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NEUROPATHIC PAIN AND NABILONE

While most current neuropathic pain (NeP) medications act upon ion channels, the discovery of endocannabinoids and cannabinoid receptors has led to a new understanding of pain pathophysiology in animal models. This study assessed the efficacy of nabilone, a CB1 receptor agonist, as an adjunctive treatment for neuropathic pain due to diabetic peripheral neuropathy.

This single-center, parallel group, double-blind, placebo controlled trial included adults 18 to 80 years of age with diabetic peripheral neuropathy associated neuropathic pain. At baseline, the patients were screened for daily pain severity and sleep disruption severity over four weeks. The subjects were randomized to receive either a flexible dose of nabilone at 1 to 4 mg per day or a placebo. The primary efficacy outcome measure was the average daily pain score during the fifth week of the double-blind phase.

Eleven of 13 subjects in the nabilone group and five of 13 in the placebo group enjoyed at least a 30% reduction in pain from baseline ($p<0.05$). Four of thirteen subjects in the nabilone group and one of 13 in the placebo group achieved a 50% reduction in pain. A significantly greater reduction was seen in Hospital Anxiety Depression Scores (HADS) among patients receiving nabilone, as compared to those receiving placebo ($p<0.05$). The evaluation of sleep using the Medical Outcomes Study Sleep Scale indicated an improvement in the overall sleep problems among those receiving nabilone ($p<0.05$). Medication related confusion resulted in the withdrawal of 5.4% of the subjects.

Conclusion: This study of diabetic peripheral neuropathy found that nabilone, an oral cannabinoid receptor agonist, is effective in reducing pain, sleep disturbance and improving quality of life.

Toth, C., et al. An Enriched Enrollment Randomized Withdrawal, Flexible Dose, Double-Blind, Placebo -Controlled, Parallel Assignment Efficacy Study of Nabilone as an Adjuvant in the Treatment of Diabetic Peripheral Neuropathic Pain. **Pain**. 2012, October; 153(10): 2073-2082.

IN VITRO FERTILIZATION AND RELAPSE OF MULTIPLE SCLEROSIS

Previous studies have demonstrated a correlation between hormonal status and the risk of relapse in patients with multiple sclerosis (MS) after pregnancy and delivery. This study investigated the influence of *in vitro* fertilization (IVF) treatments on the risk of relapse in women with MS.

Data for this study were obtained over an 11-year period from 13 French University Hospital databases and referring neurologists. During that time, 35 patients were identified with a diagnosis of MS, each of whom had undergone at least one IVF treatment. The mean age of these patients was 32 years at the time of onset of MS, with mean disease duration of 6.6 years. The relationship between IVF and the occurrence of MS relapse was analyzed.

In this cohort, 26 relapses were noted among 19 women, in the 3 month period following the 70 IVF procedures. The relapse rate was significantly increased during the three months following IVF, as compared to the same period just prior to the treatment, and to that during a control period one year prior to IVF. The significant increase in relapse was associated with both the use of gonadotrophin releasing hormone agonists ($p=0.025$) and IVF failure ($p=0.019$).

Conclusion: This study of patients with multiple sclerosis found a relationship between *in vitro* fertilization and the risk of subsequent relapse of multiple sclerosis. This correlation was especially true among those for whom *in vitro* fertilization had failed.

Michel, L., et al. Increased Risk of Multiple Sclerosis Relapse After *in Vitro* Fertilization. **J Neurol Neurosurg Psychiatry**. 2012, August; 83(8): 796-802.

TISSUE PLASMINOGEN ACTIVATOR BEYOND THE THREE-HOUR TIME WINDOW

Among patients with acute ischemic stroke, the early administration of tissue plasminogen activator (t-PA) has been found to increase the likelihood of a favorable functional outcome. The American Stroke Association and the American Heart Association have recently issued a scientific advisory recommending the administration of t-PA up to 4.5 hours after symptom onset. This study examined the effect of later administration.

This prospective, multicentered study included 53 hospitals tracking patients with acute ischemic stroke. Between 2005 and 2010, 1,070 patients received t-PA during the acute stroke hospitalization. Those receiving t-PA at three hours or less were defined as the early group, and those receiving t-PA later were defined as the late group. The main outcome was any adverse clinical outcome, including in hospital deaths, hemorrhages and other complications.

Of the 886 eligible patients who received t-PA, 781 received t-PA within three hours and 105 between three and six hours after symptom onset. Adverse events occurred in 16.3% of those in the early group and 14.3% of those in the late group. The

proportion of patients experiencing in hospital hemorrhage or death was similar between the two groups. The adjusted mean length of hospital stay was longer for the early group than for the late group ($p<0.04$).

Conclusion: This study of patients admitted with acute ischemic stroke found that administration of t-PA more than three hours after symptom onset did not result in an increased risk of in hospital mortality or hemorrhage, and did not result in an increased hospital length of stay.

O'Brien, E., et al. Clinical Outcomes among Stroke Patients Receiving Tissue Plasminogen Activator Therapy Beyond the Three-Hour Time Window. **J Stroke Cerebrovasc Dis**. 2012, October; 21 (7): 541-546.

FRACTALKINE AND STROKE OUTCOME

Fractalkine is a chemokine, expressed on neurons, which serves as an adhesion molecule, whose receptor is expressed by monocytes, lymphocytes, natural killer cells, macrophages and microglia. In its soluble form it serves as a chemoattractant for these cells. Mice deficient in Fractalkine have smaller infarct volumes and improved survival after middle cerebral artery occlusion. This study was designed to determine whether Fractalkine levels are associated with outcome after stroke.

This longitudinal study included 85 adult patients who were hospitalized for ischemic stroke. Blood was drawn for Fractalkine and inflammatory marker level assessment at baseline, and the at three, seven ,90 and 180 days after stroke onset. Clinical and demographic data were collected on all patients. Stroke severity was measured with the National Institutes of Health Stroke Scale (NIHSS).

Patients with more severe strokes had lower plasma concentrations of Fractalkine at days one and seven. At day 180, higher circulating concentrations of Fractalkine were associated with better clinical outcome. Patients with poor neurological outcome at 180 days after stroke had significantly lower levels of Fractalkine than did patients with better outcomes. However, plasma concentrations of Fractalkine early after stroke were not predictive of long-term outcome.

Conclusion: This study of patients with ischemic stroke found that lower levels of Fractalkine immediately after stroke are associated with worse stroke outcome.

Donahue, M., et al. Higher Plasma Fractalkine Is Associated with Better Six-Month Outcome from Ischemic Stroke. **Stroke**. 2012, September; 43 (9): 2300-2306.

MEMANTINE PLUS VITAMIN D FOR ALZHEIMER DISEASE

Patients with Alzheimer disease (AD) suffer not only decreased brain cholinergic activity, but also a glutamatergic excitotoxicity that leads to loss of synaptic plasticity and increased neuronal death. Treatment with memantine, a modulator of glutamatergic excitotoxicity, may alter plasticity and delay neuronal death. Clinical results from the use of this medication have been minimal, with some suggesting the need for combination treatment. Among the candidates to combine with memantine is vitamin D, a hormone with neurotrophic, anti-inflammatory, antioxidant, anti-ischemic and neuroprotective properties. This study was designed to determine whether memantine combined with vitamin D is more effective than either substance alone for improving global cognitive performance in patients with AD.

The subjects included 43 patients identified from the patient database of the memory clinic of Angers University Hospital in France. All patients had a new diagnosis of AD, an absence of delirium and a prescription for memantine and/or vitamin D supplements. Memantine was given orally and titrated by 5 mg increments over four weeks to a full dose of 20 mg per day. Vitamin D supplements were given orally with a dose range of between 400 and 1,000 international units per day or between 100,000 and 200,000 international units per month. Patients were followed for changes over six months in the Mini Mental State examination (MMSE)

Of the 43 patients, 41.9% received memantine alone, 39.5% received vitamin D alone and 18.6% received both. Those taking

memantine plus vitamin D had a mean improvement in MMSE scores of four points, while participants taking memantine alone remained stable, and those taking vitamin D alone worsened by a mean of 0.6 points. The change in MMSE scores in the combined group was greater than the change among those taking memantine alone or vitamin D alone (p=0.008, and p=0.004 respectively).

Conclusion: This study of patients with Alzheimer disease found that those treated with memantine combined with vitamin D for six months demonstrated a significant and clinically relevant improvement in Mini Mental State Exam scores, with this combination more effective than taking either drug alone.

Annweiler, C., et al. Effectiveness of the Combination of Memantine Plus Vitamin D on Cognition in Patients with Alzheimer Disease: A Pre- Post-Pilot Study. **Cogn Behav Neurol.** 2012, September; 25(3): 121-127.

CHOCOLATE CONSUMPTION AND STROKE AMONG MEN

Previous studies have demonstrated that chocolate consumption is associated with a lower risk of stroke among women. This Swedish study was designed to examine the association between chocolate consumption and the risk of total stroke in men.

Data were obtained from the Cohort of Swedish Men study, which began in 1997 with men 45 to 79 years of age. Questionnaires were sent, including 350 items regarding diet and lifestyle factors. Chocolate consumption was assessed using a self-administered food frequency questionnaire. Chocolate consumption, in grams, was assessed by age specific portion sizes. These data were compared with the incidence of first stroke occurring between 1998 and 2008. In addition, a meta-analysis of chocolate consumption and stroke was performed using data through January 2012.

During a mean follow-up period of 10.2 years, 1,995 cases of first stroke were identified. High chocolate consumption was associated with a significantly lower risk of total stroke, with those in the highest quartile of consumption having a 17% lower risk of stroke, as compared to those in the lowest quartile, after adjusting for other risk factors. The meta-analysis revealed that the overall, relative risk of stroke for the highest versus lowest category of chocolate consumption was 0.81.

Conclusion: This study of Swedish men found that those who consumed at least 62.9 g per week of chocolate had a significantly reduced risk of stroke, with a 17% reduced risk as compared to those with no chocolate consumption.

Larsson, S., et al. Chocolate Consumption and Risk of Stroke: A Prospective Cohort of Men and Meta-Analysis. **Neurol.** 2012, September 18; 79(12): 1223-1229.

LOW VITAMIN D LEVELS AND STROKE RISK

Human observational studies have provided evidence that vitamin D, a hormone that regulates calcium, may be beneficial in reducing the risk of hypertension and diabetes. Studies examining vitamin D status in relation to the risk of stroke morbidity or mortality have been inconsistent. This study further examined the relationship between plasma 25 (OH) D levels and the risk of ischemic stroke among healthy women.

Data were collected from the Nurses Health Study. From 1989 to 1990 blood samples were collected from 32,826 participants who were stroke free at the time of the blood draw. Among these, 483 incident strokes were subsequently identified. Cases and control subjects were categorized into tertiles according to the distribution of serum 25 (OH) D levels. In a separate meta-analysis, six studies were identified explicitly evaluating 25(OH) D levels in relation to incident stroke or stroke mortality.

After adjusting for body mass index and physical activity, women in the lowest tertile of vitamin D had a nonsignificant increase in the risk of ischemic stroke. When adjusted for dietary lifestyle risk factors and history of chronic conditions, the risk was mildly strengthened (p=0.06). This result was mirrored by findings of a meta-analysis pooling prospective studies that demonstrated the same inverse associations between blood 25(OH) D levels and various stroke outcomes.

Conclusion: This study using data from the Nurses Health Study found a modest association between low levels of vitamin D and an elevated risk of ischemic stroke.

Sun, Q., et al. 25-Hydroxy Vitamin D Levels and the Risk of Stroke: A Prospective Study and Meta-Analysis. **Stroke**. 2012, June; 43(6): 1470-1477.

INTERMEDIATE WEIGHT HYALURONIC ACID AND OSTEOARTHRITIS

Hyaluronic acid (HA) is a glycoasaminoglycan constituent of synovial fluid and cartilage matrix. The molecular weight and concentration have been found to be decreased in joints with osteoarthritis (OA). While viscosupplementation with exogenous HA is an established treatment for OA, studies concerning the efficacy of this treatment have provided mixed results. Some authors have suggested that the heterogeneity of the molecular weight of different HA formulas may have influenced these mixed results. This study compared the effects of low molecular weight HA with an intermediate molecular weight HA for the treatment of symptoms of knee OA.

This randomized, controlled, double-blind, parallel group trial included patients 50 to 80 years of age with a diagnosis of knee OA. The subjects were randomized to receive either an intermediate molecular weight HA (GO-ON) or a low molecular weight HA (Hyalgan), injected into the knee joint weekly for three consecutive weeks. The primary endpoint was the change in scores on the Western Ontario and McMaster Universities (WOMAC) Pain Subscale, with secondary endpoints including several efficacy variables.

After six months, changes on the WOMAC pain subscale averaged 22.9 in the GO-ON group and 18.4 in the Hyalgan group (p=0.026). This superiority pattern was seen for the majority of the secondary endpoints, including pain and clinical response.

Conclusion: This study of patients with knee osteoarthritis found that three weekly injections of intermediate molecular weight hyaluronic acid is superior in reducing

symptoms when compared to low molecular weight hyaluronic acid.

Berenbaum, F., et al. A Randomized, Double-Blind, Controlled Trial Comparing Two Intra-Articular Hyaluronic Acid Preparations Differing by their Low Molecular Weight in Symptomatic Knee Osteoarthritis. **Ann Rheum Dis**. 2012, September; 71(9): 1454-1460.

BURDEN OF CAREGIVERS OF PATIENTS IN A VEGETATIVE OR MINIMALLY CONSCIOUS STATE

With medical advances, the number of patients surviving an acquired severe brain injury has gradually increased. Those in a vegetative or minimally conscious state need constant assistance, placing continuous and significant demands on caregivers. This study was designed to better understand the burden experienced by caregivers of patients with disorders of consciousness (DOCs).

This observational, multicenter, cross-sectional study was conducted in Italy between June of 2009 and March of 2010. This investigation included 69 centers where patients were cared for with diagnoses of vegetative or minimally conscious state. The primary caregivers were assessed using the Caregiver Needs Assessment, Family Strain Questionnaire, Short Form-12, State-Trait Anxiety Inventory-Y, Beck Depression Inventory, Prolonged Grief Disorder Questionnaire and the Coping Orientation to Problem Experiences.

Data were obtained from 487 consecutive caregivers, including 36 caregivers of children. Over 60% of the participants spent more than three hours per day with their relatives. Most caregivers were female. The participants reported reduced leisure activities, in particular meeting friends (67.6%) and walking or riding a bicycle (50%). Data from the Beck Depression Inventory determined that 59.5% had reached the most severe level of depression. Both mental and physical health were rated as low ($p<0.001$ for both) compared with a normative sample.

Conclusion: This study of caregivers of patients in a minimally conscious or vegetative state found specific deficits in emotional, social and economic performance, and unmet communications needs with the care team.

Leonardi, M., et al. Burden and Needs of 487 Caregivers of Patients in Vegetative State and in Minimally Conscious State: Results from a National Survey. **Brain Inj.** 2012, September; 26(10): 1201-1210.

HYALURONIC ACID VS. STEROIDS FOR SUBACROMIAL IMPINGEMENT

Previous studies have demonstrated the efficacy of both corticosteroids and hyaluronic acid as treatments for symptomatic subacromial impingement. This study compared injections combining lidocaine with hyaluronic acid versus licocaine with corticosteroids for the treatment of pain associated with subacromial impingement.

Subjects included 159 patients with subacromial impingement who were randomized into one of three groups for subacromial injections. Group A received a mixture of 8 mL lidocaine 1% and 2 mL hyaluronic acid. Group B received 8 mL of lidocaine 1% with 2 mL of triamcinolone acetonide 10mg/ml. Finally, group C, a placebo group, received 8 mL lidocaine 1% with 2 mL of sodium chloride 0.9%. Injections were repeated, if necessary, after three and six weeks. The primary outcome measure was pain, as measured on a visual analogue scale (VAS), and expressed as the proportion of patients indicating a reduction in or resolution of pain.

At weeks three, six and 12, the corticosteroid group was superior to the hyaluronic acid group in improvement on the VAS ($p=0.004$, $p<0.001$ and $p=0.006$, respectively). Compared with placebo, corticosteroids were significantly better only at week six ($p=0.006$). The mean reductions in pain at 12 weeks were seven percent in group A, 28% in group B and 23% in group C.

Conclusion: This study of patients with subacromial impingement found that corticosteroids were slightly better than hyaluronic as a treatment to reduce pain, although neither treatment was superior to placebo at 26 weeks.

Penning, L., et al. The Effectiveness of Injections of Hyaluronic Acid or Corticosteroids in Patients with Subacromial Impingement. **J Bone Joint Surg-Br.** 2012, September; 94-B: 1246-1252.

ACCURACY OF DIFFERENT SUBACROMIAL INJECTION ROUTES

A common technique, both for the diagnosis and treatment of rotator cuff tendinopathy, is injection into the subacromial space. As the efficacy of these injections may hinge on the precise delivery of the medication, this study was designed to determine the relative accuracy of various therapeutic injection routes.

Seventy-five patients with complaints of pain with overhead shoulder activity, night pain and a positive impingement sign were enrolled in this study. The patients received injections of 5 mL of 1% lidocaine, 1 mL of triamcinolone and 2 mL of contrast medium. The subjects were randomly selected to receive injections using the posterior, lateral or anterior approach. The primary outcome variable of interest was accuracy of injection into the bursa as verified by radiographs read by radiologists held blind to the injection route.

The injections were accurate in 56 % of the posterior route, 84% of the anterior route and in 92% of the lateral route procedures. Compared with the posterior injection, injection accuracy was 1.6 times greater for the lateral route, and 1.5 times greater for the anterior route. Pain reduction was significantly better among those with accurately placed injections.

Conclusion: This study of patients with shoulder pain suggests that anterior and lateral approach injections are more accurate in medication delivery than is the posterior route.

Marder, R., et al. Injection of the Subacromial Bursa in Patients with Rotator Cuff Syndrome. **J Bone Joint Surg (Am**). 2012, August 15; 94 (16):1442-1447.

NSAIDS AND THE PROGRESSION OF AXIAL SPONDYLOARTHRITIS

Nonsteroidal anti-inflammatory drugs (NSAIDs) are a preferred therapy for patients with axial

spondyloarthritis (SpA). This study investigated the influence of these drugs on the radiographic progression of the spine in patients with ankylosing spondylitis and nonradiographic axial SpA.

This study included patients with definite clinical diagnoses of axial SpA, with the participants further classified based on radiographic findings as having AS or non-radiographic SpA. Radiographs of the spine and sacroiliac joints were obtained at baseline and after two years of follow-up. Data concerning NSAID intake were collected at baseline and every six months thereafter during two years of follow-up. Medication doses and durations were recorded, with an index of NSAID intake determined as recommended by the Assessment of the Spondyloarthropathies International Society (ASAS).

Overall, 27% of the patients with AS and 25% of those with SpA had a high NSAID intake index during the two years of follow-up. Those with high intake were found to have a lower likelihood of radiographic progression than did those with a low intake (p=0.045). The positive effect of NSAID intake was most evident among those with baseline syndesmophytes and an elevated CRP.

Conclusion: This study of patients with ankylosing spondylitis found that NSAID use seems to retard new bone formation.

Poddubnyy, D., et al. Effect of Nonsteroidal Anti-Inflammatory Drugs on Radiographic Spinal Progression in Patients with Axial Spondyloarthritis: Results from the German Spondyloarthritis Inception Cohort. **Ann Rheum Dis.** 2012, October; 71(10): 1616-1622.

POWER TRAINING AFTER STROKE

It is unclear whether improvements in upper extremity function after stroke are due to acquisition of compensatory movements, or, rather, to the restoration of more normal movement patterns. While compensatory mechanisms may enable task performance in the short term, these may be harmful over time. This study assessed the effect on mechanisms of motor recovery of two different forms of upper extremity rehabilitation, dynamic high-intensity resistance training (POWER) and functional task practice (FTP).

This randomized, controlled, crossover design trial including 14 patients with upper extremity hemiparesis secondary to stroke. All subjects were involved in treatment blocks lasting 10 weeks and involving 30 sessions of 90 minutes each. Group 1 received 10 weeks of POWER training, followed by 10 weeks of FTP, while group two received a similar schedule of FTP followed by POWER training. All subjects were evaluated before and after each block of training with a battery of clinical assessments.

After each block, both groups demonstrated improvement on clinical assessments, with no significant differences seen between the groups. Kinematic evaluations demonstrated that FTP led to compensatory movement strategies, decreased active range of motion and increased trunk excursion. The POWER group demonstrated more normal patterns of movement, with significantly reduced trunk displacement. Those who received POWER training followed by FTP demonstrated the greatest overall improvement.

Conclusion: This study of patients with upper extremity hemiparesis after stroke demonstrated that functional task practice may lead to more compensatory movement patterns than dynamic high-intensity resistance training.

Gorti, M., et al. Differential Effects of Power Training versus Functional Task Practice on Compensation and Restoration of Arm Function after Stroke. **Neurorehab Neural Repair.** 2012, September; 26(7): 842-854.

VERY EARLY MOBILIZATION AFTER STROKE

Very early mobilization is considered an important component of improved outcome among patients with acute stroke. Data have suggested that early mobilization training is important to utilize brain plasticity and to hasten recovery, in addition to preventing complications. This study compared the outcomes resulting from mobilization within 24 hours with those of mobilization 24-48 hours after hospital admission.

This prospective, randomized, blinded, controlled study included 56 adult patients, all admitted to a stroke unit with acute ischemic stroke. The subjects were randomized to a very early mobilization group, mobilizing within 24 hours of admittance (n=27), or a control group, mobilizing between 24 and 48 hours (n=29). Patients were mobilized out of bed several times per day, with treatment based upon standard protocols. The participants were assessed on admission, at discharge and at three months post-stroke. The primary outcome measure was the proportion of patients with poor outcomes, based on the modified Rankin scale. Secondary outcomes included death rate and change in neurologic function, based upon National Institutes of Health Stroke Scale Scores (NIHSS), as well as the Barthel index.

At three months' follow-up, more patients in the early mobilization group had a poor outcome than did those in the control group, although this difference did not reach statistical significance. At three months, death had occurred in 25.9% in the early group and 6.9% in the control group. (p=0.07). All three deaths occurring in the hospital were in the early group.

Conclusion: This study of patients with acute stroke found that mobilization within 24 hours is marginally associated with a worse outcome, including death and dependency, as compared to that for patients mobilized at 24 to 48 hours.

Sundseth, A., et al. Outcome after Mobilization within 24 Hours of Acute Stroke: A Randomized, Controlled Trial. **Stroke**. 2012, September; 43: 2389-2394,

REHABILITATION AFTER HIP FRACTURE

Hip fractures remain a health problem in developed countries, with significant mortality and disability resulting from these injuries. This study compared different care pathways and their effect on functional outcomes after hip fracture.

This prospective cohort study involved 806 elderly patients admitted to one of three regional hospitals in Italy, all diagnosed with hip fracture. Fracture management was

determined by orthopedic surgeons and medical care management by geriatricians. The data collected included time to surgery, type of surgery, length of hospital stay and discharge destination. Rehabilitation interventions recorded included time to weight bearing, time to ambulation and time to transfer to an acute or postacute rehabilitation facility. The participants were contacted at three, six and 12 months after surgery in order to assess their functional status, living arrangements and amount of assistance required.

Fewer than 50% of the patients underwent surgery within 48 hours. A longer time to surgery increased one year mortality by 12% for every day that the surgery was delayed. All rehabilitation options improved one year mortality, including early ambulation and post acute rehabilitation ($p<0.001$ –$p=0.021$). After controlling for baseline characteristics, the risk of losing at least one functional ability was lower in those subjects who received both intensive early rehabilitation (ambulation within the third post operative day) and access to post-acute rehabilitation units/facilities, as compared to those who received only standard rehabilitation during the hospital stay.

Conclusion: This study of patients with hip fractures requiring surgical intervention revealed that surgical delays may increase mortality and morbidity, while access to rehabilitation can reduce mortality and morbidity, in the first year after injury.

Pioli, G., et al . Time to Surgery and Rehabilitation Resources Affect Outcome in Orthogeriatric Units. **Arch Geront Geriat**. 2012, Sept-Oct; 55(2): 316-322.

NORMATIVE DATA FOR IDENTIFYING IMPAIRMENTS AFTER CONCUSSION

Recent concussion consensus statements have urged clinicians to establish pre-injury baseline scores for athletes using computerized neurocognitive testing. Nevertheless, several concerns have been voiced regarding the application of baseline testing. This study was designed to determine whether post-concussive scores are best compared with individualized baseline scores or gender specific normative values.

Gender specific normative means were generated from preseason baseline measures collected from a subsample of 673 athletes with no history of self-reported concussion, learning disability or attention deficit disorder. In addition, between 2001 and 2010, 1,060 Division I male and female collegiate student-athletes completed preseason baseline testing, which included a computerized neurocognitive test (the ANAM). Of those, 258 were later diagnosed with concussion. These athletes were retested, with their results compared to both the baseline and the normative test values.

Baseline testing identified 2.6 times more impairments on the simple reaction time test than did the normative comparison method ($p=0.043$). In contrast, the normative comparison identified 7.6 times more impairments in mathematical processing than did the baseline testing ($p<0.01$). No significant differences were found between the methods for any of the other ANAM scores.

Conclusion: This study of collegiate athletes found that, after concussion, comparing post-concussion neurocognitive scores to normative values may provide an appropriate evaluation approach, and differs very little from comparisons to individualized baseline testing.

Schmidt, J., et al. Identifying Impairments after Concussion: The Normative Data versus Individualized Baseline. **Med Sci Sports Exerc.** 2012, Sept; 44(9): 1621-1628.

DIETARY SUPPLEMENTS AND RECREATIONAL ATHLETES

It is estimated that, among athletes, between 40% and 80% use dietary supplements. This study was designed to determine the knowledge of plant derived nutritional supplements among physically active individuals.

Over a period of six months, 740 subjects who were in athletic training were enrolled in the study. Each subject completed an anonymous questionnaire providing information concerning their knowledge and/or personal experiences with plant derived nutritional substances. Those who declared themselves users of these supplements were asked to provide a blood sample for analysis.

Of the 740 athletes surveyed, 26 subjects claimed to be users of plant derived supplements. Of these 23 agreed to have their blood tested. Of those who denied the use of nutritional supplements, 30 were recruited as matched controls. Of the respondents, 45% did not know any of the plant derived substances on the list, while 24% reported knowing only phytoestrogens and 26% only vegetal sterols. Laboratory tests revealed the absence of any sign of organ toxicity/damage in any of the subjects. In addition, no significant differences were found between users and controls in the values of cortisol, LH, FSH, TSH, FT3 or FT4. On the contrary, sex hormone profiles revealed marked alterations in 15 (65%) of the 23 of users of plant derived supplements, while no alterations were found in the control group.

Conclusion: This study of recreational athletes revealed that these individuals have very little knowledge and very little use of plant derived nutritional supplements. The data suggest that these supplements may affect sex hormone levels.

Borrione, P., et al. Consumption and Biochemical Impact of Commercially Available Plant Derived Nutritional Supplements. An Observational Pilot Study on Recreational Athletes. **J Intern Soc of Sports Nutrition**. 2012, June; 9: 28.

DIETARY THERAPY FOR NEURAL PROTECTION IN SPINAL CORD INJURY

Cervical spondylotic myelopathy (CSM) is a debilitating disorder caused by primary mechanical and secondary biologic injury to the spinal cord. One of the issues in treating patients with CSM is the inability to directly treat the insidious, secondary, biological injury that occurs with this disorder. In recent years, interest has grown in the influence of dietary factors on molecular systems and mechanisms within the central nervous system. Among these, the omega-3 fatty acid DHA has been shown to reduce inflammation and provide structural material to plasma membranes, while curcumin has been shown to possess strong antiinflammatory and antioxidant capacity. This study investigated the effect of dietary supplementation with these two substances in an animal model of myelopathy.

This animal study included 27 rats, randomly assigned to one of

three groups: spinal compression and diet supplemented with saturated fats, designed to mimic a Western diet (WD), spinal compression and dietary supplements with the DHA and curcumin (DHA-cur) and a standard diet. All subjects were assessed by magnetic resonance imaging and behavioral testing, and were then euthanized 42 days after the surgical procedure for spinal cord molecular analysis.

In the WD group, worsening gait function was observed at post-operative day 21 and remained worse than baseline throughout the study. The DHA-cur group had significantly better gait function than did the WD group at the final postoperative day 42 time point ($p<0.05$). Cellular membrane damage, confirmed by the elevation of spinal cord 4-HNE was similar in the DHA-cur group and the non-injured animals, but worse in the WD group. The brain-derived neurotrophic factor levels were significantly lower in the WD group than in both the intact group ($p<0.05$) and the DHA-cur group ($p<0.05$)

Conclusion This study demonstrates that dietary supplementation with DHA and curcumin can counteract the effects of chronic spinal cord compression, resulting in the preservation of neurologic function.

Holly, L., et al. Dietary Therapy to Promote Neural Protection in Chronic Spinal Cord Injury: Laboratory Investigation. **J Neurosurg: Spine.** August; 17: 134-140.

YOGA FOR CHRONIC LOW BACK PAIN

Pain represents a significant burden to healthcare and society. Yoga has been found effective in improving function in patients with chronic or recurrent low back pain (LBP). This study was designed to determine the cost-effectiveness of this intervention.

This multi-center, randomized, controlled trial included 39 general practices in the United Kingdom. From among these, 313 consenting participants were randomized, with 157 assigned to a usual care group and 156 assigned to a yoga group.

The yoga group participated in a 12-week progressive course of yoga, with weekly 75 minute classes, a relaxation compact disc, a student yoga manual, a yoga mat and a copy of *The Back Book*. Participants were followed at three, six and 12 months after randomization, with back function the primary outcome measure. Economic valuation considered both the national health services and societal perspectives, with the incremental cost per quality adjusted life-year serving as the main outcome.

The cost of yoga intervention was estimated to be £293 for each student. Those in the treatment group gained 0.0 37 quality adjusted life-years more than did those in the usual care group, at a £213.9 lower cost than usual care.

Conclusion: This economic evaluation of patients with low back pain found that yoga is a cost-effective intervention for the treatment of with chronic low back pain.

Chuang, L., et al. A Pragmatic, Multicentered, Randomized, Controlled Trial of Yoga for Chronic Low Back Pain. **Spine.** 2012, August 15; 37(18): 1593-1601.

PHYSICAL ACTIVITY AND MORTALITY AMONG DIABETICS

Diabetes mellitus is a pandemic, increasing both morbidity and mortality. Efforts to reduce the impact of diabetes have been aimed at controlling hyperglycemia, hypertension and dyslipidemia. In the general population, physical activity has been associated with a lower risk of overall and cardiovascular disease mortality. This study was designed to determine whether physical activity is associated with cardiovascular disease and total mortality rates among patients diagnosed with diabetes.

This study included 5,859 men and women with diabetes, ranging in age from 35 to 70 years. At baseline, patients received a lifestyle questionnaire, including queries about occupational activity and the duration and frequency of walking, cycling, gardening, household work and other activities including sports during the past year. Based upon these data, the patients were divided into four categories, including inactive, moderately inactive, moderately active and active levels. Outcome measures included diabetes duration, dietary intake, alcohol consumption, height, weight, systolic and diastolic blood pressure, hemoglobin A-1 C, tobacco use, education level and prevalence of myocardial infarction, stroke and cancer. In addition, a meta-analysis was completed, encompassing 12 cohort studies of patients with diabetes followed for a mean of 12.5 years.

Higher levels of total physical activity, leisure time physical activity and walking were associated with a lower risk of total and cardiovascular mortality as compared with inactivity. The lowest HR was observed in persons categorized as moderately active, with a hazard ratio of 0.62 for total mortality and 0.51 for cardiovascular disease mortality, as compared to those with low activity. In the meta-analysis of prospective studies, the highest levels of total and leisure-time physical activity and walking were associated with a lower risk of total and cardiovascular disease related mortality as compared with a low activity level.

Conclusion: This study of patients with diabetes found that physical activity is associated with a lower risk of total mortality and cardiovascular disease mortality.

Sluik, D., et al. Physical Activity and Mortality in Individuals with Diabetes Mellitus. A Prospective Study and Meta-Analysis. **Arch Intern Med.** 2012, September 24; 172(17): 1-11.

FACTORS ASSOCIATED WITH RAPID PROGRESSION TO KNEE ARTHROPLASTY

Knee arthroplasty is a common surgical intervention for patients with severe osteoarthritis (OA) of the knee. However, research examining prognostic indicators for future knee arthroplasty has been limited. This study was designed to better clarify prognostic indicators for near-term arthroplasty.

The subjects included 4,670 patients ages 40 to 79 years with knee pain or OA, or who were at risk for developing OA due to known risk factors. Of these, 1,609 had unilateral knee pain, 1,982 reported bilateral knee pain and 1,069 reported no knee pain at the time of the examination. Data collected included demographic and socioeconomic variables, arthritis related health measures, physical examination, performance, and self-report measures of disability and pain. The patients were followed for three years.

Of the 4,672 patients followed during the study, 116 underwent a total of 128 knee arthroplasties. After

(Continued from page 2)

*Rachel Hallmark, M.D., Ph.D.
UVA, Charlottesville, VA

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

*Bonnie Weigert, M.D.
Michelle Faull, D.O.
Jeannie K. Harden, M.D.
University of Wisconsin, Madison, WI

*Donald Tower, D.O.
Jeffrey Zecker, M.D.
William Carter, M.D.
Mohammed Agha, MD
Teresa Kerge, M.D.
VCU, Richmond, VA

*Mahathy Goli, M.D.
Mark F. Adderley, D.O.
Shawna Arsenault, M.D.
Washington University, St. Louis, MO

adjusting for known prognostic factors, previously unidentified predictors were found, including a past history of knee surgery, knee flexion contracture and pain with active knee flexion. Among the known prognostic variables were whether the patients were considering knee arthroplasty in the next three years, radiographic osteoarthritis grade, knee pain severity, global rating of the effect of knee pain on daily life, use of arthritis medication, care by an arthritis physician, and age.

Conclusion: This prospective study of patients with knee osteoarthritis or at risk for osteoarthritis found previously unknown predictors of future arthroplasty, including a past history of knee surgery, knee flexion contracture and pain with active knee flexion.

Riddle, D., et al. Factors Associated with Rapid Progression to Knee Arthroplasty: Complete Analysis of Three-Year Data from the Osteoarthritis Initiative. **Joint Bone Spine.** 2012, May; 79(3): 298-303.

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