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Volume 25 Number 6

Published by Physicians  
In Physical Medicine and Rehabilitation

June 5, 2017

## STERIOD VERSUS SALINE FOR KNEE OSTEOARTHRITIS

Symptomatic knee osteoarthritis (OA) affected more than nine million individuals in the United States in 2005. As evidence suggests that OA is an inflammatory condition, treatments to suppress inflammation in these patients have included intra-articular corticosteroids. This study further tested the benefits of intra-articular corticosteroids for the treatment of knee OA.

This two-year, double-blind study included 140 patients, 45 years or older, with symptomatic knee OA. The subjects were randomized to receive injections every three months for two years, with either one mL of triamcinolone 40 mg/mL or one mL of 0.9% sodium chloride. In each case, synovial fluid was aspirated prior to the injection. All underwent MRI scans at months zero, 12 and 24 to assess cartilage volume, bone marrow lesion volume, effusion volume and cartilage damage.

The rate of cartilage loss was greater in the treatment group for cartilage thickness ( $p=0.01$ ) and as assessed by the Secondary Cartilage Damage Index ( $p=0.048$ ) than in the saline group. There were no significant differences between the two groups in the progression of cartilage denudation, bone marrow lesion, effusion volume, or trabecular morphology. Improvements in WOMAC scores of pain, function and stiffness, as well as VAS pain scores, did not differ significantly between the two groups.

**Conclusion:** This study of patients with osteoarthritis of the knee did not find that intraarticular triamcinolone is superior to placebo for the treatment of pain or the suppression of cartilage damage.

McAlindon, T., et al. Effect of Intra-Articular Triamcinolone versus Saline on Knee Cartilage Volume and Pain in Patients with Knee Osteoarthritis.

A Randomized Clinical Trial. *JAMA*. 2017, May 16; 317(19): 1967-1975.

## TISSUE FLOSSING FOR ANKLE RANGE OF MOTION AND JUMP PERFORMANCE

The partial occlusion of blood flow during range of motion activities (tissue flossing) has become a popular strategy to increase joint range of motion and improve athletic performance. This study analyzed the effect of floss band use on range of motion and jump height.

Subjects were 52 recreational athletes with a mean age of 20 years, who reported regular physical exercise. At baseline, all participants were assessed by the Weight-Bearing Lunge test (WBLT), dorsiflexion and plantarflexion range of motion, and the Single-Leg Vertical Jump Test (JUMP) with wrap pressures measured with the Kikuhime pressure monitor. Those randomized to an active treatment group had a floss band applied using a standard ankle bandaging technique, with a mean pressure of 182 mmHg. With the band applied, the subjects performed both plantarflexion and dorsiflexion to their extreme ranges of motion, and completed the mobility exercises. After two minutes, the band was removed. The control group underwent the same procedure with no band applied.

Compared to baseline, significant improvements were found in all test measures in the treatment group (WBLT, PF, DF JUMP<sub>H</sub>, JUMP<sub>V</sub> ( $p < 0.01$  for all comparisons). The differences in gains between the treatment and the control group were all in favor of the treatment group but failed to reach statistical significance.

**Conclusion:** This study of floss bands applied to recreational athletics found that ankle range of motion and jump performance could be enhanced with this blood restriction technique.

Driller, M., et al. Effects of Tissue Flossing on Ankle Range of Motion and Jump Performance. *Phys Ther Sport*. 2017, May; 25: 20-24.

## LIGHT THERAPY AND SLEEPINESS IN PARKINSON'S DISEASE

Among patients with Parkinson's disease (PD), excessive daytime sleepiness and nocturnal sleep fragmentation affect up to 90%. As supplementary exposure to bright light has shown benefits in the treatment of sleep quality and daytime vigilance in healthy, older adults, this study assessed the effect of light therapy on patients with PD.

This randomized, placebo controlled, clinical intervention included 31 patients with PD and excessive daytime sleepiness. Those with an Epworth Sleepiness Scale (ESS) score of 12 or greater were randomized to receive two weeks of light therapy, twice per day, at 10,000 lux (bright light) or at less than 300 lux (dim-red light). During the study, all subjects wore an actigraphy monitor 24 hours per day and completed a daily sleep log. All completed a visual analog score (VAS) for daytime sleepiness every two hours.

Patients in the bright light group experienced significant improvement on the Excessive Daytime Sleepiness Scale of the ESS as compared to baseline ( $p<0.001$ ), as well as daytime total physical activity ( $p<0.001$ ). Both bright light and dim-red light were associated with improvements in sleep quality as measured by the Pittsburgh Sleep Quality Index ( $p=0.006$ ). Overnight awakenings, sleep quality and ease of falling asleep were significantly improved in those treated with bright light, while all participants improved in sleep latency, total sleep time, and wake time after sleep onset. All participants reported being more

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refreshed in the morning during light therapy.

**Conclusion:** This study of patients with Parkinson's disease and excessive daytime sleepiness revealed that light therapy, administered twice daily for two weeks, significantly improved excessive daytime sleepiness and sleep wake cycles.

Videnovic, A., et al. Timed Light Therapy for Sleep and Daytime Sleepiness Associated with Parkinson's Disease. A Randomized, Clinical Trial. **JAMA Neurol.** 2017, April; 74 (4): 411-418.

### BRAIN-CONTROLLED MUSCLE STIMULATION IN TETRAPLEGIA

Patients with high cervical spinal cord injury (SCI) events have difficulty performing the reaching and grasping movements required for many activities of daily living. This study explored the ability of an intracortical brain-computer interface to recognize cortical signals sufficiently to command functional electrical stimulators (FES) for arm movement.

The subject was a 53-year-old man with a C-4 ASIA-A injury. Two 96 channel microelectrode arrays were implanted into the hand area on the precentral gyrus of his motor cortex. The patient practiced movements of a three-dimensional virtual arm for four months, and then received 36 percutaneous muscle stimulating electrodes applied to his right arm. These were placed to restore finger and thumb, wrist, elbow and shoulder movements. The subject was then tested for cortically commanded, single-joint and coordinated, multi-joint arm movements for target acquisition.

The single-joint and coordinated, multiple-joint arm movements were completed using the FES at 80 to 100% accuracy. At 463 days after implantation, the subject was able to successfully reach and drink a mug of coffee on 11 of 12 attempts and by day 717 was able to feed himself.

**Conclusion:** This case study of a tetraplegic patient found that an intracortical brain computer interface could be used to effectively provide commands to peripheral functional electrical stimulation devices, allowing for functional use of the hand.

Ajiboye, A., et al. Restoration of Reaching and Grasping Movements through Brain-Controlled Muscle Stimulation in a Person with Tetraplegia: A Proof of Concept Demonstration. **Lancet.** 2017, May; 389(10081): 1821-1830.

### INTENSIVE SPEECH AND LANGUAGE THERAPY FOR CHRONIC APHASIA AFTER STROKE

Chronic aphasia, persisting for six or more months after stroke, affects approximately 20% of stroke survivors. This study assessed the effectiveness of intensive speech and language therapy after stroke.

This randomized, open-label, wait-list controlled study included patients with aphasia lasting six or more months after ischemic or hemorrhagic stroke. The participants were randomized to a treatment group, to receive immediate speech and language therapy, 10 hours or more per week for three weeks, or to a control group, with treatment deferred for three weeks. The primary outcome measure was the Amsterdam-Nijmegen Everyday Language Test (ANELT) A-Scale, with assessments three days before beginning and three days after the therapy completion.

Data were available for 156 patients. At three weeks, the mean changes in ANELT-A scores were 2.61 points in the treatment group and -0.03 points in the control group ( $p=0.0004$ ). After treatment, the control group had similar improvements. The treatment effect remained stable in both study groups at six months. Among the subgroup of 34 patients receiving five weeks or more of therapy, the mean change in the ANELT-A score from baseline was approximately one point greater than that of those receiving three weeks. Those with less severe stroke at enrollment had greater improvement with treatment than did those with more severe stroke ( $p<0.001$ ).

**Conclusion:** This randomized study of patients with chronic, post-stroke aphasia found that three weeks of speech and language therapy, 10 hours or more per week, could produce significant and lasting improvements in speech.

Breitenstein, C., et al. Intensive Speech and Language Therapy in Patients with Chronic Aphasia after Stroke: A Randomized and Open Label, Blinded-Endpoint, Controlled Trial in a Health Care Setting. **Lancet**. 2017, April 15-21; 389 (10078): 1528-1538.

### TAI CHI FOR KNEE OSTEOARTHRITIS IN THE ELDERLY

Knee osteoarthritis (OA) is the most common joint disorder, and is a leading cause of pain, functional limitations and physical disability. Sleep disturbances have been found to occur in more than two thirds of patients with OA. Tai chi is a traditional Chinese exercise, found to be effective in improving sleep quality and as an exercise regimen among the elderly. This study assessed the effects of tai chi on sleep quality and physical function among patients with OA.

This randomized, controlled trial included women, 60 to 70 years of age, diagnosed with OA of the knee. The subjects were randomized to either a tai chi training group or a health education control group. The tai chi group received 60-minute sessions, three times a week for 24 weeks. The primary outcome measure was the Pittsburgh Sleep Quality Index (PSQI), Chinese version. In addition, the patients were assessed with the Berg Balance Scale (BBS) and The Timed Up and Go Test (TUG).

At 24-week follow-up, the tai chi group had better scores than did the control group in the global PSQI ( $p=0.006$ ), with better improvements in sleep latency ( $p=0.031$ ), sleep duration ( $p=0.043$ ) and total sleep time ( $p=0.033$ ). Scores on the SF-36 PCS were also more improved in the tai chi group ( $p=0.006$ ). The tai chi group had significant improvement in the BBS ( $p=0.001$ ) and the TUG ( $p=0.006$ ), while the control group did not, although the differences between the groups were not significant.

**Conclusion:** This study of elderly Chinese women found that tai chi training over 24 weeks could improve sleep quality and quality of life.

Lu, J., et al. Effect of Tai Chi Training on Self-Reported Sleep Quality in Elderly Chinese Women with Knee Osteoarthritis: A Randomized,

Controlled Trial. **Sleep Med**. 2017, May; 33; 70-75.

### STEM CELLS FOR MULTIPLE SCLEROSIS

Various studies have demonstrated that the transplantation of autologous hematopoietic stem cells (AH SCT) induces bone marrow recovery and promotes immune reconstitution. Early studies in multiple sclerosis (MS) have suggested that this treatment might be effective in suppressing disease reactivation. This study evaluated the long-term outcomes of patients who underwent AH SCT for the treatment of MS.

This multicentered, observational, retrospective, cohort study reviewed data collected at transplant centers worldwide between January of 1995 and December of 2006. Eligible subjects had MS, a baseline Expanded Disability Status Scale (EDSS) score and at least one follow-up visit or report after AH SCT. The study endpoint was progression-free survival.

Subjects were 281 patients in 13 countries with 66.2% undergoing AH SCT during the second half (2001-2006) of the study. At five years, the overall progression-free survival after AH SCT was 46%, while for those with relapsing MS, progression-free survival was 73% and for those with secondary progressive MS was 33%. The overall survival rate was 93% at five years and 84% at 10 years after transplant.

**Conclusion:** This study of patients with multiple sclerosis who received autologous hematopoietic stem cell transplantation found that nearly half were free from neurologic progression for five years after transplantation.

Muraro, P., et al. Long-Term Outcomes after Autologous Hematopoietic Stem Cell Transplantation for Multiple Sclerosis. **JAMA Neurol**. 2017, April 1; 74(4): 459-469.

### OSTEOPOROSIS AND COW'S MILK

The consumption of cow's milk has been long thought to have a positive effect on bone growth and bone strength. However, a recent

study found that calcium consumption is associated with excess mortality, osteoporosis and fractures. This literature review was designed to better understand the health effects of cow's milk on human bones.

A literature review was completed, with studies reviewed that focused on the association between cow's milk and bone mineral density, fractures and bone turnover.

The literature review demonstrated that a high consumption of milk suppresses the secretion of parathyroid hormone, decreases the levels of bone resorption markers and is associated with a slower pace of bone remodeling and a higher bone mass. Studies of osteoporotic fractures have produced conflicting results. In large cohort studies, the risk of any fracture and hip fracture were higher in women consuming at least three glasses of milk per day, as compared to those consuming less than one glass. This has not been shown to be true in men.

**Conclusion:** This literature review of the effect of cow's milk on health found no conclusive evidence to suggest a modification of current consumption levels.

Fardellone, P., et al Osteoporosis: Is Milk a Kindness or a Curse? **Joint Bone Spine**. 2017, May; 84(3): 275-281.

### EXERCISE-INDUCED HYPOALGESIA

Evidence suggests that physical activity may improve pain related symptoms in patients with chronic pain conditions. A single bout of exercise has been shown to activate endogenous inhibitory pain mechanisms and reduce the sensitivity to noxious stimuli. This has been termed exercise-induced hypoalgesia (EIH). This study was designed to determine whether physical activity type and or intensity correlates with EIH.

Subjects were 50 women who met the American College of Sports Medicine's aerobic activity recommendations ( $n=11$ ) or the aerobic and resistance training recommendations ( $n=16$ ), had insufficient aerobic activity, but participated in two days or more of resistance training per week ( $n=8$ ) or were insufficiently active ( $n=15$ ). At

baseline, the subjects were assessed for mood, anxiety and pain perception. Daily physical activity (PA) was measured with a wearable device. All subjects were asked to perform isometric handgrip exercises to exhaustion. The primary outcome measure was the Pain Pressure Threshold (PPT), assessed before and after exercise, both in the exercised (right) and the contralateral arm.

The PPT increased by 7.7% in the right, and by 7.0% in the left forearm after exercise. The EIH did not differ between activity groups. The PPT values were found to be inversely related to vigorous-intensity PA.

**Conclusion:** This study found an inverse relationship between levels and types of vigorous-intensity physical activity and sensitivity to pressure stimuli, with no significant difference found between groups with differing routine exercise schedules.

Black, C., et al. Exercise-Induced Hypoalgesia Is Not Influenced by Physical Activity Type and Amount. *Med Sci Sports Exer.* 2017, May; 49(5): 975-982.

### AMBROXOL FOR FIBROMYALGIA

Previous research has suggested that fibromyalgia is a sympathetically-driven, neuropathic pain syndrome, often involving small, unmyelinated, peripheral nerve fibers. In small-fiber neuropathies, specific sodium channels in the dorsal root ganglia are involved in pain transmission. Ambroxol, a secretolytic agent used for decades to treat airway disorders, has recently been found to be a strong Nav1.8 sodium channel blocker, which is associated with small fiber neuropathy. This open-label study examined the effect of ambroxol for the treatment of fibromyalgia.

The subjects were twenty-five women who met 2010 American College of Rheumatology diagnostic criteria for fibromyalgia. Oral ambroxol was administered for one month at 30 mg, three times per day. Patients completed pre- and post-treatment questionnaires, including the Revised Fibromyalgia Impact Questionnaire (FIQ-R), a Hospital Anxiety and Depression Scale, and the American Congress of Rheumatology diagnostic criteria including: the Widespread Pain Index

(WPI), the Symptoms Severity Scale (SSS), the Polysymptomatic Distress Scale (PDS), the Composite Autonomic Symptom Score, Self-report Leeds Assessment of Neuropathic Symptoms and Signs pain scale (sLANSS) and the Patient Global Impression of Change (PGIC).

After treatment, scores on the FIQ-R decreased from 62 to 51 ( $p = 0.013$ ), with scores on the VAS improving from 77 to 56 ( $p = 0.018$ ), and those on the WPI from 14.6 to 10.4 ( $p = 0.001$ ). In addition, significant improvements were found on the SSS ( $p = 0.022$ ) and the PDS ( $p = 0.001$ ). No significant changes were found in anxiety or depression scores.

**Conclusion:** This small, unblinded, uncontrolled study of patients with fibromyalgia found that ambroxol, a Nav1.8 sodium channel blocker, may be a new therapeutic option to assist with pain control.

Martinez-Martinez L., et al. Ambroxol for Fibromyalgia: One Group Pre-Test -Post-Test, Open-Label Pilot Study. *Clin Rheumatol.* 2017; doi: 10.1007/s10067-017-3664-z.

### ANTIOXIDANT SUPPLEMENT USE AND DEMENTIA

In the United States, an estimated five million elderly persons have Alzheimer's disease (AD). A number of studies have suggested that antioxidants may be helpful for the treatment of cognitive impairment or dementia. This paper reports on the results of the Prevention of Alzheimer's disease by Vitamin E and Selenium (PREADViSE) primary prevention trial.

The PREADViSE trial enrolled 4,271 men without dementia between 2002 and 2008. All subjects were screened with the Memory Impairment Screen (MIS) with those who scored below cutoffs for intact cognition receiving a secondary screen with the modified Telephone Interview for Cognitive Status. The subjects were randomized to receive vitamin E, selenium, vitamin E plus selenium or placebo. The primary endpoint was incident dementia.

At five year follow-up, incident dementia was found in 325 of the 7,540 men (4.3%). Compared to the placebo group, the hazard ratio for incident dementia in the vitamin E group was 0.88, for the selenium

group was 0.83, and for the combined group was 1.0. There were no significant differences among any of the groups.

**Conclusion:** This study of elderly men failed to demonstrate that the supplemental use of vitamin E and/or selenium will reduce the risk of incident dementia.

Kriscio, R., et al. Association of Antioxidant Supplement Use and Dementia in the Prevention of Alzheimer's Disease by Vitamin E and Selenium Trial (PREADViSE). *JAMA Neurol.* 2017, May; 74(5):567-573.

### MIGRAINE AND COGNITIVE FUNCTION

Migraine affects approximately 14.7% of the population, and has been associated with an increased risk of vascular events, specifically cardiovascular disease. This study assessed cognitive function among patients with chronic migraine.

Subjects were 34 patients diagnosed with migraine, and 24, healthy, age-matched controls. All subjects were evaluated for cognitive function with the Montréal Cognitive Assessment (MoCA). The Rey-Osterrieth Complex Figure Test (ROCF) was used to assess visual perception, constructional praxis and visuo-spatial memory. Basic information processing speed was measured on the Digit Symbol Substitution Test. In addition, all subjects underwent electrophysiologic study for reaction time and electroencephalograms for assessment of the P3 component.

The patients with migraine suffered 3.5 headaches a month, with an average duration of 24 hours. Those with migraine performed more poorly on the MoCA than did controls ( $p=0.007$ ), including scores on language ( $p=0.005$ ), memory ( $p=0.0006$ ), executive function ( $p=0.042$ ), calculation ( $p=0.018$ ) and orientation ( $p=0.018$ ). In addition, those with migraine obtained lower scores on the Memory Trial of the ROCF Test ( $p=0.012$ ). Electrophysiologic data revealed that the P3 latency was longer in those with migraine than in the healthy subjects ( $p<0.0001$ ). The MoCA score was significantly and negatively related to the duration of migraine. The time for Digit Symbol Substitution

was positively related to the duration of headaches.

**Conclusion:** This study found that patients with migraine performed more poorly on tests of cognitive function, including memory, than did controls, with longer latencies at P3.

Huang, L., et al. Duration and Frequency of Migraines Affect Cognitive Function: Evidence from Neuropsychological Test and Event-Related Potentials. *J Headache Pain*. 2017, December; 18(1): 54.

### ERENUMAB FOR PREVENTION OF CHRONIC MIGRAINE

Chronic migraine headache affects one to two percent of the global population. Oral preventative therapies, including topiramate, beta blockers and amitriptyline, are often not fully effective. As calcitonin gene-related peptide (CGRP) is a proinflammatory vasodilating neuropeptide implicated in the pathophysiology of migraine, this study assessed the efficacy of a monoclonal antibody that competitively binds to the CGRP receptor (erenumab).

This randomized, double-blind, placebo-controlled trial included adults, 18-65 years of age, with chronic migraine. The patients were randomly assigned to receive erenumab at 70 mg or 140 mg, once every four weeks for 12 weeks, or a placebo. The primary endpoint was the mean change in monthly migraine days from baseline. Secondary efficacy endpoints were the achievement of at least a 50% reduction in monthly migraine days, change in days on which acute migraine-specific drugs were used, and change in cumulative headache hours.

Of those screened for eligibility, 637 patients completed the study. Both the 70 mg and 140 mg groups realized a greater reduction in monthly migraine days from baseline during the last four weeks of the treatment phase, as compared with placebo ( $p<0.0001$ ). In addition, 40% of the 70 mg group and 41% of the 140 mg group achieved a 50% or greater reduction in monthly migraine days, compared with 23% of the placebo group ( $p<0.0001$ ).

**Conclusion:** This study of chronic migraine patients found that the monoclonal antibody erenumab could

significantly reduce the frequency of migraine headaches.

Tepper, S., et al. Safety and Efficacy of Erenumab for Preventative Treatment of Chronic Migraine: A Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial. *Lancet Neurol*. 2017, June; 16(6): 425-434.

### BODY WEIGHT FLUCTUATION AND CORONARY DISEASE

While weight loss is commonly prescribed for patients with coronary disease, weight loss is often followed by weight gain. This study evaluated whether fluctuations in body weight are associated with cardiovascular events among patients with established coronary artery disease (CAD).

This study included a post-hoc analysis of data from the Treating to New Targets (TNT) trial. The TNT study involved 10,000 patients with clinically evident CAD, as well as levels of low-density lipoprotein cholesterol below 130 mg/dL. The participants were randomized to receive either 10 mg or 80 mg of atorvastatin. All were followed at three, six, nine and 12 months, and every six months thereafter, for a median of 4.9 years. Clinical data were evaluated at each interval, including body weight, with body weight variability calculated. The primary outcome variable was an occurrence of any coronary event. The relationship between body weight variability and the risk of outcomes was assessed.

Among the 9,509 patients completing the study, the median body weight variability was 1.76 kg. Each standard deviation increase in body weight variability increased the risk of any coronary events, any cardiovascular event, death, myocardial infarction and new onset diabetes (all  $p<0.001$ ) and stroke ( $p=0.004$ ). In the adjusted analysis, compared to those in the lowest quintile of variability, those in the highest percentile had a 64% increased risk of any coronary event, an 85% increased risk of any cardiovascular event, a 124% increase in the risk of death, a 136% increase in the risk of stroke, and a 117% increase in the risk of myocardial infarction. The risk of body weight variability was greatest

among those who were overweight or obese at baseline.

**Conclusion:** This study of patients with established coronary artery disease found that fluctuations in body weight are strongly associated with the risk of cardiovascular events and death.

Bangalore, S., et al. Body Weight Fluctuations and Outcomes in Coronary Disease. *N Engl J Med*. 2017, April; 376(14):1332-1340.

### EVOLOCUMAB FOR CARDIOVASCULAR DISEASE

Low-density lipoprotein cholesterol is a well-established risk factor for cardiovascular disease. A new class of drugs, monoclonal antibodies that inhibit proprotein convertase subtilisin-kexin type 9 (PCSK9), have been found to effectively lower LDL cholesterol levels. This study evaluated the clinical outcomes of patients treated with evolocumab.

This randomized trial included patients in 1,242 sites in 49 countries, 40 to 85 years of age, all with clinically evident atherosclerotic cardiovascular disease. The subjects were randomized to receive subcutaneous placebo or injections of evolocumab, 140 mg, every two weeks or 420 mg every month. The primary efficacy endpoint was major cardiovascular events, including cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina or coronary revascularization.

Subjects included 27,564 patients with a mean age of 63 years, with 69.3% of the patients receiving high intensity statin therapy. The mean duration of follow-up was 26 months, resulting in 59,865 patient years of follow-up. At 40 weeks, the mean percent reduction in LDL cholesterol levels in the treatment group as compared with placebo was 59% ( $p<0.001$ ). The primary endpoint was realized by 9.8% of the treatment group and by 11.3% of the placebo group ( $p<0.001$ ). The benefits of evolocumab were consistent across major subgroups based on age, gender and type of atherosclerotic vascular disease, as well as across quartiles of baseline LDL cholesterol levels.

**Conclusion:** This study of patients with atherosclerosis found

that a monoclonal antibody inhibitor, evolocumab, significantly reduced LDL cholesterol levels, as well as the risk of cardiovascular events.

Sabatine, M., et al. Evolocumab and Clinical Outcomes in Patients with Cardiovascular Disease. *N Engl J Med.* 2017, May 4; 376(18): 1713-1722.

### WORLDWIDE PREVALENCE OF SMOKING

Smoking was the second leading risk factor for early death and disability worldwide in 2015. Using data from the Global Burden of Diseases, Injuries and Risk Factors Study (GBD), this study was designed to better understand the global burden on health resulting from tobacco abuse.

Using 2,818 data sources, estimates were generated of smoking prevalence by gender and five-year age groups, starting at age 10 years, for citizens of 195 countries and territories between 1990 and 2015. In addition, data were reviewed to estimate smoking-attributable disease burden including deaths and disability-adjusted life-years.

In 2015, the age standardized prevalence of daily smoking was 25% among men and 5.4% in women. Among men, the prevalence of daily smoking was highest in middle sociodemographic index (SDI) countries, whereas, for women, high SDI countries had the highest prevalence of daily smokers. Between 1990 and 2015, the global, age-standardized prevalence of daily smoking fell significantly for both genders, decreasing by 28.4% for men and 34.4% for women. In 2015, 6.4 million deaths were attributable to smoking worldwide, a 4.7% rise in smoking-attributable deaths since 2005. More than 75% of these deaths were in men, while 52.2% occurred in four countries (U.S., China, India and Russia). Smoking was the leading risk factor for attributable disease burden in 24 countries, an increase from 16 countries in 1990.

**Conclusion:** This study, estimating the global burden of tobacco smoking, found that, in 2015, one in four men and one in 20 women was a daily smoker.

GBD Collaborators. Smoking Prevalence and Attributable Disease Burden in 195 Countries and

Territories, 1990-2015: A Systematic Analysis from the Global Burden of Disease Study. 2015. *Lancet*, 2017, May; 389(10082): 1885-1906.

### AEROBIC VERSUS RESISTANCE EXERCISES IN DIETING ELDERLY ADULTS

In designing weight loss programs for the elderly, some have expressed concern that weight loss could worsen frailty by accelerating sarcopenia and osteopenia. This study was designed to determine whether aerobic and/or resistance exercises, combined with weight loss, would result in better outcomes in physical performance and the preservation of muscle and bone.

This randomized, controlled trial included 141 adults, 65 years of age or older, with a body mass index (BMI) of 30 kg/m<sup>2</sup> or greater, who were sedentary, and had mild to moderate frailty. The subjects were randomized to one of four groups, including a control group with neither weight management nor exercise intervention. The other groups received a diet with an energy deficit of 500 to 750 cal per day, plus either 60 minutes of aerobic or resistance exercise or 75 to 90 minutes of aerobic plus resistance exercise, three times per week. Frailty was assessed with the Physical Performance Test (PPT), with measurements of body composition, bone mineral density and quality of life, with assessments repeated at six months.

Scores on the PPT improved by 21% in the combination group, by 14% in the other two exercise groups (p=0.01 and p=0.02), and by four percent in the control group (p<0.001 for all comparisons). Body weight decreased by nine percent in all three exercises groups. Lean mass decreased by three percent in the combination group, two percent in the resistance group and five percent in the aerobic group. Bone mineral density at the total hip decreased insignificantly (<one percent) in the resistance group, 2.6% in the aerobic group and 1.1% in the combined group. Peak oxygen consumption increased more in the combination (17%) and aerobic groups (19%) than in the resistance (8%) group (p<0.001).

**Conclusion:** This study of elderly adults found that weight loss plus resistance training combined with

aerobic training results in greater improvement in physical function and reduction of frailty than does either exercise regimen alone.

Villareal, D., et al. Aerobic or Resistance Exercises, or Both, in Dieting, Obese, Older Adults. *N Engl J Med.* 2017, May 18; 376 (20):1943-1955.

### LONG-TERM EFFECTS OF VERTEBROPLASTY

Vertebral perforation (VP) is a treatment for vertebral compression fractures (VCFs), aimed at improving analgesia. This study compared the long-term analgesic effects of percutaneous vertebroplasty (PVP) with those of VP.

This retrospective study included patients seen between January of 2003 and April of 2011 with osteoporotic vertebral compression fractures. All had long-term pain, despite conservative treatment. In the first half of the study, PVP was performed for 64 patients. In the second half of the study, VP was provided to 67 patients. Pain was evaluated by a visual analog scale (VAS) for pain before, and at days two and seven, at three months and at greater than 15 months post-surgery. Dynamic lumbar radiographs, MRI and CT were performed before the surgery to assess the presence or absence of vertebral mobility. New vertebral fractures after surgery were compared between groups.

The changes on the VAS at three months post-surgery were significantly larger in the PVP group than in the VP group. At 15 months post-surgery, the differences in VAS scores did not differ significantly. New VCFs were found in 52% of the PVP group, and in 23.9% of the VP group. New VCFs during the first three months post-surgery were seen in 38% of the PVP group and three percent of the VP group (p<0.0001).

**Conclusion:** This study of patients with painful vertebral compression fractures found that vertebroplasty is more effective than vertebral perforation for pain relief over the first three months, with a higher incidence of subsequent compression fractures in the vertebroplasty group.

Yokoyama, K., et al. Long-Term Therapeutic Effects of Vertebroplasty

for Painful Vertebral Compression Fracture: A Retrospective, Comparative Study. **Br J Neurosurg.** 2017; 31(2): 184-188.

### EFFECT OF DAYTIME SLEEPINESS ON BALANCE AND MOBILITY IN THE ELDERLY

Diminished ability to maintain balance is associated with a fear of falling and an increased risk of falling. As balance is sensitive to sleep deprivation, the prevalence of sleep deprivation with aging may worsen this risk. This study reviewed the association between self-reported, daytime sleepiness and balance among community dwelling, elderly adults.

Subjects were cognitively intact, community dwelling adults, 65 years of age or older, and able to walk household distances. Patient sleepiness was assessed using the Epworth Sleepiness Scale (ESS). A score of nine or more was used to indicate daytime sleepiness. Subjects were assessed for gait speed and gait characteristics, and for balance, with self-reported measures of balance and mobility also applied.

Participants were 116 adults with a mean age of 78 years, among whom 45% reported daytime sleepiness. Those with daytime sleepiness had a significantly higher body mass index, and more comorbid illnesses. Among those not reporting daytime sleepiness, 30% reported having fallen in the previous year, compared to 40% of those with daytime sleepiness ( $p=0.06$ ). Those with daytime sleepiness had a slower gait speed, a wider step width and lower Activities Specific Balance Confidence Scale scores.

**Conclusion:** This study of community dwelling, elderly individuals found that 45% reported daytime sleepiness, with gait speed and self-reported balance confidence lower among those with daytime sleepiness than among those without.

Tyagi, S., et al. Mobility in Community-Dwelling Older Adults: Effect of Daytime Sleepiness. **J Am Ger Soc.** 2017, May; 65(5): 1019-1025.

### TRAINING LOAD-INJURY PARADOX

Traditionally, workload-injury investigations have found that higher workloads were associated with greater rates of injury. However, high training loads are necessary for physiological adaptation, and increased performance. This study investigated the relationship between participation in preseason training and injuries during the following season.

Subject were 30 elite rugby players followed through a 17-week preseason and 26-round competitive season. Data collected included participation in preseason sessions, in-season training loads and injury status throughout the year. An injury was included only if it resulted in a loss of match time.

A total of 40 injuries were sustained during the competitive season. A significant inverse relationship was noted between the number of preseason training sessions and the percentage of games that were missed due to injury ( $p<0.05$ ). When controlling for training load, increased preseason participation was associated with a reduced odds of injury in the current week (OR 0.85), and the subsequent week (OR 0.83). Ten additional preseason training sessions reduced the odds of injury by at least 17% in the current and subsequent week.

**Conclusion:** This study of rugby players found that greater preseason participation was associated with a reduced risk of injury during the competitive season.

Windt, J., et al. Training Load-Injury Paradox: Is Greater Preseason Participation Associated with Lower In-Season Injury Risk in Elite Rugby League Players? **Br J Sports Med.** 2017, April; 51(8): 645-650.

### PROBIOTICS AND DEPRESSION

A growing body of evidence suggests that an abnormal composition and metabolic activity of gut microbes may play a role in irritable bowel syndrome (IBS). As alterations in the gut microbiota have also been shown to improve affective disorders, this study examined the effect of microbiota supplementation on the anxiety and depression scores of patients with IBS.

Subjects were 44 adult patients with a diagnosis of IBS with mild to moderate anxiety and/or depression scores as assessed on the Hospital

Anxiety and Depression (HAD) scale. At the screening visit a clinical history was taken with a physical exam including bloodwork and a functional MRI (fMRI). The subjects were randomized to receive 42 doses of dried *Bifidobacterium longum* (BL), or a placebo. The patients were assessed by physical exam and repeat laboratory/fMRI assessments, through week 10. The primary endpoint was a reduction in HAD scores by two or more points at six weeks.

At week six, 64% of the patients in the treatment group and 32% in the placebo group had significant improvement in HAD depression scores ( $p=0.04$  in the intention to treat analysis). This improvement was sustained at the 10-week follow-up. No significant difference was noted between the groups in anxiety scores. For IBS symptoms, the analysis demonstrated a benefit of the treatment as compared to the placebo at six but not at 10 weeks. The fMRI analysis found that the BL group had a reduced engagement of the amygdala, with this change correlated with the improvement in depression scores ( $p=0.004$ ).

**Conclusion:** This study of patients with irritable bowel syndrome and anxiety/depression found that oral supplementation with BL resulted in improved depression scores which correlated with changes in the function of the amygdala.

Pinto-Sanchez, M et al. Probiotic *Bifidobacterium longum* NCC3001 Reduces Depression Scores and Alters Brain Activity: a Pilot Study in Patients with Irritable Bowel Syndrome. **Gastroenterol.** 2017; 10.1053/j.gastro.2017.05.003.

### VITAMIN D DEFICIENCY AND SPINAL CORD INJURY

Previous studies have suggested that vitamin D deficiency might be related to a number of health issues including neuromuscular function. This literature review was designed to clarify the vitamin D status of patients with spinal cord injury (SCI).

A literature review was completed for studies published through June of 2016 which included patients with SCI and an assessment of vitamin D status. From the review, 16 studies met the inclusion criteria, with 14 of these investigating individuals with chronic SCI.



(Continued from page 2)

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Vitamin D deficiency was identified in 32-93% of the subjects, and was predominant among those with chronic SCI. Significantly higher parathyroid hormone levels were found in those with low vitamin D status as compared to those with normal vitamin D status. Vitamin D supplementation was found to normalize vitamin D and decrease parathyroid hormone concentrations. There was no link between calcium concentration and vitamin D deficiency. The relationship between vitamin D deficiency and testosterone levels was equivocal.

**Conclusion:** This literature review found that individuals with spinal cord injury are at an increased risk for vitamin D deficiency, with parathyroid hormone levels negatively correlated with Vitamin D status.

Flueck, J., et al. Vitamin D Deficiency in Individuals with a Spinal Cord Injury: A Literature Review. **Spinal Cord.** 2017, May; 55 (5): 428-434.

*Rehab in Review (RIR)* is produced monthly by physicians in the field of Physical Medicine and Rehabilitation (PM&R), with the cooperation and assistance of Emory University School of Medicine, Department of Rehabilitation Medicine. The summaries appearing in this publication are intended as an aid in reviewing the broad base of literature relevant to this field. These summaries are not intended for use as the sole basis for clinical treatment, or as a substitute for the reading of the original research.

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ISSN # 1081-1303  
[www.rehabinreview.com](http://www.rehabinreview.com)



## REHAB IN REVIEW

Produced by the Department of  
Rehabilitation Medicine, Emory  
University School of Medicine

This issue sponsored by an  
Allergan Educational Grant



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