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CARDIOPROTECTIVE EFFECTS OF ISOFLAVONE SUPPLEMENTATION IN WOMEN

The association between estrogen-based hormone therapy with an increased risk of thromboembolic events has women seeking alternative therapeutic options. This study was designed to determine whether isoflavones, with their estrogen receptor modulator like activity, might be effective in reducing atherosclerosis in postmenopausal women.

The subjects included 350 women ages 45 to 92 years with no history of diabetes or cerebrovascular disease. The women were randomized to a control group or a treatment group with the treatment group receiving 25 g of soy protein containing 91 mg of aglycon isoflavone equivalents. The control group received a similar appearing placebo. The patients were followed for an average of 2.7 years with monthly clinic visits for the first six months, and then every other month for the remainder of the trial. Assessments were completed with ultrasound to determine carotid artery intima thickening, plasma lipid levels, and isoflavone levels.

The mean carotid artery thickness progression rate was 4.77 μ m per year in the treatment group and 5.68 μ m per year in the placebo group. This reduction of progression rates by 16% did not reach statistical significance ($p=0.36$). However, among women who experienced menopause within the past five years, those in the treatment group experienced a 68% lower progression as compared with those taking placebo ($p=0.05$).

Conclusion: This study of middle age to elderly females found that isoflavone soy protein supplementation may reduce the progression of atherosclerosis if taken within five years of the onset of menopause.

Hodis, H et al. Isoflavone Soy Protein Supplementation and Atherosclerosis Progression in Healthy Postmenopausal Women: A Randomized Controlled Trial. *Stroke*. 2011, November; 42(11): 3168-3175.

ADDING KETAMINE TO EPIDURAL STEROID INJECTIONS

Epidural steroid injections have become a mainstay treatment for lumbar radiculitis. Studies have shown that steroids can reduce edema, pressure, inflammation, and adhesions within the nerve trunk. Often overlooked however is the involvement of NMDA receptors in pain processing. This study was designed to determine the efficacy and safety of the use of ketamine, a known NMDA receptor antagonist, when added to steroids for epidural injections

Two hundred patients ages 25 to 50 years, with a diagnosis of lumbar radiculitis were included in the study. Patients in group 1 were randomized to receive 80 mg of triamcinolone, 3 mL of 0.25% bupivacaine, plus 30 mg of ketamine. Patients in group 2 received the same dosage of triamcinolone, and bupivacaine with 3 mL of 0.9% saline. Pain scores were assessed before injection, immediately after, and then again at one week, and one, three, six, nine and 12 months after the injection.

No difference was found between the two groups in pain scores immediately after injections. At all additional follow-up periods, however, pain relief was significantly better in group 1 as compared to group 2. Of note, six patients in the ketamine group displayed hallucinations lasting for approximately 45 minutes after the injections.

Conclusion: This randomized trial found that adding ketamine to epidural steroid injections could improve pain outcomes in patients with chronic lumbar radicular pain.

Amr, Y et al. Effect of Addition of Epidural Ketamine to Steroid In Lumbar Radiculitis: One-Year Follow-Up. *Pain Physician*. 2011; 14: 475-481.

PRE-FRONTAL CORTEX AND EXECUTIVE FUNCTION IN PRIMARY BREAST CANCER

Breast cancer is one of the more common public health problems with a worldwide estimated incidence of 39 per 100,000 individuals. A growing body of evidence suggests that patients with this diagnosis are at an increased risk of altered brain structure and function. This study was designed to determine whether profiles of brain activation differ among breast cancer survivors treated with or without chemotherapy, as compared to healthy control women.

Twenty-five female survivors of breast cancer who had undergone chemotherapy and surgical procedures were compared with 19 female breast cancer survivors who had undergone surgery only and 18 healthy female controls with no history of breast cancer. All subjects underwent brain magnetic resonance imaging, functional magnetic resonance imaging, and tests of cognitive and affective function. The results were compared between groups.

Significant between group differences in brain activation were found, with less activation in the cancer groups in the left middle dorsolateral prefrontal cortex and the pre-motor cortex. The two breast cancer groups did not differ significantly between each other. The chemotherapy group demonstrated significantly reduced left caudal lateral prefrontal cortex activation as well as increased perseveration errors and worse processing speed as compared to the other two groups.

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Conclusion: This study of breast cancer survivors demonstrates significantly reduced left middle dorsolateral prefrontal cortex and medial frontal activation compared with controls, irrespective of treatment history.

Kesler, S et al Prefrontal Cortex and Executive Function Impairments in Primary Breast Cancer. **Arch Neurol.** 2011, November; 68(11): 1447-1453.

EFFECT OF FUNCTIONAL KNEE BRACE ON ATHLETIC PERFORMANCE

In 2004, the American Academy of Orthopedic Surgeons position statement declared that studies designed to test whether functional knee braces protect the knee against "giving way" have demonstrated some beneficial effect of the brace. Data concerning the effect of these braces on functional performance have been equivocal. This study was designed to determine whether acceleration, agility, power and speed performance levels are hindered while wearing a functional knee brace.

This study included 27 healthy male athletes with no history of reconstructive ligament surgery to either lower extremity. Each subject received a custom fitted functional knee brace. All subjects underwent five non-brace testing sessions designed to measure acceleration, agility, leg power and speed. After completing five non-brace testing sessions on days 1 to 3, the subjects were then tested while wearing their braces. Performance was compared between the braced and the non-braced conditions.

The group mean performance measures of braced subjects was significantly slower for the 10 m sprint, and lower for the vertical jump test. Group mean braced performance times were also slower compared with the non-brace performance in the 2 m acceleration and agility tests, though these differences did not reach statistical significance. However, after using the brace for approximately 14 hours, no significant differences were noted between the two testing conditions.

Conclusion: This study of healthy athletes found that after 14 hours of acclimation, the use of a functional

knee brace did not impede performance.

Rishiraj, N et al. Effect of Functional Knee Brace Use on Acceleration, Agility, Leg Power and Speed Performance in Healthy Athletes. **Br J Sports Med.** 2011, December; 45 (15): 1230-1237.

SCLEROSING TREATMENT OF JUMPER'S KNEE

A prevailing hypothesis for the pain associated with patellar tendinopathy (jumper's knee) is that the pain may be related to increased vascularity in the tendon. Previous pilot studies have suggested that sclerosing treatment may be an effective intervention. This study reports on the long-term outcome of such an intervention.

This randomized trial included 33 elite athletes with a mean age of 25 years. All had a diagnosis of jumper's knee including a history of pain in the patella tendon or the patella insertion in connection with training or competition. All had symptoms for a minimum of three months. Ultrasound examination demonstrated neovascularization at the painful area. The subjects were randomized to a placebo group or a treatment group to receive ultrasound guided injections with polidocanol, with follow-up injections within 3 to 5 weeks for those who reported continued pain. The primary outcome was the Victorian Institute of Sport Assessment (VISA) score. The secondary outcome was overall satisfaction with the treatment, using a visual analogue scale. Outcomes were recorded at baseline and at 12 and 44 months after the first injection.

Of the 33 patients in the initial study, a total of 29 patients with 37 tendons were available for 44 month follow-up. Twelve of the 29 patients who were followed up had undergone arthroscopic surgery either to the patella tendon or for intra-articular injury. Of those who did not receive any additional treatment after the sclerosing therapy, significant improvement in the VISA scores were noted at 12 months (p=0.001) with further improvements noted at 44 months (p=0.047).

Conclusion: This study of patients with patellar tendinopathy found that ultrasound guided sclerosing may provide long-term

benefits in improved function and reduced pain.

Hoksrud, A et al. Ultrasound Guided Sclerosing Treatment In Patients With Patellar Tendinopathy (Jumper's Knee): 44 Month Follow-Up. **Am J Sports Med.** 2011, November; 39 (11): 2377-2380.

HYPERBARIC OXYGEN AND DISC DEGENERATION

Degenerative disc disease is believed to be a significant cause of low back pain. The changes in the microenvironment during disc degeneration are thought to be related to chemical mediators such as interleukin, prostaglandin, nitric oxide and matrix metalloproteinase. As hyperbaric oxygen (HBO) has been shown to suppress interleukin one beta (IL-1[beta]) secretion, decrease nitric oxide production, increase glucosaminoglycan synthesis, accelerate bone healing, stimulate fibroblasts, and increase microvascular PO₂ in tissue, this study was designed to assess the effect of HBO on degenerative disc disease.

Twelve degenerative disc specimens were used to evaluate the effect of HBO on nucleus pulposus cells. The discs were harvested from lumbar intervertebral discs of patients undergoing spine surgery. The cells of the control group were maintained in a 5% CO₂/95% air mixture throughout the protocol. The HBO group cells were exposed to 100% O₂ at 2.5 atmospheric pressure. Three treatments were employed at 120 minutes per treatment. The amounts of IL-1[beta], prostaglandin E₂ and nitric oxide were measured and compared between groups.

The HBO group had lower levels of IL-1[beta] at 48, 96 and 144 hours ($p < 0.01$ to $p < 0.005$). Levels of prostaglandin E₂ and NO were also reduced in the HBO as compared to the control group. The HBO treatment group also demonstrated significantly suppressed apoptosis of nucleus pulposus cells ($p < 0.01$). The HBO group had more cells than the control group after each HBO treatment, reaching statistical significance at 144 hours ($p < 0.05$). At the time points of 48 and 144 hours, the HBO group also demonstrated a more cellular appearance with abundant matrix formation

Conclusion: This *in vitro* study found that hyperbaric oxygen treatment could inhibit IL-1[beta], prostaglandin E₂ and nitric oxide production, increasing cell number and matrix synthesis of cultured nucleus pulposus.

Wang, I et al. Effect of Hyperbaric Oxygenation on Inter-Vertebral Disc Degeneration: An In Vitro study with Human Lumbar Nucleus Pulposus. **Spine** 2011, Nov 1; 36(23) 1925-1931.

PREVENTING ACUTE HAMSTRING INJURIES USING ECCENTRIC TRAINING

Hamstring injury is most prevalent injury in soccer, accounting for 12-16% of all injuries. In addition to this high incidence, a common problem is the high risk of recurrence. While some studies have suggested a positive effect of hamstring strength training, the data remain inconsistent. This study was designed to further assess the preventive effect of hamstring exercise on recurrent hamstring injuries.

Of the 116 men's soccer teams playing in the top five Danish soccer divisions, 54 teams consented to participate in this trial. From these teams, 942 soccer players were randomized for placement to an intervention or a control group. All players followed their usual training program. In addition, those in the intervention group performed 27 sessions of Nordic hamstring exercise during a 10 week period at midseason break. After the start of the second half of the season, the exercise was conducted once a week with three sets of 12, 10 and eight repetitions. The outcome of interest was the occurrence of acute hamstring injury.

A total 67 acute hamstring injuries occurred during the study. Fifteen of these occurred in the intervention group and 52 in the control group ($p < 0.001$). This difference was based on both significantly lower rates of new injuries ($p = 0.034$) and recurrent injuries ($p = 0.003$). In addition there was a significant decrease in days absent from play in the treatment group.

Conclusion: This study of Danish soccer players found that eccentric hamstring training could result in

reduced new and recurrent hamstring injuries.

Peterson, J. et al. Preventive Effect of Eccentric Training On Acute Hamstring Injuries In Men's Soccer: A Cluster -- Randomized Controlled Trial. **Am J Sports Med.** 2011, November; 39(11): 2296-2303.

ULTRASOUND GUIDED RADIOFREQUENCY LESIONING FOR LATERAL EPICONDYLITIS

Lateral epicondylitis is a common cause of elbow pain. Pain in the lateral aspect of the elbow is the most consistent symptom. Numerous nonsurgical treatments have been reported with varying results. When the patient's condition is resistant to nonsurgical treatment, surgery is offered as a last result. Radiofrequency-based microtenotomy has been advocated as an effective method of treatment. An alternative option, radiofrequency thermal lesioning (RTL), works by means of heat dissipation from an active electrode. This study evaluated the effect of this technique on the treatment of recalcitrant lateral epicondylitis.

This prospective study included 35 elbows with the diagnosis of lateral epicondylitis. A 22-gauge cannula with a solid stylet at was advanced at an angle of 30-40°, using real-time ultrasound to the point of maximal pain. The radio energy generator was then inserted and the radiofrequency ablation was performed. After the procedure, patients were evaluated with a visual analog scale to determine the intensity of pain during rest and with activity. In addition, patients were assessed with the Disability of Arm Shoulder and Hand (DASH) tests and the modified Mayo Clinic Performance Index. Follow-up evaluation were performed at one, three and six months after the procedure.

The visual analog scores for pain were reduced by 70% with pain improvement noted at one, three and six months. The VAS scores improved from 4.9 to 0.9 at rest and from 7.6 to 2.5 at palpation. The DASH scores improved from 54 to 21 and the modified Mayo Clinic Performance Index improved from poor to excellent at six-month follow-up.

Conclusion: This study of patients with recalcitrant lateral epicondylitis found that ultrasound guided percutaneous radiofrequency lesioning can be used as a treatment option when nonsurgical treatments fail.

Lin, C et al. Clinical and Ultrasonographic Results of Ultrasonographically Guided Percutaneous Radiofrequency Lesioning in The Treatment of Recalcitrant Lateral Epicondylitis. **Am J Sports Med.** 2011, November; 39(11): 2429-2435.

AEROBIC FITNESS AND OBESITY: RELATIONSHIP TO CEREBRAL WHITE MATTER INTEGRITY

Participation in regular physical activity is related to better executive function and successful brain aging. The specific mechanisms by which this occurs are unclear. Cerebral white matter fibers are responsible for neuronal transmission and integration of cognition between brain regions and across cerebral hemispheres. There is limited information however as to whether exercise affects these fibers. This study was designed to determine the relationship between aerobic fitness and obesity ,to cerebral white matter integrity in the cingulum of healthy older adults.

One hundred twenty community dwelling older adults were prescreened for self-reported health and physical activity. Those accepted were healthy, without orthopedic, cardiopulmonary, metabolic, cognitive, or MRI testing limitations. From this group 15 subjects were recruited who completed VO2 peak testing, and MRI of the brain. Obesity risk was determined using the body mass index and abdominal girth. An MRI was completed using diffusion tensor imaging techniques using cerebral white matter indices, and fractional anisotropy(FA). Subjects were screened for cognitive status, depression, by physical exam, and by aerobic exercise testing.

Results demonstrated that VO2 peak was mildly related to FA in the left middle cingulum, explaining 28.5% of the total variance of FA. Abdominal girth and body mass index were inversely related to FA in the right posterior cingulum segment. Abdominal girth and body mass index explained 53.9% and 43.9%,

respectively, of the total variance of FA in the right posterior cingulum.

Conclusion: This study found that higher aerobic fitness and lower obesity are related to greater cerebral white matter integrity, though this relationship varied in the cingulum.

Marks, B et al. Aerobic Fitness and Obesity: Relationship to Cerebral White Matter Integrity in the Brain of Active and Sedentary Older Adults. **Br J Sports Med.** 2011, December; 45(15): 1208-1215.

PLATELET RICH PLASMA TO TREAT THE INFLAMMATORY EFFECTS OF OA

Osteoarthritis is a degenerative joint disease characterized by an imbalance of anabolic and catabolic processes in synovial joints. This imbalance results in progressive cartilage damage. To stimulate repair processes, platelet rich plasma (PRP) has been investigated. This study was designed to better understand the effects of PRP in a standardized inflammatory environment.

Human osteoarthritic cartilage was obtained from six patients undergoing total knee replacement surgery. From these, chondrocytes were harvested and cultured in the presence of interleukin one beta to mimic an osteoarthritic environment. The medium was supplemented with various concentrations of PRP. Assessments were then made of gene expression of matrix forming and matrix degrading proteins to determine the effect of the PRP on these processes.

Following treatment with PRP, a diminished expression of the interleukin one beta inflammatory cascade was demonstrated. Supplementation with PRP diminished the interleukin one beta induced inhibition of COL2A1 (p=0.003) and ACAN(p=0.001) gene expression as compared to the control group. , In addition PRP resulted in a reduced expression of ADAMTS4 (p=0.001) and PTGS2 (p=0.004).

Conclusion: This study demonstrates that platelet rich plasma can diminish multiple inflammatory interleukin one beta mediated effects on human osteoarthritic chondrocytes.

Van Buul, G et al. Platelet Rich Plasma Releasate Inhibits Inflammatory Processes in Osteoarthritic Chondrocytes . **Am J Sports Med.** 2011, November: 39 (11): 2362-2370.

SYMPTOMATIC DISC HERNIATION AND SERUM LIPIDS

A significant portion of back pain is associated with degeneration of the intervertebral disc. Insufficient blood supply has been proposed as a contributing factor to disc degeneration. This study compared the known atherosclerosis risk factors and their association with disc disease.

This study included 384 patients who underwent surgery at the author's institution. Group 1 included 169 patients undergoing surgery for symptomatic disc herniation (L5-S1), as confirmed by signs, symptoms and MRI and electromyography studies. Group 2 include 169 patients who underwent arthroscopic meniscectomy for a meniscal tear during the same reporting period. None of the latter group reported back pain. The patients were matched by age and gender. All patients underwent blood draws for lipid evaluations.

When comparing the groups, patients with symptomatic herniated discs showed significant higher triglyceride concentrations (p=0.02) and total cholesterol concentrations (p=0.01).

Conclusion: This study, comparing patients with symptomatic lumbar disc degeneration with matched controls found that those with disc degeneration had higher levels of triglycerides and total cholesterol.

Longo, U., et al. Symptomatic Disc Herniation and Serum Lipids. **Eur Spine J.** 2011, October; 20(10): 1658-1662.

DIET TO MODULATE ALZHEIMER'S DISEASE RISK

Established risk factors for pathologic brain aging include obesity, diabetes mellitus, and hyperlipidemia. These are increasing in prevalence due to high consumption of saturated fats and simple carbohydrates. This study assessed the effects of a high

saturated fat/high glycemic index diet (HIGH) compared with a low saturated fat/low glycemic index diet (LOW) on insulin and lipid metabolism, Alzheimer's associated cerebral spinal fluid markers and cognition.

Twenty healthy control and 29 subjects with amnesic mild cognitive impairment (aMCI) were randomized to receive a HIGH or a LOW diet for four weeks. Glucose and insulin levels, plasma lipids, several spinal fluid Alzheimer's disease biomarkers (A β 1-42, A β 1-40, tau protein, p-tau insulin, Apo-E, F2-isoprostanes) and measures of cognition were assessed at baseline and during the fourth week of the diet.

The LOW diet increased CSF levels of A β 1-42 in the aMCI group and decreased these levels in the healthy group ($p < 0.001$). The HIGH diet increased CSF levels of A β 1-42 for healthy adults. The CSF apolipoprotein E concentration was increased in the LOW diet group and decreased in the HIGH diet group. The HIGH diet increased and the LOW diet decreased insulin, plasma lipid levels insulin and CSF F-2 isoprostane concentration. Finally, the LOW diet was shown to improve delayed visual memory, as compared with the HIGH diet group ($p = 0.04$).

Conclusion: This study suggests that a diet high in saturated fat and simple carbohydrates may contribute to pathologic brain aging, while a diet low in saturated fat and simple carbohydrates may have a protective effect.

Bayer-Carter, J et al. Diet Intervention and Cerebral Spinal Fluid Markers in Amnesic Mild Cognitive Impairment. *Arch Neurol*. 2011, June; 66(6): 743-752.

PSYCHOACTIVE MEDICATIONS AND CRASH INVOLVEMENT IN OLDER DRIVERS

Several psychoactive medications are known to impair driving ability and increase the risk of a crash. This study was designed to determine the association between psychoactive medication and the risk of motor vehicle crash in elderly drivers.

Data for this retrospective study were obtained from the Hospital Morbidity Data System comprising data of all hospital admissions in Western Australia. All hospital

admissions between 2002 and 2008 were reviewed for cause of injury, sociodemographic information, comorbid health conditions and assessment of exposure to pharmaceuticals. The patients were matched to estimate the odds of a hospitalization for injuries sustained in a crash associated with psychoactive medication use.

Nine hundred eighty-one individuals ages 60 years and older were hospitalized as a result of a motor vehicle crash during the study period. After excluding non-drivers, the final sample consisted of 616 individuals who had been prescribed psychoactive medications. A prescription for benzodiazepine within the hazard period was associated with a 5.3 times greater likelihood of a hospitalized crash ($p < 0.001$). A prescription for an antidepressant was associated with an odds ratio of 1.8 for a hospitalized crash ($p = 0.04$). Finally, those with a prescription for an opioid analgesic had a 50% greater risk of a hospitalized crash ($p = 0.05$).

Conclusion: This study of drivers older than 60 years of age found a greater risk of motor vehicle crashes resulting in hospitalization among those taking psychoactive medication prescriptions, with the greatest risk among those prescribed benzodiazepines.

Mueleners, L et al. Psychoactive Medications and Crash Involvement Requiring Hospitalization for Older Drivers: A Population-Based Study. *JAGS*. 2011, September; 59(9): 1575-1580.

LONG-TERM MORTALITY AND RE-BLEEDING IN NON-ANEURYSMAL SUBARACHNOID HEMORRHAGE

On average, 15% of patients with spontaneous subarachnoid hemorrhage (SAH) have no obvious source of bleeding. This study sought to assess the long-term outcome of patients after non-aneurysmal SAH.

Between 1989 and 1999 a total of 1154 patients with symptoms and signs of spontaneous non-traumatic SAH were admitted to the study hospital. Of these 97 were included in the study, as the etiology of the aneurysm could not be verified by cerebral angiography. At nine year follow up, the outcome of patients

was evaluated from the most recent hospital notes or by phone call. The Glasgow Outcome scale was used to evaluate the clinical status at the time of discharge and at follow-up visits. Surviving patients within the hospital catchment area were contacted, offered an MRI examination and interviewed to assess clinical outcome. A total of 33 were studied with MRI and MRA and interviewed at an outpatient clinic.

At a mean follow up of 12 years, 13 of 97 patients had died. Of the 97, 79 patients recovered well with Glasgow Outcome Scale scores of four or five. Of the 33 patients followed by MR studies, six had infarctions and 11 had leukoaraiosis. No new vascular pathology was identified to suggest an etiology for the prior SAH. The mortality rate for patients exceeded 4% in the first year after the SAH and then returned to that of the general population.

Conclusion: This study of patients with non-aneurysmal subarachnoid hemorrhage found that after the first year, mortality is comparable to the general population.

Pyysalo, I et al. Long-Term Outcome after Subarachnoid Haemorrhage of Unknown Aetiology. *J Neurol Neurosurg Psychiatry*. 2011, November; 82(11): 1264-1266.

SYSTOLIC BLOOD PRESSURE AND RISK OF RECURRENT STROKE

While national guidelines suggest maintaining a systolic blood pressure of less than 120 mmHg and a diastolic blood pressure of less than 80 mmHg in persons with a prior stroke, limited data address the role of blood pressure levels within normal range for vascular risk reduction after stroke. This study evaluated the Independent association of systolic blood pressure on clinical outcomes among persons with recent ischemic stroke.

Between September 2003 and July 2006, 20,330 patients from 695 centers were identified with recent non-cardioembolic ischemic strokes. The original trial compared the effect of a combination of aspirin and extended release dipyridamole with clopidogrel and telmisartan and placebo after ischemic stroke. A post hoc observational analysis was completed of patients 50 years of age

and older comparing the risk of recurrent stroke with mean systolic blood pressure levels. The categories for comparison included very low normal (less than 120 mmHg) low normal (120-130 mmHg), high normal (130-140 mmHg), high (140-150 mmHg) and very high (≥ 150 mmHg).

At 2.5 year follow up, recurrent stroke was greatest in the very high systolic blood pressure group (14.1%), followed by the high systolic blood pressure group (8.7%), the very low normal systolic pressure group (8%), the low normal systolic blood pressure group (7.2%) and the high normal systolic blood pressure group (6.8%). Rates of all cause mortality and death due to vascular causes were highest in the very low normal systolic blood pressure group (9.2%, and 3.1% respectively), and very high systolic blood pressure group (9.2% and 3.2% respectively).

Conclusion: This study of patients with a recent non-cardioembolic ischemic stroke found an association between recurrent stroke and systolic blood pressures that were either less than 120 mmHg, or at least 150 mmHg.

Ovbiagele, B et al. Level of Systolic Blood Pressure within the Normal Range and Risk of Recurrent Stroke. **JAMA**. 2011, November 16; 306(19): 2137-2144.

ASPIRIN VERSUS LOW MOLECULAR WEIGHT HEPARIN AFTER HIP REPLACEMENT

A recent review of national and international guidelines on thromboprophylaxis for patients undergoing orthopedic procedures reported that the recommendation as to whether or not to use aspirin remained a significant source of conflict. This study sought to better clarify the difference in efficacy between these two drugs.

Data for the study were obtained from the National Joint Registry for England and Wales, an administrative database of hospital admissions in the English National Health Service. A total of 108,584 patients undergoing surgery between 2003 and 2008 were included, and followed for 90 days. Data were analyzed to estimate odds ratios adjusted for baseline risk factors.

Without adjustment for potential risk factors, the data did not reveal significant differences in the rate of thromboembolic events, major hemorrhage, or return to surgery between aspirin and the low molecular weight group. With risk adjustment however, the difference in mortality at 90 days increased to 0.65% among those taking aspirin and 0.51% among those taking low molecular weight heparin ($p=0.04$).

Conclusion: This study of patients undergoing total hip replacement found that aspirin may be slightly worse than low molecular weight heparin for preventing mortality within the first 90 days.

Jamison, as et al. The Effect of Aspirin and Low Molecular Weight Heparin on Venous Thromboembolism after Hip Replacement. **J Bone Joint Surg (Br)**. 2011, November; 93B: 1465-1470.

OBSTRUCTIVE SLEEP APNEA AND OUTCOMES AFTER ISCHEMIC STROKE

The vast majority of patients with obstructive sleep apnea (OSA) go undiagnosed. OSA has been linked to a multitude of cardiovascular problems, including pulmonary hypertension, systemic hypertension, cardiac arrhythmias, and cerebrovascular events. Recent data suggest a possible causal link between OSA and stroke. This study assessed the relationship between a premorbid diagnosis of being at risk of OSA, and subsequent stroke mortality and disability.

This observational cohort study included 174 consecutive adult patients presenting to an emergency department with acute ischemic stroke. OSA risk was assessed using the Berlin Sleep Questionnaire, with patients classified as either high risk, or low risk. Stroke severity was measured using the National Institute of Health Stroke Severity Scale (NIHSS) with functional outcome and discharge measured using the modified Rankin scale (mRS). Mortality rates were obtained from hospital records, with all patients followed for at least one year after stroke. The data were reviewed to determine the association between the OSA risk and functional outcomes.

The Berlin Sleep Questionnaire identified 60.4% of the subjects as being at high risk for OSA. Of these, seven patients (4%) had a previous diagnosis of OSA. Those with a previous diagnosis of OSA were more likely (relative risk 5.3) than those without OSA to die within the first month after stroke ($p=0.064$). However, patients at high risk for OSA did not demonstrate increased mortality at 30 days. In the multivariate analysis, after adjusting for age and NIHSS score, previous OSA was an independent predictor of worse mRS scores at hospital discharge ($p=0.004$).

Conclusion: This study demonstrates that a pre-morbid diagnosis of obstructive sleep apnea predicts increased morbidity and mortality following an ischemic stroke.

Mansukhani, M et al. Worse Outcome after Stroke in Patients with Obstructive Sleep Apnea: An Observational Cohort Study. **J Stroke Cerebrovasc Dis**. 2011, September – October; 20(5) 401 – 405.

TOLL LIKE RECEPTOR 4 AND OUTCOME AFTER INTRACEREBRAL HEMORRHAGE

Patients presenting with intracerebral hemorrhage (ICH) have twice the risk of severe disability as compared to patients with ischemic stroke. Multiple studies have described the presence of an intense local inflammatory response surrounding the hemorrhage. This response contributes to the poor outcome. Activation of an innate immune response culminates in the production of pro-inflammatory cytokines and chemokines. Toll like receptor four (TLR4) is activated by a number of endogenous proteins that act as danger signals in the setting of injury. This study was designed to determine the role of TLR4 in the immune response after ICH.

Male TLR4 deficient and wild type mice were subjected to intracranial hemorrhage. The inflammatory response surrounding the hematoma was quantified by immunohistochemistry, whole brain flow cytometry and polymerase chain reaction. Neurobehavioral activity was quantified and compared between groups.

The perihematomal inflammation was markedly decreased in the TLR4

deficient mice, with an associated reduced recruitment of neutrophils and monocytes, and fewer microglia, as compared to controls. On day three, the TLR4 deficient mice had a significantly better neurobehavioral outcome.

Conclusion: This study found that TLR4 has a significant role in the development of perihematomal inflammation and secondary injury after intracerebral hemorrhage.

Sansing, L et al. Toll Like Receptor 4 Contributes to Poor Outcome after Intracerebral Hemorrhage. **Ann Neurol.** 2011, October; 70: 646-656.

TRANSCRANIAL DIRECT CURRENT STIMULATION AND FIBROMYALGIA

The most accepted pathophysiological model of fibromyalgia considers an imbalance between nociception and normal physiologic pain control. Based on this theory, therapeutic approaches aiming at the modulation of the central nervous system should be beneficial. This study explored the effects of transcranial direct current stimulation (tDCS) to affect an improvement in quality of life and pain among patients with fibromyalgia.

This double-blind, placebo-controlled trial included females who fulfilled the American College of Rheumatology criteria for fibromyalgia. Twenty-three patients were randomized to receive weekly sessions of sham or anodal tDCS of the primary motor cortex. All simulations were performed before the first hour of activities of the rehabilitation program. During treatment, a constant current of 2 milliamps intensity was applied for 20 minutes once a week for 10 weeks. A blind evaluator assessed the treatment effect using the visual analogue scale for pain and quality of life indicators. These included the Fibromyalgia Impact Questionnaire (FIQ), the SF-36, a health assessment questionnaire, and for depression, the Beck Depression Inventory and Hamilton Rating Scale.

For pain, measured by the SF-36, there was a significant interaction effect with tDCS ($p=0.006$). There was no affect with sham treatment. For the remaining scores of the SF-36 there was no significant effect of the tDCS. For the FIQ there was a

tendency for improved scores after active treatment ($p=0.056$) but not after sham treatment.

Conclusion: This study of patients with fibromyalgia only partially demonstrated that transcranial direct current stimulation may be an effective add-on treatment to a multidisciplinary approach in patients with fibromyalgia.

Riberto, M et al. Efficacy of Transcranial Direct Current Stimulation Coupled with a Multidisciplinary Rehabilitation Program for the Treatment of Fibromyalgia. **Open Rheum J;** 2011; 5: 45-50.

MUSCULOSKELETAL PAIN AND CEREBRAL PALSY

Musculoskeletal pain is common in children with cerebral palsy (CP). The problem is thought to increase with age. More than half of all children with CP who experience recurrent chronic pain report that this pain interferes with self-care and sleep. This study was designed to explore the prevalence and predictors of recurrent musculoskeletal pain among children and adolescents with CP.

This cross-sectional study included a population-based group, involving adolescents born in 1992 and 1993 living in southeastern Norway. In addition a hospital-based group was defined from individuals ages 8 to 18 years of age who completed gait analyses at Oslo University Hospital. All subjects agreed to a clinical examination, an interview and to answer questionnaires. Participants responded to two questions on pain including how much and how often, in the Child Health Questionnaire. Both the pediatrician and the therapists performed a clinical assessment and were asked to judge how likely it was that recurrent pain was musculoskeletal in origin and whether it was related to the CP.

According to professional judgment, 62% of the children experienced non-procedural recurrent pain related to musculoskeletal aspects of CP. Children with recurrent musculoskeletal pain were older and had greater motor impairment than did those without recurrent pain. The children reported musculoskeletal pain to be moderate.

Parents reported pain to be more severe and with higher impact on sleep than did their children.

Conclusion: This study of children ages 8 to 18 with a diagnosis of CP found that recurrent musculoskeletal pain occurs in more than half, with worse pain among those who are older and more impaired.

Ramstad, K et al. Characteristics of Recurrent Musculoskeletal Pain In Children with Cerebral Palsy Aged 8 To 18 Years. **Developmental Medicine and Child Neurology.** 2011; 53: 1013-1018.

EMERGENCY HOSPITALIZATIONS FOR ADVERSE DRUG EVENTS IN THE ELDERLY

Hospitalizations for adverse drug events are likely to increase as Americans live longer and have a greater number of chronic conditions. In a previous study, the authors found that medications classified as always potentially inappropriate are implicated in only 3.6% of emergency visits for adverse drug events in older individuals. In the same study, three medications including warfarin, insulin, and digoxin were implicated in 33% of such visits. This study sought to better understand the contribution of specific medications for adverse drug events among persons 65 years of age or older.

National estimates of emergency department visits and subsequent hospitalizations for adverse drug events were based on data from hospitals that participate in the National Electronic Surveillance System -Cooperative Adverse Drug Event Surveillance project. This project is a nationally representative probability sample of hospitals in the United States. For this study a surveillance case was defined as a hospitalization after an emergency department visit by an individual 65 years of age and older occurring between January 2007 and December 2009. Cases were identified where the treating clinician attributed the admission to the use of a drug or a drug specific adverse event. The primary outcome measure was hospitalization after an emergency department visit for an adverse event due to a medication.

On the basis of 12,666 cases, an estimated 265,802 emergency

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department visits for adverse drug events occurred during the study period. Of these 37.5% required hospitalization. Nearly half of these involved adults who were 80 years of age or older. Hematologic agents, and endocrine agents, cardiovascular agents, central nervous system agents and anti-infective agents were the five most common therapeutic categories implicated, accounting for 88.3% of the hospital admissions. The four most commonly implicated medications were warfarin (33.3%), insulin (13.9%), oral antiplatelet agents (13.3%) and oral hypoglycemic agents (10.7%). These accounted for 67% of the hospitalizations.

Conclusion: This study demonstrates that most emergency hospitalizations for adverse drug events in older individuals result from a few commonly used medications. Relatively few of these hospitalization involved medications typically designated as high risk or inappropriate.

Budnitz, D et al. Emergency Hospitalizations for Adverse Drug Events in Older Americans. **N Engl J Med.** 2011, November 24; 365(21): 2002-2012.

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