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Stem Cell And Regenerative Therapies For Meniscus Disease And Osteoarthritis Of The Knee

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INTRODUCTION:

Osteoarthritis (OA) is not a disease of only the cartilage but bones below cartilage, the membranes around the knee and ligaments. Knee osteoarthritis is commonly viewed as the final common pathway for aging and injuries of joints. Because of medical advances the population of the world is growing older and the average life expectancy is extended, leading to an increase in the incidence of osteoarthritis of the large joints. Osteoarthritis is already one of the 10 most disabling diseases in developed countries. Osteoarthritis (OA) presents a major clinical challenge to most clinicians. Articular cartilage defects within the knee are common among the elderly population causing pain, reduced function and significant disability in affected patients. There is a poor capacity for "self prepare" of cartilage defects making management rather difficult. Current treatment emphasizes on reducing pain, maintaining mobility and minimizing disability. Regardless there has been until recently no therapies available that have the potential of regenerating the affected tissue.[1] According to the Agency for Healthcare Research and Quality more than 600,000 knee replacements and 285,000 total hip replacements are performed each year in the US. The demand for repeat joint replacement or revision of the previous joint replacement will double in the next 10 years. As the demand for joint replacement surgery increases the supply of orthopedic surgeons performing this procedure are on the decline which may lead to a demand crisis.[2]

Many individuals have lived active and healthy lifestyles that have preserved their health except they suffer from orthopedic problems such as osteoarthritis of the knees and hips, dramatically affecting the quality of their life. If we have enjoyed success we want to live, run, jump, play golf, walk on the beach and enjoy an active life through our senior years. It may please you to know that we have entered a new area of regenerative orthopedic medicine were alternatives to surgical procedures are now an option.

BASIC KNEE ANATOMY:

We are going start with some basic knee anatomy for those who may not be familiar with the knee. We are going to be making a number of references in this article to anatomical parts of the knee that we will need to be familiar with. We are not going to do a detailed review, but there are several keep points that we want to cover.

An important part of knee anatomy that we will be referencing is the hyaline cartilage coving the end of the bone which is colored purple in the picture to the right. This area is representative of the "articular cartilage" that overlies the end of the bone. There is also a similar layer of cartilage on the under surface of the knee cap (patella) and the top of the tibia as well. The articular cartilage that covers the surface of the patella is thicker than most areas in joints and will be an important point of discussion later in this article. There are also some additional cartilage structures in the knee which is the medial and lateral meniscus shown in the picture below on the left.

The femur was removed and looking down on the meniscus in the picture below. Notice the moon shaped meniscus. Since the meniscus is shaped like a cow horn we call the part from the anterior horn and the part of the back the posterior horn. This region and the posterior horn are important

because this is the most common location for tears and early wear and tear. Most individuals that have undergone surgery for meniscus tear will have undergone the surgery for a tear in this region. The posterior aspect of the meniscus takes a lot of torque and pressure and therefore wears down very easily. The meniscus is attached to the bone on the periphery by small short ligaments called “coronary ligaments” that I have colored in green in the picture on the picture to the left. The small short ligaments are a very important target for injection therapy in regenerative injection procedures.

One of the very first “regeneration” procedures that I personally began using over 25 years ago was the use of “prolotherapy” which I have discussed in the article entitled “Regenerative Injection Therapy and Pain Medicine” that you can find on this website. Prolotherapy utilizes typically natural substances such as dextrose sugar directed to the ligaments which causes a fibrous connective tissue proliferation which help strengthen ligament and connective tissue attachments. In fact there are other ligaments of the knee that are also important targets for prolotherapy injections. We will not spend a great deal of time discussing the various ligaments of the knee, but it’s important to discuss how critical these structures are in supporting and stabilizing the knee joint and how important they are as a target for physician specializing in regenerative injection therapies. Many years ago my primary method of treatment of knee injuries and osteoarthritis was utilizing dextrose based injection solutions directed to the various ligaments of the knee. We found this to be empirically speaking quite helpful in many patients with knee pain and arthritis. Today the technology of regenerative medicine has advanced and we now are able to provide a whole host of different treatment strategies that are more effective.

Before we begin to explore treatment of the knee with stem cell therapies we need to cover a couple of critical topics. Before we begin to explore treatment of the knee with stem cell therapies we need to cover a couple of critical topics. The first is to address some of the important stress that is placed on the knee that causes the knee to degenerate in the first place. If you do not deal with the mechanical stressors that are breaking down the knee it is more difficult to maintain improvement once it is accomplished. We will discuss to important topics that are the major contributors to distress applied to the knee with walking.

This first is the foot and ankle. The shape of your foot and ankle is critically important and governs the function of your foot during walking and can apply variable degrees of stress to the knee and lower extremity with walking..

FOOT PRONATION:
Foot pronation is a natural motion of the foot however an individual who excessively pronates places excessive stress throughout the lower extremity hip and pelvis. The picture to the right demonstrates a foot in excessive pronation. As the foot pronates the tibia and femur excessively internally rotate placing undue torque on the knee. This causes malalignment of the kneecap which causes excessive wear of the articular cartilage in the joint as well as wear on the meniscus.

This also places excessive tension on the previously described coronary ligaments and other important ligaments of the knee. This contributes to the
wear and tear that ultimately leads to osteoarthritis.

OBESITY:
Obesity has been shown to be a significant risk factor in development of osteoarthritis of the knee.[3] The increased mechanical forces and weight bearing of the joint is probably the primary factor leading to joint degeneration. Individuals who are obese also have an abnormal angulation to the knee worsening the compression force on the cartilage and causing malalignment of the kneecap. This results in increased joint reactive forces in the inside compartment of the knee accelerating degeneration.[4]

Obesity and osteoarthritis is a vicious cycle. The worse the arthritis becomes the more pain and reduced activity tolerance an individual has. The less activity the more obesity and the cycle continues. Many individuals become so functionally disabled they can hardly move and then seek our care for stem cell therapies and other regenerative interventions. Many of these individuals have already been offered a total joint replacement. These individuals often expect a cure for their condition and come in for stem cell therapies expecting the can experience this cure. They have made many attempts at diet and weight loss but in the end they have made little change. Stem cell therapies may provide symptomatic relief and may even offer a means to allow them to become at least more physically active but if the weight does not come off the disease will progress. Despite the great potential of moderate regenerative therapies the mechanical forces on the joint will cause deterioration of articular cartilage. Although the deterioration may be slower with stem cell therapies it still is going to progress without aggressive measures taken to lose weight. Therefore individuals with significant osteoarthritis and obesity require much more comprehensive management then simply stem cell and regenerative intervention.

THE EFFECT OF MENISCUS THE SURGERY ON ARTHRITIS PROGRESSION:
Many individuals with osteoarthritis have a previous history of a damaged meniscus where an arthroscopic procedure was done to remove part of the torn cartilage. It has been known for a long time that removal of damaged meniscus or cartilage from the knee substantially increases the risk of progression of joint failure.[5-7] The picture to the right demonstrates atypical meniscus tear above and the colored portion below represents a typical pattern what portion of the meniscus would be removed by the surgeon to eliminate the tear. This type of surgical procedure does lead to short-term benefit but orthopedic research scientists are beginning to question the value of this procedure. When a portion of the meniscus is removed it increases the surface contact area and perpetuates a more rapid progression to osteoarthritis. We have known this for many years.[8-10]

For example Dandy in 1975 described problems with breakdown in the cartilage of the kneecap, overlying the femoral condyle, retained meniscus fragments and other issues following arthroscopic meniscectomy.[11] Katz and his numerous colleagues published last year an article in the New England Journal of Medicine demonstrating the patients with meniscus tears had similar outcomes whether or not they underwent arthroscopic surgery or simply physical therapy.[12] In individuals over 50 years of age 35% have meniscus tears that can be incidentally discovered and are asymptomatic.[13] One must then ask how important is the finding of a meniscus tear? Another important point is that individuals with osteoarthritis frequently have meniscus tears which we will discuss later in this paper.[14,15] So, the question is what we do with individuals with meniscus tears with or without osteoarthritis present?

Recently a study was published which evaluated patients receiving either “sham arthroscopic surgery” compared to arthroscopic debridement of cartilage and showed that the debridement procedure was no better or equivalent to a placebo procedure in improving the pain and self-reported function.[16] In addition post procedural follow-up demonstrated the objective function was worse in the debridement group than the placebo group![16] With mounting evidence that arthroscopic procedures may not be the answer to meniscus lesions there is going to be a need for advancing technology and alternatives to arthroscopic surgery and debridement of the meniscus or debridement procedures for osteoarthritis.

WHAT IS OSTEOARTHRITIS?
Before we discuss the treatment of osteoarthritis of the knee with current regenerative medicine technology including stem cell therapy we need to look carefully at the pathology of osteoarthritis. Osteoarthritis of the joint can have multiple causes. There are individuals who are into their 90s with no signs of clinical or functional problems of the disease. And we can see individuals in their 30s with advancing arthrosis and functional disability. One possible source is injury to or breakdown of ligaments. An example would be the 38- year-old which MRI is noted to the right. At the asterix on the MIR image you may notice more light-colored signal indicating edema in the

bone from a cruciate ligament injury and the meniscus on the inside (medial) knee is extruding out of the joint from injuries to supportive ligaments running alongside the knee. This phenomenon of displacing of the meniscus is relatively common. The picture to the left provides a simple graphic representing a meniscus displacement caused by injury to the ligaments that support the meniscus.

Meniscus extrusion can be a cause of joint space narrowing which has been largely overlooked. Although standard x-rays may show evidence of joint space narrowing it will not demonstrate the meniscus displacement. This finding can only be seen on ultrasonography or MRI.[17] When we see this particular disorder we often use a special stem cell grafting procedure placing a graft behind the ligament to support the meniscus while we try to stimulate it to heal.

The meniscus does not need to be displaced to cause progressive osteoarthritis. Studies have shown that tears in the posterior horn of the meniscus can cause dynamic changes in the function with abnormal loading resulting in progressive osteoarthritis.[18,19]

Researchers have proposed that the small coronary ligaments previously described attached to the meniscus (ligaments of Humphrey and Wrisburg) may play an important role in osteoarthritis progression.20 There are many physicians performing so-called “regenerative injection procedures” that are completely ignoring the ligamentous structures of the knee and thereby are not obtained the outcomes with treatment that is possible if a comprehensive regenerative approach is directed to the knee.

As previously described in our anatomy section the bone within the joint is covered by “articular cartilage”. The bone directly underneath the cartilage is called “subchondral bone” which means the bone under cartilage. The bone under the cartilage has a shock absorbing property which is essential for protecting the overlying cartilage from damage.[21] In the picture above on the right the articular cartilage is represented in Gray. Over time articular cartilage begins to erode away from bone and the bone under the cartilage has many adaptive changes including bone edema, etc. which can be seen on MRI. As bone under cartilage begins to thicken it loses its property for shock absorption and cartilage protection.[21] As cartilage cells erode from bone they float in the synovial fluid and then stick to the membrane around the knee. This membrane is called the “synovial membrane”. Typically this membrane’s role is to secrete lubricating fluid that nourishes articular cartilage.[22] Special cells in the synovial membrane secrete not only substances used for lubrication and nutrition of cartilage but also contain immune cells that can respond to foreign antigens. Small molecules of necrotic cell material and fragments of degenerating cartilage can activate the immune response resulting in inflammation and thickening of this membrane and result in pain and swelling.[23] It is this inflammation that is linked to both initiation and progression of osteoarthritis.[24] The fluid in the joint becomes full of these harmful substances that contribute to the breakdown of the joint.

Part of the critical component of treating osteoarthritis is using a stem cell technique that can “reset” and alter this significant inflammatory response within the joint that secrete numerous chemicals that damage the articular cartilage and produce pain. As we will discuss adipose derived stem cells do exactly this by dampening the immune/inflammatory response.25-27 It is important to understand that while steroids do cause reduction of inflammation they are damaging to your articular cartilage.

Part of the inflammatory pathway involved in osteoarthritis and pain is inflammatory substances mediated by chemicals called “cytokines”. These “cytokines” unfortunately besides causing inflammation can induce cartilage cells to produce enzymes and inflammatory substances that drive the destruction of the cartilage cells and cartilage architecture.[28] Obviously it is important to target this pathologic process with treatment that is going to be effective. Autologous stem cells taken and concentrated from your body provide a means of targeting these destructive cytokines chemicals. It is important to understand that MRI has basically replaced the conventional use of x-ray in diagnosing the various pathologies involved in osteoarthritis.[29,30]

A common surgical practice today is to use a technique called “microfracture”. This is a method whereby under arthroscopic surgery the surgeon will drill holes in the bone overlying the areas that cartilage has eroded away as shown in the picture to the right. The idea is to let the bone bleed and induced stem cell repair and replacement of articular cartilage. Although this has shown some short-term benefit this technique has not shown any significant improvements with long-term results,[31] Once again we find common methods of treatment used today that fall short and again provide a strong impetus to search for alternatives.

A few years ago we entered a new era in regenerative medicine. Having spent my entire career utilizing various regenerative medicine technologies I began to see a significant change in the direction in this field. Just a few years ago there was a significant paradigm shift in the stem cell science and research. The US began to fall behind in utilizing various stem cell strategies because of politics and federal government regulation creative physicians and stem cell scientists turned to the use of “autologous” stem cell therapies. Autologous stem cells means stem cells we obtain from your own body and transplant the cells back to your body for therapeutic application.

Federal regulations currently still restrict the use of your own cells and we are unable to culture and expand cells and undergo significant “manipulation” of these cells. Despite these limitations there are technologies and methods of using regenerative and stem cell therapeutic procedures especially in the field of orthopedics that have revolutionized the treatment of arthritis, articular cartilage, tendon and soft tissue injuries. This has led to the development of various sequential centrifugation techniques to concentrate autologous stem cells and create cell complex mixtures concentrated from fat and bone marrow derived cells primarily It has taken several years and travel around the world comparing methodologies before I have finally arrived at the methods we now use.

We will reference adult mesenchymal stem cells (MSCs) throughout the article. Mesenchymal stem cells are found in a number of locations but we will be referencing cells that we obtain from your bone marrow and fat. Mesenchymal stem cells are cells that have the potential to become many other types of cells when exposed to specific growth factors or environments. Our interest is in the cells for osteoarthritis and their ability to differentiate into cartilage lineage which can be a great potential for cell-based articular cartilage repair.[32-34] Fibrocartilage tissue within an individual’s knee has a limited repair capacity on its own. The application of mesenchymal stem cells have the potential of healing damage to meniscus tissue and is currently being studied extensively.35 These mesenchymal stem cells have the properties of “developmental plasticity” which means they can change to other tissues when placed in the right environment.[36,37] Fat cells and its associated connective tissue can be used as a “scaffolding” for stem cells. We utilize this technique extensively when repairing rotator cuff tears and other orthopedic injuries.

One of the big problems with meniscus tears in the knee is where the injury to the meniscus is located. If you notice on the picture to the left there is a section of the meniscus which has good blood supply and there is a section of the meniscus that does not. We often refer to these 2 zones as the “red zone” and the “white zone” of the cartilage. For years my predominant concern has been whether or not a tear exists in the “red zone” or the “ white zone” of the cartilage. If patients would have red zone tears I typically would treat them with regenerative injection therapies including stem cell and if they had a white zone tear I often referred the patient to surgery. Today this is a much more difficult decision in lieu of emerging research on the potential benefit of stem cell therapies and problems associated with arthroscopic meniscectomy as we have already discussed. The decision that I would make personally may be different than what another individual would make. Cartilage even in the presence of stem cell and regenerative injection procedures heals slowly. Many patients seeking care want immediate gratification and want the pain gone within days of an injection procedure. Therefore the question is going to be whether you want to give stem cell therapies a chance or do want or need immediate improvement. Surgery in my experience has provided rapid short-term benefits with more long-term complications, whereas stem cell therapies provide no immediate gratification but better long-term outcome. This is based on empirical experience and research data that is currently

available. Clearly, additional outcomes research is desperately needed in this area and we are participating in clinical trials to provide data on making future decisions in patient care. You may be in fact requested to be part of the study where we will be tracking your clinical outcomes on a regular basis and your willingness to have your outcome documented will help other patients in the future.

WHAT IS THE RESEARCH TO SUPPORT CARTILAGE AND ARTHRITIS IMPROVEMENT?
I use to be concerned with meniscus tears and their potential to heal. More studies however are beginning to emerge demonstrating that in the presences of stem cell therapies there is an abundance of extracellular matrix, the substance that cartilage cells make, that appear to be restoring a meniscus-like tissue even in the avascular zone of the cartilage.[38-41] We have to realize that some of this research involving healing of the meniscus also involves implantation of a scaffolding device embedded with stem cells.[42] The use of implantable scaffoldings embedded with stem cells is still in early infancy and requires further research before this can be approved by the FDA and implemented in clinical practice. Current clinical outcomes research however is encouraging. Once again we desperately need long-term outcome studies that we will be participating in over the course of the next 3 years. In addition this will require repeat MRI studies and on certain cases possibly even a second look with arthroscopic procedures.

Believe it or not there has been arthroscopic second look research! In other words physicians have injected adipose derived stem cells after arthroscopic inspection of the joint and lavage with saline43. After stem cell injection surgeons went back and reevaluated the knee under arthroscopic surgery to evaluate whether or not there was improvement. Almost all patients showed significant improvement in all clinical outcomes of follow-up. All of the patients in this study improved at 2 years compared to the 12 month follow-up! 87.5% of elderly patients greater than 65 years of age (14 out of 16) improved or maintained cartilage status at least 2 years postoperatively. More importantly none of these patient underwent total knee arthroplasty (joint replacement) during the 2 year follow-up.[43] The type of stem cell therapies utilized in this study was a technique called “stromal vascular fraction” which is a technique that we also utilize.

It is always more complicated when the patient is seen for potential treatment who has already undergone 2 or more previous arthroscopic debridement procedures in the knee and now presents with progressive worsening arthritis and pain. These patients will demonstrate rapid progression of osteoarthritic disease, and ultimately culminating in a total joint arthroplasty procedure. The question is what to do with these patients. Is there research to support the possible beneficial effect of mesenchymal stem cells delivered via injection to the knee in these patients? Actually yes there is. For example a study done by C. Thomas Vangsness, Jr. and his colleagues demonstrated that after stem cell injection and patient’s having undergone arthroscopic meniscectomy there was increased meniscus volume determined by MRI in much more patients in the study then those injected with Synvisc-like injections which are often the most commonly offered treatment after arthroscopic failure. This study demonstrated that there was evidence of meniscus regeneration and improvement in knee pain after stem cell injection and that there may be some protective effects of the stem cell injection treatment. This does not mean that every patient who undergoes a stem cell injection after a failed arthroscopic surgery is going to benefit! People who are undergoing stem cell injection therapies need to realize that the treatment can fail.

CHONDROMALACIA PATELLA:
One of the frustrating conditions that I have been working with for 30 years in practice is what to do with patients who have pain under the kneecap and degenerative changes in the articular cartilage under the kneecap. Over time early arthritis of the patellofemoral joint can occur because of obesity, foot pronation, misalignment of the kneecap for many reasons including muscular strength and imbalance, etc. The cartilage begins to wear. The top picture on the right demonstrates a normal smooth articular cartilage surface under the kneecap. Notice the picture on the bottom that demonstrates a fragmentation of the articular cartilage that makes it look like “crab meat”. This is what softening and breaking down of the cartilage appears like. This causes

symptoms of crepitation and grinding noises under the kneecap with squatting, ascending and descending stairs and movement of the knee.

We use the term “chondromalacia patella” which basically means a softening of the cartilage under the kneecap. Once this cartilage becomes fragmented the cartilage begins to erode until areas of bone are showing and arthritis progresses. Besides orthotic correction, exercise, physical therapy, etc. I have used various regenerative strategies including PRP injections. More recently however with the development of adipose derived stem cells research is beginning to show that this condition may have a treatment for the cartilage destruction that occurs with this condition. In a recent study one month after injection of autologous adipose derived stem cells patient’s pain improved 50-70% and after 3 months patient’s improved 80-90% and continued to improve over 1 year.[44] More importantly the MRI findings demonstrated recovery of the articular cartilage.[44] I have had some success in treating chondromalacia patella over the years however, I have never encountered a method of treatment that demonstrated such significant benefit from a single treatment session as I have with current stem cell and regenerative technology. The use of adipose derived stem cell therapies with her without bone marrow derived stem cell therapies has been a “game change or” in the treatment of both traumatic injuries and arthritic changes in the knee. We desperately need more research to continue to develop this technology and to do research on long-term clinical outcomes. We have started a nonprofit foundation that we hope will eventually be able to fund these research efforts.

WHY DO I WANT STEM CELLS IN MY KNEE?

Autologous stem cells have been shown to protect cartilage cells in osteoarthritis against cell death and progression of degeneration.[45] Even though osteoarthritis is not considered an inflammatory arthritis like rheumatoid arthritis, there are still pro-inflammatory chemicals which include cytokines, metalloproteinases, reactive oxygen species which are present in osteoarthritis joints. These pro- inflammatory cytokines are down regulated in the presence of autologous stem cells.[46] In addition to adipose derived stem cells having significant anti-inflammatory effects bone marrow derived stem cells have similar anti-inflammatory effects of osteoarthritis.47 Therefore injection of adipose derived stem cells or bone marrow derived stem cells has a number of beneficial effects in osteoarthritic joints which include inhibition of bone spur formation (osteophyte), decreased synovial inflammation, reduced cartilage degeneration with less fibrosis and cartilage cell death as well as stimulation of proliferation of cartilage cells and secretion of extracellular matrix important as a component of cartilage production.[47,48] In traumatic injuries of joints intra-articular injection of bone marrow derived stem cells have demonstrated that it can prevent the development of posttraumatic arthritis.[49] As I have stated before additional studies of also shown that injection of mesenchymal stem cells from bone marrow demonstrated its relative safety with improved pain, functional status in knee pain following injection and MRI studies of these patients demonstrated increased cartilage thickness and decreased subchondral bone (bone below the cartilage) reduction in edema and half the patients.[50] Research has also shown that regardless of whether it is bone marrow derived or adipose tissue derived stem cell preparations there are protective effects of cartilage cells from death and degeneration.[45]

In conclusion, this is just beginning of the new revolution and therapeutic interventions not only for orthopedic application but for many disease processes. Autologous stem cell therapy is probably going to revolution eyes the treatment of arthritis and the treatment of joint injuries. More research obviously needs to be done and the technology advanced.

HOW DOES A STEM CELL KNOW WHERE TO GO?

One of the most fascinating parts of moderate stem cell therapy is our understanding of cell “homing”. Stem cells “home” to injured tissues![51-53] Activated stem cells express certain receptors on the surface of the cell that are sensitive to chemicals secreted by inflamed and injured tissues. These chemicals are called chemokines. There are special small proteins that are secreted in the area and circulate around your body that tell a stem cell where to go. Studies have been done where the stem cell have been “tagged” with the radioisotope so that it could be

tracked like a homing beacon. When stem cells are injected via IV one can see that they accumulate in the area of a focal inflammation. This is the process we call “homing”. Typically stem cells are injected and at the focal site of local injury but can also be given IV.

In our practice because we focused more on orthopedic conditions we use ultrasonography to place stem cells in a precise location of tissue injury.

STROMAL VASCULAR FRACTION & STEM CELLS CONTROL INFLAMMATION:
One of the important observations and discoveries that we noticed when first utilizing adipose derived stem cells was the rapid improvement that patients experience with inflammation and pain in arthritic joints. We had grown accustomed to having some patients undergo significant post injection flare following areas regenerative injection procedures. After utilizing adipose arrived stem cells the first thing we noticed was how rapidly patient start to feel better. It turns out that stem cells especially those derived from adipose cells have profound effects on inflammation and immune system.[54-56] In fact the profound effects on inflammation and immune function is why stem cells are currently now being looked at for treating not only osteoarthritis but also rheumatologic disorders such as rheumatoid arthritis and autoimmune conditions.[57,58] In fact the anti-inflammatory and immune mediated responses caused by adipose derived stem cells is showing promise in the treatment of conditions such as multiple sclerosis.[59]

Stem cells and the many supportive cells that are found with them maintain a homeostatic environment which promotes growth and regeneration. For those interested in the biochemistry of the autoimmune effects of stem cell therapy I briefly discussed some of the autoimmune effects of stem cells below which include its properties and ability to suppress inflammation through the secretion of mediators including IL-10 [60], IL-17 [61], TGF-B superfamily [62], LIF [63], soluble HLA-G [64], and IL-1 receptor antagonist. [65] In addition the expression of immune regulatory enzymes such as cyclooxygenase [66], and, indolamine 2,3 deoxygenase [67] are seen which help cells “take” to the area and promote regeneration. The cells induce generation of “T regulatory cells” which have a profound effect on the local inflammatory environment.

T Regulatory cells (Treg).[68] Stem cells are capable of directly suppressing the immune systems inflammatory response by depleting certain inflammatory cells (T cells).[69] Because stem cells expressed CD34 receptors they may play a “Immunosurveillance” role for circulating CD34+ cells in circulation via activation and differentiation of these cells into dendritic cells (DC) via of toll-like receptors (TLR) agonists.[70]

Although this is a complex subject and part of this article is written for those who have a science background or who are interested in the biochemistry the important concept here is that there is a profound effect on a inflammation in a local environment such as a joint or soft tissue.

WHAT KIND OF STEM CELL THERAPY DO WE PROVIDE IN THE US?
There are actually many types of stem cell therapies that have become available worldwide. There are many stem cell procedures that are completely unavailable in the United States because of FDA regulations. We have organized a national organization of an elite team of stem cell physicians and researchers to create a laboratory and technology that will allow us to work more closely with the FDA and to develop investigational new drug licensing for our future research and development. This will hopefully someday allow us to begin to explore some of the technologies that are not available to us in the US and procedures that are often done outside the US borders. However at present time we are limited to some basic surgical transplantation technology that has been discussed in the context of this article. When you extract tissues such as adipose tissue and bone marrow and centrifuge this tissues isolate specific cells you actually obtain a tissue “complex” which is a mixture mesenchymal stem cells and a host of regulatory cells. It is this complex mixture of the cells that is responsible for the therapeutic effect in orthopedic application.

There is rapidly emerging technology that involves taking your own stem cells and culturing and expanding specific cells in the mixture. There are methods to take mesenchymal stem cells and placing them in culture and expand them in a laboratory. There are emerging methods to manipulate cells with various growth factors while they are in tissue culture to cause them to express a specific lineage such as cartilage, muscle, etc. Imagine being able to have one cell harvesting procedure and placing your cells in a "cell banking" institution where your cells can be cultured, expanded, and you can come in periodically to have "withdrawal" of stem cells that have been cultured, expanded and designed for specific use for your particular specific disease process. This technology exists but this does not occur much in the US again because of FDA regulations such as the "minimal manipulation rule". Because of these various regulations we are unable to utilize this technology unless it is authorized and used typically in clinical research.

Currently, the procedures being done today are more simple procedures that involves cell harvesting and condensation of cells by using a centrifuge and transplanting these cells shortly after harvesting by reinjecting them for therapeutic application. Fortunately as I stated before for orthopedic applications this is typically adequate. An example of this would be a process were bone marrow blood is aspirated and the cells are centrifuge to concentrate a specific set of cells with a specific weight. The cells have potential regenerative capabilities and they are simply placed in a syringe and injected at a target site. My personal opinion is that the US is falling behind rapidly in stem cell therapy. Although I do understand the importance of the regulations to protect the public and to eliminate unsafe practices for certain physicians it does limit our ability to treat specific types of diseases and conditions at present time with current technology. This limitations does not affect our personal practice quite as much because our focus is orthopedic application.

WILL STEM CELL INJECTION CURE MY ARTHRITIS?

There are countless stem cell applications for various knee injuries and arthritic conditions. For example one may have a osteochondral defect such as what is shown a picture to the right. This is a focal area of articular cartilage that has either been injured and lifted off the bone or has been worn off. Orthopedic physicians have been working for years on various techniques to try and heal these osteochondral defects with various surgical transplantation procedures, etc. There are rapidly emerging simple stem cell therapy treatments that are beginning show good efficacy in healing these types of defects. However, most individuals seeking our care have much more severe degenerative arthritic disease. The big question is how severe is your arthritis condition. Are we managing an early stage arthritic condition or a later stage arthritic condition?

Current stem cell technology is not a method that provides a "cure for arthritis". These techniques does provide an important method to help manage the disease. If you do nothing…the arthritic disease progresses. If we were to monitor your knee with osteoarthritis with MRI or inspection the inside of your knee with arthroscopy periodically we would see a continued progression of articular cartilage degeneration. With stem cell injections done periodically it modifies the disease slowing or halting disease progression depending on the severity of your condition. This method of treatment offers the most effective method of managing osteoarthritis of the knee that I have encountered in my 30 years of practice. There are times when knee replacement surgery is the best option when disease severity and functional disability is just simply too advanced or a specific patient does not respond to this type of treatment. What is interesting is that specifically with knee osteoarthritis there are some individuals with rather severe arthritic disease that do extremely well and others that do not.

The clinical manifestation of your particular arthritic condition is not the same as the next individual. There are many factors that need to be considered. That is part of the consultation process that we will go through to evaluate your specific disease process. We will have to evaluate how bad the meniscus degeneration is, articular cartilage damage, instability and a host of other factors that are contributing to the pain and disability you experience.

WHAT TO EXPECT FROM A STEM CELL THERAPY PROCEDURE:

I have written a detailed article on what to expect from stem cell procedure which also discusses risks and benefits. That document is available upon request and is always sent to all of our patients considering stem cell therapy. In short we utilize a lipoaspirate/and procedure to obtain fat or a special bone marrow aspiration procedure to obtain bone marrow cells. We described this in some degree in our article on this website entitled “beyond stem cell therapy”. And we go through a great deal of detail in our article what to expect from the stem cell therapy procedure which will be submitted upon request.

IN SUMMARY:
Current methods of stem cell therapies utilized today represent great progress with the treatment of osteoarthritic disease of the knee. In my 30 years of practice I have never encountered a therapeutic intervention that has greater promise. I have used countless injection procedures and techniques including prolotherapy, platelet rich plasma injection, and a host of complimentary and alternative medicines including prolozone all of which does not match the outcome we are seeing with the use of adipose and bone marrow drive stem cell therapies. We are heavily involved in documenting and researching clinical outcomes utilizing this method of treatment and in the development of new technology for the future.

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