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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. **Osteoarth Cartil.** 2014, January; 22(1): 128-132.

FIBRIN SEALANT FOR SYMPTOMATIC DISC DISRUPTION

Chronic low back pain (LBP) has been associated with fissures in the annulus fibrosis. 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, ≥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.

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 acetyl-cholinesterase 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.

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.

ADALIMUMAB FOR ACTIVE ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS) is characterized by inflammation of the axial skeleton, and can cause considerable disability and pain. Anti-tumor necrosis factor therapy is recommended for those who do not respond to conventional therapies. This study was designed to determine the safety and efficacy of adalimumab for the treatment of AS in Chinese patients.

Eligible patients were between 18 and 65 years of age, all diagnosed with AS. Following screening, the subjects were randomized to receive either adalimumab at 40 mg or a matching placebo subcutaneously every other week. A 12-week, double-blind phase was followed by a 12-week open label phase in which all patients received the treatment medication. Efficacy and safety of the treatment and placebo were assessed at weeks zero, two and four, and then every four weeks thereafter. The primary efficacy endpoint was the percentage of patients achieving the ASAS20 response criteria at week 12, defined as an improvement of ≥20% and an absolute improvement of ≥10 units from baseline in at least three of four domains.

One hundred fifteen patients were randomized to the placebo group and 229 to the treatment group. A total of 67.2% of the treatment group and 30.4% of the placebo group achieved the ASAS20 response at week 12 ($p<0.001$). The ASAS20 rates were significantly different as early as week two. At week 12, the efficacy of the treatment was demonstrated for several secondary efficacy variables, including chest expansion.

Conclusion: This study of Chinese patients with ankylosing spondylitis found that adalimumab can provide significant improvement in symptoms, physical function and

quality of life, as compared with placebo.

Huang, F., et al. Efficacy and Safety of Adalimumab in Chinese Adults with Active Ankylosing Spondylitis: Results of a Randomized, Controlled Trial. **Ann Rheum Dis**. 2014, March; 73(3): 587-594.

PIMAVANSERIN FOR PARKINSON'S DISEASE PSYCHOSIS

Up to 10 million people worldwide have Parkinson's disease (PD). This neurodegenerative disease is marked by motor dysfunction and non-motor symptoms, including psychosis. Typical antipsychotics can cause profound dopamine D-2 antagonism and worsen Parkinsonism. Therefore, atypical antipsychotics are commonly used. Pimavanserin is a selective serotonin five 5-HT2A inverse agonist without dopaminergic, andrenergic, histaminergic or muscarinic affinity. This study assessed the efficacy and safety of this medication for the treatment of PD related psychosis.

This randomized, double-blind, parallel group, placebo-controlled trial included patients 40 years of age or older, all diagnosed with PD psychosis. The subjects were randomized to receive either Pimavanserin at 40 mg per day or a matched placebo. The primary outcome measure was the antipsychotic benefit, as assessed with the PD adapted scale for the assessment of positive symptoms (SAPS-PD), at baseline and at 15, 29 and 43 days. Secondary outcomes included change by day 43 in clinical global impression of severity.

A total of 185 patients were randomized and included in the analysis. In the primary analysis, SAPS-PD scores at day 43 demonstrated significantly greater improvement in psychosis in the treatment group than in the placebo group (p=0.001). More patients in the treatment group had a greater than 20% reduction in SAPS-PD scores (p=0.02). Ten patients in the treatment group and two in the placebo group discontinued the study due to adverse events.

Conclusion: This study of patients with PD found that the atypical antipsychotic, Pimavanserin, may be effective for the treatment of psychosis in this population.

Cummings, J., et al. Pimavanserin for Patients with Parkinson's Disease Psychosis: A Randomized, Placebo-Controlled Phase 3 Trial. **Lancet.** 2014, February; 383:9916: 533-540.

IMMEDIATE BLOOD PRESSURE REDUCTION AFTER ACUTE ISCHEMIC STROKE

Clinical trials have documented that lowering blood pressure reduces the risk of stroke in hypertensive and normotensive patients with a history of stroke or transient ischemic attack. However, the effect of immediate antihypertensive treatment in patients with acute ischemic stroke who present with elevated blood pressure is much less certain. This multicenter, randomized, controlled trial tested whether moderate lowering of blood pressure within the first 48 hours after the onset of acute ischemic stroke can reduce death and major disability.

This randomized, controlled trial was conducted in 26 hospitals across China. Eligible patients had an ischemic stroke with systolic blood pressure elevated between 140mmHg and 220mmHg. The participants were randomly assigned to receive antihypertensives aimed at lowering blood pressure 10 -25% within the first 24 hours and achieving blood pressure less than 140/90mmHg within seven days, or to a control group discontinuing all antihypertensive medications during their hospitalization. The primary outcome measure was the combination of death and major disability at 14 days or hospital discharge.

Of the 4,071 patients eligible, 2,038 were assigned to receive antihypertensive treatment and 2,033 to the control group. At 14 days or hospital discharge, 33.6% in the treatment group and 33.6% in the control group experienced death or major disability. The odds of a higher modified Rankin scale score were not associated with antihypertensive treatment. At three months, 25.2% in the treatment group had died or had experienced major disability, as compared with 25.3% in the control group. The median modified Rankin scale score, death rate and vascular disease events were similar between the two groups. None of the differences were statistically significant.

Conclusion: This study of patients with acute ischemic stroke found that blood pressure reduction during hospitalization does not reduce the likelihood of death or major disability at 14 days.

He, J., et al. Effects of Immediate Blood Pressure Reduction on Death and Major Disability in Patients with Acute Ischemic Stroke: The CATIS Randomized Clinical Trial. **JAMA.** 2014, February 5; 311(5): 479-489.

QUETIAPINE FUMARATE FOR MAJOR DEPRESSION WITH COMORBID FIBROMYALGIA

Patients with fibromyalgia (FM) are at increased risk for mood disorders, with concurrent depression as high as 22 to 40%. This study assessed the efficacy of quetiapine fumarate extended-release (XR), an antidepressant/atypical antipsychotic, for the treatment of depression and pain in patients with FM and major depressive disorder.

This eight-week, double-blind, randomized, controlled trial included patients diagnosed with major depressive disorder as well as FM. A treatment group received quetiapine XR, starting at a dose of 50 mg per day for the first two days, and then titrated up to 150 mg per day. After two weeks, the dosage could be doubled to 300 mg per day at the discretion of the investigator. Patients in the placebo group received tablets identical in appearance to the investigational medication. The primary outcome measure was the mean change on the Hamilton-D from baseline to week eight.

A total of 120 patients were randomized, including 61 in the treatment arm and 59 in the placebo arm. The mean dosage of quetiapine was 224 mg per day, with 300 mg received by 34 of the 50 patients. The mean change from baseline to week eight in Hamilton D scores was significantly greater in the treatment group than in the placebo group (p= 0.001). At week eight, improvements in all secondary outcome scores except the Sheehan Disability Score were significantly greater in the quetiapine XR group than in the placebo group. These measures included the Brief Pain Inventory-

Short Form (p=0.007) and the Fibromyalgia Impact Questionnaire (p=0.022).

Conclusion: This study of patients with fibromyalgia and major depression found quetiapine extended-release to be effective in treating both conditions.

McIntyre, A., et al. Quetiapine Fumarate Extended-Release for the Treatment of Major Depression with Comorbid Fibromyalgia Syndrome. **Arthr Rheum.** 2014, February; 66(2): 451-461.

HYPOGLYOSSAL 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.

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.

ADALIMUMAB AND JOINT DAMAGE IN EARLY RHEUMATOID ARTHRITIS

Given the significant impact that biologic therapies have on rheumatoid arthritis (RA), some have advocated for the earlier use of these medications. The efficacy and safety of the tumor necrosis factor-alpha inhibitor, Adalimumab, has been well established as a monotherapy or combined with methyltrexate (MTX). This study compared the efficacy and safety of early intervention with adalimumab plus MTX versus MTX alone for inhibiting radiographic progression in MTX-naive Japanese patients with RA.

This study included patients at least 20 years of age, all diagnosed with RA. The subjects were randomized to receive either subcutaneous adalimumab, 40 mg, or a placebo every other week in combination with oral MTX at 6 mg/ wk or MTX alone at up to 8 mg/wk. All participants were assessed by radiographs of the hands and feet and scored by two independent readers held blind to the treatment assignment.

A total of 171 patients received the combination medications and 163 received MTX alone. Radiographic progression was significantly more reduced in the combination group at 26 weeks than in the MTX group alone (p<0.001).

Conclusion: This study of patients with rheumatoid arthritis found that a combination of methyltrexate and adalimumab is superior to methyltrexate alone in preventing joint deterioration.

Takeuchi, T., et al. Adalimumab , a Human Anti-TNF Monoclonal Antibody, Outcome Study for the Prevention of Joint Damage in Japanese Patients with Early Rheumatoid Arthritis: The HOPEFUL

1 Study. **Ann Rheum Dis.** 2014, March; 73: 536-543.

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.

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 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.

CORONARY ARTERY BYPASS GRAFTING VERSUS PERCUTANEOUS CORONARY INTERVENTION

Coronary artery disease is a leading cause of death worldwide. Noting that recent trials comparing coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) have been under-powered, the authors of this study employed a meta-analysis of randomized trials to better understand the difference in outcomes between these surgical techniques.

A systematic search of the medical literature was completed, reviewing randomized, controlled trials which paired CABG and PCI. All studies had dedicated CABG and PCI arms, had an average follow-up duration of at least one year, used arterial grafting and used stents in at least 70% of the PCI arm.

Of the trials reviewed, six were included in the analysis, for a total of 6,055 patients. The analysis revealed a 27% greater reduction in total mortality with the use of CABG, as compared with PCI (p=0.001). In addition, a 42% greater reduction was found in myocardial infarction among those treated with CABG as compared with PCI (p<0.001). The analysis revealed an insignificant trend towards excess strokes among those treated with CABG as compared with PCI (p=0.06). Repeat revascularizations (p<0.001) and major, adverse cardiac and cerebrovascular events were significantly more reduced with CABG than with PCI (p<0.001).

Conclusion: This meta-analysis of randomized, controlled trials found that, among patients with multivessel coronary disease, coronary artery bypass grafting significantly reduces long-term, all-cause mortality and myocardial infarctions as compared with percutaneous coronary intervention.

Sipahi, I., et al. Coronary Artery Bypass Grafting versus Percutaneous Coronary Intervention and Long-Term Mortality and Morbidity in Multivessel Disease: Meta-Analysis of Randomized Clinical Trials of the Arterial Grafting and Stenting Era. **JAMA Intern Med.** 2014, February; 174(2): 223-230.

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.

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 $50x10^{6}$, group B at a concentration of $150x10^{6}$ 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.

PLATELET RICH PLASMA FOR TENNIS ELBOW

Lateral epicondylitis, commonly referred to as tennis elbow, was first described in 1883. If conservative treatments fail to improve pain and tenderness, second line treatments such as cortisone injections or platelet rich plasma injections have been suggested. This study evaluated the efficacy of needling, with and without the injection of platelet rich plasma, as a treatment for chronic lateral epicondyle tendinopathy.

This double-blind, prospective, multicenter, randomized trial included patients diagnosed with lateral epicondylitis, with pain of at least 50 mm on a 100 mm visual analogue scale, and all unresponsive to conventional treatment. Participants had their extensor tendons needled, with the treatment group receiving two to three mL of platelet rich plasma. The active control group received bupivicaine without platelet rich plasma. The primary outcome measure was pain upon resisted wrist extension, as measured by a visual analogue scale at four, eight, 12 and 24 weeks. Secondary outcome measures included the Patient-Rated Tennis Elbow Evaluation, and an extended wrist examination.

At each follow-up, the platelet rich plasma group reported more improvement in pain scores as compared to the active control group. These differences were statistically significant at eight and 24 weeks. At final follow-up, the treatment group reported improvement of 71.5%, as compared with 56.1% in the active control group ($p=0.019$).

Conclusion: This double-blind, controlled study of patients with lateral epicondylitis found clinically meaningful improvement in patients treated with platelet rich plasma as compared with controls.

Mishra, A., et al. Efficacy of Platelet Rich Plasma for Chronic Tennis Elbow. A Double-Blind, Prospective, Multicenter, Randomized Controlled Trial of 230 Patients. **Am J Sports Med.** 2014, February; 4(2): 463-471.

PHYSICAL ACTIVITY, COGNITION AND WALKING IN MULTIPLE SCLEROSIS

Slowed cognitive processing speed (CPS) is common among patients with multiple sclerosis (MS). While evidence exists of a coupling between walking performance and CPS among those with MS, no randomized trials have directly studied this effect. This study examined the efficacy of physical

activity behavioral intervention for improving CPS and walking performance among patients with MS.

Eighty-two patients with MS who were randomly allocated to an intervention or a wait list control group. Over a six-month period, those in the intervention group visited a study website, wore a Yamax SW-401 Digiwalker pedometer, completed a log book, used Goal Tracker software and participated in one-on-one video coaching sessions. All were assessed for CPS using the Symbol Digit Modalities Test (SDMT), for walk performance using the six-minute walk test (6MW), for physical activity with the Physical Activity Questionnaire (IPAQ) and for disability using the Patient-Determined Disease Steps (PDDS) scale.

A total of 39 patients were included in the wait list control group and 37 in the testing group. The overall compliance with the behavioral intervention was 80.6% in the treatment group. The intervention increased walking performance as measured by the 6MW regardless of disability status, while deterioration was seen in the control group. Using a mixed model analysis of variance, a time by condition by disability group interaction was noted for SDMT test scores, with a significant time by condition action seen in 6MW distance, as compared with the control group.

Conclusion: This study of patients with multiple sclerosis found that cognitive scores improve with physical activity intervention.

Sandroff, B., et al. Randomized, Controlled Trial of Physical Activity, Cognition, and Walking in Multiple Sclerosis. **J Neurol**. 2014, February; 261(2): 363-372.

INITIATING PHYSICAL ACTIVITY IN LATER LIFE AND HEALTHY AGING

Emerging evidence suggests that regular physical exercise is among the most important lifestyle factors for the maintenance of good health as one ages. This study examined the association between physical activity and healthy aging over an eight-year follow-up in the English Longitudinal Study of Ageing (ELSA).

The ELSA cohort consists of men and women born before February 1952. This prospective study of community dwelling older adults measured self-reported physical activity, assessed at baseline, 2002 to 2003. The subjects were reassessed every two years, and then for healthy aging at eight years. With repeated questionnaires, researchers were able to determine new onset activity. Healthy aging was defined as surviving without major chronic disease, depressive symptoms or physical or cognitive impairment. Physical activity was measured as the frequency and regularity of exercise routinely practiced.

The final sample comprised 3,454 individuals with an average age of 63.7 years at baseline. A dose response association was found between baseline physical activity and healthy aging after eight years, with those reporting moderate or vigorous activity 3.1 fold and 4.3 fold, respectively, more likely to be healthy agers as compared with inactive participants. Of those who became active during the study period, this activity was associated with improved healthy aging as compared with those who remained inactive.

Conclusion: This study of community-based individuals found that remaining active, or beginning active exercise in later life, is associated with healthier aging.

Hamer, M., et al. Taking up Physical Activity in Later Life and Healthy Ageing: The English Longitudinal Study of Ageing. **Br J Sports Med**. 2014, February; 48(3): 239-243.

LEVODOPA INTESTINAL GEL FOR PARKINSON'S DISEASE

Over time, patients with Parkinson's disease (PD) receiving long-term oral levodopa treatment experience a duration of response that becomes shorter, with motor fluctuations and dyskinesias developing. Levodopa/carbidopa intestinal gel (LCIG) has been found to produce a more stable plasma concentration of levodopa in patients with advanced PD. This prospective study assessed the efficacy of LCIG on patients' symptoms and subjective response.

The subjects were 59 patients with advanced PD, with optimized oral medication, but with continued fluctuations in motor symptoms and dyskinesias. The study medication, LCIG, was initially administered by a temporary naso-duodenal tube for three to four days, followed by permanent percutaneous endoscopic gastrostomy (PEG). The patients were assessed for motor complications, gait disorders, dysphagia, dysarthria, quality-of-life (QOL) and clinical global improvement. After seven years, 41 patients remained in the study.

The perceived QOL improved in all patients, with 44% noting great improvement. Autonomy was rated as greatly improved in 30% and moderately improved in 51%. Clinical global improvement was found to be greatly improved in 62% and moderately improved in 28%. The majority of patients (54%) reported improvement in gait, whereas dysphagia improved in only 33% and dysarthria in only 18%.

Conclusion: This study of patients with advanced Parkinson's disease found that the use of levodopa/carbidopa intestinal gel results in improvement in quality-of-life, autonomy and global status.

Zibetti, M., et al. Levodopa/Carbidopa Intestinal Gel Infusion and Advanced Parkinson's Disease: A Seven-Year Experience. **Euro J Neurol.** 2014, February; 21(2): 312-318.

ROMOSOZUMAB 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 regiments of subcutaneous Romosozumab, a group receiving alendronate at 70 mg weekly, a group

(Continued from page 2)

receiving Teraparatide at 20 µg 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 observed in the Romosozumab 210 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 associated with increased bone 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.

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