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ASPIRIN RESISTANCE AND STROKE SEVERITY

A pooled analysis of the International Stroke Trial and Chinese Acute Stroke Trial found a relative risk reduction of 11% of nonfatal stroke or death among patients with short-term aspirin use. However a proportion of patients treated with aspirin demonstrate poor clinical outcomes, which may be attributed to aspirin resistance. This study investigated the association between aspirin resistance and stroke severity.

This study included adult patients with at least seven days of aspirin therapy prior to ischemic stroke onset. Stroke severity was assessed using the National Institute of Health Stroke Scale (NIHSS) on admission with the size of infarction measured by computed tomography scan. Blood samples were taken after aspirin ingestion with aspirin resistance measured by a platelet function assay, and expressed as aspirin reaction units (ARU). A cutoff of 550 ARU was used to determine the presence of aspirin resistance.

Of the 90 patients enrolled 26 were aspirin resistant. This group was more likely to have sustained a myocardial infarction, transient ischemic attack or stroke within the last two years (odds ratio 8.04; $p=0.001$). Five percent of the aspirin sensitive patients sustained a total anterior circulation infarction compared with 35% of the aspirin resistant patients. Aspirin resistance was significantly associated with severity of stroke, with aspirin resistant patients more likely to sustain a severe stroke ($p=0.002$).

Conclusion: This study of patients taking aspirin prior to the onset of ischemic stroke found that aspirin resistance is associated with an increase clinical severity and stroke infarction volume.

Zheng, A., et al. Association of Aspirin Resistance with Increased

Stroke Severity and Infarct Size. *JAMA Neurol.* 2013, February; 70(2): 208 – 213.

ORAL HEALTH AND COGNITIVE DECLINE

Antibodies to common periodontal pathogens are associated with the risk of stroke and atherosclerosis. This study was designed to further investigate the association between oral health status and cognitive decline.

The Health, Aging and Body Composition study (Health ABC) is a longitudinal cohort study including 3075 well-functioning individuals aged 70 to 79. A subset of 1843 participants was enlisted to participate in the study of periodontal disease. A periodontal clinical assessment was completed at baseline, with global cognitive function measured at baseline and at years three and five.

Of the 1171 participants, 89.9% also had year five cognitive data. Worse oral health on all measures except bleeding on probing was associated with cognitive decline. In a fully adjusted analysis, gingival inflammation was an independent risk factor for significant cognitive decline between years three and five.

Conclusion: This longitudinal study of elderly individuals found that gingival inflammation is an independent risk factor for cognitive decline.

Stewart, R et al. Adverse Oral Health and Cognitive Decline: The Health, Aging and Body Composition Study. *J Am Ger Soc.* 2013, February; 61 (2): 177-184

HEARING LOSS AND COGNITIVE DECLINE IN OLDER ADULTS

Some studies have suggested that hearing loss is independently

associated with poorer cognitive function and incident dementia. This study investigated the association of hearing loss with cognitive trajectories and incident cognitive impairment among community based older adults without prevalent cognitive impairment.

The participants were enrolled in the Health ABC study of community dwelling adults ages 70 to 79 years, all without cognitive impairment at baseline. Audiometric testing was conducted in year five, with participants followed for six years. Of those who underwent testing, 2,206 had no evidence of cognitive impairment as assessed with the Modified Mini Mental State Exam (3MS). Those patients were followed with the Digit Symbol Substitution Test (DSS) and the 3MS at years five, eight, 10 and 11.

Individuals with hearing loss demonstrated annual rates of cognitive decline that were 41% greater than those with normal hearing ($p=0.004$). Those with hearing loss had annual rates of decline on the DSS that were 32% greater than those of subjects with normal hearing ($p=0.02$). Rates of cognitive decline and risk of incident cognitive impairment were linearly associated with the severity of the baseline hearing loss.

Conclusion: This study found that hearing loss is associated with accelerated cognitive decline and incident cognitive impairment among community dwelling older adults.

Lin, F., et al. Hearing Loss and Cognitive Decline in Older Adults. *JAMA Intern Med.* 2013, Feb 25; 173(4): 293-299.

ASYMPTOMATIC CAROTID STENOSIS AND RISK OF STROKE

The treatment of asymptomatic carotid stenosis (ACS) remains controversial. This study was

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designed to determine whether ultrasound (US) monitoring of moderate ACS can provide markers to identify those at higher risk for developing vascular events.

This prospective study included patients with carotid stenosis of 50 to 70%. At 12 months, a follow-up US was completed to assess the degree of progression. The increase in stenosis was defined by an increase of at least one category of either greater than 70% stenosis, near occlusion or occlusion. The patients were then followed clinically every three months by telephone. Outcome measures included transient ischemic attack, ischemic stroke, myocardial infarction and death.

Of 523 subjects identified, with a median of nine months for the second ultrasound evaluation, progression of stenosis was detected in 129 subjects (24.7%). Eighty-one subjects had clinical events, including 35 ipsilateral strokes, 22 transient ischemic attacks, eight myocardial infarctions and one death. Of the patients with progression of stenosis, 53.7% experienced a vascular event, with 21% experiencing an ipsilateral stroke. Of those without progression, 96.7% remained free of vascular events.

Conclusion: This study of patients with moderate carotid stenosis found that progression of stenosis, as detected by ultrasound, helps to identify those at risk for vascular events.

Balestrini, S., et al. One-Year Progression of Moderate, Asymptomatic Carotid Stenosis Predicts the Risk of Vascular Events. *Stroke*. 2013, March; 44(3): 792-794.

PREVENTING KNEE OSTEOARTHRITIS

Osteoarthritis (OA) of the knee is a widely prevalent phenomenon with no proven strategy to prevent its progression. Those with OA of one knee are at high risk for OA of the contralateral knee. This study was designed to determine whether those with OA in one knee have concurrent OA in the contralateral knee, and whether reducing the medial load in the affected knee reduces the damaging loading in the contralateral knee.

Longitudinal data were obtained from the Framingham Osteoarthritis

study. That study included weight-bearing anteroposterior knee radiographs obtained from subjects at baseline and, on average, 8.6 years later. From these data, 152 patients with radiographic medial OA were selected. For a second portion of the study, participants with knee pain were recruited for a trial testing of shoe inserts. These individuals underwent gait analysis involving footwear with no insoles, and then with lateral wedge insoles posted just proximal to the fifth metatarsal head at 5°. The primary outcome measure was external knee adduction moment (EKAM) of the ipsilateral and the contralateral knee. EKAM was used as a surrogate measure of medial loading, as higher values have been associated with an increased risk of developing knee OA.

Among the Framingham data, 14.5% had at least one knee with radiographic OA. The mean age of the subjects was 58.7 years. Of these patients, 90% either had, or later developed, medial OA of the contralateral knee. Gait analysis, with wedge use for the affected knees, revealed a significant reduction in EKAM. The contralateral limb also demonstrated significant reductions in early stance EKAM.

Conclusion: This study suggests that individuals with medial joint osteoarthritis of the knee can reduce the medial loading of both the ipsilateral and contralateral knee by using a wedge insole posted by 5°.

Jones, R., et al. A New Approach to Prevention of Knee Osteoarthritis: Reducing Medial Load in the Contralateral Knee. *J Rheum*. 2013, March 1; 40: 309-315.

MUSCLE STRENGTH AND PERFORMANCE IN KNEE OSTEOARTHRITIS

Knee osteoarthritis (OA) is a leading cause of disability and deterioration in quality-of-life among community dwelling elderly individuals. Lifestyle modification, including regular exercise, is a first-line treatment for knee OA. This study compared factors associated with physical performance in a geriatric sample with radiographically severe knee OA.

This study included community dwelling Korean individuals, 65 years of age or older. Data collected from

the 533 participants included standing knee x-rays, anthropometric measures, Western Ontario McMaster University (WOMAC) index scores, isokinetic knee extension strength, data regarding depressive symptoms and physical performance data using the Short Physical Performance Battery (SPPB). Knee OA severity was divided into three groups, including no-or doubtful, minimal-to-moderate and severe. To identify the factors predicting poor physical performance, backward stepwise logistic regressions were performed in each radiographic knee OA severity group.

Physical performance differed significantly among the three knee OA severity groups in those with lower muscle strength, with those demonstrating more severe OA performing more poorly than those with less severe OA. However, in those with higher muscle strength, no significant differences in SPPB scores were found among the three OA severity groups. Among those identified with mild or moderate OA of the knee, variables associated with poor physical performance included muscle strength, knee pain, body mass index and age. Among those with severe OA, only muscle strength was significantly related to function.

Conclusion: This study indicates that patients with severe knee osteoarthritis who have good muscle strength do not show the decrease in physical performance usually seen in severe knee OA.

Chun, S., et al. Muscle Strength is the Main Associated Factor of Physical Performance in Older Adults with Knee Osteoarthritis, Regardless of Radiographic Severity. *Arch Geriatr Geriatr.* 2013; 56(2): 377–382.

CHANGES IN FUNCTIONAL MAGNETIC RESONANCE IMAGING WITH EXERCISE AFTER CONCUSSION

Recent studies have supported the use of standardized exercise testing and controlled aerobic exercise to treat postconcussion syndrome. Among patients with concussion, studies have demonstrated larger functional magnetic resonance imaging (fMRI) activation patterns among symptomatic patients with delayed recovery. This study investigated the

fMRI activation patterns of patients with postconcussion syndrome treated with exercise.

This study included 10 patients with postconcussion syndrome and five control subjects. At baseline, and after 12 weeks, all subjects completed a mathematics processing task during fMRI and performed an exercise treadmill test. Five participants were placed in an exercise group. That group performed progressive aerobic exercise for 20 minutes per day, six days per week. The subjects were considered ready for a second fMRI when they were able to exercise up to the age predicted maximum heart rate without exacerbation of symptoms. A stretch group was provided with low-impact breathing and stretching routines. All underwent an fMRI examination at baseline and after 12 weeks.

At 12 weeks, postconcussion syndrome symptoms significantly improved in the exercise group ($p < 0.0004$), but not in the stretching group ($p < 0.16$). No differences were found among the three groups in average accuracy and reaction times during the mathematics processing task. At 12 weeks, no significant differences were seen between the exercise group and the healthy control group on the fMRI, with less activity in the cerebellum, cingulate gyrus and thalamus in the stretching group compared to the control group.

Conclusion: This small study of patients with postconcussion syndrome found that exercise may help normalize cerebral blood flow distribution in this population.

Leddy, J., et al. Exercise Treatment for Postconcussion Syndrome: A Pilot Study of Changes in Functional Magnetic Resonance Imaging Activation, Physiology and Symptoms. *J Head Trauma Rehab.* 2013 DOI: 10.1097/HTR.0b013e31826da964

IMAGING OF MILD TRAUMATIC BRAIN INJURY

Occult, mild traumatic brain injury (mTBI) damage can be studied with quantitative methods such as diffusion tensor, functional MRI and proton MR spectroscopy. Multi-voxel proton MR spectroscopy imaging (H-MRSI) has improved sensitivity to subtle pathologic changes, as compared to other MR sequences.

This study further investigated whether diffuse axonal imaging is quantifiable by H-MRSI.

Twenty-six patients with closed head mTBI between the ages of 18 and 56 were recruited following emergency room visits. All underwent H-MRSI, with N-acetylaspartate (NAA), choline (CHO), creatine (CR) and myo-inositol (ml) concentrations and gray-matter/white-matter (GM/WM) and cerebrospinal fluid fractions obtained in each voxel. Statistical analysis was used to compare the mean of each metabolite between patients and controls.

Compared with controls, H-MRSI demonstrated a lower concentration of NAA in white matter, indicating neuronal damage. This difference was present diffusely in the brain areas imaged. Positive correlations were found between the duration after mTBI and increased concentrations of CHO and CR, suggesting a possible progression of axonal dysfunction with time, consistent with wallerian degeneration. No between group differences were found in metabolites measured within the gray matter or related to glial white matter, suggesting a lack of neural cell body damage and the absence of glial hypertrophy or proliferation.

Conclusion: This study of patients with mild traumatic brain injury demonstrates that H-MRSI may be useful in identifying changes consistent with diffuse axonal injury.

Kirov, I., et al. Diffuse Axonal Injury in Mild Traumatic Brain Injury: A 3-D, Multi-Voxel, Proton MR Spectroscopy Study. *J Neuro.* 2013, January (1);260: 242–252.

AQUATIC EXERCISES FOR LOW BACK PAIN

Among the treatment options for low back pain (LBP), exercise seems to have broad applications in its effectiveness. This study reviewed the literature concerning aquatic therapy for LBP.

This literature review included randomized, controlled studies of aquatic exercise as a treatment for LBP, with outcome measures including pain or disability. Of the 541,000 articles reviewed, three studies fitting the inclusion criteria were selected. The main outcome

measure was the visual analogue scale (VAS) for pain.

The studies reviewed included aquatic or land based therapy 3-5 times per week for four to seven weeks. The land based therapies included both supervised and home based programs. The improvement in VAS at the end of treatment was significant and equivalent between the two therapies, in two of the three studies and superior in the aquatic treatment group in one study. One study with a one year follow up found better VAS scores in the land based group.

Conclusion: This study of patients with low back pain found that aquatic therapy is an effective treatment, although not more effective than land based therapy.

Olson, D., et al. Aquatic Exercise for Treatment of Low Back Pain: A Systematic Review of Randomized, Controlled Trials. **Am J Lifestyle Med.** 2013, March/April;7(2): 154-160.

ANTIHYPERTENSIVE MEDICATIONS AND COGNITIVE FUNCTION

Hypertension is associated with cognitive impairment, especially in the executive domain. Recent evidence has suggested that the renin angiotensin system is involved in the regulation and maintenance of cerebral blood flow. Some have hypothesized that angiotensin converting enzyme (ACE) inhibitors have greater positive effects on cerebral hemodynamics, and, therefore, on executive function, than do other antihypertensive treatments. This study compared the effects of this class of antihypertensive medication with angiotensin receptor blockers, which block only type I receptors.

This 12-month, double-blind, randomized, controlled trial included patients sixty years of age or older, all diagnosed with hypertension, and all exhibiting executive dysfunction. The patients were randomized to receive one of three study medications, including lisinopril up to 40 mg, candesartan up to 32 mg or hydrochlorothiazide up to 25 mg. Medications were titrated to achieve systolic blood pressure of under 140 mg Hg and diastolic blood pressure of under 90 mg Hg. Cerebral

hemodynamics including cerebral blood flow velocity (BFV) and cerebrovascular reserve as measured by reactivity to carbon dioxide (CO₂) were assessed. The subjects were followed for 12 months, with tests including the Trail Making Test, The Hopkins Verbal Learning Test (HVLT) and a digit span task.

Forty-seven participants completed six-month evaluations, and 31 completed 12-month evaluations. Blood pressure parameters were equivalent among treatment groups. After adjusting for age and baseline Mini Mental Status Examination results, those randomized to receive candesartan demonstrated the greatest improvement on the Trail Making Test ($p=0.008$), as well as improved performance on the recognition portion of the HVLT. Vasoreactivity to CO₂ declined in both the lisinopril and hydrochlorothiazide groups, but not in the candesartan group.

Conclusion: This study of elderly hypertensive patients found that treatment with an angiotensin receptor blocker preserves cerebral hemodynamics and improves executive function to a greater extent than does angiotensin converting enzyme inhibitors or hydrochlorothiazide.

Hajjar, I., et al. Antihypertensive Therapy and Cerebral Hemodynamics in Executive Mild Cognitive Impairment: Results of a Pilot, Randomized, Clinical Trial. **J Am Geriatr Soc.** 2013, February; 61: 194-201.

CARDIOVASCULAR DISEASE PREVENTION WITH THE MEDITERRANEAN DIET

A recent systematic review ranked the Mediterranean diet as the most likely dietary model to provide protection against coronary heart disease. This randomized trial tested the efficacy of two Mediterranean diets in primary cardiovascular prevention.

This parallel group, multicenter, randomized trial included individuals 55 to 80 years of age with no cardiovascular disease at the time of enrollment. All participants had either type II diabetes or at least three other major risk factors for cardiovascular disease. Beginning in October of 2003, the participants were

randomized to one of three dietary interventions, a Mediterranean diet supplemented with extra virgin olive oil (approximately 1 L per week), a Mediterranean diet supplemented with nuts (30 grams of mixed nuts per day) or a control diet. No total calorie restriction was advised, nor was physical activity promoted. The primary endpoint was a composite of myocardial infarction, stroke and death from cardiovascular causes.

During the study, 7,447 subjects were randomized to one of the three study groups. The participants were followed for a median of 4.8 years. A total of 288 primary outcome events occurred, including 3.8% in the extra-virgin olive oil group, 3.4% in the extra nuts group and 4.4% in the control group. Compared to the control diet, both Mediterranean diets demonstrated significant improvement in the primary endpoint ($p=0.015$). Of the components of the primary endpoint, only the comparisons of stroke reached statistical significance ($p=0.003$).

Conclusion: This study of individuals at high risk for cardiovascular disease found that an energy unrestricted Mediterranean diet, supplemented with either virgin olive oil or nuts, resulted in a relative risk reduction of approximately 30%.

Estruch, R., et al. Primary Prevention of Cardiovascular Disease with a Mediterranean Diet. **N Eng J Med.** 2013, Feb 25. DOI: 10.1056/NEJMoa1200303

PROGNOSTIC FACTORS FOR PATELLOFEMORAL PAIN

Patellofemoral pain (PFP) is aggravated by activities that load the patellofemoral joint, and can affect participation in daily work and exercise. This study was designed to determine predictors of prognosis among those with PFP.

Prospective data were derived from two, randomized, clinical trials investigating the effectiveness of conservative interventions for PFP. Potential prognostic factors were selected from the baseline data, and included age, gender, body mass index, work type, sports participation, knee pain duration, laterality and baseline scores of pain and function.

An unfavorable outcome was reported by 55% at three months and by 40% at 12 months. A multivariate

model for worst or activity related severity at three months revealed that longer PFP duration, greater baseline severity of worst or activity related pain, and lower baseline anterior knee scale (AKP) scores were associated with greater pain severity. Baseline PFP duration of longer than two months was associated with unfavorable recovery at 12 months. Unfavorable recovery at 12 months was associated with a baseline PFP duration of longer than two months, an AKP Scale score of less than 70/100 and a pain severity of greater than 35/100 (usual/resting) and greater than 60/100 (worst/activity-related).

Conclusion: This study found that patellofemoral pain of greater than two months' duration at baseline, and anterior knee pain scale scores of less than 70, are consistent prognostic factors for pain persisting at one year.

Collins, N., et al. Prognostic Factors for Patellofemoral Pain: A Multicenter, Observational Analysis. *Br J Sport Med.* 2013, March; 47(4): 227 -233.

MYOTENDINOUS LENGTHENING FOR ELBOW SPASTICITY FOLLOWING BRAIN INJURY

Among patients with abnormal patterns of muscle activation, antagonist muscles can be fractionally lengthened at the myotendinous junction to increase the functional arc of motion. This study was designed to investigate a new surgical technique for patients with volitional motor control and spastic elbow flexion deformities after brain injury.

This retrospective review included patients seen between 2004 and 2009 with upper motor neuron disease and volitional muscle control who had undergone myotendinous lengthening of the elbow flexor muscles. Active ROM began on the first postoperative day, with resistance exercises allowed at three weeks post-surgery. The patients were assessed with the modified Ashworth scale, as well as active and passive range of motion evaluation.

Forty-two patients, including 26 men and 16 women with an average age of 51 years, were followed for an average of 14 months. The total passive arc of motion improved from 103° preoperatively to 131°,

postoperatively ($p<0.01$). The total active arc of motion improved from a mean of 77° preoperatively to a mean of 113° postoperatively ($p<0.001$). The mean modified Ashworth scale spasticity score improved from 2.7 preoperatively to 1.9 postoperatively ($p<0.001$).

Conclusion: This study of patients with spasticity due to upper motor neuron disease found that myotendinous lengthening of the elbow flexors improves the arc of motion and also improves modified Ashworth scale scores.

Anakwenze, O., et al. Myotendinous Lengthening of the Elbow Flexor Muscles to Improve Active Motion in Patients with Elbow Spasticity following Brain Injury. *J Shoulder Elbow Surg.* 2013, March; 22(3): 318 -322.

DECLINE IN ISCHEMIC STROKE MORTALITY AND CHANGES IN INCIDENCE

In Western Europe, mortality from stroke has declined over several decades. However, it remains unknown whether these mortality trends reflect favorable changes in risk factors, versus improvement in acute treatment and secondary prevention. This study was designed to better understand this trend.

A cohort of incident hospitalized ischemic stroke (IS) patients was reviewed for the period of 1997 to 2005. Data from the national hospital discharge registry, the Dutch population registry and the national cause of death register were linked. Those with a previous admission for IS were excluded. Thirty-day fatality and one-year mortality (mortality between 31 and 365 days) were both computed by age and gender.

The IS mortality rate declined continuously between 1980 and 2000, with an acceleration in this decline thereafter. Mortality per 100,000 declined between 1997 and 2005. In addition, in all age and gender groups, the 30-day case fatality rate declined between 1997 and 2005. In contrast to the decline in IS mortality, the IS incidence remained stable over time, or slightly increased.

Conclusion: This Dutch study demonstrates that, despite a significant decline in mortality from ischemic stroke, the number of

incident, nonfatal, ischemic stroke events has not changed.

Vaartjes, I., et al. Remarkable Decline in Ischemic Stroke Mortality is Not Matched by Changes in Incidence. *Stroke.* 2013, March; 44(3): 591-597,

ROPINIROLE FOR RESTLESS LEG SYNDROME

Restless leg syndrome (RLS) is a chronic, sensorimotor neurologic disorder characterized by leg discomfort, with nocturnal aggravation, sleep disturbance and somatic symptoms. Non-ergot derived dopamine agonists, such as ropinirole, are first-line drugs for treating RLS. This study further investigated the effect of ropinirole on the quality-of-life (QoL) of patients with RLS.

This multicenter, Korean study enrolled 107, consecutive, primary RLS patients over the age of 18. All subjects received ropinirole two hours before bedtime, with the dose titrated over four weeks from an initial dose of 0.25 mg. The participants were then maintained at their optimal doses for an additional four weeks. Quality-of-life was evaluated using the Korean version of the RLS QoL (K-RLS QoL) questionnaire and the Short Form-36 health survey (SF-36).

The QoL of patients significantly improved as measured by K-RLS QoL ($p<0.001$) and the total SF-36 scores ($p=0.004$). Individual domains of the SF-36 found significant improvement in bodily pain, general health, vitality, physical domains and mental domains. The average daily dose of ropinirole after eight weeks was 0.62 mg.

Conclusion: This Korean study of patients with restless leg syndrome found that ropinirole, at an average dose of 0.62 mg per day, can significantly improve quality of life.

Cho, Y., et al. Effect of Ropinirole on the Quality of Life in Patients with Restless Leg Syndrome in Korea: An Eight Week, Multicenter, Prospective Study. *J Clinical Neurol.* 2013, January; 9(1): 51-56.

EFFECT OF RESIDUAL LIMB LENGTH ON GAIT ANALYSIS

Previous studies have suggested that more proximal amputations may

lead to greater gait asymmetries. This study compared residual transfemoral amputation length and orientation to functional gait parameters.

Twenty-six military personnel with acute, trauma related transfemoral amputations, all between the ages of 18 and 32 years, were recruited for participation in this study. Each subject underwent gait analysis more than 24 months postoperatively while wearing the currently preferred prosthesis. The participants were separated into groups for analysis based upon either the femoral angle or the residual limb length. For residual femoral length analysis, the subjects were separated into two groups based upon residual limb length relative to intact limb length.

A significant, direct relationship ($p=0.004$) was observed between walking speed and residual limb ratio, indicating that patients with longer residual limbs walked at a faster self-selected pace than did those with shorter residual limbs. A good correlation was observed between residual femoral length forward lean ($r=-0.683$), lateral flexion ($r=-0.628$), pelvic tilt ($r=-0.691$), and obliquity ($r=-0.398$). Subjects with shorter residual limbs experienced a greater excursion in the torso and pelvis, while walking at a slower self-selected pace.

Conclusion: This study of soldiers with traumatic amputation found that the residual femur length significantly influences gait outcomes, with length found to be the most important variable.

Bell, J., et al. Transfemoral Amputations: The Effect of Residual Limb Length and Orientation on Gait Analysis Outcome Measures. *J Bone Joint Surg.* 2013, March 6; 95(5): 408-414.

FESOTERODINE FOR OVERACTIVE BLADDER

The prevalence of overactive bladder (OAB) increases with age. While antimuscarinic drugs are a first-line pharmacologic treatment, few placebo-controlled studies have evaluated the efficacy of these medications in the elderly population.

This multi-center study of fesoterodine in an aging population (SOFIA) trial recruited men and women, 65 years of age or older, all with OAB symptoms of at least three

months' duration. The patients were randomized to once daily treatment with fesoterodine or placebo. The study medication was begun at 4 mg, with patients allowed an increase to 8 mg at weeks four and eight. The subjects completed a three-day bladder diary, the OAB questionnaire, the Patient Perception of Bladder Condition (PPBC) questionnaire and the Urgency Perceptions Scale (UPS) at baseline and at weeks four, eight and 12.

Seven hundred ninety-four patients were randomized, with 392 to the study group and 393 to the placebo group. Seventy-eight (20%) participants in the fesoterodine group and 52 (13%) in the placebo group discontinued the study. At week 12, greater improvement was noted in the treatment group in episodes of urgency ($p<0.001$), micturitions ($p<0.001$), nocturnal micturition ($p=0.003$), severe urgency episodes ($p<0.001$) and incontinence pad use ($p=0.01$). The most frequently reported adverse events in the study group were dry mouth and constipation.

Conclusion: This study of elderly patients with overactive bladder found that the antimuscarinic medication fesoterodine improves urgency episodes, micturition frequency and patient reported outcomes.

Wagg, A., et al. Flexible-Dose Fesoterodine in Elderly Adults with Overactive Bladder: Results of a Randomized, Double-Blind, Placebo-Controlled Study of Fesoterodine in an Aging Population Trial. *J Am Geriatr Soc.* 2013, February; 61(2): 185-193.

FREEZING OF GATE AND GAIT ASYMMETRY IN PARKINSONIAN PATIENTS

Gait disturbances in patients with Parkinson's disease (PD) can affect quality-of-life, mobility and safety. The etiology of freezing of gate (FOG) in PD is poorly understood, but is hypothesized to be related to gait asymmetry (GA). This study evaluated the relationship between GA and FOG in patients with PD.

This cohort study involved 60 patients with idiopathic PA, including 30 with FOG (FOG+) and 30 without FOG (FOG-). All subjects underwent the same four-week rehabilitation program using a treadmill with visual

and auditory cues. Outcome measures included gait speed, stride length, time on each foot, a six-minute walk test, the Unified Parkinson's Disease Rating Scale (UPDRS), the Berg Balance Scale (BBS), the timed up and go test, comfortable-fast gait speeds and a FOG questionnaire (FOGQ).

After treatment, an analysis of variance demonstrated improvement in all variables in both groups, showing a time effect, at a level of significance of $p < 0.0001$ for all variables, except gait speed ($p = 0.007$) and gait asymmetry ($p = 0.0002$). Following treadmill training, greater improvements were noted on the FOG+ for scores on the UPDRS and the BBS.

Conclusion: This study of patients with Parkinson's disease found that treadmill based gait training is effective in improving asymmetry of gait and balance, as well as in improving freezing of gait.

Fraxitta, G., et al. Asymmetry and Freezing of Gate in Parkinsonian Patients. *J Neurol.* 2013, January; 260(1): 71-76.

LEUKOARAIOSIS AND OUTCOME AFTER SPONTANEOUS INTRACEREBRAL HEMORRHAGE

Intracerebral hemorrhage (ICH) results in a high risk of disability and death, with only 20% of patients functionally independent after six months. Leukoaraiosis (LA) produces neuroimaging findings of white matter changes thought to result from ischemic injury and demyelination. Whereas LA is related to poorer outcomes in ischemic strokes, its impact on ICH is uncertain.

This prospective study included patients hospitalized with nontraumatic ICH. Data collected included demographics, medical history, clinical data, including National Institute of Health Stroke Scale (NIHSS) Scores, and ICH scores. MRI scans were reviewed and graded for severity of LA, and recorded as Fazeka scores. The NIHSS score was recorded at 14 days and a modified Rankin scale (mRS) score was recorded at 14, 28 and 90 days.

No significant association was seen between Fazeka scores and acute infarction on MRI. Total Fazeka score (periventricular (PV) plus deep

white matter (DWM)) was significantly related to mRS scores at 14 days and at 90 days ($p=0.02$ for both comparisons), driven by the PV score. The Fazeka PV score was significantly related to the NIHSS score at 14 days ($p=0.03$) and to the mRS score at 14 ($p<0.001$), 28 ($p=0.004$) and 90($p=0.005$) days.

Conclusion: This study found that increased leukoariosis is an independent predictor of worse functional outcomes after spontaneous intracerebral hemorrhage.

Caprio, F., et al. Leukoariosis on Magnetic Resonance Imaging Correlates with Worse Outcomes after Spontaneous Intracerebral Hemorrhage. *Stroke*. 2013, March; 44(3): 642–646.

LIDOCAINE INFUSION WITH WOUND VACUUM ASSISTED CLOSURE REMOVAL

Wound vacuum assisted closure (VAC) is a common modality for treating acute and chronic wounds. As the removal of the polyurethane foam from the wound bed is often reported to be painful, techniques for reducing this pain could reduce the morbidity of the procedure. This study evaluated the effect of lidocaine injection in decreasing the pain of this procedure.

This randomized, double-blind, placebo-controlled trial included patients treated with wound VAC between 2008 and 2009. All participants were 18 years of age or older and underwent at least two wound VAC replacements during a hospital admission. Using a double blind design, at twenty minutes before VAC sponge removal, either lidocaine 1%, or saline was injected through the VAC suction tube and into the sponge. Pain scores were obtained 20 minutes before, during the VAC change and at five, 10 and 20 minutes after the procedure. Narcotics use was recorded as a secondary outcome measure.

The patients in the lidocaine group experienced 2.4 points less pain on a 10-point VAS during the VAC sponge removal than did those in the saline group ($p<0.001$). In addition, pain scores were significantly lower at all time points after VAC removal among patients treated with lidocaine. The lidocaine

group used significantly less narcotic medication ($p<0.001$) than did the saline group.

Conclusion: This study of patients with wound VAC use found that injecting lidocaine into the sponge prior to removal significantly reduces the pain of the procedure.

Christiansen, T., et al. Lidocaine Analgesia for Removal of Wound Vacuum Assisted Closure Dressings: A Randomized, Double-Blind Placebo-Controlled Trial. *J Orthop Trauma*. 2013, February; 27(2): 107-112.

NOVEL LOW MOLECULAR WEIGHT COMPOUND FOR FRACTURE REPAIR

The clinical use of recombinant human bone morphogenic proteins (rhBMP-2) to enhance bone healing has been limited by cost and side effects. The low molecular weight synthetic compound, SVAK-12, has been found to potentiate rhBMP-2 induced transdifferentiation of pluripotent myoblasts into the osteoblastic phenotype. This study investigated whether a single injection of this compound enhances healing in a rodent fracture model.

In this two-part study, SVAK-12 was tested in a standard chest ectopic bone formation model. RhBMP-2, with or without SVAK-12, was loaded onto a type I collagen disc, with SVAK-12 injected at a range of doses. At four weeks, the amount of bone in each implant was assessed. In the second study, a closed femoral fracture model with intramedullary fixation was used. Twenty-four hours after the creation of the fracture, the animals were randomized to receive a placebo or SVAK-12 at 250 μg . At five weeks post-surgery, the fracture sites were investigated for gap size, bone in the gap and mineralized callus, as well as by biomechanical and histologic analysis.

In the first study, a dose dependent increase was seen in the rhBMP-2 induced bone formation, with histologic analysis verifying characteristics of normal bone. In the fracture study, the radiographic healing scores were significantly better in the treatment group ($p=0.028$.) Biomechanical testing revealed that the mean torsional strength and stiffness of the treatment group was significantly better than

that of the control group at five weeks. The relative torsional stiffness of the treated group was more than twice that seen in the control group.

Conclusion: This animal study found that a new low molecular weight molecule, SVAK-12, can accelerate bone formation and improve the quality of bone-healing. The authors suggest that this treatment is cost-effective and can potentially be used in a clinical setting to enhance rhBMP-2 efficacy.

Wong, E., et al. A Novel Low Molecular Weight Compound Enhances Ectopic Bone Formation and Fracture Repair. *J Bone Joint Surg*. 2013, March 6; 95(5): 454-461.

FRONTAL GRAY MATTER CHANGES AFTER CANCER CHEMOTHERAPY

Cognitive changes related to breast cancer and its treatments have been reported to most prominently involve executive functions. The neural mechanisms underlying these changes have been the subject of numerous investigations. This study evaluated possible risk factors for gray matter changes after chemotherapy.

Participants included female breast cancer patients treated with ($n=27$) and without ($n=28$) systemic chemotherapy, as well as healthy controls ($n=24$). Study measures were completed at baseline, before radiation, chemotherapy or anti-estrogen treatment, and approximately one month after completion of therapy. The patients were assessed for self-reported executive function using the Behavior Rating Inventory of Executive Function – Adult Version (BRIEF – A). In addition each subject was assessed for APOE genotype, and with MRI, using a T1 weighted, three-dimensional, magnetized, prepared rapid gradient echo (MPRAGE). Changes in MRI after chemotherapy were compared with those of the control groups.

At one month after therapy completion (M1), relative to baseline, the chemotherapy group demonstrated decreased gray matter density in the left middle and superior frontal gyri. This correlated with BRIEF-A scores demonstrating that the chemotherapy patients experienced more perceived

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symptoms concerning the ability to initiate problem-solving or activity, with a similar trend seen on the Working Memory Scale. No similar gray matter changes were seen in the group without chemotherapy or the controls. Gray matter and executive symptom changes were not related to APOE status.

Conclusion: This study demonstrates that breast cancer chemotherapy is associated with frontal gray matter changes and related changes in perceived cognitive function, which are not found in patients treated with antiestrogen therapies.

McDonald, B., et al. Frontal Gray Matter Reduction after Breast Cancer Chemotherapy and Association with Executive Symptoms: A Replication and Extension Study. **Brain, Behavior and Immunity**. 2013, March 15; 30: S117–S125.

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