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YOGA INJURIES

Though promoted as physically and emotionally therapeutic, some have questioned the safety of the practice of yoga. This systematic review was completed to better understand the prevalence of injuries associated with yoga.

A literature review was conducted, with nine observational studies chosen for inclusion in this study. Subjects were 9,129 yoga practitioners and 9,903 non-yoga practitioners. Injury was defined as a trauma requiring discontinuation of participation for that day.

The risk of yoga associated injuries was estimated to be 1.45 per 1,000 hours of yoga practice. The lifetime prevalence of yoga–associated injuries or other adverse events ranged from 21-35%. Those yoga moves commonly associated with injuries were the headstand, shoulders stand, lotus posture, handstand, and forward or backward bending.

Conclusion: This systematic review of nine observational studies found that the risk of injury was 1.45 per 1,000 hours of yoga practice.

Crameret, et al. Injuries and Other Adverse Events Associated with Yoga Practice: A Systemic Review of Epidemiological Studies. **J Sci Med Sport.** 2018, February: 21(2) 147-154.

COFFEE CONSUMPTION AND CORONARY ARTERIES

Cardiovascular diseases are the leading cause of noncommunicable death. As coffee is one of the most popular beverages in the world, this study explored the association between coffee intake and atherosclerosis.

Data were derived from ELSA-Brasil, a cohort involving six cities, designed to identify risk factors for diabetes and cardiovascular disease. The subjects, 35 to 74 years of age at baseline, were assessed in 2008 and 2010 with a seven-hour evaluation including sociodemographics, health and medical history, work history, health care history, physical activity and dietary habits, including their daily coffee consumption. This consumption was placed in one of four categories of daily use, (a) never/ almost never, (b) one or less cups, (c) 1-3 cups or (d) more than three cups. The Sao Paulo cohort of the study underwent a CT examination to quantify coronary artery calcium (CAC), a known independent marker of future cardiovascular events.

The 4,426 participants averaged 50 years of age with 56% reporting consuming at least two cups of coffee per day. Compared to those who never drank coffee, the odds ratio (OR) of a CAC of over 100 was 0.85 for those who drank one or less cups per day, 0.73 for those who drank one to three cups per day, and 0.33 for those who drank over three cups per day (p=0.015 trend). These effects were dramatically reduced among smokers and former smokers.

Conclusion: This study found an inverse relationship between coffee consumption and coronary calcification, a marker of subclinical coronary atherosclerosis, with this protective effect dramatically reduced by tobacco use.

Miranda, A., et al. Coffee Consumption and Coronary Artery Calcium Score: Cross-Sectional Results of ELSA-Brazil (Brazilian Longitudinal Study of Adult Health). **J Am Heart Assoc**. 2018, April 3, 2018; 7(7): e007155.

SEVENTH CERVICAL NERVE TRANSFER FOR ARM PARALYSIS

Spastic arm paresis is a cause of long-term disability in patients with cerebrovascular accidents or other intracranial pathology. This study assessed the efficacy of a C7 nerve graft from the non-paralyzed to the spastic paralyzed arm.

This randomized, controlled trial included patients with hemiplegia after a stroke, a traumatic brain injury or cerebral palsy, manifesting as spasticity and weakness in the upper extremity, contralateral to the cerebral lesion. All had functionally plateaued after at least five years of rehabilitation. A surgical group underwent mobilization of the C7 nerve on the ipsilateral side with anastomosis directly to the C7 nerve on the paralyzed side. No surgery was performed on the control group. Both groups underwent identical rehabilitation therapy. The primary outcome variable was change in the total score on the Fugl-Meyer upper extremity scale from baseline to one year.

Subjects were 36 adults with an average time since injury of 15 years. The mean changes in total Fugl-Meyer scores were 17.7 in the surgical group and 2.6 and the control group ($p<0.001$). A significant portion of that improvement occurred in months 10 and 12. Changes in spasticity from baseline to month 12, as measured on the modified Ashworth Scale, significantly favored the surgical group in all joints, including elbow extension, forearm rotation, wrist extension, thumb extension, and extension of fingers two through five.

The mean changes in active range of motion from baseline to 12 months in the surgery group were 23° in the elbow, 36° in forearm rotation and 49° in the wrist, with corresponding changes in the control group of 0°, 1° and 1°($p<0.001$). Transcranial magnetic stimulation (TMS) and functional imaging demonstrated connectivity between the ipsilateral hemisphere and the paralyzed arm.

Conclusion: This randomized study of patients with hemiparesis and spasticity secondary to stroke, TBI or cerebral palsy found that transfer of cervical nerve 7 from the ipsilateral to the contralateral side significantly improved functional arm movement.

Zheng, M., et al. Trial of Contralateral Seventh Cervical Nerve Transfer for

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Spastic Arm Paralysis. **N Engl J Med.** 2018, Jan 4; 378(1): 22-34.

OMEGA-3 FATTY ACID SUPPLEMENTS AND CARDIOVASCULAR DISEASE

Early observational studies reported that regular consumption of fish once or twice a week is associated with a lower risk of death from coronary heart disease. These observations have prompted an interest in consumption of marine-derived very long chain omega-3 fatty acids (omega-3-FA). This meta-analysis assessed the association between supplementation with omega -3-FAs and cardiovascular and cerebrovascular mortality.

A literature search was completed, with ten trials, with a total of 77,917 subjects identified for inclusion. For each trial, the observed outcome of those who supplemented with omega-3-FA was compared to that expected in the general population.

Compared to the reference group, those randomized to receive omega-3 -FA had no better outcome for any coronary heart disease (CHD) events, major vascular events, stroke or revascularization events. No better outcome was found for the omega-3-FA group in studies which targeted subgroups, defined by sex, history of CHD, history of diabetes, pretreatment levels of total cholesterol, high-density lipoprotein cholesterol levels, low-density lipoprotein cholesterol levels, triglyceride levels, or prior use of statin therapy.

Conclusion: This meta-analysis of randomized trials of omega-3 fatty acid supplements found no significant associations between supplementation and fatal or nonfatal coronary heart disease or any major vascular events.

Aung, T., et al. Associations of Omega-3 Fatty Acid Supplement Use with Cardiovascular Disease Risks. MetaAnalysis of 10 Trials Involving 77,917 Individuals. **JAMA Cardio**. 2018, March; 3(3): 226-234.

POST-STROKE COGNITIVE DECLINE

Previous studies have shown that stroke is associated with an acute decline in cognitive capacity and is associated with accelerated and persistent cognitive decline for years. The REGARDS study (Reasons for Geographic and Racial Differences in Stroke) reviewed the effects of established risk factors on this cognitive decline.

This study involved 30,239 participants, all 45 years of age or older, recruited between January of 2003 and October of 2007. All were assessed for stroke and cognitive decline risk factors, including age, educational status, race, gender, referral location, stroke belt residence, hypertension, diabetes, elevated cholesterol, physical inactivity and current smoking. Cognitive function was assessed periodically, with cognitive decline compared with risk factors.

Of the 22,875 participants, 694 experienced an incident stroke during a median of 8.2 years follow-up. After a stroke the rate of acute decline in global cognition was greater in patients who were black ($p=0.04$), male ($p=0.04$), and in those who sustained cardioembolic ($p=0.001$) and large artery strokes ($p=0.001$). After this acute decline, faster declines in global cognition were noted in those who were older ($p<0.01$), resided outside of the Stroke Belt ($p=0.005$) or sustained a cardioembolic stroke ($p=0.01$). Faster declines in executive function over the years after stroke were greater in survivors who were older ($p<0.01$) or lacked hypertension ($p=0.03$).

Conclusion: This study demonstrates that incident stroke alters a patient's cognitive trajectory, with this effect accelerated among those with increased age and cardioembolic stroke.

Levine, D., et al. Risk Factors for Post Stroke Cognitive Decline. The REGARDS Study (Reasons for Geographic and Racial Differences in Stroke). **Stroke**. 2018, April; 49(4): 987-994.

COGNITION AFTER CAROTID ENDARTERECTOMY

Studies have demonstrated that microembolic and microvascular infarcts may number as many as 11 million per year in United States, with these associated with cognitive decline. This study assessed the effect of carotid endarterectomy (CEA) on the course of vascular cognitive decline among patients with carotid stenosis.

Subjects were 46 patients with greater than 60% carotid stenosis who underwent CEA. Of these, 25 were symptomatic by previous stroke or TIA. All participants underwent

screening for family history, clinical demographics and medical history. All also underwent ultrasound and transcranial Doppler (TCD) to assess plaque stability, and a neuropsychological evaluation before and one year after surgery. These results were compared with age and gender norms. A subset of 24 subjects further underwent MRI scans.

At baseline, all subjects demonstrated vascular cognitive decline as compared with norms. This decline correlated with the degree of plaque stability. At one year post-surgery, both groups demonstrated no further decline in cognitive function, with significant improvements found on two of the tests. Of the baseline variables, only baseline hypertension and better cognitive performance correlated with better cognitive outcome.

Conclusion: This study of patients scheduled for carotid endarterectomy found that all had vascular cognitive decline at base-line, with this decline found to be stable at one year after carotid endarterectomy.

Dempsey, R., et al. The Preservation of Cognition One Year after Carotid Endarterectomy in Patients with Prior Cognitive Decline. **Neurosurg.** 2018, March; 82 (3): 322-328.

CHRONIC INFLAMMATION, ACHILLES TENDINOPATHY AND RUPTURE

Achilles tendinopathy and rupture are frequent causes of pain and disability. As recent studies have found immune cells in specimens of non-ruptured chronic Achilles tendinopathies, this study was designed to better understand the association between inflammation and tendon rupture.

Subjects were 17 adults, ranging from 41 to 74 years of age, all with Achilles tendinopathy, presenting for treatment, and 19 adults, presenting with Achilles tendon rupture. For the control, healthy hamstring tendons were studied of 15 patients presenting for ACL repair. Specimens from each group were studied using immunohistochemistry, in order to assess the expression of CD14 and CD68 cells, with those findings compared to those of controls.

Compared to controls, an increased expression of CD14+ ($p=0.0015$) and CD68+ ($p=0.0015$) cells was noted in tendinopathic and ruptured Achilles (collectively labelled *diseased*). Using antibodies associated with macrophage activation, the diseased specimens revealed markers of interferon (IRF5, IRF1), STAT-6 (CD206) and glucocorticoid receptor (GCR) (CD163) macrophage activation pathways. Using CD31 as a marker of vascularization, an increased expression was noted in tendinopathic ($p=0.02$) and ruptured tendons ($p=0.0002$).

Conclusion: This study found that chronic inflammation is a feature of both Achilles tendinopathy and Achilles tendon rupture.

Dakin, S, et al. Chronic Inflammation Is a Feature of Achilles Tendinopathy and Rupture. **Br J Sports Med**. 2018, March; 52(6): 359-367.

RISK FACTORS FOR PROGRESSION OF RADIOGRAPHIC KNEE OSTEOARTHRITIS

Osteoarthritis (OA) of the knee is the most common form of OA affecting the elderly. This study assessed the incidence, progression and worsening of radiographic knee OA over time, and explored prospective risk factors for this progression.

Subjects were participants in the Hallym Aging Study, which began in 2004, and assessed residents 50 years of age or older. Subjects completed face-to-face interviews for socioeconomic and medical data, with a subgroup undergoing radiographic studies of both knees. The participants were divided into four age groups; 50 to 59 years, 60 to 69 years, 70 to 79 years and 80 to 89 years of age. Age specific, three-year incidence, progression and worsening of radiographic OA were calculated and compared with risk factors.

The subjects were a median age of 71 years, with incident OA of the knee observed in 10.2%. Progression was noted at three years in 13.6%. Univariate analysis revealed progression (defined as an increase of the Kellgren/Lawrence grade at follow-up from grades 2 or 3 at baseline) of OA for females (OR 4.4) and those with osteoporosis (OR 1.18). Factors associated with less progression were smoking (OR 0.79), alcohol consumption (OR 0.78), marriage (OR 1.11 for singles) and higher education level (OR 0.59 for 10 or more years of education). A body mass index of 25 or more was not associated with progression of OA. However, the multivariate analysis indicated that the only risk factor for progression of radiographic knee OA was female gender (OA 4.4), and the only risk factor for worsening (defined as an increase in the K-L grade at follow-up from any other grade (including grades 0 and 1) of OA, was being female (OR 1.41), and having a lower level of education (OR 0.52)

Conclusion: This prospective Korean study of 50-80 years of age found that 10.2% had OA of the knee at baseline, and that yearly progression was greater among females, and yearly worsening was greater in those with less than 10 years of education.

Yoo, J., et al. Risk Factors for Progression of Radiographic Knee Osteoarthritis in Elderly Community Residents in Korea. **BMC Musc Disord**. 2018; 19: 80.

DO PHYSICAL ACTIVITIES TRIGGER ACUTE LOW BACK PAIN

Low back pain (LBP) is a leading cause of years lived with disability (YLD) worldwide. This longitudinal, case crossover study examined whether physical activities are associated with a transient risk of pain flare-ups in patients who are experiencing acute low back pain (LBP).

The participants were adults experiencing a new episode (flare-up) of LBP, preceded by at least one month without LBP. The subjects were asked to specify age, gender, race, employment status and LBP history at the initial consultation. Back pain intensity was measured on an 11 -point numerical rating scale. Functional limitations were assessed using the Oswestry Disability Index (ODI). The patients reported specific physical activity exposures and emotional triggers during the most recent 24 hours.

The 48 adult patients had a mean age of 50 years and reported 81 flare-up periods and 247 control periods. Of the physical activities, prolonged sitting was the only activity significantly associated with a LBP flare-up, with an odds ratio (OR) of 4.4 ($p<0.001$). The multivariate analysis revealed that prolonged sitting (OR 4.2; $p<0.001$) and stress or depression (OR 2.8; $p=0.02$) were independently and significantly associated with an increased risk, while involvement with PT (OR 0.4; $p=0.05$) was associated with a decreased risk.

Conclusion: This study of patients with acute low back pain found that the only physical activity associated with an exacerbation (flare -up) of this condition was sitting for more than six hours.

Suri, P., et al. Do Physical Activities Trigger Flare-ups During an Acute Low Back Pain Episode? A Longitudinal, Case-Crossover, Feasibility Study. **Spine.** 2018, March 15; 43 (6):427-433.

KAATSU FOR KNEE OSTEOARTHRITIS

In patients with osteoarthritis (OA) of the knee, quadriceps weakness is associated with progression of the OA. Strengthening can be difficult, however, due to the pain associated with knee loading. As blood flow restriction (BFR) exercise (also known as Kaatsu) can allow strengthening at much lower loads, this study assessed the effect of BFR exercises on patients with OA of the knee.

Subjects were women, 50 to 65 years of age, diagnosed with OA of the knee. The participants were randomized to perform either 12 weeks of strengthening with high loads (HL), defined as 80% of the one repetition maximum (1 Rep Max), or strengthening at a low load (LL), defined as 20% of the 1Rep Max, without or with blood flow restriction (LL-BFR). The BRF was achieved by BP cuffs at 70% of the systolic blood pressure during exercise. Measurements made at baseline and follow up included quadriceps cross-sectional area, function (the timed-stands test and the timed-up-and-go test) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

Increases in knee strength were found in the HL and LL-BFR groups, with no significant gains in the LL group. No significant difference in gains was found between the LL-BFR and HL groups. WOMAC pain scores were significantly improved in the HL and LL-BFR groups (p=0.001 and p=0.02, respectively), but not in the (LL) group. WOMAC stiffness scores and physical function scores were significantly improved in the LL-BRF and HL conditions but not in the LL condition.

Conclusion: This study of patients with osteoarthritis of the knee found that blood flow restriction training was similar in efficacy to traditional strengthening for increasing muscle strength, quadriceps muscle mass and functionality while inducing less joint pain.

Ferraz, R., et al. Benefits of Resistance Training with Blood Flow Restriction in Knee Osteoarthritis. **Med Sci Sport Exerc.** 2018, May: 897-905.

FRANKINCENSE EXTRACT FOR RELAPSING-REMITTING MULTIPLE SCLEROSIS

Previous studies of frankincense derivatives have shown some positive activity in targeted multiple sclerosis (MS) inflammatory molecules and pathways. This study assessed the efficacy of standardized frankincense extract (SFE) as an anti-inflammatory and immunomodulatory therapy for patients with MS.

Subjects were 28 patients with relapsing remitting MS (RRMS). After a three-month baseline observation, the participants underwent an eight-week introduction period with SFE capsules of 400 mg, titrated up to a maximum of 4,800 mg per day. During the baseline, contrast-enhanced lesions (CELs) were assessed by MRI scans, with clinical follow-up and MRI studies completed monthly until month eight, and again at month 12 and every three months thereafter. The main outcome variable was the change in CELs from baseline to treatment phase.

The number of monthly CELs was reduced from a baseline median of 1.00 to a follow-up median of 0.50 ($p< 0.0001$), realized at months five to eight. In addition, brain atrophy was noted at baseline scan, with increased volume found during the treatment phase ($p=0.0081$). An immunological evaluation demonstrated that CD4+ T cells showed an increase in CTLA-4 surface expression, with the frequency of CD4+ CD25 FoxP3+ T cells increasing significantly during treatment. The IL-17A-producing CD8+ T cells decreased, while the frequency of IL-10-producing CD8+ T cells increased simultaneously, during treatment ($p<0.001$ for all). Of these, only the frequency of CD4+ CD25 FoxP3+ T cells showed a significant, negative correlation with the number of CELs.

Conclusion: This phase II trial of patients with relapsing remitting multiple sclerosis found that standardized frankincense extract is safe and demonstrates beneficial immunomodulatory effects.

Strüner, K., et al. A Standardized Frankincense Extract Reduces Disease Activity in Relapsing-Remitting Multiple Sclerosis (The SABA Phase IIa Trial). **J Neurol Neurosurg Psychiatry**, 2018; 89 (4): 330-338.

EFFECTIVENESS OF RITUXIMAB FOR MULTIPLE SCLEROSIS

Multiple sclerosis (MS) is a chronic autoimmune disease which often results in significant neurologic disability. The ability to treat these patients has changed in the past few years with the introduction of several new disease-modifying treatments (DMTs). This study assessed the efficacy of rituximab (RTX), an anti-CD20 B-cell depleting agent, for patients with newly diagnosed relapsing remitting MS (RRMS).

This retrospective study included all individuals in Stockholm and Vasterbotten Counties who were diagnosed with RRMS from January of 2012 to October of 2015. Patient records were reviewed for age, gender, hospital, DMT, relapses, lesions identified on magnetic resonance imaging reports, medications used, discontinuation date and cause, Expanded Disability Status Scale Scores and adverse events.

The final cohort included 494 patients, among whom 43.5% received an injectable DMT; 17.4%, dimethyl fumarate; 3.4%, fingolimod; 10.1%, natalizumab; 24.3%, rituximab; and 1.2% other DMTs. The rates of clinical relapse and/or neurological disease activity were significantly lower for patients treated with RTX as compared with injectable DMTs ($p<0.01$) and dimethyl fumarate ($p<0.05$). The annual discontinuation rate for RTX, injectable DMTs, dimethyl fumarate, fingolimod, and natalizumab were 0.03, 0.53, 0.32, 0.38, and 0.29, respectively, with continued disease activity as the main reason for discontinuation. Contrast enhancing MRI lesions were lower with RTX as compared with injectable DMTs and dimethyl fumarate ($p<0.02$ and $p<0.05$, respectively).

Conclusion: This retrospective Swedish study of patients with new onset relapsing remitting multiple sclerosis found that those treated with RTX had superior efficacy and discontinuation rates as compared with those receiving injectable DMTs or dimethyl fumarate.

Granqvist, M., et al. Comparative Effectiveness of Rituximab and Other Initial Treatment Choices for Multiple Sclerosis. **JAMA Neurol.** 2018, March; 75(3): 320-327.

HEALTH OF THE UNITED STATES FROM 1990 THROUGH 2016

According to the Global Burden of Disease Study 2010 (GBD 2010) US Burden of Disease Report, the main causes contributing to total disability–adjusted–life–years were poor diet, smoking, high blood pressure and obesity. This study used the GBD 2016 to evaluate the change and distribution of burden of disease from 1990 to 2016.

The GBD study used a systematic analysis of published studies and available data. From these sources, calculations were made of the incidence, prevalence, mortality, cause of death, years of life lost (YLL) and years lived with disability (YLD) and the sum of these, disability-adjusted life-years (DALYs).

Between 1990 and 2016, death rates in the U.S. declined from 745.2 per 100,000 to 578 per 100,000. Hawaii had the highest (81.3 years) and Mississippi the lowest (74.7 years) life expectancy in 2016.

The ten leading causes of disability-adjusted life-years (DALY) in 2016, from greatest to least, (with percentage change from 1990) were ischemic heart disease (-49.7%), lung cancer (-32.5%), COPD (+5%), diabetes (+11%), low back pain (-12.1%), Alzheimer's disease (+4%), opioid use disorders (+47.9%), other musculoskeletal disorders (-2.6%), major depression (+0.1%) and migraine (-1.4%).

Conclusion: This study demonstrates a rising life expectancy in United States, with great discrepancies among regions, and a shifting landscape of years lived with disability.

The U.S. Burden of Disease Collaborators. The State of U.S. Health, 1990-2016. Burden of Diseases, Injuries and Risk Factors among US States. **JAMA.** 2018, April 10; 319(14): 1444-1472.

TRENDS IN POST-ACUTE CARE USE AMONG MEDICARE BENEFICIARIES

Since the affordable care act was passed in 2010, Medicare has implemented payment reforms, shifting responsibility to hospitals and clinicians for the quality of care. The effects of these reforms on the use of post-acute care is not known. This study documents recent trends in use of institutional post-acute care, as well as hospital and post-acute care lengths of stay.

The MEDPAR file was used to identify Medicare beneficiaries, 65 years of age or older, discharged from acute care hospitals between 2000 and 2015. Changes during those 15 years were documented. Among the 137,973,633 hospital discharges, 20% were discharged to skilled nursing facilities (SNFs) and 3.7% to inpatient rehabilitation facilities (IRFs). The percentage of discharges to post-acute care increased from 21% in 2000 to 26.3% in 2015 ($p<0.001$), while the percentage of discharges to home decreased from 79% to 73.6% ($p<0.001$). Among those discharged to post-acute care, hospital length of stay decreased from nine days to 7.3 days ($p<0.001$), while, among those discharged to home, the length of stay decreased from 5.7 days to 4.8 days ($p<0.001$). The length of stay in post-acute care increased from 21.7 days to 25.1 days.

Conclusion: This study of Medicare recipients found that a decrease in length of stay in acute care hospitals was mirrored by an increase in length of stay at post-acute care hospitals.

Werner, R., et al. Trends in Post-Acute Care Use among Medicare Beneficiaries: 2002 to 2015.**JAMA.** 2018, April 17; 319 (15): 1616.

MEDICAL SPECIALTIES PROVIDING MECHANICAL THROMBECTOMY IN THE UNITED STATES

Optimal acute stroke management has evolved over the past several years with the emergence of mechanical thrombectomy. However, little is yet known regarding the United States workforce concerning this recently established procedure.

This cross-sectional study used data from the United States centers for Medicare and Medicaid services from January 1, 2009, through September 30, 2015. From a representative sampling of five percent of the cases of ischemic stroke involving mechanical thrombectomy, the clinicians' self-designated specialties were determined through national provider identity numbers (NPIs).

Of the 555 thrombectomies reviewed, the treating physicians were radiologists (61.4%), neurosurgeons (16.4%), neurologists (19.8%), and other specialists (2.4%).

Conclusion: With growing evidence of the importance of intra-arterial thrombectomy, this study reviewed the breakdown of specialists performing this procedure.

Kamel, H., et al. Medical Specialties of Clinicians Providing Mechanical Thrombectomy to Patients with Acute Ischemic Stroke in the United States**.** **JAMA Neurol.** 2018, April; 75(4): 515 -517.

DIFFUSION TENSOR IMAGING AND NEUROLOGICAL OUTCOME AFTER CARDIAC ARREST

As MRI of the brain with diffusion tensor imaging (DTI), with calculated fractional anisotropy (FA), can quantify white matter injuries after global anoxia, this study assessed the utility of FA in patients who were comatose for seven days after cardiac arrest.

This multicenter, cohort study enrolled 185 adult patients who remained unconscious at seven days following cardiac arrest. For each patient, the Glasgow Coma Scale was administered at hospital admission and on day seven. MRIs were completed between days seven and twenty-eight following cardiac arrest, with an electroencephalogram recorded within 72 hours after return of spontaneous circulation. An MRI DTI was acquired, with FA calculated. The primary outcome measure was the Glasgow Pittsburgh Cerebral Performance Categories (CPC) measure, with outcomes classified at six months as favorable (CPC 1-2) or unfavorable (CPC 3-4).

Of the 185 patients, 22% demonstrated a favorable outcome at six months. Normalized whole brain white matter FA (WWM–FA) and whole brain FA by DTI were significantly lower in patients with unfavorable outcomes than in those with favorable outcomes. A normalized WWM-FA score of lower than 0.91 had a negative predictive value for an unfavorable outcome of 71.4%, and a positive predictive value of 100%, with a sensitivity of 89.7%, and a specificity of 100%.

Conclusion: This study of patients who had remained unconsciousness for seven days following cardiac arrest found that the normalized whole-brain white matter fractional anisotropy, measured by

diffusion tensor imaging between days seven and 28, can be useful in predicting neurologic outcome at six months.

Velly, L., et al. Use of Brain Diffusion Tensor Imaging for the Prediction of Long-Term Neurological Outcomes in Patients after Cardiac Arrest: A Multi-Center, International, Prospect Observational Cohort Study. **Lancet Neurol.** 2018, April; 17(4): 318-326.

SURGICAL TREATMENT OF LATERAL EPICONDYLITIS

Many agree that the structure responsible for the symptoms of lateral epicondylitis is the origin of the extensor carpi radialis brevis (ECRB). While this condition is usually self-limiting, surgical excision of the degenerated portion of the ECRB has been introduced as an intervention for recalcitrant cases. This study assessed the efficacy of this surgery.

This prospective, randomized, double-blind, placebo-controlled trial included adults with a diagnosis of lateral epicondylitis persisting after six months of medical therapy. The subjects were randomized to a placebo surgical arm or a surgical arm to receive surgical excision of unhealthy tendinosis tissue, with both groups undergoing identical postoperative rehabilitation protocols. The patients were assessed preoperatively and post-operatively at two, six, 12, and 26 weeks.

Both groups reported a significant reduction in the frequency of pain with activity, as well as the frequency of pain at rest at 26 weeks and at 2.5 years. There was no significant difference between the placebo and the surgical groups at any time, on measures of frequency or severity of pain, or on clinical tests of function.

Conclusion: This prospective, randomized, placebo-controlled study of patients with lateral epicondylitis demonstrates no better improvement with surgical intervention than with conservative treatment.

Kroslak, M., et al. Surgical Treatment of Lateral Epicondylitis. A Prospective, Randomized, Double-Blinded, Placebo-Controlled, Clinical Trial. **Am J Sports Med**. 2018, May; 46 (5): 1106–1113.

PROTEIN INTAKE AND LEAN BODY MASS IN OLDER MEN

While studies of protein intake greater than the recommended daily allowance (RDA) have been shown to enhance training effects in some athletes, it is not known whether higher protein intake can help preserve muscle mass in vulnerable populations. This study was designed to determine whether increasing protein intake in older adult males with functional limitations would increase lean body mass (LBM) and performance measures.

Subjects were 92 men 65 years of age and older whose average daily protein intake was less than or equal to 0.83 g/kg/d. The men were divided into four groups: a) 0.8 g/kg per day of protein with placebo, b) 1.3 g/kg per day of protein with placebo, c) 0.8 g/kg per day of protein plus testosterone supplementation, and d) 1.3 g/kg per day of protein plus testosterone supplementation. The primary outcome measure was the change in LBM with secondary outcome measures including muscle strength and quality of life.

At six-month follow-up, no significant difference in LBM was noted based upon level of protein. However, fat mass decreased in men receiving higher doses of protein ($p=0.02$). Men randomized to receive testosterone gained significantly more LBM than did those randomized to the placebo group, regardless of protein intake ($p<0.001$). Changes in leg press strength, chest press strength and leg press power did not differ significantly between the protein groups but were greater among those administered testosterone. No significant effects of testosterone or protein supplementation were found in scores of overall health-related quality of life or physical component scores of quality of life.

Conclusion: This study of men 65 years of age or older found that protein intake above the recommended daily allowance did not increase lean body mass, muscle performance, physical function or well-being, unless accompanied by testosterone supplementation.

Bhasin, S., et al. Effect of Protein Intake on Lean Body Mass in Functionally Limited Older Men. A Randomized, Clinical Trial. **JAMA Intern Med.** 2018, April; 178(4): 530-541.

CARDIOVASCULAR SAFETY OF FEBUXOSTAT OR ALLOPURINOL IN GOUT

Previous studies have demonstrated that gout is associated with an increased risk of cardiovascular and chronic kidney disease. Febuxostat is an inhibitor of xanthene oxidase, used for the management of hyperuricemia in patients with gout. This study compared the cardiovascular safety of febuxostat with that of allopurinol.

This randomized, multicenter, double-blind, non-inferiority trial included patients with gout and a history of major cardiovascular disease. The subjects were randomized to receive either allopurinol, with doses modified according to kidney function, or febuxostat at 40 mg per day, titrated to 80 mg per day as needed. The primary endpoint was a composite of the first occurrence of cardiovascular death, nonfatal myocardial infarction, unstable stroke or urgent revascularization for unstable angina.

Subjects were 6,198 patients from 320 sites. Overall, 56.6% of the patients discontinued treatment prematurely. The primary endpoint was realized in 10.8% of the febuxostat group and in 10.4% of the allopurinol group ($p=0.66$). Cardiovascular mortality and death from any cause were greater in the febuxostat group than in the allopurinol group ($p=0.03$ and $p=0.04$, respectively).

Conclusion: This study of patients with gout found higher risks of cardiovascular death and death from any cause among those using febuxostat than among those using allopurinol.

White, W., et al. Cardiovascular Safety of Febuxostat or Allopurinol in Patients with Gout. **N Engl J Med**. 2018, March 29; 378 (13): 1200-1210.

TRANSCRANIAL DIRECT CURRENT STIMULATION FOR STUTTERING

Researchers have found that the left inferior frontal cortex (LIFC) is underactive during speaking among patients who stutter. This study assessed the effect on stuttering of stimulating the LIFC using transcranial direct current stimulation (tDCS).

Subjects were 30 male adults who stuttered. Those participants were randomized to receive behavioral fluency intervention by a speech pathologist with or without tDCS. Anodal stimulation was delivered at one mA over the left inferior frontal cortex for 20 minutes per day for five consecutive days, while a control group received sham stimulation. Fluency was assessed at one and six weeks after intervention.

The change from baseline in percent of dysfluent syllables decreased significantly more in the tDCS group than in the sham group ($p=0.012$) as measured at one week after the intervention. At six weeks,

this improvement was maintained during reading, but not during conversation. Outcomes on the stuttering severity instrument at one and six weeks demonstrated significantly greater improvement in the treatment than did the sham treatment group.

Conclusion: This study demonstrates that anodal transcranial current stimulation is effective in improving speech fluency in patients who stutter.

Chestersm J., et al. Transcranial Direct Current Stimulation over Left Inferior Frontal Cortex Improved Speech Fluency in Adults Who Stutter. **Brain.** 2018, April; 141(4): 1161-1171.

REPERFUSION WITH BRAIN EDEMA IN PATIENTS WITH ACUTE ISCHEMIC STROKE

Therapeutic reperfusion with endovascular treatment has been shown to improve the long-term functional outcomes of patients with anterior circulation acute ischemic stroke. This study was designed to clarify the association between reperfusion and edema in patients with stroke.

MR CLEAN was a prospective multicenter randomized clinical trial of endovascular treatment for acute ischemic stroke in the Netherlands. Subjects were admitted with a National Institutes of Health Stroke Scale score of two or more, with a proximal intracranial arterial occlusion of the anterior circulation, and the ability to start endovascular treatment within six hours of stroke onset. Imaging was performed at baseline and at follow-up, with midline shift assessed. Reperfusion status was assessed using the Modified Thrombolysis in Cerebral Infarction score. Outcome measures included the modified Rankin score (mRS), at 90 days.

Of the 462 patients included the analysis, 46.8% had a midline shift at follow-up. Successful reperfusion and recanalization were associated with a reduced likelihood of having a midline shift ($p<0.001$). The presence of a midline shift was associated with a worse mRS score ($p<0.001$).

Conclusion: This study demonstrates that endovascular reperfusion results in a reduced risk of midline shift (a factor associated with a worse functional outcome).

Kimberly, W., et al. Association of Reperfusion with Brain Edema in Patients with Acute Ischemic Stroke. A Secondary Analysis of the MR CLEAN Trial. **JAMA Neurol.** 2018, April; 75(4): 453-461.

WAKEFULNESS AND D1 RECEPTORS IN THE NUCLEUS ACCUMBENS

The Nucleus Accumbens (NAc) is known to be involved in behaviors that require heightened wakefulness. The NAc is primarily composed of two subtypes of GABAergic projection neurons. Animal studies have found that NAc D1R neurons, but not D2R neurons, play important roles in functional modulation of arousal-based behaviors. This study investigated the activity of NAc D1R neurons during the spontaneous sleep-wake cycle.

This animal study used *in vivo* fiber photometry to record and manipulate the activity of a subpopulation of cells in the NAc. Chemogenetic and optogenetic approaches combined with polysomnographic recordings were used to investigate the relationship between NAc D_1R neurons and arousal. The sleep-wake cycles were determined by EEG/EMG and compared to cell activity.

Sleep-wake stages were consistently associated with changes in the D1R neuron population activity during non-rapid eye movement (NREM) sleep. The NAc D1R neurons displayed a lower GCaMP during sleep than during either wakefulness or rapid eye movement (REM) sleep. The NAc D1R cells began to increase neuronal activity before NREM-to-wake and NREM-to-REM transitions, and to decrease neuronal activities before wake-to-NREM transitions.

Conclusion: This animal study found that D1R expressing neurons in the NAc are essential in controlling wakefulness.

Luo, Y., et al. Nucleus Accumbens Controls Wakefulness by a Subpopulation of Neurons Expressing Dopamine D1 Receptors. **Nature Commun.** 2018; 9: 1576.

SURGERY FOLLOWING CERVICAL SPINAL CORD INJURY WITH PRE-EXISTING CORD COMPRESSION

The functional prognosis following traumatic spinal cord injury (SCI) depends upon a number of factors, including the presence of pre-existing cord compression. This study examined the effectiveness of late decompressive surgery for pre-existing cord compression following traumatic cervical SCI (CSCI).

This retrospective cohort study included 78 consecutive patients with CSCI without bony injury, admitted for rehabilitation between April 2012 and September 2015. The patients were divided into four groups, based upon the compression rate of the injured spinal cord and whether or not decompression surgery was conducted. Neurologic status was evaluated with the American Spinal Injury Association (AIS) impairment scale, with functional recovery evaluated with modified Barthel index (mBI) and the Spinal Cord Independence Measure (SCIM).

Of the 32 patients in the severe compression group (with a mean of 52% cord compression), 63% underwent surgery, compared with 24% in the minor compression group (with a mean of 21% cord compression). Of those in the severe compression group who underwent surgery, 30% improved by more than two grades on the AIS, and 80% improved by at least one grade. In the minor compression group, of those undergoing surgery, 18% improved by more than two grades, and 91% by one grade. In the severe compression group, the mBI and SCIM improvement rates were significantly improved at the time of discharge only in the surgical treatment group.

Conclusion: This retrospective cohort study found that surgical decompression can improve the functional status of those with severe cord compression.

Konomi, T., et al. Clinical Outcomes of Late Decompression Surgery following Cervical Spinal Cord Injury with Pre-Existing Cord Compression. **Spinal Cord.** 2018, April; 56(4): 366-371.

ANTICHOLINERGIC DRUGS AND DEMENTIA RISK

As the use of anticholinergic drugs among people with dementia is regarded as inappropriate by both the Beers and the STOPP criteria, this study assessed the association between a new diagnosis of dementia and previous exposure to chronic anticholinergic drugs.

This nested case-control study employed data of the Clinical Practice Research Data Link, accessing records of over 11.3 million patients in the United Kingdom. The participants were 65 through 99 years of age, with a diagnosis of dementia. Using the date of diagnosis, each case was matched to a maximum of seven controls without dementia. Exposure to anticholinergic drugs was calculated and compared with

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*Jennifer Haewon Lee, M.D.
Kenton Hagan, M.D.
Supriya Shah, M.D.
Tulsi Singh, M.D.
Univ. of Pennsylvania, Philadelphia, PA

*William Hodgson, M.D.
John Lattin, M.D.
University of Virginia, Virginia St. Univ, VA

*Anna Coles, M.D.
Alicia Fuhrman, M.D.
Sean Matsuwaka, M.D.
U*niversity of Washington, Seattle, WA*

*Sean Smith, M.D.
Rahul Bijlani, M.D.
Michael Krill, M.D.
Washington U in St. Louis, St. Louis, MO

Executive Editor Emeritus
Donald F. Langenbeck, Jr., M.D.

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Michael P. Burke, M.S.

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the diagnosis of dementia.

Subjects were 40,770 patients with dementia, and 283,933 controls. From this group, 35% of the dementia cases and 30% of the controls were prescribed at least one anticholinergic drug with an Anticholinergic Cognitive Burden (ACB) score of three (definite anticholinergic activity).

A significant association with the development of dementia was found between prescriptions of any drug with an ACB score of one, two or three and dementia (respective odds ratios of 1:10, 1:10 and 1:11). In addition, a significant association was found between dementia incidence and any prescription of an antidepressant, antiparkinsonian or urological drug with an ACB score of three, up to 15 to 20 years prior to the index date.

Conclusion: This study found an increased risk of dementia in patients exposed to drugs with anticholinergic properties, persisting for up to 20 years after exposure.

Richardson, K., Anticholinergic Drugs and Risk of Dementia: A Case Control Study. **BMJ.** 2018; 361: K 1315.

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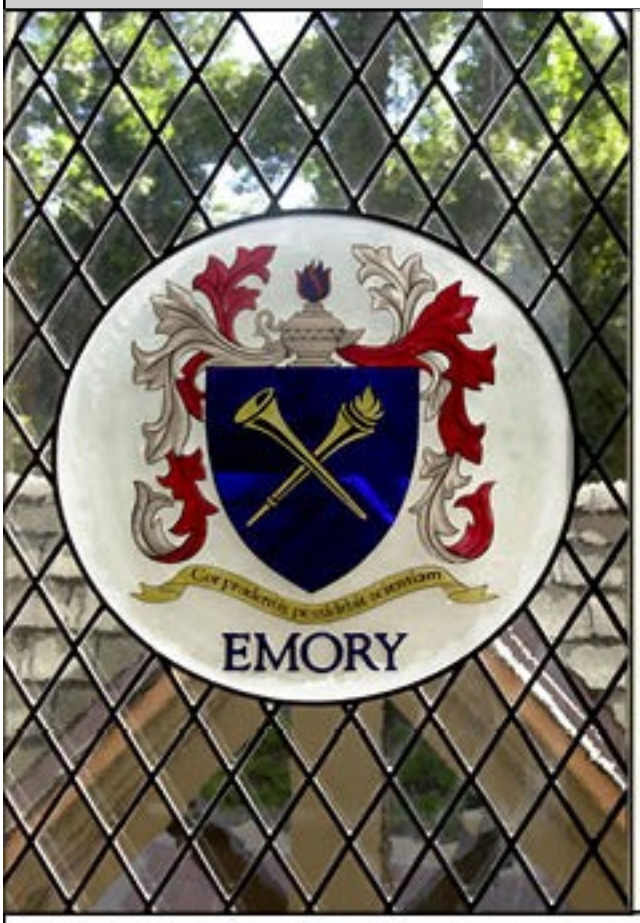

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