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SODA AND CELL AGING

Sugar sweetened beverages are the largest source of added sugar in the United States diet. As such, these beverages have emerged as an important target of public health efforts and policies. Telomeres are the DNA-protein caps at the end of chromosomes that promote chromosomal stability. Shorter telomeres have been associated with increased risks of chronic diseases. This study examined the association between sugar-sweetened beverage consumption and telomere length.

The National Health and Nutrition Examination Survey (NHANES) involved 5,309 adults, ages 20 to 65 years, who provided dietary data and underwent measurement of leukocyte telomere length in the 1999 to 2002 period. A dietary recall was used to determine the consumption of sugar-sweetened sodas, noncarbonated sugar-sweetened beverages, diet sodas, 100% fruit juice and all sugar-sweetened beverages. Associations between beverage consumption and telomere length were determined.

After adjusting for sociodemographic characteristics and health-related variables, sugar-sweetened soda consumption was found to be inversely associated with telomere length ($p < 0.05$). In contrast, a positive association was observed between 100% fruit juice and telomere length ($p < 0.05$). For a daily consumption of a 20 ounce serving of sugar-sweetened soda, 4.6 additional years of aging were estimated. No such associations were observed between diet soda or noncarbonated sugar sweetened beverages and telomere length.

Conclusion: This study of a nationally representative sample of healthy adults found that consumption of sugar-sweetened soda is associated with shorter immune cell telomere length, a biologic risk factor for aging.

Leung, C., et al. Soda and Cell Aging: Associations between Sugar-Sweetened Beverage Consumption and Leukocyte Telomere Length in Healthy Adults from the National Health and Nutrition Examination Surveys. *Amer J Public Health*. 2014, December; 104(12): 2425-2431.

FROZEN FECAL MICROBIOTA FOR RELAPSING CLOSTRIDIUM DIFFICILE

Recurrent and refractory *Clostridium difficile* infection (CDI) is a major cause of morbidity and mortality among both adult and pediatric patients. Previous studies have demonstrated that fecal microbiota transplantation (FMT), the reconstitution of normal flora by a stool transplant from a healthy individual, is effective in treating relapsing CDI. As the use of fresh donations has met with logistic challenges, this study explored the use of frozen FMT for treating acute CDI.

This open label feasibility study included patients seven to 29 years of age with refractory or recurrent CDI. Active CDI was defined as diarrhea (> 3 loose stools per day), with positive stool test results. Donors were healthy, nonpregnant adults, ages 18 to 50 years, taking no medications, with a normal body mass index. Fecal matter was placed into size 00 capsules stored at -80°C . Participants were given 15 capsules on two consecutive days. Those who showed no improvement in symptoms after 72 hours were retested and offered repeat treatment. The primary endpoints were safety and clinical resolution of diarrhea.

Twenty recipients were treated using stool from four donors. Of those, 14 had clinical resolution of diarrhea after the first administration and remained symptom free at eight weeks. All six nonresponders were

retreated, with five demonstrating resolution after the second treatment.

Conclusion: This study of patients with relapsing CDI found that frozen capsules of donor feces could successfully resolve symptoms.

Youngster, I., et al. Oral, Capsulized, Frozen Fecal Microbiota Transplantation for Relapsing *Clostridium Difficile* Infection. *JAMA*. 2014, November 5; 312(17): 1772-1778.

TELOMERE LENGTH AND BRAIN VOLUME

Telomeres are specialized structures at the end of chromosomes which undergo shortening with each cell division. Telomere length is emerging as a promising biomarker of biological age and an indicator of susceptibility to age related diseases. This longitudinal study was designed to understand whether peripheral blood telomere length is associated with brain volume.

Participants ranged in age from 18 to 85 years, with a median age of 50 years. The subjects were initially involved in a population-based probability sample of Dallas County, Texas, residents. Measurement of peripheral blood leukocyte telomere length was determined for 3,302 individuals, a subset from the original cohort study. Of those, 2,082 underwent MR imaging. The data were used to determine the association between telomere length and brain atrophy.

Regions in which telomere length had the largest effect on size included the precuneus, the inferior and posterior central regions of the parietal lobe, the hippocampus, the amygdala, the fusiform and the inferior segment of the temporal lobe ($p < 0.001$ for all). Telomere length was a significant predictor of total cerebral volume, cortical white matter volume and cortical gray matter

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volume ($p < 0.001$, $p = 0.002$ and $p < 0.001$, respectively). Telomere length was associated with cerebellar white matter volume, but not with cerebellar gray matter volume.

Conclusion: This prospective, longitudinal study demonstrates that leukocyte telomere length is a biomarker associated with regional brain size, independent of age.

King, K., et al. Effect of Leukocyte Telomere Length on Total and Regional Brain Volumes in a Large, Population-Based Cohort. **JAMA Neuro.** 2014, October; 71(10): 1247-1254.

AUDIOVISUAL MANIFESTATIONS OF PSORIATIC ARTHRITIS

Sensorineural hearing loss (SNHL) and acute audiovestibular dysfunction have been found in individuals with rheumatic diseases. However, little is known about auditory manifestations in patients with psoriatic arthritis (PsA). This study examined whether the frequency of sensorineural hearing loss is increased among patients with PsA.

Sixty patients with PsA and 60 matched controls were divided by predominant rheumatic manifestations (according to the Moll and Wright classification). Audiologic and vestibular assessments were performed to assess for speech reception threshold and sensorineural hearing loss. Computerized dynamic posturography was also performed. Associations between audiovestibular tests and epidemiological and clinical features were determined.

Of the patients with PsA, 60% demonstrated abnormal hearing loss, as compared to 8.3% of the controls ($p = 0.001$). Audiometric tests revealed symmetric sensorineural hearing loss as the predominant pattern. Compared to controls, patients with PsA more commonly experienced abnormal oculcephalic response ($p = 0.006$), caloric tests ($p < 0.001$) and computerized dynamic posturography ($p < 0.001$).

Conclusion: This study found evidence that audiovestibular compromise is common among patients with psoriatic arthritis, suggesting that audiovestibular screening may be warranted in this patient population.

Amor-Dorado, J., et al. Investigations into Audiovestibular Manifestations in Patients with Psoriatic Arthritis. **J Rheum.** 2014, October; 41(10): 2018-2026.

EFFECT OF STATIN USE DURING HOSPITALIZATION FOR INTRACEREBRAL HEMORRHAGE

Decisions regarding the prescription of statins in the acute setting of intracerebral hemorrhage (ICH) may be influenced by conflicting data regarding the effect of statins on the risk of brain hemorrhage. This study explored the effect of inpatient statin use, on the outcomes of patients with ICH.

This study included a cohort of 3,481 patients, seen over 10 years, with a primary discharge diagnosis of ICH. Records were reviewed to obtain information on both inpatient and outpatient statin use which predated the admission for ICH. Baseline demographic characteristics and medical histories were obtained for all patients. The main outcome measures were 30-day survival and discharge to home or to an inpatient rehabilitation facility.

Patients treated with a statin during hospitalization had an unadjusted 30-day mortality rate of 18.4%, while those not treated had a 30-day mortality rate of 30.7% ($p < 0.001$). Multivariable logistic regression indicated that inpatient statin users were more likely than nonusers to be alive at 30 days (odds ratio: 4.25). Those treated with statins during hospitalization for ICH were discharged to home or inpatient rehabilitation 51.1% of the time, compared to 35% of those who were not treated with statins ($p < 0.001$). Patients who entered the hospital as statin users, whose therapy was discontinued at admission were less likely to be alive at 30 days than were patients who continued statin therapy ($p < 0.001$).

Conclusion: This large cohort study of patients admitted with intracerebral hemorrhage found that inpatient statin use is associated with improved outcomes, while cessation of statin use is associated with poorer outcomes.

Flint, A., et al. Effect of Statin Use during Hospitalization for Intracerebral Hemorrhage on Mortality and Discharge Disposition.

TRUNK POSTURE INFLUENCES PATELLOFEMORAL JOINT STRESS DURING RUNNING

Despite the positive health benefits associated with running, runners experience a high incidence of injuries, with approximately half of these occurring at the knee joint. Among these, the most common diagnosis is patellofemoral pain (PFP). Recent studies have suggested that sagittal plane trunk posture may be associated with tibiofemoral joint mechanics. This study was designed to better understand the association between sagittal plane trunk posture and patellofemoral joint stress during running.

Twenty-four recreational runners between the ages of 18 and 39 years were recruited. Three-dimensional trunk and lower extremity kinematics were collected at a motion analysis lab. Ground reaction forces were determined using a single force plate. Participants were instructed to run at a controlled speed of 3.4 m/s on a 14 m runway using three different trunk positions, self-selected, flexed and extended. Patellofemoral biomechanics were compared between conditions.

An analysis of variance revealed that peak patellofemoral joint stress was significantly lower during the flexed condition and significantly higher during the extended condition, as compared to the self-selected condition. In addition, peak patellofemoral joint reaction force at the time of peak stress was significantly lower during the flexed condition ($p < 0.001$) and significantly higher during the extended condition ($p < 0.001$). The adjusted knee extensor moment at the time of peak stress was significantly lower during the flexed condition ($p < 0.001$), and significantly higher during extended condition ($p < 0.001$), as compared to the self-selected position.

Conclusion: This study found that upright trunk posture during running may expose the runner to greater patellofemoral joint stress and higher risk of injury than does forward flexed running.

Teng, H., et al. Sagittal Plane Trunk Posture Influences Patellofemoral

CEREBROVASCULAR CHANGES IN MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a chronic, autoimmune, inflammatory condition, associated with varying degrees of neurodegeneration and cognitive dysfunction. As elevated levels of nitric oxide have been noted in patients with MS, some have speculated that cerebral blood flow (CBF) may be altered in this population. This study assessed the cerebrovascular reactivity of patients with MS.

This prospective, observational trial included 19 patients with clinically definite MS and 19 age-matched, healthy controls. All subjects underwent perfusion MRI evaluation, with scans initially taken while breathing room air, and then while breathing a five percent carbon dioxide gas mixture, designed to promote CBF. Cerebrovascular reactivity was calculated as the percent increase of normocapnic to hypercapnic CBF.

Individuals with MS demonstrated significantly decreased global gray matter CBF, as compared to controls ($p = 0.001$). Additionally, patients with MS had significantly less change in CBF in response to hypercapnia (31.7% versus 44.8%; $p = 0.01$). Both of these effects were significantly, negatively correlated with an increased cerebral volume of MS lesions, and significantly positively correlated to gray matter atrophy.

Conclusion: This quantitative MRI study demonstrated a diffuse decrease in cerebrovascular reactivity in patients with multiple sclerosis, as compared with healthy controls.

Marshall, O., et al. Impaired Cerebrovascular Reactivity in Multiple Sclerosis. **JAMA Neurol.** 2014, October; 71(10): 1275-1281.

HIP AND CORE VERSUS KNEE MUSCLE STRENGTHENING FOR PATELLOFEMORAL PAIN

Treatment of patellofemoral pain (PFP) has traditionally focused on the quadriceps, suggesting that an imbalance between the vastus medialis oblique and the vastus lateralis can lead to increased PFP.

More recently, PFP was proposed to be related to reduced hip strength and core endurance. This study compared the efficacy of a hip and core focused, versus a knee focused, rehabilitation protocol for the treatment of PFP.

This single-blind, multicenter, randomized, controlled trial involved 199 patients with PFP of at least four weeks duration. Those in the hip protocol group received progressive core strengthening and balance exercises targeting the core. Those in the knee protocol underwent knee focused exercises. The subjects were asked to repeat the exercises five times per week. At six weeks, treatment success was defined as a minimum of a 2 cm improvement on the visual analogue scale (VAS) for pain and a minimum of an eight-point increase on the Anterior Knee Pain Scale (AKPS).

Both groups achieved significant improvements on both the VAS and AKPS, as compared with baseline. However, those in the hip protocol had a significant reduction in self-reported pain starting at week three, while those in the knee protocol had a significant reduction starting at week four.

Conclusion: This study of patients with patellofemoral pain found that both hip and core exercises and knee focused exercises can improve pain and function, although hip and core exercises resulted in an earlier resolution of pain.

Ferber, R., et al. Strengthening of the Hip and Core versus Knee Muscles for the Treatment of Patellofemoral Pain: A Multicenter, Randomized Controlled Trial. **J Athletic Training.** 2014; 49(3). DOI:10.4085/1062-6050-49.3.70

DIAGNOSING PERIPROSTHETIC JOINT INFECTION

Periprosthetic joint infection accounts for 25% of failed knee arthroplasties and 15% of failed hip arthroplasties. This study evaluated the diagnostic characteristics of synovial fluid biomarkers as a means to detect postoperative periprosthetic joint infection.

This prospective study included 95 patients undergoing 66 arthroplasties, believed to be aseptic failures, and 29 arthroplasties diagnosed as periprosthetic joint

infection. Among those with periprosthetic joint infection, 23 were culture positive and six were culture negative. Synovial fluid was taken to assess for 43 biomarkers. The sensitivity and specificity of each biomarker was calculated at various thresholds for correct test results. Biomarkers were compared for ability to predict the diagnosis of infection, as defined by the Musculoskeletal Infection Society (MSIS).

Five biomarkers correctly predicted a periprosthetic joint infection. These biomarkers had a sensitivity of 100% and a specificity of 100%. These predictors included α -defensin, ELA-2, BPI, lactoferrin, and NGAL. No significant relationship was seen between these biomarkers and synovial fluid white blood cell count.

Conclusion: This study evaluated potential biomarkers for diagnosing periprosthetic infection after joint replacement surgery, finding five which have 100% sensitivity and specificity for identifying these infections.

Deirmengian, C., et al. Diagnosing Periprosthetic Joint Infection. Has The Era of the Biomarker Arrived? **Clin Ortho Related Research.** 2014, November; 472(11): 3254-3262.

LAYLA AND CELECOXIB FOR KNEE OSTEOARTHRITIS

While nonsteroidal anti-inflammatory drugs are known to improve symptoms of osteoarthritis (OA), they also have cautionary side effects. PG 201, (Layla), is an ethanol extract of 12 plant sources, all with known disease modifying characteristics. This study compared the efficacy of celecoxib with that of Layla for the treatment of symptomatic knee OA.

This randomized, double-blind, controlled trial included 309 patients ages 14 to 80 years with symptomatic knee OA. At baseline, the subjects were screened by physical examination, including a visual analogue scale for pain, as well as by WOMAC scores and laboratory profiles. The participants were randomized to receive either Layla at 600 mg once per day or celecoxib at 200 mg twice per day for eight weeks. The patients were followed at four and eight weeks after medication onset. At study end, all underwent laboratory profiling.

Visual analogue scale scores improved for the Layla group from 65.7 at baseline to 46.9 at week four, and 36.6 at week eight. In the celecoxib group, pain improved from 64.3 at baseline to 42.3 at week four, and 37.9 at week eight. The placebo group had no improvement in pain scores. Both groups demonstrated significant improvements in pain scores, with no differences noted between the two groups. No significant difference was noted between the groups in the tolerability profile of the medication.

Conclusion: This study of patients with osteoarthritis demonstrates that both celecoxib and Layla are effective in reducing pain, with no significant difference between the groups in efficacy or side effects.

Yoo, W.-H., et al. Efficacy and Safety of PG201 (Layla) and Celecoxib in the Treatment of Symptomatic Knee Osteoarthritis: A Double-Blind, Randomized, Multicenter, Active Drug Comparative, Parallel Group, Noninferiority, Phase 3 Study. **Rheum Internat.** 2014, October; 34: 1369-1378.

LUMBOSACRAL ORTHOSES FOR THE MANAGEMENT OF BACK PAIN

Lumbosacral orthoses (LSO) are commonly used in the management of low back pain (LBP). Studies that evaluate clinical outcomes among patients wearing LSOs have not compared the efficacy of these orthoses by their stiffness properties. This study addressed short-term, clinical outcomes in patients with LBP, comparing an inextensible LSO (iLSO) with an extensible LSO (eLSO).

This randomized, clinical trial included 98 patients with LBP, randomized to receive either standard care alone, standard care with an eLSO or standard care with an iLSO. Participants were instructed to wear the orthoses daily, particularly during activities that were noted to aggravate symptoms. The primary outcome measure was the modified Oswestry Disability Index (ODI), with secondary outcomes including the Patient Specific Activity Scale, the Fear Avoidance Beliefs Questionnaire, for both work and physical activity, and levels of pain,

assessed with a numerical pain rating scale.

The mean improvement in both the eLSO and iLSO treatment groups reached the predetermined minimal clinically important difference, but the standard care group did not. A logistic model of success (>50% improvement) revealed that, compared to the standard care group, those in the iLSO group had 4.7 times higher odds, and those in the eLSO group had 3.0 times higher odds of success.

Conclusion: This study of patients with low back pain suggests that inextensible lumbosacral orthoses are superior to extensible lumbosacral orthoses in treating this complaint.

Morisette, D., et al. A Randomized, Clinical Trial Comparing Extensible and Inextensible Lumbosacral Orthoses and Standard Care Alone in the Management of Lower Back Pain. **Spine.** 2014, October; 39(21): 1733-1742.

NEAR INFRARED LIGHT AFTER RESISTANCE EXERCISE

Near infrared light has shown promise as a therapeutic modality for treating acute and chronic musculoskeletal injuries. This study evaluated the ergogenic effect of near infrared light therapy to attenuate strength loss after resistance training.

Thirty-one, healthy men and women underwent measurements of range of motion, muscle point tenderness and muscle strength. Before exercise, those in the laser group received a dose of 360 J covering 15 points oriented along the biceps brachialis muscle, administered for three to four seconds to each point. The subjects then underwent elbow flexor resistance exercising, including maximal concentric and eccentric contractions. Immediately after exercise, strength was reassessed to determine the percentage decline from beginning to end of the exercise protocol. The participants were again assessed after two days for recovery, and returned at one week for the crossover procedure.

Muscle strength declined by 56.48% in the active group and 60.75% in the control group ($p=0.05$). After two days, no difference was seen in muscle point tenderness or

range of motion, including pain-free flexion, full extension, pain-free extension and resting arm angle.

Conclusion: This study of 39, healthy adults found that near infrared light therapy can attenuate strength loss after resistance exercise.

Larkin-Kaiser, K., et al. Near Infrared Light Therapy to Attenuate Strength Loss after Strenuous Resistance Exercise. *J Athletic Training*. 2014; 49(3): doi:10.4085/ 1062-6050-49.3.82

BOTOX PLUS TRANSCRANIAL STIMULATION FOR SPASTIC HEMIPLEGIA

Among the established therapeutic interventions for spasticity, focal injection of botulinum toxin type A (BoTN-A) has proven beneficial. In addition, low-frequency, repetitive transcranial stimulation (rTMS), combined with intensive occupational therapy (OT), has been reported to improve motor function after stroke. This study compared clinical outcomes of patients treated with rTMS/OT, with and without BoTN-A injections.

Subjects were patients with spastic hemiparesis, twelve to 254 months post-stroke. Both groups received rTMS/OT, while the intervention group also received BoNT-A into the spastic muscles of the upper extremity. All patients were hospitalized for 15 days, receiving one session of 40 minutes of low-frequency rTMS and two sessions of intensive OT daily. Those in the BoNT-A group received injections on the first day. Outcomes were assessed with the Fugl Meyer Assessment (FMA), the Wolf Motor Function Test (WMFT) and the Modified Ashworth Scale (MAS).

Both groups demonstrated significant improvement in FMA scores (<0.001 for both), with greater improvement in the treatment than in the control group ($p < 0.05$). The WMFT log performance time improved significantly in both groups, but did not differ between groups ($p = 0.147$). The MAS for finger flexors improved significantly in both groups, with the difference more pronounced in the treatment group ($p < 0.05$).

Conclusion: This study of post-stroke patients with upper limb hemiparesis, complicated by marked

spasticity, found that Botulinum Toxin Type A seems to facilitate the beneficial effects of repetitive transcranial stimulation combined with OT.

Yamada, N., et al. Local Muscle Injection of Botulinum Toxin Type A Synergistically Improves the Beneficial Effects of Repetitive Transcranial Magnetic Stimulation and Intensive Occupational Therapy in Post-Stroke Patients with Spastic Upper Limb Hemiparesis. *Europ Neurol*. 2014, November; 72(5-6): 290-298.

RETURN TO SPORT AFTER VALGUS OSTEOTOMY

Valgus osteotomy is considered the surgical option of choice for the treatment of early-stage, medial compartmental osteoarthritis (OA) of the knee among patients ages 65 years or less. As return to sport after osteotomy is poorly documented in the literature, this study evaluated recovery of physical and sporting activity after this surgery.

Subjects were 83 patients with a mean age of 50.4 years, each of whom underwent medial osteotomy for symptomatic OA of the knee. The patients were assessed with KOOS, Lysholm, Tegner and UCLA scores. Sports levels before and after the surgery were compared. The participants were followed for an average of 5.75 years.

At follow-up, 85.5% of the patients had resumed sporting activity, with 79.5% noting that their sporting level had not declined postoperatively. Mean Lysholm scores improved significantly after surgery, while Tegner and UCLA scores did not reach significance in change. The frequency of weekly sport activity did not decrease significantly, although the duration of activity declined from 4.68 hours to 4.25 hours ($p = 0.04$). Of the 20 patients who ran before surgery, 85% were able to return to running.

Conclusion: This study of patients with moderate medial compartment osteoarthritis of the knee found that a valgus osteotomy allowed most to return to their sporting activity, with most also able to return at the level at which they had been participating before developing osteoarthritis.

Saragaglia, D., et al. Return to Sports after Valgus Osteotomy of the Knee Joint in Patients with Medial Unicompartamental Osteoarthritis. *Intern Ortho*. 2014, October; 38(10): 2109-2114.

PALISADE SACROILIAC RADIOFREQUENCY NEUROTOMY FOR ANKYLOSING SPONDYLITIS

Ankylosing spondylitis (AS) frequently causes sacroiliac (SI) joint pain. Intra-articular injections have been found to reduce pain and improve joint activity, with relief typically limited in duration. This study compared the efficacy and safety of palisade SI joint radiofrequency neurotomy (PSRN) and celecoxib for the treatment of this disease.

Subjects with AS and SI joint pain were 155 patients who met the inclusion criteria and were randomized to receive either celecoxib at 400 mg per day for 24 weeks or PSRN. The primary outcome measures were pain intensities at 12 and 24 weeks, based upon a visual analogue pain scale. Disease activity, functional capacity, mobility capacity and adverse events were assessed with the Ankylosing Spondylitis Disease Activity Score (ASDAS), the Bath Ankylosing Spondylitis Metrology Index, and the Bath Ankylosing Spondylitis Functional Index.

Both interventions resulted in significant improvement in global pain intensity at 12 and 24 weeks. Reduction in adjusted global pain intensity was more robust in the PSRN group than in the celecoxib group at both 12 and 24 weeks ($p < 0.0001$). Improvement was also more significant in patients receiving PSRN for total and nocturnal back pain. The two arms did not differ in the proportion of patients who achieved 20% improvement from baseline and ASDAS scores at either 12 or 24 weeks.

Conclusion: This study of patients with ankylosing spondylitis related sacroiliac joint pain found that radiofrequency neurotomy is superior to celecoxib for pain control, functional status improvement and spine mobility.

Zheng, Y., et al. Tomography Guided Palisade Sacroiliac Joint Radiofrequency Neurotomy versus Celecoxib for Ankylosing Spondylitis:

An Open Label, Randomized and Controlled Trial. **Rheum Intern.** 2014, September; 34(9): 1195-1202.

ADVANCED CRYOTHERAPY AFTER KNEE ARTHROPLASTY

Despite pain management advances in anesthetic techniques, total knee arthroplasty (TKA) remains a challenging procedure for most patients. Cryotherapy, the application of cold to skin surrounding the injured soft tissues, is designed to reduce intra-articular pressure and decrease the local inflammatory reaction. This study was designed to determine whether advanced cryotherapy techniques could produce better post-operative pain control.

This randomized, controlled trial included 116 patients undergoing primary TKA. The subjects were quasi-randomized to receive advanced cryotherapy (AC) or traditional cold packs. The AC group received four hours of continuous cooling at 11°C immediately after surgery, as needed during the night after surgery and for four hours the following day. The control group received 15 minutes of cold pack treatment upon arrival in the recovery room, and again upon arrival in the ward. This treatment was repeated at two hours and four hours post-surgery. On the following days, the patients received the same therapy 15 minutes after physical therapy sessions at 11:00 a.m. and 3:00 p.m. The primary outcome measures were a visual analogue scale of pain at rest and analgesics consumed, with secondary outcomes including postoperative ROM, swelling and blood loss.

No significant differences were observed between the treatment and control groups in pain scores at rest. Further, no significant between group differences in pain scores were noted on day two, and none were found for pain medication consumption or length of stay. Functional results at six weeks were equivalent between groups.

Conclusion: This study of patients undergoing knee arthroplasty did not find that continuous cooling after surgery is superior to traditional cold packs for reducing pain or improving function.

Thienpoint, E., et al. Does Advanced Cryotherapy Reduce Pain and Narcotic Consumption after Knee

Arthroplasty? **Clinical Orthopedics and Related Research.** 2014, November; 472(11): 3417-3423.

ATOMOXETINE FOR HYPERTENSION AFTER BRAIN INJURY

Deficits in attention remain a significant problem for patients recovering from a traumatic brain injury (TBI). As atomoxetine, a norepinephrine reuptake inhibitor, has demonstrated efficacy in the treatment of attention deficit disorder, this study examined the effects of this medication on TBI-related attention deficit and hypo-arousal.

Adult patients who had been treated for moderate to severe TBI at an inpatient rehabilitation facility were invited to participate in this study. By telephone, potential subjects were administered the Adult ADHD Self-Report Scale and the Cognitive Failures Questionnaire. Eligible patients were randomized to receive either atomoxetine, 40 mg twice daily, or a placebo for 14 days. The patients then returned for repeat testing. The medication assignments were then reversed for 14 days. The primary outcome measure was the Cognitive Drug Research (CDR) Computerized Cognitive Assessment System, a battery of computer-controlled tasks. From this test, the Power of Attention factor was selected as the primary outcome measure. Secondary outcome measures were the CDR Quality of Episodic Memory and Speed of Memory factors.

Fifty-six subjects in the drug first group, and 24 in the placebo first group, completed the trial. No significant differences were seen between groups in either the primary or secondary outcome measures.

Conclusion: This study of patients with moderate to severe traumatic brain injury did not find that atomoxetine is effective in treating attention impairments.

Ripley, D., et al. Atomoxetine for Attention Deficits following Traumatic Brain Injury: Results from a Randomized, Controlled Trial. **Brain Inj.** 2014; 28(12): 1514-1522.

VAGUS NERVE STIMULATION FOR TRAUMATIC BRAIN INJURY

Previous studies have demonstrated that vagus nerve

stimulation may be important for neuroprotection in diseases such as epilepsy, Parkinson's disease and Alzheimer's disease. This animal study explored the neuroprotective effects of vagus nerve stimulation for traumatic brain injury.

Twenty-eight, healthy, adult, male rabbits were randomized to a control group, a sham surgery group, and explosive injury group with and without vagus nerve stimulation. The injury groups were exposed to an explosive injury to the cortex. Those animals in the vagus group received continuous stimulation for 20 minutes. Six hours after surgery, blood was collected from each rabbit. At 24 hours after injury, rabbits from each group were sacrificed for analysis.

Animals in the stimulation group had a significant reduction in brain tissue edema compared with the explosive injury group, although they were still worse than the sham surgery group. In the vagus stimulation group, brain water content was significantly higher than that in the control and sham surgery groups ($p < 0.05$), but lower than that in the explosive injury group ($p = 0.06$). Levels of the proinflammatory cytokines, TNF- α and IL-1 β , were significantly higher in the vagus nerve stimulation group than those in the control and the sham surgery ($p < 0.01$) groups, but significantly lower than those in the explosive injury group ($p < 0.01$).

Conclusion: This animal study, involving a cranial cerebral explosive injury, found that vagus nerve stimulation can reduce the degree of edema, delay the edema process, and decrease TNF- α and IL-1 β levels.

Zhou, L., et al. Neuroprotective Effects of Vagus Nerve Stimulation on Traumatic Brain Injury. **Neural Regeneration Research.** 2014, September; 9(17): 1585-1591.

EFFECT OF LUMBAR SURGERY ON LUMBOSACRAL NERVE ROOTS

Since the 1970s, pedicle screw instrumentation for the spine has been widely used to treat various pathologic conditions, including degenerative disease, trauma, tumors and deformity. Reported postoperative neurologic deficit rates after this procedure range from one to 11%. This study evaluated the path of

physiologic effects of lumbar instrumentation on lumbosacral nerve roots in the vertebral foramen.

This study included 18 patients with L4 degenerative spondylolisthesis with lumbar spinal canal stenosis at the L3–L4 and L4–L5 segments. The patients underwent L3–L4 and L4–L5 laminotomy with L4–L5 posteriorlateral fusion (PLF). Local pressure was measured before and after surgery, with the spine in neutral and in extension.

At the L4–5 vertebral foramen, the average pressures with the spine neutral and extension postures were 29.74 and 51.57 mmHg before fixation and 39.13 and 41.71 mmHg after fixation, respectively ($p < 0.001$ for presurgery only). At L5–S1, these values were 26.91 and 54.36 before fixation and 24.82 and 58.46 after fixation ($p < 0.001$ for both).

Conclusion: This study demonstrates that, after lumbar instrumentation, higher external dynamic stresses may occur in nerve roots caudal to fixed segments, while nerve roots in fixed segments experience less external dynamic stresses with positional changes.

Morishita, Y., et al. Pathophysiologic Effects of Lumbar Instrumentation Surgery on Lumbosacral Nerve Roots in the Vertebral Foramen. *Spine*. 2014, October; 39(21): E1256–E1260.

TREATMENT OF OLECRANON BURSTITIS

Olecranon bursitis can be characterized as aseptic or septic, with the most common causal organism of infection being *Staphylococcus aureus*. The optimal treatment for this condition lacks consensus. This systematic review assessed clinical outcomes following the treatment of both aseptic and septic bursitis.

Data from eligible studies were extracted, including patient characteristics, treatment protocols and clinical outcomes. The results of various interventions were compared.

Twenty-nine studies reporting on 1,278 patients were included in this systematic review. Patients exclusively received nonsurgical management in 10 of 29 studies, including antibiotic therapy, aspiration, corticosteroid injection and/or nonsteroidal anti-inflammatory drugs alone. Patients exclusively received surgical management in

seven studies. Treatments for septic bursitis included antibiotics in 100%, aspiration in 82% and surgery in 47.1%. When septic and aseptic bursitis were analyzed together, clinical resolution was more common after nonsurgical than surgical management ($p = 0.0476$).

Complications were more common in patients treated for aseptic bursitis, as compared to those treated for septic bursitis ($p = 0.0108$). In patients with aseptic bursitis, persistent infection was more likely after surgical than nonsurgical treatment ($p = 0.006$).

Conclusion: This literature review suggests that nonsurgical management of olecranon bursitis leads to better clinical resolution and lower rates of complications than does surgical management.

Sayegh, E., et al. Treatment of Olecranon Bursitis: A Systematic Review. *Arch Ortho Trauma Surg*. 2014, November; 134(11): 1517–1536.

SUSTAINED REMISSION WITH ENTARCEPT TAPERING IN EARLY RHEUMATOID ARTHRITIS

As high rates of clinical remission have been observed in patients with early rheumatoid arthritis (RA) who were treated with a combination of anti-tumor necrosis factor agents and methotrexate (MTX), this study explored whether remission can be achieved and maintained after the dose of the biologic agent is reduced or discontinued.

This multicenter, three-phase study involved patients receiving subcutaneous injections of 50 mg of etanercept plus oral MTX weekly for 52 weeks. Those who met the criteria for response in the open label phase were randomized to one of three treatment groups, etanercept 25 mg subcutaneously plus oral MTX, placebo subcutaneously plus oral MTX, or placebo subcutaneously plus oral placebo. The primary efficacy endpoint was the percentage of patients with sustained remission, defined as a DAS28 of less than 2.6 at weeks 24 and 39.

Among the 193 patients, the mean DAS28 score after all treatment was withdrawn remained significantly lower in the combination-therapy group than in the placebo group at week 52 ($p = 0.002$) and week 65 ($p = 0.003$). A significantly higher proportion of patients in the

combination therapy group than in the MTX alone or the placebo group met the primary study endpoint of sustained remission (63% versus 40% in the MTX group and 23% in the placebo group). At 65 weeks, 44% in the combination group, 29% in the MTX alone group and 23% in the placebo group achieved remission.

Conclusion: This study of patients with early rheumatoid arthritis found that, among those who achieved remission with etanercept plus MTX, continued combination therapy at a reduced dose maintained remission better than did MTX alone.

Emery, P., et al. Sustained Remission with Etanercept Tapering in Early Rheumatoid Arthritis. *N Eng J Med*. 2014, November 6; 371(19): 1781–1792.

GLUCOCORTICOIDS AND ION- CHANNEL-MEDIATED TOXICITY

The cellular and molecular mechanisms underlying rotator cuff tendon degeneration have included both intrinsic tendon failure and mechanical impingement. The neuronal changes in tendinopathy appear consistent with a failed healing response and an upregulation in the excitatory, glutamergic system. This study was designed to further understand the histological and immunohistochemical effects of glucocorticoid injections on rotator cuff tendons.

Supraspinatus tendon biopsies were taken from eight patients undergoing rotator cuff repair, and from 12 patients undergoing subacromial glucocorticoid injection for rotator cuff tendinopathy. For those in the injection group, biopsies were taken before and after injection. For those in the surgery group, biopsies were taken at the time of surgery and at seven weeks post-surgery. Patients in the injection group received one ultrasound guided injection of 40 mg of Depo-Medrol and 4 mL of 2% lignocaine into the subacromial bursa. Biopsies were assessed for histology and immunohistochemistry.

A significant increase in nuclei count and vascularity was noted after rotator cuff repair, although not after glucocorticoid injection ($p = 0.008$ for both comparisons). In addition, hypoxia inducible factor 1 alpha and cell proliferation were increased after

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*Thiru Annaswamy, M.D.
Jason Petrasic, M.D.
UTSW Medical Center, Dallas TX

*Ryan Solinsky, M.D.
University of Washington, Seattle, WA

*Angel Chang, M.D.
Udayan Kulkarni, M.D.
Michael Kwasniewski, M.D.
James Newman, M.D.
Jack Smith, M.D.
Sean Stockhausen, D.O.
VCU, Richmond, VA

*Prateek Grover, M.D., PhD
Mark F. Adderley, D.O.
Jeremy Hartman, M.D.
Adam J. Schulte, M.D.
Washington University, St. Louis, MO

Executive Editor Emeritus
Donald F. Langenbeck, Jr., M.D.

Subscription Manager
Michael P. Burke, M.S.

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rotator cuff repair, and not after glucocorticoid injection. The N-methyl-D aspartate receptor-1 glutamate receptor was increased after glucocorticoid injection and not after rotator cuff repair. An increase in the receptor metabotropic glutamate receptor seven was noted, but only seen after the rotator cuff repair ($p=0.016$).

Conclusion: This study of patients with rotator cuff tears or rotator cuff tendinopathy found that, after steroid injection, indicators of proliferative healing response were absent in a glucocorticoid treated group, with increases in glutamate receptor NMDAR 1 after steroid injection suggesting excitotoxic tendon damage.

Dean, B., et al. Glucocorticoids Induce Specific Ion-Channel-Mediated Toxicity in Human Rotator Cuff Tendon: A Mechanism Underpinning the Ultimate Deleterious Effect of Steroid Injection in Tendinopathy? **Br J Sports Med.** 2014, December; 48(22): 1620-1626.

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