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DRIVING AFTER STROKE

While approximately 50% of persons with stroke wish to continue driving, the majority do not undergo formal driving assessment. On-road evaluations last approximately 40 minutes and cost between \$300 and \$400. This systematic review and meta-analysis sought to identify the best office-based determinants of fitness to drive, and to investigate whether drivers with stroke are at increased risk of car crashes.

Twenty databases were searched for articles on stroke and automobile driving. From among these, 30 articles were included in the systematic review, and 27 in the meta-analysis. The evidence levels ranged from case series to randomized controlled trials. The designation of "fit to drive" was defined as passing the on-road evaluation. Off-road assessment results were compared between those who did, and those who did not, pass the on-road test.

The median patient age and time between stroke onset and driving assessment were 61.1 years and 8.8 months, respectively. Five, clinically relevant, in-office determinants of fitness to drive were identified. These included the Cube Copy, Road Sign Recognition, Compass, Stroke Driver's Screening Assessment and Trail Making Test, Part B. These examinations primarily assessed cognition, focusing on executive function.

On average, those assessments took 15 minutes to complete. Fitness to drive was not affected by age, driving experience, location of lesion, motor symptoms or visual deficits. Twelve studies examining the accident potential in post-stroke patients found no increased risk among those who had passed the on road evaluation as compared with controls.

Conclusion: This systematic review and meta-analysis found that the assessment of readiness to drive in post-stroke patients could be aided

by in-office batteries with a focus on cognitive function. Patients who pass an on-road examination had no increased accident risk as compared to normal controls.

Devos, H. et al. Screening for Fitness to Drive after Stroke: A Systematic Review and Meta-Analysis. **Neurology.** 2011, February; 76(1): 747-756.

DECOMPRESSIVE CRANIECTOMY AND DIFFUSE TRAUMATIC BRAIN INJURY

Among patients who are hospitalized with severe traumatic brain injury (TBI), 60% either die or survive with a severe disability. After injury, medical and surgical therapies are performed to minimize secondary brain damage. Increased intracranial pressure is an important secondary insult. While many patients with severe TBI have increased intracranial pressure that is refractory to first tier therapies, surgical decompressive craniectomy is often performed. This study was designed to test the efficacy of bifrontotemporoparietal decompressive craniectomy for patients in whom first tier intensive care and/or surgical therapy had not maintained intracranial pressures at acceptable levels.

Patients ages 15 to 59 years with non-penetrating TBIs, all of whose intracranial pressures were greater than 20 mmHg, were included in this trial if, within the first 72 hours, intracranial pressures were not reduced sufficiently. The participants were randomized to receive either bifrontotemporoparietal decompressive craniectomy plus standard care or standard care alone. The final, primary outcome measure was the extended Glasgow Outcome Scale, administered at six months post-injury.

Of the 3,478 patients who were assessed for trial eligibility, 155 were

enrolled. Of those, 73 were randomized to the craniectomy group and 82 to the standard care group. After randomization, the mean intracranial pressure was found to be significantly lower in the surgical group than in the standard care group ($p < 0.0001$). Those in the surgical group had a shorter duration of mechanical ventilation and a shorter stay in the intensive care unit than did the standard care group. However, six months after injury, the primary outcome measure was worse in the surgical group than in the standard care group ($p = 0.03$). Unfavorable outcomes occurred in 51 patients in the surgical group (70%) and 42 patients (51%) in the standard care group ($p = 0.02$).

Conclusion: This study of adults with severe, diffuse traumatic brain injury and refractory intracranial hypertension found that, while decompressive craniectomy decreases intracranial pressure and length of stay in the intensive care unit, this procedure is associated with more unfavorable outcomes than is standard care.

Cooper, D., et al. Decompressive Craniectomy and Diffuse Traumatic Brain Injury. **N Engl J Med.** 2011, April 21; 364 (16):1493-1502

LATE SEIZURES FOLLOWING TRAUMATIC BRAIN INJURY

The cumulative, five-year probabilities of post-traumatic seizures are estimated at 0.5% after mild traumatic brain injury (TBI), 1.2% after moderate TBI and 10% after severe TBI. This prospective study evaluated the characteristics of patients with moderately severe TBI, in an effort to determine the risk factors for late onset seizures.

Participants included 39 adults with moderate TBI and cerebral contusions. All were admitted to an inpatient neurologic department between 2002 and 2005. Exclusion

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criteria included Glasgow Coma Scale scores of less than nine and the need for neurosurgical intervention. All subjects were evaluated by computed tomography and magnetic resonance imaging to identify and classify contusions. Past medical history was determined in order to assess vascular and social risk factors. All patients underwent electroencephalogram (EEG) at discharge. The participants were followed for at least three years after discharge for late onset seizures, defined as those occurring more than two weeks post-TBI.

Fourteen patients developed late onset seizures, with a median onset time of seven months post-injury. Vascular risk factors and alcohol abuse were more frequent in the seizure group than in the non-seizure group. Normal EEG findings were observed in 28.5% of the seizure group, as compared to 72% in the non-seizure group ($p=0.002$). Seizure recurrence occurred in 85.7% of these patients, despite the use of antiepileptic drugs.

Conclusion: This study of patients with moderate traumatic brain injury found that an abnormal electroencephalogram is highly predictive of late onset seizures. In addition, vascular risk factors and alcohol abuse may predispose their occurrence.

DeReuck, J., et al. Risk Factors for Late Onset Seizures Related to Cerebral Contusions in Adults with a Moderate Traumatic Brain Injury. **Clin Neurology Neurosurg.** 2011 DOI: 10.1016/j.clineuro.2011.02.004.

MAGNETIC STIMULATION AND DEMYELINATING NEUROPATHIES

Proximal demyelination may be difficult to distinguish with standard nerve conduction studies, which primarily assess distal peripheral pathways. The use of a magnetic coil for paravertebral neuromagnetic stimulation is both noninvasive and relatively painless. This study sought to determine whether differentiation between demyelinating and axonal neuropathies can be enhanced by the use of magnetic stimulation.

Subjects included normal controls and those presenting for electrodiagnostic studies for a variety of neurologic conditions. The patients were categorized by disease states using standard clinical and

neurophysiological testing as well as radiological studies. Responses using a large, twin magnetic coil for stimulation at proximal and distal cauda equina while recording from muscles of the foot, shin, and thigh were compared to those for standard cathode stimulation of the tibial nerve in the leg. Responses in the abductor hallucis, vastus medialis, and tibialis anterior were recorded with magnetic stimulation. Compound muscle action potentials were elicited by cathodal stimulation of the tibial nerve at the ankle and popliteal fossa,

Results of paravertebral neuromagnetic stimulation, comparing amplitudes and segmental conduction times, distinguished demyelinating neuropathy from neuropathy and axonal neuropathy, even with reduced amplitude compound motor action potentials. Low threshold activation sites and ectopic activation limited some magnetic stimulation parameters. However, this technique was able to distinguish subtypes of demyelinating neuropathies.

Conclusion: Magnetic stimulation can be used as an adjunct to clinical nerve conduction studies to help distinguish demyelinating from axonal neuropathies, as well as to distinguish demyelinating subtypes.

McAbee, P., et al. Upper Leg Conduction Time Distinguishes Demyelinating Neuropathies. **Musc Nerve.** 2011, April; 43: 518-530.

EPIDURAL CLONIDINE VERSUS STEROIDS FOR RADICULOPATHY

Radiculopathy due to intervertebral disc herniation (IDH) is a common cause of pain and other neurologic symptoms. Mechanical compression of the nerve root, as well as inflammation, may contribute to the clinical picture. Treatment options include oral pain medications, physical therapy, epidural steroid injection and surgery. Epidural clonidine is an approved treatment for cancer pain and may also have anti-inflammatory activity. This study compared clonidine and steroids for the treatment of radicular pain secondary to IDH.

This randomized, double-blind, prospective trial included 26 patients with approximately three months of low back and leg pain attributed to IDH. The participants were randomized to receive transforaminal

epidural steroid injections with either two percent lidocaine and 40 mg of triamcinolone, or two percent lidocaine and 200 to 400 mcg of clonidine. The primary outcome measure was performance on an 11-point pain intensity rating scale, administered at one month. Each patient received one to three injections, administered two weeks apart. Two patients in the clonidine group and seven in the steroid group received all three injections.

Both groups demonstrated significant improvement in pain scores at two weeks and at one month as compared with baseline ($p < 0.05$). However, no significant difference was seen between the groups on the primary outcome measure. The steroid group showed greater additional functional improvement at one month as compared to the clonidine group.

Conclusion: This pilot study of patients with acute lumbosacral radiculopathy found that epidural clonidine may be as effective as steroids in reducing pain in this population.

Burgher, A., et al. Transforaminal Epidural Clonidine Versus Corticosteroid for Acute Lumbar Sacral Radiculopathy Due to Intervertebral Disc Herniation. *Spine*. 2011, March 2; 36(5): E293-E300.

CAUDAL EPIDURAL INJECTIONS, WITH AND WITHOUT STEROIDS

Epidural injections are commonly performed for nonspecific, chronic back pain without disc herniation. However, limited research has addressed the effectiveness of epidural injections for these patients. This study was designed to investigate the effectiveness of epidural injections, both with and without steroids, in patients with nonspecific back pain without evidence of discogenic, radicular or facet origin.

This randomized, double-blind study involved 120 patients with chronic, nonspecific back pain, without radiologic evidence of disc herniation, and without facet pain as determined by diagnostic anesthetic blocks. The subjects were randomized to receive injections with local anesthesia only (group I), or with local anesthetic plus corticosteroid (group II). At the end of one year, pain level, functional status,

opioid intake, weight and employment status were evaluated.

At 12 months, 63% of participants in Group I and 72% of participants in Group II showed significant pain relief. A greater percentage of patients in the combined treatment group realized more than a 50% reduction in back pain. Of those who responded well to the initial injection, over 80% in both groups experienced back pain relief of greater than 50% at the end of one year. Both groups showed increased employment.

Conclusion: This study of nonspecific low back pain found that epidural injections can be effective in reducing that pain and returning patients to work.

Manchikanti, L., et al. One-Year Results of a Randomized, Double-Blind, Active Controlled Trial of Fluoroscopic Caudal Epidural Injections, with or without Steroids in Managing Chronic Discogenic Low Back Pain without Disc Herniation or Radiculitis. *Pain Physician*. 2011, January/February; 14(1): 25-36.

CLINICAL OUTCOME IN ULNAR NEUROPATHY AT THE ELBOW

Ulnar neuropathy at the elbow is the second most common entrapment neuropathy. Electrodiagnostic testing is often used to confirm and further classify the ulnar lesion. However, it remains unclear which specific electrodiagnostic results predict the outcome. This investigation was designed to determine which test result, or combination of results, is most closely associated with subsequent recovery in ulnar neuropathy.

This retrospective study included 15 years of electrodiagnostic laboratory results from one clinic. From these data, 59 patients with definite ulnar neuropathy at the elbow were identified. Associations between primary outcomes (recovery and surgery) and various electrodiagnostic and clinical parameters were calculated.

Of the 59 patients, 22 enjoyed full recovery, while 37 demonstrated incomplete recovery. No patient reported a progression of symptoms. Significant correlates of subjective recovery included conduction block across the elbow, recorded over the first dorsal interosseus muscle, and a normal abductor digiti minimi (ADM) compound action potential (CMAP).

Of the patients with these two features, 86% achieved full subjective recovery, as compared to only seven percent without conduction block and with an abnormal CMAP at the ADM. No electrodiagnostic finding was significantly associated with the need for subsequent surgery.

Conclusion: This study of patients with definite ulnar neuropathy at the elbow found that the combination of conduction block across the elbow and a normal ADM CMAP is the most significant predictor of subjective recovery.

Frederich, J., et al. Prognostic Indicators from Electrodiagnostic Studies for Ulnar Neuropathy at the Elbow. *Muscle Nerve*. 2011; April (43): 596-600.

RADIOFREQUENCY TREATMENT FOR KNEE OSTEOARTHRITIS

Chronic knee osteoarthritis (OA) is a common disease of advanced age. Pharmacologic and nonpharmacologic treatments are temporizing measures, with knee replacement being the definitive treatment. With advancing age, however, comorbidities may limit surgical options. As the genicular nerves supplying the knee joint are potential targets for treating knee pain, radiofrequency (RF) neurotomy of the geniculate nerve may be a treatment option. This study examined the effect of RF genicular neurotomy on chronic knee pain and knee function in elderly patients with OA.

This randomized, double-blind, sham lesion, controlled study included 38 patients, ranging in age from 50 to 80 years, all with chronic knee OA. All subjects complained of severe knee pain for at least three months' duration, had experienced a positive response to a diagnostic geniculate nerve block and had failed other conservative management. The diagnostic blocks were performed with two percent lidocaine applied to the superior lateral, superior medial and inferior medial geniculate nerves. The treatment group received percutaneous RF geniculate neurotomy under fluoroscopic guidance, with a control group receiving the same procedure without activation of the RF generator.

Visual analogue scale (VAS) scores, Oxford knee scores and global perceived effect, rated on a

seven-point scale, were determined at baseline and at one, four and 12 weeks' follow-ups. On the VAS, the RF group had less pain at four ($p<0.001$) and at 12 ($p<0.001$) weeks than did the controls. At weeks one, four and 12, at least 50% pain relief was realized by 59%, 65% and 59%, respectively, of the treatment group.

Conclusion: This randomized, double-blind study demonstrated that radiofrequency neurotomy of the geniculate nerves may be a minimally invasive therapeutic option for patients with chronic pain due to knee osteoarthritis.

Choi, W., et al. Radiofrequency Treatment Relieves Chronic Knee Osteoarthritis Pain: A Double-Blind, Randomized, Controlled Trial. **Pain**. 2011, March; 152(3): 481-487.

STROKE AND DELIRIUM

Delirium is a common problem among elderly patients, characterized by decreased attention and disturbance of consciousness or disorganized thinking. This disorder develops over a short time and fluctuates during the course of the day. These authors investigated the incidence, risk factors and outcomes of patients with delirium after stroke.

Five hundred twenty seven patients admitted to a stroke unit after ischemic or hemorrhagic stroke were studied. Baseline data were collected, including age, gender, medications at admission, alcohol use and auditory and/or visual impairments. All participants underwent CT scans, with stroke subtypes classified. The severity of clinical deficits was scored using the NIH stroke scale and the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE).

Delirium screening was performed between days two and four, and again between days five and seven, using the Confusion Assessment Method (CAM). If the CAM was positive, the severity of delirium was assessed daily using the Delirium Rating Scale. Metabolic complications, anticholinergic medications, cerebral atrophy and white matter changes were also evaluated. The outcome was assessed using the Barthel Index.

Of the patients evaluated, 11.8% developed delirium, with 9.7% diagnosed between days two and four and 1.9% diagnosed at the second screening. The risk of

delirium was increased three-fold with infection, 3.4 fold with anterior circulation large vessel stroke and over 50-fold with pre-existing cognitive decline. Other risk factors included right hemisphere stroke, scores within the highest tertile on the NIH stroke scale and brain atrophy. In-hospital mortality and length of hospitalization were higher for patients with delirium

Conclusion: This study found that approximately 12% of patients admitted for stroke develop delirium within the first week of admission. Pre-existing cognitive decline, infection and anterior circulation large vessel stroke were found to be independent risk factors for the development of delirium.

Oldenbeuving, A., et al. Delirium in the Acute Phase after Stroke: Incidence, Risk Factors and Outcomes. **Neurology**. 2011, March 15: 76(11): 993-999.

SMALL VESSEL DISEASE AND STROKE SURVIVAL

The short-term prognosis after an ischemic stroke due to small vessel disease (SVD) is generally favorable. This large cohort study compared long-term survival after stroke due to SVD with those of strokes due to other causes.

Patients with suspected stroke who were admitted to Helsinki University Central Hospital between 1993 and 1995 were followed over the course of 12 years. A detailed medical history was obtained, including education, cardiac risk factors and smoking history. Survival data were obtained, and cause of death was categorized as cardiac, brain associated, infectious, traumatic, cancer or other. These data were compared by stroke subtype.

In all strokes (486), the most frequent stroke risk factor was current or former smoking (49.8%), followed by arterial hypertension (47.3%), diabetes (24.7%), cardiac failure (22.1%), atrial fibrillation (20.2%), previous stroke (20.2%), myocardial infarction (19.1%) and peripheral artery disease (11.9%). Patients with SVD were more often current or former smokers ($p=0.011$), and more often had a history of cardiac risk factors ($p<0.001$).

Poor survival outcomes in SVD were associated with advanced age

($p<0.001$) and male gender ($p<0.012$). SVD was associated with cardiac cause of death, but not with brain-related or other causes of death. Previous stroke was not a predictor of mortality. Compared to other subtypes of stroke, SVD related strokes had a shorter overall survival period ($p=0.002$).

Conclusion: This long-term follow-up study found that acute stroke due to small vessel disease is associated with poorer long-term survival and a higher risk of cardiac related death, as compared to other stroke subtypes.

Melkas, S., et al. Small Vessel Disease Relates to Poor Post Stroke Survival in a 12-Year Follow-Up. **Neurology**. 2011, February 22; 76 (8): 734-740.

RELIABILITY OF VITAL SIGNS FOR ESTIMATING PAIN SEVERITY

Pain experience has been substantiated from patients' self-reports, and validated with vital signs in clinical practice. This study examined the strengths of the relationships between pain severity scores and systolic blood pressure, heart rate and respiratory rates among adults reporting pain.

This retrospective cohort study utilized a convenience sample of 3,357 patients during a seven-month period in 2005. The authors analyzed ambulance records for all patients ages 14 years or older with Glasgow Coma Scale Scores of greater than 12 who were transported to hospitals by paramedics. Paramedics in this setting were required to document at least two sets of vital signs. Pain was reported by the patients on a numeric rating scale. Descriptive statistics and tests of correlation were used to identify any relationships between initial pain severity scores and vital signs. The primary outcome variables were the associations between the first recorded pain severity score and the patient's heart rate, respiratory rate and systolic blood pressure.

No significant relationships were found between the subjective pain ratings and heart rates ($p=0.61$) or blood pressures ($p=0.81$). However, a significant relationship was found between initial pain scores and respiratory rates ($p=0.0001$), with each one point increase in pain scale score associated with an increase in respiratory rate of 0.16 breaths per

minute. Nevertheless, that finding was not thought to be of clinical significance.

Conclusion: This study found no clinically relevant association between subjective pain reports and vital signs. The authors note that these data suggest that vital signs cannot be used to estimate or validate the severity of episodes of pain reported by adult patients.

Lord, B., et al. The Reliability of Vital Signs in Estimating Pain Severity among Adult Patients Treated by Paramedics. **Emerg Med J.** 2011, February; 28(2): 147-150.

LIPID PARADOX IN RHEUMATOID ARTHRITIS

Several studies have demonstrated a continuous increase in cardiovascular risk with increasing serum cholesterol levels. In addition, the evidence is convincing for excess cardiovascular risk in patients with rheumatoid arthritis (RA). However, some evidence suggests that a decline in inflammatory markers among patients with RA coincides with increases in serum lipid values. This study assessed the impact of serum lipids and systemic inflammation on cardiovascular disease in patients with RA.

Data were drawn from the Rochester Epidemiology Project for this retrospective cohort study. Records were obtained for 651 patients with RA who were at least 18 years of age. All had been first diagnosed between 1980 and 2008. Data were collected concerning age, gender, rheumatoid factor, antirheumatic drugs, biological responses to modifiers and use of corticosteroids, statins and other lipid lowering drugs. Erythrocyte sedimentation rates (ESRs), C-reactive protein (CRP) measures and fasting serum lipid levels were also abstracted from the medical records. Cardiac events such as ischemic heart disease and heart failure were further documented. The association of lipids and inflammation with the risk of cardiovascular disease and mortality was examined.

More than one third of the patients had abnormal lipid levels at some time during follow-up. Nearly 1/3 of the subjects were treated with lipid lowering drugs, including statins. An increased ESR was significantly associated with an adjusted

increased risk of CVD and mortality. In addition, CRP was significantly associated with the risk of heart failure and mortality.

Interestingly a 3.3 fold increased risk of CVD was noted for those with total cholesterol of less than four mmol/l, while no increased risk was seen for those with total cholesterol of 4 mmol/l or more. In addition, low-density lipoprotein cholesterol levels of less than 2mmol /l were associated with a marginally increased risk of CVD, while no increased risk was noted for those with levels of 2 mmol/l or more.

Conclusion: This study of patients with rheumatoid arthritis found that the risk of cardiovascular disease among these patients is inversely related to total cholesterol and low-density lipoprotein levels.

Myasoedova, B., et al. Lipid Paradox in Rheumatoid Arthritis: The Impact of Serum Lipid Measures and Systemic Inflammation on the Risk of Cardiovascular Disease. **Ann Rheum Dis.** 2011, March; 70(3): 482-487.

DECREASED ACETYLCHOLINESTERASE ACTIVITY IN TRAUMATIC BRAIN INJURY

Due to brain anatomy and injury biomechanics, the major cholinergic centers are situated in regions that are especially vulnerable in traumatic brain injury (TBI). Vigilance, attention and memory are at least partly mediated by the cholinergic system and are frequently compromised after TBI. Therefore, cholinergic stimulation may be beneficial in improving chronic cognitive symptoms of TBI. In this study, acetylcholinesterase (AChE) activity of patients with TBI was compared by PET scan to that of normal controls.

Subjects included 17 patients with chronic TBI (an injury sustained at least one year previously) and 12 normal controls. All participants had been without centrally acting drugs for at least four weeks prior to the study. Cholinergic function was assessed with a lipophilic AChE analogue. The results were analyzed with a statistical parametric map (SMP) and a "regions of interest" (ROI) analysis.

SMP results revealed significantly lower AChE activity in subjects with TBI, most notably in the parietal/occipital regions. The ROI analysis

revealed lower AChE activity in TBI subjects than in controls, except in the medial temporal cortex. When corrected for multiple comparisons, the results for the parietal and cingulate cortices remained significant.

Conclusions: This PET scan study of patients with chronic cognitive symptoms after traumatic brain injury reveals widely lowered AChE activity across the neocortex.

Ostberg, A., et al. Cholinergic Dysfunction after Traumatic Brain Injury: Preliminary Findings from a PET Study. **Neurology.** 2011, March; (76): 1046-1050.

PREDICTION RULE FOR AMBULATION AFTER SPINAL CORD INJURY

After traumatic spinal cord injury (SCI), recovery of the ability to walk is a high priority for the patient. Prognostic indicators have been studied in the past, although no prediction rule has been identified to assess the patient's chances of walking. This study sought to develop a validated prediction rule for an adult's ability to walk independently after traumatic SCI.

This longitudinal cohort analysis included 492 patients with traumatic SCI. Data were extracted from the European Multicenter Study on Human SCI, a database with 19 centers, encompassing patient data from July of 2001 through July of 2008. Physical examinations were performed within the first 15 days and at months one, three, six and 12. The ability to walk independently was assessed using the Spinal Cord Independence Measure indoor mobility item (SCIM). Multiple analyses of the data were conducted in an effort to assess the predictive values of multiple variables.

The final prediction rule significantly discriminated patients who were able to walk independently from those who were not (p<0.001). That rule included age under 65, and four neurological predictors including, quadriceps femoris muscle grade (L3), gastrocsoleus muscle grade (S1), light touch sensory (LTS) at L3 and LTS at S1. Temporal validation confirmed the discriminatory ability of the prediction rule (p<0.0001).

Conclusion: This study identified clinical prediction rules, including age and four neurological predictors, that

can be used to anticipate ambulation outcome after traumatic spinal cord injury.

Van Middendorp, J., et al. A Clinical Prediction Rule for Ambulation Outcomes after Traumatic Spinal Cord Injury: A Longitudinal Cohort Study. **Lancet**. 2011, March 19; 377: 1004-1010.

INTERNET TRAINING FOR CHILDREN WITH CEREBRAL PALSY

Children with cerebral palsy (CP) suffer from both motor and cognitive disabilities. These children require multifaceted treatment over many years, involving local health professionals. It is thought that, in order to drive neuroplastic changes in the brain, much more intensive and long lasting training is necessary than was previously assumed. This study was designed to determine whether an interactive home-based computer program system, individualized for a child with CP, provides an efficient means of interactive training over an extended period of time.

This pilot study included nine children diagnosed with spastic CP. All were provided with a computer with specific software, a WebCam and a high-speed Internet connection. The children were trained in their own homes during a 20-week period. The program ensured that the training lasted for at least 30 minutes per day. The training system provided a combination of cognitive and motor challenges, in order to train cognitive, perceptual and motor abilities at the same time. The different modules were combined uniquely for each child according to specific cognitive and motor deficits. The children were tested for strength, balance, gait and visual perception.

The children trained for an average of 74 hours during the 20 weeks of the study. After treatment, significant improvement was seen in functional muscle strength, visual perceptual abilities, processing skills and endurance. Subjective improvement in motor abilities and self-esteem were noted by both the children and their families.

Conclusion: This pilot study demonstrates the concept of home-based, interactive Internet training for patients with cerebral palsy, which may offer the longer training

necessary for favorable results in this population.

Peder, B., et al. Individualized, Home-Based Interactive Training of Cerebral Palsy Children Delivered through the Internet. **BMC Neurology**. 2011, March; 11: 32.

CARDIAC REHABILITATION REFERRAL STRATEGIES AFFECT UTILIZATION RATES

Cardiovascular disease remains the leading cause of mortality worldwide, and is chiefly attributable to modifiable risk factors. Cardiac rehabilitation offers a comprehensive approach to chronic disease management by addressing these risk factors. There is sound evidence that participation in cardiac rehabilitation can reduce morbidity and mortality by approximately 25% over one to two years as compared with usual care. However, data from the United States, Canada and the United Kingdom demonstrate that 70% to 80% of eligible patients do not receive cardiac rehabilitation after hospital discharge. This study compared four referral strategies, in an effort to determine their effect on cardiac rehabilitation referral and utilization.

A total of 2,635, stable cardiac inpatients were recruited. Each hospital unit was identified as having used one of four referral strategies, including 1) automatic 2) liaison, 3) a combination of both or 4) usual referral at the discretion of the health care provider. The liaison referral was one in which the referral was facilitated through personal discussion with a health care professional and/or a peer graduate. One year later, the participants completed a mail survey assessing cardiac rehabilitation utilization. The referral strategies were compared by success in obtaining a cardiac rehabilitation referral.

The referral strategy was significantly related to cardiac rehabilitation referral and subsequent enrollment. The combined liaison and automatic strategies enrolled the most patients (73%), followed by the automatic (60%), liaison (50%) and usual care conditions (29%). Referral strategy did not affect cardiac rehabilitation attendance rates among those enrolled.

Conclusion: This study demonstrates that, for patients in

need of cardiac rehabilitation, automatic referral and liaison result in significantly more referral and enrollment in cardiac rehabilitation among eligible patients than does usual care.

Grace, R., et al. Effect of Cardiac Rehabilitation Referral Strategies on Utilization Rates. **Arch Intern Med**. 2011, February; 171(3): 235-241.

ORAL BISPHOSPHONATE USE AND RISK OF FEMORAL SHAFT FRACTURE

Oral bisphosphonate have been found to reduce the risk of osteoporotic fractures, although recent concerns have emerged that they may suppress remodeling and adversely influence bone strength. This study sought to determine whether prolonged bisphosphonate therapy is associated with an increased risk of subtrochanteric fracture.

The trial was a population-based, nested, case-control study examining the association between bisphosphonate use and fractures in a cohort of Ontario women age 68 years or older who had initiated treatment with a bisphosphonate between 2002 and 2008. Demographic information was obtained from the Registered Persons Database, which contains a record for all Ontario residents ever issued a health card.

Of those treated with a bisphosphonate, cases were identified with a subtrochanteric or femoral shaft fracture between 2003 and 2009. For each case, five controls were selected who were not hospitalized with a subtrochanteric or femoral shaft fracture. From the bisphosphonate exposure values, the participants were categorized as long-term users (five or more years of therapy), intermediate users (three to five years of therapy) or short-term users (100 days to three years of therapy).

Over the seven-year study period, 716 women sustained a subtrochanteric or femoral shaft fracture following the initiation of bisphosphonate therapy. These subjects included 411 women with a subtrochanteric fracture and 305 with a femoral shaft fracture. The use of bisphosphonate for five years or longer was associated with a greater risk of subtrochanteric or femoral

shaft fracture, as compared with transient use. A secondary analysis revealed long-term use to be associated with a decreased risk of fracture, as compared with transient use, at the typical sites of osteoporotic fractures, including the femoral neck and intertrochanteric region.

Conclusion: This study demonstrated that bisphosphonate use for more than five years is associated with an increased risk of subtrochanteric or femoral shaft fracture. However, the overall risk of these fractures was still quite low, occurring in 0.22% of the patients within seven years of treatment.

Park-Wyllie, L., et al. Bisphosphonate Use and the Risk of Subtrochanteric or Femoral Shaft Fractures in Older Women. *JAMA*. 2011, February 23; 305(8): 783-789.

METABOLIC SYNDROME: DIET AND EXERCISE

The prevalence of obesity is increasing at an alarming rate in both developed and developing countries. Obesity is a serious public health problem, as it plays a central role in the progression of cardiovascular and metabolic pathology. The metabolic syndrome is an important predictor of all cause and cardiovascular mortality. Evidence from numerous epidemiological studies indicates that the national recommendations for physical activity, diet and combined diet and exercise can prevent the progression of cardiovascular disease and associated risk factors. This animal study examined the effect of exercise and/or a normal fat diet on existing cardiometabolic complications linked to obesity. These factors included hyperlipidemia, insulin resistance, endothelial dysfunction and hypertension.

Six-week-old male rats were paired and given a control diet (CD) or a high fat diet (HFD) for 12 weeks. The HFD animals were then divided into four groups: sedentary rats on the high fat diet (HFD-S), exercise rats on the high fat diet (HFD-Ex), sedentary rats switched to the control diet (HF/CD-S) and exercise rats switched to the control diet (HF/CD-Ex). Blood pressure was measured every two weeks. After 24 weeks, the rats were sacrificed and blood samples collected. Subjects in the

exercise groups were trained on a motorized treadmill five days per week for 12 weeks. Cardiovascular risk parameters associated with the metabolic syndrome were measured.

The high fat diet was found to significantly increase the body weight of the HFD-S rats as compared to the CD-S rats ($p < 0.001$). The retroperitoneal and epididymal fat pad mass and heart rate were greatly increased in the HFD-S group, but no significant difference was found in the other groups. Systolic blood pressures were significantly increased in the HFD-S group, and were decreased in the exercise group. Lipid profiles and glucose levels were much better in the CD-S group, but even better in the exercising groups. Exercise alone was found to improve all of the metabolic syndrome features, even without switching to a normal caloric diet.

Conclusion: This animal study suggests that exercise reverses the metabolic syndrome induced by high fat diets in rats, even without dietary modification.

Touati, S., et al. Exercise Reverses Metabolic Syndrome in High Fat Diet Induced Obese Rats. *Med Sci Sports Exerc*. 2011, March; 43: 398-407.

STEM CELL TREATMENT FOR MULTIPLE SCLEROSIS

In 1995, these authors initiated an unblinded trial of intense immunosuppressive chemotherapy and stem cell transplantation to treat aggressive multiple sclerosis (MS) unresponsive to standard therapies. The intention was to create a renewed state of immune tolerance by replacing the aberrant immune system via hemopoietic stem cell transplantation. The authors found an 80% probability of disease progression free survival (PFS) at five years. The current study reports on the long-term results for those same 35 patients.

Hemopoietic stem cell transplantation was performed between June of 1995 and May of 2001 in patients progressing clinically with or without new or enlarging lesions on MRI. The median follow-up time was 11 years. Progression was defined as an increase of 0.5 or one point on the Expanded Disability Status Scale.

The median PFS was 5.4 years in secondary and relapsing MS, and 1.5 years in primary progressive disease ($p = 0.338$). Progression free survival was 44% at 15 years in patients with active MRI lesions, in comparison to 10% in patients without active lesions ($p = 0.01$). The results were better for patients with a short interval from diagnosis to stem cell transplantation, as well as for those below the age of 35 years. A total of five deaths occurred, ranging from two months to 14 years after transplantation.

Conclusion: This long-term follow-up study of patients with aggressive multiple sclerosis, unresponsive to standard therapies, found that stem cell transplantation resulted in improved progression free survival rates and a reduction in the number and volumes of lesions on MRI.

Fassas, A., et al. Long-Term Results of Stem Cell Transplantation for MS. *Neurology*. 2011, March 22; 76(12): 1066-1070.

UTILITY OF CUTANEOUS SILENT PERIODS IN ASSESSING DIABETIC NEUROPATHY

Small-fiber neuropathy (SFN) can be defined as sensory polyneuropathy that predominantly affects small-diameter, thinly myelinated A-delta and unmyelinated C fibers. SFN is often difficult to assess by standard nerve conduction studies (NCSs), which reflect large fiber function. Most tests that evaluate small fiber function have limited clinical utility, as they require invasive or time-consuming procedures. A readily available electrophysiologic method for evaluating SFN is the cutaneous silent period (CSP). This technique consists of a brief suppression of voluntary contraction after a strong cutaneous stimulation. This study evaluated the diagnostic utility of the CSP in distal small fiber neuropathy.

Thirty-one, consecutive, diabetic patients with clinically suspected SFN and normal NCS results were included in this trial. Control subjects were individuals without risk factors for neuropathy or abnormalities on neurological examination. All participants underwent evaluation with NCSs, F wave latency tests, heart rate variability to deep breathing, sympathetic skin responses and assessment of the cutaneous silent period.

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All patients had normal NCS results, with no differences in motor, sensory, or F-wave parameters noted between the two groups. In the upper extremity, the latencies and durations of the CSP did not differ significantly between the patients and the controls. However, the patients had significantly prolonged CSP latencies ($p=0.018$) and shortened CSP durations ($p<0.001$) in the lower extremities, when compared with controls. The sensitivity of the CSP duration in the lower extremities was 32.3%, and the specificity was 96.7%, for defining diabetic patients with small-fiber neuropathy.

Conclusion: This study found that the cutaneous silent period is an easily reproducible and noninvasive technique for evaluating patients with diabetic small fiber neuropathy.

Koytak, P., et al. Assessment of Symptomatic Diabetic Patients with Normal Nerve Conduction Studies: Utility of Cutaneous Silent Periods and Autonomic Tests. *Musc Nerve*. 2011, March; 43(3): 317-323.

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