologous Platelet-rich Plasma (A-PRP) system







Outline

- What is PRP?
- Why does it Work?
- How does it Work?
- What is the Evidence for Use for specific conditions
- What is our post injection protocol for joints? Tendons?
- Eccentric strengthening







What is PRP?

Platelet Rich Plasma (PRP) is a plasma solution with concentrated platelets above that in whole blood

PLATELETS:

- Role in hemostasis and tissue healing
- "architects of healing process" they initiate and guide healing
- When activated, they change shape and become stick, to provide fibrin-base scaffold for tissue healing
- Activated platelets degranulate and release growth factors, bioadhesive proteins and other bioactive factors, eg fibrinogen, fibronectin and vitronectin

PLASMA:

Contains biofactors and proteins involved in healing (growth factors IGF and HGF) also, leukocytes (also release growth factors)





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What are Growth Factors?

PRP has growth factors contained in the platelet alpha-granules

- TGF-B Transforming growth factor
- IGF Insulin-like growth factor
- PDGF Platelet derived growth factor
- >300 distinct cytokines and growth factors

Murray et al. J Bone Joint Surg Am. 2017;99:809-19



These factors play an important role in all phases of healing of the tissue by recruiting mesenchymal cells and also during the synthesis of the extracellular matrix.





Why Leukocyte Rich vs Leukocyte Poor

- Rich Facilitate wound debridement, wound healing, and subsequent tissue regeneration
- Poor Unexpected exacerbation of inflammation
- To date, exclusion of leukocytes seems to yield better outcomes

Kawase et a. Bioengineering (Basel), 2020.





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Avoid NSAIDs Pre-injection

Autologous PRP produced from subjects after NSAID medication shows significantly impaired platelet function and may result in lower quality regarding the content of bioactive compounds.

Should not take NSAIDs until after the blood is drawn.

Schippinger G et al. Autologous Platelet-Rich Plasma Preparations: Influence of Nonsteroidal Anti-inflammatory Drugs on Platelet Function. Orthop J Sports Med. 2015





Safety is good with PRP

- May feel inflammation
- No risk of hypersensitivity and graft reactions versus host reactions
- Autologous blood no risk of infection from PRP
- Systems are considered sterile





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Two additional factors causing variations in PRP products

- Presence or absence of white blood cells in the final product
- +/- activation of platelets with exogenous thrombin



Courtesy: Brian Feeley MD

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RegenTHT™

Instructions For Use

For additional details please refer to the RegenKit THT Instructions for Use and Centrifuge Manual



Using the butterfly needle and the blood collection set, draw 8cc of venous blood into the Regen THT tube. Invert the filled tube 5 times for mixing.





Spin

utilized.

Close the lid and select the appropriate centrifuge settings for 1,500 RCF (Stryker Universal Centrifuge = 3,400 RPM) and 8 minutes. Start centrifuge.



Platelet Preparation

After centrifugation, gently invert the Regen THT tube 5 to 10 times. Collect the supernatant fraction using the syringe equipped with the blood transfer device. The A-PRP is ready for use.



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Example RegenTHT™





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Step 2: Centrifuge

Example RegenTHT™

Spins for 8 minutes





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Step 3: Separate PRP

Example RegenTHT[™]





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Step 4: Administer PRP

Example RegenTHT™





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Ultrasound +/- Tenotomy

Ultrasound guidance for this procedure is essential to ensure that the abnormal region of the tendon is accurately targeted.

Jacobson JA et al. Ultrasound-Guided Percutaneous Tenotomy. Semin Musculoskelet Radiol. 2016 Nov;20(5):414-421.





What is needle tenotomy ?

"A needle is repeatedly passed into the abnormal tendon with the goal of converting a **chronic degenerative process** to an **acute inflammatory condition** that will progress to tendon healing."

Jacobson JA et al. Semin Musculoskelet Radiol. 2016.

4/17 articles met criteria, show positive results (34-56% VAS, 19 VISA)

Krey D. Tendon needling for treatment of tendinopathy: A systematic review. Phys Sportsmed. 2015 Feb;43(1): 80-6.





Jill Cook:

- 3 phases of tendinopathy
- A continuum
- 1. Reactive tendinopathy (young athletes)

Non-inflammatory proliferative phase

- From acute overload or a direct blow
- Short term adaptive thickening of tendon
- 2. Tendon Dysrepair attempt at tendon healing but w greater matrix breakdown
 - Increase in proteoglycans results in separation of collagen and disorganization in matrix, may be increase in vascularity
- 3.Degenerative tendinopathy: cell death, cellularity, disordered matrix, little collagen, less capacity to reverse pathological changes
 - Islands of deign pathology interspersed bwtn other stages of pathology or normal tendon

In elite athlete w chronically overloaded tendon or older person





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2 dysrepair/ degenerative tendon

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No local anesthetic or lidocaine

Association of local anaesthetics with PRP injections resulted in a significant decrease of platelets functionality, assessed by their capacity of aggregating.

Bausset O, et al. Muscles, Ligaments and Tendons Journal, 2014.



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Post Injection Protocols

- Highly variable, little evidence
- Not many studies on physical therapy, though eccentric exercises are usually recommended after a period of rest
- Return to sport is very variable



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Think About Healing

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Minutes	Hours	Days	Weeks	Months	
	Inflammat	ion			
Hemostasis					
Platelets	Fibrin clot fo	rmation			
	Vasoactive r	nediator release			
	Cytokine and	d growth factor release			
Inflammation		20.00			
Master cells	Platelet-activ	vating mediator release	lance		
	vasoactive a	and chemotacticmediator re	Hease		
Neutrophils and	Chemotaxis,	inflammation			
Monocytes	Killing and p	hagocytosing, wound debri	dment		
Macrophages	Chemotaxis, inflammation				
	Killing and p	hagocytosing, wound debri	dment		
	Cytokines ar	nd growth factor release	,		
		Prol	iferation		
		Skin resurfacing	1		
		Keratinocytes	Reepithelialization		
		Dermal restoration			
		Endothelial cells	Angiogenesis		
		Fibroblasts	Fibroplasia		
				Remodeling	
			Keratinocytes	Epidermis maturation	
			Myofibroblasts	Wound contraction	
			Endothelial celle	Apoptosis and scar maturation	
			Endothenal cells	Apoptosis and scar maturation	

Protection

- Use post-op principles
- For partial or complete tears, consider protect and limit weight bearing
- Consider Crutches
- Consider walking boot for Achilles, foot and ankle tendons
- Consider post-op knee hinge brace for patellar tendon, degenerative meniscus
- I use locked in extension knee brace for patellar tendon
- Consider an Off loader brace for osteoarthritis



My protocol for tendons

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Post PRP Rehabilitation

PHASE	LENGTH	RESTRICTIONS	REHABILITATION
	OF TIME		
Phase I Tissue protection	Days 0-3	 Consider using crutches or walking boot for certain lower extremity procedures, especially if in pain No weight training Avoid NSAIDS (Ibuprofen, Aleve, Advil, etc.) and ice 	 Relative rest Activities as tolerated; avoid excess loading or stress to treated area Gentle movement of the extremity (active range of motion)
Phase II Early Tissue healing; facilitation of collagen deposition	Days 4-14	 Progress to full weight bearing without protective device if using Avoid NSAIDS and ice 	 Light activities to provide motion to tendon; aerobic exercise which avoids loading of the treated tendon for lower extremities Gentle prolonged stretching May work on core strengthening and strengthening away from the injury site
	Weeks 2-6	 Avoid eccentric exercises (this is the part of exercise when the weight is being lowered) Avoid NSAIDS and ice 	 Progress load bearing activities Low weight, high repetition exercise w/ pain <3/10 - hand or foot should be free to move; not placed on fixed object (consider using machines) Soft tissue work on the tendon, such as deep tissue massage "Dvnamic" stretching
Phase III Collagen strengthening	Weeks 6- 12		 Eccentric exercises w/ pain <3/10) -2 sets of 15 repetitions, now w/hand or foot placed on immovable object, such as the ground or other firm surface Plyometrics; proprioceptive training and other sport-specific exercises Progress load bearing activities and consider return to sport if pain <3/10
	Months 3+	Reassess improvement; if not > 75 % improved consider repeat injection and return to Phase I	Progress back to functional sport specific activities with increasing load on tendon as pain allows.





Phase 1: 0-3 days

- Protect tissue
- Pain control (tylenol, warm bath, gentle ROM)
- Immobilization:
 - Sling for rtc, elbow tendons
 - PWB +crutches for patellar/squad tendons, knee extension brace
 - PWB +Boot and crutches for achilles/ankle tendons/plantar fascia

Gentle AROM and PROM outside of brace



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Phase 2: Early tissue healing, collagen deposition

Days 4-14: d/c immobilization

- Daily activities, WB as tolerated, wean off braces/crutches, take it easy!
- Light stationary cycling, aerobic NWB activities to promote ROM and blood flow
- Gentle prolonged stretching, AROM BID-TID

Weeks 2-6: progress load bearing activities and strengthening

- isometric, concentric exercises, higher reps
- Soft tissue work
- Stretching
- Proprioception work





Phase 3: collagen strengthening weeks 6-12

- Cont stretching, may add light soft tissue work
- Progress strengthening to eccentric work
- More focus on strength and endurance
- Work on mechanics, balance, core strength
- Cont nonimpact activities for endurance
- Eg, band work for shoulders, light weights for elbow,
- Single leg leg press, drop squats for knee, heel raises for achilles/ankle
- Progress weight bearing and functional work, core and balance
- Return to run/sport begins when full strength,

Painfree







Isometric vs Eccentric

- Eccentric begins at or after 6 weeks
- Eccentric exercise has been shown to increase collagen production in abnormal tendons and
- Eccentric exercise beneficial for pain, function and return to activity
- Pain is guide: OK for pain to increase 1-2/10 on pain scale with treatment but not more and just return to baseline again
- Studies show that exercise induced pain in degenerative stage of tendinopathy will not affect outcome
- Ref: "Is tendon pathology a continuum? A pathology model to explain the clinical presentation of load-induced tendinopathy." JL Cook, CR Purdam. BJSM 43 (6)



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Nordic Hamstring Curl







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Results: Lateral Epicondylosis (Tennis elbow)

At 12 weeks (n = 192), the PRP-treated patients reported 55.1% improvement in pain scores vs. 47.4% in the active control group (P=0.163).

At 24 weeks (n = 119), the PRP-treated patients reported 71.5% improvement in pain scores vs. 56.1% in the control group (P=0.019).

ehabmypatient

Mishra AK et al, Am J Sports Med, 2014



Results: Rotator Cuff Tears



22 RCTs: 18 surgical and 3 conservative show lack of beneficial effects.

Filardo G et al. Knee Surg Sports Traumatol Arthrosc. 2016

Use of PRP in rotator cuff repair results in improved healing rates

Hurley ET et al. Am J Sports Med, 2018

PRP may be more advantageous for small and medium tears to prevent re-tears.

Charles et al. Curr Rev Musculoskelet Med. 2018





Results: Patellar Tendinopathy

6 RCTs: 4 surgical and 2 conservative show benefits.

Filardo G et al. Platelet-rich plasma in tendon-related disorders: results and indications. Knee Surg Sports Traumatol Arthrosc. 2016.



Results: Gluteus Medius Tendinopathy

- 21 subjects in registry study with prospective follow-up
- Ultrasound-guided intratendinous PRP injections showed better post vs pre functioning with ADL's and Sports
- No RCT's yet

Lee JJ et al. Orthop J Sports Med, 2020.



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Results: Knee Osteoarthritis



- 10 randomized controlled trials with a total of 1069 patients
- 6 months postinjection, PRP and hyaluronic acid (HA) had similar effects with respect to pain relief and functional improvement (WOMAC)
- At 12 months, PRP was associated with significantly better pain relief
- PRP did not increase the risk of adverse events compared with HA and saline
 - •Dai WL, et al. Arthroscopy. 2017



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Results: Knee Osteoarthritis PRP vs HA?



- 49 patients randomized to PRP and 50 randomized to treatment with Hyaluronic Acid. No difference was seen between the groups in the primary outcome measure (WOMAC pain score)
- Significant improvements were seen in other patientreported outcome measures, with results favoring PRP over HA.

• Cole BJ, Karas V, Hussey K, Pilz K, Fortier LA. Am J Sports Med. 2017



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Multiple Injections? (Knee osteoarthritis)

- Systematic Review
- Single injection was as effective as multiple PRP injections in pain improvement
- Multiple injections seemed more effective in joint functionality than a single injection at 6 months

Vilchez-Cavazos F, et al. Orthop J Sports Med.

2019





Achilles Tendinopathy?



Efficacy of Platelet-Rich Plasma Versus Placebo in the Treatment of Tendinopathy

A Meta-analysis of Randomized Controlled Trials

Dai, Wenli MD; Yan, Wenqiang MD; Leng, Xi MD; Wang, Jian MD; Hu, Xiaoqing MD; Cheng, Jin MD; Ao, Yingfang PhD

CJSM Aug 2, 2021

- Prp vs placebo, outcomes on intention to treat w randomized effects models
- No difference in PAIN at 4-6 weeks, >/=24 wks, or in FUNCTION at 4-6 weeks, 12 wks, >/=24 wks
- NO improvement over placebo at 12 wks for different types of tendinopathies, treatment regimens, leukocyte concentrations, or cointerventions



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PRP Summary

- There is evidence that it works in tendon issues and early knee osteoarthritis
- All PRP is not the same, though they all demonstrate some positive results
- The post injection recovery and therapy are extremely important for improvement
- More RCT studies are needed to demonstrate efficacy
- Be Familiar with PRP



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Thank you!





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