

OMED[®] 16

Renew your purpose.
Renew your passion.

SEPTEMBER 17-20 | ANAHEIM, CA



HEALTH LINK
MEDICAL CENTER



Regenexx[®]

updates in interventional management of low back pain

Shounuck I. Patel, DO FAAPMR
Board-certified PM&R

Board-certified Sports Medicine
AAO/AOASM/AOCPMR 09/18/2016

Disclosures

- Regenexx Network Physician
- Discussion will involve
 - Off-label administration of epidural corticosteroids
 - Experimental devices
 - Experimental manufactured injectates
 - Experimental autologous injectates
- Opinions are my own

Credits

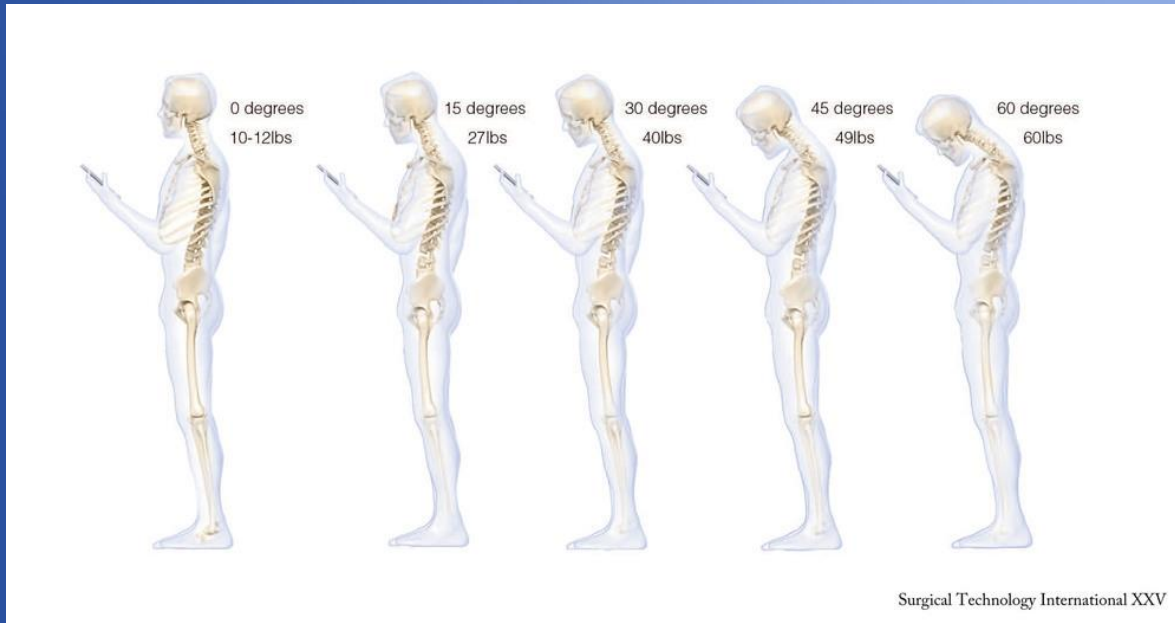
- Information from various sources
 - Case reports
 - Published and ongoing research
 - Presentations from other conferences
 - Regenexx registry data
 - Personal experience

...a little about me

- Regenerative Sports & Spine
 - Health Link Medical Center in Beverly Hills/Newport Beach/Oceanside
- Stem Cell & Regenerative Orthopedics Training
 - Regenexx Centeno-Shultz Clinic
- Sports & Interventional Pain Fellowship
 - Orthopedic & Spine Specialists of PA
- PM&R Residency
 - Kessler Institute / Rutgers University (formerly UMDNJ)
- Osteopathic Internship
 - Plainview Hospital
- Osteopathic Medical School
 - Midwestern U – CCOM

Outline

- “Pain Generators”
- Current Interventional Spine Treatments
 - AKA what insurance covers
- Philosophy
- Regenerative/Orthobiologic Spine Tx
- Paradigm shift





Neck & Back Conditions

- **The Young Athlete**

- Discogenic pain <-> Disc Annular Tears (+/- radiculitis)
- Spondylolysis / -lithesis
- Sacroiliac Joint Dysfunction
- Ligament Sprains and Laxity
- Trigger Points
- Whiplash & Facet pain
- Stingers & Burners
- Peripheral Nerve Injuries
- Rib contusion / Intercostal Neuralgia - Strain

- **The Aging Athlete**

- Degenerative Disc Disease
- Radiculitis & Piriformis Syndrome
- Facet & Sacroiliac Joint Arthropathy
- Stenosis
- Peripheral Mono- & Poly-Neuropathies

- **The Female Athlete**

- Ligamentous Laxity
- SIJ, Pelvic Pain, and Coccydynia
- Diastasis Recti

A vertical illustration of a human spine, showing the vertebrae and intervertebral discs. The top portion is white, and the bottom portion is blue, matching the background of the slide.

Current standard interventional treatments

- Epidural steroid injections
- Facet steroid injections
- Lumbar Radiofrequency Ablation
- Sacroiliac joint steroid injections
- Percutaneous discectomy
- Spinal cord stimulation
- Kyphoplasty/vertebroplasty
- Sympathetic blocks
- Intrathecal pain pumps

Corticosteroids: The Good

- Decrease inflammation
 - Limit capillary dilation and vascular permeability
- Dec accumulation of neutrophils/macrophages
- Inhibit release of destructive enzymes
- Smart business

ESI for discogenic back pain

[Spine J.](#) 2016 Aug 20. pii: S1529-9430(16)30886-5. doi: 10.1016/j.spinee.2016.08.024. [Epub ahead of print]

The efficacy of interlaminar epidural steroid administration in multilevel intervertebral disc disease with chronic low back pain: a randomized, blinded, prospective Study.

[Ökmen K¹](#), [Ökmen BM²](#).

⊕ Author information

Abstract

BACKGROUND CONTEXT: Epidural steroid injection is commonly used in patients with chronic low back pain. Applying a mixture of a local anesthetic (LA) and steroid using the interlaminar (IL), transforaminal, and caudal techniques is a preferred approach.

PURPOSE: The present study aims to investigate the efficacy of interlaminar epidural steroid administration in patients with multilevel lumbar disc pathology (LDP) and to assess the possible correlation of the procedure's success with age and body mass index (BMI).

STUDY DESIGN: A randomized controlled trial was performed.

PATIENT SAMPLE: We administered interlaminar epidural steroid to a total of 98 patients with multilevel LDP.

OUTCOME MEASURES: The visual analogue scale (VAS) and Oswestry Disability Index (ODI) scoring were performed on the study population at pretreatment (PRT), posttreatment, and 1, 3, 6, and 12 PRT months. A possible correlation of BMI and age with the procedure success was evaluated.

METHODS: The LA group (Group L, n=50) received 10 mL 0.25% bupivacaine, whereas the steroid+LA group (Group S, n=48) received 10 mL 0.25% bupivacaine+40 mg methylprednisolone at L4-L5 intervertebral space in prone position under the guidance of C-arm fluoroscopy.

RESULTS: There was no statistical difference in the PRT VAS and ODI scores between the groups ($p < .05$), whereas the VAS and ODI scores at 1, 3, 6, and 12 posttreatment months were higher in Group L, compared with Group S ($p < .05$). Age and BMI were not found to be related with the success of the procedure.

CONCLUSIONS: Our study results showed that the VAS and ODI scores were lower in patients with multilevel LDP receiving steroid, following the administration of IL epidural injection. However, further studies are required to establish a robust conclusion on the dispersion of IL epidural injections in the epidural area and the dose of steroid.

Copyright © 2016 Elsevier Inc. All rights reserved.

Epidural steroid injection therapy for low back pain: a meta-analysis.

Choi HJ¹, Hahn S, Kim CH, Jang BH, Park S, Lee SM, Park JY, Chung CK, Park BJ.

+ Author information

Abstract

OBJECTIVES: The aim of this study was to systematically assess the long-term (≥ 6 months) benefits of epidural steroid injection therapies for patients with low back pain.

METHODS: We identified randomized controlled trials by database searches up to October 2011 and by additional hand searches without language restrictions. Randomized controlled trials on the effects of epidurals for low back pain with follow-up for at least 6 months were included. Outcomes considered were pain relief, functional improvement in 6 to 12 months after epidural steroid injection treatment and the number of patients who underwent subsequent surgery. Meta-analysis was performed using a random-effects model.

RESULTS: Twenty-nine articles were selected. The meta-analysis suggested that a significant treatment effect on pain was noted at 6 months of follow-up (weighted mean difference [WMD], -0.41; 95 percent confidence interval [CI], -0.66 to -0.16), but was no longer statistically significant after adjusting for the baseline pain score (WMD, -0.19; 95 percent CI, -0.61 to 0.24). Epidural steroid injection did not improve back-specific disability more than a placebo or other procedure. Epidural steroid injection did not significantly decrease the number of patients who underwent subsequent surgery compared with a placebo or other treatments (relative risk, 1.02; 95 percent CI, 0.83 to 1.24).

CONCLUSIONS: A long-term benefit of epidural steroid injections for low back pain was not suggested at 6 months or longer. Introduction of selection bias in the majority of injection studies seems apparent. Baseline adjustment is essential when we evaluate pain as a main outcome of injection therapy.

ESI for radiculopathy

Accepted Manuscript

The Clinical Efficacy for Two-Level Transforaminal Epidural Steroid Injections

Jaspal R. Singh, M.D., Eliana Cardozo, D.O., George C. Christolias, M.D.



- 721 pts
- 2 mos

- 152 pts
- 1 yr

J Clin Diagn Res. 2016 Jul;10(7):RC05-11. doi: 10.7860/JCDR/2016/18208.8127. Epub 2016 Jul 1.

Efficacy of Epidural Steroid Injection in Management of Lumbar Prolapsed Intervertebral Disc: A Comparison of Caudal, Transforaminal and Interlaminar Routes.

Pandey RA¹.

⊕ Author information

Abstract

INTRODUCTION: Epidural steroid is an important modality in the conservative management of prolapsed lumbar disc and is being used for over 50 years. However, controversy still persists regarding their effectiveness in reducing the pain and improving the function with literature both supporting and opposing them are available.

AIM: To study the efficacy of epidural steroid injection in the management of pain due to prolapsed lumbar intervertebral disc and to compare the effectiveness between caudal, transforaminal and interlaminar routes of injection.

MATERIALS AND METHODS: A total of 152 patients with back pain with or without radiculopathy with a lumbar disc prolapse confirmed on MRI, were included in the study and their pre injection Japanese Orthopaedic Association (JOA) Score was calculated. By simple randomization method (picking a card), patients were enrolled into one of the three groups and then injected methyl prednisone in the epidural space by one of the techniques of injection i.e. caudal, transforaminal and interlaminar. Twelve patients didn't turn up for the treatment and hence were excluded from the study. Remaining 140 patients were treated and were included for the analysis of the results. Eighty two patients received injection by caudal route, 40 by transforaminal route and 18 by interlaminar route. Post injection JOA Score was calculated at six month and one year and effectiveness of the medication was calculated for each route. The data was compared by LSD and ANOVA method to prove the significance. Average follow-up was one year.

RESULTS: At one year after injecting the steroid, all three routes were found to be effective in improving the JOA Score (Caudal route in 74.3%, transforaminal in 90% and interlaminar in 77.7%). Transforaminal route was significantly more effective than caudal ($p=0.00$) and interlaminar route ($p=0.03$) at both 6 months and one year after injection. No significant difference was seen between the caudal and interlaminar route ($p=0.36$).

CONCLUSION: The management of low back pain and radicular pain due to a prolapsed lumbar intervertebral disc by injecting methyl prednisone in epidural space is satisfactory in the current study. All three injection techniques are effective with the best result obtained by transforaminal route.

Role of Epidural Injections to Prevent Surgical Intervention in Patients with Chronic Sciatica: A Systematic Review and Meta-Analysis

Adnan Bashir Bhatti ¹, Sunny Kim ²

1. Medical Director of Clinical Research, Spine Surgery, Tristate Brain and Spine Institute, United States

2. Spine Surgery, Tristate Brain and Spine Institute

✉ **Corresponding author:** Adnan Bashir Bhatti, dr.adnanbashir@gmail.com

Disclosures can be found in Additional Information at the end of the article

Abstract

Objective: The aim of this study is to evaluate the efficacy of the different types of epidural injections (EI) to prevent surgical intervention in patients suffering from chronic sciatica due to lumbar disc herniation (LDH).

Material and Methods: Studies were identified by searching PubMed, MEDLINE, and Google Scholar to retrieve all available relevant articles. Lists of references of several systematic reviews were also used for scanning further references. Publications from the past ten years (2006-2016) were considered, and all studies selected were in the English language only. The studies employed specified the use of EI to treat sciatica caused by LDH. A total of 19 papers meeting the eligibility criteria (mentioned below) were included in this study. The pain scores, functional disability scores, and surgical rates from these studies were considered, and meta-analysis was performed.

Outcome measures: Pain scores, functional disability scores, and surgical rates were assessed from the included studies. The Numeric Rating Scale (NRS) and Visual Analogue Scale (VAS) have been the most commonly used baseline scales for pain evaluation followed by the Verbal Numerical Rating Scale (VNRS) and Japanese Orthopedic Association (JOA). The Oswestry Disability Index (ODI) and Roland Morris Disability Questionnaire (RMDQ) scales were used for the functional disability scoring system in the literature.

Results: Significant improvement in the pain scores and functional disability scores were observed. Additionally, greater than 80% of the patients suffering from chronic sciatica caused by LDH could successfully prevent surgical intervention after EI treatment with or without steroids.

Conclusion: The management of sciatica with EI treatment results in significant improvements in the pain score, functional disability score, and surgical rate. We concluded that EI provides new hope to prevent surgical intervention in patients suffering from sciatica caused by LDH.

ESI for stenosis

[Br J Neurosurg](#). 2016 Aug 22:1-4. [Epub ahead of print]

Transforaminal epidural steroid injection in lumbar spinal stenosis: an observational study with two-year follow-up.

[Davis N¹](#), [Hourigan P²](#), [Clarke A³](#).

⊕ Author information

Abstract

BACKGROUND CONTEXT: Transforaminal epidural steroid injection (TFESI) is recognised as a treatment for symptomatic lumbar disc herniation, whilst surgical decompression is generally thought to be the most effective treatment option for lumbar spinal stenosis. There is little available literature examining the effect of TFESI on symptomatic lumbar spinal stenosis.

PURPOSE: To evaluate the use of TFESI as an alternative to surgery in patients with symptomatic stenosis.

STUDY DESIGN/SETTING: An observational study which took place between May 2010 and July 2013. All patients were seen by the Extended Scope Physiotherapist (ESP) injection service.

PATIENT SAMPLE: A total of 68 consecutive patients were included. Thirty-one were male and 37 were female. The average age was 75 years.

OUTCOME MEASURES: The primary outcome measure was the avoidance of decompressive surgery.

METHODS: Patients with radicular leg pain were seen by an ESP in an Outpatient setting. Concordant clinical examination and magnetic resonance imaging were required for diagnosis. Peri-radicular bupivacaine hydrochloride 0.25% (3 ml) and triamcinolone (40 mg) were then injected. Outcome measures were recorded at 6 weeks, 1 year and 2 years.

RESULTS: Of 68 patients with spinal stenosis, 22 (32%) had opted for surgery at two year follow-up. Thirty (44%) patients were satisfied with non-surgical management at 2 years, required no further treatment, and were discharged. Of the remaining 24%, nine patients were referred for further injection, four declined surgery but were referred to the Pain Relief Clinic, two still had a similar level of pain but declined surgery and one had died.

CONCLUSIONS: Our study reports a considerably lower percentage patients opting for surgery than previously demonstrated by the available literature. TFESI is a reasonable treatment for lumbar spinal stenosis and can result in long-term relief from symptoms in a high proportion of patients.

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 3, 2014

VOL. 371 NO. 1

A Randomized Trial of Epidural Glucocorticoid Injections for Spinal Stenosis

Janna L. Friedly, M.D., Bryan A. Comstock, M.S., Judith A. Turner, Ph.D., Patrick J. Heagerty, Ph.D., Richard A. Deyo, M.D., M.P.H., Sean D. Sullivan, Ph.D., Zoya Bauer, M.D., Ph.D., Brian W. Bresnahan, Ph.D., Andrew L. Avins, M.D., M.P.H., Srdjan S. Nedeljkovic, M.D., David R. Nerenz, Ph.D., Christopher Standaert, M.D., Larry Kessler, Ph.D., Venu Akuthota, M.D., Thiru Annaswamy, M.D., Allen Chen, M.D., M.P.H., Felix Diehn, M.D., William Firtch, M.D., Frederic J. Gerges, M.D., Christopher Gilligan, M.D., Harley Goldberg, M.D., David J. Kennedy, M.D., Shlomo Mandel, M.D., Mark Tyburski, M.D., William Sanders, M.D., David Sibell, M.D., Matthew Smuck, M.D., Ajay Wasan, M.D., Lawrence Won, M.D., and Jeffrey G. Jarvik, M.D., M.P.H.

 Open Access Full Text Article

REVIEW

Epidural injections with or without steroids in managing chronic low back pain secondary to lumbar spinal stenosis: a meta-analysis of 13 randomized controlled trials

This article was published in the following Dove Press journal:
Drug Design, Development and Therapy
13 August 2015
[Number of times this article has been viewed](#)

Systematic Review

Epidural Injections for Lumbar Radiculopathy and Spinal Stenosis: A Comparative Systematic Review and Meta-Analysis

Laxmaiah Manchikanti, MD¹, Nebojsa Nick Knezevic, MD, PhD², Mark V. Boswell, MD, PhD³, Alan D. Kaye, MD, PhD⁴, and Joshua A. Hirsch, MD⁵

Data Synthesis: Thirty-nine randomized controlled trials met inclusion criteria. There were 9 placebo-controlled trials evaluating epidural corticosteroid injections, either with sodium chloride solution or bupivacaine, compared to placebo injections. There were 12 studies comparing local anesthetic alone to local anesthetic with steroid.

Results A meta-analysis of 5 studies utilizing sodium chloride or bupivacaine with steroid showed a lack of efficacy.

A comparison of lidocaine to lidocaine with steroids in 7 studies showed significant effectiveness from baseline to long-term follow-up periods. Meta-analysis showed a similar effectiveness for pain and function without non-inferiority of lidocaine compared to lidocaine with steroid at 3 months and 12 months.

Limitations: The review was restricted to the data available with at least 3 months of follow-up, which excluded some studies. The inclusion criteria were restricted to English language studies.

Conclusion: Epidural corticosteroid injections for radiculopathy or spinal stenosis with sodium chloride solution or bupivacaine were shown to be ineffective. Lidocaine alone or lidocaine in conjunction with steroids were significantly effective.

Facet steroid injections

J Craniovertebr Junction Spine. 2016 Jan-Mar;7(1):38-42. doi: 10.4103/0974-8237.176622.

Factors affecting results of fluoroscopy-guided facet joint injection: Probable differences in the outcome of treatment between pure facet joint hypertrophy and concomitant diseases.

Albayrak A¹, Ozkul B¹, Balioğlu MB¹, Atici Y¹, Gultekin MZ², Albayrak MD³.

⊕ Author information

Abstract

STUDY DESIGN: Retrospective cohort study.

PURPOSE: Facet joints are considered a common source of chronic low-back pain. To determine whether pathogens related to the facet joint arthritis have any effect on treatment failure.

MATERIALS AND METHODS: Facet joint injection was applied to 94 patients treated at our hospital between 2011 and 2012 (mean age 59.5 years; 80 women and 14 men). For the purpose of analysis, the patients were divided into two groups. Patients who only had facet hypertrophy were placed in group A (47 patients, 41 women and 6 men, mean age 55.3 years) and patients who had any additional major pathology to facet hypertrophy were placed in group B (47 patients, 39 women and 8 men, mean age 58.9 years). Injections were applied around the facet joint under surgical conditions utilizing fluoroscopy device guidance. A mixture of methylprednisolone and lidocaine was used as the injection ingredient.

RESULTS: In terms of Oswestry Disability Index (ODI) and visual analog scale (VAS) scores, no significant difference was found between preinjection and immediate postinjection values in both groups, and the scores of group A patients were significantly lower ($P < 0.005$) compared with that of group B patients at the end of the third, sixth, and twelfth month.

CONCLUSION: For low-back pain caused by facet hypertrophy, steroid injection around the facet joint is an effective treatment, but if there is an existing major pathology, it is not as effective.



Corticosteroids: The Ugly

- Particulates
- Micro effects
- Macro systemic effects



The NEW ENGLAND JOURNAL of MEDICINE

[HOME](#)[ARTICLES & MULTIMEDIA](#) ▾[ISSUES](#) ▾[SPECIALTIES & TOPICS](#) ▾[FOR AUTHORS](#) ▾[CME](#) ▸

Perspective

Serious Neurologic Events after Epidural Glucocorticoid Injection — The FDA's Risk Assessment

Judith A. Racoosin, M.D., M.P.H., Sally M. Seymour, M.D., Laurelle Cascio, Pharm.D., and Rajdeep Gill, Pharm.D.
N Engl J Med 2015; 373:2299-2301 | [December 10, 2015](#) | DOI: 10.1056/NEJMp1511754

[Pain Manag.](#) 2015;5(4):261-72. doi: 10.2217/pmt.15.17. Epub 2015 Jun 10.

Key safety considerations when administering epidural steroid injections.

[Manchikanti L](#)^{1,2}, [Benyamin RM](#)^{3,4}.

⊕ Author information

Abstract

Neurological and other complications of epidural steroid injections have been widely discussed in recent years. Consequently, the US FDA issued a warning about serious neurological events, some resulting in death, and consequently is requiring label changes. Neurological adverse events numbering 131, including 41 cases of arachnoiditis, have been identified by the FDA, and 700 cases of fungal meningitis following injection of contaminated steroids. A review of the literature reveals an overwhelming proportion of the complications are related to transforaminal epidural injections, with the majority of them to cervical transforaminal epidural injections. This perspective describes the prevalence of administering epidural injections, complications, pathoanatomy, mechanism of injury and various preventive strategies.

Corticosteroids

- Globally inhibit cell growth and production
- Widespread negative effect on healing
- Stabilize lysosomes
 - Decreased phagocytosis by PMNs/macrophages
- Inhibit epithelial regeneration
- Direct inhibitor effect on fibroblast genome
- Decreased collagen deposition/maturation

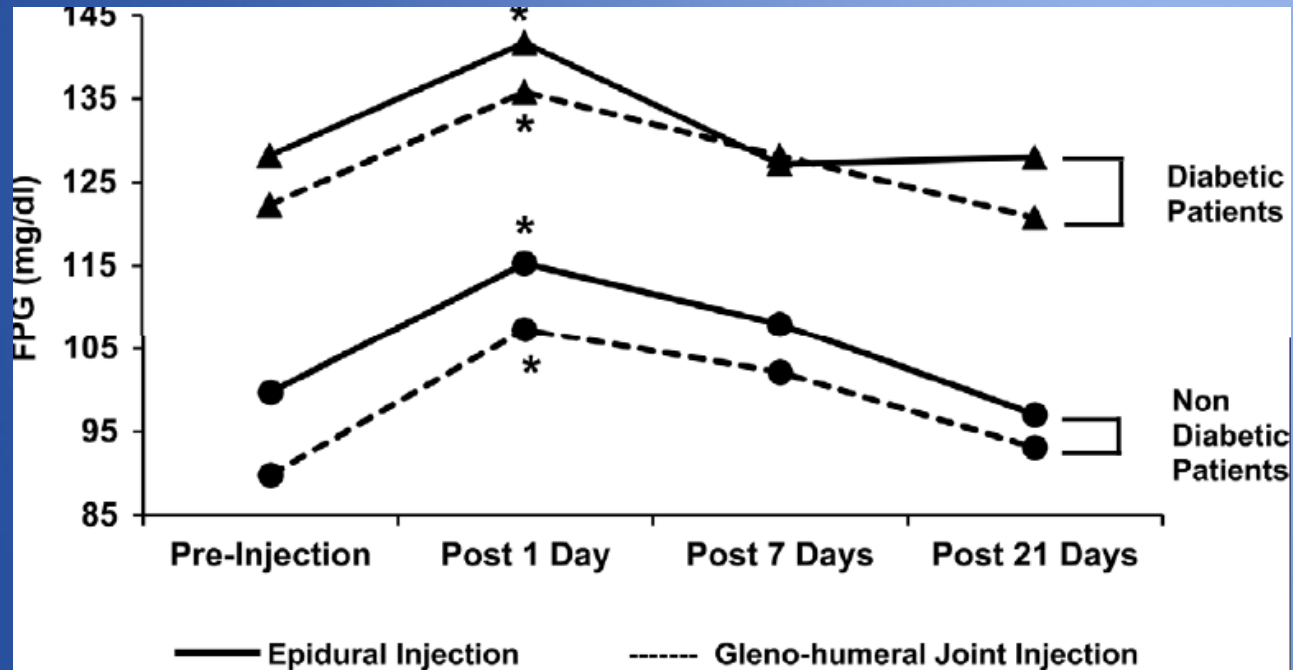
» Broughton 2006

Corticosteroids

- Systemic side effects
 - Post-procedure flare (2-25%)
 - Infection (rare)
 - Adrenal suppression
 - Jacobs et al 1983 -> central effect via CSF
 - Cartilage damage
 - Increased serum glucose

Adapted from Andre Panagos MD at AAPMR 2014

Corticosteroid



- Moon et al 2014
 - Serum cortisol levels effected for 21 days
 - Epidural worse - Diabetic worse

Corticosteroids in Joints

- Steinberg et al 1962
 - Charcot-like arthropathy post IA hydrocortisone
- Shapiro et al 2007
 - Rabbit cartilage
 - Saline vs. Corticosteroid vs. NSAID
 - Infarcted cartilage & fragmentation

About ▼ Member Services ▼ Education ▼ Advocacy ▼



Epidural Steroid Injections and Hyperglycemia FactFinder

Various studies: rise for up to 2 days or up to 2 weeks in susceptible patients

Pain Physician 2013; 16:557-568 • ISSN 1533-3159

Prospective Evaluation

Effects of Two Different Doses of Epidural Steroid on Blood Glucose Levels and Pain Control in Patients with Diabetes Mellitus

Won Ho Kim, MD¹, Woo Seog Sim, MD, PhD¹, Byung Seop Shin, MD, PhD¹, Chul Joong Lee, MD, PhD², Hyun Seung Jin, MD¹, Jin Young Lee, MD¹, Hee Jin Roe, MD¹, Chung Su Kim, MD,

Kenalog 20mg better than 40mg for diabetics without difference in pain effect



Current Standard Non-Steroid Interventions

- Radiofrequency ablation

Facet Medial Branch RFA

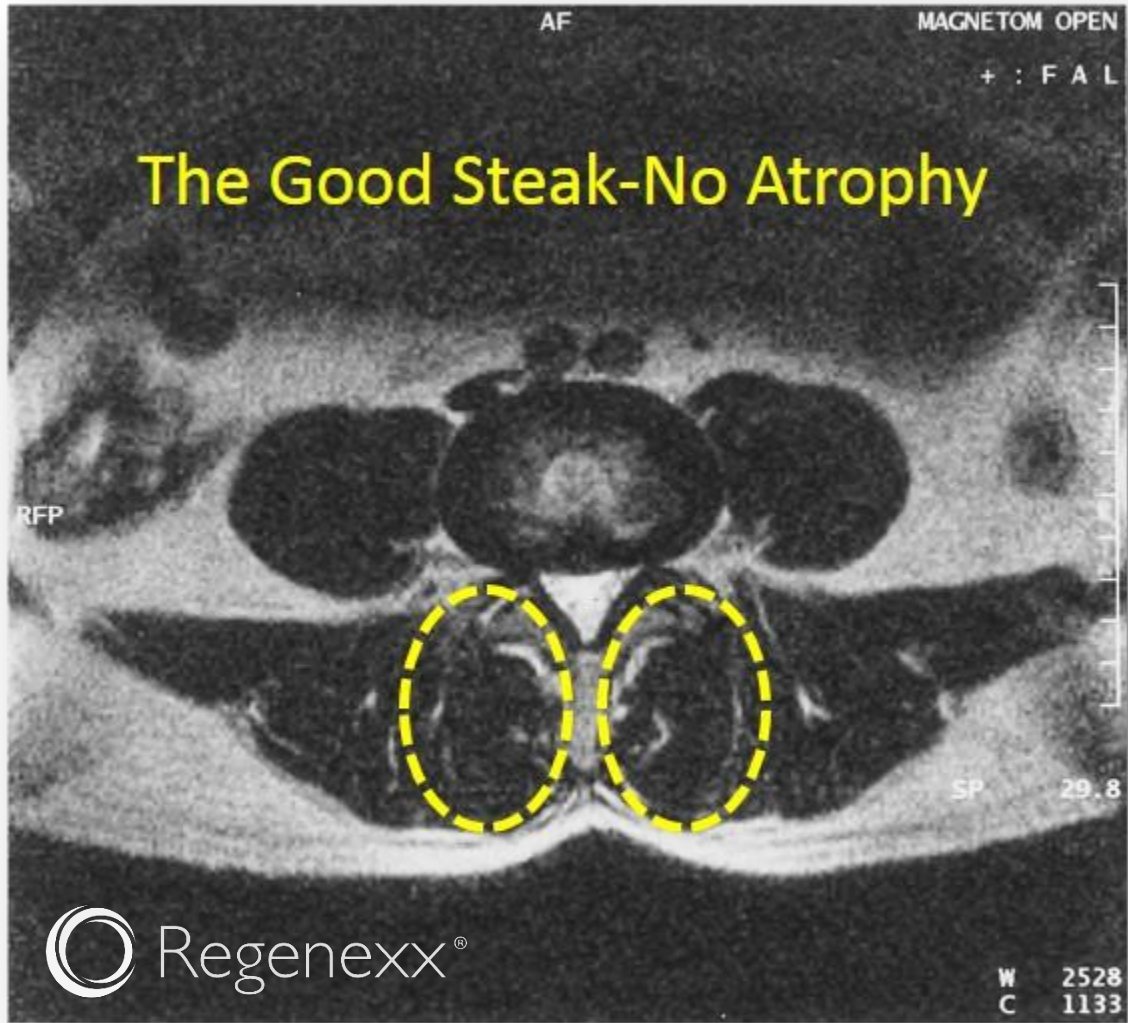
Cochrane Database Syst Rev. 2015 Oct 23;(10):CD008572. doi: 10.1002/14651858.CD008572.pub2.

Radiofrequency denervation for chronic low back pain.

Maas ET¹, Ostelo RW, Niemisto L, Jousimaa J, Hurri H, Malmivaara A, van Tulder MW.

MAIN RESULTS: In total, we included 23 RCTs (N = 1309), 13 of which (56%) had low RoB. We included both men and women with a mean age of 50.6 years. We assessed the overall quality of the evidence as very low to moderate. Twelve studies examined suspected facet joint pain, five studies disc pain, two studies SI joint pain, two studies radicular CLBP, one study suspected radiating low back pain and one study CLBP with or without suspected radiation. Overall, moderate evidence suggests that facet joint RF denervation has a greater effect on pain compared with placebo over the short term (mean difference (MD) -1.47, 95% confidence interval (CI) -2.28 to -0.67). Low-quality evidence indicates that facet joint RF denervation is more effective than placebo for function over the short term (MD -5.53, 95% CI -8.66 to -2.40) and over the long term (MD -3.70, 95% CI -6.94 to -0.47). Evidence of very low to low quality shows that facet joint RF denervation is more effective for pain than steroid injections over the short (MD -2.23, 95% CI -2.38 to -2.08), intermediate (MD -2.13, 95% CI -3.45 to -0.81), and long term (MD -2.65, 95% CI -3.43 to -1.88). RF denervation used for disc pain produces conflicting results, with no effects for RF denervation compared with placebo over the short and intermediate term, and small effects for RF denervation over the long term for pain relief (MD -1.63, 95% CI -2.58 to -0.68) and improved function (MD -6.75, 95% CI -13.42 to -0.09). Lack of evidence of short-term effectiveness undermines the clinical plausibility of intermediate-term or long-term effectiveness. When RF denervation is used for SI joint pain, low-quality evidence reveals no differences from placebo in effects on pain (MD -2.12, 95% CI -5.45 to 1.21) and function (MD -14.06, 95% CI -30.42 to 2.30) over the short term, and one study shows a small effect on both pain and function over the intermediate term. RF denervation is an invasive procedure that can cause a variety of complications. The quality and size of original studies were inadequate to permit assessment of how often complications occur.

AUTHORS' CONCLUSIONS: The review authors found no high-quality evidence suggesting that RF denervation provides pain relief for patients with CLBP. Similarly, we identified no convincing evidence to show that this treatment improves function. Overall, the current evidence for RF denervation for CLBP is very low to moderate in quality; high-quality evidence is lacking. High-quality RCTs with larger patient samples are needed, as are data on long-term effects.





Radiofrequency side effects...



OMED[®] 16



HEALTH LINK
MEDICAL CENTER

Facet Capsule RFA

Clin Neurol Neurosurg. 2016 Sep 5;150:96-104. doi: 10.1016/j.clineuro.2016.09.004. [Epub ahead of print]

Percutaneous radiofrequency facet capsule denervation as an alternative target in lumbar facet syndrome.

Moussa WM¹, Khedr W².

⊕ Author information

Abstract

OBJECTIVES: Percutaneous radiofrequency denervation of the medial dorsal branch is often used in chronic low back pain of intervertebral facet etiology, which is sometimes difficult to perform and recurrence of pain often ensues. We theorized that shifting the target of RF coagulation to the facet joint capsule would provide an easier target and a longer-lived pain relieving response.

PATIENTS AND METHODS: A prospective randomized controlled trial where 120 patients diagnosed with CLBP of a confirmed facet origin were randomly divided into three equal groups, the first was submitted to percutaneous radiofrequency coagulation of the facet joint capsule, the second underwent percutaneous denervation of the medial dorsal branch and the third did not receive radiofrequency lesioning. All the three groups received local injection of a mixture of local anesthetic and steroid. Cases were followed for up to 3 years.

RESULTS: 87(72.5%) patients were females. By 3 months' post procedure, improvement in VAS was significantly better than pretreatment levels in all groups ($p < 0.05$). The control group lost improvement by 1-year follow-up ($p = 0.017$). At 2 years' follow-up, the joint capsule denervation group maintained significant improvement ($p = 0.033$) whereas the medial branch denervation group lost its significant effect ($p = 0.479$). By the end of follow-up period, only joint capsule denervation group kept significant improvement ($p = 0.026$).

CONCLUSION: In CLBP of facet origin, shifting the target of percutaneous radiofrequency to the facet joint capsule provides an easier technique with an extended period of pain relief compared to the medial dorsal branch of the facet joint.

Copyright © 2016 Elsevier B.V. All rights reserved.

Philosophy

- **Hippocratic Oath**
 - Primum non nocere – First, do no harm.
- **Osteopathic Medicine**
 - The body is a unit
 - Structure and Function are interrelated
 - The body possesses self-regulatory & self-healing mechanisms
 - Rational treatment is based on applying these principles
- **Physiatric Medicine**
 - Restore maximum function by addressing the whole person with non-surgical treatments
- **Interventional Pain Management**
 - Decrease pain with minimally invasive procedures to allow for optimal functioning
- **Regenerative Medicine**
 - Restore function to damaged tissues and organs by boosting the body's natural ability to heal itself

A vertical illustration of a human spine, showing the vertebrae and intervertebral discs. The top half is white and the bottom half is blue, matching the slide's background.

Regenerative 101

- Prolotherapy
- Allogenic Biologics
 - Amniotic products – NOT stem cells
- Autologous Biologics
 - PRP
 - PL
 - Stem Cells

Prolotherapy



Prolotherapy

- Prolotherapy = Proliferative Therapy
 - Coined by George Hackett MD
 - Trained Hemwall & published in 1956
 - Irritant into joint, ligament, tendon insertion
 - Trigger healing cascade
 - Repair connective tissue

Prolotherapy

- Hyperosmolar Dextrose
- Sodium Morrhuate
 - Salt of morrhuic acid which is more inflammatory than dextrose
- Phenol
 - Carboic acid – caustic
- Ozone
 - Inflammatory, free radicals

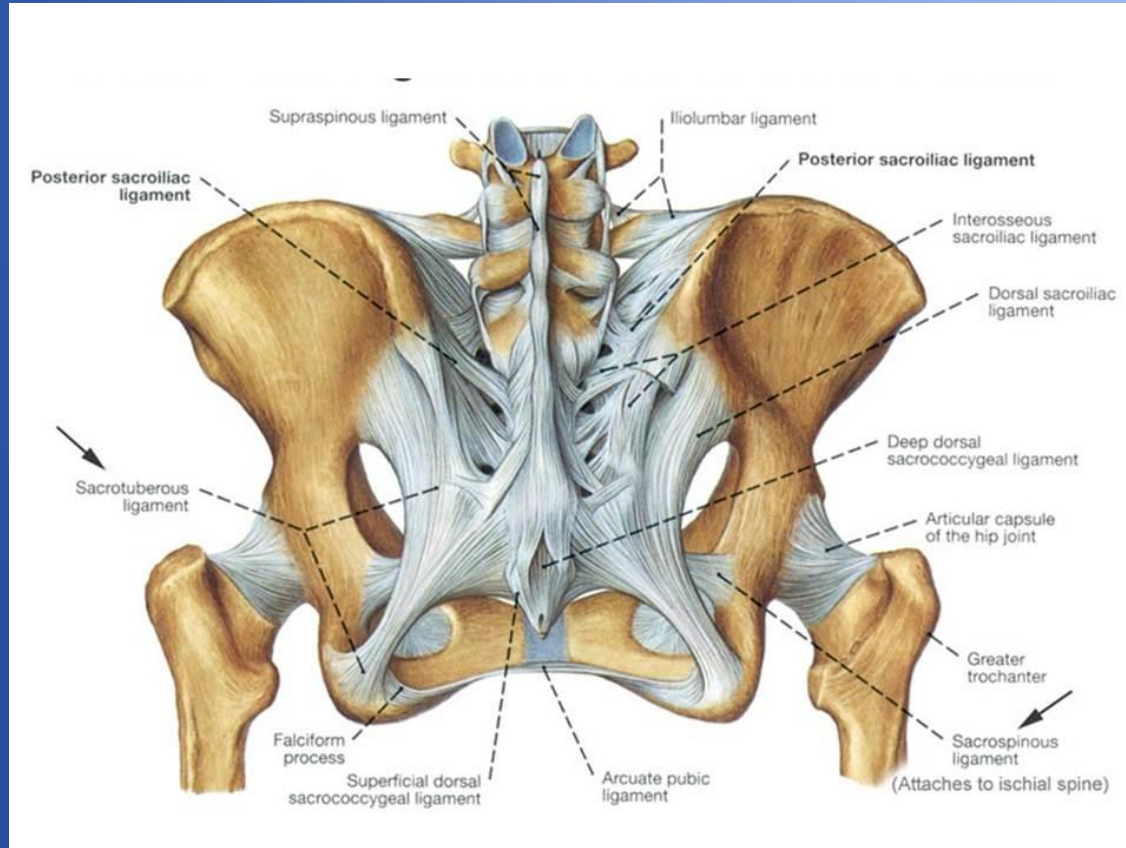
Dextrose

- Stimulation of healing cascade
 - Hyperosmolar dextrose > 10%
 - Hypertonic -> Osmosis -> Cell Rupture
 - Temporary inflammation GF elevation
- Murphy et al. 1999
 - 20 min exposure to 0.45% glucose
- Needling effect
- Neuromodulation (not prolo)

GFs that Dextrose Elevates						
	P	T	E	b	I	C
	D	G	G	F	G	T
	G	F	F	G	F	G
	F	β		F		F
Lig/Tend Healing	X	X	X	X	X	X
Cartilage Healing	X	X		X	X	
Dextrose Effect	↑	↑	↑	↑	↑	↑

<http://www.drreeves.com>

Dextrose prolotherapy



Facetogenic Pain

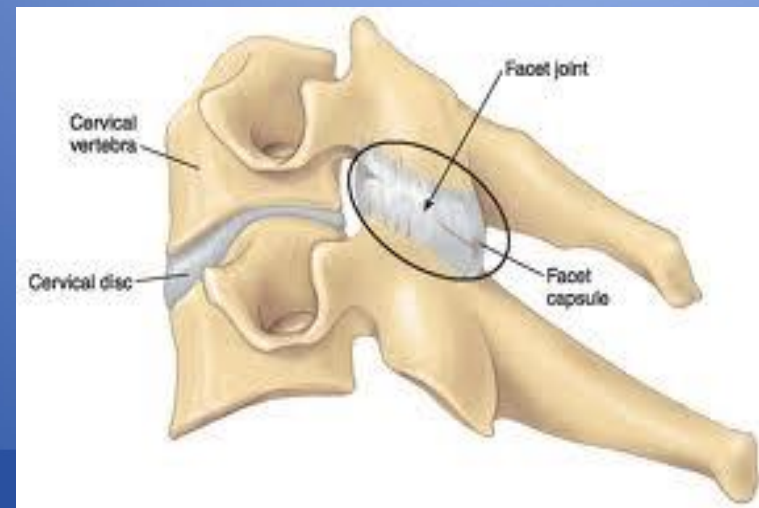
326

The Open Orthopaedics Journal, 2014, 8, 326-345

Open Access

Chronic Neck Pain: Making the Connection Between Capsular Ligament Laxity and Cervical Instability

Danielle Steilen*, Ross Hauser*, Barbara Woldin and Sarah Sawyer



NOT PROLO

- “Neural prolotherapy” or “Perineural Subcutaneous Injection”
 - Hilton’s Law
 - Cutaneous sensory nerves over a joint also supply the joint/ligaments/tendons themselves.
- Dextrose Hydrodissection or “Perineural Deep Injection”, and “Sweet Caudals”
 - Mechanical dissection from fascial layers

Platelet products

- PRP
- PL



Platelet Rich Plasma

- Concentrated platelets
- First to arrive at injury -> healing cascade
- Alpha Granules -> secrete growth factors
- Dense Granules
 - Serotonin, ADP, Histamine, Calcium
- “Pro-inflammatory” & “Anti-inflammatory”

PRP

- Alpha Granules
 - Platelet Derived Growth Factor (PDGF)
 - Transforming Growth Factor (TGF)
 - Epidermal Growth Factor (EGF)
 - Vascular Endothelial Growth Factor (VEGF)
 - Connective Tissue Growth Factor (CTGF)



The American Orthopaedic
Society for Sports Medicine

The American Journal of Sports Medicine

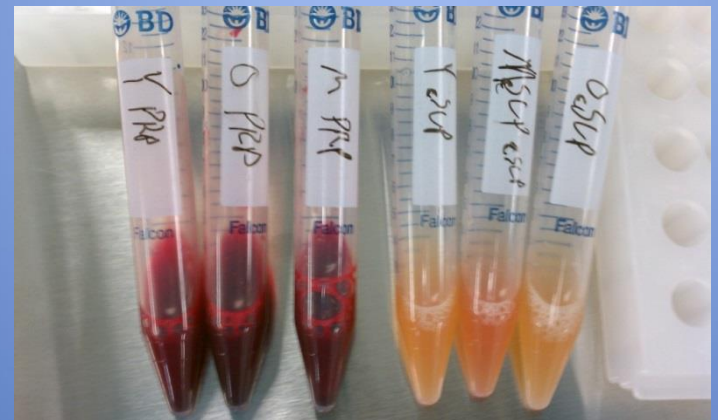
Platelet-Rich Plasma Increases Anti-inflammatory Markers in a Human Coculture Model for Osteoarthritis

Chelsea Osterman, BA^{*}, Mary Beth R. McCarthy, BS^{*}, Mark P. Cote, DPT^{*},
Knut Beitzel, MA, MD[†], James Bradley, MD[‡], Gregory Polkowski, MD[§] and
Augustus D. Mazzocca, MS, MD^{*,||}

Am J Sports Med. 2015 Feb 25. pii: 0363546515570463. [Epub ahead of print]

PRP Differences

- Most PRP is prepared by bedside centrifuge using kits
 - Different set concentrations, etc.
- PRP can be processed manually to produce different results
 - RBCs are removed
 - Keep or remove WBCs
 - Customize concentration based on patient/treatment



What can PRP treat?

- Facet Joints
 - Repair? Chondrogenesis?
 - Micro-environment
 - Pro- vs. Anti-inflammatory
- Paraspinal muscles
- Intra-discal: Greg Lutz MD - HSS
- Ligamentum Flavum hypertrophy (kinking)
- Ligaments



The American Orthopaedic
Society for Sports Medicine

The American Journal of Sports Medicine

Stimulation of the Superficial Zone Protein and Lubrication in the Articular Cartilage by Human Platelet-Rich Plasma

Ryosuke Sakata, MD^{*}, Sean M. McNary, PhD^{*}, Kazumasa Miyatake, MD^{*},
Cassandra A. Lee, MD^{*}, James M. Van den Bogaerde, MD^{*}, Richard A. Marder
MD^{*} and A. Hari Reddi, PhD^{*,†}

Am J Sports Med. 2015 Mar 26. pii: 0363546515575023. (knee – no facet lit)

Effect of autologous platelet leukocyte rich plasma injections on atrophied lumbar multifidus muscle in low back pain patients with monosegmental degenerative disc disease

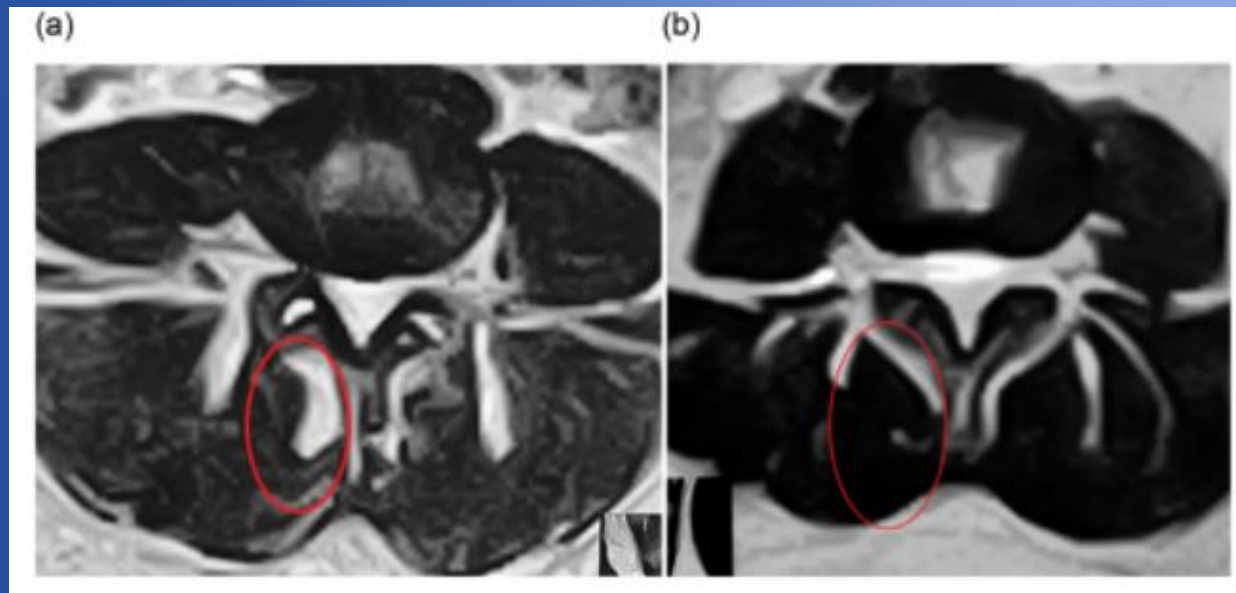
Mohamed Hussein^{1,*} and Tamer Hussein²

¹ Department of Orthopedics and Traumatology, Surgery New Hospital, Zagazig University Hospitals and Faculty of Medicine, Zagazig University, 44519 Zagazig City, Sharkiah, Egypt

² Department of Anesthesiology and ICU, Surgery New Hospital, Zagazig University Hospitals and Faculty of Medicine, Zagazig University, 44519 Zagazig City, Sharkiah, Egypt

Received 30 May 2015, Accepted 7 January 2016, Published online 22 March 2016

104 pts with maximal improvement in 12-18 months



Disc degeneration

- Cellular
 - Irreversible loss of IVD cells
 - Poor repair capacity
- Molecular
 - Extracellular Matrix
 - Decreased production, increased degradation
- Pain
 - Pro-inflammatory & trophic cytokines

Molecular level

- Dehydration & Loss of disc height
 - Pro-inflammatory cytokines
 - IL-1 β , IL-6, TNF- α , prostaglandin E2
 - Matrix degradation enzymes
 - MMP's, **ADAMTS's**
 - Collagen Type II to Type I
- Annular tears \leftrightarrow disc protrusions & extrusions
- Discogenic pain \leftrightarrow chemical/mass radiculitis

Intradiscal PRP

- As presented at TOBI 2014, 2015
- Greg Lutz – HSS
 - Prospective Double-Blind RCT
- Refractory axial LBP >6 mos
- IVD height maintained at least 50%
- Disc protrusion <5mm on MRI or CT
- Concordant pain on Discography
- Grade 3-4 annular tear on discography

HSS Intradiscal PRP

- Outcomes
 - Pain Numeric Rating Scale (NRS)
 - Modified NASS Outcome Questionnaire
 - Functional Rating Index (FRI)
 - SF-36 (physical functioning and pain sections)
- Follow-up at 1 wk, 4 wks, 8 wks, 6 mo, 1 yr

HSS Intradiscal PRP

- Significant improvement at 8 weeks & 1 year
- No significant change in control
- 58% success in PRP group vs. 13% in controls
- No complications



PM R 8 (2016) 1-10

www.pmrjournal.org

Original Research—CME

Lumbar Intradiskal Platelet-Rich Plasma (PRP) Injections: A Prospective, Double-Blind, Randomized Controlled Study

Yetsa A. Tuakli-Wosornu, MD, MPH, Alon Terry, MD, Kwadwo Boachie-Adjei, BS, CPH,
Julian R. Harrison, BS, Caitlin K. Gribbin, BA, Elizabeth E. LaSalle, BS,
Joseph T. Nguyen, MPH, Jennifer L. Solomon, MD, Gregory E. Lutz, MD

Abstract

Objective: To determine whether single injections of autologous platelet-rich plasma (PRP) into symptomatic degenerative intervertebral disks will improve participant-reported pain and function.

Design: Prospective, double-blind, randomized controlled study.

Setting: Outpatient physiatric spine practice.

Participants: Adults with chronic (≥ 6 months), moderate-to-severe lumbar diskogenic pain that was unresponsive to conservative treatment.

Methods: Participants were randomized to receive intradiskal PRP or contrast agent after provocative diskography. Data on pain, physical function, and participant satisfaction were collected at 1 week, 4 weeks, 8 weeks, 6 months, and 1 year. Participants in the control group who did not improve at 8 weeks were offered the option to receive PRP and subsequently followed.

Main Outcome Measures: Functional Rating Index (FRI), Numeric Rating Scale (NRS) for pain, the pain and physical function domains of the 36-item Short Form Health Survey, and the modified North American Spine Society (NASS) Outcome Questionnaire were used.

Results: Forty-seven participants (29 in the treatment group, 18 in the control group) were analyzed by an independent observer with a 92% follow-up rate. Over 8 weeks of follow-up, there were statistically significant improvements in participants who received intradiskal PRP with regards to pain (NRS Best Pain) ($P = .02$), function (FRI) ($P = .03$), and patient satisfaction (NASS Outcome Questionnaire) ($P = .01$) compared with controls. No adverse events of disk space infection, neurologic injury, or progressive herniation were reported following the injection of PRP.

Conclusion: Participants who received intradiskal PRP showed significant improvements in FRI, NRS Best Pain, and NASS patient satisfaction scores over 8 weeks compared with controls. Those who received PRP maintained significant improvements in FRI scores through at least 1 year of follow-up. Although these results are promising, further studies are needed to define the subset of participants most likely to respond to biologic intradiskal treatment and the ideal cellular characteristics of the intradiskal PRP injectate.



Platelet Lysate

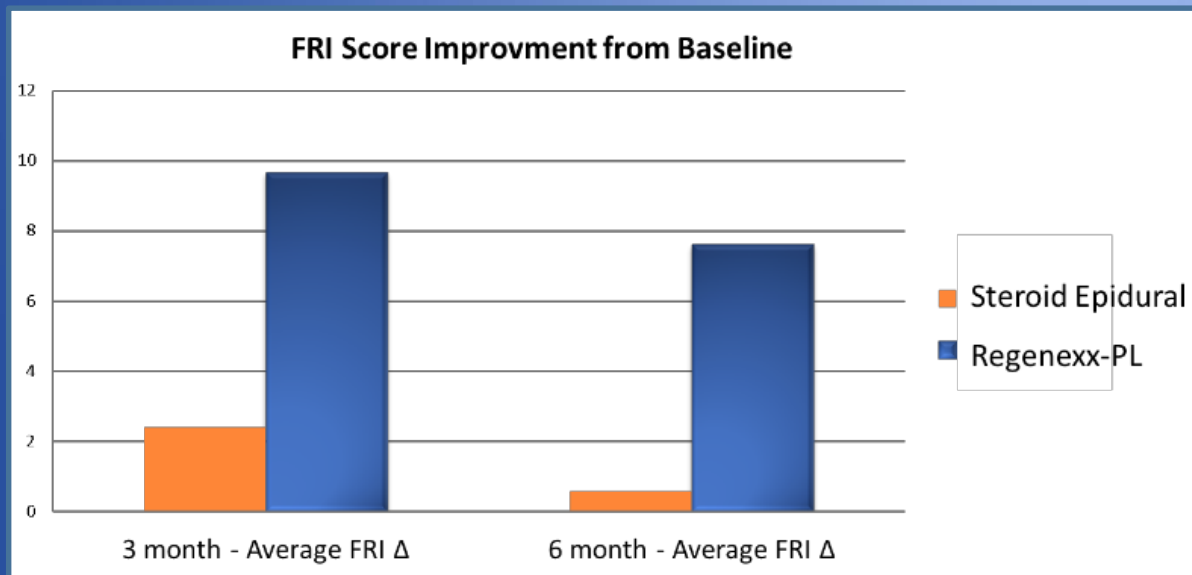
- Manual processing techniques can lyse platelets and release Alpha Granule growth factors from platelet membranes
- PL Immediate vs. PRP sustained release
- Net anti-inflammatory effect
- Neuromodulatory?

Platelet Lysate Epidural

- Regenexx patient registry outcome data demonstrates that PL-Disc when compared to Steroid injection
 - 392% more effective at 3 months
 - 1,500% more effective at 6 months

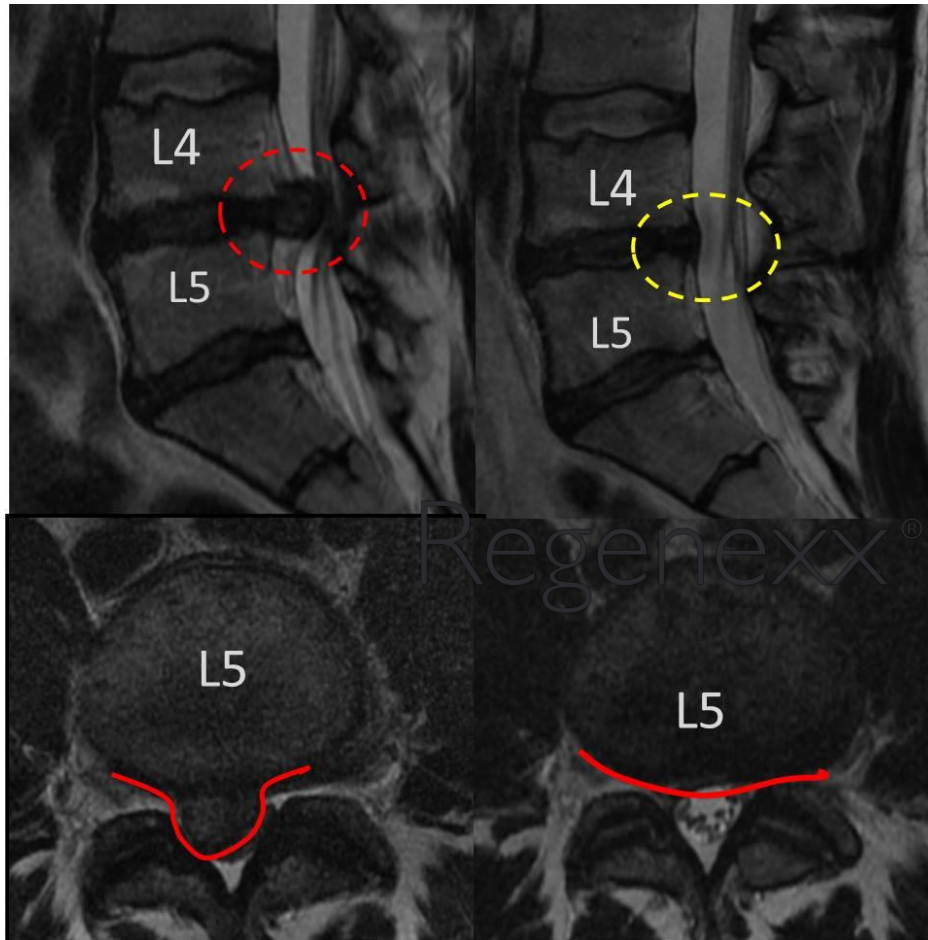
This is registry data, which is not the same as a controlled trial. This means it was collected as patients were treated.

	Regenexx-PL	Steroid Epidural
Number of Patients	147	85
Average # Injections	1.25	1.44
Cross-over #	PL/Dex→ESI: 0	ESI→PL/Dex: 11
Average time to Cross-over	N/A	56 days



Details: n=60 for patients responding after PL procedure at 3 months and n=48 at 6 months. N=24 at 3 months for steroid epidural patients and n=19 at 6 months.

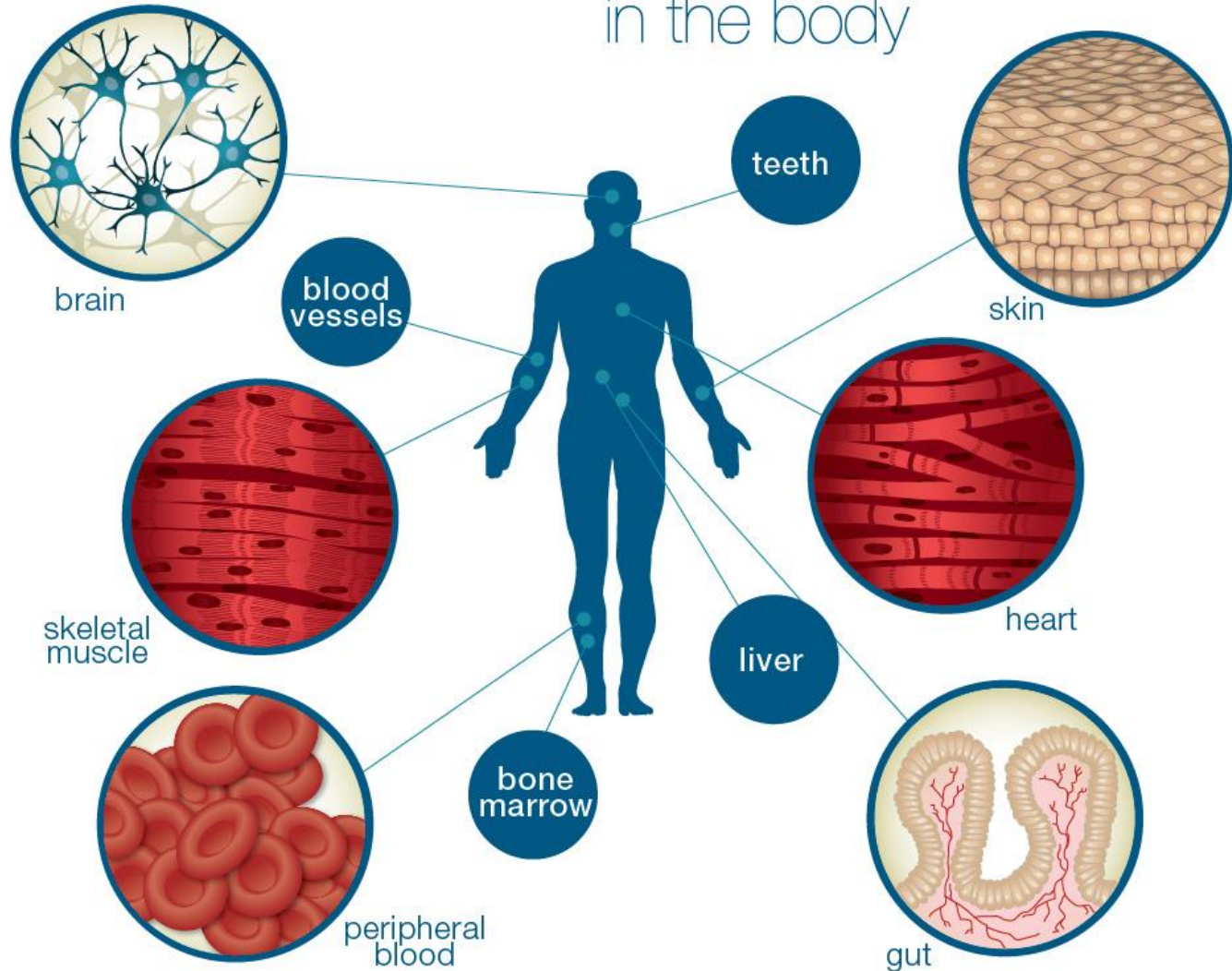
MRI: 6.26.2012 (PRE-INJECT) MRI: 11.21.2012 9 (POST-INJECT)



Stem Cells

- Adult – not embryonic
- Autologous
- Undifferentiated cell in reserve until replacement or repair is needed

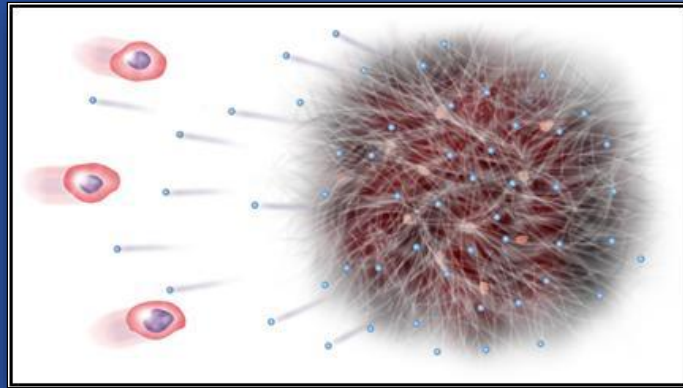
Locations of **Somatic Stem Cells** in the body



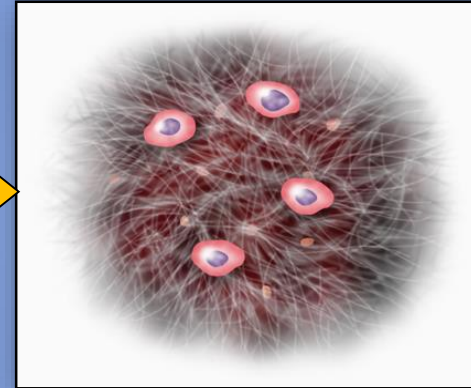
<http://learn.genetics.utah.edu/content/stemcells/quickref/>

Types of Adult Stem Cells

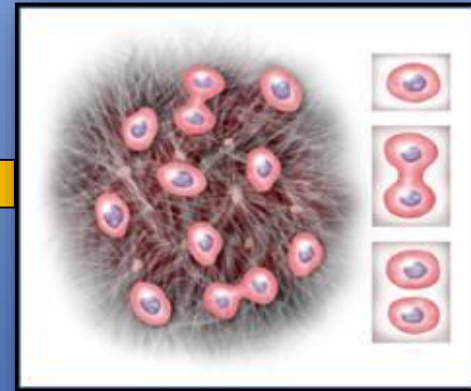
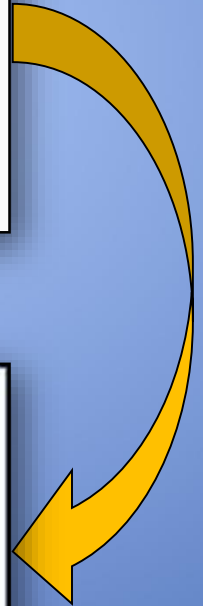
- Endothelial progenitor cells (CD146/MCAM/MUC18/S-endo-1, CD34, CD133/prominin, Tie-2, Flk1/KD/VEGFR2)
- Hematopoietic stem cells (CD34, CD117/c-Kit, Sca1)
- **Mesenchymal stem cells** (CD146/MCAM/MUC18/S-endo-1, STRO-1, Thy-1, CD106, CD105, C166)
- VSEL (Very Small Embryonic Like): (Sca 1, CD45)
- Neural stem cells (CD133/prominin, nestin, NCAM)
- Mammary stem cells (CD24, CD29, Sca1),
- Intestinal stem cells (NCAM, CD34, Thy-1, CD117/c-Kit, Flt-3).



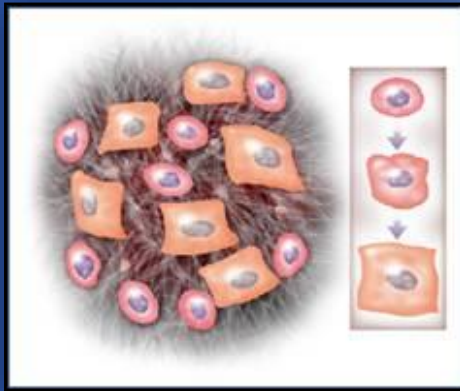
Chemoattraction



Migration

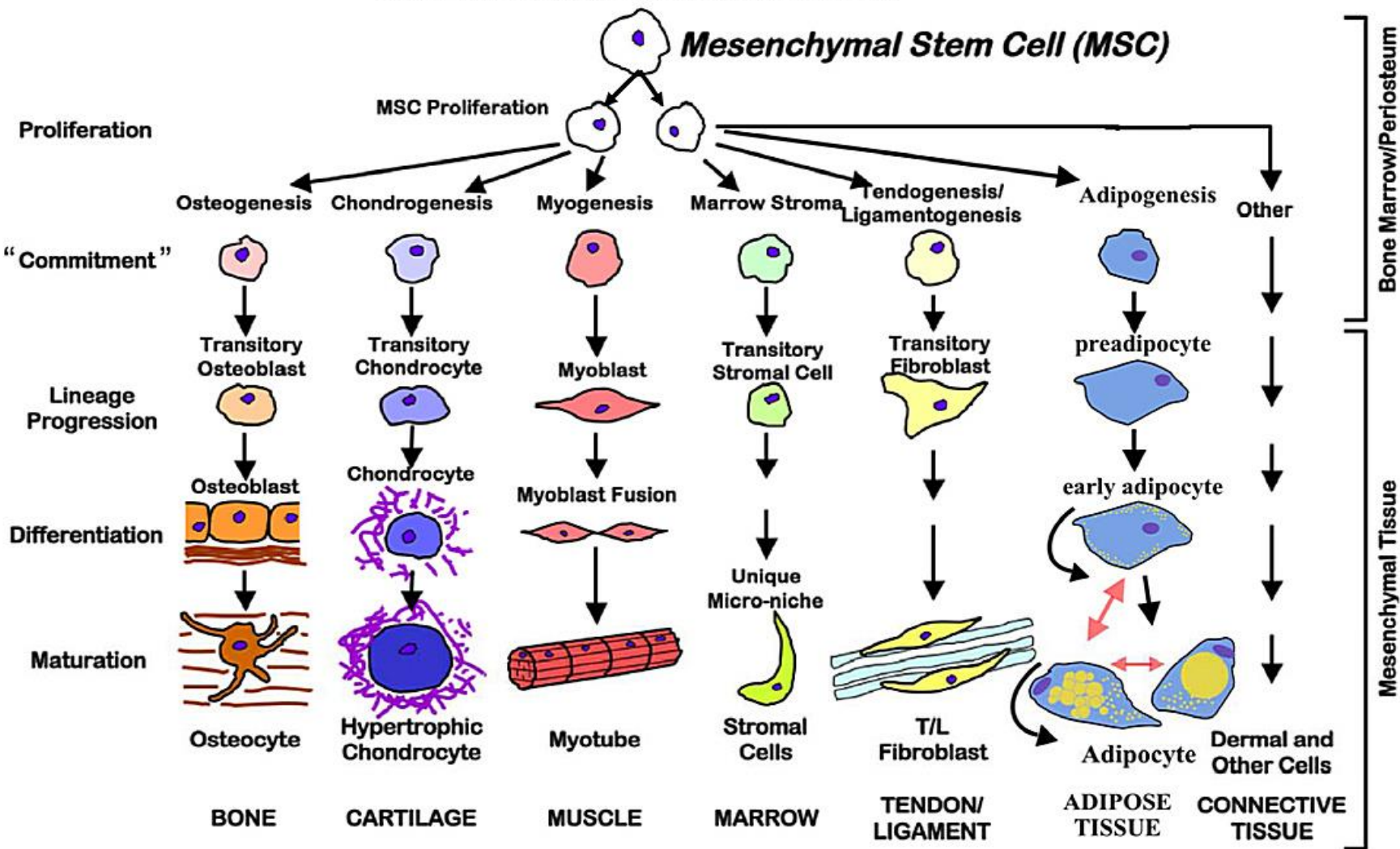


Proliferation



Differentiation

THE MESENGENIC PROCESS



<http://www.discoverymedicine.com/Tracey-L-Bonfield/2010/04/15/adult-mesenchymal-stem-cells-an-innovative-therapeutic-for-lung-diseases/>

Medicinal Signaling Cells

Hofer and Tuan *Stem Cell Research & Therapy* (2016) 7:131
DOI 10.1186/s13287-016-0394-0

Stem Cell Research & Therapy

REVIEW

Open Access

Secreted trophic factors of mesenchymal stem cells support neurovascular and musculoskeletal therapies



Heidi R. Hofer and Rocky S. Tuan*

OPEN

Experimental & Molecular Medicine (2013) 45, e54; doi:10.1038/emm.2013.94
© 2013 KSBMB. All rights reserved 2092-6413/13
www.nature.com/emm

REVIEW

Mesenchymal stem cells: environmentally responsive therapeutics for regenerative medicine

Matthew B Murphy¹, Kathryn Moncivais¹ and Arnold I Caplan²

MSC sources

- **Bone Marrow Aspirate**
 - Same Day: Regulated by state practice of medicine
 - Cultured: Regulated by FDA and needs drug approval
- **Adipose Tissue**
 - Whole or Micronized Adipose Graft:
 - Regulated by state practice of medicine
 - Stromal Vascular Fraction:
 - Chemically digested to release stem cells
 - Regulated by FDA and needs drug approval
- Amniotic fluid products are **NOT** stem cells

BMAC vs AD

Artif Cells Blood Substit Immobil Biotechnol. 2011 Feb;39(1):31-8. doi: 10.3109/10731191003776769. Epub 2010 Nov 30.

Comparing the chondrogenic potential in vivo of autogenic mesenchymal stem cells derived from different tissues.

Li Q¹, Tang J, Wang R, Bei C, Xin L, Zeng Y, Tang X.

Biotechnol Lett (2011) 33:1257–1264

DOI 10.1007/s10529-011-0541-8

ORIGINAL RESEARCH PAPER

A comparison between osteogenic differentiation of human unrestricted somatic stem cells and mesenchymal stem cells from bone marrow and adipose tissue

Abbas Shafiee · Ehsan Seyedjafari ·
Masoud Soleimani · Naser Ahmadbeigi ·
Peyman Dinarvand · Nasser Ghaemi

Orthopedic Bone Marrow Stem Cell Research Summary (1997-2016)

Some physicians and scientists argue that we don't have much research supporting the use of bone marrow stem cells to treat orthopedic conditions. While this may be true for some stem cell types, nothing could be farther from the truth for bone marrow. Here I list all significant publications from the late 90s through April 2016. Each circle represents a research study and is hyperlinked to the abstract in the U.S. National Library of Medicine or the full text article. The main author is listed, the area of treatment, the number of patients involved, and the type of bone marrow stem cells used (either Autologous Bone Marrow Concentrate (BMC) or Cultured Mesenchymal Stem Cells (Cult MSC) [autologous or allogeneic]. The scalpel or injection icons represent the three types of delivery techniques: injection, surgical, or both. Centeno-Schultz publications are highlighted.

1997

2000

n=8,207

(The patient n is approximate as a few studies list joints instead of patients. On the other hand, several later case studies and small case series were also excluded due to significance. In addition, this number represents total publishing activity as patients from prior studies are likely repeated by later studies.)

If you're interested in using this slide in presentations, please request permission in writing from Chris Centeno, M.D. at centenooffice@centenoschultz.com.

2005

2010

2015

2016



MSCs

- Severe Facet Degeneration (no lit)
- Sacroiliac joint (no lit)
- Intra-discal (lit)

[Spine \(Phila Pa 1976\)](#). 2010 May 15;35(11):E475-80. doi: 10.1097/BRS.0b013e3181cd2cf4.

Disc regeneration therapy using marrow mesenchymal cell transplantation: a report of two case studies.

[Yoshikawa T](#)¹, [Ueda Y](#), [Miyazaki K](#), [Koizumi M](#), [Takakura Y](#).

[Transplantation](#). 2011 Oct 15;92(7):822-8. doi: 10.1097/TP.0b013e3182298a15.

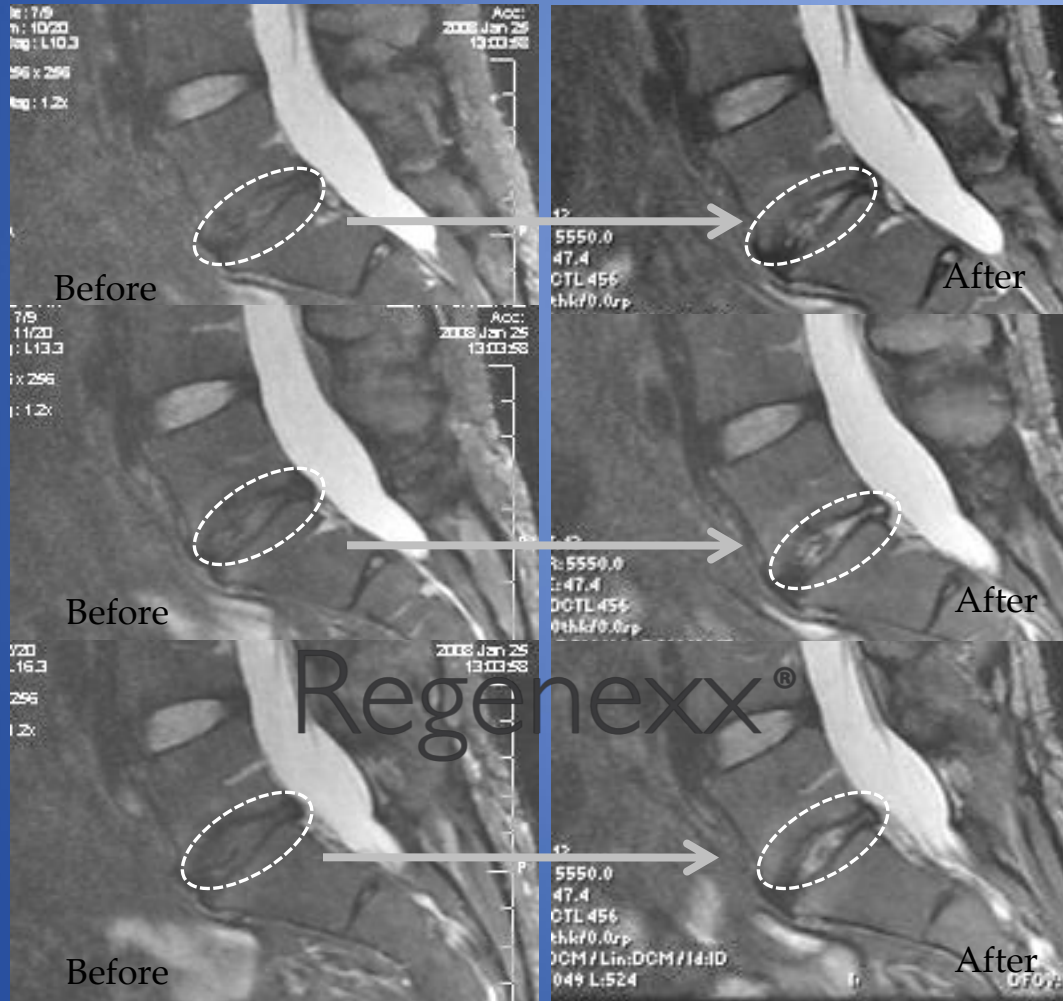
Intervertebral disc repair by autologous mesenchymal bone marrow cells: a pilot study.

[Orozco L](#)¹, [Soler R](#), [Morera C](#), [Alberca M](#), [Sánchez A](#), [García-Sancho J](#).

[Stem Cells](#). 2015 Jan;33(1):146-56. doi: 10.1002/stem.1845.

Percutaneous injection of autologous bone marrow concentrate cells significantly reduces lumbar discogenic pain through 12 months.

[Pettine KA](#)¹, [Murphy MB](#), [Suzuki RK](#), [Sand TT](#).



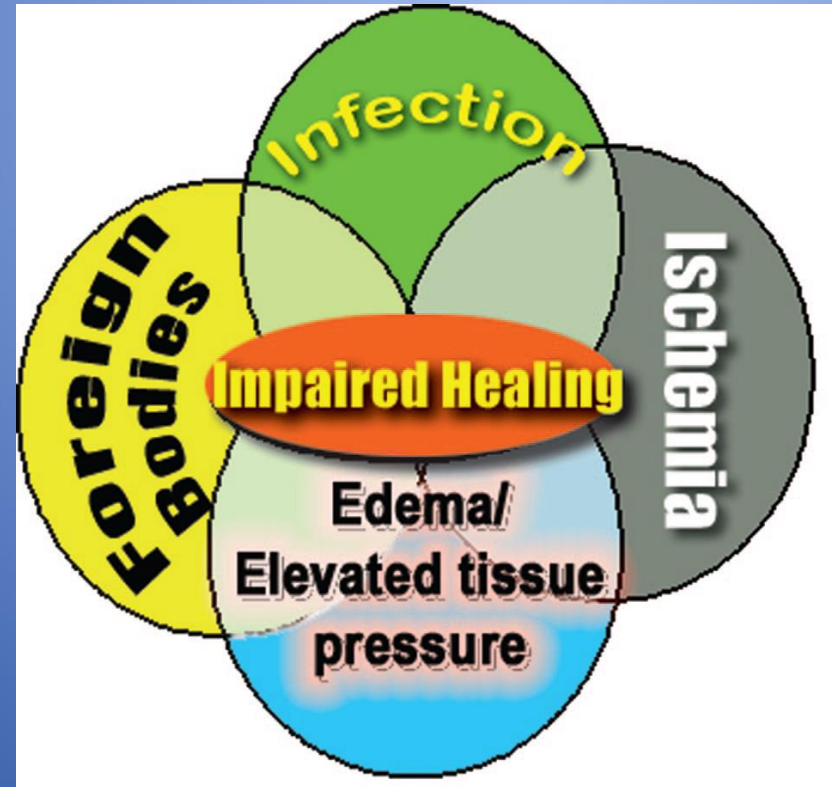
Paradigm shift

- Remove barriers
- Treat the whole picture

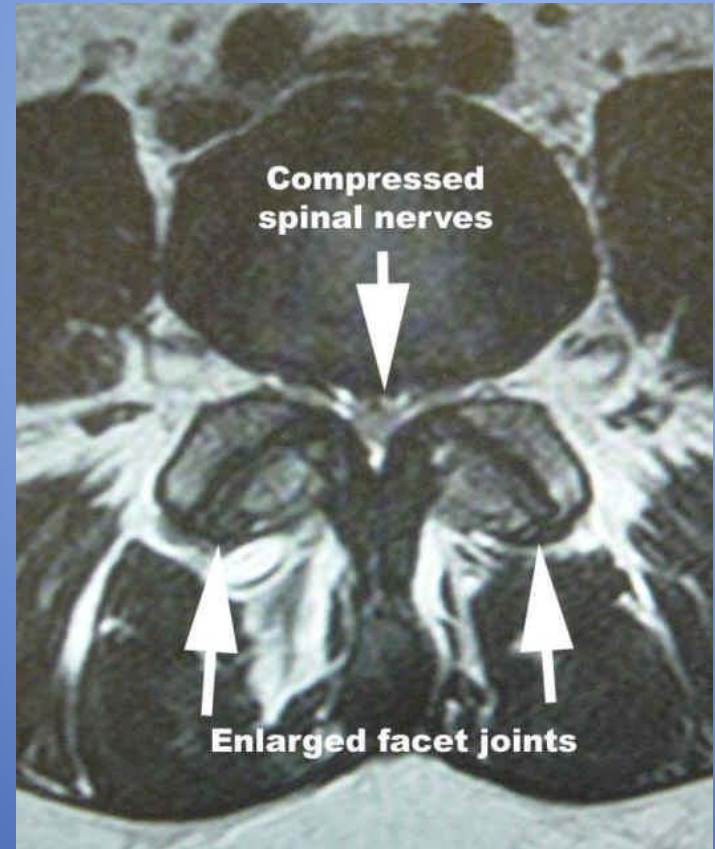
Barriers to healing

Systemic Obstacles

- Diabetes
- Hypothyroidism
- Age
- Tissue Perfusion
- Nutrition
- Smoking
- **DYSFUNCTION**
- **PAIN**
- **NSAIDs**
- **STEROIDS**



Putting it together



- Don't just treat the “pain generator”
- Multi-factorial condition needs multi-factorial treatment

Conclusions

- Epidural steroid = short term benefit
 - **But** only for:
 - Radiculopathy due to disc herniations
 - Possibly axial back pain due to disc herniations
- Stenosis: Lidocaine alone = epidural steroid!
- Facet Medial Branch Denervation NOT recommended for young and active old pts

Conclusions

- Regenerative treatments provide a safe and effective alternative
- Paradigm shift to treating the whole picture, not just the “pain generator”
- ... But more research is needed
... so please Track Your Outcomes!



questions?

HEALTH LINK
MEDICAL CENTER



Regenexx[®]

References

Various slides, and images: www.regenexx.com

Healing cascade image: <https://classconnection.s3.amazonaws.com/804/flashcards/1758804/png/untitled1346084557506.png>

Healing cascade image: http://commons.wikimedia.org/wiki/File:Wound_healing_phases.png

Broughton G, Janis JE, Attinger CE. Wound Healing: An Overview. *Plast. Reconstr. Surg.* 117: 1e-S, 2006.

Prolotherapy information and slides: <http://www.drreeves.com/>

Murphy M, Godson C, Cannon S, Kato S, Mackenzie HS, Martin F, Brady HR: Suppression subtractive hybridization identifies high glucose levels as a stimulus for expression of connective tissue growth factor and other genes in human mesangial cells. *J Biol Chem* 1999;274(9):5830-5834.

Castillo TN et al. Comparison of Growth Factor and Platelet Concentration from Commercial Platelet-Rich Plasma Separation Systems. *Am J Sports Med.* 2011 Feb;39(2):266-71.

Kusida S et al. Platelet and growth factor concentrations in activated platelet-rich plasma: a comparison of seven commercial separation systems. *J Artif Organs.* 2014; 17:186-192.

Drago JL et al. Comparison of the acute inflammatory response of two commercial PRP systems in healthy rabbit tendons. *Am J Sports Med.* 2012 Jun;40(6):1274-81.

Osterman C et al. Platelet-rich plasma increases anti-inflammatory markers in a human coculture model for osteoarthritis. *Am J Sports Med.* 2015 Feb 25. [Epub ahead of print]

Locations of stem cells image: <http://learn.genetics.utah.edu/content/stemcells/spin/kryf/>

Lundgreen K et al. Lower muscle regenerative potential in full-thickness supra-spinatus tears compared to partial-thickness tears. *Acta Orthopaedica* 2013; 84(6):565-570.

The mesengenic process image: <http://www.discoverymedicine.com/Tracey-L-Bonfield/2010/04/15/adult-mesenchymal-stem-cells-an-innovative-therapeutic-for-lung-diseases/>

Li Q et al. Comparing the chondrogenic potential in vivo of autogenic mesenchymal stem cells derived from different tissues. *Artif Cells Blood Substit Immobil Biotech.* 2011 Feb;39(1):31-8.

Shafiee A et al. A comparison between osteogenic differentiation of human unrestricted somatic stem cells and mesenchymal stem cells from bone marrow and adipose tissue. *Biotechnol Lett.* 2011;33:1257-1264.

Steilen D et al. Chronic neck pain: making the connection between capsular ligament laxity and cervical instability. *Open Ortho J.* 2014;8:326-345.

Degenerative spondylolisthesis slide: http://www.homeorizon.com/images/user_files/degenerative-spine-disease8a.jpg

Friedly JL et al. A randomized trial of epidural glucocorticoid injections for spinal stenosis. *N Engl J Med* 2014; 371:11-21

Andersson BJ. Epidural glucocorticoid injections in patients with lumbar spinal stenosis. *N Engl J Med* 2014;371:75-76.

Wei AS et al. The effect of corticosteroid on collagen expression in injured rotator cuff tendon. *J Bone Joint Surg Am.* 2006;88(6):1331-1338.

Jacobs S et al. Adrenal suppression following extradural steroids. *Anaesthesia.* 1983;38(10):953-956.

Steinberg CLR et al. Charcot-like arthropathy following intra-articular hydrocortisone. *JAMA.* 1962;181(10):851-854.

Shapiro PS et al. The effect of local corticosteroid or ketorolac exposure on histologic and biomechanical properties of rabbit tendon and cartilage. *Hand.* 2007 Dec;2(4):165-172.

Moon et al. Changes in blood glucose and cortisol levels after epidural or shoulder intra-articular glucocorticoid injections in diabetic or nondiabetic patients. *Am J Phys Med Rehabil.* 2014;93(5):372-8.

Palmieri M. Pain, functional and behavioral outcomes in patients undergoing platelet rich plasma (PRP) injection for cervical and lumbar facet arthropathy. Poster presented at AAPM 31st Annual Meeting.

Sakata R et al. Stimulation of the superficial zone protein and lubrication in the articular cartilage by human platelet-rich plasma. *Am J Sports Med.* 2015 Mar 26. [Epub ahead of print]

Lutz G et al HSS unpublished data as presented at TOBI 2014.

Yoshikawa T et al. Disc regeneration therapy using marrow mesenchymal cell transplantation: a report of two case studies. *Spine* 2010;35(11):E475-80.

Orozco et al. Intervertebral disc repair by autologous mesenchymal bone marrow cells: a pilot study. *Transplantation.* 2011;92(7):822-8.

Pettine KA et al. Percutaneous injection of autologous bone marrow concentrate cells significantly reduces lumbar discogenic pain through 12 months. *Stem cells.* 2015;33(1):146-56.

