REGENERATIVE MEDICINE

Stem Cell injections using bone marrow
Definition of MSCs
• Adult STEM CELLS are an **early stage** cell (in the cells development)
• MSC's are isolated from adult tissues.
• STEM CELLS is a generic term used to describe immature or PROGENITOR CELLS with the capability of self-renewal and also the ability of differentiation into multiple cell lines.
• Adult STEM CELLS are capable of developing into other types of cells.
  o Chondrocytes (which goes into cartilage)
  o Osteoblasts (which goes into bone)
  o Adipocytes (which goes into muscle and adipose tissue)
• They have the potential to regenerate damaged tissues (Arthritis for example)
• They act as the body’s repair cell.
• They have a super anti-inflammatory property to help fight pain and inflammation
• They are responsible for the maintenance and repair of unhealthy tissues.
Three Generations of Biologic Injectates

• **Hyaluronic Acid (First Generation)**
  o Successful in the treatment of painful Osteoarthritis of the knee.
  o Benefits covered by insurance.
  o Limits include:
    • Temporary effect.
    • Best used in early osteoarthritis.

• **PRP (Second generation)**
  o Has demonstrated superior results compared to Hyaluronic Acid.

• **Adult MSC's (Third Generation)**
  o More powerful than PRP.
  o Function like MINI DRUG STORES to repair injury sites.
  o Come from multiple sources like bone marrow and adipose.
  o The adult STEM CELL is an undifferentiated cell that is held in reserve until replacement or repair is needed.
  o It can turn into many cells.
  o It can orchestrate a repair response in joints, muscles and tendons.
Overview of Stem Cells
A.T. Still: Founder of Osteopathic Medicine:

- "The body of man [is] God’s drug-store and [has] in it all liquids, drugs, lubricating oils, opiates, acids, and anti-acids, and every sort of drug that the wisdom of God thought necessary for human happiness and health."

- “Man should study and use the drugs compounded in his own body."
THE STEM CELL ORTHOPEDIC INSTITUTE OF TEXAS offers MESENCHYMAL STEM CELL and PLATELET RICH PLASMA (PRP) procedures as viable alternatives for individuals suffering from:

- joint pain,
- joint and tendon degeneration,
- soft tissue injury.
- joint replacement or fusion

The patient may therefore avoid a lengthy post-operative period after surgery, an invasive procedure, and a lengthy rehabilitation.
• In recent years, Scientists and Doctors have made tremendous advances to make tissue regeneration (with STEM CELLS) a reality.

• Through Regenerative Medicine, a person can take advantage of their body’s ability to heal itself by using their own adult STEM CELLS that can be found throughout the body.

• This may provide the patient an alternative to surgery for certain treatments.
More Powerful Alternative: Adult (Autologous) Stem Cells

- Types:
  - Mesenchymal (MSC) “Medicine Signaling Cells”
    - Function like mini drugstores and mobile paramedics to repair injury sites
    - Multi-potent, from sources including bone marrow and adipose
  - Hematopoietic (HSC)

*Images courtesy of: Caplan, Arnold ICRS Stem Cells & Scaffolds Meeting, Bologna Italy Dec 2013.*
THE STEM CELL ORTHOPEDIC INSTITUTE OF TEXAS offers Regenerative Medicine treatments (STEM CELLS / PRP (PLATELET RICH PLASMA) for specific degenerative and inflammatory conditions of the:

- Hip.
- Knee.
- Shoulder.
- Low back.
- Hand/wrist.
- Foot/ankle.
• MSC's are used in the TREATMENT for:
  o Osteoarthritis treatment of joints (knee, hip, etc.)
  o Rotator Cuff Tears
  o Meniscal tears
  o Tendinopathies
  o Spine Degenerative Disc Disease
<table>
<thead>
<tr>
<th>KNEE</th>
<th>HIP</th>
<th>SHOULDER</th>
<th>ELBOW</th>
<th>BACK &amp; SPINE</th>
<th>ANKLE</th>
<th>HAND &amp; WRIST</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arthritis</td>
<td>Avascular Necrosis</td>
<td>Rotator Cuff Tears</td>
<td>Laeral Epicondylitis (Tennis Elbow)</td>
<td>Spinal Degeneration (Degenerative Disc Disease)</td>
<td>Osteoarthritis</td>
<td>Arthritis</td>
</tr>
<tr>
<td>Patellofemoral Syndrome (Chondromalacia)</td>
<td>Bursitis</td>
<td>Arthritis</td>
<td>Medial Epicondylitis (Golfer’s Elbow)</td>
<td>Discogenic Low Back Pain</td>
<td>Rheumatoid Arthritis</td>
<td>Rheumatoid Arthritis</td>
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<tr>
<td>Patellar Tendinopathy</td>
<td>Tendinopathy</td>
<td>AC Joint Dysfunction</td>
<td>Elbow Arthritis</td>
<td>facet Joint Arthritis</td>
<td>Chronic Ligament Sprain or Tear</td>
<td>Trigger Finger</td>
</tr>
<tr>
<td>Meniscal Tear</td>
<td>Labral Tears</td>
<td>Bicep Tendinosis</td>
<td>Elbow Bursitis</td>
<td>Sacroiliac Joint Dysfunction</td>
<td>Plantar Fascitis</td>
<td>(Dupuytren’s Contracture)</td>
</tr>
<tr>
<td>MCL Sprain or Tear</td>
<td>Greater Trochanteric Bursitis</td>
<td>Glenohumeral Joint Arthritis</td>
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<tr>
<td>ACL Sprain or Tear</td>
<td>Sacroiliac Dysfunction</td>
<td>Sub-Acromial Bursitis</td>
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<tr>
<td>LCL Sprain or Tear</td>
<td>Ischial Tuberosity Bursitis</td>
<td>Impingement Syndrome</td>
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<tr>
<td>Biceps Femoris Tendinopathy</td>
<td>Labral Tears of Degeneration</td>
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<tr>
<td>Hamstring Tendinopathy</td>
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<tr>
<td>Baker’s Cyst</td>
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<tr>
<td>Iliotibial Band Syndrome</td>
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</table>
Osteoarthritis
DEFINED
• Once considered only in the elderly, now osteoarthritis is seen in younger patients.

• Osteoarthritis is a progressively debilitating and irreversible disease that affects mostly cartilage and associated changes in the bone and synovium.

• All joints can be affected in Osteoarthritis with hand, knee, hip and spine being the major sites.

• Manifestations of Osteoarthritis include:
  o Joint pain.
  o Impairment to movement.
  o Local tissue inflammation surrounding the joint.
• Current treatment strategies for Osteoarthritis are inadequate.

• MSCs have been shown to possess anti-inflammatory function and so they are suitable cell types to treat OSTEARTHRITIS

• MSC's isolated from patients with end stage OSTEARTHRITIS are functionally deficient in their proliferative and differentiation abilities whereby they had reduced ability to produce cartilage, fat and bone.
Current Treatment In Osteoarthritis

• Non-pharmacological and pharmacologic treatments are used for early cases of Osteoarthritis, but protection of the articular cartilage has not been shown.

• It is a striking fact that no appropriate pharmacological intervention, biological therapy or procedure prevents the progressive destruction of the osteoarthritic joint.

• Total joint replacement can be successful resulting in enhanced mobility and reduction in pain.

• Total joint replacement risks includes thrombosis, infection and very high cost in hospitalization and rehabilitation.
MSC's – Base procedures (STEM CELL injection) has had therapeutic effects in OSTEOARTHRITIS through their trophic effect (what they secrete) and anti-inflammatory and immunosuppressive activities which can significantly affect their local environment in carrying out the regenerative function.
MSC’S in the Treatment of Osteoarthritis

• Osteoarthritis is associated with progressive and often severe inflammation.

• Because MSC's have been shown to possess anti-inflammatory function, they are a suitable cell type for this purpose.

• Several characteristics of MSC's make them attractive in this respect.
  
  o MSC's migrate to and engraft onto multiple musculoskeletal tissues, especially sites of injury.
  
  o MSC's at site of injury undergo site specific differentiation.
  
  o **MSC's at the site can exert significant effects on the local environment and on resident endogenous tissue progenitor cells through direct or indirect interactions and soluble factors.

  o MSC's have shown potent anti-inflammatory and immunosuppressive activities.

  o All the above make MSC's a promising candidate for cell therapy for diseases that often involve the immune system (OA and RA).
Where MSCs Are Found
• MSCs are isolated from:
  o Bone marrow.
  o Fat.
  o Synovium.
  o Periosteum.
  o Blood Vessels
  o Etc.
MSC’s = “Pericytes”: Cells that live on microvessels

(images courtesy of Arnold Caplan PhD)
Differentiation Potentials of STEM CELLS

1. SYNOVIAL derived MSC's have:
   - A greater CHONDROGENESIS ability than BONE MARROW derived MSCs (DAVID DAVID DAVID)

2. ADIPOSE derived MSC's have the highest number of cell colonies.

3. The CHONDROGENIC potential of ADIPOSE has a lesser robust response than bone marrow derived.

4. BONE MARROW derived MSC's have greatest multi-lineage differentiation potential (but do not exhibit the greatest cell growth – adipose does).

5. BONE MARROW derived MSC's produce better repair of bone/cartilage than adipose.

6. Bone marrow derived MSC's are favored to work best for degenerative bone/cartilage disease.

7. UMBILICAL CORD derived STEM CELLS isolates have been found to heal non-union (bone defects) the fastest
   - Muscle derived MSC's work best for muscle related application.
TYPES OF STEM CELLS
# Types of Stem Cells

## Adult VS Embryonic Stem Cells

<table>
<thead>
<tr>
<th>ADULT MSCs</th>
<th>EMBRYONIC STEM CELLS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exist in all tissue</td>
<td>Exist only in early developmental stages of the body</td>
</tr>
<tr>
<td>Not cancerous</td>
<td>Potentially cancerous</td>
</tr>
<tr>
<td>No ethical issues</td>
<td>Ethical issues exist</td>
</tr>
<tr>
<td>Contact inhibition</td>
<td>Don’t stop growing</td>
</tr>
<tr>
<td>Limited DIFFERENTIATION potential to 1 germ layer</td>
<td>Can DIFFERENTIATE into 3 germ layers</td>
</tr>
<tr>
<td>No immune rejection</td>
<td>Immune rejection</td>
</tr>
</tbody>
</table>
ADIPOSE STEM CELLS

• Greatest risk of the procedure is getting DEAD CELLS.
• Have potential application in cartilage regeneration. (But usually has to be cultured)
• Have proliferation potential superior to that of MSC's from bone marrow.
  ○ But BONE MARROW derived STEM CELLS have greater CHONDROGENIC potential in both quality and quantity in the cartilage they produce.
Types of Stem Cells

- Bone Marrow Aspirate
  - Isolated from Bone Marrow
- Adipose (Fatty Tissue)
  - Cells taken from fatty tissue

Autologous

Allogeneic

- Cord Blood
- Amniotic
- Embryonic
- Synovial
Function of MSCs
The Power of Stem Cells

- MSC's do the following:
  - **ANTI-INFLAMMATORY**–
    - by releasing certain proteins that decrease inflammation (called CYTOKINES).
  - **DIFFERENTIATION**
    - MSC's at the site of injury undergo a differentiation into bone, muscle or cartilage, depending on the environment they reside.
  - In orthopedics, adult BONE MARROW STEM CELLS have the ability to differentiate into the cells of the chondrocyte lineage
    - These MSCs have the greatest potential for cartilage repair.
  - **MSC's secrete GROWTH FACTORS (PARACRINE FUNCTION)** that will:
    - Increase blood vessel growth in injured areas and assist in tissue repair.
    - Increase collagen production in tissues.
  - **REGENERATION**
    - MSC's self-replicate and produce new bone, cartilage and muscle.
  - **CYTO-PROTECTIVE**
    - STEM CELLS stop the death of injured cells by increasing blood vessel growth and nutrition.
  - **STEM CELLS inhibit certain bad cancer cells to grow (IMMUNOMODULATION)**
    - They inhibit the maturation of immune cells.
  - **STEM CELLS MIGRATE** to injured areas or areas showing inflammation and engraft there. While there, they can differentiate into tissue specific cells and therefore substitute for loss cellular function.
  - **STEM CELLS PROTECT** the host cells.
  - Promote cell proliferation
    - Tissue remodeling and promote a more viable environment to exist
  - Recruit local cells called PROGENITOR CELLS to replace damaged cells.
Treatment

• MSC's are used in the TREATMENT for:
  - Rotator cuff tears
  - Meniscal tears
  - Osteoarthritis treatment of joints
  - Tendinopathies
Where MSCs Are Found

MSC's are found in all joints

- They contribute to the maintenance of healing tissues by two mechanisms:
  - Tissue repair and HOMEOSTASIS
    - MSC's provide a reservoir of repair cells that are activated in response to growth remodeling or repair.

- REDUCE inflammation and limit T-Cell activation

- MSC's might reside in cartilage in order to replenish the surface proteoglycan LUBRICIN.
  (Which is crucial for reducing friction).
MSCs in Tendon Repair
Tendon injuries range from acute traumatic ruptures to chronic tendinopathy.

The healing and injured tendon tissue in most cases results in formation of a poor quality tissue such as the following:
- Scar tissue.
- Fatty infiltration.
- Matrix disorganization.

MSC's injected into tendons can:
- Increase collagen fiber density.
- Restore a nearly normal tendon – bone junction.
- Increase the presence of fibrocartilage at the defect site (which has been associated with increased biomechanical strength).
- Produce greater organization of collagen.
Moderate Improvements to Complete Resolution of Symptoms for the Most Commonly Treated Tendons

<table>
<thead>
<tr>
<th>Injury Location</th>
<th>Subjects (%)</th>
</tr>
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<tbody>
<tr>
<td>Lateral Epicondyle</td>
<td>93</td>
</tr>
<tr>
<td>Patella</td>
<td>59</td>
</tr>
<tr>
<td>Achilles</td>
<td>100</td>
</tr>
<tr>
<td>Rotator Cuff</td>
<td>81</td>
</tr>
<tr>
<td>Hamstring</td>
<td>82</td>
</tr>
<tr>
<td>Gluteus Medius</td>
<td>81</td>
</tr>
<tr>
<td>Medial Epicondyle</td>
<td>82</td>
</tr>
</tbody>
</table>
Conclusion

• MSC's:
  o Promote vascularization
  o Promote cell proliferation
  o Promote cell differentiation
    • Cartilage
    • Bone
    • Tendon
  o Inhibit osteoarthritis progression
  o Decrease an inflammatory response
  o Immunomodulation
CONCLUSION

• The above literature presented indicates that Bone Marrow-derived MSC's for tendon repair are:
  o Safe.
  o Potential to enhance tendon repair.
Safety of MSCs
Safety of MSCs

• Bashir et al:
  - A large review study investigating the safety of MESENCHYMAL STEM CELL application for Musculoskeletal conditions revealed no neo-plastic complications in 339 patients.

• A recently published report showed that there was no risk for tumor formation at the site of autologous bone marrow concentrate injection. This is a study of 1,873 patients who were treated for orthopedic diseases with an average follow up of 12.5 years, which includes one group of patients who have no evidence of tumor formation after 22 years.
Summary of large MSC Studies for Cancer risks

- Centeno – 2365 cases
- Hernigou – 1800 cases
- Centeno – 700 cultured cases

No concern for increased cancer rates for the above cases.
Allowed Use of MSCs
Regulatory guidelines of stem cells
FDA GUIDELINES

• Adipose is a drug that requires digestion or breakdown of the collagen matrix into a liquid suspension
  o Therefore ALTERS the biologic characteristic of that tissue (Not FDA approved)

• In bone marrow, the tissue already exists in a liquid suspension
  o Cellular digestion of the collagen matrix IS NOT REQUIRED.
Stem Cell
Procedure Overview
• The patient is given intravenous light sedation and laid on their stomach to relax.

Bone marrow biopsy.

  o Dr. Hirsch/Dr. Hall place a very small needle into the hip to numb the specific area. The hip location is rich in **MESENCHYMAL STEM CELLS**.
  o Then a larger needle is inserted (under live x-ray) into the intended area of the posterior hip.
  o Then 60 cc’s of bone marrow (rich in **STEM CELLS**) are extracted (aspirated) from this area of the hip (The iliac crest which has the highest number of cells).

• These cells are then processed through a bedside centrifuge for approximately 10 minutes (in order to retrieve the **STEM CELL** concentrate and removing the undesirable cells).
• The STEM CELL concentrate has 3 layers:
  o Plasma
  o Red Blood Cells
  o BUFFY COAT
    • Which has platelets, leukocytes, granulocytes, monocytes, and progenitor cells.
    • This is the layer that is useful in regenerative healing.

• The concentrated STEM CELLS are then re-injected into the injured region.

• The injection is accomplished by using image guidance (live x-ray or ultrasound) in order to put the STEM CELLS in the exact anatomic area intended.
• Our goal is to deliver much greater numbers of **STEM CELLS** to an injured area of the body than the body could deliver on its own.

• The Stem Cell Orthopedic Institute of Texas may in certain patients add **PLATELET RICH PLASMA** to the stem cell concentrate (to make a super mix or an anti-pain cocktail).

• The **STEM CELL/PLATELET RICH CONCENTRATE** offers different anti-inflammatory potentials and different mechanisms to aid in the body repair.

• **PLATELETS** do have a stimulatory effect on the **STEM CELLS**.
• Typically, the process takes less than 60 minutes.
• After the procedure, you leave the office with appropriate instructions and a customized rehabilitation program to support your recovery.
• The Stem Cell Orthopedic Institute of Texas will track your outcomes through follow up visits, by phone or by email.
• All patients are tracked in a patient registry for outcomes and complications.
• This is a SAME DAY PROCEDURE which includes the bone marrow aspiration and the STEM CELL injections.
EXERCISES AND POST STEM CELL PROCEDURE PROTOCOLS
THE STEM CELL ORTHOPEDIC INSTITUTE OF TEXAS
POST PROCEDURE PROTOCOL

What can I expect post procedure?

• STEM CELL procedures are done as an outpatient, so no overnight stay is required. Most should expect to walk out of the clinic without assistance.

• Some patients have reported experiencing mild pain for the first 48 to 72 hours post STEM CELL procedure. This pain can primarily be from the bone marrow biopsy in the hip. The pain also can be from the absence of the patient taking their normal anti-inflammatory medications (nonsteroidals) prior to the procedure. -- Do not restart an anti-inflammatory (nonsteroidals and/or aspirin) for 2 weeks after the procedure.

• Taking Tylenol, Tylenol #3, Lortab, Hydrocodone, Norco, etc. is allowed for pain.

• Celebrex is also allowed for pain relief.

• Ice should be applied to the affected area 15-20 minutes at a time (no longer) for 3-5 times in a 24 hour period over the donor site (hip) and injected area. This should take place for about 2 days.

• Encourage re-hydration (drinking fluids) after the procedure for the next 24 hours.

• Stop tobacco use, if possible.

• Consider supplements of zinc and vitamin D3.
When can I resume physical activity?

• For the procedure to have the best chance to yield lasting benefits, we recommend:
• No anti-inflammatory medications for the first 2 weeks post procedure.
• Rest as much as possible for the first 24-48 hours.
• Restrict the joint to just *general use* for the first 2 weeks.
• For weeks 3-4, walking and cardio activities are allowed.
• After 4 weeks, weightlifting and running are permitted.
Stem Cells

Treatment of knees and cartilage repair
The challenge in repairing meniscus is the poor blood supply and nutrient supply of the inner two-thirds of the meniscus (where many tears occur) versus the outer third.

- Surgical repair is more successful in the outer one-half.
- So, many surgeons perform a partial meniscectomy for tears which can lead to significant biomechanical abnormalities in the knee.
- MSC's may be able to overcome the problem of the poor repair in the AVASCULAR ZONE by using MSC's transplanted into a fibrin matrix.
There are many studies that show MSC's ability to enhance meniscal repair.

• Centeno
  o In 202 knee and hip osteoarthritis treated with injections of MSC's
  o Only 6 patients eventually needed total knee or hip replacements. **DAVID, DAVID, DAVID GET THE NUMBERS**

• MRI data shows the following after MSC injection:
  o Cartilage fill of the defect.
  o Improved integration of the repair tissue in the surrounding normal cartilage. (Extension of repair tissue over the subchondral bone).
  o Increased height of the medial meniscus.
  o Increased cartilage volume and thickness.
  o Decrease in subchondral edema.
• Resection of ACL and medial meniscus repair showed advanced osteoarthritic changes induced by surgery.
  o Joint Degeneration.
  o Cartilage Fibrillation.
  o Osteophyte Formation.
  o Subchondral Sclerosis.
## Injectable Stem Cells Vs Knee or Hip Arthroplasty

<table>
<thead>
<tr>
<th></th>
<th>Stem Cells</th>
<th>Knee/Hip Arthroplasty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain associated with procedure</td>
<td>Minimal</td>
<td>Considerable</td>
</tr>
<tr>
<td>Post procedure recovery time</td>
<td>Minimal</td>
<td>Considerable</td>
</tr>
<tr>
<td>Joint Infections</td>
<td>0.0% (reports of 2 patients with infections at bone marrow draw sites)</td>
<td>0.72%</td>
</tr>
<tr>
<td>DVT/PE</td>
<td>0.0%</td>
<td>as high as 3.76%/1.19% (with anticoagulation)</td>
</tr>
<tr>
<td>Nerve injury</td>
<td>0.0%</td>
<td>Up to 0.03%</td>
</tr>
<tr>
<td>Limb length discrepancy</td>
<td>0.0%</td>
<td>Up to 62%</td>
</tr>
<tr>
<td>Cost of procedure</td>
<td>Up to $11,000</td>
<td>Up to $25,000/$44,816</td>
</tr>
<tr>
<td>Need for Revision</td>
<td>Unknown</td>
<td>5,082/7,852 in UK in 2010</td>
</tr>
</tbody>
</table>
• Surgery of the joints ultimately:
  o Requires long rehabilitation for strength loss and range of motion.
  o Costly.
  o Increased complications.
  o Recent study has shown that 50% of the patients reported significant improvement in pain and activities of daily living.
  o 25% of patients who undergo a single joint replacement will require another joint replacement in 2 years
Conclusions to the Centeno 999 procedure registry that had STEM CELLS injected into the knee or knees

- Decreased pain score
- The mean improvement in pain at 2 years was 71%.
- No association between body weight and outcome.
- No association between older age and outcome.
- No association between arthritis severity and outcome.
- There was a significant decreased pain score.
- Increased range of motion of the joint.
- Activities of daily living improved considerably
Stem Cell Treatment

LUMBAR DISC DENERGATION (DDD)
Chronic low back pain is the condition of the axial lumbar spine in which symptoms have lasted longer than 3 months.

Symptoms may be recurrent, and in some patients unremitting.

Improvement in function and pain is the most important goal in treating this condition.

The spinal components work together to provide function and mobility to the body.

If an area in the back is injured, the entire structure begins to compensate for the injury causing problems with spinal stability and function.

Restoring stability and functionality by reducing your pain is possible when treating:

- Discogenic low back pain.
- Bulging discs.
- Degenerative disc disease.
- Facet joint arthritis.
- SI joint arthritis.
Symptoms

• Lumbar pain (low back pain) that may radiate to one or both buttocks is the main symptom of degenerative disc disease.

• Often the pain is mechanical

• Aggravated by activities such as:
  o Bending,
  o Stooping,
  o Lifting,
  o Twisting.

• Patients may have a history of sciatica (pain radiating down the back of the leg).

• Pain in the low back is the predominant symptom.

• Symptoms may last for years, typically presenting between the third and sixth decades of life.
Symptoms Cont.

- Some pain is relieved with a night’s rest. Sleep can be disturbed though.
- Chronic pain often causes
  - Mood disturbances,
  - Sexual changes and
  - Concentration problems.
  - Deconditioning may also develop.
- The patient usually reports stiffness when rising from a seated position and there may be tenderness about the lumbar spine and sacroiliac joints.
TREATMENT (POSSIBLE OPTIONS)

- Nonsteroidals (NSAID’s)/muscle relaxants.
- Narcotics.
- Antidepressants for pain and mood changes.
- Physical therapy to include traction and spinal exercises.
- Weight reduction.
- Spinal injection.
- Spine surgery (Fusion).
• STEM CELLS hold promise that it may be possible to treat degenerative disc disease or its components to hopefully prevent spinal fusion.
Alternative to Back Surgery

• Millions of people undergo painful lumbar spine surgeries yearly.
• Sometimes lumbar surgery is extremely helpful and life changing.
• Traditional spinal surgery for DDD has had disappointing results (Deyo 1993 and Fritell 2003)
• When a failed low back surgery occurs, the patient can be left with
  o Decreased back motion
  o Decreased activity levels
  o Chronic pain
  o Chronic muscle spasms,
  o Depression
  o Employment issues

Most low back surgeries (fusions) require a lengthy recovery

• The Stem Cell Orthopedic Institute of Texas offers spinal stem cell injections for:
  o Degenerative disc disease/discogenic low back pain.
  o SI joint arthritis.
  o Facet joint arthritis.
• The **STEM CELL** injections are a walk in/walk out procedure with return to activities as tolerated that day.

• The **STEM CELL** procedure is super anti-inflammatory injection into the discs or joints to help with pain and hopefully restore some disc height.

• With significant disc degeneration of the lumbar spine
  o The spine vertebral bodies get closer together, and this
  o Ultimately puts more pressure on the affected spinal segment joints.
  o Arthritis and pain can develop with time as well as compression of nerve roots.
• With **STEM CELL** injections, there is
  - No scarring
  - No cutting of the spinal musculature
    (Which can cause muscle injury and residual low back pain after surgery)
  - Limited complication rates and morbidity.

• The combination of **STEM CELL** and **PLATELET** Injections help with low back pain healing.

• The patient’s platelets contain growth factors that help blood vessels to grow and increase blood supply to the disc.
  - This aides the disc in healing and pain.

• **STEM CELL** and **PLATELETS** injected into the disc can also help with decreasing pain.

• **STEM CELLS** may restore a partially collapsed and degenerative disc.

• **STEM CELLS** can cause architectural changes that occur as well.
Patient Satisfaction

• Number of Patients in study = 15
• The average pain relief was 79% improvement between 3-6 months after injection.
• The WOMAC score improved 42% average. The WOMAC questionnaire measures pain, ability to walk, sit, bend, stand, lift, and other activities of daily living.
• Positive outcomes took place in our research:
  o Pain
  o ADLs (Activities of daily living)
  o Function
  o Well being
FUTURE HOPE FOR STEM CELLS
• Worldwide, there are more than 400 clinical trials involved in MSC's. MSC's may permit the engineering and repair of cartilage not only for local repair of lesions but also for the treatment option for osteoarthritic changes.

• MSC's may be used earlier in the treatment of muscle, joint, ligament and tendon injuries

• MSC's use in orthopedic treatments may decrease the number of total hip, total knee and total joint replacements and tendon surgery.

• MSC’s injected into the degenerative disc may prevent future spinal fusions
• There are new sources of MSC's:
  o Synovial Fluid-Derived Stem Cells.
  o Peripheral Blood-Derived Stem Cells (also known as Progenitor Cells) – These cells can increase growth of cartilage and thickness of cartilage.

• Increased effectiveness of MSC's when used with PRP.

• Hyperbaric oxygen may increase the number of Stem Cells in the body naturally.

• MSC injections may possibly replace steroids as the first line of treatment for pain injections
THE NEED FOR ULTRASOUND
Interventional injections of target structures by pain physicians are expensive. The failure of getting to the target structure such as nerve, tendon sheath, bursa, joint space, muscle can lead to the following:

- Failure of treatment.
- An additional expense.
- Possible surgery because of failure in conservative treatment.

Because of these potential situations, **ULTRASOUND** has become the mainstream treatment for musculoskeletal medicine. The delivery of **STEM CELLS / PLATELETS** into the appropriate designated structure is priceless.
The following terms compare CAT SCAN/FLUOROSCOPIC guided injections vs ULTRASOUND guided injections and the utility for using ULTRASOUND for many procedures, which is the mainstream for pain injections today:

• Ultrasound imaging has several attributes that make it an attractive soft tissue injection guidance modality:
  - Ultrasound provides excellent soft tissue images of structures such as muscles, nerves, tendons, bursa, bones which enhance the accuracy of needle placement and assist in the prevention of complications.
  - The ability of ultrasound to provide real time imaging assist in anatomic structure identification and proper needle placement.
  - Ultrasound does not expose the patient or clinician to IONIZING RADIATION like CAT scan.
  - ULTRASOUND IMAGING IS MUCH LESS EXPENSIVE THAN CAT SCAN.
  - Ultrasound is portable and can be done at the bedside and is quick and easy.
  - Ultrasound is fast and often technically easy to perform.
  - Ultrasound guided injections can be used in a large variety of musculoskeletal interventional problems:
ULTRASOUND VERSUS MRI OF ROTATOR CUFF TEARS

1. Ultrasound sensitivity is 95.6 %
2. MRI sensitivity was 97.7 %
3. Greater specificity with ultrasound versus MRI
4. The Conclusion – Ultrasound was almost equally effective in detecting partial tears compared to MRI
5. The Ultrasound has a spatial resolution of 150 microns
6. MRI has a spatial resolution of 450 microns
7. Digital fluoroscopy has a spatial resolution of 125 microns
   a) Red blood cells is 10 microns
   b) Dust particle is 25 microns
   c) A hair is 100 microns

• Jacobson’s study compared MRI versus ultrasound in tendons (very similar results except you see the anterior talo-ligament tear better with ultrasound)
<table>
<thead>
<tr>
<th>Shoulder</th>
<th>Hip</th>
<th>Knee</th>
<th>Wrist / Hand</th>
<th>Ankle / Foot</th>
<th>Elbow</th>
<th>Spine</th>
<th>Misc.</th>
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</thead>
<tbody>
<tr>
<td>Sub-acromial Bursa</td>
<td>Hip Joint Recess</td>
<td>Supra-patellar Recess</td>
<td>Carpal Tunnel Injection</td>
<td>Anterior Joint</td>
<td>Distal Biceps Tendon Sheath</td>
<td>Caudal Epidural Injection</td>
<td>Piriformis Injection</td>
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<tr>
<td>AC Joint</td>
<td>Femoral Nerve</td>
<td>MCL / LCL injection</td>
<td>Duputryns Contractures (Trigger Finger)</td>
<td>Tarsal Tunnel</td>
<td>Common Flexor Tendon</td>
<td>Cervical Medial Branch Block</td>
<td>Intercostal Nerve</td>
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<td>Infraspinatus Sheath</td>
<td>Saphenous Nerve</td>
<td>Common Peroneal Nerve</td>
<td>De Quervains Injection</td>
<td>Morton’s Neuroma</td>
<td>Olecranon Bursa</td>
<td>SI Joint Injection</td>
<td>Pudendal nerve</td>
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<tr>
<td>Gleno-Humeral Joint</td>
<td>Trochanteric Bursa</td>
<td>Prepatellar Bursa</td>
<td>Superficial Radial Nerve</td>
<td>Achilles Tendon</td>
<td>Median Nerve at Elbow</td>
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<td>Brachial Plexus</td>
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<tr>
<td>Sub-scapularis Sheath</td>
<td>Iliopsoas Muscle / Tendon Injection</td>
<td>Pes Anserine Bursa</td>
<td>Radio-Carpal Joint (radial &amp; ulnar side)</td>
<td>Saphenous Nerve at Ankle</td>
<td>Common Extensor Tendon</td>
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<td>Iliohypogastric Nerve</td>
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<tr>
<td>Supra-scapular Nerve</td>
<td>Baker’s Cyst Aspiration</td>
<td>Guyon’s Canal</td>
<td>Plantar Fascia</td>
<td>Cubital Tunnel</td>
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<td>Trigger Point Injections</td>
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<td></td>
<td></td>
<td>Infrapatellar Bursa</td>
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</tbody>
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5/25/2015  75
Musculoskeletal Ultrasound

Therapeutic and Diagnostic Applications
Shoulde

ANATOMY

• Supraspinatus
• Sub-Acromial Bursa
• Biceps Tendon
• Subscapularis
• AC Joint
• Glenohumeral Joint
• Infraspinatus
• Supraspacular Nerve
• Pectoralis Major Tendon
• Rotator Interval
• Deltoid Muscle
Supraspinatus Tendon

- Normal Tendon
- Supraspinatus Tear
Sub-Acromial Injection
Biceps Effusion

Left Bicep Tendon

Effusion

Left Bicep Tendon

Effusion

Longitudinal
Supra-patellar Recess
Carpal Tunnel

ANATOMY

• Median Nerve
• Radial / Ulnar Arteries
• Flexor Tendons
• Carpal Bones
• Flexor Retinaculum
Carpal Tunnel Injection
Cubital Tunnel

ANATOMY

• Medial Epicondyle
• Olecranon
• Medial Head of Triceps
• Ulnar Nerve
Hip Joint / Trochanteric bursa

ANATOMY

Anterior
• Femoral Neck / Head
• Joint Recess
• Iliopsoas Muscle / Tendon

Lateral
• Gluteus Min. / Med. Tendons
• Trochanteric Bursa
• Iliotibial Tract
Hip Injection

Right Joint Recess
Plantar Fascia

ANATOMY

• Calcaneus
• Plantar Aponeurosis
Plantar Fascia Injection

+ Dist 0.57 cm

Right Plantar Fascia PRP
Platelet Rich Plasma
• PRP (PLATELET RICH PLASMA) is where a small volume of blood plasma is concentrated through a centrifuge to produce the resultant high potency PLATELETS.

• Platelets are blood cells that aide in clotting.
• PLATELETS are rich in GROWTH FACTORS that help in the initiation of:
  o Pain reduction
  o Tissue healing
  o Tissue repair
  o Bone regeneration
  o Development of new blood vessels
  o Stimulate wound healing

• **PRP stimulates the growth of collagen which is the main component of connective
tissue such as tendons and cartilage.

• **PRP contains GROWTH FACTORS that attract and recruit STEM CELLS to the area
of tissue damage.

• PRP also increases the effectiveness of the STEM CELLS to help decrease
inflammation.

• Medical literature indicates that the most successful areas to treat PRP are:
  o HEEL (Plantar Fasciitis pain)
  o KNEE (Patella Tendonitis)
  o ELBOW (Lateral Epicondylitis)
  o SHOULDER (Tendonitis or Rotator Cuff tear)
• Tendinopathy is a common and perplexing problem facing clinicians.
• It is the most important common reason (30%) that patients seek medical attention for a musculoskeletal condition.
• Tendon pain is common in recreational and professional athletes as well as sedentary people.
• Initially, tendinopathy was considered inflammatory (*itis for example tendonitis*), but this has changed over the years whereby now it is considered degenerative (*opathy*) and characterized by the following:
  o Hypercellularity.
  o Vascular hyperplasia.
  o Collagen disorganization.
We are now trying to REGENERATE the TENDON by using PRP and/or STEM CELLS, and also decreasing the pain.

- Tendinosis is when healing becomes chronically impaired as evidenced by:
  - Lack of inflammatory cells in the tissue.
  - Abnormal tissue repair.
  - Collagen degeneration.
  - Neovascularization.
  - Thickening of the tendon.
THE POWER OF PLATELETS in treatment

- Platelets are not just for clotting any more.
- They are cells involved in wound healing.
- Platelets are the first cells to arrive at the site of injury.
- They are responsible for the initiating of the healing cascade.
- They secrete alpha granules and dense granules each of which have certain functions in regeneration and inflammation.
The PRP Procedure

• Platelet rich plasma injections have been proposed as a promising alternative for treating tendinopathies:

• PRP is an ideal blood product from the patient that promotes the body’s own natural healing.

• The blood (10 cc’s) taken from the patient’s arm is then centrifuged until the red blood cells and platelets separate, after which the platelets concentrate is extracted from the platelet rich section of the centrifuged plasma.

• The PRP is then filtered and separated. This increases the concentration of platelets and GROWTH FACTORS to approximately 400%. The number of platelets in PRP is approximately 4 to 8x normal.

• This concentrate is then injected into the tendon sheath (for example tennis elbow) under ultrasound guidance to help in decreasing inflammation and pain and increasing architectural changes and increasing positive architectural changes within the tendon.
Functions and Benefits

- Platelets contain GROWTH FACTORS which are very important in the repair of tissues.
- When stimulated by tissue injury, platelets release these GROWTH FACTORS that do the following:
  - Decrease pain.
  - Promote wound healing.
  - Increase collagen production for tendon healing and repair.
  - Increase blood vessel growth for nutrition to the injured areas.
  - Platelet GROWTH FACTORS attract and recruit MESENCHYMAL STEM CELLS.
  - The GROWTH FACTORS can recruit other cells to help with repair.
  - The GROWTH FACTORS can cause cells in the local area to DIFFERENTIATE into newly needed tissue. (differentiation)
  - The GROWTH FACTORS can prevent further soft tissue degeneration from occurring.
  - It promotes tenocytes proliferation and production
  - Stimulates gene expression of extracellular matrix constituents
  - No major risk of adverse effects.
  - Lower cost and shorter recovery time when compared to surgical management.
Research

• **Several studies have revealed under ultrasound that there are changes in tendon size (decrease) and good architectural changes suggesting that structural changes may occur after treatment with PRP.

• PRP is an effective and safe treatment for patients with chronic tendinopathy in a variety of locations to include, Achilles tendon, lateral epicondylitis, the patella tendon, and several other tendons.
Research Cont.

In a major study by Finnoff et al

• patients injected with PRP:
  o 83% of subjects were satisfied with their outcome after the procedure.
  o 83% would recommend the procedure to a friend.
  o 82% had an improvement in the ultrasound analysis of the tendon echotexture.
  o 82% had a decrease in the tendon vascularity (DAVID DAVID DAVID) RE-READ
  o 38% had resolution of the intra-tendinous calcifications.

• No complications were reported.

• There was a mean improvement in the subjects function and worse pain scores of 68% and 58% respectively.
Research Cont.

- In conclusion, Finoff’s study demonstrated improvements not only in pain but also in function and tendon structure after the PRP procedure.
- His study used tenotomy followed by PRP injection, then followed by a standardized post-procedural rehabilitation program.
Frequently Asked Questions
• What are adult STEM CELLS?
Adult STEM CELLS are unique in the body, since they can expand in number (self-renewal) without becoming a tissue cell, but they also can differentiate into various cells found in mature tissue, like cartilage. They are unspecialized or undifferentiated cells capable of two processes; self-renewal and differentiation. They are vital to maintaining tissues in the body such as internal organs, skin and blood.

• Where do adult STEM CELLS come from in the body?
In adults, STEM CELLS are present within various tissues and organ systems, but the most accessible locations of Mesenchymal STEM CELLS are the bone marrow and adipose (fat) tissue. Other sources include the liver, epidermis, retina, skeletal muscle, intestine, brain, placenta, umbilical cord and dental pulp.

• What is the difference between adult STEM CELLS and embryonic STEM CELLS?
  a. Adult STEM CELLS are found in mature adult tissues, including bone marrow and fat, while embryonic STEM CELLS (ESCs) are not found in the adult human body.
  b. ESCs are obtained from donated embryos provided during in vitro fertilization procedures, which raises many ethical concerns. Because ESCs are not obtained from your body, there is a possibility of immune rejection if the ESCs were to be implanted. Adult STEM CELLS do not raise ethical issues nor pose any risks for immune rejection.
• Is Stem Cell therapy safe?
Yes, and ask your doctor what clinical studies have been done to show that STEM CELLS are safe and effective.

• Is this procedure FDA approved?
The FDA allows Physicians to remove bone marrow from your hip, process it and then use the Stem Cell-containing preparation for-treatment.

• Are there ethical issues associated with harvesting STEM CELLS?
No, adult STEM CELLS do not raise ethical questions as they are harvested from the patient's body.

• Are there cancer-causing risks associated with adult Stem Cell treatments?
No. While embryonic STEM CELLS have been show to form teratomas (germ cell tumors), there is no data that suggests adult STEM CELLS have the same potential to promote the development of tumors. In fact, a recently published report showed that there was no risk for tumor formation at the site of autologous bone marrow concentrate injection. This is a study of 1,873 patients who were treated for orthopedic diseases with an average follow up of 12.5 years, which includes one group of patients who have no evidence of tumor formation after 22 years.
• How are adult STEM CELLS used in therapeutic procedures?

Adult STEM CELLS are used to treat patients with damaged tissues due to the aging process or trauma. During a procedure, STEM CELLS are isolated from the patient, concentrated and delivered back to the site of injury to assist in the healing process.

• What basic science data exists that shows that concentrated STEM CELLS from bone marrow can help heal orthopedic injuries?

Basic science data has been obtained that show the biological activities of adult STEM CELLS. Clinical studies have been reported starting in the 2000's showing a benefit to being treated with your STEM CELLS for both soft tissue injuries, tendon problems, and bone and joint disease.
• Will my body reject the **STEM CELLS**?
  No, since the cells are obtained from your body (autologous) and processed quickly at point-of-care, they will not be rejected.

• How long will it take to see results?
  Depending on the condition being treated, your perception of improvement might vary from 2 weeks to 4 weeks.

• How much will it cost?
  The cost of Stem Cell portion of therapy isn't covered by insurance companies, so ask your doctor for details on cost and payment options.
WHAT IS REGENERATIVE MEDICINE?

• It is an emerging clinical approach to utilizing the Power of Stem Cells to improve the repair and regeneration of damaged tissues (such as bone, tendon and joints).

• It is a relatively new field in its utilization in pain mitigation and treatment of orthopedic problems and pain.

• Regenerative medicine clinics like ours at The Stem Cell Orthopedic Institute of Texas - use ultrasound and fluoroscopy guided, minimally invasive treatments of adult STEM CELLS harvested from Bone Marrow aspiration.
WHAT ARE ADULT STEM CELLS?

- They are unique in the body since they self replicate and regulate the body’s natural healing process.
- Adult Stem Cells have the potential to differentiate into various cells found in mature tissue like cartilage, skin and bone, etc.
- Adult Stem Cells from Bone Marrow have the ability to migrate (Homing) to injured areas where environmental chemistry influences what they do. For example.
  - Tissue repair—tendon, joint, bone.
  - Differentiation into certain types.
    1. Chondrocytes.
    2. Osteocytes.
  - Pain control by reducing inflammation.
  - They suppress the breakdown of joints (such as preventing osteoarthritis progression).
  - Adult Stem Cells are the coordinators of the repair process much like a conductor directs the symphony.
WHAT IS STEM CELL THERAPY?

• Stem Cell therapy involves taking Bone Marrow from the patient's hip and concentrating the cells through a process called centrifugation.
• What results is a preparation that contains Stem Cells.
• These Stem Cells are then injected back into the patient's damaged area (Hip, Knee, Shoulder, Low Back).
• These Adult Stem Cells help the body to naturally heal itself.
• The procedure takes around 45 minutes.
• The patient can walk out of the clinic on his or her own.
• The patient's regular exercise program can be restarted in 2-4 weeks after the procedure.
WHY DO YOU TREAT PATIENTS WITH STEM CELL THERAPY?

• The use of Stem Cell Therapy has shown to be very safe and promising for patients with orthopedic and soft tissue injuries to include:
  • Bone --to enhance bone healing.
  • Tendons - -to increase strength and decrease inflammation and to increase collagen growth.
  • Joints --to increase articular cartilage growth.

• Treatment options with adult Stem Cell therapy include:
  • Hip and knee arthritis.
  • Shoulder problems (rotator cuff injuries).
  • Fractures.
  • Low back pain
  • Rheumatoid arthritis for pain.

• Regenerative Stem Cells offer an effective treatment for damaged tissues but can also prevent further tissue degeneration.

• Stem Cells help jump start the healing and repair process.
WHAT FIRST INTERESTED YOU ABOUT STEM CELL THERAPY?

• I believe Stem Cells have a big future in the treatment of pain problems and orthopedic injuries.
• We have seen in our clinical practice at South Texas Spinal Clinic terrific outcomes in their use for:
  • Pain -- From a pain point of view, our numbers showed after 3 months post injection, 79% relief of pain. All of these patients were potentially having total knee or hip replacements
  • Patient’s activities of daily living improved 42%.
• More and more data is becoming available in Pain Medicine, Physical Medicine, Orthopedics and Rheumatology to support its use.
• It is a Natural Healing Process because the patient's own Stem Cells are used to treat the patient's own damaged areas.
• The cost benefits are excellent compared to surgery and lengthy postop and rehab (for example) for total hip replacements, total knee replacements and spinal fusions.
• There is very little down time for the patient versus surgery such as the patient can return to work almost immediately.
• Hopefully decreasing pain medicine and narcotic intake.
• There are no major reported side effects as opposed surgery, such as blood clots, pneumonia or infection.
• In our clinic, we utilize ultrasound to inject injured joints, tendons and nerves. The ultrasound imaging provides an excellent way to enhance the accuracy of the needle placement into the target injured area.
• With ultrasound guided imagery, we view the tip of the needle continuously on injection in order to see:
  • The important anatomic structures (joints, bursa, nerves, tendons)
  • The proper injection site (joint, bursa, nerve, tendon) of the STEM CELL concentrate (STEM CELLS, PLATELETS, steroids) at the end of the procedure
HOW DO YOU SEE STEM CELL THERAPY AFFECTING OUTCOMES ON THESE PATIENTS?

• There is terrific evidence that using Bone Marrow concentrate (Stem Cell Therapy) can reduce pain in patients.

• We did our own unpublished study with 15 patients, and the results between 3 to 6 months post injection were the following:
  • Pain -- From a pain point of view, our numbers showed after 6 months 79.6% relief of pain from patients that required total knee and total hip replacements.
  • About 40% of the patients return to activity that they were previously not able to do

• The Stem Cells secrete certain proteins that:
  • Increase blood vessel growth needed for repair, regeneration and oxygenation
  • Decrease inflammation.
  • Increase tendon strength.
  • Increase cartilage growth.
  • Decrease scarring in joints and tendons.

• Knees exposed to Adult Stem Cells have shown:
  • Marked regeneration of the meniscus.
  • Cartilage degeneration was reduced.
IS STEM CELL THERAPY SAFE?

• There are a number of stem cell therapies that are being researched. We use adult STEM CELL therapy because they are safe. These cells are not cultured or manipulated, and they won’t be rejected because these cells come from the patient.

PATIENT HEAL THY SELF

• A recent published report showed no risk for tumor (cancer) formation at the site of STEM CELL injections. --This report included around 1,800 patients who were treated for orthopedic problems.
DO YOU SEE STEM CELL THERAPY CHANGING THE WAY YOU PRACTICE?

• Yes-- It is an emerging and viable treatment for pain mitigation and for preventing or prolonging the need for surgery.
THE FUTURE OF STEM CELL THERAPY

• Hopefully more and more research to support the claims.
• Ultrasound guided injections are a natural fit to deliver the STEM CELL concentrate precisely.
• It is effective with cartilage, bone and tendon repair.
• The patient's pain is managed earlier and more effectively without as many medications.
• STEM CELLS may replace steroids as a first line treatment for injections in the future.
• Stem cells have the potential to decrease the number of orthopedic surgeries.
• Decrease in cost.
• Improved quality of life.