

20 NSCA 22 *NATIONAL* CONFERENCE

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#NSCACon22

› *KNOWLEDGE*
› *ADVANCEMENT*
› *COMMUNITY*

CONFLICT OF INTEREST STATEMENT

I have no actual or potential conflict of interest in relation to this presentation.

Vitae

- Nova Southeastern University
 - Professor
 - Department of Physical Therapy
 - Fort Lauderdale, Florida
- Institute of Regenerative Medicine
 - Boca Raton, Florida



Lecture Topics

- Preface: Bridging the Gap
- Musculoskeletal Regenerative Medicine (Injectables)
 - Adult Stem Cell Procedures
 - Procedures, Indications, Evidence
- Regenerative Rehabilitation/Mechanotherapy
 - Post-Procedural Considerations
- Common questions

Stem Cell Therapy for Orthopedic Conditions

Hope vs. Hype?

Time For Something New?

Conservative Management
Low-Risk
P.T./O.T./Rehab
Viscosupplementation
Integrative Supplements
Latest & Greatest
Mod-Risk
NSAIDS/Corticosteroids
Opiates/Analgesics

Unsuccessful Outcome

Successful Outcome

Regenerative Medicine

Unsuccessful Outcome

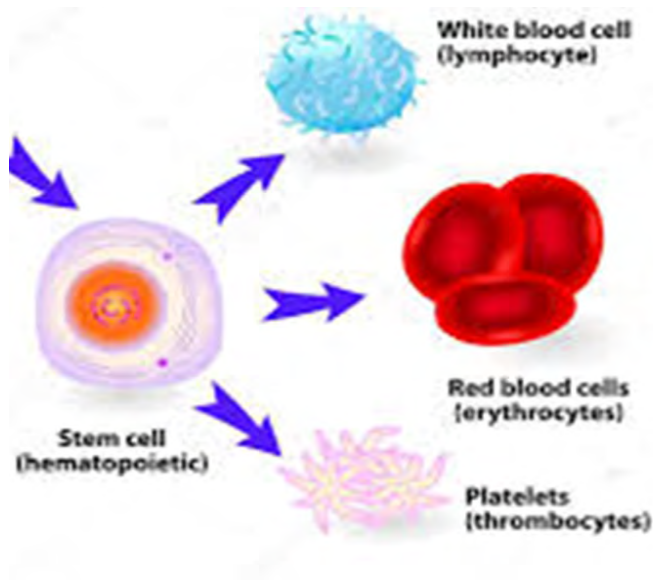
Surgical Management

Wait & See
Live With It
Pain is in the Brain
Delay Surgery

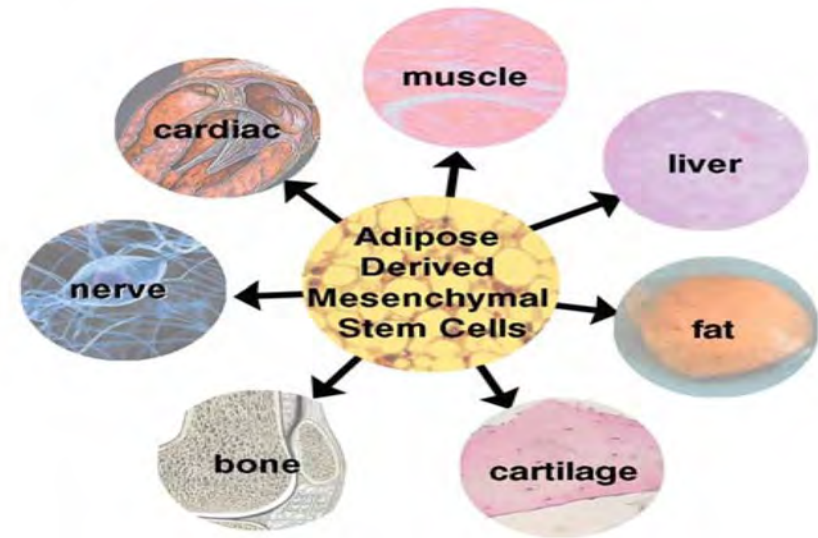
Adult Stem Cells

*Higher *potency (plasticity)* than mature cells (e.g., chondrocytes/tenocytes)

- **Hematopoietic:** blood forming
 - Bone marrow aspirate

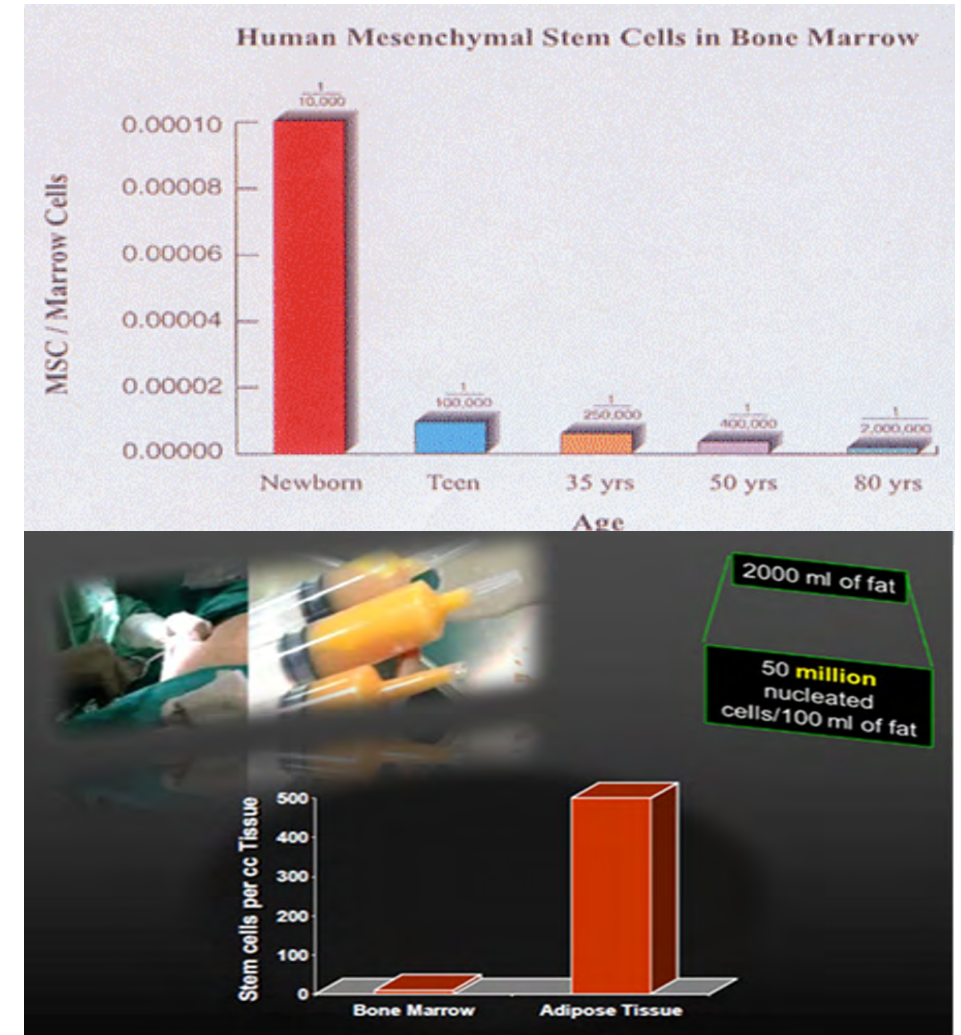


- **Mesenchymal:** musculoskeletal
 - Bone marrow aspirate**
 - Lipoaspirate



Adult Stem Cells: Potential Benefits

- Cellular differentiation
 - Age = covariate
- Growth factors & cytokines
- Activate resident cells
 - Progenitor & mature
- **Immunomodulation**
- Serve as scaffold for PRP
 - Adipose-derived
- Cushioning of joint (adipose)



Musculoskeletal Orthobiologics

- Platelet rich plasma (PRP)
- Adult “stem cell”
 - Bone marrow aspirate (BMA)
 - Lipoaspirate (fat graft)

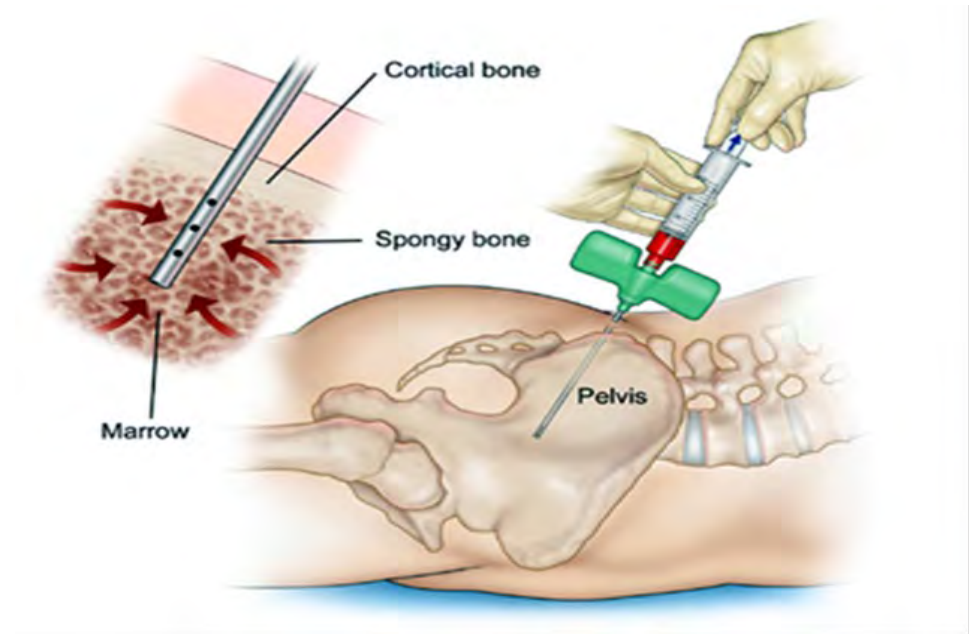


Bone Marrow Aspirate

- **BMA:** Autologous procedure that aspirates bone marrow (blood) and associated cells (*1^o hematopoietic*) from an area of high cell density. The product is both prepared (concentrated =BMAC) and used in extracted form. Mid-line/proximal regions have the highest stem cell density (PSIS).

- **Indications**

- Joint pathology
- Arthritis
- Avascular necrosis
- Chondral lesions



Lipoaspirate

- **Lipoaspirate:** Autologous procedure that aspirates adipose from flank area to procure adipose-derived stem cells (1° mesenchymal). The aspirate is cleaned/washed & injected into site of pathology. Used for stem cell content, immunomodulatory effects, & to serve as scaffold for PRP & BMA/BMAC.
- **Indications**
 - Joint pathology
 - Arthritis
 - Avascular necrosis
 - Chondral lesions
 - Soft tissue lesions



Stem Cell Clinical Evidence

- **Partial rotator cuff tear** treated with BMAC & PRP (N =12)
 - Significant improvement in pain, function, & MMT from baseline
 - ↓ tear size from 30.2 to 22.5mm at 3-months

Kim et al, *Cell Transplantation*, 2017
- **Knee OA**(KL3-4) treated w/BMA-MSK (N = 12)
 - Improvement in cartilage (MRI), function, stiffness & pain at 1-2 year

Orozco et al, *Transplantation*, 2014
- **OA** (Knee, Hip, Ankle) treated w/BMA-MSK (N =17)
 - Baseline to 12-months consistent ↑ in walking distance & improved WOMAC
 - Imaging: radiographs improved-all patients at 6-month follow up
 - MRI: Knee (↓ subchondral edema 3/6); Hip (cartilage repair in 3/5); Ankle (↓ subchondral edema 4/6)

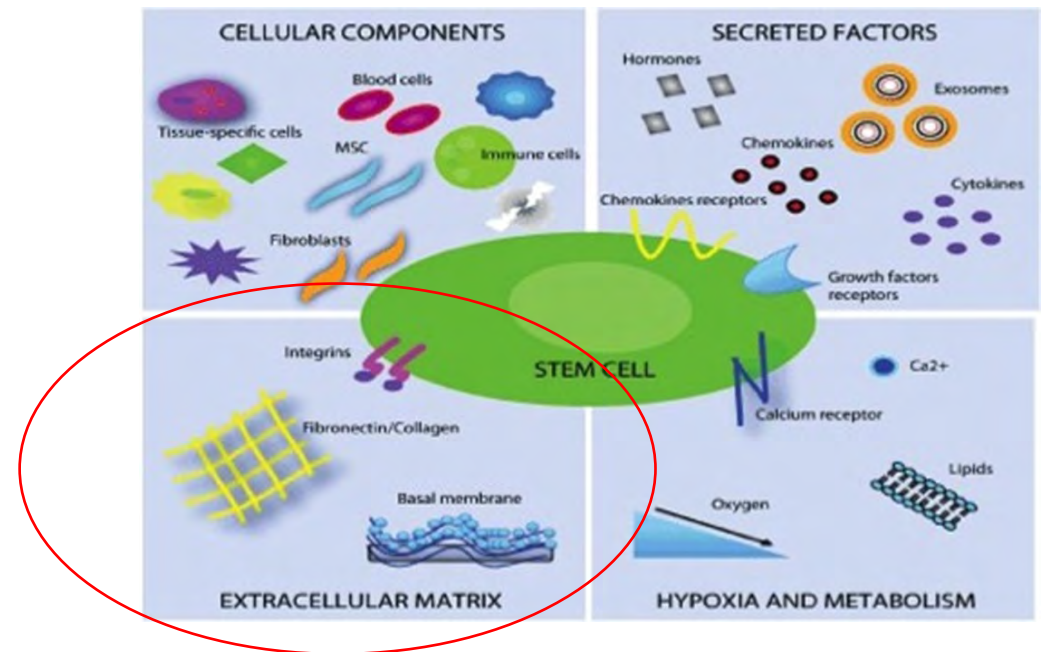
All groups-thickening of cartilage

Emadedin et al, *Arch Iran Med*, 2015
- **Hip AVN**: Lipoaspirate & PRP & HA (N =2)/**Knee OA**: lipoaspirate & PRP & HA (N =2)
 - 12-weeks MRI: Knee ↑ meniscal thickening
 - 12-weeks MRI: Hip: bone defect filling & bone matrix formation

Pak et al, *J Med Case Report*, 2011

Regenerative Rehabilitation/Mechanotherapy

- Promote interventions that work synergistically with regenerative medicine
- Target cellular & molecular responses similar to regenerative medicine
- Support anabolic responses



Exercise increases interleukin-10 levels both intraarticularly and peri-synovially in patients with knee osteoarthritis: a randomized controlled trial

Ida C Helmark^{*1}, Ulla R Mikkelsen¹, Jens Børglum², Anders Rothe², Marie CH Petersen¹, Ove Andersen³, Henning Langberg¹ and Michael Kjaer¹

- **Design:** 31 females with knee OA. Following acute resistance exercise (25 sets of 10 reps at 60% of 1 Repetition Maximum) versus no exercise, two micro dialysis catheters were positioned in two different compartments, intraarticularly and peri-synovial.
- **Main outcome measures:** Interstitial concentrations of inflammatory and cartilage biomarkers over a three-hour period.
- **Results:** One bout of exercise ↑ the concentration of IL-10 in the synovial fluid and in the peri-synovial compartment when compared to the non-exercise group. Serum *COMP was ↓ in the exercise group at the 3-hour point.
- **Bottom line:** Resistance training ↑ anti-inflammatory cytokines & ↓ *markers of cartilage degeneration (COMP)

Eccentric training in patients with chronic Achilles tendinosis: normalised tendon structure and decreased thickness at follow up

L Öhberg, R Lorentzon, H Alfredson

Br J Sports Med, 2004

- **Design:** 26 tendons from 25 patients (mean age 50) were treated for 12-weeks with an eccentric overload program for painful chronic Achilles tendinosis.
- **Main outcome measure:** Prospective evaluation of tendon thickness and structure with MSK-US at 2cm and 6cm levels before & 3.8 years after program.
- **Results:** 22/25 were satisfied w/activity levels. While all tendons had structural abnormalities prior to treatment (hypoechoic regions, ↑ thickness, & irregular structure) MSK-US was normal in 19 of 26 at 3.8 year point.
- **Bottom line:** Eccentric loading produced cellular changes (differentiation)

Changes in inflammatory mediators following eccentric exercise of the elbow flexors

Running Title : Eccentric exercise and cytokines

**Lisa Hirose¹, Kazunori Nosaka², Michael Newton²,
Andrew Laveder³, Masumi Kano¹, Jonathan Peake¹, and Katsuhiko Suzuki¹**

• *Exerc Immunol Rev*, 2004

- **Design:** 10 untrained subjects performed 2-bouts of eccentric overload (6-sets of 5 reps) biceps flexion exercise separated by 4 weeks. Blood was sampled before, immediately after, 1 h, 3 h, 6 h, 24 h (1 d), 48 h (2 d), 72 h (3 d), 96 h (4 d) following each exercise bout to measure plasma concentrations cytokines.
- **Main outcome measures:** Plasma concentrations of inflammatory mediators.
- **Results:** After 1st bout TNF α & IL-8 was $\downarrow$, whereas IL-10 was $\uparrow$ after 2nd bout.
- **Bottom Line:** Eccentric training $\downarrow$ pro-inflammatory & $\uparrow$ anti-inflammatory cytokines

Effects of eccentric cycling exercise on IGF-I splice variant expression in the muscles of young and elderly people.

Hameed et al, *Scand J Med Sci Sports*, 2008

- **Design:** 9 young (age 20-27) & 8 elderly (age 67-75) were subjected to a 60-min reverse cycling eccentric protocol.
- **Main outcome measures:** Muscle biopsy samples were obtained from the quadriceps muscle before and 2 1/4 h after completion of the exercise bout and were analyzed for IGF-1Ea & MGF mRNA levels using real-time quantitative PCR.
- **Results:** Eccentric cycling exercise resulted in a significant ↑ mechanogrowth factor (MGF (IGF-1Ec)) in young & older subjects.

Exercise: Topic Specific Evidence

- Acute exercise mobilizes stem & progenitor cells into peripheral blood (PB)
 - Immediately (15min.) & up to 1-hour Emmons et al, *Stem Cells Int*, 2016 (Review)
- Endurance training ↑ VSELS & hematopoietic stem cells in PB & bone marrow
 - Mean age 24 10km run @ 7.5 mph Marycz et al, *Stem Cells Int*, 2016
- Mobilization of stem cells through exercise is intensity dependent
 - 70 versus 30% of peak work rate on cycle ergometer or treadmill Baker et al, *J Appl Physiol*, 2016; Agha et al, *Brain Behav Immune*, 2017
- No ↑ using programs of lower intensity or habitual exercise Wardyn et al, *Exp Hematol*, 2008

Post-Procedural Strategies

- **Key considerations**
 - **Still treating same injury/condition*
 - Repeated movements
 - Resistance training: **overload**
 - Eccentric overload (anabolic, anti-inflammatory, & cellular benefits)
 - Accentuated eccentric loading
 - Isolated eccentric loading

Common Questions

- Cost?
- Ice and anti-inflammatory medications?
- Hope versus hype?

Additional Resource

Kolber MJ, Purita J, Sterling B, Stermer J, Salamh P, Masaracchio M, Hanney WJ. Stem Cell Injections for Musculoskeletal Pathology: An Overview for the Sports Medicine Professional. *Strength Cond J*. 2019;40:75-86.

Thank you

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