

REHAB IN REVIEW

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Volume 17 Number 8

Published by Physicians
In Physical Medicine and Rehabilitation

August 5, 2009

CALORIE RESTRICTION: DISEASE AND MORTALITY

Evidence that mammals have increased longevity with caloric restriction was first observed in 1935. This study sought to determine whether caloric restriction in monkeys has the same effect as was seen in the previous rodent models.

This trial used rhesus macaques including 46 males and 30 females. The animals were randomly assigned to either a calorie restriction group or to a control group. Each subject's individually determined baseline intake was reduced by ten percent per month over a three-month period, to reach a desired 30% restriction. The animals were followed for 20 years or until death, with the cause of each death determined. Age associated diseases were chronicled in the survivors. In order to assess the health and aging phenotype of each individual, the researchers assessed food intake, body weight, body composition, serum chemistry, glucose regulation, energy expenditure, activity measurement, endocrine profiles, electrocardiogram, blood pressure, brain magnetic resonance imaging, and radiography. These measures along with twice daily observation of the animals, allowed disease conditions to be identified and treated appropriately.

By study completion, 50% of the control animals and 80% of the calorie restricted animals had survived. The effect of calorie restriction in reducing disease onset was significant ($p=0.008$). Age-related diseases were detected in control animals at three times the rate of the calorie restricted animals. Radiologic studies demonstrated that calorie restriction resulted in a significant preservation of brain gray matter in subcortical regions. Calorie restriction reduced the incidence of diabetes, cancer, and cardiovascular disease.

Conclusion: This study of rhesus monkeys demonstrated that calorie restriction by 30% can extend life and reduce morbidity in these primates.

Colman, R., et al. Caloric Restriction Delays Disease Onset and Mortality in Rhesus Monkeys. *Science*. 2009, July; 325:201-203.

CORONARY RISK FACTOR INTERVENTION FROM INFANCY

It is clear that atherosclerosis develops as a result of a lifelong process often leading to coronary heart disease. A number of arguments support the concept that prevention of children's exposure to atherosclerosis risk factors should be started at an early age. Using data from a large, cross-sectional, coronary risk factor follow-up study, the Special Turku Coronary Risk Factor Intervention Project (STRIP) was launched in 1989 to study the effect of reduced exposure to coronary risk factors at an early age.

All participants were healthy children not regarded as a risk group for atherosclerosis development. Parents and siblings of the study infants and children were involved in the study as well, with their serum lipoprotein values and blood pressures measured at yearly visits. Dietary counseling was given to families by a nutritionist at three to twelve month intervals. Intervention was aimed at achieving a child's fat intake of 30 to 35% of daily energy. To maintain adequate fat intake, parents added two to three tablespoons of soft margarine or vegetable oil to the child's food from 12 to 24 months of age. During the first year, counseling was given to parents. From age 7 years onward progressively more dietary information and suggestions were given to the children. The control group received basic health

education, routinely given at well baby clinics and school health care. Throughout the study, food intake, and physical examinations were recorded including laboratory studies.

After 15 years, fifty percent of the cohort was still participating in the study. The STRIP intervention was effective in decreasing serum cholesterol in the first three years of life without reducing growth. The intervention produced significant reductions in cholesterol with no differences in neurological and cognitive development. Reviewing data at 10 years, the endothelial function in the intervention group was better than in controls.

Conclusion: This study found that low cholesterol diet counseling starting in infancy has a significantly favorable effect on certain cholesterol values and endothelial function, especially in boys, without harmful influence on the child's growth or cognitive, neurologic or puberty development.

Simell, O., et al. Cohort Profile: The STRIP Study (Special Turku Coronary Risk Factor Intervention Project), An Infant Onset Dietary and Lifestyle Intervention Trial. *Int J Epid*. 2009, June; 38:650-655.

MIDLIFE INCREASE IN PHYSICAL ACTIVITY

Physical activity is associated with decreased risks of obesity, diabetes, cardiovascular disease, osteoporosis and cancer. This study investigated the impact of physical activity on total mortality from middle age to old age, taking into account changes in activity during that period of life.

Data were obtained from the population based Upsalla Longitudinal Study of Adult Men. In 1970, all 2,841 men born in 1920-1924 and living in the municipality of Upsalla, Sweden were invited to

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participate in a health survey. Of those, 82% of the men ages 40 to 51 agreed to participate. Participants were invited for reinvestigation at ages 60, 70 and 77. At each survey the subjects were evaluated for medical conditions, and physical activity. Changes in the physical activity between the first and second survey were considered in four categories: unchanged low, unchanged high, decreased, and increased. High physical activity was defined as at least three hours of recreational sports or heavy gardening per week. The main outcome measure was all cause mortality, as determined through the Swedish national population register.

Men with low, medium and high physical activity had absolute mortality rates of 27.1, 23.6 and 18.4 per 1000 person-years. The relative reduction rate of mortality that was attributable to high physical activity as compared to low physical activity was 32%. Among men who increased their activity between ages 50 and 60 there was no clear benefit. However at 10 year follow-up, their mortality level was the same as men who had an initially high level of activity. The benefit gained from increased activity was similar to the benefit from smoking cessation. After adjusting for potential confounding factors, the years gained from high levels of physical activity were 2.3 compared to those with low activity and 1.1 compared to those with moderate activity.

Conclusion: This study demonstrates that increased physical activity in middle age is associated with a decrease in all cause mortality.

Byberg, L., et al. Total Mortality After Changes in Leisure Time Physical Activity in 50-Year-Old Men: 35 Year Follow-up of a Population-Based Cohort. **Br J of Sp Med.** 2009, July 43; 482.

ALLOPURINOL AND MORTALITY

Hyperuricemia, the culprit of gout pathogenesis, is associated with cardiovascular disease. The extent of this relationship is unclear. Recently, large-scale epidemiologic studies have found that individuals with gout have a higher risk of premature death. No previous study, however, has investigated the role of

urate lowering therapy on mortality. Therefore, this study examined the impact of allopurinol on the risk of mortality among patients with hyperuricemia.

A total of 9,924 veterans with hyperuricemia were studied. Of those, 2,483 taking allopurinol were compared to 7,441 who were not. Detailed demographics and medical information were available for the majority of patients. Eighty-three percent of the patients taking allopurinol had a diagnosis of gout as compared with only 20% of the control group. In general, the allopurinol group had a higher body mass index and an increased prevalence of hypertension, cardiovascular disease and diabetes, along with an overall greater burden of comorbidities. The use of allopurinol was associated with a 23% lower mortality rate. After adjusting for potential confounders the hazard ratio for all cause mortality for those taking allopurinol was 0.78. The magnitude of the risk reduction was comparable to that of established cardiovascular drugs, such as ACE inhibitors, angiotensin receptor blockers and beta-blockers

Conclusion: This cohort study of veterans suggests that allopurinol may provide a survival benefit for patients with hyperuricemia.

Luk, A., et al. Allopurinol and mortality in hyperuricemic patients. **Rheum.** 2009, July; 48; 804-806.

LIFE YEARS GAINED WITH IMPROVING CORONARY HEART DISEASE RISK FACTORS

Between 1980 and 2003, the life expectancy of US newborns increased by 4.8 years for males and 2.7 years for females. Much of this increase has been attributed to reductions in rates of coronary heart disease (CHD) related mortality during that period. While investigators have examined the reductions in CHD mortality rates, few have assessed gains in life years associated with these reductions. This study estimated the increase in life years among US residents associated with CHD treatments and changes in risk factors between 1980 and 2000.

The authors used the IMPACT CHD mortality model to estimate the

number of deaths prevented or postponed in 2000 that could be attributed to either increases in the use of cardiac treatments or decreases in the prevalence of CHD risk factors since 1980. This model combined data describing the number of CHD patients in each disease subcategory, the percentage of patients who received specific treatments, population trends for the prevalence of major risk factors, and the effectiveness of specific treatments.

The data revealed that 341,700 fewer CHD deaths occurred in the United States in 2000 than would have been expected had mortality rates remained the same as in 1980. Of the estimated 3,000,000 life years gained, 1,100,000 were attributed to treatments, while 2.1 million were gained through decreased levels of smoking, cholesterol, blood pressure, and physical inactivity. However, 715,000 life years were lost due to increased rates of obesity and diabetes.

Conclusion: This study demonstrated that changes in the prevalence of CHD risk factors accounted for nearly twice as many life years gained as did medical interventions. However, this improvement was offset somewhat by life years lost due to increases in obesity and diabetes.

Capewell, S., et al. Life Years Gained among US Adults from Modern Treatments and Changes in the Prevalence of Six Coronary Heart Disease Risk Factors between 1980 and 2000. *Am J Epid.* 2009, July; 170:229-236.

MEMATINE FOR PARKINSON'S DISEASE OR LEWY BODY DEMENTIA

Dementia with Lewy bodies (DLB) and dementia associated with Parkinson's disease (PD) have similar clinical and neuropathological symptoms, accounting for up to 20% of the global incidence of dementia. Mematine, a N-methyl D-aspartate (NMDA) receptor antagonist has proven to be effective for the treatment of Alzheimer's disease. Data concerning its effect for patients with DLB has been inconsistent. This study tested the hypothesis that Mematine can be an effective

treatment for PD or DLB.

Patients with mild or moderate PD or DLB were recruited at four psychiatric and neurological outpatient clinics in Norway, Sweden and the United Kingdom. The diagnoses were made by licensed psychiatrists or neurologists. The patients were randomly assigned to receive either Mematine or an identical appearing placebo. The dosing of Mematine was titrated from 5 mg up to the maintenance of 20 mg per day. Participants were assessed at baseline, at week 12 and at week 24. The primary outcome variable was clinical global impression of change (CGIC). Secondary outcomes included the 24 weeks scores for five instruments: the mini mental status exam, a quick test of cognitive speed, the neuropsychiatric inventory (NPI), the disability assessment for dementia (DAD), and the modified unified Parkinson's disease rating scale (UPDRS) motor subscale.

Of the 72 patients included, 34 were treated with Mematine and 38 with placebo. Sixteen withdrew before the end of the study due to adverse events. At week 24, those patients randomized to the Mematine group had obtained significantly better CGIC than those taking placebo ($p=0.03$). Among these secondary outcome measures, only speed on attention tasks differed, with better performance in the Mematine group than in the placebo group ($p=0.004$).

Conclusion: This study of patients with Parkinson's disease dementia or dementia with Lewy bodies demonstrates that these patients can benefit from treatment with Mematine.

Aarsland, D., et al. Mematine in Patients with Parkinson's Disease Dementia or Dementia with Lewy Bodies: a Double-Blind, Placebo-Controlled, Multicentre Trial. *Lancet Neur.* 2009, July; 8:613-618.

MEMATINE AND ARICEPT FOR ALZHEIMER'S DISEASE

The increased longevity of the elderly populations is accompanied by a growing prevalence of dementia, especially Alzheimer's disease (AD). The introduction of Mematine, an N-Methyl D-aspartate (NMDA) receptor antagonist has altered the standard of

care for patients with AD. This study examined the effect of cholinesterase inhibitors (ChEIs) and Mematine on the time to death and time to nursing home admission among individuals with AD.

The patients in this study were participants in the Alzheimer's Disease Research Program (ADRC) or the Alzheimer's Disease Research Center (ADRC) at the University of Pittsburgh. All subjects underwent an extensive neuropsychiatric evaluation including medical history and physical examination, neurological history and examination, a semistructured psychiatric interview and a neuropsychological assessment. Of the patients followed, 15% used both ChEIs and Mematine, 45% used only ChEIs and 40% used neither. The average follow-up time was 62.3 months. The primary outcome measures included the time to nursing home admission, or death.

Neither single nor combination therapy affected the time to death. However, the patients treated with only ChEIs and those taking both drugs were less likely to be admitted to a nursing home during follow-up than were the untreated patients (relative hazard ratios: 0.37 and 0.29, respectively). The risk of nursing home admission was reduced in the combination group by a factor of 3.4 relative to the group taking only ChEIs.

Conclusion: This observational study demonstrates that the addition of an NMDA receptor modulator to a regimen of cholinesterase inhibitors provides benefits above those of cholinesterase alone by extending the time to nursing home admission.

Lopez, O., et al. Long-Term Effects of the Concomitant and Use of Mematine with Cholinesterase Inhibition in Alzheimer's Disease. *J Neurol Neurosurg Psy.* 2009; 80: 600-607.

PEG TUBE REPLACEMENT: ARE X-RAYS NECESSARY?

Percutaneous endoscopic gastroscopy (PEG), first described in 1980, has become a common and relatively safe method of providing long-term enteral feedings. Many believe that the numbers and types of placements of percutaneous feeding tubes continues to increase. It has

been estimated that at least eight percent of these tubes will eventually malfunction. The replacement of a percutaneous feeding tube in the emergency department is associated with some concern about misplacement into the peritoneum, with adverse consequences. The need for a confirmatory x-ray has been debated in the literature. This study sought to determine whether confirmatory x-ray is helpful after PEG tube replacement.

This retrospective chart review included the medical records of all encounters between 12/15/2000 and 3/23/2004. Data were tabulated for those over 18 years of age with a PEG tube requiring replacement. Measurements extracted from the chart included the patient's age, sex, initial date of and reason for the tube placement, reason for the tube replacement, whether an x-ray was completed, whether problems were encountered during tube placement, and whether a dilator was used. Trauma to the tract was defined as any action that placed force or stress on the tract, including the tube being pulled out with the balloon inflated under unknown circumstances, or difficulty with placement.

One hundred thirteen patients met the inclusion criteria. Of those, 42% did not have confirmatory x-rays and 58% had confirmatory x-rays. Among the 66 patients with confirmation by x-ray, 94% of the feeding tubes were in the correct location. Four significant complications occurred (4%). Two patients had intraperitoneal extravasations. One tube was found in the colon and one was found in a gastrocutaneous fistula.

Conclusion: This study of patients with percutaneous feeding tube replacement found that, of 113 patients with tube dislodgment, four were either malpositioned or demonstrated a compromise of the tract. Two patients had intraperitoneal extravasation.

Jacobson, G., et al. Percutaneous Feeding Tube Replacement in the ED -- Are Confirmatory X-Rays Necessary? *Am J Emer Med.* 2009, June; 27: 519-524.

DELIRIUM AFTER HIP FRACTURE

Up to 60% of elderly patients who undergo surgical repair of hip

fractures are found to suffer from postoperative delirium. Symptoms include fluctuation in cognition and consciousness which can last for days. Little is known about the pathophysiology behind this delirium. One possible etiology may be irreversible brain damage secondary to transient neuronal damage. As S100-protein (S100B) and neuron specific enolase (NSE) have been used as markers of brain damage in various diseases, this study compared the levels of these markers in patients undergoing hip fracture surgery

Between 2005 and 2008, patients admitted to an Amsterdam hospital with a diagnosis of hip fracture, who were 65 years of age or older were invited to participate in this study. Delirium was diagnosed using the Confusion Assessment Method. The subjects were then divided by subtype using the Delirium Symptoms Interview. Serum samples were obtained in order to measure levels of S100B and NSE. Those levels were compared to the results of the delirium testing.

One hundred twenty patients were included in this study, 62 of whom experienced delirium. A significant increase in S100B levels was noted among those with delirium, as compared to the non-delirious group ($p < 0.001$). No such association was found between delirium and NSE levels. The levels of S100B were highest during episodes of delirium, though those who did experience delirium had elevated levels both before and after the episodes of delirium.

Conclusion: This study of patients undergoing hip fracture surgery found that S100B may be a biomarker for patients who will experience postoperative delirium

Munster, B., et al. Markers of Cerebral Damage during Delirium in Elderly Patients with Hip Fracture *BMC Neur.* 2009; 9:21.

SACRAL NEUROMODULATION FOR NEUROGENIC LOWER URINARY TRACT SYMPTOMS AFTER INCOMPLETE SPINAL CORD INJURY

In the past, renal failure was the leading cause of death after spinal cord injury (SCI). Today, mortality

following SCI has declined dramatically, due in part to improved management of urologic dysfunction associated with SCI. Sacral neuromodulation (SNM) involves the implantation of a permanent electrode in the third sacral (S3) nerve root, connected to an implantable pulse generator (IPG). This study evaluated the efficacy and complications of treatment with SNM for partial SCI patients, who present with neurogenic lower urinary tract symptoms (NLUTS).

This retrospective study included 24 adults with incomplete SCI, who underwent implantation of SNM with at least twelve months follow-up. Individuals with a known psychiatric disorders, stress incontinence, urologic complications, abnormal urologic anatomy, and elevated creatinine were excluded. The subjects were divided into two groups: those with urinary retention ($n=13$), or overactive bladder ($n=11$). All subjects were followed at one, three, and six months, and thereafter every six months.

The mean follow-up period after implantation was 60.7 months. For those in the urinary retention group, the data revealed a fifty percent improvement in volume per catheterization, the number of clean intermittent catheterizations, urinary frequency, and voided volumes. Among the four patients with loss of efficacy of SNM, this effect was reversed by contralateral nerve root stimulation. The mean lifespan of the IPG was 63 months. In the overactive bladder group, there was a reduction in the daytime frequency. In this group the maximum bladder capacity increased and the mean detrusor pressure during filling decreased. The mean IPG lifespan in this group was 66 months. Twenty-two of the subjects reported adverse events, which all resolved with no significant lasting effects.

Conclusion: This study of patients with incomplete spinal cord injury and neurogenic lower urinary tract symptoms suggests that sacral neuromodulation may be an effective treatment option.

Lombardi, G., et al. Clinical Outcome of Sacro Neuromodulation in Incomplete Spinal Cord Injured Patients Suffering from Neurogenic Lower Urinary Tract Symptoms. *Spinal Cord.* 2009, June; 47(46): 486

THIGH HIGH COMPRESSION STOCKINGS AND THE RISK OF DEEP VEIN THROMBOSIS

Deep vein thrombosis (DVT) and pulmonary embolism are common complications of hospital admissions for surgery or acute medical conditions. Up to 42% of patients admitted with a stroke developed a DVT. Among those interventions meant to reduce this risk are graduated compression stockings and intermittent pneumatic compression devices. This study sought to determine the efficacy of thigh high graded compression stockings in reducing the occurrence of DVTs.

This randomized, controlled trial included 2518 patients hospitalized within one week of an acute stroke. Patients with peripheral vascular disease, subarachnoid hemorrhage or skin issues were excluded. The participants were randomized to receive routine care plus thigh high graduated compression stockings or routine care plus avoidance of graduated compression stockings. A technician blinded to the treatment groups performed bilateral lower extremity ultrasound examinations, first at seven to ten days and then again at 30 days post stroke. The groups were compared for new onset DVT.

A DVT was detected in 126 (10%) of those in the stocking group and 133 (10.5%) in the control group. The use of thigh high, graduated compression stockings was associated with a nonsignificant (0.5%) absolute reduction in the primary outcome. Skin breakdown was significantly more common among patients who wore compression stockings than among those who did not (5.1% versus 1.3%).

Conclusion: This study found that thigh high graduated compression stockings provide no significant reduction in the risk of deep vein thrombosis among patients with new onset stroke.

Dennis, M., et al. Effectiveness of Thigh Length of Graduated Compression Stockings to Reduce the Risk of Deep Vein Thrombosis after Stroke (CLOTS trial 1): A

Multicentre Randomized Controlled Trial, *Lancet*. 2009, May; 373:1958-1965.

POVIDONE-IODINE VS. SALINE FOR EXTERNAL FIXATORS

Since the introduction of distraction osteogenesis by Ilizarov, its indications have been extended to include correction of bone deformity and treatment of nonunion. However, this technique is associated with morbidities, including infection of the contact area at the metal/skin interface. Povidone-iodine is a common antiseptic solution for general wound dressing, despite its inhibitory effect on healing tissue. This study compared infection rates at the metal/skin interface between those lesions using using povidone-iodine and those using saline.

Between 2002 and 2003, 46 males and 16 females underwent distraction osteogenesis using external fixators. The fixators were dressed using either diluted povidone-iodine or saline. All patients were followed up every two weeks for six months. At follow-up visits, the wounds were evaluated based on a grading system which included evidence of infection.

The overall infection rate in the study was eighteen percent. More infections were noted at the pin fixation sites than at the wire fixation sites. The infection rate in the povidone-iodine group was similar to that noted in the saline group..

Conclusion: This study comparing cleansing solutions used for external fixator sites found that normal saline is as effective in preventing infection as is povidone-iodine.

Chan, C., et al. Diluted Povidone-iodine Versus Saline for Addressing Metal Skin Interfaces in External Fixation. *J Ortho Surg*. 2009, April; 17(1):19-22.

VASCULAR SMOOTH MUSCLE DYSFUNCTION AND MIGRAINES

Migraines affect almost 30 million people in the United States. Prospective studies have confirmed that individuals with migraines are at increased risk of cardiovascular events, including myocardial

infarction and ischemic stroke. The mechanistic link between migraine and cardiovascular disorders remains elusive. This study explored the activity of endothelial and vascular smooth muscle cells, as well as major molecular mediators for each, in patients with migraine headaches.

This case control study included 12 patients with migraine, without aura, and 12 matched healthy control subjects. Vascular reactivity was measured by plethymography measures of forearm blood flow (FBF) during infusions of vasoactive agents including acetylcholine and nitroprusside. Laboratory measurements included nitrous oxide and cyclic GMP.

The infusion of acetylcholine elicited an intense vasodilatory response. In patients with migraine however the FBF increase was much lower than in controls ($p < 0.001$). In addition, the dose response curve to nitroprusside, acting on vascular smooth muscle cells, was much less in patients with migraines ($p < 0.001$). Prior to acetylcholine infusion, nitrous oxide and cGMP levels were similar. After infusion, cGMP released from the vascular smooth muscle cells was markedly greater than among those with migraines ($19.1 \text{ nmol dL}^{-1} \text{ min}^{-1}$ versus $1.9 \text{ nmol dL}^{-1} \text{ min}^{-1}$).

Conclusion: This study found that patients with migraine headaches have impaired vascular reactivity that is attributable to vascular smooth muscle cell dysfunction. This may help explain the propensity for cardiovascular disease in this population.

Napoli, R., et al. Vascular Smooth Muscle Cell Dysfunction in Patients with Migraine. *Neur*. 2009, June 16; 72(4):2111-2114.

BRACING, CASTING AND VERTICAL EXPANDABLE RIB FOR INFANT SCOLIOSIS

Infantile idiopathic scoliosis (IIS) represents a small portion of the population of patients with scoliosis. IIS is defined as an idiopathic curve measuring over 20°, diagnosed in a patient under three years of age. Treatments for this disease are limited due to the difficulties accommodating growth and development as well as adequate correction of the curve. This

retrospective study compared the outcomes of the three most common treatments for IIS, bracing, casting and a vertical expandable prosthetic titanium rib (VEPTR) .

Thirty-one consecutive patients diagnosed with IIS were studied. Of these, 17 underwent bracing, 10 received serial body casts, and 10 had VEPTR implantation with serial lengthening procedures. Some of those in the bracing group were subsequently sent for other treatments. Braces were worn for 16 to 23 hours a day with adjustments made as the child grew. Casting was done under general anesthesia and recasting performed every two to three months. The VEPTR was placed through small incisions and attached superiorly to the ribs and inferiorly down to the spine or ilium. This was adjusted every six months.

Most patients were initially treated with bracing or casting and were then referred for surgery when conservative measures failed. Typically, those patients with curves of less than 30° received bracing, while those with angles of 30° to 60° received casting. Those above 60° received VEPTR. Of the three, only bracing failed to control curve progression, observed in nine of 17 of the patients. The ten patients who received body casts had a mean precasting angle of 50.4° and demonstrated an average correction of 59%. The ten patients treated with VEPTR had a mean preoperative angle with 90° with an average correction of 33.8%.

Conclusion: This study of patients with IIS found that bracing alone was effective in fewer than half of the patients. Casting provided excellent maintenance of curve correction with no patient progressing to surgical intervention from this group.

Smith, J., et al. The Role of Bracing, Casting, and Vertical Expandable Prosthetic Titanium Rib for the Treatment of Infantile Idiopathic Scoliosis: a Single Institution Experience with 31 Consecutive Patients. *J Neurosurg Spine*. 2009, July; 11(1):3-8.

ASSOCIATION BETWEEN DIABETES AND ALCOHOL CONSUMPTION

In observational studies relating

individual dietary factors to health outcomes, confounding by dietary components is often controlled by limiting the number of dietary factors. No prior study relating a single food or nutrient to a health outcome has addressed the issue of residual confounding by correlated foods and dietary patterns. Thus this study sought to quantify the potential confounding effect of dietary patterns on the association between alcohol consumption and incident type II diabetes mellitus (DM).

This study used data collected by the Framingham offspring study. During the fifth examination cycle, 3,799 participants underwent a standardized medical examination. Nutrient intake of various foods were calculated by multiplying the frequency of a food item with each prespecified portion size and the nutrient composition for that item. Consumption data included habitual alcohol intake. Individuals who had been diagnosed with type 2 DM at baseline were ineligible for further analyses. Using those data, the authors modeled the longitudinal association between alcohol consumption and the seven-year risk of developing type II DM.

Compared with the abstainers, those with the highest frequencies of alcoholic beverage consumption were less likely to be women, or to have a parental history of DM. They had a lower mean body mass index, dietary glycemic index, and intake of dietary fiber, saturated fats, and trans-fatty acids. Those with the highest frequency of alcohol consumption had significantly higher mean blood concentrations of total cholesterol, high-density lipoprotein, low density lipoprotein, and fasting glucose, as well as higher mean diastolic blood pressure. Results of a Cox proportional hazards regression analysis demonstrated that individuals with a higher frequency of alcoholic beverage consumption had a lower risk of DM. The findings of the crude model and the model adjusted for DM risk factors were 0.45 and 0.47, respectively. However, adjusting for dietary patterns increased this inverse relationship, suggesting that dietary patterns of those who drink enhance the risk of developing diabetes.

Conclusion: This study suggests that alcohol intake, rather than dietary patterns associated with alcohol intake, is responsible for an inverse

association with the risk of developing type II diabetes mellitus.

Imamura, F., et al. Confounding by Dietary Patterns of the Inverse Association between Alcohol Consumption and Type 2 Diabetes Risk. *Am J Epid*. 2009, July 1; 170:37-45.

CARDIOVASCULAR AND GASTROINTESTINAL EVENTS AMONG USERS OF SELECTIVE NSAIDS

Cumulative data have raised concerns about the cardiovascular safety of some of the cyclooxygenase two (COX-2) inhibitors. Few studies however have attempted to balance the cardiovascular and gastrointestinal effects of COX-2 inhibitors and those of the traditional nonsteroidal anti-inflammatory drugs (NSAIDs). The study sought to simultaneously assess cardiovascular and gastrointestinal risks of various NSAIDs

This nested, case control study obtained data from the PHARMO record linkage system. This system includes the drug dispensing records from community pharmacies and hospital discharge records of over 40 demographically defined areas of the Netherlands. In addition, hospital records were reviewed which included detailed information concerning the primary discharge diagnoses and dates of hospital admissions and discharges. Subjects were classified as current users or remote users of the study medications. Medication use was compared to acute myocardial infarction (MI), cardiovascular, and gastrointestinal (GI) events.

A total of 485,059 subjects were studied. Compared to remote use, MI risk was increased among current users of COX-2 inhibitors combined (adjusted odds ratio (OR) 1.73) and traditional NSAIDs combined (OR 1.41). The MI risk with celecoxib (OR 2.53), rofecoxib (OR 1.60), ibuprofen (OR 1.56) and diclofenac (OR 1.51) was significantly increased. The cardiovascular risk with current use of individual COX-2 inhibitors and traditional NSAIDs was significantly increased (OR from 1.17 to 1.64), as was GI risk with current use of rofecoxib (OR 1.99), naproxen (OR 4.44), ibuprofen (OR 1.90), diclofenac (OR 4.77), other traditional NSAIDs

(OR 2.59), but not celecoxib (OR 1.36). Compared to current use of celecoxib, the MI risk was significantly decreased with current use of naproxen (OR 0.48) only. GI risk was increased with current use of naproxen (OR 3.26) and diclofenac (OR 3.50).

Conclusion: This study found that acute MI and other cardiovascular risks increased similarly with both COX-2 inhibitors and traditional NSAIDs. However the risk of gastrointestinal is greater with naproxen and diclofenac than with the COX-2 inhibitors

Van der LINDIN, M et al The Balance between Severe Cardiovascular and Gastrointestinal Events among Users of Selective and Nonselective Nonsteroidal Anti-Inflammatory Drugs. *Ann Rheum Dis.* 2009, May; 668-673.

ACUPRESSURE AND MONTESSORI ACTIVITIES FOR AGITATION

Agitated behavior among cognitively impaired elderly individuals has generated considerable attention over the past several decades. Some have explored non-pharmacologic intervention techniques such as acupressure, Montessori methods, and massage to manage agitation and increased relaxation in patients with dementia. This study explored the efficacy of acupressure and Montessori-based activities in decreasing the agitated behavior of elderly individuals with dementia.

Subjects were chosen from six, long-term special care units for residents with dementia in Taiwan. A total of 133 residents were randomly assigned to different groups to compare the effects of the three different interventions. These groups included acupressure, Montessori methods, and the presence of a visitor. On each intervention day, the residents were given their assigned intervention. Acupressure or the presence of a visitor was introduced in 15 minute sessions once per day, six times per week, for four weeks. The group-based Montessori methods were introduced in 45-minute sessions every day, six days per week for four weeks. Between each intervention period, there was a one-week period of testing, two

weeks of washout, and one-week of pretesting before the next intervention. During each pretest period, baseline data were collected consisting of the cumulative frequency and intensity of agitated behaviors during daytime care activities. During the posttest period, the same cumulative data were collected to determine the effect of the various treatments.

At follow up, the acupressure and Montessori-based groups demonstrated greater decrease in agitation behaviors, aggressive behaviors, and physically nonaggressive behaviors than did the control group. Those results were also reflected in the ease of care ratings. Neither the acupressure nor the Montessori-based activities resulted in decreased verbally agitated behaviors.

Conclusion: This randomized controlled trial of elderly patients with agitated dementia found that a noninvasive, traditional Chinese medicine procedure, acupressure, coupled with a Western activities program could be useful in reducing agitation and aggression.

Lin, L et al. Using Acupressure and Montessori-Based Activities to Decrease Agitation for Residents with Dementia: a Crossover Trial. *J Am Ger Soc.* 2009, June; 57:1022-1029.

CONSTRAINT INDUCED THERAPY AND INFARCT LOCATION

Several studies have suggested that infarct location influences spontaneous recovery of motor function after stroke. Despite these findings, the influence of infarct location on specific motor rehabilitation outcomes remains unclear. As constraint induced therapy (CIT) has been shown to produce functional changes in brain metabolism, blood flow and electric excitability, this study sought to determine whether infarct location can predict motor improvements in chronic stroke patients who are given CIT.

All participants studied had chronic post-stroke upper extremity hemiparesis. Study included two groups of patients: those who received full CIT and those who received attenuated versions of the therapy. The location of the infarct was used to compare groups on

changes in motor scores after CIT.

Full CIT produced significant improvements on the Wolf Motor Function Tests (WMFT) and the Motor Activity Log (MAL) ($p < 0.0001$ and $p < 0.0001$, respectively). Infarction of the centrum semiovale, contralateral to the more affected arm was significantly associated with poorer performance at pretreatment, as measured by the WMFT ($p < 0.004$). However, infarct location was not significantly correlated to treatment outcome as measured by either the WMFT or the MAL.

Conclusion: This study of patients with chronic stroke found that the improvement realized by constraint induced movement therapy is independent of infarct location.

Gauthier, L., et al. Improvement after Constraint Induced Movement Therapy Is Independent of Infarct Location in Chronic Stroke Patients. *Stroke.* 2009, July; 40:2468-2472.

ELECTROACUPUNCTURE AND CEREBRAL EDEMA

While many advances have been made in the pharmacotherapy of stroke, clinical treatment of this disorder is often insufficient. After the discovery of the endogenous cannabinoid system, research has focused on the apparent protective effects of this system against ischemic damage in the heart and brain. In addition, previous research has demonstrated that pretreatment with electroacupuncture (EA) at the Baihui acupoint (GV 20) can induce a rapid tolerance to cerebral ischemic insult. This study, therefore, sought to determine whether the endocannabinoid system is involved in the mediation of neuroprotection resulting from electroacupuncture pretreatment.

Male Sprague-Dawley rats and male 10-week-old C57BL/6 mice were housed under controlled conditions before the study's onset. Two hours after the end of the electroacupuncture pretreatment, focal cerebral ischemia was induced by middle cerebral artery occlusion for 120 minutes. Neurobehavioral scores, infarction volumes, and neuronal apoptosis were evaluated at 24 hours or seven days after reperfusion in the presence or absence of a selective cannabinoid receptor antagonist, AM251.

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Electroacupuncture pretreatment reduced the size of the infarction, and improved neurological recovery to a significantly greater extent than did the control condition. In addition, those treated with electroacupuncture demonstrated inhibited neuronal apoptosis at 24 hours and at seven days after reperfusion. These beneficial effects were blocked by the introduction of AM251. Acupuncture pretreatment was found to upregulate the expression of aCB1 receptors in the brain and elevate the brain tissue content of an endocannabinoid in the brain.

Conclusion: This animal study demonstrates that, if introduced before cerebral ischemia, electroacupuncture can reduce the consequences of cerebral infarction, through its effect on the endocannabinoid system.

Wang, Q., et al. Pretreatment with Electroacupuncture Induces Rapid Tolerance to Focal Cerebral Ischemia through Regulation of Endocannabinoid System. *Stroke*. 2009; June 1 40:2157-2164.

Rehab in Review is a monthly publication produced by physicians in the field of Physical Medicine and Rehabilitation (PM&R). The summaries appearing in this publication are intended as an aid in reviewing the broad base of literature relevant to this field. These summaries are not intended for use as the sole basis for clinical treatment, or as a substitute for the reading of the original research.

Rehab in Review is produced with the cooperation and assistance of Emory University School of Medicine, Department of Rehabilitation Medicine. *Rehab in Review* is affiliated with the Association of Academic Physiatrists, the World Health Organization and the Chinese Society of PM&R. Funding for academic training subscriptions is provided by corporate sponsorship.

Private subscriptions are available by mail at P.O. Box 183, Lampe, MO 65681, or by fax or phone at (800) 850-REVU (7388).

ISSN # 1081-1303



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