

Regenerative Medicine

An Unbiased Patient Guide

A Patient Guide

*Regenerative Medicine: a branch of medicine concerned with developing therapies that regenerate or replace injured, diseased, or defective cells, tissues, or organs to restore or establish function and structure*¹

Regenerative medicine is far more than just two buzz words. This revolutionary industry is leading the way in medical advancements, addressing conditions that would otherwise require more invasive solutions.

Regenerative medicine has existed for hundreds of years. In fact, records dating back to the 8th century BC confirm that the theory of regeneration was indeed acknowledged, although not entirely understood.² Years of research and exploration have catapulted this industry into a new medical generation, one that science has shown may achieve the goal of using the body's own substances and cells to repair, restore, and rejuvenate.³

In recent years, a regenerative boom has taken place, with clinicians and practitioners alike utilizing various forms of regenerative medicine to treat countless conditions. Regenerative applications have made an impact on the medical industry, changing the treatment landscape so that patients may have less down time and, potentially, faster and more effective results.

Healthcare is an investment, and it's important that patients have the necessary tools to make an educated decision. We know that choosing what type of regenerative medicine treatment best suited for your diagnosis may be confusing. For that reason, we have created this booklet to provide a thorough review of several regenerative medicine products and applications. Together with your physician, this booklet aims to assist you on your regenerative journey and provide the knowledge necessary to feel confident in your treatment plan.



What is Regenerative Medicine?

When people think of regenerative medicine, it is often associated with stem cells. Stem cell therapy is taking the regenerative medicine world by storm... but should stem cells get all the credit? It's a common misconception that stem cells are the only component needed in regenerative medicine to kickstart the healing and regenerative. That misconception couldn't be more wrong.

“Stem cell” regeneration can at times be misleading, especially when speaking to regenerative forms that derive stem cells from your own body. Stem cells age as your age, meaning the number of viable stem cells taken at advanced age will not be as plentiful. Stem cells, when truly present, may be beneficial, but it's really the other components that are the true heroes.

One of the most valuable aspects of regenerative medicine is that our understanding evolves with science, but certain aspects tend to remain constant, specifically the dream team of healing components contained within regenerative medicine. These components are comprised of growth factors, cytokines, collagens, proteins, hyaluronic acid, and peptides, all of which enhance the body's natural ability to heal.

Regenerative Components

Wharton's Jelly

The amount of growth factors, cytokines, hyaluronic acid, cellular components and extracellular vesicles are higher in Wharton's Jelly compared to other biologics. These components aid in strength, flexibility, cushioning, covering, compressibility and response to friction in the body. It also plays a vital role in reducing inflammation.

Hyaluronic Acid

Naturally present in the body, hyaluronic acid acts as a cushion and lubricant for the joints and other tissues. Hyaluronic acid can be used for various joint disorders and aging among other conditions. It may promote healthier, more supple skin, speed up wound healing and preserve bone strength

Proteins

Required for the structure, function and regulation of the body's tissues and organs, proteins help repair tissues and allow metabolic reactions to occur. Some proteins are chemical messengers between cells, tissues and organs while others provide structure and support.

Elastin

As the most dominant protein found in skin, elastin provides resilience and elasticity to tissues and organs. It is 1000 times more flexible than collagen and one of the body's most enduring proteins.

Collagens

Collagens form a scaffold to provide strength and structure throughout the body delivering a platform for new tissue growth.

Chemokines

A form of cytokine that stimulates movement and plays a crucial role in immunological reactions.

Cytokines

These molecules serve as messengers between cells, mediating and regulating immunity, inflammation and hematopoiesis. They stimulate the production of blood cells and provide growth and differentiation functions that function in development, tissue maintenance and repair.

Carbohydrates

Vital in supporting life's basic functions, carbohydrates produce and store energy, build macromolecules, extra proteins and assist in lipid metabolism.

Growth Factors

Regulate cell division and cell survival to stimulate the growth of a specific tissue.

Amino Acids

The building blocks of proteins, amino acids are vital for protein synthesis, tissue repair and nutrient absorption.

HOW DOES REGENERATIVE MEDICINE WORK?

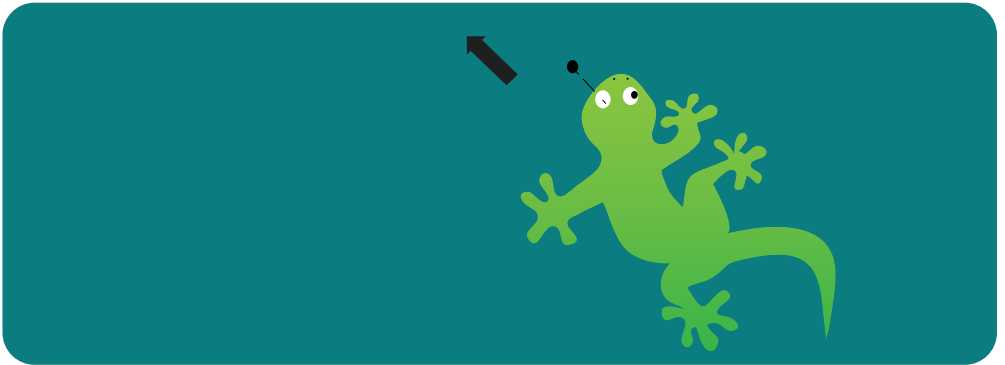
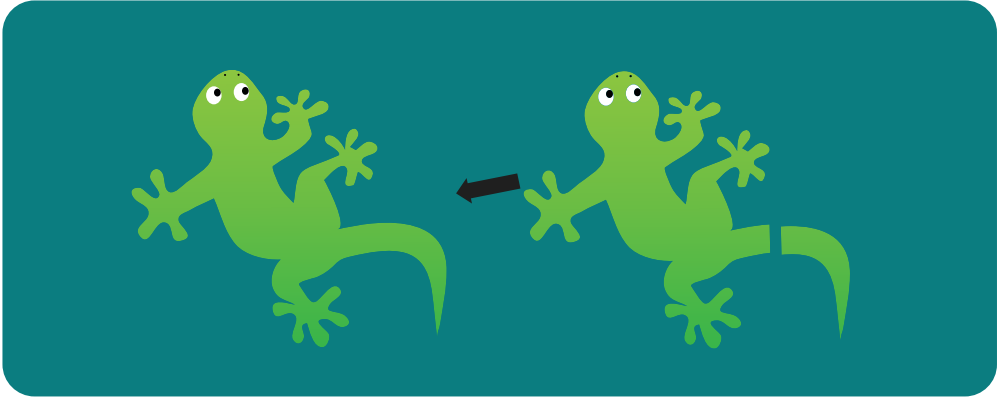
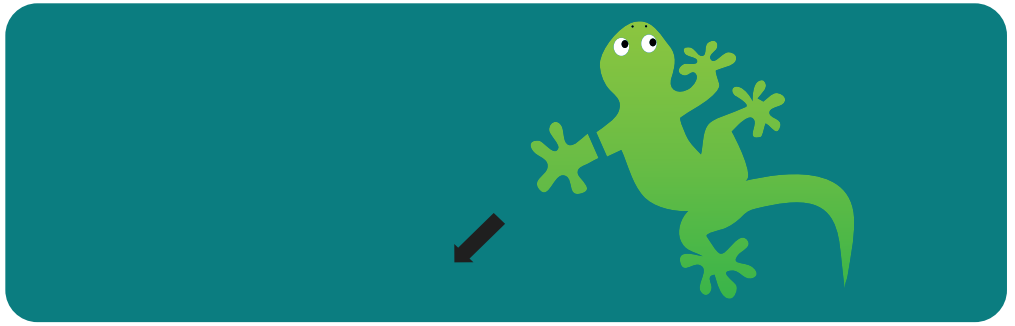
Cells are the building blocks of tissue, and tissues are the basic unit of function in the body.

Wait... what? To put it simply, cells build tissue and tissue allows our bodies to function and maneuver.

Generally, when cells group together, they create their own support structures. These structures are called the extracellular matrix.⁴ This matrix does more than just support the cells; it also acts as a relay station. These cells receive messages from many sources that become available from the local environment. Each message can start a chain of responses that determine what happens to the cell.

Through medical technology we can now understand how individual cells respond, interact with their environment and organize themselves into a healing process. The extracellular matrix created utilizes various regenerative medicine treatments allowing the tissue to "self-assemble".





Epimorphosis is defined as the regeneration of a specific part of an organism caused by cell growth, reverse of cells to create structural change, and reformation. Like with a lizard and its tail, epimorphosis restores the anatomy of an organism that existed before the destruction of tissue or structure occurred. This process is similar to utilizing regenerative medicine treatments for joint degeneration, hair loss, and more.

WHAT CAN REGENERATIVE MEDICINE BE USED FOR?

PAIN MANAGEMENT

Pain for most of us comes and goes; some stays and you live with it day in and day out. Imagine a life where pain is constant, taking control of you and, in some ways, the life of those close to you. Imagine having to rely on a narcotic to somewhat lessen the pain just to make it through the day. In 2016, an estimated 20.4% of U.S. adults had chronic pain and 8.0% of U.S. adults had high-impact chronic pain.⁵

In 2011, a study publicized by the Institute of Medicine reported that approximately 100 million U.S. adults suffered from pain at a cost of approximately \$560 billion to \$635 billion a year. The publication acknowledged that an underfunding of research was a significant barrier to progress, with only about 1% of a National Institutes of Health (NIH) budget that exceeded \$30 billion devoted to the study of pain. Relabeling pain a “biopsychosocial” phenomenon, the report urged a new recognition of its complex, multidimensional nature, as well as the wide range of individual variations in susceptibility to pain, cultural and emotional interpretations of pain, and responses to treatment.⁶

Drugs are typically the first line of treatment for most forms of pain. To date, the goal of successful pain management is to effectively control patient pain without causing side effects from the medication prescribed. Common prescription medications that can be considered for management of acute and chronic pain are often opioids. Although effective for moderate to severe acute pain, the effectiveness of opioids beyond three months requires more evidence. A recent study demonstrated that treatment with opioids alone was not superior to treatment with trials of various combinations of non-opioid medications for improving pain-related function over 12 months.⁷

With the effectiveness of opioid medications for pain management in question, many find the risks outweigh the benefits. Side-effects from opioid use can be severe, including addiction and potential overdose. People suffering from chronic pain are in constant search for alternative treatments with fewer side effects and long-lasting relief.



SPORTS INJURIES

Sports for professional and recreational purposes are mainstays in American society, but unfortunately so are sports-related injuries. As recent studies increasingly prove the inefficiency and harm of commonly-used treatments like anti-inflammatory medications and corticosteroid injections, more injured athletes are seeking regenerative medicine therapies to heal.

Regenerative medicine is now at the forefront of offering such treatments to help athletes overcome injuries without surgery or invasive measures.

Sports injuries are most often musculoskeletal conditions that occur in the hip, knee, elbow, ankle, shoulder and foot. (Figure 4) Since tendons, ligaments, cartilage, and bones in that area of the body don't receive a great deal of blood flow, the body can't always heal and regenerate itself effectively. Regenerative medicine treatments offer a new and efficient treatment option that can augment the body's natural healing process and rebuild damaged tissue.



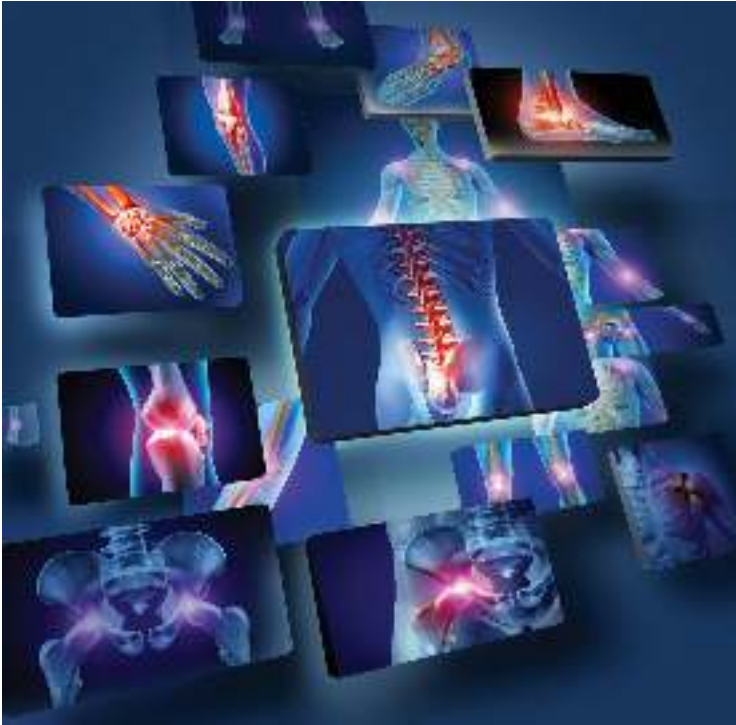


FIGURE 4

When treating articular cartilage injuries, for example, regenerative medicine treatments can both overcome the limited ability of the cartilage to self-repair by providing either new cells or growth factors needed to repair the existing cells. Studies indicate that such techniques can improve the efficacy and consistency of treatment and reduce the potential for future injuries in the same location. Professional and recreational athletes now have a safe and efficient alternative to surgery that not only resolves pain but also thoroughly heals difficult injuries.

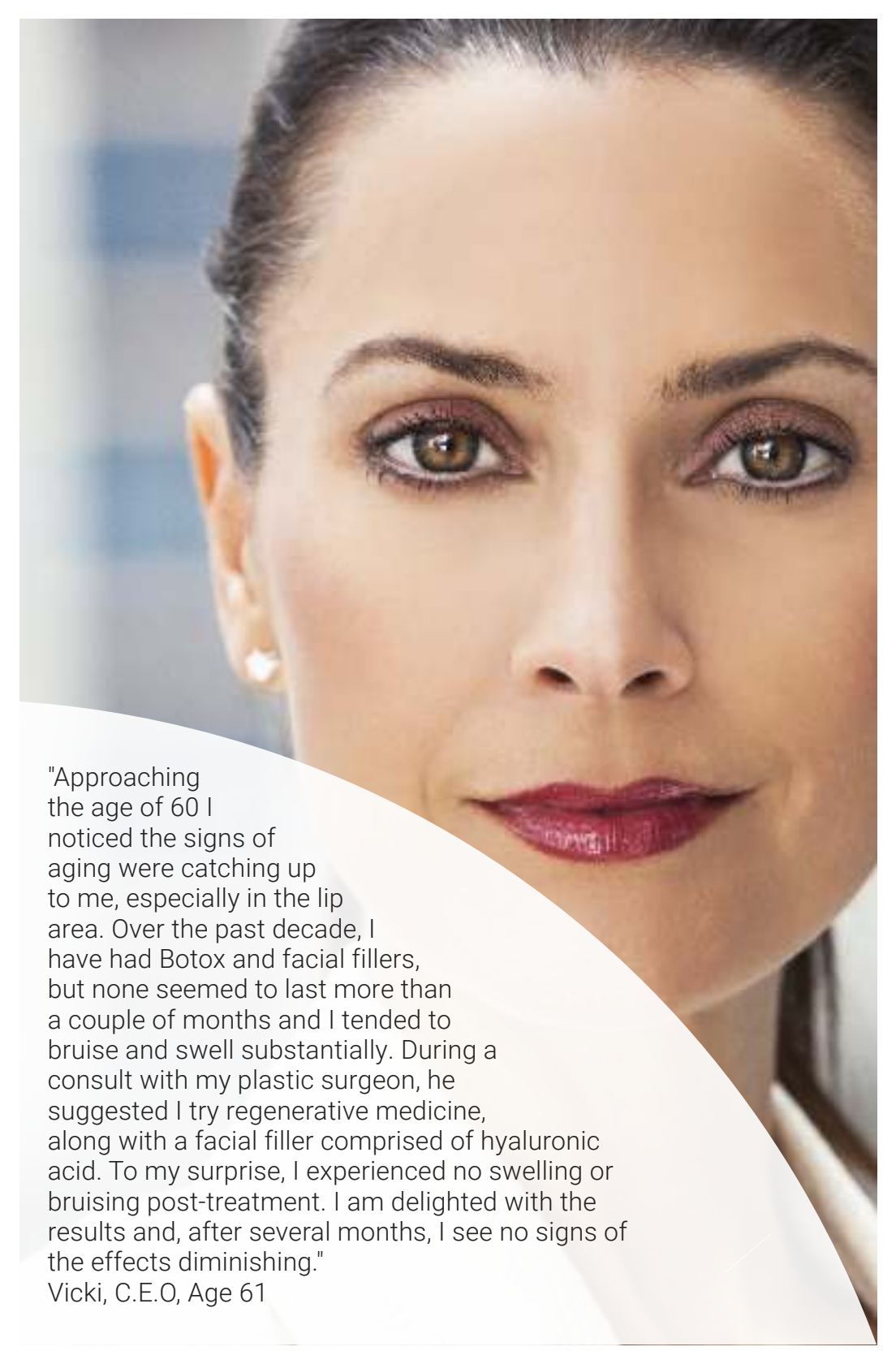
ANTI-AGING

In addition to baby boomers, now being an average age of sixty-four, the younger generation is feeling the pressures of today's society which has placed a tremendous focus on personal appearance. As recent as ten years ago, the average age for a woman having some type of anti-aging procedure was forty-seven; today that average age is thirty-five. Patients, both men and women, are having cosmetic treatments prior to the aging process becoming apparent in their appearance.

Regenerative medicine is gaining popularity in the fight against aging. Anti-aging procedures are becoming the fastest growing treatments in cosmetics. Treatments being utilized include platelet-rich plasma, also known as the Vampire Face Lift, bone marrow aspirate, amnion liquid, and umbilical cord tissues and blood, all being marketed as "stem cell therapy." (Figure 5)



FIGURE 5



"Approaching the age of 60 I noticed the signs of aging were catching up to me, especially in the lip area. Over the past decade, I have had Botox and facial fillers, but none seemed to last more than a couple of months and I tended to bruise and swell substantially. During a consult with my plastic surgeon, he suggested I try regenerative medicine, along with a facial filler comprised of hyaluronic acid. To my surprise, I experienced no swelling or bruising post-treatment. I am delighted with the results and, after several months, I see no signs of the effects diminishing."

Vicki, C.E.O, Age 61

HAIR RESTORATION

According to the American Hair Loss Association, two-thirds of men will experience hair loss by the age of 35. But women are also affected, making up 40% of all hair loss sufferers. Hair loss around the face affects 90% of all males and females during the aging process and is one of the strongest contributing factors to low self-esteem. In addition, the psychological damage caused by hair loss and feeling unattractive can be just as devastating as any serious disease, and in fact, can take an emotional toll that directly affects physical health.

The most common cause of hair loss is a hereditary condition called male-pattern baldness or Female-pattern baldness. It usually occurs gradually and in predictable patterns—a receding hairline and bald spots in men and thinning hair in women. Alopecia Areata is also a major cause of hair loss.

During the last ten years or so, there has been great promise for being able to treat hair loss by using regenerative medicine therapies. Regenerative medicine may work in numerous ways to improve and regenerate hair by providing nutrition and promoting new blood supply to the follicle; increasing hair shaft size for additional growth. Additionally, studies show growth factors contained within regenerative medicine reduce inflammation in the scalp and turn on follicular stem cells to promote hair growth.



**PATIENT TREATED WITH
UMBILICAL CORD TISSUE AND PRP**



**PATIENT TREATED WITH
WHARTON'S JELLY AND PRP**

WOUND CARE

Chronic skin wounds affect an estimated 6.5 million people in the United States, with treatment costs accounting for up to \$25 billion per year.

Populations at risk for chronic wounds include the elderly and those with comorbidities such as diabetes and obesity. If not treated properly, chronic wounds can lead to severe local infection, sepsis, tissue or limb amputation, or death.

You're more likely to get skin ulcers if you have certain risk factors. These include:

- Pregnancy.** During pregnancy, hormonal changes and increased blood volume may cause leg vein problems.

- Cigarette smoking.** Tobacco smoke hardens your arteries and disrupts proper blood flow.

- Limited mobility.** Being bedridden, paralyzed, or using a wheelchair puts your skin under constant pressure. Leg injuries and arthritis can limit your movement.

- Increasing age.** Age is linked to atherosclerosis and venous insufficiency.

- High blood pressure.** Hypertension, or high blood pressure, damages the arteries and disrupts blood flow.



WHAT THERAPIES ARE AVAILABLE?

BIRTH TISSUES

Birth tissue is donated by healthy mothers at the time of normal delivery. Through an informed consent process, expectant mothers submit their past medical and social history which is prescreened through an extensive and complete medical review and pre-natal evaluation. This process is performed before delivery utilizing the protocols established by various regulatory agencies. Additionally, prior to delivery, the mother is tested for communicable diseases following the requirements of the Food and Drug Administration (FDA), Center for Disease Control (CDC), and the American Association of Tissue Banks (AATB). (Figure 6) The recovery is performed by specifically trained technicians at the time of the delivery.

TESTING	PURPOSE
HIV I/II Ab	Antibody to HIV Virus Type 1
HBsAG	Hepatitis B Surface Antigen
HBcAb	Hepatitis B Core Antibody
HCV Ab	Hepatitis C Antibody
HIV I/II NAT	HIV and HCV Nucleic Assay Testing
RPR	Syphilis Detection Test
WNV	West Nile Virus

FIGURE 6

Birth tissue has been used for over 100 years for a broad range of therapeutic applications. However, it is only recently that birth tissue was discovered to have great clinical benefit when cryo-preserved to protect its residual cells. Since the discovery of birth tissue as a viable regenerative treatment in 2005, there have been no reports of disease transmission. Additionally, birth tissue is considered immune-privileged, meaning there is little risk of rejection.

Finally, birth tissue products are easy to use as it can be applied directly to the injured site. To date, tens of thousands of patients have been treated with these types of products.

Some people may hesitate at the idea of birth tissue. Be assured that the tissue is obtained from healthy, carefully screened mothers at the time of a normal delivery and causes no harm to her or her newborn.



AMNIOTIC FLUID THERAPY

Patients considering invasive stem cell injection treatment to aid in pain management, recovery, or healing may want to consider the rejuvenating qualities provided by amniotic fluid. This all-natural regenerative therapy is a liquid amnion allograft composed of amniotic fluid and features many components that enhance the body's natural healing process. (Figure 7)

Just as the amnion (innermost layer of the placenta) protects the fetus during development, it can also provide the same protection to injured or traumatized tissue. Amnion contains collagen substrates, a full range of growth factors, amino acids, carbohydrates, cytokines, hyaluronic acid, fibroblasts, epithelial cells, and extracellular matrix. Amniotic fluid has proven to be multipotent and capable of differentiating into many different types of cells contained within the body.

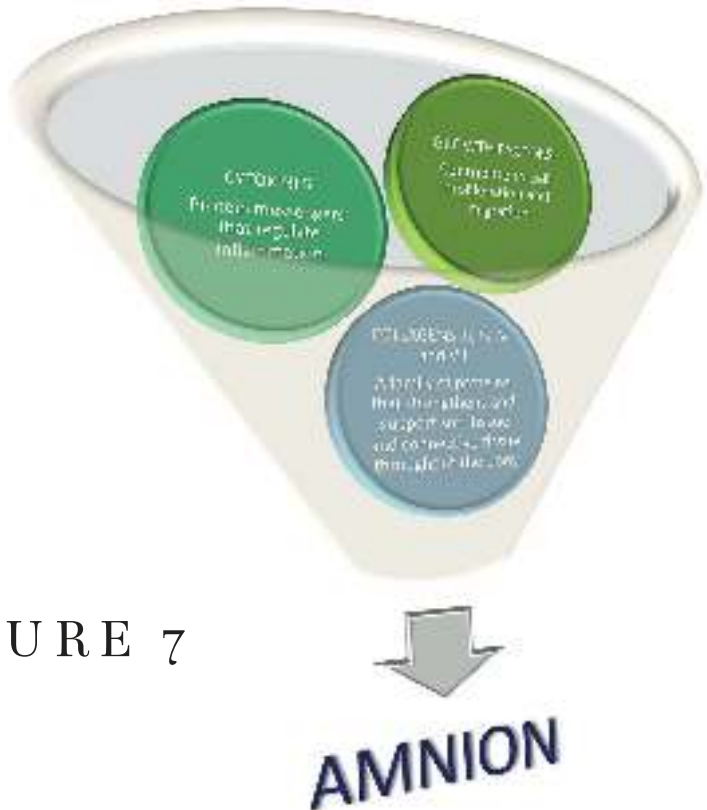


FIGURE 7

Amnion membrane is rich with the basic components necessary for tissue regeneration. It also contains anti-inflammatory characteristics with the capability to reduce scarring internally and externally. To remove the risk of graft-host reaction*, the chorion* is removed. This will maximize the potential benefits of amniotic membrane in a variety of medical specialties. Additionally, the immunologically privileged nature of amnion membrane has been shown in a multitude of research papers.



**Graft-versus-host reactions occur when the patient's healthy cells view the newly implanted cells as foreign objects. The patient's healthy cells then attack and damage the new cells.*

**Chorion is the outermost layer of the amniotic sac.*

UMBILICAL CORD TISSUE

Also derived from birth tissue within the umbilical cord is the Wharton's Jelly. Wharton's Jelly is the tissue surrounding the umbilical vein and vessels in the cord. (Figure 8)

When the vessels are removed closer to the fetal side of the cord, you have remaining tissue which contains cells termed medicinal signaling cells or MSCs. MSCs are undifferentiated cells (not changed) that can change into any specific cell type in the body. These cells, once deployed to any area of injury or disease, can readily change into the cell type that is needed to repair. Moreover, MSCs are directed to the body's cell signals that recruit them to the site of the injury. Once they reach this area, they dock and begin repairing by releasing cytokines, growth factors and other components that are needed in the healing process.

When the vessels are removed closer to the maternal side of the umbilical cord, this tissue contains up to 50 times more growth factors and other components than the amniotic fluid, but does not contain MSCs. Wharton's Jelly products are especially beneficial for patients over forty that, due to the aging process, have less viable cells than a younger patient would have. (Figure 9)

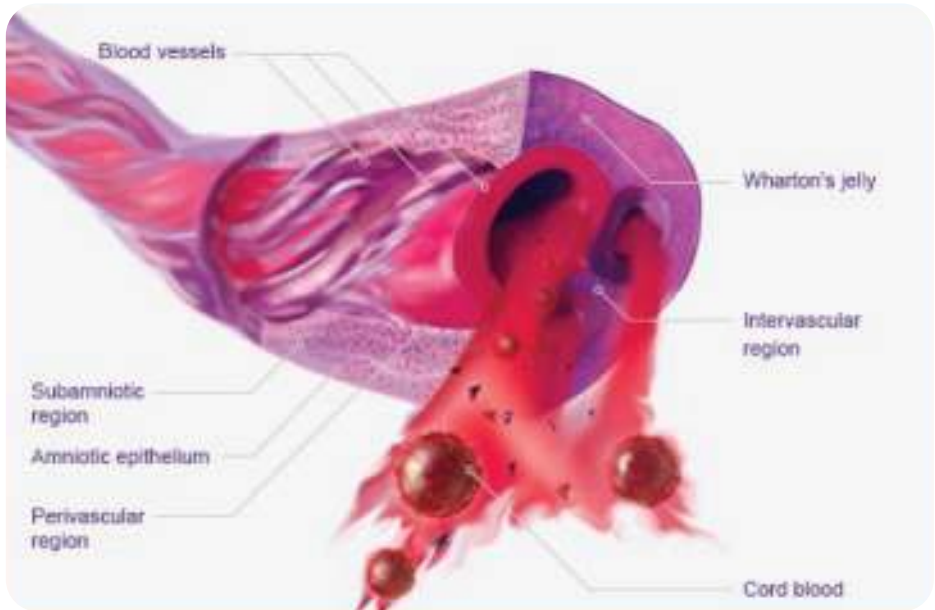


FIGURE 8

IMPACT OF AGING ON THE RATIO OF MSCS TO BONE MARROW CELLS (A. CAPLAN 1994)

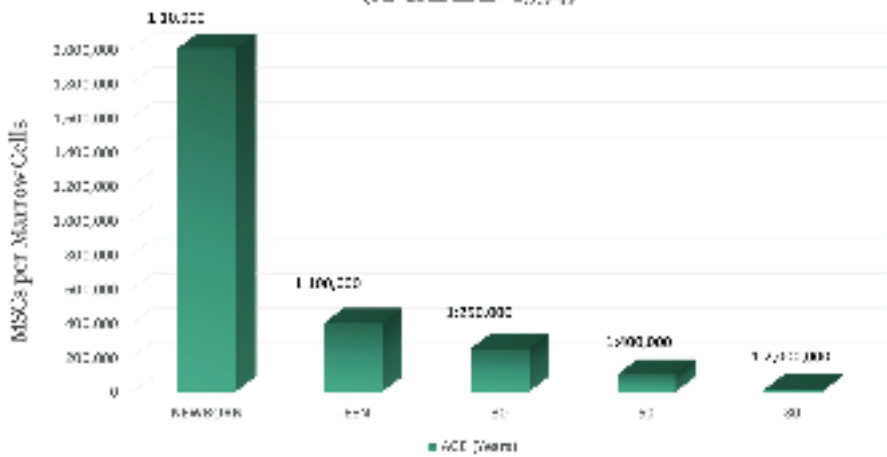
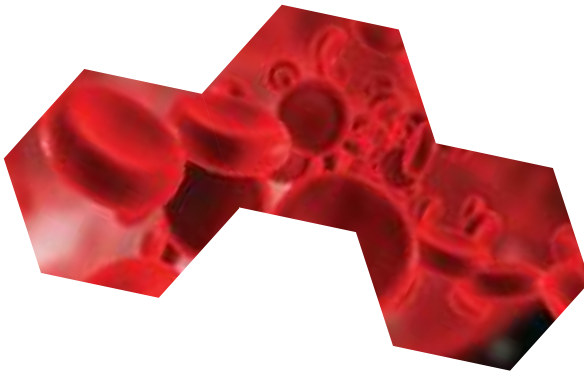


FIGURE 9

UMBILICAL CORD BLOOD

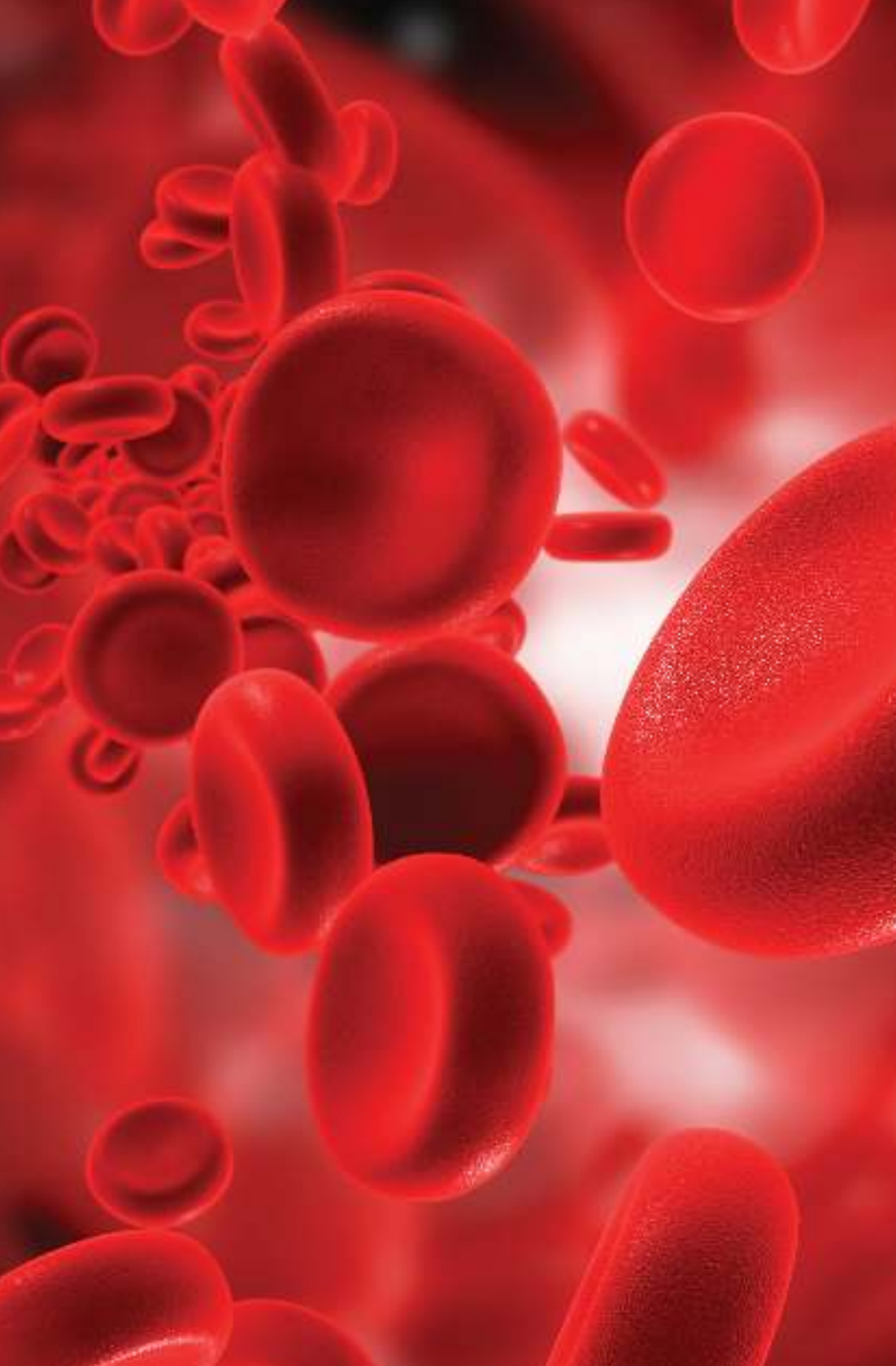
Umbilical cord blood is blood that remains in the placenta and the attached umbilical cord after childbirth. Umbilical cord blood contains two types of cells, primarily hematopoietic stem cells* and a small number of medicinal signaling cells*. These cells have the capacity to self-renewal, release growth factors and cytokines, as well as change into more mature cells.

As an extension of fetal cells, umbilical cord blood cells exhibit high plasticity. Umbilical cord cells have been used for over twenty years for hematopoietic cell reconstitution as a substitution for bone marrow reconstitution. Additionally, due to the high plasticity of umbilical cord cells, there is a significantly decreased risk of graft-versus-host disease (GVHD) and if GVHD does occur it is less severe than most other types of transplants.



**Hematopoietic Cell: immature cells that can develop into all types of blood cells, including white blood cells, red blood cells, and platelets.*

**Medicinal Signaling Cell: plays an important role in many regeneration processes in the human body.*

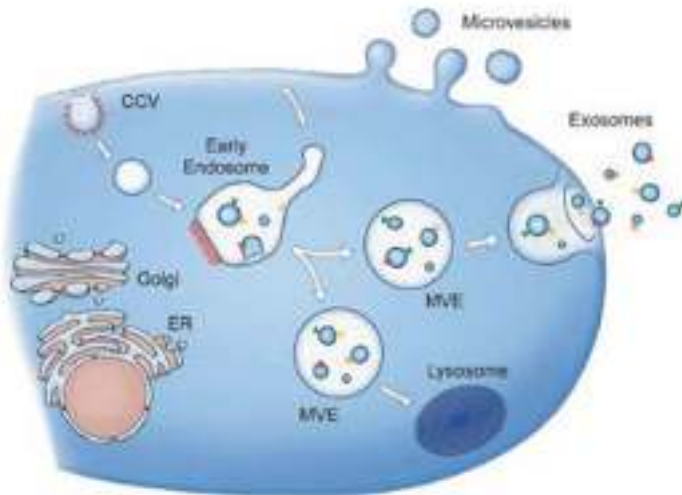


EXOSOMES

Older cells are less robust in the production of components necessary for healing. One option for older patients seeking regenerative medicine treatments is exosomes. Exosomes provide many therapeutic benefits by exhibiting regenerative and immune responses that assist the cells contained within the body to heal and correct.

Not all cells in the body are active. Some lie dormant, not working to complete the needs of the body. This population of cells are particularly versatile and once activated penetrate or travel to the sites of injury where they can develop specific characteristics to repair and remodel. Exosomes possess the capability to activate these dormant cells.

Exosomes derived from healthy connective tissue cells do not contain DNA. This means that there is no risk of cells developing cancerous characteristics. Additionally, as the cells contained within do not come from the patient's own body, the number of cells is not limited by the patient's age





PLATELET RICH PLASMA (PRP)

Often misrepresented as stem cell therapy, PRP is created by drawing blood from a patient with an anticoagulant, injecting it in a special tube and placing the tube in a centrifuge. The high speed of the centrifuge separates the platelets (Figure 10) from the red blood cells.

The product is then re-coagulated and sometimes mixed with calcium chloride* to induce the release of growth factors. The PRP is then ready to be used as an autologous tissue* injection or introduced to a surgical site.

Platelets are normally known for their responsibility to clot blood, but they also contain proteins known as growth factors that play a vital role in healing injuries. Since the location of most sports injuries does not receive an abundant flow of blood, the injuries are deprived of the platelets and growth factors needed to regenerate damaged tissue. Studies show that PRP treatment can resolve that problem by delivering the injured part of the body with the platelets necessary to support healing.

While not as "potent" as other therapies, PRP does contain growth factors and other cytokines that are said to recruit cells to an area of injury to coordinate a repair response. Additionally, PRP activates tenocytes to proliferate quickly and produce collagen to repair tissue.

PRP is said to begin working in a few weeks but, alone, can take 6-9 months for its full effect. However, PRP mixed with New Life Regenerative Medicine products may enhance the healing process and cut the time down by more than eighty percent.

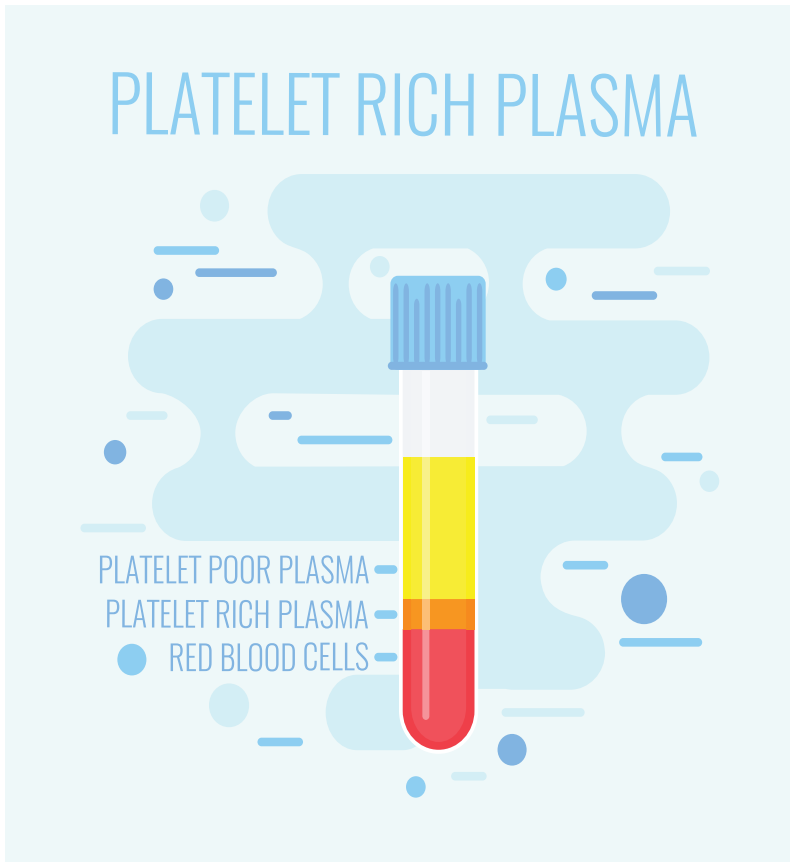


FIGURE 9

**Calcium chloride is a calcium salt and an inorganic chloride*

**Autologous: Cells or tissues obtained from the same individual*

ADIPOSE DERIVED STEM CELLS

Adipose (fat) is collected from the patient via mini-liposuction. This procedure should be performed by a licensed physician in a hospital setting under light general anesthesia. The physician will determine the most appropriate location(s) to perform the incision(s) for the required fat tissue extraction. One of the most frequently used areas is commonly referred to as the "love handles." The procedure typically takes about an hour. After the procedure, patients are observed for one hour in the post-op recovery room and then an additional one to two hours in another recovery room. Pain medication is prescribed for those who need it although most patients require very little medication.

While recovering, your cells will be separated from your fat tissue and the doctor will then inject those cells (just like getting a shot or an IV) back into your body. (Figure 11) The entire procedure normally takes four to five hours and the number of viable cells obtained is greatly dependent on the age of the patient.

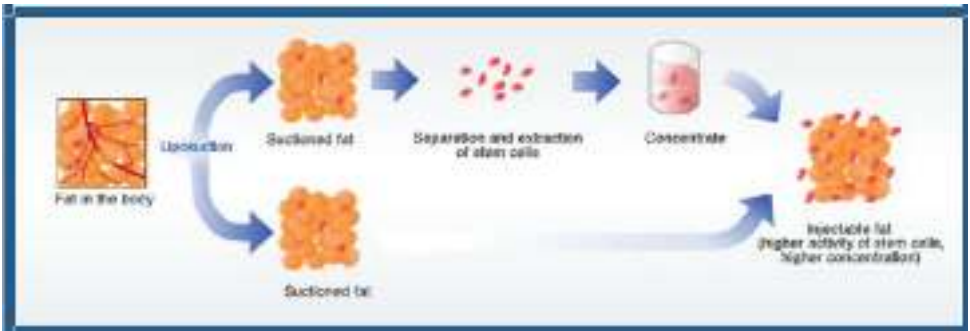


FIGURE 11

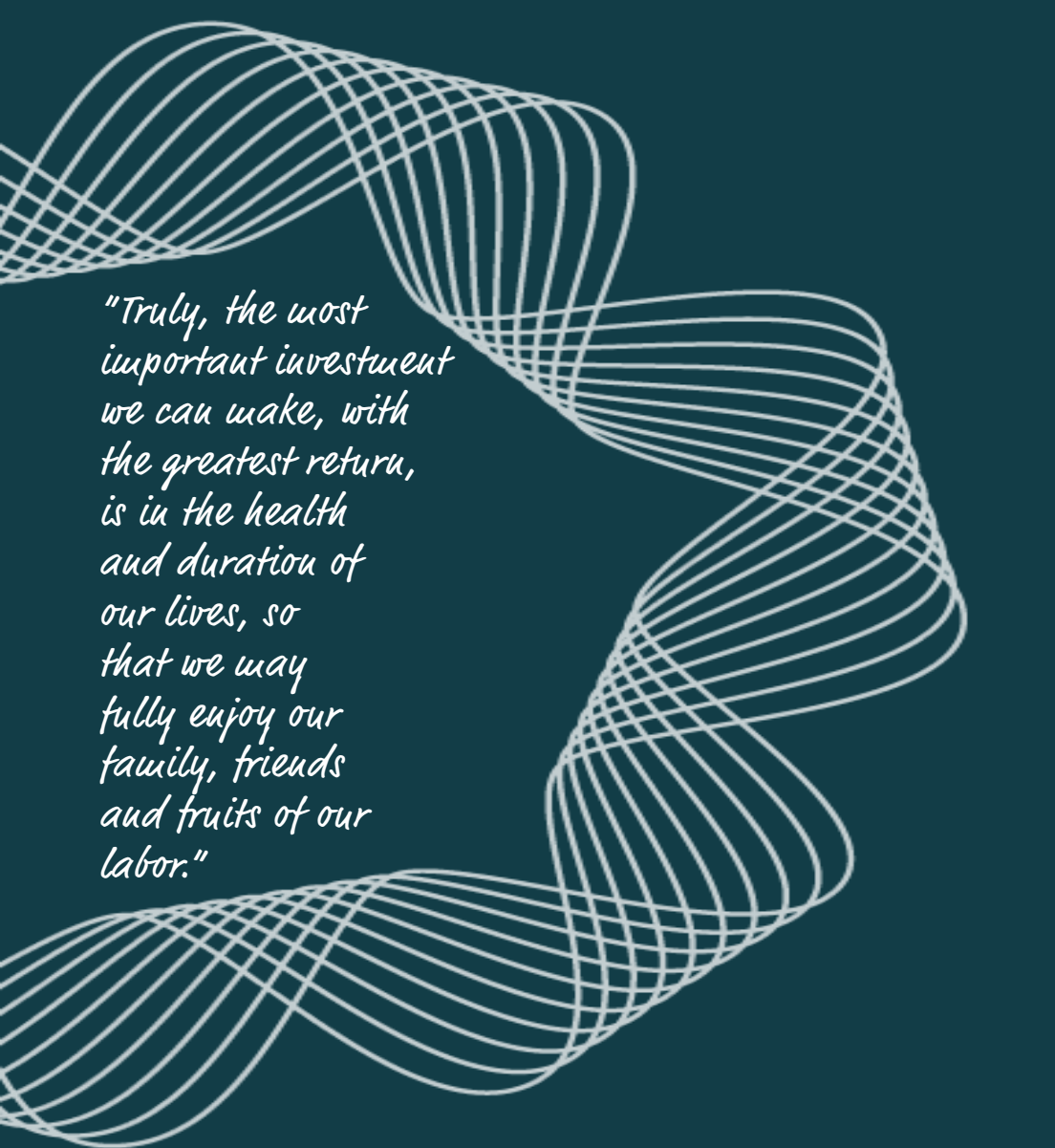
BONE MARROW ASPIRATE STEM CELLS

Bone marrow aspirate concentrate is made from fluid taken from bone marrow. A needle is used to remove bone marrow from within the bone. This is typically done under sedation or general anesthesia. Marrow is commonly taken from the pelvis but may be taken from other sites. The pelvis is marked and prepped to keep the site sterile. A hollow needle is inserted into the bone and a syringe is used to withdraw fluid from the bone marrow. (Figure 12) After enough fluid has been collected, the needle is removed. Pressure is applied to the needle site to stop the bleeding. A small dressing is then applied. After aspiration, there usually is pain at the pelvis that goes away within several days. A small dressing or bandage is kept at the aspiration site until it has healed.

The sample of bone marrow is removed and then spun down in a centrifuge to separate the cells. A liquid is produced that has a high concentration of cells. The physician injects the stem cells directly into the surgical site. This method is avoided in patients who have an infection or cancer. Complications may include pain, bleeding, infection and nerve injury. An intra-abdominal injury may occur because of the needle. The success of bone marrow aspirate cells is dependent on the age of the patient



FIGURE 12



"Truly, the most important investment we can make, with the greatest return, is in the health and duration of our lives, so that we may fully enjoy our family, friends and fruits of our labor."