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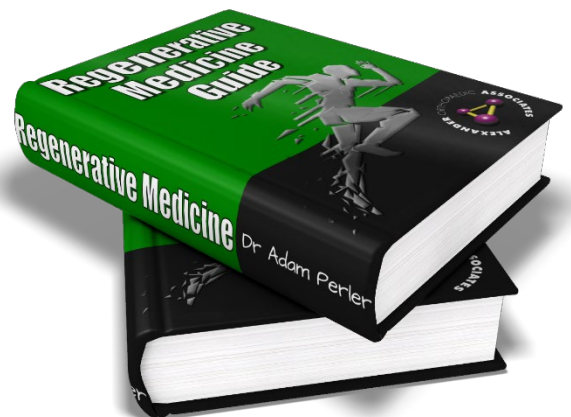
REGENERATIVE MEDICINE PRIMER

“We aren’t made of drugs, we’re made of cells. Stem cells, or stem cells in combination with pharmaceuticals, will be the future of medicine.”

Cade Hildreth, President/CEO of BioInformant

CELLULAR THERAPY AND REGENERATIVE MEDICINE

In the following section, I will attempt to give you an overview of an exciting and evolving field of medicine that will likely change the way we treat common injuries and conditions that affect normal function of the feet. Unfortunately, as with any new and exciting treatments, there is a lot of mis-information that can often lead to confusion and poor decision making regarding what is best for you on your pathway to recovery.



WHAT IS REGENERATIVE MEDICINE?

Regenerative medicine is a branch of translational research in tissue engineering, cellular and molecular biology which deals with the "process of replacing, engineering or regenerating human cells, tissues or organs to restore or establish normal function".

Though great progress has been made in medicine, current evidence-based and traditional treatments are increasingly unable to keep pace with patients' needs, especially given our aging population. In reality, there are few effective ways to truly treat the root causes of many of the diseases, injuries and congenital conditions that present to our office on a daily basis which are capable of restoring them back to their original/intended state. In many cases, we effectively can

only manage patients' symptoms using a traditional approach via medications, corrective surgeries and/or devices such as braces or insoles.



Although it has gained more recent attention, the field of regenerative medicine is actually not new. In fact, it has been around ever since the first successful bone marrow and organ transplant which were performed decades ago. But advances in developmental and cell biology, immunology, and other fields have unlocked new opportunities to refine existing regenerative therapies and develop newer ones. In the following article, you will learn about how regenerative medicine can be used to help you heal... perhaps the way nature originally intended.

Today, regenerative medicine is recognized as a game-changing and constantly evolving area of medicine with the potential to fully heal damaged tissues and organs, which were previously thought impossible by offering more natural/organic based solutions thus providing hope for people who have conditions that today are beyond repair by

more traditional mean. To delve deeper into the subject, lets take a look at how the body tries to repair itself after an injury.

HOW DOES THE BODY REPAIR ITSELF?

Inflammation is key to natural healing, however there are two different kinds of inflammation... a good type (acute) and a less productive type (chronic). Acute inflammation is your body's initial response to injured tissue. It may be due to trauma or repetitive stress to an area such as a tendon or ligament resulting in conditions such as Achilles tendonitis or plantar fasciitis. This type of inflammation generally resolves itself within a few weeks to months with proper care. Conservative treatments may include devices such as boots or braces to reduced stress to the area of damage thus giving it an opportunity to heal, anti-inflammatories, physical therapy and occasionally cortisone injections which aim to suppress and/or eliminate the inflammation.

If your injury remains untreated, the body develops chronic inflammation. During this chronic phase, macrophage cells (a special cell that feeds on non-viable cells or tissues) multiply in the injured area and can cause further problems. When body gives up on "actively" healing the injury, the chronic situation becomes the new norm and cannot heal itself. This is a big reason why it's so important to seek treatment when an injury does not improve after a number of days, instead of weeks or months. When a patient is seen with a chronic inflammation or condition, they usually explain that their level of pain is becoming intolerable.

WHAT ARE STEM CELLS, WHERE DO THEY COME FROM AND CAN THEY HELP ME?

Perhaps easiest way to define a true stem cell is to describe it as an immature “teenager” cell that hasn’t decided what it wants to be when it grows up. We call this pluripotency... in other words the cell can develop by a process of differentiation into many different types of cells such as skin cells, nerve tissues, cells that make up bone, cartilage or soft tissues such as ligaments and tendons. Thus, stem cells are a key component of regenerative medicine, as they hold the key to open the door to many new and exciting clinical applications.

There are mainly two different types of stem cells... embryonic and adult. While embryonic stem cells hold the most promise, there are often numerous ethical concerns that arise from their use since they are best harvested from a developing fetus. Scientists are trying to understand how these cells work and hoping to be able to replicate these types of immature pluripotent cells without crossing any ethical barriers. Currently, the closest we can get to fetal tissue without crossing an ethical barrier is to harvest tissue from the afterbirth of a healthy mommy and child such as the placenta or umbilical cord. While not true stem cells, these tissues can replicate part of the function of a stem cell which have been shown to stimulate new tissue growth by delivering high concentrations of growth factor to the site of injury and deliver something called extracellular matrix, which acts as a protein scaffolding for new tissue growth.

Adult stem cells, by definition are matured stem cells that typically come from ones own tissues such as blood (platelet rich Plasma or PRP), bone marrow or even belly fat aspiration. However, these cells are not considered to be nearly as viable in regards to regenerative properties since they have already been exposed to a number of stresses that occur to our bodies such as exposure to illnesses, food and drug toxicities as well as the typical and gradual degradation that comes with normal aging.

STEM CELL TECHNOLOGY AVAILABILITY

While true embryonic/fetal stem cells are difficult to get due to governmental restrictions and further discussion is needed regarding the ethics involved, embryonic derived tissues such as amnion/chorion and umbilical cord (Wharton’s Jelly) are readily available for use today. With that being said, most insurance companies have not developed coverage policies for this as they are often deemed as “investigational” or “experimental” and will likely not consider them until



more research is published regarding its efficacy. It is important to note that to my knowledge, there have been no reports in the current literature of any negative or adverse effects of amniotic derived tissues. In other words, the main risk of their use is typically financial as if they do not work, they will not make your condition worse, but you will be out the money you spent to acquire them... which depending on the clinic you get them from can be quite expensive. While there is a lot of excitement and recent media coverage about the emerging field of regenerative medicine, unfortunately there are several clinics that are taking advantage of this and making false claims about their use of “stem cells”... and charging a small fortune for access.



Insurance typically doesn't cover adult stem cell harvesting procedures such as Platelet Rich Plasma or bone marrow or fat aspirates. While there are no ethical issues in taking tissues from your own body, several recent studies have shown that the actual amount of growth factor that is available in these tissues varies greatly per individual, per harvesting method and viability when compared to embryonic derived tissues, especially umbilical cord with Wharton's Jelly. Also, I have personally found that the body has a pretty intense inflammatory response to the use of these tissues which can lead to more post procedural discomfort, especially when injected into a joint, ligaments or tendons. With that being said, there are certain indications/applications where this may be beneficial such as when cadaveric bone grafting is used and soaked with a patient's own bone marrow aspirate to mimic their own bone and increase the body's "acceptance" of the graft tissue.

At Alexander Orthopaedic Associates, we have incorporated many of the benefits of regenerative medicine into our approach and can provide access to both embryonic derived tissues for injection in the clinic or use during surgery, as well as adult stem cell harvesting. Please discuss this with one of our doctors to see if any of these options are right for you.



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REGENERATIVE MEDICINE MENU

“... the bone is a plant, with its roots in the soft tissue, and when its vascular connections are damaged, it often requires, not the techniques of a cabinet maker, but the patient care and understanding of a gardener.”

-Robert Gathorne Girdlestone, 1932

A Word About Inflammation

It is important to understand that regenerative medicine is based on a cellular process of repair. After tissue damage has occurred, such as a tendon or ligament tear or a bone fracture, the body increases blood flow to the area and sends out signals to its repair system to recruit and deliver the proper cells and proteins to the damaged area needed for healing. Therefore, the goal of regenerative medicine is to augment this process. If a condition is chronic in nature, the injury site may be stagnant and needs to be converted back to more of an acute healing mode, so the body can properly recruit the proper cells for repair. Perhaps the best way to think about this organic process is to compare it to another, more familiar one. In order for a plant to produce flowers, it needs to have a stable home in nutrient rich soil and have lots of water and sun. If a plant is struggling to produce flowers, this could indicate a situation where plant has been physically damaged or it is not in a conducive and nurturing environment. Before you dig up the plant and put a new one, one should consider what is causing the problem in the first place as planting a new plant in nutrient poor soil will likely lead to the same result, which is similar to chronic inflammation where the body is just not capable of turning the situation around. A regenerative approach would call for aerating the soil around the ailing plant to convert it to more an acute process, adding nutrients to the soil with the addition of fertilizer and perhaps Scott's Miracle Grow (which can be compared to using nutrient rich placental/amniotic tissue) to enhance the environment and convert it back to a state that is

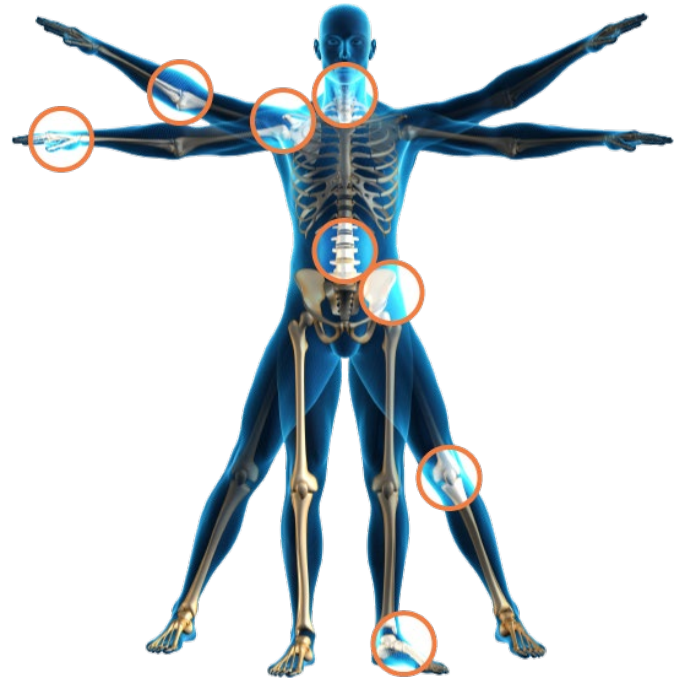


optimal for the plant to thrive and eventually produce flowers. In the body, this technique is what we are trying to simulate by agitating a chronically damaged site to convert it to an active repair site and then stimulating new tissue growth by seeding the area with stem-cell based technologies which rejuvenate the “soil” via the deliverance of growth factors and extracellular matrixes (proteins) that the body can utilize to heal itself.

SO, WHAT’S THE DEAL WITH CORTISONE?

Cortisone is one of the main hormones that are naturally released by our bodies as a result of stress or injury. Cortisone injections contain a synthetic version of this hormone and are traditionally injected directly into the injured area to reduce the inflammation that occurs with tissue damage, therefore reducing pain. While it is a strong anti-inflammatory, cortisone works in a totally different way than the regenerative medicine approach and can often be associated with some very serious downsides. Unfortunately, cortisone is often mistaken to be a miracle drug due to its ability to almost instantly get rid of pain. In reality, it actually retards the body’s natural response to injury and ultimately blocks the repair process. Less pain? Yes, however cortisone almost instantly reduces or eliminates the proper inflammatory response associated with either tendon and muscle injuries.

Furthermore, it has been well documented in the literature that cortisone use near tendons can compromise the tendon to the point where it can eventually fail and rupture. Cortisone by an acute bone fracture will prevent it from healing. Repetitive cortisone injections into an arthritic joint will actually cause further cartilage degradation and actually lead to an advancement of the arthritis. So is it all bad?



While we usually try to avoid cortisone injections when we can, one or two at the most may calm severe/chronic swelling and pain. In very limited cases, it helps break the inflammation cycle of conditions such as capsulitis, Morton’s neuroma or plantar fasciitis. It can bring almost immediate short-term relief from pain and, sometimes, longer-term relief which can help a patient get through more meaningful therapeutic exercises necessary to address the underlying condition.

It’s very important to note that we never inject cortisone into the Achilles tendon. Cortisone can make the Achilles injury worse and increase the risk of a complete tendon rupture. Cortisone injections do not stimulate healing, nor do they address the core issue of the pain, whatever that may be. The benefit of regenerative medicine is that unlike cortisone injections, use of stem cell-like therapies to stimulate healing have never been associated with a derogatory

effect nor do they lead to weakened or damaged tissues. Rather, they regenerate the body's ability to heal itself.

CONVERTING CHRONIC TO ACUTE

In a situation where inflammation has been present for an extended period of time, the body has likely given up on the healing process. In order to get the area ready for productive healing through tissue regeneration, it must be converted back to an acute process so that the body can send out signals to its repair cells and attract them to the damaged tissue. This can be done in a number of ways. Traditional open surgical repair is one way to “stir the pot”. In the event a ligament or tendon is repaired via a traditional open surgical approach, use of an amniotic tissue matrix membrane or injection into/around the repair site will insure that there are additional nutrients (growth factors and proteins) are available to further stimulate an optimal healing environment. In the event a more minimally invasive method is chosen, the amniotic derived tissue may be injected into the repair site. To optimize healing, the site may benefit from a procedure that is geared towards micro-debriding the soft tissue and therefore causing a controlled amount of acute damage to encourage the body to convert the site into the more productive form of inflammation that can trigger the natural repair process.



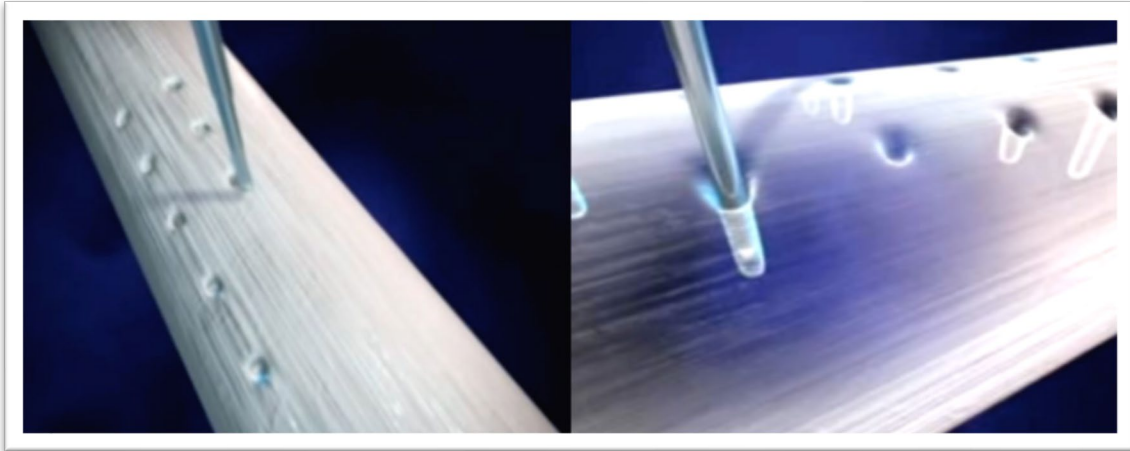
Micro-Debridement Techniques (Aeration) of Damaged Soft Tissues

- **Topaz Procedure:** minimally invasive radiofrequency treatment for tendons and fascia

The Topaz Procedure (or Topaz MicroDebrider) is a minimally invasive, state-of-the-art procedure used to treat chronic tendon and ligament conditions such as **chronic Achilles tendonitis** and **chronic plantar fasciitis**. Topaz is typically intended for patients who have not responded to more traditional conservative treatments, such as supportive insoles, oral anti-inflammatory, oral steroids, physical therapy, stretching, or massage. I have utilized this particular technology successfully for over 10 years in my practice and since its introduction have reduced the need for open surgical repair for issues such as plantar fasciitis and mild to moderate Achilles tendinosis by almost 90%.

How Does the Topaz Procedure Work?

The entire process takes only 5 minutes and is performed under light/twilight sedation using an intravenous sedation anesthetic (you are asleep but breathing on your own). The Topaz wand, which looks like a specialized sewing needle, is placed through a small poke-hole through the skin into the damaged area of fascia or tendon and radiofrequency is utilized for a split-second to create a small hole in the ligament/tendon. The Topaz wand uses cobalation technologies, which create the radiofrequency waves that gently cause microscopic “trauma” to the scar tissue that body wasn’t able to heal on its own. The procedure brings blood flow back to the affected area and reinitiates the healing process by converting a chronic form of inflammation into more of an acute and productive healing process. The strategically placed Topaz wand greatly minimizes any damage to surrounding healthy tissue.



The wand is used to create a grid like pattern of fenestration sites spread about a quarter-inch from each other in the affected area. Once this is accomplished, the area is then typically “seeded” with regenerative properties by injection of amniotic/placental materials or adult derived stem cell spin down products (harvested from the patient during the procedure) such as platelet rich plasma or bone marrow aspirate. Because the method is minimally invasive, recovery time from the Topaz procedure can be measured in weeks instead of months. After a week in a walking boot, most patients can begin wearing athletic shoes with orthotics. Also, there is no incision made and the dressings are removed the day after the procedure.

What is the Success Rate?

In my experience over the past 10 years, the topaz treatment mixed with a regenerative medicine component has been up to 90% successful in the avoidance of more traditional open surgical procedures/repairs. It’s important to note that the pain relief is not instantaneous and it may actually get worse before it gets better. However, once your recovery is complete, the pain is relieved, and the tendon/ligament are back to normal function. After a successful treatment, it

should be emphasized that continued support to the area with proper shoes and/or insole and daily stretching is what it takes to avoid a recurrence of the condition.

Is Topaz Covered by Insurance?

Most insurance plans will cover the Topaz microdebridement procedure. We have had it covered in our practice and are happy to help you should you require this procedure. On the other hand, the use of injectable amniotic/placental tissue is still not typically covered by insurance. Since AOA has extensive experience/utilization of these tissues, we have been able to secure very affordable options for our patients so that they will continue to have access to the latest and greatest that regenerative medicine technologies have to offer.

- **Tenex: A Cutting-Edge Achilles Tendon and Plantar Fascia Treatment**

If you're one of 8 million Americans experiencing pain and discomfort in the Achilles tendon or plantar fascia, the Tenex Health Procedure, a minimally invasive treatment for soft tissue damage, may help. Developed with Mayo Clinic, Tenex uses very precise microscopic cutting and removes the diseased tissue. When tissue is unhealthy, blood flow is reduced and healing is impaired, if not halted.

Tenex is performed in a surgery center or hospital setting with light sedation and local. It's covered by most insurance plans. After the procedure, a small bandage closes the miniscule incision.

What to Expect During the Tenex Procedure

Dr. Perler uses a diagnostic ultrasound to pinpoint the exact area(s) of scar tissue within the damaged tendon or ligament. The ultrasound uses a specific frequency can locate the difference between healthy tissue and scar tissue. The actual Tenex Procedure usually takes only about 15 minutes. In most cases, an injection of amniotic tissue can help to both stimulate and accelerate the healing process. Afterward, there can be minor swelling. Recovery time is greatly reduced from several months (with traditional surgery) to one to two weeks with Tenex. In most cases, you can begin light weight-bearing exercise within two weeks. Dr. Perler has stood on the forefront of this exciting new procedure. He aims to maximize every traditional and advanced technological modality to safely heal your foot and ankle challenges. If you're suffering from foot and ankle pain and need to have it evaluated or have tried conventional healing elsewhere and still have not received adequate relief, please contact us today to setup an appointment for a consultation.

