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COMPARISON OF PLATELET RICH PLASMA FORMULATIONS FOR CARTILAGE HEALING

Although platelet rich plasma (PRP) has been studied as a means to deliver autologous growth factors, the optimal method of preparing PRP for cartilage repair is not known. This study investigated the mechanisms of action of different PRP formulations on human chondrocytes.

Platelet rich plasma and platelet poor plasma (PPP) were obtained from 10, healthy, male volunteers. In this one-step method, 45 mL of venous blood was divided into five tubes. From these, three formulations were prepared, including PRP with a low concentration of platelets and very few leukocytes (L-PRP), pure PRP with high concentrations of both platelets and leukocytes (P-PRP) and platelet poor plasma (PPP). These different formulations were applied to cartilage samples from patients undergoing knee replacement surgery. Chondrocyte growth in the presence of each formulation was evaluated after zero, three and seven days of culture.

The five percent, 10% and 20% concentrations of each formulation induced a dose-dependent enhancement of chondrocyte proliferation, with the only difference between the formulations being greater cell growth on day seven with P-PRP as compared to the other formulations ($p < 0.05$). At each concentration, P-PRP induced greater cell proliferation on day seven when compared with L-PRP and PPP ($p < 0.05$).

Conclusion: This study of cartilage response to different platelet rich plasma (PRP) formulations found that PRP with a low concentration of platelets and very few leukocytes had superior effects on cell growth and resulted in higher levels of growth factors and

cytokines than did other formulations.

Cavallo, C., et al. Comparison of Platelet Rich Plasma Formulations for Cartilage Healing: An *In Vitro* Study. *J Bone Joint Surg.* 2014, March 5; 96(5): 423-429.

DIABETES AND CERVICAL LAMINOPLASTY

Cervical spondylotic myelopathy (CSM) is an increasingly common condition in the geriatric population. Treatment for this condition includes cervical laminoplasty. As diabetes mellitus is a frequent comorbidity, this study was designed to better understand the impact of diabetes on the outcome of this surgical procedure.

Between January of 2007 and March of 2011, 700 patients underwent laminoplasty for the treatment of CSM. Of the 528 eligible patients, 505 were followed for over 12 months, and were included in this study. All patients were followed for clinical outcomes, with measures including the Japanese Orthopedic Association (JOA) score for cervical myelopathy, as well as radiographic and functional assessments. These outcomes were compared between those with, versus those without, a diagnosis of diabetes at the time of the surgery.

Machino, M., et al. Impact of Diabetes on the Outcome of Cervical Laminoplasty. *Spine.* 2014 39(3) 220 -227.

HOME-BASED EXERCISE AFTER HIP FRACTURE

Hip fractures occur in more than 250,000 people in the United States each year. Two years after these fractures, more than half of men and 39% of women are dead or living in long-term care facilities. This study was designed to determine the efficacy of a six-month, functionally oriented rehabilitation program,

designed to extend the benefits of the initial hip fracture rehabilitation.

This randomized, clinical trial included two parallel groups, 60 years of age or older, with a primary diagnosis of hip fracture. All patients were discharged from rehabilitation services within 20 months of the baseline assessment. An intervention group was instructed to perform a home exercise program three times per week for six months, initially taught by physical therapists. A control group received dietary nutritional education during a single home visit, followed by telephone calls and mailings. The frequency of contact with dietitians was matched to that of the physical therapists in the treatment group. Function was measured with the Short Physical Performance Battery (SPPB) and the Active Measure for Post-Acute Care (AM-PAC).

Of the 232 randomized patients, 195 were followed up at six months. The treatment group showed significant improvement relative to the control group on the SPPB in both the adjusted and the unadjusted analyses ($p < 0.001$ for both analyses). Significant differences were also noted at six months in favor of the treatment group on the mean AM-PAC mobility scores ($p = 0.01$), and mean AM-PAC daily activity scores ($p = 0.01$). The benefits persisted at nine month follow up.

Conclusion: This study demonstrates that, among patients who had undergone a standard rehabilitation program after hip fracture, home-based, functionally oriented exercise significantly improved physical function at six and nine months after initiation.

Latham, N., et al. Effect of a Home-Based Exercise Program on Functional Recovery following Rehabilitation after Hip Fracture. A Randomized Clinical Trial. *JAMA.* 2014, February; 311(7): 707-709.

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PHYSICAL ACTIVITY, LOW BACK PAIN, AND OBESITY

Combined, obesity and back pain are thought to be associated with 30% of United States healthcare expenditures. While studies of back pain often list obesity as a confounding factor, research has failed to consistently establish this association. This study examined the interrelationships among physical activity, obesity and low back pain (LBP).

Data were obtained from the 2003-2004 survey of the National Health and Nutrition Examination Survey (NHANES). From these data, LBP was determined by a questionnaire. Body mass index (BMI) was calculated during the physical examination and divided into four groups: normal weight (BMI < 25 kg/m²), overweight (BMI 25-30 kg/m²), obese (BMI 31-35 kg/m²) and morbidly obese (BMI 36 kg/m² and above). Physical activity was reviewed and characterized by intensity, frequency and duration.

The risks of LBP were 2.9% for normal weight, 5.2% for overweight, 7.7% for obese and 11.6% for morbidly obese subjects. Tobacco abuse was the strongest predictor of LBP across the BMI spectrum. The best physical activity predictors of LBP were found in the moderate- and high-intensity ranges with small predictive effects. For the average overweight American, a modest increase in moderate activity time (17.6 minutes each day) reduced the LBP risk by 32%. For the average morbidly obese American, an increase in moderate activity average bout duration from 1.3

minutes to 2.1 minutes reduced the risk of back pain risk by 38%.

Conclusion: This study found that an elevated body mass index is a risk factor for low back pain, and that increases in the total amount and time per bout of moderate physical activity decreases this risk.

Smuck, M., et al. Does Physical Activity Influence Relationship between Low Back Pain and Obesity. *Spine J.* 2014, February; 14(2): 209-216.

PLATELET RICH PLASMA FOR PATELLAR TENDINOPATHY

Patellar tendinopathy (PT) is a degenerative disease of the patella tendon, resulting in anterior knee pain. Among the newer therapies introduced to address PT, platelet rich plasma (PRP) has been suggested as a potential intervention. This study investigated whether the combination of the eccentric exercise and PRP may be effective for the treatment of PT.

This double-blind, randomized, controlled trial included 23 patients with PT who had failed conservative treatment. The subjects underwent either a single injection of PRP or a placebo dry needling (DN) technique. These treatments were combined with a standardized, five-phase program of eccentric exercise. For the primary outcome measure, patients were assessed at baseline and at three, six, nine, 12 and >26 weeks with the Victorian Institute of Sport Assessment (VISA) score for patella tendinopathy. Secondary outcome measures included the Tegner Activity Scale, the Lysholm Knee Scale and the Short Form (SF-12) Questionnaire.

A total of 13 patients were randomized to the DN group and ten to the PRP group. At 12 weeks, the PRP group demonstrated significantly more improvement, as measured by the VISA, than did the DN group ($p=0.02$). However, the significance of that difference had dissipated by week 26 ($p=0.66$). Measurement of activity using Tegner scores revealed no significant difference between the groups at 26 weeks. Measurement of function and stability using Lysholm scores demonstrated better function at 26 weeks in the DN group ($p=0.006$). No significant differences were noted between the groups in measures of pain (VAS) or of health-related quality of life (SF-12).

Conclusion: This study of patients with patella tendinopathy demonstrates that combining eccentric exercise and platelet rich plasma injection accelerates the recovery from patella tendinopathy relative to exercise alone. However, time.

Dragoo, J., et al. Platelet Rich Plasma as a Treatment for Patellar Tendinopathy: A Double-Blind, Randomized, Controlled Trial. *Am J Sports Med.* 2014, March; 42: 610-619.

PLATELET RICH PLASMA VERSUS WHOLE BLOOD FOR CHRONIC TENNIS ELBOW

Lateral elbow epicondyle tendinosis (tennis elbow) is a common condition, occurring at the common extensor tendon. Newer treatment options have included platelet rich plasma (PRP), autologous blood, prolotherapy and extracorporeal shockwave therapy. Both PRP and autologous blood contain platelets with strong growth factors which may help the healing process from chronic injuries. Given the high cost of autologous PRP therapy, this study compared the efficacy of whole blood injections with that of PRP.

Patients diagnosed with chronic lateral epicondylitis with a duration of more than three months and a pain severity of at least five on a 10-point scale were included in the sample. Those subjects were randomized to receive 2 mL of autologous PRP into a maximal tenderness point at the elbow under aseptic techniques, or 2 mL of autologous peripheral whole blood using the same technique. Pain severity was assessed before injection and at four weeks, eight weeks, and six and 12 months post-injection. Additional outcome measures included the Modified Mayo Clinic Performance Index and the Pressure Pain Threshold (PPT).

Sixty-one patients completed this study. The mean pain score decreased significantly in both treatment groups at each follow-up evaluation ($p<0.001$). Mayo and PPT scores significantly improved in both treatment groups at 12 months ($p<0.001$ and $p<0.002$, respectively). No significant differences were noted between the groups in pain scores and function scores at any follow-up examination.

Conclusion: This study of patients with chronic lateral epicondylitis found that both platelet

rich plasma and autologous whole blood injections are effective treatments, both for reducing pain and increasing function.

Raeissadat, S., et al. Is Platelet Rich Plasma Superior to Whole Blood in the Management of Chronic Tennis Elbow: One-Year, Randomized Clinical Trial. **BMC Sports Sci, Med Rehab.** 2014; 6: 12.

RETURN TO PITCHING AFTER TOMMY JOHN SURGERY IN MAJOR LEAGUE PITCHERS

The medial ulnar collateral ligament (UCL) of the elbow provides stability to valgus stress during throwing sports. The outcome of UCL reconstruction surgery, often referred to as the Tommy John surgery, has enjoyed increased use over the years. This study was designed to determine the rate of return to pitching and to clarify the performance of those pitchers after this reconstructive procedure.

Major League Baseball (MLB) pitchers with symptomatic UCL injury, who underwent reconstruction were included in the study. Data were obtained from the MLB database. A player was deemed to have returned to pitching if he pitched in any MLB game after the surgery. Controls were matched by age, body mass index, position, handedness, and MLB experience and performance.

A total of 179 pitchers with UCL tears who underwent reconstruction were included in the analysis. Of these 148 were able to return to play in the major leagues and 174 in the major or minor leagues combined. The pitchers returned at a mean of 20 months after reconstruction. After surgery, pitchers had significantly fewer innings pitched per season and had both fewer wins and losses per season as compared to before surgery. Pitchers who had undergone the surgery had lower earned-run averages and walks plus hits per inning, had significantly lower losing percentages and gave up fewer hits per inning as compared with controls. Two years after surgery there were no significant differences between cases and controls.

Conclusion: This study of Major League Baseball pitchers with ulnar collateral ligament injury reconstruction found that the majority return to major-league baseball, and were successful as measured by multiple performance variables.

Ericsson, B et al. Rate of Return to Pitching and Performance after

Tommy John Surgery in Major League Baseball Pitchers. **Am J Sports Med** 2014, March; 42(3): 536– 543.

REVIEW OF OPIOID PRESCRIPTION GUIDELINES

Currently, 8 to 30% of patients with chronic non-cancer pain received opioids. Given the current rates of opioid overdose, a number of organizations have created guidelines for opioid prescribing. This review paper was designed to summarize the current guidelines for the treatment of chronic pain

Several medical databases were searched for guidelines addressing the use of opioids in the treatment of chronic pain published between 2007-2013. The content of the guidelines meeting selection criteria were reviewed and appraised.

Thirteen guidelines met the selection criteria and were screened for quality. Ten received poor to fair scores and two received high scores according to standardized assessment tools. Most guidelines were based on observational data or expert consensus. In describing the guideline content, the authors note that the majority of guidelines recommend that physicians avoid prescribing greater than 90-200 morphine equivalents per day, reduce doses by 25 to 50% when rotating opioids, acquire additional knowledge before prescribing methadone, and recognize the risks of fentanyl patches. Most guidelines recommend the use of opioid risk assessment tools, written treatment agreements, and urine drug screen.

Conclusion: This review of current guidelines for chronic pain found agreement on upper dosing thresholds, cautions with certain medications and the use of risk assessment tools, treatment agreements and urine testing.

Nuckols, T et al. Opioid Prescribing: A Systematic Review and Critical Appraisal of Guidelines for Chronic Pain. **Ann Intern Med.** 2014, January 7: 38 – 47.

SOCCER BOOTS AND PLANTAR PRESSURE

Foot and ankle injuries are common among soccer players, with footwear and playing surface thought to impact these injuries. This study assessed plantar pressures in elite soccer players, comparing differences in these pressures in soccer boots versus running shoes.

Seventeen, elite, German, male soccer players were equipped with sensor loaded insoles designed to measure pressure and force. In a first trial, all players ran at 3.3 m/s in a straight line in running shoes. In a second trial, the players ran with soccer boots equipped with a 12-stud profile. The preferred and nonpreferred feet were identified for each player. Changes in peak plantar pressure between soccer boots and running shoes were compared for nine, predefined foot locations for each foot.

The subjects had an average age of 23 years and a mean weight of 81 kg. Significantly increased plantar pressures were noted with the use of soccer boots, as compared to the running shoes at the lateral midfoot, first metatarsal head, fourth and fifth metatarsal heads and great toe, for both the preferred and nonpreferred foot. The greatest differences were noted at the lateral midfoot and great toe.

Conclusion: This study of elite soccer players found that, compared with running shoes, running in soccer boots results in significant loading, particularly at the lateral midfoot.

Hands – Dieter, C., et al. Soccer Boots Elevate Plantar Pressures in Elite Male Soccer Professionals. **Clin J Sports Med.** 2014, January; 24(1):58-61.

TESTOSTERONE LEVELS IN MEN WITH RHEUMATOID ARTHRITIS

Risk factors for rheumatoid arthritis (RA) include genetic, environmental and hormonal factors. In cross-sectional studies, lower levels of serum testosterone have been found in both male and female patients with RA. This study investigated the significance of hormonal concentrations among men who subsequently develop RA.

This population-based, case-control study screened 22,444 males born between 1921 and 1949, and

10,902 females born between 1925 and 1938. A health survey was designed to screen large strata of the adult population to identify individuals for preventive intervention. All subjects underwent physical examination, including laboratory tests and self-administered questionnaires focusing on health and lifestyle factors. From laboratory tests, serum total free testosterone, sex hormone binding globulin (SHBG), luteinizing hormone (LH) and follicle stimulating hormone

(FSH) concentrations were quantified. All medical records were reviewed to determine individuals who developed RA. Two matched controls were found for each validated case.

From the cohort, 104 cases with RA were identified. After adjustments for confounding factors of tobacco abuse and body mass index, low testosterone levels were found to be weakly associated with the development of rheumatoid factor-negative RA (odds ratio 0.31), with a weaker association with rheumatoid factor-positive RA. Those who developed RA had lower mean concentrations of all measured hormones except SHBG, as compared with controls. Serum levels of FSH were positively associated with the development of rheumatoid factor-negative RA, and negatively associated with the development of rheumatoid factor-positive RA.

Conclusion: This study demonstrates that low levels of testosterone are associated with the subsequent development of rheumatoid factor-negative RA.

Pikwer, M., et al. Association between Testosterone Levels and Risk of Future Rheumatoid Arthritis in Men: A Population-Based, Case-Control Study. *Ann Rheum Disease*. 2014, March 1; 73(3): 573-579.

TRANSCRIPTION FACTOR DECOY AYX1 PREVENTS ACUTE AND CHRONIC PAIN

As Early Growth Response 1 (ERG1) is a transcription factor essential for the early response to noxious injury, it is thought that its immediate activation after injury triggers the delayed, long-term transcription and neuronal excitability changes necessary for the development of chronic pain and mechanical hypersensitivity. A DNA decoy, AYX1, with high affinity and specificity for EGR1, was developed to block ERG1 function. This study examined the effect of the intrathecal administration of this molecule on the development of postoperative pain.

This placebo controlled, animal incisional knee pain model used the vehicle only, or AYX1, injected via a single intrathecal bolus, one hour before surgery for the incisional and knee surgery models, once at the time of surgery for the chronic neuropathic (SNI) model and at -24 hours, -1 hour, +24 hours, and +72 hours relative to injury for the

inflammatory (CFA) model. The animals were tested for mechanical hypersensitivity and functional recovery after surgery.

In the mechanical hypersensitivity model, the treatment group was noted to have significantly less response to light and robust mechanical stimuli, suggesting an effect on allodynia and hyperalgesia. In addition, greater spontaneous activity was noted, as compared with the control groups, demonstrating the ability of AYX1 to suppress reduced function post-surgery.

Conclusion: This animal study demonstrates that a DNA decoy drug, administered by a single intrathecal injection, can significantly reduce mechanical and neuropathic pain after surgery.

Mamet, J., et al. Single Intrathecal Administration of the Transcription Factor Decoy AYX1 Prevents Acute and Chronic Pain after Incisional, Inflammatory or Neuropathic Injury. *Pain*. 2014, February; 155(2): 322-333.

TRANSFUSIONS AND WOUND INFECTION AFTER TOTAL KNEE AND TOTAL HIP ARTHROPLASTY

Previous studies have demonstrated that perioperative transfusions may increase the morbidity and mortality associated with surgery. This study compared the effects of perioperative allogenic and autologous transfusions on the risk of reoperation for suspected infection after primary total hip or total knee arthroplasty.

This retrospective study reviewed the cases of 3,352 patients undergoing primary total knee arthroplasty or total hip arthroplasty, performed between 1997 and 2007. Outcomes were compared between those receiving no transfusions, those receiving allogenic transfusions and those receiving autologous transfusions. The groups were compared by the number of repeat surgeries within three months for suspected acute joint space or extra-capsular tissue infection.

Of the patients studied, 1,746 perioperative transfusions were received, with 836 patients having allogenic exposure and 910 autologous-only exposure. The rate of reoperations for suspected infection was higher among patients with allogenic exposure (1.67%) as compared with all others (0.72%, $p = 0.014$). Autologous transfusion was

not associated with a higher reoperation rate. A multivariable regression analysis revealed that the total number of units transfused ($p = 0.011$) and American Society of Anesthesiologists scores of >2 ($p = 0.008$) were significant predictors of reoperation.

Conclusion: This retrospective study of patients undergoing total knee or total hip arthroplasty found that the total number of blood units transfused was a significant risk factor for reoperation for acute infection, although allogenic exposure itself was not significantly predictive.

Newman, E. Impact of Perioperative Allogenic and Autologous Blood Transfusion on Acute Wound Infection following Total Knee and Total Hip Arthroplasty. *J Bone Joint Surg*. 2014, February; 96(4): 279-284.

TREATMENT OF PHANTOM LIMB PAIN WITH AUGMENTED REALITY

Phantom limb pain is experienced by up to 70% of amputees, with multiple medical and nonmedical interventions proposed. Virtual reality mirror therapy has been introduced as an upgrade to a previously introduced mirror therapy. This study investigated whether a higher degree of realism provided by augmented reality (AR) could improve the efficacy of this therapy.

A patient with chronic, phantom limb pain, 48 years in duration, was studied after failing a variety of treatments. For this patient, myoelectric activity at the residual limb was used to assess the intended phantom limb motions. Using this input a virtual arm was superimposed on his residual limb. The patient was then instructed to perform specified movements. The protocol was applied once weekly for 18 weeks and then twice weekly. Pain was recorded at baseline and throughout the training period.

After four weeks of training, the patient reported episodes of lower pain intensity. At 10 weeks, episodes of near absent pain began to occur, developing into completely pain free episodes, which were new to the patient since amputation.

Conclusion: This case study of a patient with chronic, phantom limb pain found that pain levels can be significantly reduced by using augmented reality and gaming, controlled by myoelectric pattern recognition.

ACETYLCHOLINESTERASE INHIBITORS AND HEALING OF HIP FRACTURES

Adrenergic activity is associated with bone resorption. Drugs that inhibit this activity have been found to increase bone accrual and reduce the risk of hip fractures. By contrast, cholinergic activity has been found to have a positive effect on bone accrual, although the utility of this mechanism for accelerating the healing of bone has not been explored. As cholinergic activity is stimulated by the administration of acetylcholinesterase inhibitors (AChEIs), this study was designed to determine the effect of these medications on hip fracture healing.

This retrospective study reviewed the records of patients with Alzheimer's disease who had sustained a hip fracture, seen over an eight-year period. All subjects were female between the ages of 75 and 95 years at the date of the fracture, with smokers and those with diseases affecting bone metabolism excluded.

All participants underwent postsurgical plain pelvic radiographs at five weeks after the procedure, with radiographs examined by musculoskeletal radiologists held blind to the patient's treatment group. The progress of the fracture was compared between those who were receiving AChEIs and those who were not.

Patients receiving acetylcholinesterase inhibitors had better radiographically demonstrated union at the fracture site [relative rate (RR), 2.7], better bone quality (RR, 2.0), and fewer healing complications (RR, 0.8) than did those who were not receiving this medication.

Conclusion: This study of female patients with Alzheimer's disease and hip fracture found that the use of acetylcholinesterase inhibitors at the time of surgery may produce better fracture healing and minimize complications.

Eimar, H., et al. Acetylcholinesterase Inhibitors and Healing of Hip Fractures in Alzheimer's Disease Patients: A Retrospective Cohort Study. *J Musculoskelet Neuronal Interact.* 2013, December; 13(4): 454-463.

ALTERNATIVE MEDICINE USE BY OLDER WOMEN WITH BACK PAIN

In Australia, back pain is the second most common complaint seen in general practice, representing a significant economic burden. Among those who seek treatment for back pain, many use complementary and alternative medicine (CAM) in addition to conventional medical treatment. Few studies have investigated CAM use specific to back pain. This study examined the patterns of CAM use among Australian women with back pain.

Data were obtained from the Australian Longitudinal Study on Women's Health (ALSWH), which investigated factors affecting the health and well-being of women over a 20-year period. The focus of the study was on women from the 1946 to 1951 cohort, ranging in age from 60 to 65 at the time of the survey. For this sub-study, 1,851 women who had indicated in a 2010 survey that they had experienced back pain were mailed a questionnaire. Within the survey, women were asked whether they had consulted CAM practitioners for back pain in the previous 12 months, and to specify which CAM practice they had used.

Of the 1,310 women who responded to the survey, 76.4% consulted one or more types of CAM practice for back pain. Of these, the modal practitioner was a massage therapist (41%), followed by chiropractor (37.3%), acupuncturist (13.3%), herbalist or naturopath (9.5%) and osteopath (8.8%). Other forms of CAM used included Reiki therapists, reflexologists, traditional Chinese medicine practitioners, aromatherapists and craniosacral therapists (24.8%).

Conclusion: This Australian study found that, among women with low back pain, a substantial number seek treatment from complementary and alternative medicine practitioners, with the most common being massage therapists, chiropractors and acupuncturists.

Murthy, V., et al. Consultation with Complementary and Alternative Medicine Practitioners Amongst Wider Care Options for Back Pain: A Study of a Nationally Representative Sample of 1,310 Australian Women Aged 60 to 65 Years. *Clin Rheum.* 2014, February; 33(2): 253-262.

ANXIOLYTIC MEDICATION AS AN ADJUNCT TO MORPHINE FOR ACUTE LOW BACK PAIN

For patients with acute low back pain (LBP), numerous medication options are available for pain relief. Anxiety has been associated with increased pain intensity in this patient population, with anxiolysis by nonpharmacological measures found to have a positive effect on pain management. As antihistamines have been found to have a strong anxiolytic-sedative effect, this study evaluated the effectiveness of promethazine as an adjunct to morphine analgesia for acute LBP.

Patients were selected from among those presenting to an emergency department with acute LBP. The participants were randomized to receive either intravenous morphine at 0.1 mg per kilogram or up to 10 mg, administered over 30 minutes, or to a group to receive the same dose of morphine with promethazine 25 mg administered in a similar infusion. The patients rated their pain and anxiety using a 100 mm visual analogue scale before and two hours after completion of the analgesia.

Of a total of 250 patients with acute LBP, 65 were included in the study. Pain relief was similar between the two groups, as was anxiety relief ($p=0.26$ and $p=0.37$, respectively). Drowsiness was noted in 6 of the 30 monotherapy patients and in 27 of the 29 combination therapy group (20% vs. 93.1%, respectively; $p < 0.001$). Mean emergency department stays were 246 minutes in the morphine group and 324 minutes in the combination group ($p=0.01$).

Conclusion: This randomized trial of patients with acute low back pain presenting to an emergency department found that adding an anti-anxiety medication to the intravenous administration of morphine does not significantly affect recovery from acute pain nor relief of anxiety.

Behrbalk, E., et al. Anxiolytic Medication as an Adjunct to Morphine Analgesia for Acute Low Back Pain Management in the Emergency Department. *Spine.* 2014, January; 39 (1): 17-22..

EFFICACY OF PIASCLEDINE FOR OSTEOARTHRITIS OF THE HIP

Osteoarthritis (OA) of the hip affects many individuals, particularly in the

older population. Current treatment strategies include mainly symptom relieving agents, as we still lack an approved disease modifying therapy. Piascledine is an herbal supplement containing avocado- soybean unsaponifiable (ASU), which has an inhibitory effect on interleukin 1, a stimulating effect on collagen synthesis in articular chondrocyte cultures and a potential action on subchondral bone osteoblasts. This study sought to determine whether Piascledine can reduce radiographic progression of symptomatic hip OA.

This randomized, controlled trial included 345 patients with symptomatic hip OA. The subjects were randomized to receive either piascledine at 300 mg daily or a placebo. Radiographs of the standing pelvis, both anterior posterior and oblique views, were taken yearly, with the joint space width (JSW) recorded. The primary outcome measure was the change in JSW on the AP target hip view at year three.

No significant difference was seen in mean JSW between the piascledine and placebo groups. The placebo group had 20% more patients with radiographic evidence of JSW loss of greater than 0.5 mm, as compared to the treatment group ($p=0.04$). No significant difference was found between the groups on clinical measures.

Conclusion: This study of patients with osteoarthritis of the hip found that Piascledine, at 300 mg per day, does not reduce average joint space loss, but reduces the percentage of patients with joint space width deterioration when compared with placebo.

Cadet, M., et al. Randomized, Controlled Trial of Avocado-Soybean Unsaponifiable (Piascledine) Effect on Structure Modification in Hip Osteoarthritis: The ERADIAS Study. *Ann Rheum Dis.* 2014, February 1; 73(2): 376-384.

BOSWELLIC ACID AND OSTEOARTHRITIS

By the age of 65 years, 80% of the population demonstrates radiographic evidence of osteoarthritis (OA). In the treatment of OA, several agents have been used topically, including analgesics. Boswellic acids are potent inhibitors of 5-lipoxygenase (5-LO), an enzyme that catalyzes the generation of leukotrienes, strongly implicated in

OA associated inflammation. This animal study assessed the efficacy of topical and oral boswellic acid preparations for the treatment of posttraumatic OA.

Using a surgical mouse model of OA, medial menisci were destabilized, resulting in articular cartilage loss and synovitis similar to that observed in human OA. Starting on the day of surgery, boswellic acid was administered either orally, at 10 mg/kg, or topically twice-daily for 12 weeks. Control mice received a placebo cream. The mice were assessed for tissue and plasma levels of boswellic acid, cartilage degeneration, osteophytes and synovitis.

At 12 weeks, both the oral and topical preparations were found to significantly attenuate cartilage erosion ($p<0.01$) as compared to placebo. Both preparations significantly reduced knee synovitis and osteophyte formation ($p<0.01$ for each comparison).

Conclusion: This animal model of osteoarthritis found that both oral and topical application of boswellic acid can reduce cartilage loss, synovitis and osteophyte formation as compared with placebo.

Wang, Q., et al. Oral and Topical Boswellic Acid Attenuates Mouse Osteoarthritis. *Osteoarthr Cartil.* 2014, January; 22(1): 128-132.

CONCUSSION REPORTING RATES AT THE CONCLUSION OF COLLEGE ATHLETICS

Many clinicians note that underreporting of concussion remains a significant issue. This study explored potentially unrecognized concussion rates among college student athletes who competed during their college careers.

A 21-item questionnaire was developed, addressing injuries experienced during an intercollegiate athletic career. The three dependent variables for analysis included the reported concussion rate, the acknowledged unreported concussion rate, and the potentially unrecognized concussion rate.

Among participants who self-reported a concussion, most reported one concussion, with 22.2% reporting three or more. Responses identified 26.1% with potentially unrecognized concussions. Overall, 49.7% reported at least one potential concussion that was reported,

unreported or unrecognized. Of those not reporting a concussion, 52.6% reported not knowing that it was a concussion, 52.6% reported not wanting to be removed from future games, 42.1% reported not wanting to be removed from the current game and 42.1% reported not wanting to let down their teammates.

Conclusion: This study found that nearly half of student athletes suffer a potential concussion during their collegiate careers.

Llewellyn, T., et al. Concussion Reporting Rates at the Conclusion of an Intercollegiate Athletic Career. *Clin J Sports Med.* 2014, January; 24(1): 76-79.

FIBRIN SEALANT FOR SYMPTOMATIC DISC DISRUPTION

Chronic low back pain (LBP) has been associated with fissures in the annulus fibrosus. Fissures extending to the outer annulus expose nociceptive nerves to elevated concentrations of pro-inflammatory cytokines. This study assessed the efficacy of intradiscal fibrin sealant as a potential treatment for patients with chronic, discogenic LBP.

Subjects were patients with LBP for more than six months, refractory to pharmacologic conservative and nonoperative modalities. After receiving preintervention intravenous antibiotics, the participants received fibrin sealant injected into the central third of the target disc nucleus. Neurologic examination was performed prior to discharge, with follow-up at 72 hours and at one, four, 13, 26, 52 and 104 weeks after the procedure. Efficacy outcomes included a visual analogue score for LBP, the Roland Morris Disability Questionnaire (RDMQ), a subject global assessment, a subject satisfaction questionnaire and subject employment status.

Fifteen subjects were studied. Clinically significant pain relief, defined as a greater than 30% reduction in LBP, was observed in 87% of subjects at the 26-week endpoint. The mean, individual reduction in LBP was 40.7 mm, and the mean reduction in LBP VAS was 55.6%. Clinically significant improvements in function (RMDQ score, $\geq 30\%$ reduction) were achieved by 73% of the subjects at the 26-week endpoint.

Conclusion: This study of patients with chronic lumbar disc pain

found that intradiscal injection of fibrin sealant may improve pain and function.

Yin, W., et al. Intradiscal Injection of Fibrin Sealant for the Treatment of Symptomatic Lumbar Internal Disc Disruption: Results of a Prospective, Multicenter Pilot Study with 24-Month Follow-Up. **Pain Med.** 2014, January; 15(1):16-31.

HYPOGLOSSAL STIMULATION FOR OBSTRUCTIVE SLEEP APNEA

Obstructive sleep apnea is related to multiple medical morbidities, with sequelae including excessive sleepiness and impaired quality of life. Upper airway stimulation, through the use unilateral stimulation of the hypoglossal nerve, has been developed as a possible treatment option. This multicenter, prospective study assessed the clinical efficacy and safety of this technique.

One hundred twenty-six patients with moderate to severe obstructive sleep apnea were enrolled in this trial. The subjects underwent a surgical procedure, implanting an upper airway stimulating system, with the stimulation electrode placed on the hypoglossal nerve to recruit tongue protrusion. The patients were then followed at months two, three, six, nine and 12. The primary outcome measure was the change in severity of obstructive sleep apnea, as assessed with the apnea-hypopnea index (AHI) and the oxygen desaturation index (ODI).

The median AHI decreased 68% from baseline ($p < 0.001$), with ODI scores decreasing by 70% ($p < 0.001$). Two participants had serious device related adverse events requiring repositioning and fixation of the neurostimulator to resolve discomfort. Temporary tongue weakness occurred in 18%, resolving over days to weeks. At 12 months, clinically meaningful improvements were noted on the Functional Outcomes of Sleep Questionnaire ($p < 0.001$) and the Epworth Sleepiness Scale ($p < 0.001$).

Conclusion: This study of patients with moderate to severe obstructive sleep apnea who had failed CPAP therapy found that hypoglossal nerve stimulation may improve the severity of obstructive sleep apnea and self-reported sleepiness and quality of life.

Strollo, P., et al. Upper Airway

Stimulation for Obstructive Sleep Apnea. **N Engl J Med.** 2014, January 9; 370(2): 139-149.

OMEGA-3 AFTER HEAVY ECCENTRIC EXERCISE

Epidemiologic studies have demonstrated that those who consume more fish and less red meat have a lower incidence of inflammatory diseases. Some studies have found that increased consumption of omega-3 fatty acid can improve lipid profiles, reduce oxidative stress and reduce inflammation. This study tested whether subjects with a higher systemic omega 3 (N3) index display differences in the incidence of delayed onset muscle soreness (DOMS), inflammatory biomarkers and quality of life following vigorous exercise.

Subjects were men and women over the age of 18, randomized to take either six capsules of omega-3 dietary supplement each day or a placebo, prior to exercise. All subjects underwent multiple sets of maximum eccentric forearm extensions, performed on the nondominant arm. Blood was drawn at zero, 24, 48, 70 to 96 hours post exercise for measurement of C-reactive protein (CRP), and creatine kinase. Functional measurement of DOMS was measured on a visual analogue scale, as well as by assessment of extension range of motion and torque. A profile of mood states (POMS) questionnaire was administered to every subject at each time point.

Subjects were 69 male and female college students. At 72 and 96 hours, significant differences were found between the two groups in DOMS worst pain scores ($p = 0.031$ and $p = 0.035$, respectively). No significant differences were found between the two groups on measurements of extension and torque. Scores on the POMS demonstrated greater emotional stability at 72 hours among those in the higher N3 index (> 4) group than in the lower N3 index (< 4) group ($p < 0.05$). In addition, an elevated N3 index was related to reduced CRP levels at 24 hours ($p = 0.001$) and blood lactate levels immediately after exercise ($p = 0.03$).

Conclusion: This study of college students performing maximum eccentric exercise found that omega-3 supplementation can reduce delayed onset muscle soreness and positively affect subjective quality-of-life.

Lembke, P., et al. Influence of Omega

-3(N-3) Index on Performance and Well-Being in Young Adults after Heavy Eccentric Exercise. **J Sports Sci Med.** 2014, January; 13(1): 151-156.

ROMOSUZUMAB FOR OSTEOPOROSIS

Antiresorptive drugs for osteoporosis increase bone mineral density (BMD) and prevent the progression of structural damage, but may not restore bone structure. Sclerostin, an osteocyte-secreted glycoprotein, has been identified as a pivotal regulator of bone formation. This substance impedes osteoblast proliferation and function, thereby decreasing bone formation. Romosozumab is a humanized monoclonal sclerostin antibody designed to affect postmenopausal osteoporosis. This phase 2 trial evaluated the efficacy and safety of this medication for the treatment of postmenopausal women with low bone mass.

This randomized trial included 367 elderly women with low BMD, randomized to either one of five dosing regimens of subcutaneous Romosozumab, a group receiving alendronate at 70 mg weekly, a group receiving Teraparotide at 20 μ g daily or a placebo control group. BMD was measured at baseline in the lumbar spine and femur, and then again at three, six and 12 months. In addition, levels of bone formation markers were compared among groups.

At 12 months, patients taking Romosozumab had significantly increased BMD at the lumbar spine, regardless of the dose frequency and dose level ($p < 0.001$). Similar gains were also seen at the total hip and the femoral neck ($p < 0.001$ for all comparisons). The largest gains were mg/month group, with the increases significantly greater than those observed in the alendronate or teriparatide groups ($p = 0.001$ for all comparisons). In all of the Romosozumab groups, transitory increases were noted in bone formation markers and sustained decreases in bone resorption markers.

Conclusion: This study of postmenopausal women with low bone mineral density found that treatment with Romosozumab is mineral density and bone formation, with decreased bone resorption.

McClung, M., et al. Romosozumab in Postmenopausal Women with Low Bone Mineral Density. **N Eng J Med.** 2014, January 30; 412-420.

STEM CELLS AS AN ADJUNCT FOR MENISCAL REPAIR

The majority of arthroscopic knee surgeries in the United States are performed for surgical repair or partial excision of a meniscal tear. As recent data has questioned the efficacy of that surgery, there is a strong interest in improving the outcomes of patients in need of surgical repair. This study was designed to determine whether mesenchymal stem cells can improve the outcome of meniscal repair surgery, and to assess their effects on osteoarthritis of the knee joint.

This double-blind, randomized, controlled trial included 60 patients with meniscal injuries who were candidates for partial medial meniscectomy. A single, intra-articular knee injection was given to all subjects seven to 10 days post-surgery. The participants were randomized to receive one of three injections. Group A received allogenic mesenchymal stem cells, at a concentration of 50×10^6 , group B at a concentration of 150×10^6 and group C, a control group, received the vehicle only. The subjects were

followed for two years for adverse events, shifts in immunological outcomes, MRI changes in meniscal volumes, total Lysholm knee scores and changes in pain.

At two years, visual analog scale scores for pain were significantly improved in group A, as well as in group B, as compared with controls ($p=0.05$ and $p=0.04$, respectively). Using a predefined criterion of significance as a greater than 15% improvement in meniscal volume at 12 months, this criterion was achieved by 24% of the patients in group A, six percent in group B ($p=0.022$) and none in the control group.

Conclusion: This study of patients with meniscal tear injury found that the addition of stem cells following partial medial meniscectomy may result in improved outcomes as compared to surgery alone.

Vangsness, C., et al. Adult Human Mesenchymal Stem Cells Delivered via Intra-Articular Injection into the Knee following Partial Medial Meniscectomy. *J Bone Joint Surg.* 2014, January; 96-A (2): 90-98.

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