

All You Need is Blood

by: Karen Stassi

Ortho Docs Look at
Platelet Rich Plasma

Blood.

In the world of medicine, it holds a preeminent position both as essential for life and as a pathway for, or indicator of, illness. Now doctors are looking more closely at blood, specifically the platelets, as a conduit for natural growth factors that can jumpstart healing after surgery or injury. Used for several years by dentists and oral surgeons, platelet rich plasma (PRP) therapy is now gaining a following among orthopaedic specialists as a treatment for chronic tendonitis and muscle injury. Its use on a few high profile athletes in the NFL and MLB has generated a buzz both in medical journals and the popular media, but the jury is still out on whether it is truly effective.

Platelet rich plasma is exactly what it sounds like. Whole blood is drawn from the patient, treated with an anticoagulant and spun down in a centrifuge. When the blood separates into its different components, you are left with a dark layer of red blood cells and a clear yellow layer of plasma. In between is a barely visible layer, the buffy coat, of white blood cells (leukocytes) and platelets. The platelet rich plasma is simply that layer of platelets concentrated in a small amount of plasma to about five times the amount in whole blood. When used in clinical applications, that platelet rich plasma is then injected directly into the site of the tendon injury or tendonitis. "The reason we believe it works is that platelets have various growth factors such as vascular endothelial growth factor, transforming growth factor, and platelet-derived growth factor, and those growth factors have several effects," said Dr. Joseph Broyles, an orthopaedic surgeon at the Bone & Joint Clinic of Baton Rouge. "One of the most important effects is that it increases new blood vessel growth in that area." That's important because tendonitis is an avascular, non-inflammatory condition and the limited blood supply in the tendons tends to slow the healing process. The theory is that injecting platelets with growth factors directly into the tendon will cause an inflammatory reaction, boost new blood vessel growth, and improve the chance of actual tendon healing. Broyles indicated that the healing effect has been clearly shown to be the case in animal studies. "When tendons are transected and then injected with platelet concentrates, the new blood vessel growth that we see on histologic slides occurs much sooner and to a greater degree than in situations where the platelets are not used. It also heals at a faster rate or reaches improved mechanical strength earlier," he said.

Despite clear animal evidence, there have not been many long-term, randomized human studies. Those that have been done are too small or too uncontrolled to produce definitive answers, but for the most part do support the evidence seen in animal studies. One of the first studies was conducted by Dr. Allan Mishra, an orthopaedic surgeon in California. He published an article in the *American Journal of Sports Medicine* in 2006 in which he discussed using platelet rich plasma to treat tennis elbow in several patients. For his small control group, he injected five patients with Marcaine, a local anesthetic. The other fifteen subjects received PRP therapy. Each of Mishra's patients had already explored conservative treatments for tennis elbow including anti-inflammatories, physical therapy, and cortisone shots. "Those patients had done just about everything else and those patients in my experience don't get better unless you operate," said Broyles. Three members of the control group opted out before the study's conclusion and required surgery. However, all members of the treatment group were able to avoid surgery and at final follow-up, which was between one and three years, reported a 93% improvement in symptoms.

Mishra's study inspired Dr. Broyles to ultimately engage in a prime example of "physician heal thyself." Suffering from a chronic case of tendonosis in his quadriceps tendon for two years, Broyles began to research the latest treatments. He came across Mishra's article and thought the science behind it made sense. So, in August of 2008 he tested PRP on himself. It was a painful, but ultimately successful experiment. "I have to admit that for the first two days I wondered, 'What have I done?'" laughed Broyles. "The pain increased initially and I was on crutches." However, the immediate pain subsided after a few days and after four months the pain in his leg was totally gone. "I could lift as much weight as I wanted with no pain for the first time in two years." Encouraged by his results, he tried the therapy again on a family member with tennis elbow. The family member also showed improvement. Broyles decided that he would begin to offer PRP to his patients. "It's a very safe procedure, there's really no downside, no significant risks involved with it," said Broyles.

The fact that the procedure is minimally invasive, uses the patient's own blood, and usually involves no additives other than the anticoagulant, does mean that besides the initial pain, there is little risk of infection or adverse reaction to PRP therapy. Some studies suggest that PRP used in spinal injuries might actually slow healing, but like many other PRP

studies to date, the results are inconclusive. Most, but not all, suggest a benefit to using PRP for tendon injuries in the shoulder, arm, knee, and leg. Dr. Joseph Laughlin, an orthopaedic surgeon at Baton Rouge Orthopaedic Clinic who has also used PRP, noted, however, a recent study published in the January 13, 2010 issue of the *Journal of the American Medical Association* in which platelet rich plasma was used for Achilles tendonopathy. In that study Robert J. de Vos, MD and colleagues observed that while all of their 54 patients improved, no additional benefit was seen in those receiving PRP over patients who received just a saline injection. The study's authors therefore did not recommend PRP for Achilles tendonopathy. Broyles indicated that he had also read the article with interest, because, "Obviously I don't want to do anything that isn't going to work," but he had some questions about both the inclusion criteria and the controls used in the study. The study published in *JAMA* required that patients have tendonosis symptoms for at least two months, which is significantly shorter than the time period Broyles considers for his patients before recommending PRP. "With patients that have symptoms of this for two months, in my experience, a lot of those patients, no matter what you do, they're going to get better because they haven't had that condition long enough to tell me that it's truly going to be an ongoing, chronic problem," said Broyles. "Part of what we are probably seeing in that

study is that even the patients with the saline injection got better because they were going to get better anyway. It wasn't that bad of a case of tendonosis." Broyles said that in addition, both groups engaged in eccentric stretching exercises, which have been shown to be beneficial in tendonosis. He believes the stretching could be considered confounding treatment. However, Broyles said the study does raise the question of whether "the science that we clearly see in animal studies and in vitro conditions and the known effects of these various growth factors, in the long term will pan out to be something that we continue to use in clinical practice."

In the meantime, Broyles believes the therapy has helped people that probably would not have gotten better otherwise and is keeping careful data on his own results. One



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of his patients, referred to him by a physical therapist, had plantar fasciitis for two years, had received cortisone shots, engaged in physical therapy off and on for 18 months, and was considering surgery. The patient's pain score before the injection, on a scale of zero to 100 was approximately 70. Two months after the injection his pain score was a 12 and he was reportedly ecstatic. "I've had other cases like that, but I can't tell you that it's helped every single patient because there have been some who didn't get any benefit from it," said Broyles. "I think that the patients who are much more active early on probably have more pain than someone who is resting. The big thing is they need to understand it's not an immediate fix. It's a gradual process and as time goes by they should notice more good days and fewer bad days." Laughlin has also heard mixed reactions on the effectiveness of PRP, but estimates about a 60 to 70% success rate in the cases he has heard about. He also acknowledges that many patients will get better on their own, pointing out that only about 10% of people with tennis elbow require surgery. That means that 90% will eventually get better, but perhaps PRP can speed up that process.

As noted, PRP is most commonly being used to treat tendonitis in the knee, elbow, and shoulder but has also been used to treat plantar fasciitis and knee osteoarthritis. It's also used in knee replacement, Achilles tendon repair, muscle

repair, anterior cruciate ligament reconstruction, and spinal injury, with varying results, particularly in the latter two instances. Dr. Laughlin has treated tennis elbow with PRP and has used it to assist in healing after arthroscopic knee surgery. He also injected PRP into the knee of one of his partners at Baton Rouge Orthopaedic Clinic, Dr. Robichaux, who had treated patients with PRP and was of the personal opinion that it would help the area of his torn meniscus heal faster, said Laughlin. Several other doctors at the clinic have used the therapy, primarily for tennis elbow, according to Laughlin. Broyles indicated that other orthopaedic surgeons at the Bone and Joint Clinic had tried it and/or had referred patients to him for treatment. PRP therapy can be rendered in an outpatient setting with a variety of delivery systems now on the market or may be used during surgical repair. While one injection is standard, some studies report using as many as three at multi-day intervals. PRP therapy may be offered alone or in conjunction with stretching or exercise. All of these factors make it difficult to compare results on an "apples to apples" basis.

There is some speculation, furthered by the recent study in *JAMA*, that tendonitis may not be responding to PRP, but may be merely getting better on its own or that patients may be experiencing a placebo effect based on some intervention having been taken. Broyles concedes that's a valid argument

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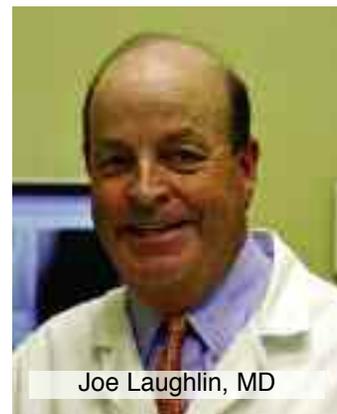
and the only way we'll know is through further studies. "However, when we do surgery we are cutting out that diseased tendon. The surgery itself causes an inflammatory response, which is going to increase blood flow to that area. If we can inject something that will increase the growth of new blood vessels it seems logical to me that this has a real chance of solving the problem." While he and his colleagues have used the therapy, Laughlin said PRP, "hasn't so far, passed the test of time and there's no double-blinded studies out there." However, he indicated that doctors often use therapies that seem to work before the scientific studies that support them are in place. "That's very usual for the way medical advances come along," said Laughlin, pointing to the high cost of doing the studies. "I've heard that to run a very good double-blinded study can cost between \$5 million and \$10 million and you need a statistically significant group of patients." In the meantime, doctors are seeing some promising results so they are giving it a try. Treatments like these can also be driven by public demand and given recent articles about PRP's use in professional athletes, patients may start to ask about it although, "I haven't had anybody personally come to me and say, "I want some platelet rich plasma," said Laughlin.

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- JOE LAUGHLIN, MD

Instead, PRP is generally only offered to patients who have chronic conditions, have exhausted other options first, and are considering surgery. "If a patient comes to me with tennis elbow, even if they've had it for four months, I give them a cortisone shot first," said Broyles. "A lot of times patients will get better with that...it's a quick fix, they get immediate relief and if it goes away then fine." Broyles has also had patients opt for surgery rather than a single PRP injection. That may or may not surprise you depending on how familiar you are with the vagaries of insurance coverage. Because PRP therapy is still relatively unknown and lacking large, long-term, randomized studies to back its efficacy, some insurance companies won't cover the treatment. However, orthopaedic surgery to correct a chronic condition generally is covered. If insurance won't cover the treatment, Broyles charges \$500 per PRP procedure. Based on reports from around the country, PRP therapy can cost as little as \$150 to as much as \$2000 per shot. It's a

significant cost, but may still be less than many patients' deductibles and is certainly less invasive than surgery. Laughlin said some of the doctors at his clinic only use PRP during surgery because the cost is more likely to be covered. It can be used to reduce bleeding and promote healing during rotator cuff repair or knee replacement.



Joe Laughlin, MD

It may also come as no surprise that any procedure that involves talk of growth factors and professional athletes has drawn close scrutiny. "I've seen that question come up before and in my opinion as a physician and knowing what this is, I don't think there should be any controversy about the use of this in athletes," said Broyles. "If you were to ban this you would have to ban any other intervention that we do for athletes including therapy, including surgery. Surgery is much more invasive than this—we're changing the natural course of events—this is simply giving the patient his own platelets." He said there should be no suspicion because the only thing that's added is an anticoagulant to keep the blood from clotting when you spin it down. It is not enhancing performance, just healing. "I guess that's a way to look at it," said Dr. Laughlin who indicated that the Olympic sports committees, particularly the World Anti-doping Agency, have not approved PRP for use in athletes because it is a blood product that is helping something heal outside of the ordinary process. "From the Olympics' perspective, the big, rich countries would have an added advantage over other countries that don't have this therapy available," he said.

Laughlin said that while the evidence supporting PRP is better than anecdotal, it's still a technique looking for definite indications. "Nobody knows if we should do it after they've had the pain for three months or six months. How deep do we inject it? What we really need is double-blinded, controlled studies. In a perfect world we would have evidence-based medicine for everything that we do." While Broyles agrees the studies are needed, he thinks PRP is a promising technology. "I think twenty years from now or maybe before that, we won't be doing surgery for tendonosis. And it may not be platelets we're using. It may be that we have a vial of endothelial growth factor that you order from the pharmaceutical company that we inject directly into the tendon." In the meantime, blood is all you need. ❖

Sources: Robert J. de Vos, MD, Adam Weir, MBBS, Hans T. M. van Schie, DVM, PhD, Sita M. A. Bierma-Zeinstra, PhD, Jan A. N. Verhaar, MD, PhD, Harrie Weinans, PhD, Johannes L. Tol, MD, PhD, "Platelet-Rich Plasma Injection for Chronic Achilles Tendinopathy," *JAMA* 2010;303(2):144-149; Storrs, Carina, "Is Platelet-Rich Plasma an Effective Healing Therapy?" *Scientific American*, Dec. 18, 2009 <http://www.scientificamerican.com/article.cfm?id=platelet-rich-plasma-therapy-dennis-cardone-sports-medicine-injury>; Schwarz, Alan, "A Promising Treatment for Athletes, in Blood" *New York Times*, Feb 16, 2009, www.nytimes.com/2009/02/17/sports/17blood.html; Hall, Michael, MD, Band, Philip, PhD, Meislin, Robert J., MD, Jazrawi, Laith, MD, Dardone, Dennis, DO, "Platelet Rich Plasma: Current Concepts and Application in Sports Medicine," *Journal of the American Academy of Orthopaedic Surgeons*, October 2009, Vol. 17, No. 10. P. 602-608; Boyan, Barbara D., PhD, Schwartz, Zvi, DMD, PhD, Patterson, Thomas E., PhD, Muschler, George, MD, "Clinical use of platelet-rich plasma in orthopaedics," *American Academy of Orthopaedic Surgeons*, September 2007, *AAOS Now*, <http://www.aaos.org/news/bulletin/sep07/research2.asp>; Mishra A, Pavelko T. Treatment of chronic elbow tendinosis with buffered platelet-rich plasma. *Am J Sports Med*. 2006;10(10):1-5; Mandelbaum, Bert, "Platelet rich plasma injection graft for musculoskeletal injuries: a review, *Curr Rev Musculoskeletal Med.*, DOI 10.1007/s12178-008-9032-5.