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ANTI-INFLAMMATORY TREATMENT AFTER ACL INJURY

More than 50% of patients with anterior cruciate ligament (ACL) rupture develop radiographic abnormalities and post-traumatic osteoarthritis within five to 15 years post-injury. This study was designed to determine whether steroid injections affect the inflammatory biomarkers evident in the joint after such injuries.

Patients with ACL tears received intra-articular injections at four days and two weeks post-injury. Group one received a corticosteroid injection (triamcinolone, 40 mg) at four days and a placebo at two weeks. Group two received a placebo saline injection at four days and a corticosteroid injection at two weeks. Group 3 received corticosteroid injections at both time intervals. Group four received placebo injections at both intervals.

Arthrocentesis was performed on the day of initial presentation, between six and 10 days after the initial visit and on the day of surgery. Patient-reported outcomes were collected at the initial visit and at the time of surgery, with outcome scores obtained from the 5 KOOS subscales, the International Knee Documentation Committee Measure, visual analog scale pain scale and the Pain Catastrophizing Scale.

Both chondrodegenerative and inflammatory markers worsened over the first five weeks, while all patient-reported outcomes improved during this time. Patient-reported outcomes did not differ between those of patients in the corticosteroid group and those in the placebo group. Increases in CTX-II, associated with greater type II collagen breakdown, were significantly greater in the placebo group than either of the two groups receiving steroids within the first several days post-injury.

Conclusion: This study of patients with ACL ruptures found that biochemical indicators of early osteoarthritis were evident before surgery, with intra-articular steroids able to suppress some of these.

Latterman, C., et al. A Multicentered Study of Early Anti-Inflammatory Treatment in Patients with Acute Anterior Cruciate Ligament Tear. *Am J Sports Med.* 2017, February; 45 (2): 325-333.

ANKLE SPRAIN IN YOUTH SOCCER

Soccer is currently the most popular sport played in the world. The high incidence of injury in youth soccer is a growing concern. Ankle sprains account for approximately 20% of all injuries in youth soccer players. This study examined whether hip muscle strength is a risk factor for sustaining a lateral ankle sprain among youth soccer players.

This prospective study included youth soccer players who played in the national league of their respective age category. Data collected including demographic, anthropometric and hip strength. Isometric hip strength was measured for the flexors, extensors, abductors, adductors and external/internal rotators. Injuries were monitored by the team's medical staff, and defined as that which prohibited the player from participating in practices or games for at least 48 hours.

Of the 133 players followed, 12 sustained a lateral ankle sprain, representing 18% of all injuries. These injuries resulted in a mean time lost of 22.4 days. An adjusted multivariate regression model revealed that players with greater hip extension muscle forces had a lower risk of lateral ankle sprain ($p=0.028$).

Conclusion: This prospective study of youth soccer players found that hip muscle extension force was

significantly associated with a reduced risk of lateral ankle sprain.

De Ridder, R., et al. Hip Strength as an Intrinsic Risk Factor for Lateral Ankle Sprains in Youth Soccer Players: A 3-Season. Prospective Study. *Am J Sports Med.* 2017, February; 45(2): 410-416.

AUTOLOGOUS WHOLE BLOOD VERSUS STEROIDS FOR PLANTAR FASCIITIS

Plantar fasciitis is the most common cause of heel pain, with typical, conservative treatments including orthoses, stretching, taping and nonsteroidal anti-inflammatory drugs. When conservative treatment fails, corticosteroid injections are often used. This study compared the outcomes of treatment with autologous whole blood (AWB) with those of corticosteroids for patients with chronic plantar fasciitis.

Patients diagnosed with chronic plantar fasciitis were randomized to a control group or to receive treatment by injection with either 1 mL of autologous whole blood combined with 1 mL of 1% lidocaine or 40 mg of methylprednisolone combined with 1 mL of 1% lidocaine. The subjects returned for evaluation at four and 12 weeks after therapy. The assessment included the plantar fasciitis pain/disability scale (PFPS), a visual analog scale (VAS) and pressure pain threshold.

Both the steroid and AWB groups improved significantly on all pain measures at each of the measurement intervals ($p<0.05$ for all measures). At four weeks after treatment, the steroid group had significantly greater improvement than the AWB group on the VAS, PFPS and PPT ($p<0.05$). At 12

weeks, both treatment groups had better pain scores than the control group, with no differences between the two treatment groups.

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Conclusion: This study of patients with chronic plantar fasciitis found that both steroids and autologous whole blood injections are effective for reducing pain, with steroids demonstrating better outcomes at four weeks, but equal in outcome to autologous whole blood at 12 weeks post-injection.

Karimzadeh, A., et al. Autologous Whole Blood versus Corticosteroid Local Injection in Treatment of Plantar Fasciitis: A Randomized, Controlled, Multi-Center Clinical Trial. **Clin Rheum.** 2017, March; 36 (3): 661-669.

BARICITINIB VERSUS ADALIMUMAB FOR RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a systemic autoimmune disease associated with severe disability and increased mortality. Activated Janus Kinases (JAK) are known to play a pivotal role in intracellular signaling for multiple cytokines that have been implicated in the pathological processes of RA. Baricitinib is an orally available small molecule that provides a reversible inhibition of JAK1 and JAK2. This study compared the effects of baricitinib with a tumor necrosis factor alpha inhibitor, adalimumab, for the treatment of RA. Adult patients with active RA, with inadequate response to methotrexate were randomized to receive baricitinib, 4 mg once daily, adalimumab, 40 mg subcutaneous

every other week or oral placebo. For the primary endpoint, baricitinib was compared with placebo and adalimumab for the proportion of patients at week 12 with a 20% response according to the criteria of the American College of Rheumatology (ACR20 response).

Subjects were 1,305 patients, with 488 in the placebo group, 487 in the baricitinib group and 330 in the adalimumab group. At week 12, the ACR20 responses were 70% for baricitinib and 61% for adalimumab ($p=0.01$). In addition, baricitinib was superior to adalimumab in reducing disease activity at week 12, as assessed with the Disease Activity Score for 28 Joints (DAS28) with the use of high-sensitivity c-reactive protein ($p<0.001$). A reduction in radiographic progression was observed for both treatment groups as compared to placebo at weeks 24 and 52.

Conclusion: This study of patients with rheumatoid arthritis and inadequate response to methotrexate found that an oral dose of baricitinib resulted in significantly greater clinical improvement than placebo or adalimumab.

Taylor, P., et al. Baricitinib versus Placebo or Adalimumab in Rheumatoid Arthritis. **N Engl J Med.** 2017, February 16; 376(7): 652-662.

BETA ALANINE USE AMONG PROFESSIONAL FOOTBALLERS

A number of studies have demonstrated that supplementation with beta alanine can improve high-intensity and intermittent exercise. However, little is known about the use of this supplement among professional athletes. This study was designed to estimate the prevalence of beta alanine supplementation among professional rugby and Australian Rules Football (ARF) players.

An anonymous questionnaire, consisting of 38 questions, was administered to professional athletes from teams in the Australian Football League (ARL), in the National Rugby League (RL) and Super Rugby (RU) football competitions. Questionnaires were designed to gather information regarding demographics, knowledge, use, side effects and sources of information regarding beta alanine.

Of the 785 surveys sent, 570 were returned. Of those who responded, 61% reported that they used beta

alanine. Nonusers reported a lack of knowledge as the primary reason for nonuse. Of the users, 15% supplemented with the recommended dose of 46 g per day, while 50% were consuming less than half of the recommended dose. Of those supplementing, 37% were supplementing one to three times per week, 21% four to six times per week and 12% more than six times per week. The main sources of information influencing the decision to use this supplement were the strength and conditioning coach, followed by the dietitian.

Conclusion: This study of Australian professional football players found that the majority of athletes supplement with beta alanine, although the majority use the supplement in a manner inconsistent with recommendations.

Kelley, V., et al. Prevalence, Knowledge and Attitudes Relating to Beta Alanine Use among Professional Footballers. **J Sci Med Sport.** 2017, January; 20(1): 12-16.

CONCUSSED ATHLETES MORE PRONE TO INJURY

Previous studies have demonstrated that athletes who sustain a concussion have a higher risk of sustaining another serious injury during the 21 days after return to play. This study employed a large database of patients who had presented to the emergency department with concussion, to better understand the rate of subsequent injuries.

Patient data were collected from the Umea Injury Data Base in northern Sweden, the only hospital within a 120km radius. Data were collected concerning participants in four contact sports, (ice hockey, soccer, handball and floorball), who were treated for concussion between 1995 and 2009. Data were reviewed for injuries treated 24 months before through 24 months after the index concussion. A control group of athletes with an ankle sprain, but no concussion, was used for comparison.

Between 1995 and 2009, 4,961 concussions were documented, of which 699 occurred during the participation in the sports identified. These athletes were compared to 1,259 athletes without concussion. Compared to the control group, those

with concussion had a higher risk of injury in the 24 months after the index concussion (OR 1.72), as well as in the 24 months before the injury (OR 1.98). This was not true for the athletes with ankle injury.

Conclusion: This study found that, while athletes who suffer a concussion are more likely to sustain injuries during the two years after the concussion, this risk is no greater than during the two years before the concussion.

Burman, E., et al. Concussed Athletes Are More Prone To Injury both Before and After Their Index Concussion: A Data Base Analysis of 699 Concussed Contact Sports Athletes. **BMJ Open Sport Exer Med.** 2016; 2(1).

EMERGENCY ROOM OPIOID PRESCRIBING AND RISK OF LONG-TERM USE

Rates of opioid prescribing and opioid related overdoses have quadrupled in the past three decades. This study examined a national sample of Medicare beneficiaries in an effort to understand how the initial exposure to an opioid relates to subsequent outcomes.

Data were retrieved using the Centers for Medicare and Medicaid Services carrier files. From these, a 20% random sample of beneficiaries from January of 2008 through December of 2011 was used to identify those who were assessed and treated in emergency rooms (ERs). From these visits were identified new prescription claims corresponding to an opioid. For this and subsequent opioid prescriptions, the number of days for which opioids were supplied was determined. The primary outcome was long-term opioid use, defined as 180 days or more of opioid supplied in the 12 months after the emergency room visit. The secondary outcome variable was the rate of hospital encounters. Physicians within the same ER were categorized by their rate of opioid prescribing.

The sample consisted of 215,678 patients treated by low intensity opioid prescribers and 161,951 treated by high-intensity opioid prescribers. Long-term opiate use at 12 months was significantly higher among those treated by high-intensity prescribers than among those treated by low intensity prescribers. Rates of opioid-related hospital encounters and encounters for fall or fracture were

significantly higher in the 12 months after the index emergency department visit among patients treated by high-intensity opioid prescribers than among those treated by low intensity opioid prescribers ($p=0.02$).

Conclusion: This study of elderly patients seen in the same emergency department found that long-term opioid use was significantly higher among those treated by physicians who were high-intensity opioid prescribers than among those treated by low intensity prescribers.

Barnett, M., et al. Opioid-Prescribing Patterns of Emergency Physicians and Risk of Long-Term Use. **N Engl J of Med.** 2017, February 16; 376: 663-673.

EXERCISES FOR PARKINSON'S DISEASE

While short-term exercise may improve health, well-being and function in patients with Parkinson's disease (PD), there is a lack of evidence of long-term benefits. This study was designed to better understand these benefits.

This phase II, randomized, controlled trial included patients with idiopathic PD, who were able to walk at least 100 m. The subjects were randomized to perform exercises or receive handwriting training, twice per week for six months. Exercise included 30 minutes of aerobic training followed by 30 minutes of resistance training. A control group underwent handwriting exercises, using workbooks at home. Outcome measures were performed at baseline, and at three, six and 12 months. The primary outcome measure was the two-minute walk test. Mobility was also assessed using the Timed Up and Go Test, the Nine Hole Peg Test and global motor function assessed using the Motor Examination of the MDS-UPDRS (III). At 12 months, during the two-minute walk test, the exercise group was able to walk 144.6 m, while the control group walked 137.9m ($p=0.06$). The largest effect was found on the MDS-UPDRS III at 12 months ($p<0.05$), indicating an improvement in motor symptoms ($p<0.05$). Small, statistically insignificant better gains were found in the exercise group than in the control group in improvement in leg power, aerobic capacity and perceived health-related quality of life.

Conclusion: This study of patients with Parkinson's disease suggests that twice weekly aerobic and resistance exercise may improve physical function.

Collett, J., et al. Phase II, Randomized, Controlled Trial of a Six-Month Self-Managed Community Exercise Program for People with Parkinson's Disease. **J Neurol Neurosurg Psychiatry.** 2017, March; 88(3): 204-211.

HAMSTRING FLEXIBILITY VERSUS HAMSTRING INJURIES IN SOCCER

Among amateur soccer players, hamstring injuries account for 16% of all injuries. In addition, the risk of recurrence is thought to be over 15%. Some have suggested that increasing hamstring flexibility may reduce the risk of this injury, though this relationship remains unclear. This study investigated the relationship between hamstring flexibility and hamstring injuries in male amateur soccer players. Between October and November of 2002, all male first-class, amateur soccer teams in the Netherlands were invited to participate in the study. All participants received information providing details of the study. Of those who agreed to participate, patient characteristics were collected using a questionnaire that queried age, years of soccer experience, field position and hamstring injuries in the year before the study. To measure hamstring flexibility, the Sit and Reach Test (SRT) was conducted by the medical staff for the soccer team. The players were then followed for hamstring injuries.

The final analysis was completed using data from 450 participants, with a mean age of 24.5 years. During the year of the study, 23 injuries were reported, resulting in a hamstring injury rate of 5.1%. The multivariate analysis revealed no significant relationship between hamstring flexibility and hamstring injury. Age and previous hamstring injuries were also not significantly related to hamstring injuries in either the univariate or the multivariate analyses ($p=0.176$ and $p=0.285$, respectively).

Conclusion: This study of high-level, male, amateur soccer players found no significant relationship between hamstring flexibility and the risk of hamstring injury.

Doormaal, M., et al. No Relationship between Hamstring Flexibility and Hamstring Injuries in Male, Amateur Soccer Players. *Am J Sports Med.* 2017, January; 45(1): 121-126.

INTERMITTENT LOWER LIMB OCCLUSION FOR MUSCLE RECOVERY

Strenuous eccentric muscle contractions can lead to exercise-induced muscle damage (EIMD.) This effect can decrease muscle performance and lead to pain in the days following exercise. Therapies to reduce EIMD include antioxidants, nonsteroidal anti-inflammatory drugs, cryotherapy and compression garments. Recently, the use of intermittent vascular occlusion (OCC) has been found to be effective for improving the recovery process. This study was designed to further evaluate the effect of OCC on the recovery processes following EIMD.

Subjects were 16 healthy recreationally active male participants, with a mean age of 22 years. After an initial familiarization session, the participants reported to the laboratory for four consecutive days. Muscle damage was induced by repeated drop jumps from a 0.6 m height, with five sets of 20 repetitions, separated by two minutes of recovery. Following this EIMD protocol, bilateral arterial occlusion cuffs were placed on the proximal thigh and inflated to either 220 mmHg (OCC) or 20 mmHg (control) for five minutes followed by five minutes of reperfusion. This process was repeated three times, totaling 30 minutes. Muscle performance was measured for maximum voluntary contraction (MVC) and vertical jump height (JH) at baseline and again at 24, 48 and 72 hour extension peak torque of the dominant leg was measured, with labs taken to determine plasma creatinine kinase (CK).

Compared with the control group, the treatment group had significantly better MVC when measured at 24, 48 and 72 hours after exercise ($p < 0.05$ for all comparisons). The CK levels were lower in the treatment group at 24 and 48 hours than in the control group ($p < 0.05$ for both comparisons). Muscle soreness was also significantly lower in the treatment group than in

the control group at 24, 48 and 72 hours ($p < 0.05$ for all comparison).

Conclusion: This study demonstrated that intermittent lower limb occlusion immediately after exercise-induced muscle damage can reduce muscle soreness and decrements in the maximum isometric voluntary contraction at 24, 48 and 72 hours.

Page, W., et al. The Effect of Intermittent Lower Limb Occlusion on Recovery Following Exercise-Induced Muscle Damage: A Randomized, Controlled Trial. *J Sci Med Sport.* 2017.doi.org//10.1016/j.jsams.2016.11.015s.

NEWER ANTIDEPRESSANTS WITH PREGABALIN FOR FIBROMYALGIA SYNDROME

Studies have shown that pregabalin, in combination with serotonin-norepinephrine reuptake inhibitors (SNRI) can be beneficial for the treatment of pain, fatigue and sleep disorders in fibromyalgia (FM). This study compared the use of pregabalin with amitriptyline, venlafaxine or paroxetine for symptoms of fibromyalgia.

The subjects were 75 adult women, previously diagnosed with FM, all of whom had experienced a poor response to pain medications, physical therapy and psychological support. Each patient received a single, daily dose of pregabalin at 75 mg. In addition, the patients were randomized to receive one additional medication, including oral amitriptyline at 25 mg per day, venlafaxine at 75 mg per day or paroxetine at 25 mg per day. The subjects were assessed bimonthly for six consecutive months. The primary outcome variable was the change in somatic symptoms, as measured by the SSS-8. Secondary outcome measures included the CESDS (depression) score, life satisfaction, mood, sleep quality, fatigue, medication tolerability and adverse events.

The combination which included paroxetine resulted in significantly lower SSS-8 scores from 10 weeks ($p < 0.001$) as well as 18 weeks ($p < 0.001$) after the initiation of the study medications as compared with pregabalin plus amitriptyline or venlafaxine. This combination also resulted in lower CESDS scores

from 10 weeks after the initiation of study medications until the end of the study ($p < 0.001$). This combination further resulted in higher medication tolerability ($p < 0.001$), and a greater number of patients with elevated mood, and good life satisfaction and sleep quality ($p < 0.05$).

Conclusion: This study of patients with fibromyalgia found that combining pregabalin with paroxetine improves pain, affect and function more than combining pregabalin with amitriptyline or venlafaxine.

Ramzy, E., et al. Comparative Efficacy of Newer Antidepressants in Combination with Pregabalin for Fibromyalgia Syndrome: A Controlled, Randomized Study. *Pain Practice.* 2017, January; 17(1): 32-40.

NITRATE SUPPLEMENT AND PERFORMANCE

Recent studies have demonstrated that dietary nitrate supplementation can improve performance in short duration, moderate intensity, aerobic exercise. This study investigated the influence of dietary nitrate supplementation on exercise performance.

Participants were 27 untrained, healthy males. At baseline, all were assessed by standard anthropometric measurements, VO₂ max, ventilatory thresholds (VT) and maximum work rate. The subjects were then matched for VO₂ max, and randomly assigned to either a sprint interval training plus nitrate group (SIT-nitrate) or a SIT- placebo group. The SIT-nitrate group consumed two nitrate-rich peach gels, containing eight mmol nitrate at

2.5 hours prior to each SIT session. Nine instructor led sessions of SIT occurred over a period of three weeks. Blood was drawn before and after each session to measure plasma nitrate, blood glucose and blood lactate concentrations.

Following a two-minute warm-up at 50 W, a load corresponding to 0.07 kgkg⁻¹ of body mass was applied to the bike and participants were verbally encouraged to maintain the highest cadence possible for 15 seconds. Peak

power and mean power during the sprint were calculated. Participants then completed four minutes of active recovery at 50W before repeating the process three more times.

At follow-up, VO₂ max and ventilatory threshold (VT) increased in both groups, with no significant difference between groups. The maximum work rate increased 8.7% in the nitrate group and 4.7% in the placebo group (p=0.07), with fatigue reduced more in the nitrate group than in the placebo group (p=0.058), though neither reached statistical significance.

Conclusion: In this study of previously untrained males, dietary nitrate supplementation did not significantly improve VO₂ max and VT.

Muggerridge, D., et al. The Effects of Dietary Nitrate Supplementation on the Adaptations to Sprint Interval Training in Previously Untrained Males. *J Sci Med Sport*. 2017, Jan; 20(1): 92-97.

OUTCOME MARKER FOR IVIG TREATED GUILLAIN-BARRÉ SYNDROME

Intravenous immunoglobulin (IVIG) has been the treatment of choice for Guillain-Barré syndrome (GBS), with varying recovery and outcome. As serum albumin has been identified as an independent factor associated with outcome in amyotrophic lateral sclerosis and Kawasaki disease, this study aimed to determine whether serum albumin levels can serve as a prognostic marker in patients with severe GBS treated with IVIG.

A cohort of patients with GBS participated in two previously conducted clinical trials between May 5, 1986, and August 2, 2000. Serum samples were obtained from 174 patients before and after IVIG treatment at four standardized time points. The main outcome measures were muscle weakness, respiratory failure and ability to walk. Serum albumin levels were measured before and after treatment.

Before treatment, the median serum albumin level was 4.2g/dl, with hypoalbuminemia in 20 (albumin<3.5g/dl) participants. Two weeks following treatment with IVIG, the median serum albumin level fell to 3.7g/dl. The number of

participants with hypoalbuminemia increased to 60 (p<0.001). Hypoalbuminemia was associated with respiratory failure (p<0.001), muscle weakness at four weeks (p<0.001) and six months (p<0.001) and inability to walk (p<0.001). A logistic regression analysis identified serum albumin as an independent factor associated with outcome.

Conclusion: This study found serum albumin to be an independent factor associated with the prognosis of patients with Guillain-Barré syndrome treated with IVIG.

Fokkink W., et al., Association of Albumin Levels with Outcome in Intravenous Immunoglobulin-Treated Guillain-Barré Syndrome. *JAMA Neurol*. 2017, February; 74 (2): 189-196.

PELVIC AND HIP FRACTURE RISK ASSOCIATION WITH ANTIHYPERTENSIVE MEDICATIONS

People with hypertension have more osteoporotic fractures than do people without hypertension. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) was a large, randomized, clinical trial comparing the effects of different classes of antihypertensive drug therapy in preventing heart disease. This study used data from the ALLHAT database to compare specific antihypertensive use with the risk of hip fracture.

This randomized, double-blind, active controlled, clinical trial included hypertensive women 55 years of age or older. The study compared first- step treatment with the thiazide-type diuretic, chlorthalidone (n=15,255), the calcium channel blocker, amlodipine, (n = 9048), the α -receptor blocker, doxazosin, (n = 9061) and the angiotensin-converting inhibitor, lisinopril (n = 9054). The doxazosin arm was dropped early, due to the higher risk of CVD compared with chlorthalidone. Hip and pelvic fractures were determined by hospital data between 1994 and 2006. The incidence of fractures was calculated, beginning one year after study enrollment.

During a mean follow up of 4.9 years, 34 participants had pelvic

fractures and 307 had hip fractures. A fully adjusted hip and pelvic fracture hazard ratio revealed that chlorthalidone was associated with a significantly lower risk of fracture than amlodipine or lisinopril. This finding was true for all subgroup comparisons.

Conclusion: This study found that the thiazide-type diuretic, chlorthalidone, is associated with a lower risk of pelvic fracture than are amlodipine and lisinopril.

Puttman, R., et al. Association of Three, Different Antihypertensive Medications with Hip and Pelvic Fracture Risk in Older Adults: Secondary Analysis of a Randomized, Clinical Trial. *JAMA Internal Med*. 2017, January; 177 (1):67-76.

PLASMA TAU AND RETURN TO PLAY AFTER CONCUSSION

Despite the 3.8 million sports-related concussions (SRCs) occurring annually in the United States, there are still no prognostic biomarkers to predict recovery. Tau has been found to be linked to axonal damage, as well as to return to play, among ice hockey players. This study was designed to better understand the relationship between increases in tau following a concussion and time to return to play (RTP).

Between 2009 and 2014, 632 National Collegiate Athletic Association Division I and division III contact sport athletes underwent plasma tau baseline sampling and cognitive testing prior to the beginning of the sports season. Those with an SRC underwent plasma sampling within six hours of injury, and then at two, three and seven days post-injury. Plasma sampling was also performed for noncontact athletic controls and nonathletic controls. Return to play was determined by the athletic trainers or team physicians. Clinical outcome after concussion was determined by changes in cognitive performance, post concussive symptoms and postural stability.

During the study, 48 athletes were diagnosed with SRC and were compared with 37 non-concussed athletes. Both athletic groups had significantly higher mean tau concentrations than did non-athletes at baseline, as well as at all other time points. Compared with the

control athletes, the concussed athletes had lower mean tau levels at 24 (p=0.03) and 72 hours (p=0.04). Compared to those allowed RTP within 10 days, those restricted from RTP for more than 10 days had higher overall concentrations of tau at six (p<0.01), 24 (p<0.01), and 72 hours (p<0.01). Plasma tau level at six hours post-concussion was a significant predictor of a RTP of 10 days or more (p<0.01).

Conclusion: This study demonstrates that plasma tau concentration within six hours after sports-related concussion is related to a prolonged return to play.

Gill, J., et al. Acute Plasma Tau Relates to Prolonged Return to Play after Concussion. *Neurol.* 2017, February 7; 88: 595-602.

U.S. HIGH SCHOOL SOCCER INJURIES

Soccer is one of the fastest growing sports in the United States, with male participation growing by four-fold and female participation by 35-fold between 1973 and 2014. This study reviewed the change in the number of soccer injuries in high school athletes between 2005/2006 and 2013/2014.

This prospective, epidemiologic study used data collected from the National High School Sports-Related Injury Surveillance System, High School Reporting Information Online (RIO). Data were gathered by board certified athletic trainers who reported exposure and injury data for athletes participating in sanctioned high school soccer programs. Athletic trainers completed detailed reports for each injured athlete, with injuries defined as occurring as a result of participation, requiring medical attention and resulting in the restriction of the athlete's participation for at least one day beyond the date of the injury.

Overall, the injury rate was 2.06 per 1,000 athletic exposures. The most common diagnoses were ligament sprains in 29.7%, concussions in 17.9% and muscle strains in 16.1% of the injuries. Compared with practice, injury rates were significantly higher in competition (RR 3.55). Injury rates were significantly higher in girls (RR 1.27) than in boys. Between 2005/2006 and 2013/2014, non-

concussion injuries decreased in boys, but not in girls. During that same time interval, concussion rates increased in both girls and boys.

Conclusion: This study of injuries in high school soccer players found that, over the past nine years, overall injuries decreased in boys and increased in girls, while concussion diagnoses increased in both genders.

Khodaei, M., et al. Nine-Year Study of U.S. High School Soccer Injuries: Data from International Sports Injury Surveillance Program. *Br J Sports Med.* 2017, February; 51(3): 185-193.

OUTCOME OF FEMOROACETABULAR IMPINGEMENT SURGERY

Femoroacetabular impingement (FAI) is a common cause of hip pain and dysfunction. This study was designed to better understand the functional outcome of patients at least two years after arthroscopic surgical treatment of FAI.

This prospective study included 289 patients with FAI who had failed nonsurgical intervention. At baseline, the subjects underwent physical exams, including radiologic evaluation. All participants completed web-based, patient reported outcome measures at baseline and at 24 months postoperatively. These included the International Hip Outcome Tool (iHOT-12), the Copenhagen Hip and Groin Outcome Score (HAGOS) the Hip Sports Activity Scale (HSAS), a visual analog scale for overall hip function and a standardized instrument for the measurement of health (ED-5Q). In addition, the subjects were asked whether they were satisfied with the surgery. Postoperatively, the patients were allowed free range of motion and full weight bearing during the early rehabilitation phase, with crutches recommended for one month for outdoor and longer ambulation.

The subjects' average age was 37 years, with an average symptom duration prior to surgery of 3.8 years. At two-year follow-up, significant improvements were found for all measured outcomes (p<0.05). Satisfaction with surgery was endorsed by 82%, with 13% expressing dissatisfaction. Symptom duration was significantly

and negatively related to both the iHOT-12 and the HAGOS-QoL.

Conclusion: This study of patients with femoral acetabular impingement found that surgical intervention resulted in statistically and clinically significant improvement in patient outcome.

Sansone, M., et al. Outcome after Hip Arthroscopic for Femoral Acetabular Impingement in 289 Patients with Minimum Two-Year Follow-Up. *Scand J Med Sci Sports.* 2017, February; 27(2); 230-235.

CRIZANLIZUMAB FOR PAIN IN SICKLE CELL

Patients with sickle cell disease experience sickle cell related pain crises. These are thought to be caused by vascular occlusion in the microcirculation, with the process of leukocyte adhesion to the endothelium believed to be initiated by P-selectin. Crizanlizumab is a humanized monoclonal antibody that binds to P-selectin and blocks its interaction with P selectin glycoprotein ligand 1. This study assessed the efficacy of this medication in reducing the rate of sickle cell related crises.

Patients eligible for study inclusion had sickle cell disease, sickle cell hemoglobin C disease, sickle beta⁰ thalassemia or sickle cell beta⁺ thalassemia, were 16 to 65 years of age and had experienced two to 10 sickle cell related pain crises in the prior 12 months. The participants were randomized to receive Crizanlizumab, 2.5 mg/kg, 4.5 mg/kg or placebo, administered intravenously 14 times over a period of 52 weeks. The primary efficacy endpoint was the yearly rate of sickle cell related pain crises.

At the end of the treatment phase, the median crisis rates in the intention to treat population were 1.63 in the high-dose group, 2.01 in the low dose group and 2.98 in the placebo group. The difference between treatment and placebo was only significant for the high dose group (p=0.01). A crisis rate of zero was achieved by 36% in the high-dose, 18% in the low-dose and 17% in the placebo group.

Conclusion: This study of patients with sickle cell disease found that treatment with Crizanlizumab resulted in a

significantly lower rate of sickle cell related pain crises, and was associated with a low incidence of adverse events.

Ataga, K., et al. Crizanlizumab for the Prevention of Pain Crises in Sickle Cell Disease. *N Engl J Med.* 2017, February 2; 376: 429-439.

LOW INTENSITY PULSED ULTRASOUND FOR BONE HEALING

The U.S. Food and Drug Administration has approved Low Intensity Pulsed Ultrasound (LIPUS) to accelerate fracture healing. This systematic review further assessed the efficacy of LIPUS for radiographic healing and clinical efficacy.

Medical databases were searched for controlled studies concerning the efficacy of LIPUS for the healing of fractures, published through November of 2016. The outcomes included time to return to work, full weight bearing, pain reduction, bone healing and subsequent fractures.

The search identified 42 studies, of which 26 were randomized, controlled trials. The authors found significant heterogeneity in the studies and found that, among those with a low risk of bias, treatment with LIPUS did not significantly reduce pain, days to weight bearing, or days to radiographic healing.

Conclusion: This literature review, focusing on those with a "low risk of bias", failed to identify low intensity pulsed ultrasound as an effective treatment to accelerate healing, pain or functional outcome in patients with fractures.

Schandelmaier, S., et al. Low Intensity Pulsed Ultrasound for Bone Healing: Systematic Review of Randomized, Controlled Trials. *BMJ.* 2017; 356: j656.

RHEUMATOID ARTHRITIS TRIPLE THERAPY COMPARED WITH ETANERCEPT

Among patients with rheumatoid arthritis (RA) treated with methytrexate (MTX), it is estimated that 70% will need additional therapy. Previous studies have demonstrated that triple therapy (SSZ and HCQ added to MTX) was non-inferior to MTX, and that TNF

inhibition produces similar results, to triple therapy. This study examined the difference in infectious disease and GI adverse events (AEs) between patients treated with triple therapy and those treated with a tumor necrosis factor inhibitor (etanercept).

Subjects were 353 patients with active RA despite treatment with MTX. The participants were randomized to triple therapy (T) with SSZ and HCQ added to MTX, or Etanercept added to MTX therapy (E). Those without improvement of 1.2 or greater on the DAS28-ESR at 24 weeks were switched in a blinded fashion to the other therapy. Both GI and infectious disease adverse events (AEs) were recorded for both groups.

For both therapies, the majority of infectious AEs were non-serious, with a greater number occurring in the E group than in the T group ($p=0.02$), remaining significant after adjusting for comorbidities ($p=0.01$). No significant difference was found between groups for serious infectious disease AEs. For non-serious GI AEs, T therapy had a higher incidence ($p=0.02$), with no significant difference between the groups in serious GI AEs. Further, there was no significant difference between the treatment groups in the number of patients who switched treatment groups due to poor improvement in RA symptoms.

Conclusion: This study of patients with active RA, treated with methytrexate, found that there is no difference in treatment outcome, or serious adverse outcomes among those treated with triple therapy (SSZ + HCQ + MTX) and those treated with TNF-inhibitor therapy (MTX+ Etanercept).

Quach, L., et al. Rheumatoid Arthritis Triple Therapy Compared with Etanercept: Difference in Infectious and Gastrointestinal Adverse Events. *Rheum.* 2017, March; 56 (3): 378-383.

SEDENTARY BEHAVIOR AND LOW BACK PAIN

Low back pain (LBP) is among highest causes of disability in the world. Previous studies have assessed the association between sedentary behavior and LBP, although no prior study has explored the influence of sedentary behavior

on the occurrence of LBP. This study was designed to better understand the association between sedentary behavior and the occurrence of LBP.

Data were collected from a population based registry of monozygotic (MZ) and dizygotic (DZ) twins, registered in a population-based twin registry of adult multiples born between 1940 and 1966. Data were collected between 2009 and 2011, including demographic information and self-reported health-related questionnaires. The main outcomes in the longitudinal analysis were the occurrence of new cases of LBP, with data on sedentary behavior sectional and the longitudinal analysis collected using a categorical self-report questionnaire. The data were reviewed for an association between sedentary behavior and LBP outcome for both the cross-sectional and the longitudinal analysis.

Data were collected from 2,148 twins, with an overall lifetime prevalence of persistent LBP of 32%. A multivariate analysis revealed that sedentary behavior was weakly associated with a lifetime prevalence of persistent LBP ($p=0.06$). Further analysis found that, among DZ twins, sedentary behavior was associated with an increased prevalence of persistent LBP in females, but not males. The MZ twins analysis found no significant difference between males and females.

Conclusion: This study of twins found that sedentary behavior is only weakly associated with low back pain, with this relationship more evident in females than in males.

Amorim, A., et al. Sedentary Behavior Increases the Risk of Low Back Pain? A Population Based, Co-Twin Study of Spanish Twins. *Spine J.* 2017.doi.org/10.1016/j.spine.2017.02.004.

THROMBOPROPHYLAXIS AFTER KNEE ARTHROSCOPY

The use of pharmacologic thromboprophylaxis after most orthopedic interventions is well established. Whether such prophylaxis is effective after arthroscopic knee surgery is less certain. The Prevention of

Thrombosis after Knee Arthroscopically (POT-KAST) and the Prevention of Thrombosis after Lower Leg Plaster Cast (POT-CAST) trials were designed to assess the effect of low molecular weight heparin for the prevention of symptomatic venous thromboembolism (VTE).

Subjects 18 years of age or older who were scheduled to undergo knee arthroscopy were enrolled in the POT-KAST study and those treated for at least one week with casting of the lower leg with or without surgery were enrolled in the POT-CAST study. Eligible patients in the two trials were randomly assigned to receive either a prophylactic dose of low molecular weight heparin or no anticoagulant therapy. In the POT-KAST study, heparin was administered once daily for eight days, while in the POT-CAST study, heparin was administered for the full period of immobilization. The primary outcome measure was the cumulative incidence of symptomatic VTE within three months of the procedure.

Subjects were 1,543 patients, with 773 assigned to receive low

molecular weight heparin and 770 to a control group. In the intention to treat analysis, in the POT-CAST trial, the cumulative incidences of symptomatic VTE within three months were 0.7% in the treatment group and 0.4% in the control group. This finding represented a relative risk of 1.6. One patient in each group had a major hemorrhagic event. The POT-KAST study revealed that the cumulative incidence of symptomatic venous thromboembolism was 1.6% in the treatment group and 1.8% in the control group. In neither study was the prophylaxis found to be effective.

Conclusion: This study found that administering low molecular weight heparin for eight days following knee surgery performed arthroscopically or during immobilization due to casting was not significantly effective for preventing symptomatic venous thromboembolism.

Adrichem, R., et al.
Thromboprophylaxis after Knee Arthroscopically and Lower Leg Casting. *N Engl J Med.* 2017, February 9; 376(6): 515-525.

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