Place name of Medical Policy: Platelet-Rich Plasma Therapy			
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Specialty:	Orthopedic Surgery	**Reviewed Date:**	07/06/17
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POLICY

- Not recommended. Platelet-Rich Plasma injections are experimental and do not warrant use.
- Platelet-rich plasma therapy (PRP) involves drawing the patient's blood and spinning it in a centrifuge to separate out the platelets. The layer of platelet-rich plasma is then injected into the patient's pathological body part. The platelets then release growth factors to promote healing. It is an office procedure that lasts less than an hour.
- There is no supporting data to validate this treatment. While the results are promising, the science is still very limited.
- Not recommended as adjunct therapy as it is impossible to determine whether the injections are effective.
- Only in the elbow, is evidence of sufficient quality to support its use. However, based on a review of the available literature, the number of patients reported in these studies were extremely small and there is lack of histological data to show that these injections in fact treat the underlying pathology and produce healing of the soft tissues.

CRITERIA FOR USE

1. Epicondylalgia lasting at least 6 months
2. Unresponsive or insufficiently responsive to other treatments including NSAID(s), straps, stretching and strengthening exercises, and at least one glucocorticosteroid injection.

SUPPORTING DOCUMENTATION

ODG Ankle and Foot (updated 04/27/17) - Online Version
Platelet-rich plasma (PRP)
Not recommended, with higher quality evidence showing this treatment to be no better than placebo.
Also see other chapters where this is covered: the Elbow Chapter; the Shoulder Chapter; the Knee Chapter; the Hip Chapter; the Wrist/Hand Chapter; the Low Back Chapter; the Burns Chapter; & the Pain Chapter. See also Autologous blood-derived injections; Injections (corticosteroid).
Platelet-rich plasma (PRP) is a bioactive component of whole blood with a high concentration of platelets containing growth factors, including platelet-derived growth factor, transforming growth factor, insulin-like growth factor, and vascular endothelial growth factor. PRP has been popular among professional athletes, but there is inadequate science to support general use. Based on a prospective study of 30 patients with chronic refractory Achilles tendinopathy treated with PRP, it was suggested that this should be reserved only for the "worst of the worst" patients. (AAOS, 2010) A systematic review concluded that PRP for Achilles tendinopathy did not improve health

outcomes. Case reports had previously highlighted rapid recovery of competitive athletes, with one case series of 14 patients reporting dramatic improvements. These claims were not confirmed in a high quality, double-blinded, sham-controlled randomized trial, which found no such benefit. PRP for chronic Achilles tendon disorders (tendinopathy, tendinitis, tendinosis) did not reduce pain or improve activity compared to sham injections, with no significant distinction between the 2 groups during any measurement period. Both treatment groups showed equivalent but positive clinical progression, as seen in previous PRP studies, likely due to the strict associated exercise protocols. Stretching and strengthening programs have been proven to be moderately effective. (de Vos, 2010) A follow-up study on the same 54 patients using ultra sonographic tissue characterization revealed no differences in tendon structure or neovascularization between groups. (de Vos, 2011) At one-year, no differences in outcome were ultimately seen. (de Jonge, 2011)
There are certainly different techniques for processing and activating PRP, so it is possible that the specific method used was not effective, but that others might be proven in the future. (Tice, 2010) A Cochrane Database systematic review extensively covering 1088 patients from 19 clinical trials for multiple conditions included only the single RCT for Achilles tendinopathy and another for post-surgical repair. The evidence for all primary outcomes was judged to be of very low quality, with 16/19 studies having high or unclear risk of bias. Lack of standardization and varying preparation techniques were areas of concern. It was concluded that there was insufficient evidence to support any platelet-rich therapies for musculoskeletal soft tissue injuries. (Moraes, 2014) Another systematic review also found that only the single RCT was available, also noting the paucity of high-level literature. (Di Matteo, 2015) A small case series initially suggested that treating chronic plantar fasciitis with PRP injections can be safe, with some potential to reduce pain. (Martinelli, 2012) 2 RCTs comparing PRP vs. corticosteroid injections showed similar results up to 6 months, but sustained better outcomes were seen at 12 months with PRP. (Jain, 2015) (Monto, 2014) However, a systematic review has questioned these plantar fascia studies for failure to compare to sham injections (true control), and noted that previous research had already demonstrated no differences between PRP and dextrose prolotherapy outcomes. (Franceschi, 2014)

ACOEM Practice Guidelines: Ankle and Foot Disorders. https://new.mdguidelines.com/Resources/ACOEM-Practice-Guidelines/Disorders/Ankle-and-Foot-Disorders. (effective September 1, 2015)
ANKLE AND FOOT DISORDERS
DIAGNOSTIC AND TREATMENT RECOMMENDATIONS
PLANTAR HEEL PAIN (PLANTAR FASCIITIS)
TREATMENT RECOMMENDATIONS
Injection Therapies
Platelet Rich Plasma
Injected platelet rich plasma has been used for treatment of plantar fasciitis.
Platelet Rich Plasma Injections for Plantar Fasciitis
No Recommendation. There is no recommendation for or against the use of platelet rich plasma injections for treatment of plantar fasciitis.
Strength of Evidence - No Recommendation, Insufficient Evidence (I)
Level of Confidence - Low

ODG Elbow (updated 06/27/17) - Online Version
Platelet-rich plasma (PRP)
Recommend single injection as a second-line therapy for chronic lateral epicondylitis after first-line physical therapy such as eccentric loading, stretching and strengthening exercises, based on recent research below.
See also Autologous blood injection.
This small pilot study found that 15 patients with chronic elbow tendinosis treated with buffered platelet-rich plasma (PRP) showed an 81% improvement in their visual analog pain scores after six months, and concluded that PRP should be considered before surgical intervention. Further evaluation of this novel treatment is warranted. (Mishra, 2006) This review concluded that there is strong pilot-level evidence supporting the use of prolotherapy, polidocanol, autologous whole blood and platelet-rich plasma injections in the treatment of lateral epicondylosis (LE). Rigorous studies of sufficient sample size, assessing these injection therapies using validated clinical, radiological and biomechanical measures, and tissue injury/healing-responsive biomarkers, are needed to determine long-term effectiveness and safety, and whether these techniques can play a definitive role in the management of LE and other tendinopathies. (Rabago, 2009) Using a Gravitational platelet separation system, whole blood can yield platelet-rich plasma. Specially prepared platelets taken from the patient are then re-injected into the tendon of the affected elbow. Platelet-rich plasma contains powerful growth factors that initiate healing in the tendon, but may also send signals to other cells in the body drawing them to the injured area to help in repair. Treatment with PRP is still considered investigational and further research is needed before it can be made available to the general

population. According to the author, "The body has an extraordinary ability to heal itself. All we did was speed the process by taking blood from a different area, concentrating it, and putting it back into an area where there was relatively poor blood supply to help repair the damage." Early studies have shown PRP therapy may be useful in maxillofacial surgery, wound healing, micro fracture repair, and in the treatment of plantar fasciitis. PRP looks promising, but it is not yet ready for prime time. PRP has become popular among professional athletes because it promises to enhance performance, but there is no science behind it yet. PRP was better than corticosteroid injections in relieving pain and improving function in patients with chronic severe lateral epicondylitis, but the study concluded that PRP should be reserved for the most severe cases since 80% of tennis elbows will be cured spontaneously without doing anything within a year. (AAOS, 2010)
Recent research: This RCT showed that 49% of patients in the corticosteroid group while 73% of patients in the PRP group were successful. The corticosteroid group was better initially and then declined, whereas the PRP group progressively improved. The authors concluded that treatment of patients with chronic lateral epicondylitis with PRP reduces pain and significantly increases function, exceeding the effect of corticosteroid injection. (Peerbooms, 2010) These benefits persisted even after a follow-up of 2 years. (Gosens, 2011) This RCT found success with both autologous blood and PRP, but PRP was superior to autologous blood in the short term. (Thanasas, 2011) At 6 months the authors observed a 66% success rate in the platelet-rich plasma (PRP) injections group versus 72% in the autologous blood injections (ABI) group, but there was a higher rate of conversion to surgery in the ABI group (20%) versus the PRP group (10%). In patients who are resistant to first-line physical therapy such as eccentric loading, ABI or PRP injections are useful second-line therapies to improve clinical outcomes. In this study, up to seven out of 10 additional patients in this difficult to treat cohort benefit from these surgery-sparing interventions. (Creaney, 2011) (Bisset, 2011) According to this short-term RCT, neither steroids nor platelet-rich plasma injections are any better than injections of inactive salt water for treating tennis elbow. After one month, pain had dropped by almost 10 points on a 50-point scale among people who'd had steroid injections, compared to less than two points for the PRP and saline groups. Elbow function had also improved significantly more for people injected with steroids. However, at three months, any extra benefit due to steroids had disappeared and pain and functioning were similar across all three groups. The study did not follow patients for enough time to see the long-term effects of platelets. In other studies, PRP patients continue to improve, and the glucocorticoid patients revert to normal, as steroids only provide short-term relief and may damage the tendon further with repeat injections. For people who have had tendon problems for weeks rather than months or years, watchful waiting might be the most appropriate treatment, since after a year, 80% of people with tennis elbow will be cured. (Krogh, 2013) The results of this study indicated that PRP is an effective option to successfully treat partial ulnar collateral ligament (UCL) tears of the elbow in athletes. At an average follow-up of 70 weeks, 88% of athletes had returned to the same level of play without any complaints, and the average time to return to play was 12 weeks. (Podesta, 2013) Results from this systematic review of injection therapies in lateral epicondylitis found that both autologous blood and platelet-rich plasma were statistically superior to placebo, but there were issues of potential bias. (Krogh, 2013) According to Cochrane, the evidence for all primary PRP outcomes is very low quality. When pooling data for all conditions, not just epicondylitis, they concluded that there is insufficient evidence to support the use of PRP for treating musculoskeletal soft tissue injuries, and said there is need for standardization of PRP preparation methods. (Moraes, 2014) In this double-blinded RCT patients had their extensor tendons needled with or without PRP. No significant differences were found at 12 weeks, but at 24 weeks, clinically meaningful improvements were found in patients treated with leukocyte-enriched PRP compared with an active control group. Success rates for patients with 24 weeks of follow-up were 84% in the PRP group compared with 68% in the control group. (Mishra, 2014)
As an autologous preparation, PRP has been introduced into clinical practice without being subject to the stringent development required of new drugs. Commercially available PRP preparation devices have FDA approval, but this is based on device performance and safety, not evidence of clinical efficacy. Routine use of PRP in clinical practice cannot be recommended given the lack of high-quality clinical evidence supporting its efficacy. Patients should only be offered PRP for musculoskeletal soft tissue injuries within the context of well-designed clinical trials. Clinicians offering PRP should ask manufacturers for the evidence of the platelet and growth factor concentrations, the constitution, and the viability of their PRP product (platelet activation levels). (Keene, 2016)

ACOEM Practice Guidelines: Elbow Disorders.
https://new.mdguidelines.com/Resources/ACOEM-Practice-Guidelines/Disorders/Elbow-Disorders. (effective April 15, 2013)
Elbow Disorders
Diagnosis and Treatment Recommendations
Lateral Epicondylalgia
Treatment Recommendations
Platelet-rich Plasma Injections for Chronic Lateral Epicondylalgia

Recommended. Platelet-rich plasma injections are recommended for the treatment of chronic lateral epicondylalgia. Strength of Evidence - Recommended, Insufficient Evidence (I)

ODG Knee and Leg (updated 06/27/17) - Online Version
Platelet-rich plasma (PRP)
ODG Criteria for Platelet-rich plasma (PRP) intra-articular injection:
(1) Significantly symptomatic osteoarthritis:
(a) Not responded adequately to recommended conservative non-pharmacologic (e.g., exercise) and pharmacologic treatments or are intolerant of these therapies (e.g., gastrointestinal problems related to anti-inflammatory medications), after at least 6 months; &
(b) Documented symptomatic mild-moderate (not advanced) osteoarthritis of the knee; &
(c) Under 50 years of age; &
(d) Pain interferes with functional activities (e.g., ambulation, prolonged standing) and not attributed to other forms of joint disease; &
(e) Failure to adequately respond to aspiration and injection of intra-articular steroids; &
(f) Generally performed without fluoroscopic or ultrasound guidance; &
(g) Single injection highly concentrated WBC-poor (filtered); &
(h) Maximum once yearly if previous injection documented significant relief for over 6 months; OR
(2) Refractory patella tendinosis:
(a) Not responded adequately to recommended conservative non-pharmacologic (e.g., exercise) and pharmacologic treatments or are intolerant of these therapies (e.g., gastrointestinal problems related to anti-inflammatory medications), after at least 12 months; &
(b) Single injection, not multiple.

ODG Shoulder (updated 05/12/17) - Online Version
Platelet-rich plasma (PRP)
Not recommended.
PRP has been popular among professional athletes but the science behind it remains unconvincing. In a blinded, prospective, randomized trial of PRP vs. placebo during rotator cuff repair, there were no differences in pain relief, functional outcome, or residual defects on MRI. (AAOS, 2010) Platelet-rich fibrin matrix (PRFM) applied to the site of rotator cuff tendon repair also did not improve healing, with significantly higher failure rate with PRFM vs. control for double-row repairs. (Rodeo, 2012) PRP during surgery for large to massive rotator cuff repairs reportedly improved structural outcomes with a decreased re-tear rate (20% vs. 56%) and increased cross-sectional area of the supraspinatus compared to repairs without PRP augmentation, although no differences in clinical results were seen. (Jo, 2013) The same author claiming such dramatic differences for giant tears then reported on medium to large tear repairs with 3% vs. 20% re-tearing (not clearly defined) with and without PRP, again with similar clinical outcomes. (Jo, 2015).
In contrast, a Cochrane systematic review of 19 clinical trials including 6 rotator cuff repair and 1 impingement surgery application, noted high or unclear bias, variable preparation techniques and lack of standardization causing the evidence for primary outcomes of PRP to be of very low quality. Specifically, the cuff repair trials showed no statistical or clinically significant differences with PRP. The authors concluded that overall, and for individual clinical conditions, there is currently insufficient evidence to support PRP for musculoskeletal soft tissue injuries. (Moraes, 2014) A systematic review of 7 meta-analyses of several thousand patients concluded that PRP with cuff repair does not universally improve re-tear rates and does not affect clinical outcome scores. It appears that the author reporting much lower re-tear rates in several published RCTs has not been verified by other investigators. It is suggested that currently reported but not yet verified beneficial applications might involve a solid PRP matrix, applied only to the bone-tendon interface, with small/medium sized double-row repairs. (Saltzman, 2015) Another meta-analysis and cost-effectiveness analysis reviewing 13 studies from 2010-2014 noted some statistical difference in favor of PRP regarding re-tears, but concluded that in large tears PRP was simply insufficient to make any difference, and even though it might promote improved healing in small/medium tears, the application was not cost-effective. (Vavken, 2015) Several other SR/MA studies showing no proven benefit of PRP for cuff repair are available. (Warth, 2015) (Zhao, 2015) (Li, 2014)
In addition, an RCT with 2 post-operative PRP injections similarly failed to improve tendon-bone healing or functional recovery. (Wang, 2015) A single RCT with PRP injections for rotator cuff tendinopathy showed some reduction up to six months of pain and disability compared to dry needling. (Rha, 2013) However, an RCT with and without PRP tendon injections in combination with arthroscopic needling for calcific rotator cuff tendonitis showed no differences in clinical outcomes or residual cuff defects. (Verhaegen, 2016) PRP injections in a wheelchair population with biceps tendinopathy noted some mild overall positive effects. (Ibrahim, 2013)

REFERENCE(S)

ODG Ankle and Foot (updated 04/27/17) - Online Version

ACOEM Practice Guidelines: Ankle and Foot Disorders. https://new.mdguidelines.com/Resources/ACOEM-Practice-Guidelines/Disorders/Ankle-and-Foot-Disorders. (effective September 1, 2015)

ODG Elbow (updated 06/27/17) - Online Version

ACOEM Practice Guidelines: Elbow Disorders. https://new.mdguidelines.com/Resources/ACOEM-Practice-Guidelines/Disorders/Elbow-Disorders. (effective April 15, 2013)

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ODG Shoulder (updated 05/12/17) - Online Version