

Regenerative Therapies - Stem Cell & Platelet Rich Plasma (PRP)

An Introduction to Regenerative Medicine

Platelet Rich Plasma (PRP) and Stem Cell injections are part of an emerging field called regenerative medicine, which uses various biologic substances to heal and regrow damaged tissue naturally. Today, regenerative therapies are being used by a growing number of medical specialties to induce a therapeutic response by utilizing the body's own native healing capacities. PRP injections are used for a variety of therapeutic interventions including musculoskeletal injuries that involve damage to tendons, ligaments, cartilage, disc, joints, and sometimes bone. Many professional athletes have turned to regenerative therapies to hasten recovery and return to the playing field. In this document, I will provide a brief overview of the current uses of regenerative therapies in the treatment of musculoskeletal injuries.

Regenerative Therapy treatments represent one of the major breakthroughs in medical science over the last 10-15 years, offering a less invasive treatment option for those suffering from a variety of musculoskeletal injuries. These treatments can make a real difference in patient's lives and healthcare costs due to their ability to help avoid more invasive, risky, and expensive open surgery. Some of the reported benefits include shorter recovery, less invasive, lower risks, healing the body more naturally, maintenance of the body's normal biomechanics, and less time out of work. Today, there are a variety of biologic substances/products that may be injected but the main stay of therapy continues to be PRP and stem cell injections.

Regenerative therapies tends to target structures that are typically avascular by nature (tendons, ligaments, discs, and cartilage all have poor blood supply) and therefore the body's normal reparative cells are not able to reach the site of injury in sufficient numbers to heal the damaged tissue. By injecting PRP and/or Stem Cells into the area, we deliver reparative cells directly to the point of injury, to stimulate a natural healing process which replaces and repairs structurally damaged tissue. Most importantly, the injections deliver growth factors directly to the site of injury to induce a natural healing process.

PRP is indicated for a variety of musculoskeletal (orthopedic) injuries including: lateral epicondylitis (tennis elbow), medial epicondylitis (golfers elbow), partial rotator cuff tears (NOTE: complete tears with retraction are not appropriate candidates), labral tears of both the shoulder and hip, chronic hamstring tears, medial and lateral collateral ligament tears of the knee, meniscus tears of the knee, plantar fasciitis, chronic ankle sprain (triangular ligament tear), partial Achilles tendon tears, as well as a variety of other musculoskeletal injuries. It can also be used to treat degenerative arthritis. Although the arthritis may not be completely reversed, the treatment can slow progression and achieve long-term pain relief. This helps to delay and sometimes avoid the need for joint replacement or other invasive surgical procedures.

For many reasons these injections are ideal for the active patient or injured worker who does not want surgery and the associated time out of work (and/or play) for recovery. The advantages of regenerative therapies are the lower cost, less invasive nature of the procedures, extremely low risk of infection (due to the antimicrobial effects of the injectate), less time out of work for

recovery, and minimal risks/complications. If regenerative therapies do not work, conventional surgery can still be performed.

Research is being produced at a frenzied rate in this emerging field, with thousands of studies worldwide looking at various regenerative therapies for a multitude of indications. For some conditions, multiple studies have shown good results already, such as the very high success rate in the treatment of lateral epicondylitis (as high as 93% success in one study). For many conditions, the data/research is simply not available yet and so today many of the treatments are based on a combination of research and the anecdotal experience of the physician. At Connecticut Pain Care, we have seen high success rates with most of our regenerative treatments, (over 80% of our patients achieve at least 50% relief of their symptoms and avoid surgery), with approximately 80% requiring a single treatment to achieve this result. Unlike steroids, once the injury heals, symptoms typically won't recur except with a new injury to the area. Note: Larger injuries or more significant tissue damage may require more than one treatment.

Regenerative therapies are safe, minimally invasive treatments that are low cost, low risk, high benefit, associated with shorter and easier recovery, less need for postoperative opioid medications, and do not result in the later development of post-surgical (post-traumatic) osteoarthritis. It is currently being used by athletes all over the world as first line therapy (when medically appropriate) over surgical treatment. While there is resistance to these treatments within some portions of the medical community, it has been embraced and accepted by many physicians (including surgeons). Regenerative therapy will not cure all injuries or degenerative processes, but the indications are certainly expanding and eventually insurance will begin to accept these forms of treatment as they better understand the clinical and financial benefits.

Platelet rich plasma can be used without stem cells for more simple injuries that involve tendon, ligament or muscle injury. Arthritic involvement and other injuries may require the use of direct stem cell injections, which have greater reparative potential, but are also significantly more costly to obtain (Note: PRP which comes from the patient's blood contains some limited number of stem cells). Below I will highlight some of the differences.

PRP

PRP treatment utilizes concentrated platelets obtained by centrifugation of the patient's own peripheral blood (PRP is always autologous), and then the re-injection of those platelets into the site of injury enabling natural regrowth and repair of damaged tissue. Platelets are effective in this process because they contain proteins called growth factors and cytokines. The various growth factors within platelets promote a cascade of events that enable healing and tissue growth to occur. Some of these events include enhanced blood flow, signaling the body to send healing anti-inflammatory mediators to the area, attraction of stem cells, and differentiation of cells to promote tissue growth.

Platelet rich plasma is typically produced by drawing 2 oz. or 4 tablespoons (60cc) of the patient's blood, mixing it with an anti-coagulant, and then placing it in a machine called a centrifuge. This machine spins the patient's blood at a rapid speed causing the platelets, growth

factors and white blood cells to be separated from the red cells and other blood products. Today there are many different machines that produce PRP of a variable nature including some that are RBC and WBC poor (this also removes all circulating white cells such as hematopoietic stem cells).

We then treat/expose the prepared PRP sample to a special light source (*Adistem* light), which activates the platelets and modulates the cytokines within the PRP preparation, promoting anti-inflammatory cytokines and inhibiting pro-inflammatory cytokines. This last process reduces the pain and inflammation the patient experiences when the platelets and growth factors are injected back into the injured area (this component of our regenerative protocol is not offered by most other practices).

Once introduced into the injured site, the platelet derived growth factors and other signaling proteins stimulate the body healing process. This includes the stimulation of blood flow into the area through angiogenesis and chemically signaling the body to send in more stem cells to assist with the healing process. PRP works with stem cells to repair the area.

Tissue growth takes time and thus pain and symptom relief won't occur overnight as is seen with steroid injections. Rather, this takes weeks to months to happen, and the timing of healing is highly dependent on tissue type and site of injection. Like planting a new lawn, grass doesn't grow overnight. The time each tissue takes to heal is different, some as quickly as weeks, and others can take months to see an initial effect, such as with shoulders. In fact, full benefit occurs upwards of 6 months to one year after injection (note: shoulder surgery also takes a year to recover and extensive therapy post-op). Unlike steroids, which cause breakdown (or catabolism) of tissue, often leading to other and sometimes bigger problems, PRP helps to grow new normal tissue, healing damaged structures naturally.

Stem Cells

Stem Cell Therapy is typically used (rather than PRP) for more severe injuries (I.e.- when advanced degenerative arthritis is present). The use of concentrated stem cells provides delivery of large amounts of growth factors which can theoretically stimulate a greater degree of tissue repair for more significantly damaged tissue. Stem cells should be considered when the extent of arthritis is moderate or worse, especially with significant bone marrow lesions and cartilage loss as is seen with advanced degenerative arthritis. Stem Cells can come from a variety of sources and I will discuss some of these below. Stem cell therapies are regulated by the FDA and cloning of stem cells is prohibited by law in the U.S.; some physicians have developed clinics for this purpose outside of the U.S. where they are not governed by such laws and where there is also little regulatory/safety oversight.

For more severe problems such as osteoarthritis of joints, we need more repair cells and we achieve this by delivering larger numbers of stem cells into the affected area. This is accomplished by injecting stem cells derived from adipose tissue, bone marrow, and our placental derived tissue directly into the area. Stem cells are rudimentary cells that can differentiate into other cells of the body, i.e. – cartilage and bone. There are many types of stem cells within the body and they are not all created equal in their ability to promote tissue repair;

some are pluripotent (can develop into many different tissue types) and others multipotent (tissue specific). The goal of stem cell injections into the arthritic joint is to encourage cartilaginous growth, improve blood flow to the damaged area, reverse underlying bone lesions (damaged bone under the cartilage adjacent to the joint that also begins to degenerate), and repair other diseased elements of the joint.

Stem cells have been in the news the last several years with many new advancements occurring every year. Some of the more exciting research is taking place in other areas of medicine such as spinal cord injury and diabetes. I can imagine the day when we can treat diabetes with a stem cell transplant of pancreatic islet cells (the cells in your body that make insulin), preventing the need for a lifetime of insulin shots for a young child with juvenile onset diabetes. Treatment like this should also prevent the secondary organ disease that occurs related to poor blood sugar control (i.e.- neuropathy, heart disease, strokes, renal failure, and retinopathy).

Although stem cell treatment might sound innovative and cutting edge, this therapy has been around for quite some time and has been used by many other medical fields in the treatment of a variety of diseases. The types of stem cells we are discussing are not the ones referred to by politicians (those are embryonic stem cells and not the autologous adult stem cells used in most of our therapies). In the past, these cells were very difficult and expensive to procure. However, in today's world with modern advances in our techniques and equipment, stem cells can easily be obtained (harvested) and concentrated in a simple office procedure or even purchased in placental derived products.

Stem cells exist in your body from the very beginning. The earliest stem cells (embryonic) are unspecialized and it isn't until they start to mature or differentiate that their specific cellular functions begin to be expressed. They split and divide in a pre-programmed fashion, enabling them to become the cells that make up parts of the body such as your muscles and nerves. Adult stem cells exist and in fact are required for life; your body must replace millions of cells every day or you would die. Evidence of their existence is seen in the fact that we continue to grow/replace our skin, hair, and our intestinal lining. While the human body is naturally able to entirely reproduce (i.e. - replace/repair) itself every 6 years, as you get older the absolute numbers of stem cells in your body decrease and therefore your ability to repair tissue on your own decreases.

Stem cells are integral to tissue repair and regrowth, they usually travel to the injured areas via the blood stream and are responsible for much of the healing process. If the injured area has a poor blood supply, then stem cells and other reparative cells such as platelets cannot get delivered in sufficient numbers to repair the damaged tissue. This is often an area of hypoxia or low oxygen content. Regenerative injections help reverse this problem by increasing blood flow into the area through angiogenesis stimulation (or blood vessel growth) so that the body can deliver the nutrients and cells it needs to repair the damaged tissue.

Mesenchymal stem cells repair and regenerate muscle, bone, cartilage, or tendons and the richest source of these types of cells in the body is found in adipose tissue, your fat! New fat stem cell harvest procedures have been developed that accomplish this process with consistency, but the safety has been questioned by the FDA and they have blocked some practices from doing these

therapies claiming they involve more than “minimal cell manipulation”. To avoid this issue, I have chosen to use whole emulsified fat combined with PRP and/or stem cell injections avoiding this issue of minimal manipulation. I believe the fat graft provides a source of some additional stem cells, favorable chemical mediators, and a scaffold or template which will help keep the stem cell injectate localized. The fat graft is typically harvested from the lower abdomen or flank (love handles).

Bone marrow is also a rich source of stem cells. It contains various types of stem cells (mostly hematopoietic but some mesenchymal) and is FDA approved. Bone marrow aspirate is typically accomplished by aspirating from the bone marrow in the back of the pelvis (the iliac crest), using a simple technique to draw fluid from inside the bone. There is minimal discomfort with this procedure as the area is first well anesthetized before placing the needle (although you will feel the local anesthetic injection). After the bone marrow fluid is aspirated, it may be centrifuged depending on the technique and treatment indication.

Tissue repair usually takes months, and possibly a year for a full effect, but early improvement of the symptoms is usually noted within 2-3 months. Approximately 4-6 weeks after the stem cell injection, a platelet rich plasma injection may be performed to re-stimulate, recruit, and promote the growth of additional stem cells to effectuate repair of the surrounding tissue.

Today, there are a number of placental derived regenerative products, including amniotic and umbilical cord blood derived. These typically contain concentrated quantities of tissue growth factors, and some of these products may contain variable amounts of live cells. The viability of these stem cells has been questioned by some who feel that the primary effect comes from the high concentration of growth factors in these products. Stem cells contain hundreds of different growth factors which can induce or inhibit the healing process, the balance of these various growth factors seems to hold the key to inducing a successful therapeutic response. These growth factors can be both angiogenic and highly chemotactic for autologous/native stem cells and other reparative cells inducing the bodies natural delivery of repair cells to the area. Most placental products contain predominantly growth factors and not live cells.

Frequently Asked Questions

Are these stem cells the same as embryonic stem cells?

No. They are your own adult stem cells. Embryonic stem cells can transmit genetic diseases that an embryo may carry. These genes could turn on certain cancers. In a young person, this might not initially be a problem but as this person ages the cancer chances will increase. If we use your own stem cells, there is no increased risk of cancer, therefore autologous adult stem cells are theoretically safer. Placental derived stem cells/products are also not embryonic but obtained from a fully formed placenta at birth, with donors being screened in an intense process, as is done with blood donation today.

Is it better to get stem cells from the bone marrow and then grow them in a lab to increase their numbers?

Cloning of stem cells is illegal in this country because there is speculation and some limited evidence that growing these stem cells out of the body may cause mutations to the cells, possibly causing increasing the risk for tumor line development.

What is the downtime from a stem cell or platelet procedure?

Essentially, there is no downtime from either procedure, although there will be some post-procedure discomfort for several days (sometimes a week or more). On the contrary, we encourage our patients to go out and use the affected area. We want the area to heal along normal stress lines and so resuming activity sooner than later is important. Your activity will be most limited by when the postop pain resolves/improves, however you must build back slowly into your full exercise regimen. We will discuss and guide you with this postoperatively, including specifically as to how it relates to your injury. Of course, one should expect some post-procedure discomfort (the degree will vary based on the area being treated and your own pain tolerance), but this is usually limited to a few days or a week. Stem cells and fat grafts usually hurt for a bit longer than PRP.

How do we know that this is a safe procedure?

There have been thousands of procedures performed worldwide safely and with limited adverse effects. There have been few reports in the literature of adverse reactions from stem cells or platelets especially when using the patient's own cells and putting them back into the same body the same day. It is hard to imagine something safer than re-injecting one's own body. In addition, the risk of infection is extremely low as both PRP and BMAC are bactericidal (i.e. - contain white cells and other products that help the body fight infection). Most adverse reactions in regenerative medicine have been related to added chemicals such as enzymes or preservatives in the injectate.

Is this procedure covered by insurance?

Unfortunately, likely not; we have found almost no carriers willing to cover PRP treatments at this time. Typically this treatment is labelled as investigational or experimental. The carriers will of course cover more invasive, riskier, more expensive, and quite frankly not always entirely proven surgery. It is also highly unlikely that your insurance carrier will cover stem cells at this time since this is a new cutting-edge procedure that most carriers still consider investigational.

How often does the procedure work?

In our practice, we have performed many PRP procedures, on many different areas of the body, with the vast majority of these patients having achieved greater than 50% relief, marked improved function, and as important, most of these patients have been able to avoid surgery. This is in part because of good patient selection; I wouldn't offer you this treatment if I didn't think it could potentially help you. By avoiding surgery, there is substantially less downtime and a much shorter recovery. Lost time from work after a regenerative treatment (if you are currently working) is typically 0-3 days. The results around the country (and the world) from stem cell

injections have also been good with some studies reporting 75% success for the knee and 50% success for the hip), but this is an area that also remains under active investigation.

Can the procedure fail?

Like any other procedure there is no 100% guarantee that the procedure will work. While simpler injuries typically respond to a single treatment, more complex injuries or advanced degeneration may require more than one treatment. It is also possible that your disease is too advanced to respond to these therapies as with severe end stage arthritis or complete tears of tendons and ligaments.

If the stem cells or platelets do not work can I still have surgery?

Yes, there is nothing about these procedures that would preclude you from having or effect the results of traditional surgery. If a regenerative therapy does not work, you can always have surgery.

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