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EFFECTS OF GROWTH HORMONE ON FRACTURES AND QUALITY-OF-LIFE

In a previous study, women with postmenopausal osteoporosis, treated for three years with growth hormone (GH), were found to have increased bone mineral density (BMD) at one year after treatment termination. This study reviewed the BMD data and fractures, after 10 years, of women who had received growth hormone for at least three years.

This randomized, double-blind, placebo-controlled trial involved 80 postmenopausal women with osteoporosis. All women received 750 mg of calcium and 400 units of vitamin D and were randomized to receive either recombinant human GH at one unit per day, two point five units per day, or a placebo. The GH injections continued for three years. All women were followed for 10 years. The subjects were invited for reevaluation after a mean of 12 years' follow-up at the age of 67 to 76 years. At follow-up, measurements included body composition, bone measurements, quantitative ultrasound measurements, lifestyle factors and quality-of-life measures. A random population sample of 2,400 men and women served as population controls.

Before treatment, 56% of the women in the treatment group had sustained a fracture, while 28% sustained fractures in the 10 years of the study (p=0.0003). In the control group, three percent had sustained a fracture before the study and 32% sustained a fracture in the 10 years of the study (p=0.0008). At 10 years, BMD had decreased to similar levels as before treatment, but was still higher in the 2.5 U GH group than in the other two groups.

Conclusion: This long-term follow-up study of postmenopausal women with osteoporosis found that growth hormone treatment can reduce the incidence of fracture seven years after treatment cessation.

Krantz, E., et al. Effect of Growth Hormone Treatment on Fractures and Quality-Of-Life in Postmenopausal Osteoporosis: A 10-Year Follow-Up Study. The **J Clin Endocrin Metab.** 2015, September; 100(9): 3251-3259.

BALANCE PROGRAM FOR FALL PREVENTION FOR OLDER WOMEN

While previous studies have demonstrated that balance training may be effective in reducing falls in older, community dwelling individuals, most trials have lacked the power to show the effect of this training on injurious falls. This study was designed to better understand the effect of balance training on the rate of injuries resulting from falls in the elderly.

This multicenter, randomized, controlled trial included 20 sites across France, from December of 2007 to June of 2013. Women ages

35 to 85 years of age, living in the community were examined. Those deemed to be at high risk of falling were included. Of those included, 352 patients in the treatment group underwent one-hour weekly sessions for two years, focusing upon improving postural stability, balance and coordination. Subjects in the control group were given brochures concerning fall prevention. The primary outcome measure was the number of serious injuries (resulting in fractures) and moderate injuries (bruising resulting in a functional decline of at least three days' duration or requiring medical attention) resulting from falls.

During the study period, 397 falls with injury occurred among the 189 women in the control group, and 305 among the 170 women in the intervention group. Over the two-year intervention period, the fall injury rate was 19% lower in the intervention group than in the control group (p=0.004). The rates of moderately serious falls decreased by similar magnitudes.

Conclusion: This study of elderly women at risk for falls found that once per week progressive balance training can reduce the risk of injurious falls by 19%.

El-Khoury, F., et al. Effectiveness of Two-Year Balance Training Program on Prevention of Fall Induced Injuries in at Risk Women Aged 75 to 85 Living in Community: Ossebo Randomized, Controlled Trial. **Br Med J**. 2015; 351: H3830.

TESTOSTERONE ADMINISTRATION AND SUBCLINICAL ATHEROSCLEROSIS IN OLDER MEN

Testosterone sales have increased significantly over the past decade, especially to older men. Some studies have raised concern that testosterone supplementation might increase the risk of cardiovascular disease events. This study was designed to determine the effect of increasing circulating testosterone concentrations to a mid- normal range for young men with low or low-normal testosterone levels on subclinical atherosclerosis.

The Testosterone's Effects on Atherosclerosis Progression in Aging Men (TEAAM) trial was a randomized, double-blind, placebo-controlled, trial involving community dwelling men, 60 years or older with low or low-normal testosterone levels. Eligible participants were randomized to daily receive either a placebo gel or testosterone gel, with the latter adjusted such that the total testosterone concentrations were

between 500 ng/dL and 900 ng/dL. Distal common carotid intima media thickness was measured at baseline and every six months during the intervention period. The total coronary artery calcium score was determined using multidetector-row computed tomography (MDCT) at baseline and at 18 and 36 months. The participants were also assessed for sexual function and health-related quality-of-life.

Subjects were 306 men with a mean age of 67.6 years and a body mass index of 28.1. The per year rate of change in intima-media thickness and the change in coronary artery calcium did not differ significantly between groups (p=0.30 and p=0.48, respectively). Intercourse satisfaction scores improved significantly more in the treatment group, although the differences were thought to be modest (p=0.05). Self-reported physical function, composite health- related quality-of-life and adverse events did not differ significantly between the two groups.

Conclusion: This study of older men with low or low normal testosterone levels found that three years of testosterone supplementation did not affect the change in common carotid artery intima media thickness or coronary artery calcium, nor did it improve overall sexual function or health-related quality-of-life.

Basaria, S., et al. Effects of Testosterone Administration for Three Years on Subclinical Atherosclerosis Progression in Older Men with Low or Low Normal Testosterone Levels. **JAMA**. 2015, August 11; 314(6): 570-581.

EXERCISE AND PATELLAR CARTILAGE IN WOMEN WITH MILD KNEE OSTEOARTHRITIS

Knee osteoarthritis (OA) is characterized by a loss of, and degeneration of, hyaline cartilage. This study investigated the effects of 12 months of supervised aerobic/step aerobic exercise program on patellar cartilage.

This 12-month, randomized, controlled trial included postmenopausal women with knee pain on most days, and grade one to two Kellgren-Lawrence radiographic tibiofemoral joint OA. The subjects were randomized to one of two experimental arms; an aerobic/step aerobic training group or a non-training control group.

The exercise group performed 55-minute sessions of an aerobic and step aerobic jumping exercise program three times per week, progressing in intensity for 12 months. The control group was asked to maintain their usual activities. Daily activity of all participants was measured with an accelerometer. Cartilage measurements were made through MRI, with the secondary outcomes including muscle force, muscle power and cardiorespiratory fitness.

At 12-month follow-up, the full patellar cartilage T2 relaxation time values had improved in the exercise group, suggesting improved cartilage quality (p=0.018). Positive effects were noted in the lateral and medial segments of the joint, as well as in the total deep zone (p=0.013). While the exercise group showed better improvement in pain, OA symptoms, and quality-of-life scores, the difference between the exercise and control groups did not reach statistical significance.

Conclusion: This randomized, controlled, high-impact exercise trial involving postmenopausal women with mild osteoarthritis of the knee found that T2 relaxation time decreased, indicating improved patellar cartilage quality, after 12 months of exercise.

Koli, J., et al. Effects of Exercise on Patellar Cartilage in Women with Mild Knee Osteoarthritis. M**ed Science in Sports Exer**. 2015, Sept; 47(9): 1767 -1774.

FUNCTIONAL EFFECTS OF FAMPRIDINE FOR MULTIPLE SCLEROSIS

The potassium channel blocker 4-aminopyridine (Fampridine) has been found to improve nerve conduction in demyelinating neurons, and has been approved by the European Medicines Agency for the treatment of patients with Multiple Sclerosis (MS) with walking disability. This study investigated the benefits of Fampridine SR on parameters of gait, fatigue and quality-of-life among patients with MS.

This prospective, open label, cohort study enrolled 120 adults with MS. All were assessed for walking with the Timed 25 Foot Walk Test (T25FW), the Two-Minute Walk Test (2MWT) and the Self Perceived Multiple Sclerosis Walking Scale (MSWS-12) at baseline and at 14 days. Those in the treatment group received Fampridine SR, 10 mg twice per day, for 14 days, continuing for three months only among responders (at least 50% improvement by day 14 on one of these tests). Additional assessments included the Nine Hole Peg Test, a self-assessed fatigue visual analogue scale (F-VAS), the Fatigue Severity Scale (FSS), the GAITRite Walkway System for gait parameters and the 12-Item Short Form Health Survey (SF-12). Outcomes were compared between responders and non-responders at day 14.

Of the initial cohort, 112 completed drug treatment and measures at day 14. Of those, 74% were responders, with significant improvements on the T25FW ($p<10^{-4}$), the 2MWT ($p<10^{-4}$) and the MSWS–12 ($p<10^{-4}$). Responders also demonstrated improvement on the secondary outcomes for hand function ($p<0.001$), fatigue ($p<001$) and quality-of-life ($p<0.001$). Findings were sustained at three-month follow- up.

Conclusion: This study of patients with multiple sclerosis found that treatment with Fampridine SR can improve several parameters of gait, as well as hand function and fatigue.

Allart, E., et al. Sustained Release Fampridine In Multiple Sclerosis: Effects on Gait Parameters, Arm Function, Fatigue and Quality-Of-Life. **J Neurol.** 2015, August; 262: 1936-1945.

HAND EXERCISES FOR OSTEOARTHRITIS

Hand osteoarthritis (HOA) is highly prevalent, and poses functional burdens on those affected. Evidence of the effectiveness of non-pharmacologic therapies such as range of motion and strengthening exercises is controversial, and lack randomized, controlled studies. This study further examined the effect of hand exercises on women with HOA.

This prospective study included

80 women with HOA between the ages of 18 and 80 years of age. The patients were randomized to receive either information regarding HOA and an exercise program or information alone. The exercise program involved a rubber ball to provide resistance in the grip while rubber bands were used to provide resistance to the thumb abduction/extension. The patients were assessed at baseline and at three months with activity measured by the Patient-Specific Functional Scale (PSFS). Data regarding grip strength and webspace were also collected at baseline and at study completion.

A significant difference was found between groups in the PSFS scores, favoring the exercise group ($p<0.001$). Better improvements were also noted in the treatment group as compared to the control group in joint pain ($p=0.02$), grip strength ($p<0.001$), thumb webspace ($p=0.018$ (right) and $p=0.007$ (left)) and hand fatigue ($p=0.05$).

Conclusion: This randomized, controlled trial demonstrated that home-based hand exercises are effective in improving activity performance and pain in patients with hand osteoarthritis.

Hennig, T., et al. Effect of Home-Based Hand Exercises in Women with Hand Osteoarthritis: A Randomized, Controlled Study. **Ann Rheum Dis**. 2015, Aug; 74(8): 1501-1508.

HIGH-VOLUME INJECTION FOR RECALCITRANT PATELLAR TENDINOPATHY

Preliminary studies of patients with recalcitrant tendinopathy and evidence of neovascularization have suggested that high-volume, image- guided injection (HVIGI) may decrease pain and improve functional activities. This study was designed to determine the short-term effect of HVIGI on patients with recalcitrant tendinopathy of the patellar tendon.

Patients were included if they had a clinical and imaging diagnosis of patellar tendinopathy, unresponsive to three months of eccentric exercise and other common treatments. All thirty-two participants underwent an ultrasound guided bolus of 40 ml of normal saline, mixed with 10 ml of 0.5% bupivacaine and 62,500 IU of apoprotinin, placed posterior to the patellar tendon, immediately adjacent to the area of neovascularization. At 15 months' follow-up, an independent observer assessed the patients on the VAS scale of pain and the Victorian Institute of Sport Assessment-Patellar Tendon (VISA-P) questionnaire. The subjects were asked to rate the results of the procedure according to the presence of pain and to return to their sporting activity.

In all patients, neovascularization disappeared immediately after the injection. At last follow-up, the mean VISA-P, pain VAS and function VAS scores had significantly improved as compared with baseline. Of the 32 active patients, 72% return to sport at the same level as before the onset of symptoms. In twenty-five cases a further injection was performed at an average of 2.7 weeks. At final follow-up, 23 of 32 (72%) athletes were classified as good to excellent, and nine as poor.

Conclusion: This study of patients with recalcitrant patellar tendinopathy found that high-volume image guided injections can improve pain and function scores, with improved return to sport.

Maffulli, N., et al. High-Volume, Image-Guided Injection for Recalcitrant Patellar Tendinopathy in Athletes. **Clin J Sp Med**. 2015 DOI: 10.1097/ JSM.0000000000000242

ISOMETRIC EXERCISE FOR PATELLAR TENDINOPATHY

For patients with patellar tendinopathy (PT), eccentric exercise is commonly prescribed. However, this exercise is often painful to complete. This study was designed to determine whether isotonic or isometric exercise can induce pain relief in patients with PT.

This single blind, randomized, crossover trial included six, male volleyball athletes with PT. At baseline, tendon pain and quadriceps strength were tested. The single leg decline squat (SLDS) was used as a primary outcome measure. The athletes were asked to complete a Victorian Institute of Sport Assessment-Patellar Tendon (VISA-P) questionnaire of patellar tendon pain and function.

During a maximum voluntary isometric contraction (MVIC), the athletes completed five efforts of 45 seconds each, with a two-minute recovery between sets. During an isotonic condition, the subjects exercised at 70% of their one repetition maximum, with five sets of

45 seconds duration. Baseline measures of corticospinal excitability and short interval intracortical inhibition were obtained by transcranial magnetic stimulation.

At baseline, the participants had a mean VISA-P of 52.8, with isometric exercise reducing pain on the SLDS from a mean of 7/10 to 0.17/10, with the reduction sustained at 45 minutes ($p<0.001$). During the isotonic condition, pain on the SLDS was reduced from 6.3/10 to 3.75/10 ($p=0.04$), although this reduction was not sustained at 45 minutes. A significant increase in MVIC torque was observed immediately after isometric intervention ($p<0.001$), and was sustained at 45 minutes after intervention, that was not significant in the isotonic group.

Conclusion: This small study of volleyball athletes with patella tendinopathy found that a single bout of isometric contractions can result in immediate pain relief lasting for at least 45 minutes, with a concurrent increase in maximal voluntary isometric contraction.

Rio, E., et al. Isometric Exercise Induces Analgesia and Reduces Inhibition in Patellar Tendinopathy **Br J Sp Med**. 2015, October; 49(19):1277-1283.

MENISCAL TRANSPLANTATION

Meniscal transplantation has been performed for many years, with few long-term studies published to date. This study was designed to better understand the survivorship rates and long-term functional outcomes of patients undergoing meniscal transplantation.

Thirty-eight patients with articular cartilage deterioration underwent meniscal transplants of 40

cryopreserved menisci. In a previous evaluation at a mean of 3.3 years, the characteristics of the transplants had

been assessed by MRI. At that time, the transplants had been rated as normal in 43%, as altered in 30% and as failed in 28%. Those who did not undergo a follow-up surgery were followed for a mean of 11 years.

The mean age at surgery was 30 years. Of the original 40 patients, eleven required follow-up surgery in the initial study at 0.2 to 1.5 years, and 11 other transplants required surgery at 6.1 to 14.5 years. Therefore, of the initial 40 transplants,18 completed the long-term evaluation at a mean of 13.7 years. At follow-up, the patients were evaluated clinically and radiographically.

At baseline, 72% of the patients had moderate or severe pain with daily activities, while, at follow-up, 11% had such pain ($p<0.0001$). At baseline only one of the 18 patients participated in sports, while at follow - up, 14 of 18 were participating. A survivorship analysis revealed that the probability of transplant survival was 88% at five years, 63% at ten years, and 40% at fifteen years. The mean time at failure was 8.2 years for medial transplants and 7.6 years for lateral transplants.

Conclusion: This long-term follow-up of 40, consecutive medial and lateral meniscal transplants found that 22 required repeat surgery and that, among the others, symptoms improved, and return to sport activities occurred in the majority of patients.

Noyes, F., et al. Meniscal Transplantation in Symptomatic Patients under Fifty Years of Age. **J Bone Joint Surg**. 2015, August 5; 97(15): 1209-1219.

PHYSICAL EXERCISE AND NEUROINFLAMMATION, NEUROPLASTICITY, NEURODEGENERATION AND BEHAVIOR

The effects of exercise on the central nervous system in health and in neurodegenerative and cerebrovascular disorders have been a recent focus of research. This study reviewed the effects of different types of exercise on experimental models of neurodegenerative disorders, particularly Parkinson's disease and Alzheimer's disease.

This literature review used articles in PubMed from 1980 through August of 2014. The search focused on physical exercise, training, neuroinflammation, neuro-degeneration, intensity, high-intensity interval training, cytokines, behavior, cognition, in rodents and in humans. Exercise was found to lead to increased levels of neurotrophic factors, as well as changes in levels of different cytokines and altered microglial functions in different parts of the brain that could be beneficial for patients with neurodegenerative diseases.

Exercise was also shown to affect cell surface receptors, such as the TLR and adrenergic receptors, as well as intracellular signaling molecules involved in inflammatory pathways. Exercise intensity studies have demonstrated that high intensity training can increase anti-inflammatory cytokines and decrease pro-inflammatory cytokines. Moderate intensity exercise lowers levels of pro -inflammatory cytokines more than does mild intensity training in diabetes patients. No studies have investigated the effect of training intensity on neuroinflammation and neurodegeneration.

Conclusion: This literature review demonstrates that exercise is related to increased levels of neurotrophic factors, elevated expression of anti-inflammatory cytokines and reduced levels of pro-inflammatory cytokines and activated microglia.

Svensson, M., et al. Effects of Physical Exercise on Neuroinflammation, Neuroplasticity, Neurodegeneration, and Behavior: What We Can Learn from Animal Models in Clinical Settings. **Neurorehab Neural Repair.** 2015, July; 29(6): 577-589.

SPLINTING FOR DE QUERVAIN'S TENDINOPATHY

Thumb spica splints are frequently prescribed for the nonoperative management of de Quervain's tendinopathy. However, no consensus has been reached concerning the best splint-wear protocol. This study reviewed the outcomes of full-time versus as desired splint wear.

This prospective, randomized trial included 83 patients diagnosed with de Quervain's tendinopathy. The participants were assigned to either a cohort that was asked to wear the splints at all times or to a group wearing splints as desired. At baseline the patients completed the Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire as the primary outcome measure, as well as the Pain Anxiety Symptoms Scale (PASS) to assess anxiety regarding pain, the Center For Epidemiologic Studies Depression (CES-D) scale to measure depressive symptoms, the Pain Catastrophizing Scale (PCS) to measure a set of maladaptive cognitive conditions and the pain Numeric Rating Scale (NRS) to assess pain intensity.

At an average follow-up of 7.5 weeks, no significant differences were noted between the splinting groups in disability ($p=0.77$), grip strength ($p=0.82$), pain intensity ($p=0.36$) or treatment satisfaction ($p=0.91$). Bivariate analysis revealed that upper extremity debility was significantly related to CES-D ($p=0.001$), PCS ($p=0.001$) and PASS ($p=0.008$) test scores.

Conclusion: This study of patients with de Quervain's tenosynovitis found that full-time splinting is not superior to splinting as needed, and that depressive symptoms are strongly associated with greater disability.

Menendez, M., et al. A Prospective, Randomized, Clinical Trial of Prescription of Full-Time versus as Desired Splint Wear for De Quervain's Tendinopathy. **Intern Ortho**. 2015, August; 39(8): 1563-1569.

STAY ACTIVE ADVICE FOR SEVERE LOW BACK PAIN

As substantial evidence suggests that physical activity is beneficial for most musculoskeletal conditions, including low back pain (LBP), advice for the patient to stay active is common. This study reviewed the effect of advice concerning activity among patients with LBP.

Subjects were 109 patients with acute, severe LBP of less than 48 hours' duration. At baseline, the patients underwent an extensive physical examination including radiographic imaging, and

completed a battery of questionnaires, including questions concerning acute LBP, and a seven-day diary recording activity and pain. All were provided a digital pedometer.

The subjects randomized to the stay active (SA) group were advised to remain as physically active as possible, despite LBP. Those in an adjusted activity (AA) group were advised to adjust activity according to pain. For the 99 subjects included in the final analysis, the step count increased only in the SA group, with step counts of 9,865 steps on the last day of follow-up in the SA group and 6,609 in the AA group (p=0.008). While the SA group showed higher pain intensity and a slower decrease in pain intensity compared to the AA group, no significant difference was found between the groups in pain intensity change trajectory.

Conclusion: This study of patients with acute, severe low back pain (LBP) found that those advised to stay active despite LBP increased their activity more than those advised to adjust activity by pain level, with slightly higher, although insignificant differences in pain.

Olay-Contreras, P., et al. The Effect of the Stay Active Advice on Physical Activity and on the Course of Acute, Severe Low Back Pain. **BMC Sp Sci Med Rehab.** 2015; 7: 19 doi:10.1186/ s13102-015-0013-x

STRESS INTENSITY AND MIGRAINE FREQUENCY

Patients with headache frequently report stress to be one of their main activators. However, evidence is lacking concerning the association between stress and headache frequency. This study investigated the association between stress intensity and headache frequency.

The Longitudinal Population-Based German Headache Consortium (GHC) involved 18,000 men and women, ages 18 to 65 years of age, who were randomly selected from three German cities. Questionnaires were sent to the subjects to assess stress using a visual analogue scale (VAS). Questions were posed concerning the number of days associated with headache and the frequency of intake of acute pain medication. The participants were also queried regarding stress level, using a 100-point VAS. The subjects' headaches were classified through questionnaires as tension type headaches, migraines, migraines with coexisting tension type headaches, unclassified headache or no headache.

Of the 5,159 participants, tension type headaches were reported by 31%, migraine by 14% and migraine associated with tension type headache by 10.6%. An increase in headache frequency was positively correlated with increasing stress intensity, independent of headache subtype. The highest effects were observed in participants with tension type headaches, with each 10-point increase in stress intensity associated with a 6.4% increase in headache days per month.

Conclusion: This longitudinal population-based cohort study demonstrates that increasing stress is associated with increasing headache days for all patients with headache subtypes. This was particularly pronounced in participants with tension type headaches.

Schramm, S., et al. The Association between Stress and Headache: A Longitudinal, Population-Based Study. **Cephalalgia.** 2015, September; 35(10): 853-863.

VIRTUAL REALITY TRAINING FOR PATIENTS WITH PARKINSON'S DISEASE

Parkinson's disease (PD) is a progressive neurodegenerative disease that may affect postural stability and gait. Over two thirds of community dwelling patients with PD experience falls every year, with tripping over obstacles the major cause of these falls. This study examined the effects of virtual reality- based exercise on obstacle crossing performance and dynamic balance in patients with PD.

Thirty-six patients with PD were randomly assigned to one of three groups. Interventions included traditional exercise (TE), virtual reality-based Wii fit exercise (VRWii), with treadmill training included in both. All subjects underwent 12 sessions over six weeks. Participants in the control group received only fall-prevention education. The primary outcome variables were obstacle crossing performance and dynamic balance, assessed by the Balance Master system. Secondary outcomes included the sensory organization test (SOT), the 39-question Parkinson's Disease Questionnaire (PDQ39) and the Timed Up and Go Test. All outcomes were assessed at baseline and after training, at one -month follow-up.

At one-month follow-up, the VRWii group demonstrated greater improvement in obstacle crossing velocity (p=0.003) and crossing stride length (p=0.001) than did the control group, with no differences between the VRWii and the TE group. Both the VRWii and TE groups showed significantly greater improvements than the controls on the TUG, PDQ39 and FES-I, with no significant differences between the VRWii and TE groups.

Conclusion: This study demonstrated that virtual reality training through the use of Wii fit can improve obstacle crossing performance in patients with Parkinson's disease.

Lio, Y., et al. Virtual Reality-Based Training to Improve Obstacle Crossing Performance and Dynamic Balance in Patients with Parkinson's Disease. **Neurorehab Neural Repair**. 2015, August; 29(7): 658-667.

TLSO BRACES AND THORACOLUMBAR BURST FRACTURES

Treatments for thoracolumbar burst fractures often involve early bracing and return to activity. While thoracolumbosacral orthoses (TLSO) are commonly used for this injury, evidence concerning their efficacy is limited. This study compared the outcomes of patients treated with TLSO with those of patients without such immobilization.

This randomized, blinded, controlled trial included 96 patients with isolated burst fractures between T10 and L3. Patients in the TLSO group were placed on strict bed rest until they were fit with the TLSO, which was worn at all times for 10 weeks, except when in bed. Patients in both groups were cautioned to not exceed 90° of hip flexion or to lift more than 5 kg. The primary outcome measure was

performance on the Roland Morris Disability Questionnaire (RMDQ) at three months. Secondary outcome measures included the mental and physical component scores of the Short Form-36 (SF-36), pain, satisfaction and kyphosis.

The average RMDQ scores at three months were 6.8 points in the TLSO group and 7.7 points in the non-bracing group. At two-year follow-up, the groups did not differ in RMDQ scores or on any of the secondary outcome measures.

Conclusion: This study of patients with neurologically intact thoracolumbar burst fractures found no difference between those treated with a TLSO brace and those treated without bracing.

Bailey, C., et al. Treatment with or without an Orthosis Is Equivalent for Thoracolumbar Burst Fractures. **J Bone Joint Surg (Am)**. 2015, August 19; 97(16): 1374.

TOPICAL DICLOFENAC FOR NEUROPATHIC PAIN

Neuropathic pain results from injury to the peripheral and/or central nervous system, and is often difficult to treat. This study was designed to determine the effect of the topical nonsteroidal anti-inflammatory drug, diclofenac, as a treatment for patients with neuropathic pain.

This double-blind, placebo-controlled, crossover trial included patients with a diagnosis of post-herpetic neuralgia or chronic regional pain syndrome. The participants were assessed at baseline with a quantitative sensory test, and were then randomized to a placebo or a treatment group. Subjects topically applied 1.5% topical diclofenac or a placebo solution three times per day to the painful area for two weeks. After a one-week washout period, the participants received the alternative cream. At baseline and follow-up, the subjects were asked to complete the Pain Questionnaire and Short Form Health Survey (SF-36) and to undergo quantitative sensory testing.

After two weeks of topical application, the subjects in the treatment group obtained lower VAS pain scores than did the placebo group (4.9 versus 5.6, respectively; p=0.04). In addition, at two weeks, the VAS scores for burning pain were lower in the treatment group than in the control group (2.9 versus 4.3, respectively; p=0.02). No significant differences occurred between groups in constant pain, hypersensitivity or shooting pain.

Conclusion: This prospective, double-blind study of patients diagnosed with postherpetic neuralgia or complex regional pain syndrome found that topical diclofenac may be an effective treatment option.

Ahmed, S., et al. Effect of 1.5% Topical Diclofenac on Clinical Neuropathic Pain. **Anesthesiology**. 2015, July; 123(1): 191-198.

EFFECT OF SMOKING CESSATION ON MULTIPLE SCLEROSIS PROGNOSIS

Cigarette smoking is a risk factor for multiple sclerosis (MS). However, it remains unclear whether smoking cessation alters the course of the disease. This study evaluated the effects of continued smoking, following the diagnosis of MS on the progression to secondary progressive MS (SPMS).

This case controlled, retrospective study utilized data from the Genes and Environment in Multiple Sclerosis (GEMS) study database in Sweden, wherein all subjects completed detailed, yearly questionnaires. All selected subjects had relapsing remitting MS and documented smoking status information. A smoker was defined as someone smoking at least one cigarette per day. Smokers were further classified as continuous smokers, who remained smoking after the diagnosis, quitters, who stopped smoking after diagnosis, or intermittent smokers, with at least one year without smoking after the diagnosis, but without sustained cessation. Smokers were compared to never smokers.

Of the 728 smokers at the time of diagnosis, 332 continued smoking, 118 quit and 278 were intermittent. Of the smokers, 216 converted to SPMS. Accelerated time to progression was noted as 4.7% per year smoking after the MS diagnosis ($p< 0.001$). The median age of conversion to SPMS was 48 years in those who continued smoking and 56 years in those who quit smoking after their diagnosis($p=0.006$).

Conclusion: This study of patients with relapsing multiple sclerosis found that continued tobacco abuse after the diagnosis of multiple sclerosis is associated with accelerated progression to secondary MS.

Ramanujam, R., et al. Effect of Smoking Cessation on Multiple Sclerosis Progression. **JAMA Neurol**. 2015, October 15; 72(10): 1117-1123.

IMPLANTATION OF STEM CELLS FOR KNEE OSTEOARTHRITIS

Osteoarthritis (OA) results from the failure of chondrocytes to repair damaged articular cartilage in synovial joints. As mesenchymal stem cells (MSC) have been suggested as a potential therapy for the treatment of OA, this study compared the outcomes of patients treated with arthroscopic MSC injection to those with MSC implantation.

Subjects were patients with full thickness articular cartilage lesions with symptoms of knee joint pain and/ or functional limitations despite three months of nonsurgical treatment. Of the participants, the first 71 were treated with autologous MSC injection, and the next 94 underwentautologous MSC implantation with a fibrin glue scaffold. Among these, 52 patients in the injection group and 63 in the implantation group agreed to follow-up arthroscopic evaluation. For all patients, stem cells were harvested from adipose tissue, with a mean of 4.01×10^6 stem cells prepared. Outcome evaluations included International Knee Documentation Committee Scores (IKDC) and the Tegner activity scales to assess joint function and sports activity.

At the time of second look arthroscopy, at a minimum of 12.6 months postoperatively, significantly better improvement was noted in the implantation group for both the IKDC and the Tegner activity scores ($p<0.001$ for all comparisons). At the final follow-up, at 28.6 months postoperatively, further improvement was noted in the implanted group, with no such improvement seen in the injection group.

Conclusion: This study of patients with osteoarthritis of the knee found that mesenchymal stem cells can produce significant improvement, especially when implanted during arthroscopic surgery.

Kim, Y., et al. Comparative Matched - Analysis of the Injection versus Implantation of Mesenchymal Stem Cells for Knee Osteoarthritis. **Am J Sport Med**. 2015, September; 42 (11): 2738-2746.

EPIDURAL INJECTION OF AUTOLOGOUS SERUM

Cervical radiculopathy is a common complaint of middle to older patients at orthopedic outpatient clinics. As research has suggested that biochemical sensitizers make nerve roots susceptible to mechanical effects of a herniated mass, interleukin one and prostaglandins are commonly seen as involved in producing radiculopathy. Autologous conditioned serum (ACS) is derived by processing the patient's blood to produce high concentrations of interleukin I receptor antagonists. This study evaluated the efficacy of ACS in patients with cervical radiculopathy who had failed conservative treatments.

Forty patients with neck pain radiating into one upper limb for at least six weeks were randomized to receive either ACS or methylprednisolone (MPS). The subjects were assessed with a visual analogue scale (VAS) for pain, the Neck Pain Disability Scale (NPDS) and the Neck Disability Index (NDI). Measurements were made at baseline, and then at three weeks, three months and six months after injection.

The mean, six-month improvement in VAS scores for patients receiving ACS was 73.2%, while that for those receiving MPS was 58.4%. Over the same timeframe, the mean NPDS score decreased in the ACS group by 73.76% and in the MPS group by 55.6%. The mean NDI scores decreased by 74.47% in the ACS group and by 52.8% in the MPS group.

Conclusion: This study of patients with cervical radiculopathy found that epidural injections of autologous condition serum are at least as effective as steroid injections for reduction of pain and disability.

Goni, J., et al. Efficacy of Epidural Perineural Injection of Autologous Condition Serum in the Unilateral Cervical Radiculopathy. **Spine.** 2015, August; 40(16): E915-E921.

PREVENTION OF KNEE OSTEOARTHRITIS IN OVERWEIGHT FEMALES

Previous studies have suggested that, among overweight individuals, weight loss can prevent the occurrence of knee osteoarthritis (OA). Other studies have suggested the use of glucosamine as a treatment for OA. This study evaluated the effects of oral glucosamine sulfate and a tailored diet and exercise weight reduction program on the incidence of knee OA in a high-risk group of overweight women.

Subjects were women, 50 to 60 years of age, with no history of OA and with a body mass index of 27 kg/ m² or greater. The participants were randomized to a treatment group, to receive a tailored diet and exercise program (DEP), with or without 1,500 mg glucosamine, or to a control group who were not offered an intervention. The predefined, primary outcome measure was the difference between groups in the incidence of knee OA or joint space narrowing. The subjects were followed for a mean of 2.5 years.

A total of 407 women were studied, with a mean age of 55.7 years and a mean body mass index of 32.4 kg/m². Of these, 17% showed incident knee OA, including 19% in the DEP control/placebo group, 13% in the DEP control/ glucosamine group, 9% in the DEP / placebo group and 23% in the DEP / glucosamine group. No significant differences were seen between the groups.

Conclusion: This study of overweight women failed to demonstrate a protective effect of weight reduction or oral glucosamine for the prevention of knee osteoarthritis.

Runhaar, J., et al. Prevention of Knee Osteoarthritis in Overweight Females: The First Preventative, Randomized, Controlled Trial in Osteoarthritis. **Am J Med**. 2015, August; 128(8): 888-895.

SEXUAL FUNCTION BEFORE AND AFTER FEMOROACETABULAR IMPINGEMENT SURGERY

Chronic pain has been shown to significantly affect a patient's ability to perform activities of daily living, including sexual function. As femoroacetabular impingement (FAI) is a common cause of symptoms that may lead to chronic hip pain, this study was designed to determine the presence and significance of sexual difficulties in patients with chronic hip pain due to symptomatic FAI, before and after hip surgery.

This retrospective review included 305 patients who underwent hip arthroscopic surgery for FAI between 2011 and 2013. All patients underwent unilateral hip arthroscopic surgery with labral repair or debridement and capsular repair. An anonymous, 23-item, Likert-style questionnaire assessed preoperative and postoperative sexual function. A comparative analysis was performed between gender and age groups.

A total of 131 patients returned the questionnaire, resulting in a response rate of 43%. Of these, 66% strongly agreed or agreed that they experienced preoperative sexual difficulties. The most commonly reported contributors to altered sexual function were hip pain in 77.9%, stiffness in 47.1% and loss of interest in 21.4%. Resumption of sexual activity occurred at a mean of 29.2 days post-surgery, while sexual activity with minimum pain occurred at a mean of 40.8 days. Female patients resumed sexual activity later than did males. Postoperatively, only 10.8% strongly agreed or agreed that they experienced current sexual difficulties. The frequency of sexual activity increased in 32% of the patients and was unchanged in 40.5%.

Conclusion: This study of patients undergoing hip arthroscopic surgery for symptomatic femoroacetabular impingement found that hip arthroscopic surgery may improve sexual function postoperatively.

Lee, S., et al. Evaluation of Sexual Function Before and After Hip Arthroscopic Surgery for Symptomatic Femoroacetabular

Impingement. Am J Sports Med. 2015, August; 43(8): 1850-1856.

OXYCODONE PLUS NALOXONE FOR CHRONIC PAIN IN PARKINSON'S DISEASE

Pain is a fundamental symptom of Parkinson's disease (PD) that is often unrecognized and undertreated. This study was designed to evaluate the safety and efficacy of using opioids in patients with PD.

This eight week, single center, prospective, observational trial included 14 patients with PD and chronic pain syndromes. The participants were prescribed oxycodone hydrochloride, combined with naloxone hydrochloride dehydrate (OXN PR 5/325), beginning at once a day and titrated to twice per day after one week. Pain intensity was assessed by the 11- point Numeric Rating Scale (NRS) and the Brief Pain Inventory (BPI), motor status by the Unified Parkinson's Disease Rating Scale Section-III (UPDRS-III) and cognitive status by the Mini Mental State Examination (MMSE). In addition, the patients were assessed with the Global Impression of Change (CGI-C). All were followed with weekly examinations for eight weeks.

A significant reduction was seen in the NRS scores during the entire observation (ANOVA $p<0.05$). A 30% or greater reduction in the mean NRS scores was noted from baseline to eight weeks in 56% of the patients. The ratings were much improved for 42.86% of the patients. Bowel function was not worsened by the analgesic treatment, as demonstrated by changes in BFI scores.

Conclusion: This study of patients with Parkinson's disease found that a combination of oxycodone XR and naloxone may be a safe and effective treatment for chronic pain.

Madeo, G., et al. Efficacy and Safety Profile of Prolonged Release Oxycodone in Combination with Naloxone (OXN PR) in Parkinson's Disease Patients with Chronic Pain. **J Neur**. 2015, September; 262(9): 2164-2170.

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