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CANNABINOID NASAL SPRAY FOR NEUROPATHIC PAIN

Neuropathic pain is a chronic and potentially debilitating condition. Despite the availability of multiple treatment options, many produce only partial relief. As previous studies have demonstrated analgesic effects of the endocannabinoids, this study was designed to determine whether a nasal spray containing delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD) could impact neuropathic pain.

This study included 380 patients with peripheral neuropathic pain associated with diabetes, or allodynia. The subjects were randomized to a control group or a treatment group. The treatment group received 2.7 mg of THC and 2.5 mg of CBD, administered at a maximum of 24 times every 24 hours. The outcome was measured by change in pain severity on a numerical rating scale (NRS). Secondary outcome measures included scores on a neuropathic pain scale, sleep quality, intoxication, subjective global impressions of change and quality of life.

All patients improved on the NRS pain scale over the initial weeks of treatment. The mean numeric rating scale score decreased from 6.9 at baseline to 4.2 at the end of the study. Improvements in the neuropathic pain scores were observed after four weeks of treatment, and were maintained over the nine months of the study, without an associated increase in the daily dose of the spray. After nine months, the majority of patients reported 30% or more improvement in pain scores compared to baseline. In addition, improvements in the secondary outcome measures of neuropathic pain scale scores, quality of life and sleep quality were positive and were maintained throughout the duration of the study.

Conclusion: This open label study found that patients with neuropathic pain can respond well, and over a long period of time, to a delta-9-tetrahydrocannabinol/cannabidiol oral mucosal spray.

Hoggart, B., et al. A Multicentre, Open Label, Follow-up Study to Assess the Long-Term Maintenance of Effect, Tolerance and Safety of THC/CBD Oral Mucosal Spray in the Management of Neuropathic Pain. **J Neurol.** 2015, January: 262: 27-40.

INTRA-ARTICULAR BIPHOSPHONATE FOR KNEE OSTEOARTHRITIS

Osteoarthritis (OA) of the knee is a major cause of disability, affecting 10% of people over the age of 55 years. A prior multicenter study found intra-articular clodronate, a bisphosphonate, to be as effective as hyaluronic acid, for the treatment of OA, with significant progression in improvement of pain and functional outcomes. This study further assessed the tolerability and efficacy of intra-articular clodronate for patients with OA of the knee.

This randomized, double-blind, study included men and women between the ages of 50 and 75 years of age. All had knee OA with radiographic confirmation. The patients were randomly allocated to receive either weekly intra-articular injections of two mg of clodronate or a placebo saline solution for four weeks. The subjects were then followed for a total of 12 weeks. The primary outcome measure was pain relief, as rated on a 100mm Visual Analogue Scale (VAS) at eight weeks. Secondary outcomes included WOMAC scores, Lesquesne index scores and global knee OA (KOA) evaluations by patients and investigators.

Significant improvement was noted on all outcome measures at all time points in both groups. Patients in the clodronate group demonstrated greater improvement in VAS pain scores at eight weeks than did the saline group (by 27.4 mm). However, that difference was no longer evident at 12 weeks. The experimental group demonstrated greater improvement on the Lequesne index, global KOA evaluations of both patients and investigators and the WOMAC pain subscale.

Conclusion: This double-blind, single center, randomized, controlled trial found that intra-articular clodronate provides symptomatic and functional benefits for patients with osteoarthritis of the knee.

Rossini, M., et al. Effects of Intra-Articular Clodronate in the Treatment of Knee Osteoarthritis: Results of a Double-Blind, Randomized, Placebo-Controlled Trial. **Rheum Intern**. 2015, Feb; 35(2): 255-263.

HEMATOPOIETIC CELL TRANSPLANT FOR MULTIPLE SCLEROSIS

Relapsing remitting multiple sclerosis (RRMS) is characterized by breakthrough episodes of active central nervous system inflammation. This phenomenon often occurs despite treatment with disease modifying therapies. Autologous hematopoietic cell transplant (HCT), combined with high-dose immunosuppressive therapy, has been found to be effective in resetting the immune system. This study tested the hypothesis that early control of inflammation can prolong remission and reverse neurologic dysfunction.

This prospective, open label, multicenter, trial included 24 patients between the ages of 18 and 60 years, all diagnosed with RRMS who had failed disease modifying drugs. The procedure involved harvesting autologous CD 34+ stem cells, followed by high-dose BEAM

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chemotherapy to deplete the patient's immune system. Grafts were then used to reconstitute the immune system. The primary endpoint was time to treatment failure during five years after transplant, defined as death, worsening debility, as assessed with the Expanded Disability Status Scale (EDSS) or relapse, based upon neurologic signs or new lesions as seen on MRI.

Treatment failed in 21% of the patients. Overall, event-free survival was estimated at 95.8% at one year, 82.8% at two years and 70.4% at three years after transplant. Scores on the EDSS improved and T2 MRI lesion volume decreased after three years ($p=0.007$ and $p<0.001$, respectively). Despite the high risk of treatment, most early side effects were hematologic and/or gastrointestinal, with those reversible.

Conclusion: This study of patients with relapsing remitting multiple sclerosis found that autologous hematopoietic cell transplantation, combined with high-dose immunosuppressive therapy, can effectively induce remission for up to three years

Nash, R et al. High-Dose Immunosuppressive Therapy and Autologous Hematopoietic Cell Transplantation for Relapsing Remitting Multiple Sclerosis (HALT-MS). **JAMA-Neurol**. 2015, February; 72(2): 159-169.

CHONDROPROTECTION AND PREVENTION OF OSTEOARTHRITIS PROGRESSION

Osteoarthritis (OA) is a major cause of musculoskeletal pain and disability worldwide. Most treatment focuses on reducing symptoms, rather than modifying the disease process itself. This systematic literature review was designed to better understand the evidence for the routine use of agents to modify the progression of the OA disease process.

An initial literature search identified 12 treatment agents, each recognized as possessing potential chondroprotective properties of the joint. The authors then identified randomized, controlled trials with a minimum of 12 months' follow-up, evaluating the efficacy of each of those agents. Measures included joint space width, distance between the femoral condyle and the tibial plateau and joint space narrowing or changes in cartilage volume. Of the articles reviewed, 13 fulfilled the criteria.

The data revealed that the long-term use of both oral glucosamine and chondroitin sulfate may have a small, but significant, effect on slowing disease progression in patients with OA of the knee. No conclusions were possible for treatment using intra-articular injections of these agents. Oral vitamins, including D and E, as well as nonsteroidal anti-inflammatory drugs, did not significantly affect the progression of the joint disease.

Conclusion: This literature review supports the use of both oral glucosamine and chondroitin sulfate as structure modifying, chondroprotective drugs in patients with osteoarthritis of the knee.

Gallagher, B., et al. Chondroprotection and the Prevention of Osteoarthritis Progression of the Knee: A Systematic Review of Treatment Agents. **Am J Sports Med.** 2015, March; 43(3): 734-744.

CIRCULATING C-REACTIVE PROTEIN IN OSTEOARTHRITIS

While osteoarthritis (OA) is generally perceived as a noninflammatory disease, recent studies suggest that local inflammation may play a prominent role in its pathogenesis. This meta-analysis reviewed literature concerning the association between C-reactive protein and OA.

Literature was reviewed for the years 1992 through 2012 from multiple databases. The authors identified studies which involved patients with OA, and included serum high sensitivity C-reactive protein (hsCRP). The data were reviewed to determine the relationship between circulating levels of CRP and OA phenotypes.

The literature review produced 32 studies, including 10 case controlled, 15 cross-sectional, four longitudinal and three clinical trials. Overall, hsCRP was modestly elevated in the population with OA ($p<0.001$) as compared to controls. In addition, serum hsCRP was associated with symptoms of OA, including pain ($p<0.001$) and loss of physical function ($p<0.001$). Serum hsCRP

was not, however, significantly associated with joint space narrowing nor Kellgren Lawrence scores. The findings revealed no evidence of a predictive value of hsCRP for the progression of OA.

Conclusion: This literature review and meta-analysis found that low-grade systemic inflammation may play a role in symptoms related to OA, but not radiographic changes associated with OA.

Jin, X et al Circulating C Reactive Protein in Osteoarthritis: A Systematic Review and Meta-Analysis. **Ann Rheum Dis.** 2015, March; 74 (4): 703–710.

NSAIDS: EFFECTS ON OSTEOARTHRITIS SYMPTOMS AND DISEASE PROGRESSION

An estimated 27 million people in the United States have osteoarthritis (OA). Clinical guidelines for the management of this disease include both pharmacologic and nonpharmacologic therapies. This study was designed to estimate the extent to which prescription nonsteroidal anti-inflammatory drugs (NSAIDs), taken over the long-term, affect the symptoms and disease progression of OA.

Between 2004 and 2006, the Osteoarthritis Initiative (OAI) collected baseline data from four study sites, including a total of 4,796 patients with established OA, or who were at high risk for developing OA of the knee, and were not taking an NSAID at study onset, and who began use during the study period. The participants were evaluated for four years with annual follow-up assessments. All were assessed for changes in the Western Ontario and McMaster University Osteoarthritis Index (WOMAC), as well as for radiographic progression over four years. These outcomes were compared between NSAID users and nonusers.

Among nonusers at baseline, six percent initiated treatment by one year, with 52% reporting regular use. Any prescription NSAID reported on the most recent assessment was not associated with scores for pain, stiffness or physical function on the WOMAC or with the joint space width. However, among those reporting use of prescription NSAIDs at all three of the yearly assessments, improvements were noted in patient reports of stiffness and function, with delayed joint space width progression.

Conclusion: This study found that long-term, but not short-term, use of NSAIDS is associated with important changes in stiffness, physical function and joint space width among patients with osteoarthritis of the knee.

Lapane, K., et al. Effects of Prescription Nonsteroidal Anti-Inflammatory Drugs on Symptoms and Disease Progression among Patients with Knee Osteoarthritis. **Arthritis Rheumatol**. 2015, March; 67(3): 724-732.

NUTRITIONAL SUPPLEMENTS FOR PRESSURE ULCER HEALING

Malnutrition is known to be prevalent among patients with pressure ulcers, and is considered a factor contributing to the development of, as well as inhibiting the healing of these ulcers. As previous studies have demonstrated that supplementation with nutritional formulas enriched with arginine, zinc and antioxidants may having a healing effect, this study further investigated whether an oral nutritional supplement enriched with those substances can assist in healing pressure ulcers.

Subjects were long-term care residents or homecare patients with stage II through stage IV pressure ulcers, all demonstrating malnourishment, defined as a low body mass index, recent unintentional weight loss, low serum albumin levels and reduced food intake. The subjects were randomized to receive a control formula or an experimental formula enriched with arginine, zinc, and vitamins E and C. All patients received optimal wound care. Pressure ulcer areas were documented at baseline, and four and eight weeks.

Of the screened patients, 200 were randomized. Both groups realized improved wound healing. Compared to baseline, pressure ulcer areas were decreased by an average of 60.9% in the treatment group and 45.2% in the control group (p=0.017). In the treatment group, 16.9% experienced complete healing, as compared with 9.7% in the control group (p=0.097). Withdrawals from the study included two in the experimental group and three in the control group, with gastrointestinal intolerance as the primary cause of withdrawal.

Conclusion: This study found that, when added to optimal wound care and proper nutrition, a formula with arginine, zinc and antioxidants seems to accelerate pressure ulcer wound healing.

Cereda, E., et al. A Nutritional Formula Enriched with Arginine, Zinc and Antioxidants for the Healing of Pressure Ulcers. **Ann Intern Med.** 2015, February 3; 162(3): 167-174.

CLOSTRIDIUM DIFFICILE IN THE UNITED STATES

Data from United States death certificates reveal that Clostridium difficile (C Diff) infection is the leading cause of gastroenteritis associated death, estimated to have caused 14,000 deaths in 2007. In 2009, the Center for Disease Control and Prevention began active population and laboratory-based surveillance for these infections in seven US cities, later expanding to 10. This study calculated estimates of the national incidence and total number of infections in the U.S.

Surveillance staff at each site identified all positive C Diff test results from 88 inpatient and 33 outpatient laboratories. On the basis of the initial medical review, a case was classified as community associated if the specimen was collected at an outpatient site or within three days of hospital admission. All other cases were classified as healthcare associated, with these further classified as community onset associated with healthcare facility, hospital onset or nursing home onset.

From January 1, 2011, to December 31, 2011, 15,461 cases of C Diff were identified across all 10 sites, with an estimated national burden of 453,000 cases. Of those, 65.8% were health care associated and 24.2% were hospital-onset. Among those with health care associated infection the rate of first recurrence was 20.9% and the rate of death within 30 days was 9.3%. The incidence was higher among females than males, with a ratio of 1.26, among whites than nonwhites with an odds ratio of 1.72 and among

persons 65 years of age or older with an odds ratio of 8.65.

Conclusion: This study estimated that C Diff was responsible for almost half a million infections and 29,000 deaths in the United States in 2011.

Lessa, F., et al. Burden of Clostridium Difficile Infection in the United States. **New Eng J Med**. 2015, February 26; 372(9): 825-834.

ASSESSMENT OF GOUT TREATMENT BY ULTRASOUND

Gout is a common arthritis, resulting from the deposition of monosodium urate crystals within the joints. This disorder affects one to two percent of adults in developed countries, and may be increasing in prevalence. Crystal deposition has traditionally been identified by using joint aspirants. Gout may also be diagnosed by ultrasound (US), based upon the presence of a "double contour sign". This study evaluated the ability of US to detect a decrease or disappearance of the US features of gout after the initiation of urate lowering therapy.

This prospective study included 16 males with gout, averaging 61 years of age. Evaluations were made of the first metatarsophalangeal joints and knees at baseline and after six months of treatment. Medical intervention include either allopurinol, 100 mg per day, or febuxostat, 80 mg per day, both titrated to achieve target serum uric acid levels of less than 360 µmol per liter.

Features of gout had not disappeared in four patients who did not reach the target blood levels of serum uric acid. Among those who did achieve target levels, there was an excellent correlation with a decrease or disappearance of US features in all joints reviewed.

Conclusion: This study of patients with gout found that the disappearance of urate deposits by ultrasound analysis correlates well with the efficacy of urate lowering therapy drugs.

Ottaviani, S., et al. Ultrasound n Gout: A Useful Tool for Following Urate Lowering Therapy. **Joint Bone Spine**. 2015, January; 82: 42-44.

ULTRASOUND ASSESSMENT OF STEROID INJECTIONS TO THE KNEE

Osteoarthritis (OA) is a common form of arthritis, affecting up to 10% of the North American elderly population. In addition, the prevalence of radiographically established OA in the United States is estimated to be 33% among individuals over 63 years of age. This study was designed to determine whether ultrasound (US) can be effective in demonstrating a response to intra-articular corticosteroid injections to the knee.

Subjects included 35, consecutive subjects who met the American College of Rheumatology's radiologic criteria for OA. All subjects completed a symptom assessment and US examination at baseline, and returned for follow-up at 14 weeks. Of those, 19 participants were determined to be in need of a corticosteroid injection, and received 80 mg of methylprednisolone mixed with 2 mL of lidocaine one percent. The remaining subjects underwent no therapeutic intervention. All participants were asked to rate their knee pain on a visual analogue scale, and to complete the Western Ontario McMaster Universities Osteoarthritis Index (WOMAC). The knee joints were assessed with US at baseline and at four weeks.

At follow-up US, synovial thickness was noted to have decreased in 16 of the 19 patients in the treatment group, and in two of the 14 patients in the control group ($p=0.012$). A reduction in synovial thickness was associated with a reduction in pain greater than or equal to the predetermined minimally clinically important improvement level (> 20 mm on the VAS). With both groups combined, no substantial association was seen between changes in synovial thickness and changes in pain.

Conclusion: This pilot study suggests that US may be useful in detecting early changes in synovial pathology in response to intra-articular anti-inflammatory therapy.

Keen, H., et al. Ultrasound Assessment of Response to Intra-Articular Therapy in Osteoarthritis of the Knee. **Rheum**. 2015 DOI: 10. 1093/rheumatology/keu 529

ULTRASOUND USE AND CONTAMINATION OF INJECTION SITES

Localized corticosteroid injection is used to treat a number of musculoskeletal disorders of the knee and shoulder. Some have estimated the risk of post-injection infection to be 4.6 per 100,000 injections. As ultrasound (US) is commonly used to assist with these injections, this study was designed to determine whether the use of nonsterile gel increases the risk of contamination.

Subjects were 26, healthy volunteers whose skin was prepared in a manner simulating therapeutic intra-articular shoulder injections under US guidance. Skin swabs were taken at the injection site before skin preparation, after skin preparation, after sterile gel application, and after nonsterile gel application. In addition, swabs were taken of the US transducer, and 10 sample swabs of nonsterile US transmission gel for determination of bacterial contamination.

Increased skin contamination was found with sterile US gel use, but not with nonsterile gel use. Of those with positive cultures after the first swab, no contamination was noted after alcohol preparation. Of the cultures from the nonsterile gel, none were positive. None of the cultures from the US probe were positive for bacteria.

Conclusion: This study found that the use of US probes and transmission gel may result in greater contamination of the site. The authors suggest sterile preparation of the entire field, including the area of US use.

Sherman, T., et al. Does the Use of Ultrasound Affect Contamination of Musculoskeletal Injection Sites? **Clin Ortho Rel Res.** 2015, January; 473 (1): 351-357.

TRANSCRANIAL MAGNETIC STIMULATION FOR MOTOR SYMPTOMS IN PARKINSON'S DISEASE

Parkinson's disease (PD) is a progressive neurodegenerative disorder affecting approximately one percent of the population older than 60 years of age and four percent of those over the age of 80. Current treatments include medical therapy,

as well as surgical techniques, including deep brain stimulation. During the past two decades, repetitive transcranial magnetic stimulation (rTMS) has been examined as a possible treatment for PD. This meta-analysis was designed to better understand the effects of (rTMS) on the motor symptoms of PD.

A literature search was conducted using multiple databases through June 30, 2014. Studies included those focused on PD and rTMS which were sham controlled and randomized. Motor symptoms were measured using the motor examination of the Unified Parkinson's Disease Rating Scale (UPDRS).

Twenty studies were included, for a total of 470 patients. The effect size of rTMS on the UPDRS was 0.46, a medium effect size in reducing motor symptoms ($p<0.001$). The subgroup analysis found no significant differences in effect size between rTMS sites and between high-frequency and low-frequency rTMS. However, the treatment effects of high-frequency rTMS that targeted the primary motor cortex, as well as low frequency rTMS applied over other frontal regions, were both significant ($p<0.001$ and $p=0.008$, respectively). A meta-regression analysis revealed that a greater number of pulses per session or across sessions was associated with a greater treatment effect.

Conclusion: This systematic review and meta-analysis suggests that repetitive transcranial magnetic stimulation can improve motor symptoms in Parkinson's disease, with key modulators of effect including stimulation site, frequency and number of pulses.

Chou, Y., et al. Effects of Repetitive Transcranial Magnetic Stimulation on Motor Symptoms in Parkinson's Disease. A Systematic Review and Meta-Analysis. **JAMA Neurol.** 2015 doi:10.1001/jamaneurol.2014.4380

HOSPITAL READMISSION AFTER HIP FRACTURE

Hospital readmission following hip fracture is a frequent and serious event that may indicate a gap in care. National readmission rates following hip fracture have remained essentially unchanged from 2004 to 2009. This study examined the 30-day hospital readmission rate in a center that employs the Geriatric Fracture Center Model of care.

This retrospective study included patients 65 years of age or older, admitted between 2005 and 2010 with a unilateral low-energy hip fracture, requiring surgical correction. Readmissions were identified, with records reviewed to determine the primary cause for readmission.

Of the 1,081 patients reviewed, 129 were readmitted within 30 days of their initial discharge date. Of these, 18.6% were admitted for surgical reasons, including fixation failure, refracture, new fracture, dislocation, hematoma or wound complications. In addition, 81.4% were readmitted for medical reasons. The most common medical reason was pulmonary problems, at 27%. Of those readmitted, 18.6% died during that hospitalization. The one-year mortality rate for patients readmitted within 30 days was 56%, as compared to 21% for those not readmitted ($p<0.0001$).

Conclusion: This retrospective study of patients undergoing surgical correction for hip fracture found that 11.9% were readmitted, with 18.6% of those readmitted dying during that hospitalization.

Kates, S., et al. Hospital Readmission after Hip Fracture. **Arch Orthopaed Trauma Surg**. 2015, March 3; 135 (3): 329 -337.

HOSPITAL STAY AFTER HIP FRACTURE AND RISK OF DEATH

One strategy for controlling health service expenditures involves reducing the length of hospital stay. This study investigated the impact of changes in length of stay after hip fracture in relation to the risk of death among Swedish citizens at least 50 years of age.

Using a closed nationwide cohort, the authors identified patients who had experienced a hip fracture between January 1, 2006, and December 31, 2012. Data were obtained from the Swedish National Patient Register, covering all inpatient care in Sweden. Using a national prescription database, medication use, including that of antidepressants and neuroleptics at the time of hip fracture, was determined. The date of death and underlying cause of death were obtained through the National Cause of Death Register.

During the study period, 116,111 patients sustained a hip fracture at a mean age of 82.2 years. The mean length of stay in 2006 was 14.2 days, decreasing to 11.6 days in 2012 ($p<0.001$). Patients discharged within five days of admission had twice the risk of death within 30 days of discharge as compared to those with a length of stay of at least 15 days. In 2012, for patients with a length of stay of 10 days or less, each day's reduction in length of stay increased the risk of death within 30 days by 16% ($p<0.007$).

Conclusion: This Swedish study found that, among the elderly, after hip fracture, a shorter length of hospitalization is associated with an increased risk of death after discharge.

Nordstrom, P., et al. Length of Hospital Stay after Hip Fracture and Short Term Risk of Death after Discharge: A Total Cohort Study in Sweden. **BMJ.** 2015; 350:h696 doi: 10.1136/bmj

TOCILIZUMAB FOR ELDERLY PATIENTS WITH RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is the most common, chronic inflammatory arthritis in adults. Clinical trials have suggested that disease modifying antirheumatic drugs (DMARDs) and tumor necrosis factor antagonists are effective and well tolerated in elderly patients with this disease. However, most studies have included only a small number of patients over the age of 65 years. This study investigated the efficacy and safety of an IL-6 receptor blocker, tocilizumab, for the treatment of RA among patients over the age of 65 years.

This multicenter, retrospective French cohort study included all patients who initiated tocilizumab therapy for RA between December of 2009 and December of 2012. Response to treatment at six months was evaluated using standardized criteria according to the European League against Rheumatism (EULAR) response and remission score. In addition, the authors documented the number of patients in remission and reviewed adverse events.

A total of 222 patients with RA were entered into the cohort database. Of those, 61 were 65 years of age or older and 161 were younger. After six months of treatment, significantly fewer elderly patients had a good EULAR response than did younger subjects (40.7% versus 61%; p= 0.01), though the numbers of patients with a moderate response were similar between age groups. After adjustment for baseline C-reactive protein and disease duration, elderly patients were found to be 3.63 times more likely than were younger patients to be in a worse EULAR response category at six months.

Conclusion: This retrospective study of patients with rheumatoid arthritis found that tocilizumab is well tolerated, but less effective, in patients 65 years of age or older than in younger patients.

Pers, Y., et al Efficacy and Safety of Tocilizumab in Elderly Patients with Rheumatoid Arthritis. **Joint Bone Spine.** 2015, January; 82(1): 25-30.

SYMPTOMS IN THE LAST YEAR OF LIFE

In 1997, the Institute of Medicine described extensive patient and family suffering at the end of life, and emphasized the need for better care. This study examined a nationally representative group for trends in end -of-life symptom prevalence between 1998 and 2010.

Using data from the Health and Retirement Study, a nationally representative, longitudinal survey of community dwelling adults 51 years of age or older, data were collected for participants every two years until death. Symptom prevalence was evaluated using questions regarding the presence of pain, depression, confusion, dyspnea, fatigue, incontinence, anorexia and frequent vomiting. For each participant who died during the study interval, a proxy reported symptoms during the last year of life.

From 1998 to 2010, proxy reports of “any pain” prevalence across all decedents increased from 54.3% to 60.8%, with moderate or severe pain reported in 48.7% in 1998 and 52.4% in 2010. The proxy reported prevalence of depression, periodic confusion and incontinence increased by 26.6%, 31.3% and 11.9% respectively.

Conclusion: This study demonstrates that, despite national efforts to improve end-of-life care, between 1998 and 2010, the prevalence of pain and other symptoms experienced during the last year of life increased.

Singer, A., et al. Symptom Trends in the Last Year of Life from 1998 to 2010: A Cohort Study. **Ann Intern Med.** 2015, February 3; 162(3): 175-183.

HIP FLEXION STRENGTH FOLLOWING ANTERIOR CRUCIATE LIGAMENT REPAIR

Few studies have evaluated the biomechanics of the hip after anterior cruciate ligament (ACL) reconstruction. This study evaluated hip flexion muscle strength in ACL reconstructed patients with patellar or hamstring tendon graft use, comparing them with healthy controls.

This randomized, controlled trial included ACL deficient patients undergoing reconstruction. The subjects were randomized to receive ACL reconstruction with patella tendon or hamstring tendon grafts. In addition, 64 healthy, male athletes participated as controls. The patients were progressed to resistance and endurance training the 13th to 24th weeks post-surgery. All patients underwent isokinetic hip muscle flexion strength testing the day before surgery and one year after surgery. Healthy controls were tested at baseline and at the end of the study.

Preoperatively, no significant difference was found in hip flexion strength between the patella tendon and hamstring groups. While hip flexion strength was increased one year after ACL reconstruction, it remained significantly reduced compared with healthy controls. In addition, hip flexion strength was significantly higher in the patella tendon group than in the hamstring group at one-year postoperatively ($p<0.001$).

Conclusion: This study demonstrates that hip flexion strength of reconstructed anterior cruciate ligament deficient patients is decreased compared to that of controls at one year post-surgery.

Monzopouloa G., et al. Hip Flexion Strength Remains Decreased in Anterior Cruciate Ligament Reconstructed Patients at One-Year Follow-Up Compared to Healthy Controls. **Intern Orthoped**. 2015: Doi. 10. 1007/S00264 – 014

COGNITIVE MOTOR INTERFERENCE FOR GAIT AND BALANCE AFTER STROKE

Cognitive motor interference (CMI) occurs when cognitive and motor tasks are performed simultaneously. This technique has been used to enhance treatment in sports rehabilitation medicine. This literature review and meta-analysis investigated the efficacy of CMI for improving gait and balance in patients with stroke.

A literature search of multiple databases was made for randomized, controlled trials published from 1972 to 2014, including adult stroke patients treated with CMI and a control group. Outcome measures included assessments of gait and balance, with secondary outcomes including activities of daily living and functional independence measures.

Data were included from 15 RTCs for 395 participants. The results indicated that CMI was better than the control for improving gait speed ($p<0.003$), stride length ($p<0.004$) and cadence ($p=0.001$). In studies of balance, CMI was better than the control in improving center of pressure sway area ($p=0.01$) and performance on the Berg Balance Scale ($p=0.02$).

Conclusion: This literature review found that, among patients with stroke, treatment with cognitive motor interference results in improvements on multiple measures of gait and balance.

Wang, X., et al. Cognitive Motor Interference for Gait and Balance in Stroke: A Systematic Review and Meta-Analysis. **Euro J Neurol**. 2015, March; 22(3): 555-563.

EXERCISE FOR WHIPLASH ASSOCIATED DISORDER

Data suggest that, one year after injury, 50% of people with whiplash associated disorder (WAD) still report neck pain. Despite clinical recommendations, there remains no clinical evidence of benefit for many conservative methods of management of chronic WAD, including neck specific exercise. As chronic neck disorders may have symptoms with both physical and psychosocial contributing factors, this

study assessed the effects of incorporating a behavioral approach to neck specific exercises.

Subjects were 216 individuals with chronic WAD, with a mean age of 40.5 years. The subjects were randomized to receive either physiotherapist led neck specific exercise (NSE), twice-weekly, aimed at facilitating activity of the deep cervical muscle layers, or similar exercise combined with behavioral intervention. The behavioral treatment included education concerning pain, as well as activities aimed at pain management and problem solving (NSEB). A third group was prescribed physical activity, to be completed outside of the healthcare system (PPA). The primary outcome measure was the Neck Disability Index (NDI). Other outcome variables included self-reported general health, measured with the Euroqol 5-D instrument, and activity level, measured with the International Physical Activity Questionnaire. Pain was recorded with a pain visual analog scale (VAS).

At three months, disability levels were found to have significantly improved in both the NSE ($p<0.01$) and the NSEB ($p<0.001$) groups, with no improvement observed in the PPA group. At six months, the proportions of responders, as indicated by changes in scores on the NDI, were 21% in the PPA group, 28% in the NSE group and 54% in the NSEB group. Pain bothersomeness was significantly reduced over time in all three groups. Self-efficacy improved only in the NSE group.

Conclusion: This study of patients with whiplash associated disorder found that supervised, neck specific exercise may have better clinical benefits than a prescription for home exercise, with additional benefits found when combined with a behavioral approach.

Ludvigsson, M., et al. Effect of Neck Specific Exercise with or without a Behavioral Approach on Pain, Disability and Self-Efficacy in Chronic Whiplash Associated Disorder: A Randomized Clinical Trial. **Clin J Pain.** 2015, April:31(4) 294-303.

ASSOCIATION BETWEEN ACUTE MYOCARDIAL INFARCTION AND SPINAL CORD INJURY

According to the World Health Organization, cardiovascular diseases are among the most frequent causes of death among people with spinal cord injury (SCI). This study analyzed the incidence and hazard ratios of acute myocardial infarction (AMI), comparing patients with SCI to those without.

The Taiwan National Health Insurance Program was used to identify a population based cohort of all patients with SCI who were newly diagnosed between 2000 and 2004. Each patient was matched with four controls without SCI. The data were further analyzed for episodes of AMI during the study period. The risk of developing AMI was compared between those with SCI and the controls.

Patients with SCI were found to have a significantly higher risk of AMI than the matched controls, with a hazard ratio of 1.17 ($p<0.05$). After adjusting for age, gender and comorbidities, patients with a SCI at the thoracic level were at an increased risk of AMI, with a hazard ratio of 1.38 ($p<0.05$). Pre-existing comorbidities of COPD, hypertension, cardiovascular disease and renal disease were also significantly associated with the development of AMI.

Conclusion: This Taiwanese national population based cohort study found a significantly higher risk of acute myocardial infarction among patients with spinal cord injury.

Yang, T., et al. The Association between Spinal Cord Injury and Acute Myocardial Infarction in a Nationwide, Population Based Cohort Study. **Spine.** 2015, February 1; 40(3): 147-152.

RAPID ENDOVASCULAR TREATMENT OF ISCHEMIC STROKE

Among patients with proximal vessel occlusion in the anterior circulation, up to 80% die within 90 days of stroke, or do not regain functional independence despite alteplase treatment. Recent studies have demonstrated the efficacy of endovascular treatment as an alternative to chemical treatment. This study was designed to determine the efficacy of rapid endovascular treatment, in addition to standard care, for patients with acute ischemic stroke.

This prospective, randomized, open label, controlled trial included patients with ischemic stroke, enrolled within 10 hours of symptom onset. A contrast computed tomography (CT) and CT angiography were performed to identify participants with a small infarct core, an occluded proximal artery in the anterior circulation and moderate-to-good collateral circulation. Participants in both groups received intravenous alteplase within 4.5 hours after onset of stroke if they met accepted guidelines.

Participants in the intervention group underwent rapid endovascular treatment, using available thrombectomy devices to achieve reperfusion. The primary outcome variable was the score on the modified Rankin scale at 90 days. Secondary and safety outcomes included early recanalization and reperfusion, intracranial hemorrhage, angiographic complications, neurologic disability at 90 days and death.

Analysis of the primary endpoint showed a common odds ratio of 2.6, favoring the intervention group ($p<0.001$). The median, 90-day modified Rankin scores were two in the intervention group and four in the control group ($p<0.001$). Mortality rates at 90 days were 10.4% in the intervention group and 19% in the control group ($p=0.04$). The rates of patients with a score on the Barthel index of 95 to 100 at three months were 57 7% in the intervention group and 33.6% in the control group.

Conclusion: This multicenter, randomized, controlled trial found that, among patients with acute ischemic stroke with a small infarct core, a proximal intracranial occlusion in the anterior circulation and moderate to good intracranial collateral circulation, rapid endovascular treatment can improve clinical outcome and reduce mortality.

Goyal, M., et al. Randomized Assessment of Rapid Endovascular Treatment of Ischemic Stroke. **New Eng J Med**. 2015, March 12; 372(11): 1019-1030.

GENETIC OVERLAP IN ISCHEMIC STROKE SUBTYPES

While conventional risk factors for stroke are well-established, genetic factors are thought to contribute up to 40% of the risk. This study was designed to estimate the genetic correlations with the three major subtypes of ischemic stroke.

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Data were obtained from the Meta-Stroke study, including 15 individual studies, contributing 12,389 total ischemic strokes cases. In this study, data obtained included genotype, phenotype and demographic details. Stroke subtype was determined, identifying cases with large artery atherosclerosis (LAA), cardioembolism or small vessel (lacunar) disease (SVD). A meta-analysis of allelic effects for LAA and SVD was performed for 2,167 LAA cases, 1,854 SVD cases and 51,976 controls.

The results revealed a high genetic relationship between LAA and SVD using both linear mixed models and profile scores. The meta-analysis of LAA and SVD identified a strong association for single nucleotide polymorphisms near the opioid receptor M-1 (OPRM1) gene.

Conclusion: This study of patients with ischemic stroke found an extensive genetic overlap between large artery atherosclerotic and small vessel ischemic stroke.

Holliday, E., et al. Genetic Overlap between Diagnostic Subtypes of Ischemic Stroke. **Stroke.** 2015, March; 46: 615–619.

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REHAB IN REVIEW

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