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Volume 18 Number 4

Published by Physicians  
In Physical Medicine and Rehabilitation

April 5, 2010

## INTENSIVE MEDICAL THERAPY FOR ASYMPTOMATIC CAROTID STENOSIS

Patients with asymptomatic carotid stenosis (ACS) are at high risk of vascular disease, including myocardial infarction, as well as stroke. To date, the literature does not support arterial stenting in asymptomatic patients, as it carries a high risk of complications. This study evaluated the effects of intense medical therapy on the rate of transcranial Doppler microemboli and cardiovascular events among patients with asymptomatic carotid stenosis.

Four hundred sixty-eight patients with asymptomatic carotid stenosis of at least 60% were studied. All participants underwent baseline measurement of total plaque area, followed by annual follow-up measurements. In 2003, the clinic implemented an intensive therapy for accelerated atherosclerosis. This process included addressing smoking cessation, placing patients on a Mediterranean diet, and increasing the dose of statins to the maximum tolerated dose regardless of levels of low density lipoprotein. For those on maximum statin doses, ezetimibe was added. The researchers also added niacin for patients who did not have diabetes and added fibrates for diabetic patients or those unable to take niacin. Further, they ensured that hypertensive patients were taking an angiotensin converting enzyme inhibitor or an angiotensin receptor blocker. In addition, they optimized blood pressure control. Finally, those with insulin resistance were given metformin or pioglitazone at the onset of diabetes.

Among the patients included in the study, 199 were enrolled before December 31, 2001, and 269 were enrolled after January 1, 2003. Microemboli were apparent in 12.6% of the patients enrolled before 2003 and in 3.7% of those enrolled after 2003 ( $p < 0.001$ ). Before 2003, plaque

progressed by a mean of 69 mm<sup>2</sup>, while, after 2003, plaque progressed by 23 mm<sup>2</sup> ( $p < 0.001$ ). Before 2003, 17.6% of the patients had a cardiovascular event, as compared to 5.2% since 2003 ( $p < 0.001$ ).

**Conclusion:** This study demonstrates that cardiovascular events and measured microemboli decline significantly after the adoption of intensive medical therapy for patients with asymptomatic carotid stenosis.

Spence, J. et al. Effects of Intensive Medical Therapy on Microemboli and Cardiovascular Risk in Asymptomatic Carotid Stenosis. *Arch Neur.* 2010, February; 67(2): 180-186.

## APOPTOSIS AND MITOCHONDRIAL DYSFUNCTION IN CHONDROCYTES EXPOSED TO LIDOCAINE, BUPIVACAINE AND ROPIVACAINE

Intra-articular injection of local anesthetics is widely used to control pain. However, studies have shown that chondrotoxicity occurs after treatment with bupivacaine and other local anesthetics. The exact mechanism of this toxicity is unclear. This study compared the effects of lidocaine, bupivacaine, and ropivacaine on chondrocyte mitochondrial function, and sought to characterize the type of cell death that occurs with exposure to local anesthetics.

Primary chondrocyte cultures were obtained from patients with osteoarthritis hospitalized for total knee replacement. The cells were exposed to two percent, one percent and 0.5% lidocaine, 0.5% and 0.25% bupivacaine, and 0.5% and 0.2% ropivacaine for one hour. Cell viability and apoptosis were measured at 24 and 120 hours after treatment. To analyze whether Caspase activation was involved in the initiation of apoptosis, a Western blot analysis

was used with antibodies against Caspase-3 and Caspase-9. Cells were analyzed for mitochondrial DNA damage, changes in ATP production and mitochondrial protein levels.

After 24 hours, a two percent concentration of lidocaine caused a nearly complete loss of viable cells due to massive necrosis. Exposure to one percent lidocaine and 0.5% bupivacaine caused detectable, but not significant, decreases in viability after 24 hours. The decrease in viability at all of the concentrations of local anesthetics used was primarily due to necrosis. There was no significant increase in the number of apoptotic cells twenty-four hours after exposure. At 120 hours, a significant decrease in viability, with an increase in apoptotic cells, was seen at all concentrations of lidocaine, bupivacaine and ropivacaine except 0.2% ropivacaine.

**Conclusion:** This study demonstrates that exposure of human chondrocytes to lidocaine, bupivacaine or ropivacaine *in vitro* can decrease cellular viability and increase the induction of apoptosis. The chondrotoxicity of local anesthetics was found to result from delayed mitochondrial dysfunction.

Grishko, V., et al. Apoptosis and Mitochondrial Dysfunction in Human Chondrocytes following Exposure to Lidocaine, Bupivacaine, and Ropivacaine. *J Bone Joint Surg.* 2010, March; 92: 609-618.

## SWIMMING DURING PREGNANCY

Exercise is recommended during pregnancy, with swimming considered by many to be an ideal activity for pregnant women. However, the chemical disinfection processes in swimming pools result in the formation of disinfection byproducts through the reaction of chlorine with organic matter. Some have worried that some of these

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substances may be fetotoxic. This study examined the associations between swimming during pregnancy and several birth outcomes.

This study reviewed data obtained from the Danish National Birth Cohort, a nationwide, population-based cohort with prospectively collected data from pregnant women and their offspring. Inclusion criteria were residence in Denmark, and the ability to participate in telephone interviews during and after pregnancy. Information collected included self-reported exercise data. To be included in additional analyses, the women had to have reported swimming, bicycling, or no exercise during both interviews.

With these data, the authors generated three exposure categories: (1) any reported swimming, (2) any reported bicycling, but no swimming and (3) no exercise. The reproductive endpoints, abstracted from the national discharge registry data, included gestational age at birth, birth weight, head circumference, abdominal circumference, placental weight and congenital malformations. Preterm birth was defined as a delivery after 153 gestational days but before 259 days.

In this sample, 75% did not engage in any exercise, 14% reported swimming and 11% reported bicycling and no swimming. Fewer preterm births occurred among swimming mothers than among the other groups. Apart from this, only minor differences were seen between swimmers and bicyclists. There were fewer post-term deliveries, with more smaller for gestational age babies and a slightly higher occurrence of malformations in the offspring of non-exercising mothers than among those who swam and bicycled.

**Conclusion:** This prospective study of pregnant women in Denmark did not find that swimming in a pool is associated with adverse reproductive outcomes.

Juhl, M., et al. Is Swimming during Pregnancy a Safe Exercise? **Epidem.** 2010, March; 21(2): 253-258.

## **CHONDROCYTE DEATH AND LOCAL ANESTHETIC**

Traumatic joint injuries and inflammatory conditions are commonly treated with intra-articular administration of local anesthetics. In

addition, intra-articular anesthesia is routinely used for postoperative pain relief after joint surgery. A phenomenon known as chondrolysis has been linked to the intra-articular administration of local anesthetics in human patients and in animal studies. The data concerning the magnitude and cause of this cell death are unclear. This study attempted to determine whether lidocaine and bupivacaine cause death of bovine articular chondrocytes.

Bovine articular chondrocytes were obtained from three week old calves. The cells were placed in a suspension culture, phosphate buffered saline or human synovial fluid, and treated with either one percent lidocaine, 0.25% bupivacaine without epinephrine, 0.25% bupivacaine with epinephrine, 0.5% bupivacaine with epinephrine or 0.25% bupivacaine with epinephrine. A control group was treated with phosphate buffered saline (PBS) at pH values of 4.5, 3.8, 3.4 and 2.4, or with one percent lidocaine in Dulbecco's Modified Eagle's Medium (DMEM). In a parallel study, other cells were treated similarly to determine whether the effects on chondrocytes could be generalized to other cell types. Chondrocyte viability was analyzed after one hour of treatment in each of the study conditions.

The rates of chondrocyte cell death were 8.4% in the PBS control group, 13.3% in the one percent lidocaine group ( $p < 0.002$ ), 11.8% in the 0.25% bupivacaine group ( $p < 0.02$ ), 11.8% in the 0.25% bupivacaine plus epinephrine group ( $p < 0.01$ ), 12% in the 0.5% bupivacaine plus epinephrine group ( $p < 0.0006$ ) and 12% in the 0.25% bupivacaine plus epinephrine group ( $p = 0.003$ ).

Increased chondrocyte cell death was found when the pH value of the buffered saline dropped to less than 3.4. In contrast, when bupivacaine was mixed with cell culture medium, 100% of chondrocytes died. When lidocaine was mixed with DMEM or human synovial fluid, 99.2% or 96.3% of the chondrocytes died (both  $p < 0.01$ ). There was no significant death of C3H10T1/2 cells with exposure to any of the anesthetic mixtures.

**Conclusion:** This study found that, while minimal chondrocyte death is caused by anesthetics alone, local anesthetics combined with human

synovial fluid may result in significant chondrocyte cell death. The authors suggest that the intra-articular administration of lidocaine or bupivacaine should not be advocated.

Bogatch, M., et al. Is Chemical Incompatibility Responsible for Chondrocyte Death Induced by Local Anesthetics? *Am J Sp Med.* 2010, March; 38(3): 520-526.

### INTRAVENOUS IMMUNOGLOBULIN FOR COMPLEX REGIONAL PAIN SYNDROME

Complex regional pain syndrome (CRPS) results in severe pain that often occurs after trauma, and can adversely affect quality of life. There is some evidence for immune activation in the effected limb with this disorder. This study evaluated the efficacy of intravenous immunoglobulin (IVIG) for the treatment of long-standing CRPS.

This randomized, placebo-controlled, double-blind, crossover trial was conducted at a pain management center. Thirteen subjects with a diagnosis of CRPS participated. All subjects had failed trials of oral analgesics, as well as physical therapy. Each subject was randomized to receive either 0.5 g per kilogram of IVIG or normal saline. Each treatment lasted 28 days, including a washout period before crossover. Subjects kept a pain journal during the trial, both rating their pain levels daily on an 11-point scale and keeping a CRPS limb symptoms scale record. The final follow-up occurred eight weeks after the second infusion. Pain intensity served as the primary outcome measure, while the subject's rating of efficacy was among the secondary outcome measures.

The average pain intensity was 1.55 points lower after IVIG treatment than after saline treatment ( $p < 0.001$ ). The pain scores of five subjects decreased by at least two points with IVIG, with three of those reporting a 50% decrease in pain. Two patients receiving IVIG in the second treatment period reported pain relief for as long as 28 days following infusion. One patient reported improvement after saline infusion alone, while one reported improvement in pain after both infusions, and three reported no pain.

The major adverse event reported was moderate to severe headache.

**Conclusion:** This pilot study of patients with chronic, complex regional pain syndrome found that low dose IVIG may be helpful in reducing pain in these refractory patients.

Goebel, A., et al. Intravenous Immunoglobulin Treatment of the Complex Regional Pain Syndrome. *Ann Int Med.* 2010, February; 152: 152-158.

### METABOLIC SYNDROME AND DEMENTIA RISK IN OLDER ADULTS

Metabolic syndrome (MetS) is defined as a cluster of reversible metabolic risk factors including glucose intolerance, obesity, dyslipidemia and hypertension. Persons with the MetS are at an increased risk of developing cardiovascular disease and diabetes mellitus. In addition, all of the individual components of MetS are associated with risk of Alzheimer's disease (AD) and vascular dementia (VaD). Previous studies have suggested that, up to the age of 75, MetS works better than its individual components as a predictor of worsening performance on neuropsychological tests, especially in persons with high blood inflammatory markers. However, that association has not previously been confirmed in older persons. This study, using data from a population-based, Italian, elderly cohort, investigated the associations between the MetS and four-year risk of incident dementia, AD, and vascular dementia.

Data were obtained from the Conselice study of brain aging, which investigated the epidemiology and risk factors for cognitive impairment. In 1999 and 2000, 1,016 of the 1,353 individuals 65 years of age or older residing in the Italian municipality of Conselice participated in the prevalence study. A two-phase procedure was used with a baseline evaluation consisting of a cognitive screening phase and an extensive neuropsychological assessment of those positive at baseline screening.

Previous medical records were available for approximately 90% of the participants. Identification of incident dementia cases at follow-up

examination in the years 2003 to 2004 was performed using the same, two-phase procedure. All patients were assessed for MetS, with laboratory measures including total and HDL cholesterol, triglycerides, albumin and glucose. Covariates were defined using data collected at baseline.

The risks of overall dementia and its subtypes were not significantly associated with the MetS in any participants younger than 75 years of age. However, among those over the age of 75, the MetS was actually associated with a lower risk of AD. In addition, abdominal obesity was associated with a lower risk of overall dementia.

**Conclusion:** This study suggests that the MetS, measured late in life, may be associated with a lower risk for AD.

Forti, P., et al. Metabolic Syndrome and Risk of Dementia in Older Adults. *J Am Ger Soc.* 2010, March; 58(3): 487-492.

### CEREBROSPINAL FLUID BIOMARKERS AND COGNITIVE DECLINE

Alzheimer's disease (AD) is a neurodegenerative disorder with a disease onset that is believed to occur several decades before cognitive symptom detection. Cognitive functions first affected in AD are thought to be episodic memory, perceptual speed and executive function. This study investigated whether changes occur in cerebral spinal fluid biomarker levels over time, and whether a tendency to change is associated with changing cognitive functions.

This study included cognitively healthy, older adults who underwent a test battery including the Mini Mental State Examination and the Alzheimer's disease Assessment Scale-Cognitive Subscale (ADA-cog). In addition, all underwent cerebral spinal fluid analysis for assessment of  $\beta$ -amyloid<sub>1-42</sub> protein (A $\beta$ 42), tau protein (T-tau), and hyperphosphorylated tau protein 181 (P-tau 181). Cognitive tests and cerebral spinal fluid analyses were completed at baseline and at four-year follow-up. The laboratory results were compared to those of the cognitive assessments.

At baseline, no significant relationships were found between CSF biomarker levels and any of the cognitive test results. At follow-up, lower CSF A $\beta$ 2 levels were associated with a decrease in delayed word recall scores ( $p < 0.01$ ) and slower results on the Quick Test of Cognitive Speed ( $p < 0.001$ ). Over the four-year course of the study, those with a decrease of 15% or greater CSF A $\beta$ 2 level performed more poorly on the ADA-Cog delayed word recall and the Quick Test of Cognitive Speed at follow-up.

**Conclusion:** This study of healthy, older adults found that changes in certain CSF biomarker levels, which had previously been shown to be associated with AD, correlate with a decline in cognitive function.

Stromrud, E., et al. Correlation of Longitudinal Cerebrospinal Fluid Biomarkers with Cognitive Decline in Healthy, Older Adults. *Arch Neur.* 2010, February; 67(2): 217-223.

#### CYCLIC VOMITING SYNDROME TREATMENT

Cyclic vomiting syndrome (CVS) is defined by recurrent stereotypical episodes of nausea and vomiting. CVS is generally believed to be a variant of migraine, based on overlapping symptoms such as headache, nausea and photophobia. As the nutrient supplement, CoA Q, has demonstrated efficacy for adult migraine, some have suggested it as a treatment for CVS. This study sought to better understand the efficacy of this treatment

Individuals who had been diagnosed with CVS by health care professionals were invited to participate in this study by completing an approximately 30-minute, internet-based survey. A total of 385 subjects with a diagnosis of CVS completed the survey. Subjects taking CoA Q were compared to those taking amitriptyline, the current standard of care. Efficacy was queried with regard to four different vomiting episode-based parameters, episode frequency, episode duration, number of emeses and nausea severity. A reduction of at least 50% in each parameter was scored as positive. The data were reviewed for efficacy and tolerability of different doses of amitriptyline and CoA Q.

Eighteen subjects were excluded due to an absence of a health professional's diagnoses, and three for failure to meet the diagnostic criteria for CVS. Among the 347 remaining, 277 and 82 reported experience with amitriptyline and CoA Q, respectively. The subjects reported a 50% reduction in at least one of the four parameters, including 72% of those treated with amitriptyline and 68% of those treated with CoA Q. While no side effects were reported among subjects on CoA Q, 21% of those taking amitriptyline discontinued their treatment due to side effects.

**Conclusion:** This retrospective study of cyclic vomiting syndrome suggests that CoA Q may be as effective as amitriptyline for the treatment of this disorder. Interestingly, however, far fewer side effects occurred with CoA Q.

Boles, R., et al. Treatment of Cyclic Vomiting Syndrome with CoA Q10 and Amitriptyline: A Retrospective Study. *BMC Neur.* 2010; 10: 10.

#### NATURAL HISTORY OF CONCUSSION IN SPORTS

Concussion is a common problem in many contact sports. It has been estimated that, in the United States alone, 1.6 to 3.8 million cases of sports and recreation related traumatic brain injury (TBI) occur each year. This study sought to describe the pattern of symptoms and cognitive recovery after concussion in Australian football, and to investigate the relationship between these features and time to return to play.

This prospective, cohort study was conducted over four, competitive seasons of Australian football. A sample of 1,015, male, Australian football players between the ages of 16 and 35 years were recruited for the study. All players underwent baseline cognitive testing before the start of each season and were prospectively monitored for concussive injuries during the course of the study. All teams were cared for by highly experienced medical staff, including team doctors. These doctors were present at each injury, making the diagnosis of concussion according to standard injury definitions. Standard return to play decisions involve monitoring symptom recovery and use of a

limited cognitive assessment with either paper-and-pencil or computerized test batteries. Concussed players were monitored regularly until all of the acute features of the concussive injury had resolved. The timing of post concussion assessments reflected the individual clinical management strategies of the medical staff.

Eighty-eight concussions were observed in 78 players. The incidence of concussion was 3.5 per thousand player hours among the elite senior players, 1.3 per thousand player hours in the elite junior players, and 3.2 per thousand player hours in community-level players. Overall, the mean number of symptoms reported for each concussive injury was 3.7, with the duration of symptoms 48.6 hours. Cognitive deficits, as measured by computerized tests, recovered two or three days later. In fact, cognitive impairment was found in 35% of concussed players after other symptom resolution. Headache was the most commonly reported symptom, with fatigue, lethargy, fogginess, sleep disturbance and headache lasting the longest.

**Conclusion:** This study demonstrates that, after a concussive injury, cognitive recovery is delayed for up to three days after the resolution of symptoms. Thus, the authors surmise that symptom assessment may underestimate the time to complete recovery.

Makdissi, M., et al. Natural History of Concussion in Sports: Markers of Severity and Implications for Management. *Am J Sp Med.* 2010, March; 38(3): 464-470.

#### ANTICHOLINERGIC DRUGS AND PARKINSON'S DISEASE

Cognitive impairment and dementia are frequently seen in patients with Parkinson's disease (PD). Given the decrease in cholinergic function in patients with PD, and its association with cognitive impairment, drugs with anticholinergic activity may contribute to the observed cognitive impairment. This study investigated the impact of drugs with anticholinergic properties in a community-based sample of patients with PD.

Subjects were selected from among participants of a longitudinal,

prospective, community-based study of 245 patients diagnosed with PD. Cognition was assessed with the Mini Mental State Exam, with depression assessed with the Montgomery Asberg Depression Rating Scale (MADRS). To estimate anticholinergic activity, medications used by each patient were individually scored, with those scores summed to provide a quantitative assessment of anticholinergic activity. Relationships among cognitive decline, anticholinergic activity load and duration of treatment were assessed. The patients were assessed at baseline and then again four and eight years later.

One hundred two of the 235 patients received at least one drug with anticholinergic activity. The most common of these were antidepressants, cardiovascular agents, anxiolytics and sedatives. Seventy-two (31%) of the subjects were taking more than one drug with anticholinergic activity. At baseline, patients taking anticholinergic drugs had significantly lower cognition and higher depression scores than did those not taking these agents. During the eight years of follow-up, the cognitive decline was greater among those who were taking anticholinergic drugs than among those who were not ( $p=0.025$ ). After adjusting for confounding factors such as age, baseline cognition and depression, significant associations were found between declines on MMSE scores and for total anticholinergic activity load ( $p=0.04$ ), as well as for duration of drug use ( $p=0.032$ ).

**Conclusion:** This study suggests an association between anticholinergic drug use and cognitive decline among patients with Parkinson's disease.

Ehrt, U., et al. Use of Drugs with Anticholinergic Effect and Impact on Cognition and Parkinson's Disease: A Cohort Study. *J Neur Neurosurg Psych*. 2010, February; 81(2): 160-165.

### COGNITIVE DECLINE IN CRITICAL ILLNESS AND HOSPITALIZATION AMONG OLDER ADULTS

The incidence of critical illness syndromes is increasing in the United States, and is higher for older adults. These trends are resulting in a growing number of patients who are

survivors of critical illness. The consequence of critical illness is multiple morbidity effects, including cognitive impairment. Previous studies have linked critical illness with cognition, although none of the studies have included objective measures of cognitive function before critical illness, and few have evaluated the risk of incident dementia among survivors of critical illness. This study examined the associations between hospitalization for acute illness or critical illness and cognitive decline and dementia in older individuals.

This study involved the analysis of data from an ongoing, prospective, cohort study, the Adult Changes in Thought (ACT), a population-based longitudinal study of aging and dementia. The ACT study's sample was created from a random sample of individuals without dementia, 65 years of age or older, who were not residing in a nursing home at baseline. The original cohort was enrolled between 1994 and 1996, with an expansion cohort recruited between 2000 and 2002. From this cohort, 2,929 patients, 65 years of age or older, were randomly chosen and followed for 6.1 years. Medical and demographic data were collected using questionnaires, and cognitive screening was performed using the Cognitive Abilities Screening Instrument (CASI). Cognitive scores were compared between those who were, and those who were not, hospitalized.

Of the subjects, 1,601 had no hospitalizations, 1,287 had noncritical illness hospitalizations, and 41 had critical illness hospitalizations. The CASI results were analyzed for 94.3% of the patients. Adjusted scores averaged 1.01 points lower for acute care illness, and 2.14 points lower for critical illness hospitalizations, as compared to those with no hospitalizations. The hazard ratios for incident dementia were 1.4 following acute care illness and 2.3 following critical illness hospitalizations.

**Conclusion:** This study of older adults without dementia at baseline found that those who underwent an acute care illness hospitalization and those who underwent a critical illness hospitalization had a greater likelihood of cognitive decline than did those who were not hospitalized.

Elenbach, W., et al. Association between Acute Care and Critical Illness Hospitalizations and Cognitive Function in Older Adults. *JAMA*. 2010, February, 24; 303(8): 763-770.

### MOBILE COMPRESSION FOR THROMBOSIS PREVENTION

Without prophylaxis, the incidence of deep venous thrombosis (DVT) after total hip arthroplasty (THA) has been estimated to be as high as 50%. As 90 % of symptomatic pulmonary emboli originate in a lower extremity, prevention of these thrombi has become the standard of care after THA. Mechanical methods of prophylaxis are often used for patients with a higher bleeding risk or as an adjunct to chemoprophylaxis. However, widely available, hospital based compression devices prevent walking and are often difficult to apply. This study assessed the efficacy of a new mobile compression device for the prevention of venous thromboembolism.

This randomized, prospective trial included 386 patients (389 hips) undergoing THA. The subjects were randomized to receive 10 days of either mechanical prophylaxis or low molecular weight heparin (LMWH). Mechanical prophylaxis was begun intraoperatively, with LMWH injections started 12 to 24 hours post-surgery. The portable compression device applied intermittent, sequential pressure to the leg in correlation with the patient's respiratory-related venous phasic flow. The 1.65-lb pump and battery pack were carried with a shoulder strap. Bilateral lower extremity venous duplex ultrasound was obtained 10 to 12 days postoperatively, with spiral CT scan performed for any patient with symptomatology suspicious for pulmonary embolism (PE). DVT and PE follow-ups were also performed at 12 weeks post-surgery.

Distal and proximal DVT rates were three percent and two percent, respectively, in the compression group, and three percent and one percent, respectively, in the LMWH group. PE was found in two (one percent) patients in both groups. The overall difference in VTE between the compression and the low molecular weight heparin groups was not statistically significant ( $p = 0.953$ ). All eleven bleeding events occurred in the heparin group ( $p = 0.0004$ ).

**Conclusion:** This study of patients undergoing total hip arthroplasty found that the rates of DVT and PE are similar between groups receiving prophylaxis with LMWH and those using a portable pneumatic compression device. Significantly more bleeding events occurred in the heparin group.

Colwell, C., et al. Thrombosis Prevention after Total Hip Arthroplasty: A Prospective, Randomized Trial Comparing a Mobile Compression Device with Low Molecular Weight Heparin. *J Bone Joint Surg (Am)* 2010, March; 92: 527-535.

### ULTRASOUND MEASUREMENT OF MEDIAN NERVE SLIDING FOLLOWING NERVE REPAIR

Peripheral nerves need to slide and stretch in order to accommodate changes in length during passive or active limb movement. After median nerve repair, fibrotic scar tissue may impede the nerve's ability to slide, and may increase tension across the repair site. Previous studies have shown that such tension can compromise axon regeneration and recovery. This study used ultrasound (US) to determine the mobility and excursion of the median nerve following primary nerve repair.

This retrospective case series included 10 subjects who had undergone a division of the median nerve, with repair. The average time post-surgery was 34 months at the time of the study's onset. US was used to measure the path of excursion of the median nerve at the wrist while passively flexing the metacarpophalangeal joints from neutral to 90°. The subject's uninjured side served as the control. Nerve morphology and maximum cross-sectional area were also recorded.

The median nerve was found to be fusiform in shape and considerably larger in cross-sectional area on the injured side than on the uninjured side (median 45.7 mm<sup>2</sup> versus 12.2 mm<sup>2</sup>, respectively). Significant reductions in median nerve movement were found when comparing the injured side (2.15 mm) to the uninjured side (2.54 mm). However, much of that difference was attributed to three subjects with outlying values. Other factors contributing to decreased excursion

included scar tissue presence, changing connective tissue interface and nerve swelling. No significant relationship was found between the reduction in longitudinal nerve sliding and cross-sectional area.

**Conclusion:** This follow-up study of 10 patients who had undergone median nerve repair found that the median nerve increased in cross-sectional area following repair, with a reduction in excursion with wrist motion. As this study used ultrasound, this tool was found to be useful in defining morphological characteristics after nerve repair.

Erel, E., et al. Sonographic Measurements of Longitudinal Median Nerve Sliding in Patients following Nerve Repair. *Musc Nerve*. 2010, March; 41: 350-354.

### MOTION CONTROL SHOES AND FATIGUE IN OVERPRONATORS

Excessive rearfoot pronation may cause various overuse injuries in runners. Motion control shoe technology was developed to prevent lower leg muscle overuse in runners by limiting rear foot pronation during landing. This study examined lower leg muscle activation in different shoe conditions among individuals identified with excessive pronation.

Twenty female runners with excessive rear foot pronation (> 6°) were recruited. All were unfamiliar with motion control footwear technology, and all were tested while running 10 km. on a treadmill over two days. The participants wore either a motion control running shoe or a neutral running shoe on each of the testing days. Surface electromyography was used to assess the activity of the tibialis anterior (TA) and the peroneus longus (PL). Before each running session, every participant performed a maximum voluntary isometric contraction (MVC) for both muscles tested. The running test results were then compared against this MVC. The normalized root-mean-square electromyography and median frequency were compared between the two shoe conditions. The power spectrum was quantified by calculating the median frequency (MF) for each of the raw EMG data.

Significant differences in the normalized EMG values for the TA and PL muscles were found with

different footwear conditions ( $p < 0.001$ ) and across mileage ( $p < 0.001$ ). Comparing the two shoe conditions, a significantly larger shift in median frequency was found in the PL during the neutral shoe testing condition ( $p < 0.001$ ). For the TA, however, the difference between shoe conditions was not significant ( $p = 0.074$ ).

**Conclusion:** This study found that a motion control shoe reduced fatigue endurance of the peroneus longus muscle during a 10 kilometer run among runners who overpronate.

Cheung, R., et al. Motion Control Shoe Delays Fatigue of the Shank Muscles in Runners with Overpronating Feet. *Am J Sp Med*. 2010, March; 38(3): 486-491.

### GENERALIZED HYPERALGESIA IN CHRONIC FATIGUE SYNDROME

Patients with chronic fatigue syndrome (CFS) often suffer from generalized pain complaints. The literature indicates that up to 94% of these patients report muscle pain and 84% report articular pain. Central sensitization is known as increased central neuronal responsiveness, which causes hyperalgesia, allodynia, referred pain and hyperalgesia across multiple spinal segments, leading to chronic, widespread pain. This study sought to determine whether a difference in pressure pain thresholds exists between healthy people and patients with CFS suffering from chronic pain.

Thirty patients with CFS were randomly chosen from among consecutive referrals to a Belgian chronic fatigue clinic. All subjects fulfilled the Belgium Center of Disease Control criteria for CFS. In addition, all reported chronic, widespread pain, lasting for more than three months. Thirty, age and gender matched controls with no reports of pain were included for comparison. All subjects used the Margolis Pain Diagram to shade the body parts where they had felt pain lasting for more than 24 hours in the previous four weeks. The drawings were then converted to a total percentage of body surface. Pressure pain thresholds (PPTs) were measured bilaterally with an analog Fisher algometer. After completing a battery of questions evaluating pain, cognition, functional status and

symptomatology, a researcher held blind to those data assessed the PPTs at seven sites in both the trunk and the extremities.

The percentage of painful body area was significantly higher in the CFS group than in the controls ( $p < 0.001$ ). Patients with CFS had experienced more episodes of pain lasting for more than 24 hours during the previous four weeks. On average, 35% of their body area was marked as painful, as compared to three percent in the control group. The average PPTs were 3.3 kg/cm<sup>2</sup> in the CFS patients and 8.1 kg/cm<sup>2</sup> in the controls ( $p < 0.001$ ).

**Conclusion:** This study found lower PPTs in patients with chronic fatigue syndrome who express chronic, widespread pain, as compared to healthy controls. This was true even at pain-free locations.

Meeus, M., et al. Evidence for a Generalized Hyperalgesia in Chronic Fatigue Syndrome: A Case Control Study. *Clin Rheum.* 2010, April; 29: 393-398.

#### **POLYNEUROPATHY AND MOTOR VEHICLE ACCIDENTS**

In the United States, motor vehicles are the most common mode of transportation and the fourth most frequent cause of death and injury. The ability to drive, even among people with disability, represents mobility and independence. The influence of medical conditions on the ability to safely drive is of importance to patients, physicians and society.

Physical factors associated with peripheral neuropathy include weakness, sensory loss and pain, all having the potential to impact the ability to drive. Despite these risks, the safety of driving among individuals with neuropathy has not been previously evaluated. This study investigated the risk factors for motor vehicle accidents among patients diagnosed with neuropathy.

This cohort study surveyed patients with distal symmetric polyneuropathy. All were diagnosed by clinical examination, with electrodiagnostics performed when needed for confirmation. Information collected included severity of neuropathy, medications, current and past driving patterns and accident history. Motor vehicle accidents per million miles

travelled were calculated and compared to national data.

Two hundred sixty patients with neuropathy were studied. Of those, 43% reported at least one accident and 10% discontinued driving due to safety concerns. The rate of motor vehicle accidents was 0.11 accidents per year per driver, as compared to the other 191 million licensed American drivers, whose rate was 0.034 accidents per year per driver. Of those involved in an accident, 46% reported pain of greater or equal to 6 on the VAS, while only 15% of those without an accident experienced the same level of pain ( $p < 0.001$ ). The odds ratio of having a MVA among those with difficulty with ambulation was 1.9 ( $p = 0.026$ ). In all, 72% cited their neuropathy, and 55% cited their medications, as playing a role in their accidents. Over half reported changing their driving habits after developing neuropathy. There was no significant difference in accident rates between patients who were on medications and those who were not.

**Conclusion:** This study, comparing rates of motor vehicle accidents among patients with neuropathy to those of the general population, demonstrates that patients with neuropathy, particularly those with severe pain and weakness, are at increased risk of motor vehicle collisions.

Cho, C., et al. Driving with Polyneuropathy. *Musc Nerve.* 2010, March; 41: 324-328.

#### **ULTRASOUND GUIDED STEROID INJECTION OF THE INTERNAL OBLIQUE**

Strains of the internal oblique muscle have been described in a number of sports. These strains are characterized by sudden onset of pain and focal tenderness over the rib cage. While diagnoses can usually be made correctly, imaging can be helpful to evaluate the extent and severity of the injury. This case series describes professional major league baseball pitchers who underwent ultrasound examination for therapeutic injection of steroids to accelerate the recovery of their injuries.

Between April of 2006 and April of 2008, three professional baseball pitchers with pain in muscles along the right lower rib cage were referred

for treatment. In each case, an MRI had been performed, confirming the presence of an internal oblique strain. Ultrasound was used to isolate the strain, with the muscle injected with a mixture of 0.25% bupivacaine and dexamethasone sodium phosphate. The patients were then asked to perform provocative maneuvers, in order to determine whether their pain had receded.

All three subjects experienced significant pain relief within a few days of the injection and were able to pitch at full speed within three weeks of the injury. All returned to active status by five weeks. All three continued to pitch with none reporting re-injury of the site.

**Conclusion:** This study found that therapeutic injections of steroids and anesthesia under ultrasound guidance may speed recovery and rehabilitation of professional baseball pitchers with internal oblique muscle strain.

Stevens, K., et al. Imaging and Ultrasound Guided Steroid Injections of Internal Oblique Muscle Strains in Baseball Pitchers. *Am J Sp Med.* 2010, March; 38(3): 581-585.

#### **ORAL FINGOLIMOD FOR MULTIPLE SCLEROSIS**

Oral fingolimod is a sphingosine-1-phosphate-receptor modulator which, after phosphorylation induced receptor internalization, renders B and T cells insensitive to a signal necessary for egress from secondary lymphoid tissues. The resulting redistribution to lymph nodes reduces recirculation of auto-aggressive lymphocytes to the central nervous system. Fingolimod has been found to effectively treat experimental autoimmune encephalomyelitis, an animal model for multiple sclerosis (MS). This study compared fingolimod to standard interferon therapy for the treatment of MS.

This phase three, double-blind - double dummy study was completed between May of 2006 and September of 2007. The study randomized 1,292 patients diagnosed with MS, with 1,153 completing the study. Subjects were randomized into three groups, which compared standard dosing of interferon to fingolimod at two different strengths. Outcome measures included the annualized relapse rate, new or enlarge lesions,

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as noted on T2 weighted MRI scans, and progression of disability, sustained for at least three months.

Significantly greater reductions in relapse rates were seen in the fingolimod groups as compared to the interferon group ( $p < 0.001$ ). The fingolimod groups also had significantly fewer new or enlarged hyperintense lesions according to MRI findings ( $p < 0.001$ ). No significant difference was found between the groups when looking at progression of disability or proportion of patients with confirmed progression. Adverse reactions were similar in all groups. Serious adverse reactions that resulted in the discontinuation of treatment were most common in the high-dose fingolimod group, with 10% discontinuing, as compared to 5.6% in the lower dose group and 3.7% in the interferon group.

**Conclusion:** This study found that fingolimod is superior to intramuscular interferon beta 1A for the treatment of MS, with a superior reduction in the relapse rate.

Cohen, J. Oral Fingolimod or Intramuscular Interferon for Relapsing Multiple Sclerosis. *NEJM*. 2010, Feb 10; 362: 402-415.

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

*Rehab in Review* is produced with the cooperation and assistance of Emory University School of Medicine, Department of Rehabilitation Medicine. *Rehab in Review* is affiliated with the Association of Academic Physiatrists, the World Health Organization, and the Chinese and Indian Societies of PM&R. Funding for academic training subscriptions is provided by corporate sponsorship.

Private subscriptions are available by mail at P.O. Box 183, Lampe, MO 65681, or by fax or phone at (800) 850-REMU (7388).

ISSN # 1081-1303



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is produced by the  
Emory University Department of  
Rehabilitation Medicine.



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