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DEXTROMETHORPHAN/QUINIDINE FOR PSEUDOBULBAR AFFECT

Pseudobulbar affect (PBA) is a type of affect lability, thought to occur as a result of injury or diseases that disrupt pathways regulating emotional expression. Dextromethorphan hydrobromide and quinidine sulfate in a fixed combination (NUEDEXTA) is currently the only pharmaceutical agent approved for the treatment of PBA. This study reports on the effectiveness of NUEDEXTA for the treatment PBA.

Adults with a diagnosis of PBA secondary to dementia, stroke, or traumatic brain injury (TBI) and a Center for Neurologic Study-Lability Scale (CNS-LS) score ≥13 were enrolled in this open label, 90-day study. The participants received NUEDEXTA at 20/10 mg twice daily. Clinical assessments were performed at baseline and days 30 and 90 with telephone contact at day 60. The primary outcome was the change in the CNS–LS from baseline to day 90. Secondary measures included PBA episode count for seven days preceding each study visit, as well as the Clinical Global Impression of Change, and Patient Global Impression of Change.

The final analysis included 367 participants diagnosed with PBA of whom 134 had dementia, 113 had a stroke and 120 had a TBI. Compared with baseline scores, CNS-LS scores at day 30 and day 90 significantly improved ($p<0.001$ for both comparisons). The PBA episode counts for seven days prior to study visits decreased from a median of 12 at baseline to four at day 30 and two at day 90. The Clinical Global Impression of Change and Patient Global Impression of Change of PBA symptoms were “much”, or “very much” improved in 76.6% and 72.5% respectively. The most frequent adverse events were diarrhea in 5.4%, and headache in 4.1%.

Conclusion: This study of patients with pseudobulbar affect found that dextromethorphan hydrobromide and quinidine sulfate in a fixed combination may be an effective and well tolerated treatment.

Hammond, F et al. PRISM II: An Open Label Study to Assess Effectiveness of Dextromethorphan/ Quinidine for Pseudobulbar Affect in Patients with Dementia, Stroke or Traumatic Brain Injury. **BMC Neurol.** 2016; 16:89.

BLOOD FLOW RESTRICTED EXERCISE

In order to enhance muscle mass and strength, resistance exercises, with loads of 70-80% of a one repetition maximum (one rep max) are typically recommended. Such resistance exercises are often challenging and may be contradicted in certain patients, including the elderly and recovering athletes. Several studies in recent years have suggested that lower weights may be effective when combined with restricted blood flow, also known as Kaatsu training. This literature review and meta-analysis reviewed studies combining blood flow restriction exercise, in an effort to clarify the effectiveness of this technique and to understand which training method results in the greatest muscle strength and hypertrophy.

Medical databases were searched for articles investigating the effects of exercise combined with restricted blood flow to skeletal muscle on muscle hypertrophy and muscle strength. Among those reviewed, 47 were included in the meta-analysis. A total of 400 subjects from 19 studies focused on muscle strengthening.

Those studies that reviewed the effects of aerobic exercise combined with blood flow restriction reported a mean strength improvement of 0.4 N m greater than the control ($p=0.04$). Those studies focusing on resistance exercise for strengthening found a mean improvement of 0.3 kg greater than the controls ($p<0.01$). Of the 19 studies focusing on muscle hypertrophy, those in the blood flow restriction group had an increase in hypertrophy 0.4 cm greater than that of the control group ($p<0.001$). Training programs at >20% one rep max performed better than those at less than 20%, while cuff systolic blood pressure at >150 mmHg resulted in greater strength gains than pressures below 150 mm Hg.

Conclusion: This study found that the addition of blood flow restriction to dynamic exercise training can be effective for increasing the effects on strength and hypertrophy.

Slysz, J., et al. Efficacy of Blood Flow Restricted Exercise: Systematic Review and Meta-Analysis. **J Sci Med Sport**. 2016, August; 19(8): 669 -675.

OVERWEIGHT HIP FRACTURE PATIENT SURVIVAL

Previous studies have suggested that up to half of patients suffering from a hip fracture are malnourished upon hospital admission. Some have found an association between increased in-hospital mortality rate and low body mass index (BMI). This study evaluated the association between BMI and one-year survival in relatively healthy, elderly hip fracture patients.

Consecutive patients with a hip fracture admitted to one of four university hospitals in Stockholm were assessed for inclusion. Eligible patients were >65 years of age, living independently, with no diagnosis of dementia or severe cognitive impairment. Each patient’s physical status was assessed before surgery, with cognitive function evaluated using the SPMSQ. Living conditions

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both before the hip fracture and one year postoperatively were recorded. A BMI was calculated for each patient and compared with one-year outcome. A BMI of less than 22 kg/m^2 was used as the cutoff for underweight and risk of malnutrition.

Of the 843 patients included in the study, the one-year mortality rate was 16% in patients with a BMI of less than 22 kg/m^2, 18% among those with a BMI of 22-26 kg/m^2 and 6% among those a BMI of >26 kg/m^2. The unadjusted odds ratio for one-year survival in patients with a BMI of > 26 kg/m^2 was 2.7, compared to the group with a BMI of < 22 kg/m^2, and 3.1 compared to the group with a BMI of 22–26 kg/m^2.

Conclusion: This prospective study of patients with acute hip fracture found that survival was superior among patients with a body mass index above 26 kg/m^2, as compared with those with a lesser body mass index.

Flodin, L., et al. Increased One-Year Survival and Discharge to Independent Living in Overweight Hip Fracture Patients: **Acta Orthop.** 2016, April; 87(2): 146-151.

BALANCE TRAINING WITH MUSCLE STRENGTHENING IN OLDER ADULTS

Falls are the number one cause of injury, fractures and death among the older population. Although the cause of falls is often multifactorial, lower extremity weakness and decreased balance are two significant factors. This study evaluated the effect of a balance training program, including calf muscle strengthening, on balance and the fear of falling, and explored how well calf muscle strength correlates with other fall risk factors.

Subjects were sixty years of age or older, recruited from a senior center in Philadelphia. All were independent with community mobility, with or without an assistive device. At baseline, all participants were assessed with measures of static and dynamic balance, calf muscle strength, functional lower extremity strength and endurance, functional mobility, and fear of falling. Each subject underwent a five-week, 10-session program of 30 minutes per session, using exercises that challenged static balance, dynamic balance, and strengthening exercises. Complexity and speed of balance exercises were steadily increased over the course of 10 sessions. Strengthening included three sets of heel raises, with 15 reps per set.

Subjects were 28 adults with an average age of 70 years. At follow-up, static balance with eyes closed, heel rise and results on the Timed Up and Go Test (TUG) and the 30-Second Chair Stand Test improved significantly. Heel rise ability was significantly related to the results of the TUG and the 30-Second Chair Stand Test. None of the participants who were able to perform 10 reps or more of heel rises were at a high risk of falls based on their TUG results.

Conclusion: This study of elderly individuals found that balance training including calf muscle strengthening performed for 30 minutes, twice a week for five weeks, resulted in significant improvement in calf muscle strength, functional performance and balance, as well as improvement in balance confidence.

Maritz, C., et al. A Prospective, Cohort Study on the Effect of a Balance Training Program, Including Calf Muscle Strength, In Community-Dwelling Older Adults. **J Geriatr Phys Ther**. 2016, July/September; 39 (3): 125-131.

PREDICTORS OF FAILURE OF CONSERVATIVE TREATMENT OF FULL-THICKNESS ROTATOR CUFF TEARS

Rotator cuff tears are prevalent, affecting an estimated 10% of persons over the age of 60 years in the United States. Nonoperative treatment is effective for many patients, with surgical repair failure rates estimated at 25 to 90%. This study was designed to identify predictors of surgery among patients with these injuries.

This prospective, multicenter, cohort study included patients with full-thickness rotator cuff tears. The participants engaged in a physical therapy program developed from a systematic review of the literature, and returned for evaluations at six and 12 weeks. Those who were cured or improved were scheduled for reassessment in six weeks. Those who were no better were offered surgery. The subjects were contacted by telephone at one and

two years to determine whether they had undergone surgery since their last visit.

Of the 433 patients seen, 20% elected to undergo surgery. Using a multivariate adjusted model, patients' expectations regarding the effectiveness of rehabilitation (p<0.0001) was found to be the most significant predictor of failure of rehabilitation and ultimate surgical intervention. Those with higher activity levels and nonsmoking patients were also more likely to undergo surgery. Structural factors, including size of tear, pain scale scores, and weakness were not predictors of choosing surgery.

Conclusion: This study of patients with full-thickness rotator cuff tears found that the patient's decision to undergo surgery was influenced more by low patient expectations regarding the effectiveness of physical/occupational therapy than by the patient's symptoms or anatomic features of the rotator cuff injury.

Dunn, W., et al. Predictors of Failure of Nonoperative Treatment of Chronic, Symptomatic, Full-Thickness Rotator Cuff Tears. **J Shoulder Elb Surg.** 2016, August; 25(8): 1303-1311.

SINGLE INJECTION OF HYALURONIC ACID VERSUS CORTICOSTEROID FOR KNEE OSTEOARTHRITIS

Treatment options for patients with osteoarthritis (OA) of the knee include injections with intra-articular hyaluronic acid or corticosteroids. As both have been found to be effective treatment options, this study was designed to clarify the difference between these two for relieving pain and improving function.

This double-blind, randomized, controlled study included 110 patients with symptomatic knee OA. The subjects were randomized to receive an injection with either Hylan G-F20 or triamcinolone acetonide. The primary outcome variables were knee pain, functional improvement and knee range of motion at six-month follow-up.

At six months, both groups demonstrated significant improvement in visual analogue scale pain scores (p<0.001), modified WOMAC scores (p<0.001) and knee flexion (p<0.001). Pain was significantly more improved at 24, 48 and 72 hours, as well as one week after the injections, in the triamcinolone group as compared with the Hylan G-F20 group. WOMAC scores were similar between groups at all points except at two weeks, when the triamcinolone group obtained better scores.

Conclusion: This randomized, controlled trial of patients with knee osteoarthritis found that a single triamcinolone acetonide injection provides similar improvement in knee pain, function and range of motion at six months as does Hylan G-F20, with slight superiority of triamcinolone acetonide in the first two weeks.

Tammachote, N., et al. Intra-Articular, Single Shot Hylan G-F20 Hyaluronic Acid Injection Compared with Corticosteroid in Knee Osteoarthritis. A Double-Blind, Randomized, Controlled Trial. **J Bone Joint Surg.** 2016, June; 98 (11): 885-892.

RISK OF FRACTURES AMONG USERS OF ALENDRONATE

Clinical management of osteoporosis has progressed with the introduction of antiresorptive drugs that reduce the risk of fractures in adults. However, some have expressed concern that these drugs may lead to atypical femur fractures, which could offset the benefits of long-term use. This study reviewed the association between long-term use of alendronate and the risk of subtrochanteric and femoral shaft fractures.

Data were derived from a nationwide population-based open registry cohort study containing two nested case-controlled studies. The sample included treatment naive incident users of alendronate from 1996 to 2007 in Denmark who were ages 50 to 94 years at onset of treatment. Those who sustained a hip fracture during the study period were matched to controls. In addition, those who experienced a subtrochanteric/shaft fracture were identified as cases in a second database, also matched to controls. Exposure to alendronate was determined by pharmacy dispensations and used to determine the association between long-term use of alendronate and the risk of subtrochanteric and femoral shaft fractures.

Subjects were 61,990 alendronate users followed for a median of 6.9 years. During that time, 1,428 sustained a subtrochanteric or femoral shaft fracture while 6,784 sustained a hip fracture. Conditional logistic regression analysis demonstrated a reduced risk of subtrochanteric and femoral shaft fractures among those who were highly adherent to alendronate use, as compared to those who were poorly adherent (p=0.05), although this finding changed when adjusted for comorbid conditions (p=0.11). Higher adherence was associated with a decreased risk of hip fracture as was a cumulative use of five to 10 dose-years (p<0.001) and 10 or more dose-years.

Conclusion: This study of patients treated with alendronate for up to 10 years found a 30% lower risk of hip fracture and no increase in the risk of fractures of the subtrochanteric femur and femoral shaft with the use of this drug.

Abrahamsen, B., et al. Risk of Hip, Subtrochanteric and Femoral Shaft Fractures among Mid- and Long-Term Users of Alendronate: Nationwide Cohort Nested Case-Control Study. **BMJ.** 2016;353:i3365.

LONG-TERM RENAL FUNCTION AFTER SPINAL CORD INJURY

Patients with spinal cord injury (SCI) are at increased risk of renal deterioration and urinary tract complications. This study described the extent of renal deterioration in patients with SCI over a 45-year follow-up period.

Medical records were reviewed of all patients admitted to the Spinal Cord Clinic of the Rigshospitalet, Hornbæk, Denmark, with a traumatic SCI sustained during 1944 to 1975. Most patients attended follow-up examinations with assessment of renal function every other year. Until the 1980s, exams included plasma creatinine and x-ray of the abdomen. From the 1980s, CT scan and renography were routine. The primary outcome variable of the study was renal deterioration, based upon results of renography and gender adjusted relative GFR.

At year 45, the cumulative risk of moderate renal deterioration was 58%, while that of severe renal deterioration was 29%. The

probabilities of moderate deterioration after 20, 30 and 40 years were 14.5%, 30% and 47.5%, respectively. The probabilities of severe renal deterioration at 20, 30 and 40 years were 3.4%, 13.6% and 21.1%, respectively. A history of renal/ureter stones requiring removal was significantly associated with a decreased GFR.

Conclusion: This study of 116 patients with spinal cord injury found that the cumulative risk of severe renal deterioration was 29% after 45 years.

Elmrlund, M., et al. Forty-Five Year Follow-Up on the Renal Function after Spinal Cord Injury. **Spinal Cord.** 2016, June; 54(6): 445-451.

LOW-DOSE VERSUS STANDARD DOSE IV ALTEPLASE IN ACUTE ISCHEMIC STROKE

Thrombolytic therapy with intravenous (IV) alteplase at a dose of 0.9 mg/kg of body weight has been found to be an effective intervention for acute ischemic stroke. The Enhanced Control of Hypertension and Thrombolyzed Stroke study (ENCHANTED) compared low-dose with standard dose IV alteplase in patients with acute ischemic stroke.

Subjects were recruited from 111 clinical centers in 13 countries, all 18 years of age or older with a history of acute ischemic stroke. After demonstrating eligibility for treatment, the subjects were randomized to receive a standard dose of IV alteplase 0.9 mg/kg, or a very low dose at 0.6 mg/kg, initiated within 4.5 hours of symptom onset. The primary outcome measure was the combination of death or disability at 90 days, defined by scores of two to six on the modified Rankin scale.

A total of 3,310 patients underwent randomization, with 1,654 patients assigned to the low-dose and 1,643 to the standard-dose group. In the modified intention to treat analysis, the primary outcome occurred in 53.2% in the low-dose group and 51.1% in the standard dose group (p=0.51). Major symptomatic intracerebral hemorrhage occurred in 1% of the low-dose group and 2.1% of the standard dose group (p=0.01). Mortality at seven days was 3.6% in the low dose group and 5.3% in the standard dose group (p=0.02), with mortality at 90 days 8.5% in the low-dose group and 10.3% in the standard dose group (p=0.07).

Conclusion: This study of adult patients with acute ischemic stroke, found that low-dose alteplase was not inferior to standard dose alteplase with respect to the primary outcome of death and disability.

Anderson, C., et al. Low-Dose versus Standard-Dose Intravenous Alteplase in Acute Ischemic Stroke. **New Eng J Med.** 2016, June 16; 374(24): 2313 -2323.

PREVIOUS STATIN USE AND INTRACRANIAL ATHEROSCLEROTIC PLAQUE

The use of statins has been shown to be protective against carotid, coronary and intracranial artery atherosclerosis. This study explored the relationship between premorbid statin use and the characteristics of intracranial atherosclerotic plaque.

Data were obtained from participants in the Intensive Statin Treatment in Acute Ischemic Stroke Patients with Intracranial Atherosclerosis Trial (STAMINA-MRI), an ongoing study evaluating the efficacy of high-dose statin treatment on the stabilization of intracranial atherosclerotic plaque. Between February of 2012 and September of 2015, patients admitted for the treatment of acute ischemic stroke were invited to participate.

Eligible subjects were diagnosed with intracranial atherosclerosis. Excluded were patients who had a previous history of stroke, an incomplete history of previous medications or contradictions for MRI. Clinical data, including initial stroke severity and 90-day modified Rankin scale score were acquired. Premorbid use of statins was recorded at the time of admission. The cortical distribution and volume of ischemic brain lesions were measured using diffusion weighted imaging.

Among the patients enrolled, 38 (27.9%) were taking statins before the index stroke. Of these, 22 were taking low-dose, and 16 high-dose, statins and 29 were not taking statins. While the degree of stenosis did not differ among the three groups, the proportion of patients with plaque enhancement decreased in statin users (p=0.006) and the volume of plaque enhancement was significantly lower in the statin users than in the nonusers (p=0.011). Premorbid statin use was associated with a higher prevalence of non-embolic stroke and a reduction in large cortical infarctions.

Conclusion: This study indicates that premorbid statin use is associated with modulation of plaque enhancement in symptomatic intracranial atherosclerotic plaque, and decreases the proportion of patients with large cortical infarctions.

Chung, J., et al. Previous Statin Use and High-Resolution Magnetic Resonance Imaging Characteristics of Intracranial Atherosclerotic Plaque. The Intensive Statin Treatment in Acute Ischemic Stroke Patients with Intracranial Atherosclerosis Study. **Stroke**. 2016, July; 47(7): 1789-1796.

PROPHYLACTIC ANTIEPILEPTICS FOR SUBARACHNOID HEMORRHAGE

The development of seizures following spontaneous subarachnoid hemorrhage (SAH) has been well documented, with such seizures associated with clinical and radiographic markers of hemorrhage severity. This study evaluated whether prophylactic administration of antiepileptic drugs (AEDs) significantly decreases the incidence of post-SAH seizures.

This retrospective review of prospectively collected data included all patients presenting to the UPNC Presbyterian Hospital for spontaneous SAH from February of 2005 to October of 2010. The AED prescription characteristics and clinical course were recorded. The AED course was described as prophylactic or therapeutic. The primary outcome variable was seizure occurrence during initial hospitalization.

Of the 353 patients admitted with a diagnosis of spontaneous SAH, 43% received prophylactic AEDs on admission or after craniotomy. Seizure activity was noted in 10% of patients, with a mean seizure onset of 3.6 days. Seizure onset occurred within 24 hours in 47% of the patients with seizures. Treatment with prophylactic AEDs was not significantly associated with the risk of seizure. After adjusting for neurologic grade on admission,

multivariable regression analysis did not reveal prophylactic AED therapy to be a significant predictor of seizure risk.

Conclusion: This study of patients with spontaneous subarachnoid hemorrhage found that prophylactic antiepileptic drugs do not significantly reduce the risk of seizure during hospitalization.

Panczykowski, D., et al. Prophylactic Antiepileptics and Seizure Incidence following Subarachnoid Hemorrhage. **Stroke.** 2016, July; 47(7): 1754-1760.

MEASUREMENT ERROR WITH IMPACT TESTING

After a mild traumatic brain injury (TBI), computerized neurocognitive tests remain a cornerstone of concussive assessment. The Immediate Post Concussion Assessment and Cognitive Testing (ImPACT) is the most widely used of the neurocognitive testing programs in concussion management. This literature review was designed to better assess the reliability of the ImPACT test.

A literature review was completed using studies published between January of 1999 and November of 2014. The search was completed for studies assessing the ImPACT compared with other methods of neuropsychological testing in patients with brain injury. Studies selected were included if participants completed the ImPACT at least twice.

Of the 5,943 articles reviewed, ten were chosen for full review and meta-analysis. Seven of the nine studies reported a Pearson r as a measure of test-retest reliability. Within each study, the visual/motor processing speed was consistently the most reliable composite score, with verbal memory and visual memory demonstrating the least reliability. With the exception of processing speed, all composite scores exhibited poor to moderate reliability.

Conclusion: This literature review and meta-analysis of ImPACT testing found that the majority of ImPACT composite scores failed to reach good reliability.

Alsalaheen, B., et al. Measurement Error in the Immediate Postconcussion Assessment and Cognitive Testing (ImPACT): Systematic Review. **J Head Trauma Rehab**. 2016, July/August; 31(4): 242 -251.

RETURN TO SPORT AFTER ROTATOR CUFF REPAIR

One of the main expectations of athletes undergoing rotator cuff repair surgery is to return to sport after treatment. This systematic review and meta-analysis of the literature was designed to better understand the rate of return to sport after treatment of rotator cuff tears.

A literature search was performed using multiple databases for studies which focused on rotator cuff tear/ repair/return to play/return to sport. The final search was performed in October of 2014. Data were extracted and analyzed to determine the mean rate of return to sport. Secondary outcome variables included functional results and patient satisfaction.

The analysis included data from 25 studies, among which 22 were retrospective and five were comparative. From these, data concerning 859 patients with a mean age of 42.6 years were extracted. The mean delay between the rotator cuff injury or the beginning of symptoms and surgery was 14.5 months. The combined return to sport was 84.7%, with the time to return ranging from 4.1 to 17 months. Of those returning to sport, 65.9% reported returning at the same level as pre-injury. The rate of return to the same level of play was 49.9% in the professional athletes, 81.4% in the competitive athletes and 92.4% in the recreational athletes. Patient satisfaction with the repair ranged from 68.4% to 100%.

Conclusion: This meta-analysis of patients undergoing rotator cuff repair found that 84.7% returned to sport, with 65.9% of those returning at the same level of play as pre-injury.

Klouche, S., et al. Return to Sport after Rotator Cuff Tear Repair: A Systematic Review and Meta-Analysis. **Am J Sport Med.** 2016, July; 44(7): 1877-1887.

GABAPENTIN FOR CHRONIC LOW BACK PAIN

Chronic low back pain (LBP) is a prevalent and often disabling condition for which there are few effective interventions. As treatment with gabapentin has shown some evidence of efficacy in patients with fibromyalgia, this study evaluated the efficacy of gabapentin for patients with chronic LBP, with or without leg pain.

This prospective, randomized, double-blind, placebo controlled trial included patients 21 to 70 years of age with nonspecific LBP, present daily for six months or longer. The participants agreed to discontinue muscle relaxants, antidepressants and opioids at least two weeks before the trial. The patients were randomized to receive either gabapentin, titrated to 1,200 mg, three times per day by week four, or a placebo. The primary outcome measure was pain intensity, as determined by the Descriptor Differential Scale (DDS). The main secondary outcome measure of everyday functioning was the Oswestry Disability Index (ODI).

Of the 108 individuals who were randomized, 55 were assigned to the gabapentin group and 53 to the placebo group. Of these, 72 (71.3%) completed all 12 weeks of the study. Pain intensity decreased significantly over time for all participants, with subjects reporting pain reduction of 30% from baseline. There were no differences between groups in DDS assessed pain intensity ($p=0.423$) or change in pain unpleasantness ($p=0.523$). Similar, nonsignificant differences were noted for measures of disability.

Conclusion: This study of patients with chronic low back pain did not find that gabapentin is more effective than placebo for reducing pain and increasing function.

Atkinson, J., et al. Randomized, Controlled Trial of Gabapentin for Chronic Low Back Pain with and without a Radiating Component. **Pain.** 2016, July; 157(7): 1499-1507.

MUSCULOSKELETAL INJURIES AND CARPAL TUNNEL SYNDROME

Risk factors for carpal tunnel syndrome (CTS) include female gender, pregnancy, obesity and manual labor. As musculoskeletal injuries may force affected individuals to adopt adverse postures, this study assessed the association between

those injuries and CTS in a group of Latino manual laborers.

Subjects were Latino poultry and non-poultry manual labor workers in four rural counties in western North Carolina. The participants underwent a one-hour interview, answering questions regarding their work and health. Data were recorded of self-reported changes in health and pain in shoulders, elbows or low back that had occurred on at least two days during the preceding month. Sports medicine physicians conducted musculoskeletal examinations, with a particular focus on the site of the pain. Participants also underwent nerve conduction studies (NCSs) on bilateral wrists, with findings scored as no CTS, possible CTS, and CTS. The findings were dichotomized into CTS (combined CTS and possible CTS) and no CTS. Musculoskeletal injuries were compared with NCS findings.

A total of 512 participants, with a mean age of 34.7 years and a mean body mass index of 28.7 kg/m^2, completed the study. Of these, 14.6% had rotator cuff syndrome, 5.7% epicondylitis and 48.6% CTS in at least one extremity. The association between rotator cuff syndrome and CTS was significant for all individuals (p=0.03), with a greater odds ratio in the right arm. The association between epicondylitis and CTS failed to reach statistical significance.

Conclusion: This study found that individuals with rotator cuff syndrome have a higher prevalence of carpal tunnel syndrome.

Cartwright, M., et al. Examining the Association between Musculoskeletal Injuries and Carpal Tunnel Syndrome in Manual Laborers. **Muscle Nerve.** 2016, July; 54 (1): 31-35.

GUT MICROBIOTA AND EXTREME LONGEVITY

Given the research demonstrating its impact on human metabolism and immunology, the gut microbiome has been proposed as a possible determinant of healthy aging. This study compared the microbiota of those who had aged to beyond 100 years with those of other adults.

Subjects included 24 semi-supercentenarians (S), 105 to 109 years of age, 15 young adults (Y), 22 to 40 years of age, 15 centenarians (C), 99 to 104 years of age and 15 younger elderly adults (E), 65 to 75 years of age, all in the same geographic region. Feces were collected, with total bacterial DNA extracted from all samples. The fecal microbiota were compared among age groups.

Fecal microbiology in all age groups was dominated by three families: *Bacteroidaceae*, *Lachnospiraceae* and *Ruminococcaceae*, but their cumulative relative abundance decreased with aging (77.8% in Y, 71.1% in E, 58.7% in C and 57.7% in S), highlighting an age-dependent increase in the contribution of subdominant families. The abundance of *Coprococcus*, *Roseburia* and *Faecalibacterium*, belonging to the *Lachnospiraceae* and *Ruminococcaceae* families, was negatively associated with age. *Oscillospira* was positively related to age, as were two subdominant members of the Bacteroidales order (*Odoribacter* and *Butyricimonas*). Extremely long-living people seemed to experience a parallel increase in several health-associated taxa including *Akkermansia*, *Bifidobacterium*, and *Christensenellaceae*.

Conclusion: This study of the microbiota of the aged found that, in extremely old people, the microbiome is enriched with the health-associated bacteria, *Akkermansia*, *Bifidobacterium* and *Christensenellaceae.*

Biagi, E., et al. Gut Microbiota and Extreme Longevity. **Curr Biol.** 2016, June; 26(11): 1480-1485.

HEALTHY LIFESTYLE AND OUTCOMES OF STROKE IN WOMEN

Previous studies among women have shown a decreased risk of total and ischemic stroke among those with healthier lifestyles. This study was designed to determine the associations between healthy lifestyle and stroke severity.

Data were obtained from the Women's Health Study, a randomized, placebo controlled trial of the effects of low-dose aspirin and vitamin E on the primary prevention of cardiovascular disease and cancer. Subjects were U.S. female health professionals ages 45 years or older without a history of cardiovascular disease, cancer or other major illnesses. The subjects were randomized to receive low-dose aspirin or vitamin E. Twice during the first year, and yearly thereafter, the women were sent questionnaires asking about demographics, lifestyle and health information. Using the Healthy Lifestyle Index (incorporating information concerning smoking, physical activity, body mass index (BMI), alcohol consumption and diet), the authors evaluated the relationship between healthy lifestyle and incident stroke.

Over the 17.2 years of follow-up, 867 strokes were reported. Compared with the lowest category of the Healthy Lifestyle Index (zero to four points), higher Healthy Lifestyle Index categories were associated with reductions in the risk of mild, moderate and severe stroke outcomes. There was no significant decrease or increase in risk of hemorrhagic stroke with moderate/ severe outcome for those in higher compared to those in the lowest Healthy Lifestyle Index categories.

Conclusion: This study found that a healthy lifestyle is associated with a reduction in the risk of total and ischemic stroke with mild, moderate and severe functional outcomes among women.

Rist, P., et al. Healthy Lifestyle and Functional Outcomes from Stroke in Women. **Am J Med.** 2016, July; 129 (7): 715-724.

LUMBAR FACET SYNDROME TREATED WITH ORAL DICLOFENAC OR STEROID INJECTION

Lumbar facet joint syndrome is thought to be an important cause of low back pain (LBP). The efficacy of facet injections with steroids or oral nonsteroidal anti-inflammatory drugs (NSAIDs), while commonly performed, have yet to be fully vetted. This study compared the effectiveness of oral NSAIDs with steroid facet injections by measures of function and pain.

Consecutive patients presenting with LBP, with or without thigh pain, were evaluated for inclusion. Those diagnosed with lumbar facet syndrome were invited to participate. Subjects were randomized to one of three treatment groups: an oral diclofenac group, to receive two weeks of 50 mg tablets taken twice daily, a methylprednisolone facet injection group, to receive 80 mg injections of methylprednisolone acetate, combined with one ML 0.5% bupivacaine, or a combination group

to receive both. The primary endpoints were scores on the Oswestry Disability Index (ODI) and a visual analogue scale (VAS) of pain, both administered before treatment and at four and 12 weeks post-treatment.

Comparing treatment groups at each time point, the combined group realized significantly better ODI scores than the oral group at four- and 12-week follow-ups (p<0.001 for both comparisons). The injection group had better ODI scores than did the oral group at four- and 12-week follow-ups (p<0.001 and p=0.004, respectively). The combined group demonstrated significantly better ODI scores than did the injection group at four-week follow-up (p=0.02). Comparing VAS scores, the combined group and the injection group both realized significant reductions in VAS scores as compared to the oral diclofenac group at the four-week follow-up (p<0.001 for both comparisons).

Conclusion: This study of patients with lumbar facet syndrome found that the combination of oral diclofenac and injected methylprednisolone is more effective than either alone, with the benefit strongest within four weeks of treatment.

Sae-Jung, S., et al. Outcomes of Lumbar Facet Syndrome Treated with Oral Diclofenac or Methylprednisolone Facet Injection: A Randomized Trial. **Int Orthop.** 2016, June; 40(6): 1091-1098.

PHARMACOTHERAPY FOR DEPRESSION POST-BRAIN INJURY

The diagnosis of traumatic brain injury (TBI) carries a significantly increased risk of depression. Evidence suggests that the experience of depression following TBI is associated with greater functional impairment and poorer recovery. This literature review and meta-analysis examined the effectiveness of pharmacotherapy for the treatment of depression following TBI.

A literature review of multiple databases was completed for studies including the use of pharmacotherapy for the treatment of depression following TBI. Data abstracted included antidepressant use, treatment timing and duration, method of assessment and results of treatment. A pooled analysis was conducted to examine the effectiveness of treatment in reducing depressive symptoms over time.

From the literature review, nine clinical trials were identified for review and meta-analysis. The subjects in these trials had a mean age ranging from 28 to 50 years, with severity of brain injury predominantly mild to moderate. A pooled analysis showed that, over time, antidepressant treatment was associated with a large favorable treatment effect (P<0.001). Limiting the analysis to those with placebo-controlled trials, a significant treatment effect was also noted (p=0.02). Significant treatment effects were noted specifically with tricyclics (p<0.001) and SSRIs (p<0.001).

Conclusion: This meta-analysis of studies of patients with brain injury treated for depression found that pharmacotherapy is associated with a significant reduction in depressive symptomatology.

Salter, K., et al. Pharmacotherapy for Depression Post-Traumatic Brain Injury: A Meta-Analysis. **J Head Trauma Rehab.** 2016; 31(4): E21-E32.

FRACTURE RISK WITH PARATHYROIDECTOMY AND BIPHOSPHONATES IN HYPERPARATHYROIDISM

Primary hyperparathyroidism (PHPT) is a common endocrine disorder, which, if left untreated, leads to a loss of bone mineral density (BMD) over time. As surgery is the only definitive treatment for PHPT, this study examined changes in BMD and fracture rates among patients with PHPT, treated with parathyroidectomy, biphosphonates or observation.

The Kaiser Permanente Southern California Laboratory Management System was queried to identify patients with a biochemical diagnosis of PHPT from 1995 through 2010. Those who initiated phosphonate treatment before the date of study inclusion and those treated with less than one year of biphosphonates were excluded. The database was reviewed to identify patients who underwent a parathyroidectomy, BMD results and for fracture outcomes. The change in BMD was studied over four discrete periods: zero to two years, two to five years, five to eight years, and beyond eight years.

The study included 6,272 patients with PHPT. At baseline, 11% had normal BMD, 36% had osteopenia and 53% had osteoporosis. BMD increased in women after parathyroidectomy by 4.2% within two years and with bisphosphonates by 3.6% within two years, declining thereafter. In men, bisphosphonate treatment resulted in a sustained increase in BMD.BMD declined with observation only, in both men and women, losing 6.6% and 7.6%, respectively, at greater than eight years follow-up. In osteopenic and osteoporotic patients, parathyroidectomy was associated with reduced risks of hip fracture and any fracture, as compared with observation only, while biphosphonates were associated with an increased risk.

Conclusion: This study of patients with primary hyperparathyroidism found that the risk of fracture is reduced in those undergoing parathyroidectomy, with no reduction realized with the use of biphosphonates.

Yeh, M., et al. The Relationship of Parathyroidectomy and Biphosphonate with Fracture Risk and Primary Hyperparathyroidism**.** An Observational Study. **Ann Intern Med**. 2016, June 7; 164(11): 715-723.

MYOCARDIAL INFARCTION EVALUATION WITH HIGH SENSITIVITY TROPONIN T

Classically, to rule out an acute myocardial infarction (MI), serial biomarkers were needed during the first eight to 24 hours. This study evaluated the ability of a high sensitivity cardiac troponin (hs-cTnT) assay, which allows for measurement of low cTn concentrations with high precision, to assist in the early diagnosis of MI.

This international, multicenter study recruited patients presenting to the emergency department with symptoms suggestive of an acute MI. All participants underwent a clinical history, physical exam, 12-lead ECG, pulse oximeter reading, blood tests, including hs-cTnTand a sensitive cardiac troponin 1, and a chest radiograph. Blood samples were collected within 45 minutes of presentation. Additional samples were collected after one hour, two hours, and at four to 14 hours. A group of cardiologists were selected

(Continued from page 2)

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to determine the diagnosis, and were held blind to the hs-cTnT results. The primary outcome variable was the diagnosis of MI, with secondary outcomes including mortality at 30 days and at one year.

Among the 285 patients recruited, 64 (16.6%) were assigned a diagnosis of MI. Applying the hs-cTnT algorithm, the negative predictive value was 99.1% and the sensitivity 96.7%. At presentation, the cutoff value for hs-cTnT of14 ng/L resulted in a negative predictive value of 97.3%, and a specificity of 81.5%.

Conclusion: This study of patients presenting with chest pain found that using the change in high sensitivity troponin T levels measured at admission and one hour later allowed for a very reliable rule-out and rule-in of acute myocardial infarction.

Mueller, C., et al. Multicenter Evaluation of a Zero Hour/One Hour Algorithm in the Diagnosis of Myocardial Infarction with High Sensitivity Cardiac Troponin T. **Ann of Emerg Med.** 2016, July; 68(1): 76-87.

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