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## TANEZUMAB FOR OSTEOARTHRITIC PAIN

Approximately 12% of adults in the United States develop osteoarthritis (OA). Nonsteroidal anti-inflammatory drugs and opioid analgesics are commonly used, although these medications often result in an unsatisfactory therapeutic response. Nerve growth factor (NGF) is a neurotrophin that modulates pain processing and sensitivity. Tanezumab is a humanized monoclonal antibody that targets NGF, inhibiting NGF from activating receptors on pain signaling neurons. This large study evaluated the safety and efficacy of tanezumab in patients with OA of the hip.

This double-blind, placebo-controlled, phase III trial randomized patients to receive intravenous tanezumab at 2.5 mg, 5 mg, 10 mg, or a placebo. The medication was administered at baseline, week eight and week 16. The patients were assessed with the WOMAC Pain and Physical Function subscale scores, as well as by patient global assessment of OA. All participants were followed until week 32.

Of the patients randomized, 621 received the study medication. At week 16, treatment with the tanezumab 2.5 mg, 5 mg and 10 mg produced greater, clinically meaningful improvement for each of the primary endpoints relative to placebo ( $p < 0.001$  for all comparisons). The greatest benefits were seen in the 5 mg and 10 mg treatment groups. Of the subjects, 4.3% of the treatment patients and 3.2% of the placebo patients were categorized as having a new or worsening peripheral neuropathy. The most common of these was carpal tunnel syndrome.

**Conclusion:** This study of patients with hip osteoarthritis found that tanezumab at each of three doses was superior to placebo for the treatment of pain, physical function

and patients' global assessment of OA.

Brown, M., et al. Tanezumab Reduces Osteoarthritic Hip Pain: Results of a Randomized, Double-Blind, Placebo-Controlled Phase III Trial. *Arth Rheum.* 2013, July; 65(7): 1795-1803.

## TANEZUMAB VERSUS NAPROXEN FOR CHRONIC LOW BACK PAIN

Over two thirds of all adults experience an episode of low back pain (LBP) in their lifetime. Treatment of LBP is a difficult clinical problem, with treatment approaches including pharmacologic and nonpharmacologic methods. Tanezumab is a humanized monoclonal antibody which inhibits nerve growth factor, a key mediator in the generation and potentiation of pain signals. This study compared the effects tanezumab with those of a nonsteroidal anti-inflammatory drug, naproxen, for the treatment of LBP.

This large, randomized, double-blind, placebo controlled, parallel group phase 2B study involved 1347 patients with chronic LBP. Eligible patients were randomized to receive either tanezumab at five, 10 or 20 mg every eight weeks, naproxen at 500 mg twice daily or a placebo. The primary efficacy endpoint was the mean change in daily average LBP intensity from baseline to week 16. Secondary endpoints included the change from baseline to week 16 in Roland Morris Disability Questionnaire scores and in patients' global assessments of LBP.

Efficacy was similar with tanezumab 20 mg and 10 mg, with both showing significantly greater improvements than with either placebo or naproxen in the primary efficacy endpoint, as well as both key secondary endpoints. Adverse events were similar across all tanezumab doses, but higher than with placebo

or naproxen. The most common of these were arthralgia, pain in an extremity, headache and paresthesias.

**Conclusion:** This study of patients with chronic low back pain found intravenous tanezumab to be superior to naproxen for the improvement of pain, function and global assessment scores.

Kivitz, A., et al. Efficacy and Safety of Tanezumab versus Naproxen in the Treatment of Chronic Low Back Pain. *Pain* 2013, July; 154(7): 1009-1021.

## CARDIAC BENEFITS OF LIFESTYLE CHANGES FOR DIABETICS

The recommendation for weight loss for overweight patients with type II diabetes is based on short-term studies demonstrating numerous benefits. However, it is unknown whether weight loss reduces the risk of cardiovascular morbidity and mortality in patients with type II diabetes. This study was designed to determine whether an intensive lifestyle intervention designed to achieve weight loss through calorie restriction and activity enhancement reduces cardiovascular morbidity and mortality among patients with type II diabetes.

This study included 5,104 overweight or obese patients with type II diabetes. The subjects were randomized to an intervention group or to a control group. The intervention group underwent individual counseling sessions, with a goal of 1,200 to 1,800 kcal per day, and at least 175 minutes of moderate-intensity physical activity per week. The control group received diabetes support and education. The primary endpoint was the first occurrence of a composite cardiovascular outcome, including death from cardiovascular causes, nonfatal myocardial infarction

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or non-fatal stroke, during the 13.5-year follow-up period.

The average age of the subjects was 58.7 years, with a mean body mass index of 36, with 60% women. The median duration of diabetes was five years, with 14% of the patients reporting a history of cardiovascular disease. The study was stopped at 9.6 years after the interim analysis revealed no significant, between-group difference in the composite primary outcome and no significant between-group differences in the secondary outcomes.

**Conclusion:** This study of patients with type II diabetes found that intensive lifestyle intervention focusing on weight loss and increased exercise does not reduce the rate of cardiovascular events.

The Look AHEAD Research Group. Cardiovascular Effects of Intensive Lifestyle Intervention in Type II Diabetes. *N Eng J Med.* 2013, July 11; 368: 145-154.

### **BLOOD PRESSURE TELEMONITORING**

Hypertension is the most common, chronic condition for which patients visit primary care physicians, affecting approximately 30% of adults in the United States. This study was designed to determine the effect and durability of home blood pressure (BP) telemonitoring with pharmacist case management.

Patients with a history of elevated BP at their two most recent primary care visits were identified. Those subjects were randomized to receive either usual care (n=222) or home BP telemonitoring. The telemonitoring group initially met with a pharmacist for instruction regarding the BP telemonitoring system. The patients transmitted six BP measurements weekly, three in the morning and three in the evening. All subjects met with the pharmacist by telephone every two weeks until BP was sustained for six weeks, with the frequency then reduced to monthly. The usual care patients worked with their primary care physicians as they had in the past. All patients visited the research clinic for study enrollment, and at six, 12 and 18 months after baseline for follow-up.

At six months, BP was controlled in 71.8% of the telemonitoring group and in 45.2% of the usual care group

(p<0.001). At 12 months, BP was controlled in 71.2% of the telemonitoring group and in 52.8% of the usual care group (p=0.005). Finally, at 18 months, BP was controlled in 71.8% of the telemonitoring group and in 57.1% of the usual care group (p=0.003).

**Conclusion:** This randomized, clinical trial found that telemonitoring blood pressure to a pharmacist, with pharmacist medication adjustments, results in better blood pressure control than usual care through a physician's office.

Margolis, K., et al. Effect of Home Blood Pressure Telemonitoring and Pharmacist Management on Blood Pressure Control. A Cluster Randomized, Clinical Trial. *JAMA.* 2013, July 3; 310(1): 46-56.

### **ASPIRIN PLUS PLAVIX FOR STROKE PREVENTION**

After a transient ischemic attack or a stroke, the risk of a subsequent stroke is estimated to be approximately 10-20% within the initial three months. The role of antiplatelet therapy for secondary stroke prevention has been well established. As aspirin and clopidogrel work synergistically to inhibit platelet aggregation, this study assessed the efficacy of this combination for stroke prevention.

Subjects were patients 40 years of age or older, each diagnosed with acute minor ischemic stroke or a transient ischemic attack. The patients randomized to an aspirin group received a placebo version of clopidogrel on days one through 90, and aspirin at a dose of 75 mg per day on days two through 90. Both groups received open-label aspirin on day one. Those randomly assigned to a combination group received a loading dose of 300 mg of clopidogrel on day one, followed by a dose of 75 mg per day on days two through 90, aspirin at a dose of 75 mg per day on days two through 21, and placebo aspirin on days 22 through 90. The primary outcome measure was a new ischemic or hemorrhagic cerebrovascular accident within 90 days. The primary safety outcome measure was the occurrence of a moderate to severe bleeding event.

Of the patients randomized to the combination group, 8.2% experience a stroke, compared with 11.7% in the

aspirin group ( $p<0.001$ ). Ischemic stroke occurred in 7.9% of the combination group and in 11.4% of the aspirin group ( $p<0.001$ ). Hemorrhagic stroke occurrence did not differ between groups. The composite outcome of vascular events occurred in 8.4% of the combination group, as compared with 11.9% in the aspirin group ( $p<0.001$ ). Moderate or severe hemorrhage rates did not differ between the two groups.

**Conclusion:** This study of patients with a recent transient ischemic attack or minor ischemic stroke found that combining clopidogrel and aspirin is more effective than aspirin alone in decreasing subsequent stroke rates in the first 90 days.

Wang, Y., et al. Clopidogrel with Aspirin and Acute Minor Stroke or Transient Ischemic Attack. **N Eng J Med.** 2013, July 4; 369(1): 11-19.

#### ASPIRIN VERSUS HEPARIN FOR PROPHYLAXIS AFTER HIP ARTHROPLASTY

Venous thromboembolism (VTE) prophylaxis after total hip arthroplasty (THA) has been shown to reduce morbidity and mortality. Given the cost and complications of extended prophylaxis with low molecular weight heparins, this study compared the efficacy of aspirin to that of low molecular weight heparin for patients undergoing THA.

This multicenter, randomized, controlled trial included 778 patients undergoing elective unilateral THA. The morning after surgery, all patients received 5,000 units of dalteparin once daily for 10 days. Between postoperative days eight and 10, patients were randomly assigned to either continue receiving dalteparin or to receive 81 mg of aspirin for 20 days. The primary outcome measure was the development of symptomatic proximal deep vein thrombosis in the lower extremity or a pulmonary embolism, confirmed by objective testing within 90 days.

During the follow-up period, five patients in the treatment group and one in the aspirin group had a symptomatic event. The analysis found aspirin to be noninferior ( $p<0.001$ ), but not superior ( $p=0.22$ ), to dalteparin.

**Conclusion:** This study found that extended prophylaxis for 28 days with aspirin was as safe and as effective as dalteparin for the prevention of VTE for patients with THA who were initially treated for 10 days with dalteparin.

Anderson, D., et al. Aspirin versus Low Molecular Weight Heparin for Extended Venous Thromboembolism Prophylaxis after Total Hip Arthroplasty. **Ann Int Med.** 2013, June 4; 158(11): 800-806.

#### TREATMENT OF CALCIFIC TENDINITIS OF THE ROTATOR CUFF

Calcific tendinitis of the rotator cuff (RCCT) is reported to have a prevalence of 6.8-54% in patients with shoulder pain. Needling, lavage (barbotage) and subacromial injections of the bursa (SAI) are among the more commonly used treatments. This study compared barbotage and SAI for the treatment of RCCT.

This multicenter, double-blind, randomized, controlled trial included patients with shoulder pain and calcifications of  $>3$  mm in size on standard anteroposterior (AP) radiographs. The patients were randomized to receive either ultrasound (US)-guided barbotage, in combination with SAI (group 1) or US-guided SAI only (group 2). Shoulder function was assessed at baseline and at six, 12, 24 and 144 months. Assessments were completed with the Constant Shoulder Score, the Western Ontario Rotator Cuff Index and the Disabilities of the Arm, Shoulder and Hand Questionnaire (DASH).

At one-year follow-up, the mean Constant Score for group 1 was 86 and that for group 2 was 73.9 ( $p=0.005$ ). The mean size of the calcifications decreased by an average of 11.6 mm in group 1 and 15.1 mm in group 2 ( $p=0.001$ ).

**Conclusion:** This study of patients with rotator cuff calcific tendinitis found that treatment with barbotage, in combination with subacromial injections of the bursa (SAI), is superior to SAI alone.

De Wille, P., et al. Calcific Tendinitis of the Rotator Cuff. A Randomized, Controlled Trial of Ultrasound Guided Needling and Lavage versus

Subacromial Corticosteroids. **Am J Sports Med.** 2013, July; 41(7):1665-1173.

#### VITAMIN D AND PHYSICAL PERFORMANCE

An increasing body of evidence suggests multiple roles for the vitamin D. One tissue regulated by vitamin D is skeletal muscle. This study examined the effects of vitamin D supplementation on physical performance.

Volunteer subjects were 30 club-level athletes in Great Britain, all of whom were tested between October and April at latitude 53° north. All athletes were assessed for physical performance with the vertical jump, 20 m sprints, a one-repetition max bench press and a one-repetition max leg press. Resting venous blood samples were drawn for 25 (OH) D measurement. The subjects were then allocated to groups by block randomization, based upon baseline total 25 (OH) D levels. The participants then received either 20,000 or 40,000 IU vitamin D3 or a placebo once a week for 12 weeks. The performance tests were repeated at six and 12 weeks.

At baseline, 57% of the subjects were found to be vitamin D deficient. At 12 weeks, no significant changes were noted on any of the physical performance variables (1-RM-BP,  $p=0.17$ ; 1-RM leg press,  $p=0.18$ ; vertical jump,  $p=0.90$  and 20-meter sprint,  $p=0.64$ ).

**Conclusion:** This study of athletes with vitamin D deficiency did not demonstrate improved physical performance after vitamin D supplementation.

Fraser, D., et al. The Effects of Vitamin D3 Supplementation on Serum Total 25(OH)D Concentration and Physical Performance: A Randomized, Dose-Response Study. **Br J Sport Med.** 2013, July; 47(11): 692-697.

#### BEE VENOM ACUPUNCTURE FOR ADHESIVE CAPSULITIS

Adhesive capsulitis (AC) has been estimated to affect two to five percent of the population 40 to 60 years of age. Among the interventions used to augment manual physical therapy (PT), bee venom acupuncture (BVA)

has been suggested as an alternative for those for whom corticosteroids are not suitable. This study examined whether the addition of BVA to PT is more effective than PT alone in the management of AC.

Patients with a diagnosis of AC who were at least 18 years of age and who had a symptom duration of between one and 12 months were enlisted. All subjects received PT three times per week. The participants were also told to perform home exercises twice daily. In addition, the patients were randomized to receive BVA (in one of two doses, BV1 or BV2) or normal saline (NS) injected at each acupuncture point. The primary outcome measure was the Shoulder Pain and Disability Index (SPADI). Secondary measures included scores on a pain visual analogue scale (VAS).

At eight weeks, all three groups demonstrated significant improvement on the SPADI. The BV1 group demonstrated significantly better improvement, as compared to the NS group, at eight and 12 weeks after treatment initiation ( $p=0.025$  and  $p=0.014$ , respectively). The BV1 group further demonstrated significantly better VAS scores at rest at week eight and in motion at week 12. No significant differences were seen between the BV1 and BV2 subjects on either measure.

**Conclusion:** This study of patients with adhesive capsulitis found that bee venom acupuncture can augment physical therapy in improving pain and disability.

Koh, P., et al. Clinical Effectiveness of Bee Venom Acupuncture and Physiotherapy in the Treatment of Adhesive Capsulitis: A Randomized, Controlled Trial. *J Shoulder Elbow Surg.* 2013, August; 22(8): 1053-1062.

#### RETURN TO PLAY AFTER ANTERIOR CRUCIATE LIGAMENT RECONSTRUCTION

The anterior cruciate ligament (ACL) is commonly injured through a noncontact mechanism during sports participation. ACL reconstruction surgery is performed to allow a safe return to sports activity. This study was designed to determine whether there is a consensus concerning the factors used to determine return to

sport participation among experienced orthopedic surgeons.

A survey concerning return to play after ACL reconstruction was sent to all 274 qualified instructors of arthroscopy in Germany. The survey included six questions about recommendations for returning to competitive sports, training, sport specific rehabilitation, strengthening exercises, return to competitive level I sports and the use of clinical scores to make these decisions.

Of the 274 questionnaires mailed, 221 responded, resulting in a response rate of 80.6%. Of the surgeons surveyed, 35.3% allowed return to competitive sports at six months and 30% after eight months. A total of 63.5 % recommended a time point later than six months. Also among those surgeons, 48.6% recommended beginning training after four months and 44% after six months. The majority, 76.6%, recommended sport specific rehabilitation after four months. The most frequent criterion to allow return to sport was a negative Lachman test result (81.7 %), followed by free range of motion (78.4 %) and a negative pivot shift (60.1 %) finding. Over 80% reported that they did not use clinical scores to make return to play decisions.

**Conclusion:** This survey of experienced, German arthroscopic surgeons found that the majority who perform anterior cruciate ligament reconstruction do not consider muscle function, jump tests, alignment tests and proprioception when considering return to sports.

Petersen, W., et al. Return to Play following ACL Reconstruction: Survey among Experienced Arthroscopic Surgeons (AGA Instructors). *Arch Orthop Trauma Surg.* 2013, July; 133(7): 969-977.

#### SURGERY FOR HORIZONTAL MENISCAL TEAR

Horizontal tears of the meniscus are often considered to be degenerative, and occur more commonly in late middle age. This investigation compared the clinical results of arthroscopic meniscal repair with nonoperative treatment of horizontal tears of the posterior horn of the medial meniscus.

Subjects were 102 patients with knee pain and a degenerative

horizontal tear of the posterior horn of the medial meniscus. Fifty patients underwent arthroscopic meniscectomy and 52 were treated with strengthening exercises. The functional outcomes included Lysholm knee scores, Tegner Activity Scale scores, pain assessed using a visual analogue scale (VAS), activity, and satisfaction scales, as well as radiographic findings.

At two-year follow-up, the average VAS scores were 1.8 in the surgery group and 1.7 in the nonoperative group. Pain in the meniscectomy and nonoperative group was completely relieved in 34 of the surgical and 35 of the conservative group, improved in 13 and 12 patients, and persisted in 3 and 5 patients, retrospectively. Patient satisfaction did not differ significantly between the two groups ( $p=0.357$ ). The average Lysholm knee scores were 83 in the surgery group and 84.3 in the nonoperative group ( $p=0.237$ ). The average Tegner Activity Scale score improved in both groups, without a significant difference between the groups ( $p=0.522$ ).

**Conclusion:** This study of patients with degenerative meniscal tears found no significant difference between those treated surgically and those treated nonsurgically in measures of knee pain, knee function and patient satisfaction.

Yim, J., et al. A Comparative Study of Meniscectomy and Nonoperative Treatment for Degenerative Horizontal Tears of the Medial Meniscus. *Am J Sport Med.* 2013, July; 41(7): 1565-1570.

#### ENZOGENOL FOR TRAUMATIC BRAIN INJURY

Traumatic brain injury (TBI) leads to persistent cognitive deficits which may profoundly impact social function and employability. Previous studies suggest a link between oxidative stress and excitotoxicity following TBI, further suggesting that antioxidants may assist in recovery by decreasing oxidative damage. This study examined the safety and effects of a flavonoid extract on cognitive functioning in patients with mild TBI.

This randomized, controlled trial involved 60 adults who met the inclusion criteria for mild TBI, three to 12 months post-injury at enrollment. The patients were 18 to 64 years of

age and reported persistent cognitive deficits. This three-phase trial compared 1,000 mg per day of oral enzogenol with a placebo. Participants were assessed at six, 12 and 16 weeks with a set of well-validated tests to evaluate cognitive functioning (primarily memory), post-concussion symptoms and mood.

Greater reductions in self-reported cognitive failures were found in the enzogenol group as compared with the placebo group after six weeks (a 28% change versus a 22% change, respectively). Improvement in the frequency of self-reported cognitive failures continued until week 11 before stabilizing.

**Conclusion:** This pilot study suggests that the flavonoid, enzogenol, is safe and well tolerated, and may improve cognitive function in patients with mild traumatic brain injury.

Theadom, A., et al. Enzogenol for Cognitive Functioning in Traumatic Brain Injury: A Pilot Placebo-Controlled RCT. *Europ J Neur*. 2013, August; 20(8): 1135–1144.

### POSTTRAUMATIC MIGRAINE AS A PREDICTOR OF RECOVERY AFTER CONCUSSION

Common symptoms of athletes with concussions include headache, dizziness, difficulty with concentration, confusion and visual changes. Previous studies have suggested that posttraumatic migraine symptoms occurring early after concussion may indicate a more severe injury. This study sought to better understand the relationship between posttraumatic migraine and recovery time after concussion.

This multisite trial included male, high school football players diagnosed with sport related concussion. The subjects were followed over time for symptom resolution, with participants classified as those with rapid (<7days), versus those with prolonged (>21 days) recovery. The two groups were compared for headache type, cognitive performance and symptoms.

Of the athletes, 56 were in the posttraumatic migraine (PTM) group, 63 were in the headache group and 19 were in the no headache group. The PTM group performed worse in verbal memory than did the headache

only group at eight to 14 days post-injury. The PTM group performed worse in visual memory than did the other two groups at one to 14 days post-injury. The PTM group also performed worse on reaction time than did the other two groups at days one to 14.

The PTM group further scored significantly higher on all four of the symptom factors (cognitive, somatic, emotional and sleep) than did the headache and no headache groups throughout the course of recovery (one to 14 days). The PTM group had 7.3 times and 2.6 times increased risk of a protracted recovery than the no headache and headache groups, respectively.

**Conclusion:** This study of athletes with concussions found that posttraumatic migraine is associated with cognitive impairments and protracted recovery times but that headache without migraine symptoms was not a predictor of recovery.

Kontoa, A., et al. Posttraumatic Migraine as a Predictor of Recovery and Cognitive Impairment after Sport-Related Concussion. *Am J Sport Med*. 2013, July; 4(7): 1497-1504.

### RECOVERY OF POSTTRAUMATIC MIGRAINE

Headache is the most commonly reported symptom after a concussion. This study compared athletes with concussions who presented with versus without posttraumatic migraines.

The study included 344 student-athletes between the ages of 12 and 25 years of age, all of whom had sustained a mild traumatic brain injury (TBI) during athletic competition. Subjects were included in a posttraumatic migraine group if they reported the presence of headache, nausea and either photophobia or phonophobia on the day after the concussion. Patients reporting headaches without other migraine like symptoms were classified as a headache group. Those not reporting headaches were placed in a no headache group.

Testing was completed for all subjects using the Balance Error Scoring System, the Standardized Assessment of Concussion and a graded symptom checklist to evaluate balance performance, cognition and symptoms at baseline, at the time of

injury, after the event and at days one, two, three, five, seven and 90.

Patients with posttraumatic migraine obtained greater symptom severity scores than did headache and no headache patients at the time of injury, after the event and through day seven ( $p<0.001$  for all comparisons). No significant differences between the headache and no headache groups were observed beyond day three. Further, no group differences were seen in balance performance ( $p=0.43$ ) or cognitive testing ( $p=0.200$ ) over time. Female patients were 2.13 times more likely than males report posttraumatic migraine following concussion.

**Conclusion:** This study of patients with concussion found that athletes suffering from posttraumatic migraine take longer to recover from overall symptom severity than do those experiencing simple posttraumatic headaches or no headaches.

Mihalik, J., et al. Recovery of Posttraumatic Migraine Characteristics in Patients after Mild Traumatic Brain Injury. *Am J Sport Med*. 2013, July; 41(7): 1490-1496.

### SCHEDULED ANALGESIA FOLLOWING HIP FRACTURE SURGERY IN THE ELDERLY

After hip fracture in the elderly, early mobilization is known to decrease the incidence of pulmonary complications, deep venous thrombosis and pressure ulcers. However, pain has been found to hinder early mobilization. This prospective study compared patients with hip fracture using a medication schedule versus an as-needed pain medication management strategy.

Subjects were 400 patients ages 65 or older with a diagnosis of femoral neck, trochanteric or subtrochanteric fracture. All patients underwent arthroplasty or internal fixation. The participants were randomized to a group to receive scheduled analgesia, including Tramadol, 50 mg, and paracetamol, five mg, three times a day for the first three weeks, or to a control group administered the same medication PRN up to six times per day. Outcome measures included resting and dynamic pain intensity, mobility and functional performance.

At discharge, the scheduled analgesic group had higher ambulatory status, less wheelchair mobility and higher functional performance than did the control group. Both groups improved in resting and dynamic pain intensity, as well as postoperative pain.

**Conclusion:** This study of 400 elderly patients undergoing hip fracture surgery found that a scheduled regimen of pain medications, three times per day for three weeks, facilitates mobility and functional outcomes better than does pain medication scheduled on an as-needed basis.

Chin, R., et al. Scheduled Analgesic Regimen Improves Rehabilitation after Hip Fracture Surgery. **Clin Ortho Rel Research**. 2013, July; 471 (7): 2349–2360.

### **BALLOON KYPHOPLASTY FOR VERTEBRAL COMPRESSION FRACTURE**

Vertebral compression fractures affect 1.4 million individuals worldwide each year. Balloon kyphoplasty is a percutaneous surgical treatment designed to correct the vertebral deformity. This study sought to better understand the effect of this procedure on patients with vertebral compression fractures.

Patients with acute, painful vertebral fracture were enrolled. In the surgical arm of this study, balloon kyphoplasty was performed within 10 days following study entry, with the conservative group treated with analgesics, bed rest, bracing, physical therapy, rehabilitation and walking aids. Outcomes were assessed with subjective quality of life measures and objective function with the Timed Up and Go test.

Compared to the conservative group (n=151), the kyphoplasty group (n=149) demonstrated greater improvement on the SF-36 Physical Component summary scores at one month and at 24 months ( $p<0.001$  for both comparisons). In addition, greater mobility was found in the kyphoplasty group on the Timed Up and Go Ability Test ( $p=0.0036$ ). Greater improvement was also noted in kyphotic angulation as compared with the control group, with this finding maintained at 24-month follow-up.

**Conclusion:** This large, randomized trial of patients with vertebral fractures demonstrates that balloon kyphoplasty reduces pain and improves function better than does conservative treatment.

Van Meirhaeghe, J., et al. A Randomized Trial of Balloon Kyphoplasty and Nonsurgical Management for Treating Acute Vertebral Compression Fractures: Vertebral Body Kyphosis Correction and Surgical Parameters. **Spine**. 2013, May 20; 38(12): 971-983.

### **LOCAL LIDOCAINE FOR CHRONIC TENSION HEADACHE**

Patients with tension type headaches frequently report restrictions in daily activities. Studies concerning the central versus peripheral mechanisms of these headaches have suggested a combination of these factors. This study was designed to determine whether local lidocaine injections are effective in treating the sequelae of these headaches.

This randomized, double-blind placebo-controlled trial involved 40 patients diagnosed with chronic, tension type headaches. The participants were randomized to a treatment group, which received local lidocaine injections, or a control group, receiving local saline injections. The injections were every three days at the superior cervical ganglion, trigger points of muscles innervated by C1 to C3, trigeminal nerves and the exit point of cranial nerve five. Patients had one session every three days for three sessions. The subjects were evaluated for three months after the treatment for the number of painful days within a month, severity of pain, assessed on a visual analogue scale, number of analgesic drugs used in a month, Hamilton Depression Scale Scores and Hamilton Anxiety Scale Scores.

Compared with the placebo group, the lidocaine group had a significant decrease in the number of painful days, the number of analgesic tablets used, pain scores and depression and anxiety scores ( $p<0.001$  for all comparisons). No serious side effects were found for either treatment.

**Conclusion:** This study of patients with chronic, tension type headaches found that local lidocaine

injections may significantly improve pain, as well as anxiety and depression, associated with these headaches.

Karadas, O., et al. Efficacy of Local Lidocaine Application on Anxiety and Depression and its Curative Effect on Patients with Chronic, Tension Type Headache. **Euro Neurol**. 2013; 70(1-2): 95-101.

### **GRADUAL VERSUS ABRUPT SMOKING CESSATION**

The deleterious effects of tobacco abuse are well known, as is the difficulty with successful cessation. Based upon observational studies, the U.S. Food and Drug Administration recommends that smokers quit abruptly. However, strategies for gradual cessation remain popular. This literature review explored the evidence comparing those two approaches to tobacco cessation.

This literature review included 10, randomized, controlled trials between 1978 in 2000, including 3,760 participants, averaging 42.8 years of age. The primary outcome measures were smoking abstinence at least six months after cessation, with biochemical verification provided in 10 of the studies.

The data revealed that gradual quitting was 21% less successful than was abrupt cessation. In a real-life setting, smokers quitting abruptly with support can expect a 15% success rate. Those who use the gradual method can anticipate a 14.1% success rate. Of the studies that used nicotine replacement as a cessation aide, no serious adverse events were reported.

**Conclusion:** This literature review suggests that abrupt cessation is superior to gradual cessation as a treatment strategy for those who wish to discontinue tobacco abuse.

Lindson-Hawley, N., et al. Gradual Reduction versus Abrupt Cessation as a Smoking Cessation Strategy in Smokers Who Want to Quit. **JAMA**. 2013, July 3; 310(1): 91–92.

### **INSULIN PUMP INTERRUPTION TO REDUCE HYPOGLYCEMIA**

Sensor augmented insulin pump therapy is thought to offer substantial

glycemic benefits as compared with daily insulin injections. A new pump, with low glucose suspend features, has been available outside the United States since 2009, and is under review by the FDA. This study investigated the effects of the threshold-suspend feature with sensor-augmented insulin pump therapy in patients with documented nocturnal hypoglycemia.

Subjects were patients 16 to 70 years of age with type I diabetes of at least two years' duration. All participants had used insulin pump therapy for more than six months, and had documented nocturnal hypoglycemia. The subjects were randomized to receive either sensor-augmented insulin pump therapy with the threshold-suspend feature (threshold-suspend group) or standard sensor-augmented insulin pump therapy (control group). The primary safety endpoint was the change in the glycated hemoglobin level from randomization to study end. The primary efficacy endpoint was the area under the curve (AUC) for nocturnal hypoglycemic events.

The threshold suspend group had significantly lower weekly rates of both nighttime hypoglycemia events and combined daytime and nighttime events than did the control group ( $p < 0.001$  for both comparisons). The change in the glycated hemoglobin level from randomization to study end was negligible in both groups. Four patients in the control group had a severe hypoglycemic event, with none occurring in the threshold suspend group.

**Conclusion:** This study of patients with diabetes and a history of nocturnal hypoglycemia found that the use of a sensor augmented insulin pump with threshold suspend features can reduce nocturnal hypoglycemia without increasing glycated hemoglobin values.

Bergental, R., et al. Threshold-Based Insulin Pump Interruption for Reduction of Hypoglycemia. *N Eng J Med*. 2013, July 18; 369: 224-232.

### FEMOROACETABULAR IMPINGEMENT IN HEALTHY ADULTS

Femoral acetabular impingement (FAI) is now recognized as a risk factor for early hip osteoarthritis. The pain of FAI can be reproduced by a

positive clinical test for anterior impingement. This study was designed to determine the association between the findings using this clinical test and clinical and radiographic findings among young, healthy adults.

Medical and functional status questionnaires were distributed to 2,344 volunteers, ages 18 to 20 years. A clinical hip examination was performed, including the impingement test and hip ROM, as well as two pelvic radiographs.

A positive FAI was found in 7.3% of men and 4.8% of women. Decreased hip flexion in women and men ( $p = 0.003$  and  $p = 0.062$ ), and abduction ( $p = 0.018$ ) and internal rotation ( $p = 0.001$ ) for men were associated with positive impingement tests. Strong associations were seen between FAI and self-reported hip discomfort in women ( $p < 0.001$ ), and increased physical exercise in men ( $p = 0.001$ ). Radiographic cam-type findings were associated with positive impingement testing in men, with no such association found in women.

**Conclusion:** This study found that a positive test for anterior impingement is not uncommon among young, healthy adults, with this finding associated with increased physical activity in men and self-reported hip discomfort in women.

Laborie, L., et al. Is a Positive Femoral Acetabular Impingement Test a Common Finding in Healthy, Young Adults? *Clin Orthop Rel Res*. 2013, July; 471(7): 2267-2277.

### PRESSURE ULCER TREATMENT STRATEGIES

Pressure ulcers are thought to affect three million adults in the United States. Healing rates depend upon comorbid conditions, clinical interventions, and also severity. This study compared the effectiveness of various treatment approaches. A literature search reviewed relevant articles concerning randomized trials and comparative observational studies of treatments for pressure ulcers. The studies were reviewed for quality, with the data synthesized for analysis.

This literature review found 174 studies that met the inclusion criteria. Among those were 24 studies of support surfaces, 16 concerning nutrition, 89 examining local wound

applications, six reviewing surgical intervention and 34 involving adjunctive therapies.

From those studies, no significant differences were found in complete wound healing when comparing types of support surfaces, although moderate-strength evidence was found indicating that wound improvement was superior with air-fluidized beds, as compared to regular hospital beds. Healing was similar between alternating pressure mattresses and other support surfaces.

Among the nutrition articles, most of the studies of protein supplementation found greater reductions in ulcer size with supplementation, although no greater complete wound healing. No significant benefit was found with vitamin C or zinc supplementation. Of the wound dressings, some evidence suggested a superiority of Hydrocolloid dressings, although complete wound healing was equivalent with foam and hydrocolloid dressings. Radiant heat dressings produced a more rapid reduction in size than did other dressings. Moderate-strength evidence showed that electrical stimulation improved healing rate, although the effect on complete healing was unclear.

**Conclusion:** This meta-analysis found that pressure ulcer healing can be improved by the use of air fluidized beds, protein supplementation, electrical stimulation and radiant heat dressings.

Smith, M., et al. Pressure Ulcer Treatment Strategies: A Systematic, Comparative Effectiveness Review. *Annals Intern Med*. 2013, July 2; 159: 39-50.

### AUTONOMIC DYSFUNCTION IN THE CRITICALLY ILL

The extent to which critical illness neuropathy affects the autonomic nervous system is poorly understood. Cardiovascular autonomic dysfunction has been implied by decreased heart rate variability (HRV) in patients in the intensive care unit (ICU). This study was designed to better understand the frequency of dysfunction and feasibility of performing specific tests of autonomic dysfunction in the ICU.



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Twelve, critically ill patients were recruited from a tertiary ICU, with 12 hospital staff recruited as control subjects. Patients excluded from participation had neuromuscular disease, stroke, spinal cord injury or a history of polyneuropathy or autonomic neuropathy. Tests of autonomic function included the cold face test (CFT) and the skin wrinkle test (SWT). The CFT involved applying a cold pack to the forehead and measuring a decrease in heart rate mediated by the vagal nerve. The SWT measured peripheral sympathetic nerve fiber function by assessing wrinkle formation of the fingertips.

Of the 10 patients tested, the CFT was abnormal in nine. The SWT was performed in 11 patients, with an abnormal response found in six. Heart rate variability was found to be abnormal in all 12 patients.

**Conclusion:** This study of intensive care unit patients found that the cold face test and the skin wrinkle test are feasible, and may be used for the evaluation of autonomic dysfunction among these patients.

Wieske, L., et al. Examination of Cardiovascular and Peripheral Autonomic Function in the ICU: A Pilot Study. *J Neuro*. 2013, June; 260 (6): 1511-1517.

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