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Creatine Use May Lead to Exertional Compartment Syndrome

ABSTRACT & COMMENTARY

Synopsis: *Dietary creatine supplementation significantly increases the resting and postexercise anterior compartment pressure of the leg compared to presupplementation levels.*

Source: Potteiger JA, et al. Changes in lower leg anterior compartment pressure before, during, and after creatine supplementation. *Journal of Athletic Training.* 2002;37(2):157-163.

THERE HAS BEEN WIDESPREAD ACCEPTANCE OF THE USE OF dietary creatine supplementation to enhance muscle bulk and athletic performance. One common problem noted has been increased rates of muscle cramping with fluid shifts. Potteiger and colleagues from the University of Kansas had previously shown that creatine use also was associated with increases in lower leg anterior compartment pressure. The present study went a step further.

Sixteen athletically active males served as somewhat heroic volunteers for an elaborate set of experiments. They had not been prior users of creatine or had a history of lower leg problems. The subjects were divided into a low-dose creatine group of .03 g creatine/kg/d, and a high-dose supplementation group of .3 g creatine/kg/d for 7 days followed by .03 g creatine/kg/d until 35 days. Both groups underwent extensive testing to include determination of body mass, body composition, blood pressures, lower leg volume, and muscle biopsies. Anterior compartment pressure measurements were performed prior to exercise, immediately after exercise, and then 1, 5, 10, and 15 minutes post exercise. All of these measurements were performed prior to creatine use and then after 7 days and 35 days of supplementation as well as 28 days after stopping the supplements.

As expected, body mass and lower leg volume showed increases with creatine supplementation. Also of note there was an elevation of blood pressure, especially in the high-dose group with creatine

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supplementation. Muscle biopsies showed elevated creatine amounts that normalized after supplementation was discontinued.

Because no differences were seen between the groups in terms of compartment pressures, but only with time, the 2 groups were combined for the data analysis. Creatine use showed a rather dramatic increase in anterior compartment pressure measurements both resting and after exercise. The numbers were quite striking with an increase from baseline at rest of 18 mm Hg to 26 mm Hg after just 7 days of creatine. Immediately after exercise the pressures increased from 52 for the controls to 77 with the creatine supplementation. At 5 minutes post-exercise, when the pressure should be diminished, they were down to 24 for the control group but remained elevated at 41 for the creatine supplementation group. When patients were measured after being off the creatine for approximately 1 month, these numbers were still elevated at about 33 mm Hg. All pressure measurements both at rest and after exercise were significantly elevated from baseline for the creatine supplementation groups.

Potteiger et al note that creatine elevates compartment pressures to the point that athletes are at risk for

exertional compartment syndrome symptoms. Indeed, complaints of tightness and burning in the anterior compartments were common among the participants in this study.

■ COMMENT BY DAVID R. DIDUCH, MS, MD

Pedowitz has established formal criteria to diagnose patients with exertional compartment syndrome.¹ This is based on elevated compartment pressures 1 minute after exercise of greater than 30 mm, or 5 minutes after exercise greater than 20 mm of mercury. The mean pressure measurements for the subjects in both the high- and low-dose creatine groups were all elevated above these established criteria. Furthermore, pressures were slow to return to normal levels even after 28 days of being off of creatine. Interestingly, many of the athletes in the study had symptoms compatible with exertional compartment syndrome.

I believe Potteiger et al were successful in proving their hypothesis. Creatine supplementation can significantly increase resting and postexercise anterior compartment pressures above presupplementation levels, and there is a slow normalization of these pressure measurements after stopping creatine use. This study was well conducted, organized, and written and should heighten our awareness for exertional compartment syndromes for athletes with a history of creatine use. It should also prompt us to question athletes who present with exertional compartment syndrome symptoms as to whether they are using creatine. It would certainly be simpler and less risky to have athletes stop creatine use rather than undergoing surgical decompression.

The mechanism behind the elevated compartment pressures is less clear and could be an excellent source of further research. Potteiger et al contend that increased protein synthesis as a result of creatine supplementation may increase volume within a fixed muscular compartment. Another factor is that creatine uptake by the muscle occurs in conjunction with an influx of sodium with associated water uptake by the muscle with swelling that also would increase volume within the fixed compartment. Both of these would likely result in higher compartment pressures both at rest and after exercise due to the rigidity of the anterior compartment of the lower leg. Indeed, there has even been a previous case report of acute quadriceps compartment syndrome with rhabdomyolysis in a weightlifter using high-dose creatine.² Sports medicine care providers need to have a heightened awareness for this potential problem with creatine use. ■

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Management of the Spinal Cord Injured Football Player

ABSTRACT & COMMENTARY

Synopsis: *The helmet and shoulder pads should be left on during spine-board immobilization of the injured football player.*

Source: Tierney RT, et al. Head position and football equipment influence cervical spinal-cord space during immobilization. *Journal of Athletic Training.* 2002;37(2):185-189.

TIERNEY AND COLLEAGUES ASSESSED THE EFFECT OF head position and football equipment (helmet and shoulder pads) on cervical spinal cord space in subjects lying supine on a spine board. Magnetic resonance imaging (MRI) data from 12 subjects were analyzed for sagittal space available for the cord (SAC), sagittal diameter of the spinal cord, and cervical-thoracic angle. The MRI scans were evaluated midsagittally at each spinal level (C3-C7). The sagittal-diameter spinal canal and spinal cord measurements were taken at the midpoint of the vertebral body, and were traced manually. The spinal-canal diameter was measured as the shortest distance from the vertebral body to the spinolaminar line. The spinal-cord diameter was measured at the appropriate spinal levels. The SAC was determined by subtracting the sagittal-cord diameter from the corresponding sagittal-canal diameter. The cervical-thoracic angle was determined by drawing a line parallel with the dorsal aspect of the C2 and C3 vertebral bodies and a line parallel with the dorsal aspects of the T1 and T2 vertebral bodies.

Subjects were positioned supine on the spine board, and were MRI scanned at 0 cm, 2 cm, and 4 cm of occiput elevation with occipital padding with no helmet and shoulder pads and with helmet and shoulder pads. The sagittal-diameter spinal-cord values ranged from 6.22-8.89 mm, and the cervical-thoracic angle averages ranged from 15.43-22.88°. The findings were that the SAC was significantly greater for 0-cm than for 2-cm and 4-cm positions. The SAC was

significantly greater for the equipment condition than for the 2-cm and 4-cm positions. There was no significant difference in SAC between 0-cm and the equipment condition.

■ COMMENT BY DAVID H. PERRIN, PhD, ATC

The 0-cm of occipital padding was the most extended position assessed in this study. This position produced the greatest sagittal space available for the cord, and there was no difference between this position and the equipment condition. This supports the recommendation that the football helmet and shoulder pads should both be left on during management and immobilization of the spinal cord injured football player. This recommendation is consistent with the Inter-Association Task Force for the Appropriate Care of the Spine-Injured Athlete.¹

Access to the airway of the football player immobilized with the helmet in place can be obtained by removal of the facemask. Various instruments are available for this removal, including polyvinyl chloride pipe cutters, an anvil pruner, screwdrivers, EMT shears, rotary cutting devices, the Trainer's Angel, and the Face Mask Extractor.² The sports medicine team, on a regular basis and in advance of an actual neck injury, should practice the technique. It is also essential that the sports medicine team be on the same page with the local EMS in management of the spine-injured football player so that a debate about removal of the helmet doesn't occur during management of an actual injury.

At some point, the football helmet and shoulder pads must be removed, and this most appropriately occurs in the emergency room. It is not surprising that typical emergency room personnel are not trained in removal of this equipment in a manner that minimizes cervical spine motion. Consequently, it is imperative that a member of the sports medicine team trained in the proper technique of helmet and shoulder pad removal accompanies the injured athlete to the medical facility to provide assistance. Proper management of the potentially spine-injured athlete on the field and in the medical facility can prevent a serious injury from becoming catastrophic. ■

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Arthroscopic Subscapularis Tendon Repair

ABSTRACT & COMMENTARY

Synopsis: *A retrospective review was performed to evaluate the preliminary results of 25 consecutive arthroscopic subscapularis tendon repairs. This study concludes that: 1) arthroscopic repair of torn subscapularis tendons can be consistently performed with good-to-excellent results; 2) the Napoleon test is useful in detecting the presence and size of subscapularis tendon tears; and 3) arthroscopic repair of massive rotator cuff tears can produce durable reversal of proximal humeral migration and restoration of overhead function.*

Source: Burkhart SS, Tehrany AM. Arthroscopic subscapularis tendon repair: Technique and preliminary results. *Arthroscopy*. 2002;18:454-463.

THIS RETROSPECTIVE CASE SERIES REVIEWED Burkhart's early experience performing 32 arthroscopic subscapularis tendon repairs. Twenty-five shoulders with more than 3 months follow-up were reviewed with an average duration of just 10.7 months. Isolated subscapularis tears occurred in 8 shoulders, while massive rotator cuff tears, defined by a complete subscapularis tear combined with supraspinatus and infraspinatus tears, were identified in 6 shoulders.

The UCLA score improved from an average preoperative value of 10.7 to a postoperative average value of 30.5 ($P < 0.0001$). In the 6 patients with massive rotator cuff repairs, the UCLA score improved from 9.5 to 28.3 ($P < 0.001$). For the 8 patients with isolated subscapularis tears, the UCLA score improved from 10 to 32.8 ($P < 0.002$). Overall, forward flexion increased from an average of 96.3° to 146.1° ($P < 0.01$). There were 2 reruptures and no other clinically significant complications in this preliminary study.

The Napoleon and lift-off tests were used to evaluate the condition of the subscapularis tendon prior to surgery. To perform the Napoleon test, patients were instructed to place their hand on their stomach and push posteriorly. The Napoleon test was considered normal if the patient could push the hand against the stomach and maintain a straight wrist; positive if the wrist flexed 90° ; and intermediate if the wrist flexed 30° to 60° . The lift-off test was performed by placing the dorsum of the hand against the lower back and instructing the patient to actively "lift-off" the hand from the back. All patients tolerated the Napoleon test

during clinical examination. In contrast, the lift-off test could not be performed due to pain or restricted motion in 19 of 25 patients. The Napoleon test was thought best to correlate with the condition of the subscapularis. All patients with a negative or normal Napoleon test were found to have tears confined to the upper half of the subscapularis tendon. Eight of 9 patients with a positive Napoleon test had complete tears of the subscapularis. Incomplete tears involving more than 50% of the tendon tended to have intermediate Napoleon tests.

Proximal humeral migration, defined as an acromiohumeral interval of less than 5 mm and an inferior humeral head-inferior glenoid articular margin of greater than 5 mm, occurred in 10 patients (40%). Eight out of 10 patients had reversal of proximal humeral migration on postoperative radiographs. In 2 patients with recurrent proximal humeral migration, forward flexion improved to $< 110^\circ$ and the UCLA scores were poor and fair. Recurrent proximal humeral migration was felt to correlate with a poor outcome.

■ COMMENT BY ROBERT C. SCHENCK, Jr., MD, & JOHN C. FRANCO, MD

Isolated subscapularis tears and massive rotator cuff tears involving the subscapularis tendon can be debilitating problems and challenging to repair. Patients with isolated subscapularis tears can experience anterior shoulder instability and profound loss of shoulder internal rotation strength. Massive rotator cuff tear involving the subscapularis produces global shoulder instability and painful loss of shoulder function. Virtually all researchers recommend operative treatment of a torn subscapularis tendon.¹⁻⁴

The theoretical advantages of arthroscopic subscapularis repair include a minimally invasive approach, limited risk to extra-articular neurovascular structures, and little risk of additional functional loss to the deltoid when an irreparable rotator cuff tear is encountered. Burkhart and Tehrany report the first series of arthroscopic rotator cuff repair with remarkably good to excellent results in 92% of patients. The outcome of arthroscopic subscapularis repair in cases of isolated tendon rupture was most successful. The final UCLA shoulder score (32.8/35) compares favorably with the final Constant score (82/100) reported by Gerber² following open repair of isolated subscapularis tear.

Repair of massive rotator cuff tears, especially anterior-superior tears involving subscapularis, can be extremely difficult, results are often poor, and rerupture is not uncommon. Warner reported an average Constant

score of 69 and excellent or good results in only 8 of 19 open anterior-superior rotator cuff repairs.³ Gerber reported on 29 open massive rotator cuff repairs (13/29 involving supscapularis) and demonstrated an average Constant score of 85 and improvement in pain free forward flexion to 142°.⁴ These experiences are important benchmarks to compare any long-term follow-up of a new arthroscopic procedure. We agree that the Napoleon test is useful in diagnosing supscapularis tears, especially when shoulder internal rotation is limited and/or painful. The correlation between the Napoleon test result and the intraoperative condition of the subscapularis is an interesting finding that may prove useful in preoperative planning and patient counseling. In our experience, the use of clinical findings to verify the presence of a subscapularis tear are experience dependent with occasional presence of false negatives, and frequently require both clinical examination and MRI evaluation.

There are 2 main concerns with regards to this study. The first is the relative short follow-up. Compared to reports of open subscapularis repair with up to 3-year follow-up, final follow-up in this series averaged 10 months and deterioration in objective and subjective results, as well as a higher rate of rerupture, may occur with longer follow-up. That being said, the early results of arthroscopic subscapularis repair are very encouraging. The second concern is that of technical difficulty. The practicing clinician is best advised to repair the subscapularis with a familiar and reproducible technique, in his or her hands. Certainly, the presence of a displaced biceps tendon with a complete subscapularis tear adds to the technical challenge of such a repair, be it open or arthroscopic. Further experience in addition to longer follow-up of this group of patients is needed before arthroscopic subscapularis tendon repair is considered a routine technical exercise. ■

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SLAP Repairs in Athletes

ABSTRACT & COMMENTARY

Synopsis: *Although motion was preserved and outcomes were generally good following arthroscopic SLAP repair, it was difficult for throwers to return to pre-injury levels of activity.*

Source: Kim SH, et al. Results of arthroscopic treatment of superior labral lesions. *J Bone Joint Surg*. 2002;84-A(6): 981-985.

THE RESULTS OF ARTHROSCOPIC TREATMENT OF ISOLATED SLAP repairs have not been fully reviewed in overhead athletes. The purpose of this study was to evaluate the short-term results of arthroscopic repair with a suture anchor of isolated superior labral lesions of the shoulder in young patients. Thirty-four patients (average age, 26 years) were evaluated at a mean of 33 months following arthroscopic repair of an isolated superior labral lesion of the shoulder. The diagnosis for the SLAP lesion was made by a combination of a positive physical exam and positive MRI, and all were confirmed at arthroscopy. Eighteen athletes competed in overhead sports and 12 in contact sports, including 12 collegiate and 11 professional. The surgical outcomes were evaluated with the UCLA shoulder score, a visual analogue scale, and on the basis of the patient's ability to return to prior activities.

Arthroscopic repair of the SLAP lesion resulted in a satisfactory shoulder score in 94% of the patients. Pre-injury shoulder function was obtained in 91% of patients overall. Athletes participating in overhead sports had significantly lower shoulder scores and a lower percentage of return to their preinjury level of shoulder function compared with patients who did not participate in overhead activity. Kim and colleagues conclude that arthroscopic repair of an isolated SLAP lesion is successful in young athletic patients but further state that poor results were noted in athletes participating in overhead sports.

■ COMMENT BY JAMES R. SLAUTERBECK, MD

This is a nice study of repair of SLAP lesions in young patients, many of whom were athletic and competing in overhead sports. History, physical exam, MRI, and arthroscopy documentation of all lesions highlighted the inclusion criteria and those patients with additional pathology were excluded. A single surgical procedure was performed that used the mini-Revo screw-type

suture anchor. However, no control group was used for comparison of results.

This study identifies that arthroscopic repair of SLAP lesions is a successful procedure in the young, athletic population. However, as expected, lower shoulder scores and functional scores were identified in the overhead-throwing athletes. This does not come as a surprise because of the significant loads placed upon the shoulder during throwing. Full, uncompromised activity level was achieved by 63% of the non-throwing and just 22% of the throwing athletes. This diminished throwing ability was not due to stiffness, as this type of SLAP repair did not compromise shoulder ROM. This is a major success because significant loss of external rotation to the throwing athlete can end a career.

Shoulder surgeons who treat overhead throwing athletes need to be facile with a technique of repairing the superior labrum that does not limit motion and restores function. It is important to tell throwing athletes that SLAP repairs may not return them to the same function they had prior to injury. We must continue to search for better techniques to treat SLAP lesions in the throwing athlete. Until then, SLAP lesions remain difficult to treat in the challenging population of overhead throwers. ■

Meniscal Repair with the Mitek (Fastner) Device

ABSTRACT & COMMENTARY

Synopsis: *Laprell and colleagues report clinical success with the Mitek Fastner; however, they had several problems, including 1 case of cartilage injury, 5 failures, and 8 patients who had difficulty with duck walking at 1-year follow-up.*

Source: Laprell H, et al. Arthroscopic all-inside meniscal repair using a new refixation device: A prospective study. *Arthroscopy*. 2002;18(4):387-393.

THERE ARE SEVERAL MENISCAL REPAIR DEVICES that have been recently introduced. Although many of them are easier and quicker to insert than conventional inside-out sutures, sutures are still the standard with which they must be compared. One of these devices, the Mitek meniscal repair system, was evaluated in this European study. Thirty-seven patients were treated with this device, with a roughly equal distribu-

tion of men and women and medial and lateral meniscal repairs. Most of the repairs were within the vascular zone of the meniscus. Seventeen patients had a concomitant ACL tear that was reconstructed 6 to 8 weeks after the meniscal repair, giving the surgeon a chance to evaluate the repair. Depending on the size of the tear, 1-4 anchors were used. Patients were followed for at least 1 year postoperatively.

The most common intra-operative problem was loosening of the implant (1 in 6 cases). Subcutaneous migration was seen in one case. In the 17 cases re-evaluated at the time of ACL reconstruction, 5 had a residual cleft and 1 had a prominent device with superficial articular cartilage abrasion. At 1-year clinical follow-up, there were 5 reruptures (all in the red/white zone) and 3 additional cases of degenerative fraying of the inner rim of the meniscus. Eight additional patients had difficulty with duck walking. Eight of the 17 ACL reconstructions had a 1+ Lachman and 3 had a pivot shift. Despite these problems, Laprell et al conclude that their clinical results are promising.

■ COMMENT BY MARK D. MILLER, MD

Although many of these new meniscal repair devices are appealing because of their ease of insertion, I do not consider the results of this short-term report promising. Clearly the most stringent review of meniscal repair results is with second-look arthroscopy. Evaluation at 6-8 weeks showed residual clefts in 5 of 17 menisci and articular cartilage abrasion in 1. Clinical evaluation at 1 year, which is less stringent, demonstrated 5 reruptures and 8 patients with difficulty in duck walking. That means that 13 of 37 patients, which is more than one third of the group, had an unacceptable result with their meniscal repair. Although there are known problems associated with inside-out meniscal repair (nerve injury, technical difficulty, etc), numerous studies have shown better results with this technique.

The problem I have with this particular device is that there is very little flexibility in ensuring that adequate tension can be applied to the meniscal fixation. Some of the newer devices (such as the Smith & Nephew Fas-T-Fix and the Mitek Rapid Loc) do allow meniscal tensioning. Even these newer devices still have the risks of all all-inside devices, which include migration, late laxity, and articular cartilage injury. Additionally, all repairs in the red-white zone (where the 5 failures occurred in this study) should be treated with enhancement techniques (aggressive rasping, fibrin clot, etc) at the time of repair. I was surprised that Laprell et al still prefer to stage combined ACL and

meniscal repairs. If these patients are followed closely postoperatively, combined ACL reconstruction with meniscal repair has been shown to be extremely successful. Additionally, some surgeons have proposed that bleeding from the ACL reconstruction may actually increase the success of meniscal repair. Perhaps a newer generation meniscal repair device will allow all of the features of traditional inside-out repair with the ease of insertion associated with all-inside repair, but we are not there yet! ■

Mechanical Injury and Chondrocyte Viability

ABSTRACT & COMMENTARY

Synopsis: *In both in vitro and in vivo trials, the number of apoptotic cells increased significantly in response to mechanical loading. Furthermore, caspase inhibitors reduced chondrocyte apoptosis following mechanical injury.*

Source: D'Lima DD, et al. Impact of mechanical trauma on matrix and cells. *Clin Orthop Relat Res.* 2002;391:S90-S99.

IT HAS BEEN SUGGESTED THAT CHONDROCYTE DEATH may be a critical factor in the response of cartilage to injury. Although articular cartilage responds differently to different types of mechanical stimuli, the contribution of cell death to matrix degradation has not been fully characterized. The present study sought to determine the effect of mechanical injury on chondrocyte viability and matrix degradation.

Both in vivo and in vitro effects of mechanical loading on cartilage were examined. The models of mechanical injury investigated were transient static compression, impact loading, and creation of a cartilage defect in articular cartilage. The release of glycosaminoglycan (GAG) and percentage of apoptotic cells were measured to determine the response to the mechanical loading. The inhibition of chondrocyte apoptosis by a pan-caspase inhibitor, z-VAD-fmk, in human articular cartilage explants was also determined.

The bovine and human cartilage explants were mechanically loaded by an Instron 8511 servohydraulic testing machine (Instron Corporation, Boston, Mass). The simulation of acute joint injury followed either a dose response model (low, moderate, high) or a repetitive model where following a small preload, a 30% strain was applied to the explants at a rate of 3/sec last-

ing for 500 ms. To stimulate traumatic injury, 3-mm drill holes in weightbearing portions of bovine femoral condyles and human talar domes were created (no penetration of subchondral bone), and 5 mm disks from around the drill holes were harvested. Additionally, unilateral patellas in eight anesthetized rabbits were subjected to an impact load by dropping a 3 kg weight from a height of 100 cm.

For the dose-response experiments, it was determined that GAG release increased with the intensity of the loading at 48 hours after loading. The moderate load and high load groups showed significantly higher apoptosis rates than the control groups. A correlation of GAG release with apoptosis rate was observed ($r = 0.67$; $P = 0.02$). For the repetitive injury model, explants subjected to 30% strain had a mean apoptosis rate of 34% (± 12) compared to those cultured in the presence of caspase inhibitor which exhibited a mean apoptosis rate of 21% (± 11) with a significant reduction in GAG release.

All bovine cartilage explants with drill holes showed a higher rate of apoptosis along the margin of the drill holes ($55.2\% \pm 30.2$) as compared to the sharply punched out margins of the disks ($26.8\% \pm 8.6$; $P = 0.02$). In vivo impact loading of patellar cartilage demonstrated 15% apoptosis compared to 1% in the unimpacted cartilage ($P < 0.01$).

■ COMMENT BY BRIAN J. COLE, MD, MBA

The present study has shown that chondrocyte apoptosis can be induced both in vitro and in vivo proportional to the level of mechanical loading and injury. However, the level of apoptosis following injury in vivo is much lower than that found in vitro. The findings from this study also indicate that, in vitro, apoptosis induced by mechanical loading can be reduced through the use of caspase inhibitors. These results should be considered when clinicians harvest the patellar bone block during ACL reconstruction, harvest and handle chondrocytes for cell transplantation, and harvest or impact osteochondral grafts. Clearly, our current techniques must minimize the chance for iatrogenic injury. Additionally, our postoperative rehabilitation protocols may benefit from considering this data. Additional research focused on maturing tissue (ie, fibrocartilage, hyaline like cartilage, integration of osteochondral grafts) may help to fine tune our rehabilitation protocols. In order to determine the clinical efficacy of caspase inhibitors in patients exposed to surgical trauma of cartilage, further in vivo studies are required. ■

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CME Questions

8. Creatine supplementation was associated with increased compartment pressure measurements of the lower leg:

- a. pre-exercise.
- b. 1 minute postexercise.
- c. 5 minutes postexercise.
- d. even 28 days after stopping the creatine.
- e. All of the above

9. Which of the following most accurately reflects proper spine-board immobilization of the spine-injured football player?

- a. Occipital padding should be placed under the shoulder pads.
- b. The helmet should be left on and the shoulder pads should be removed.
- c. The helmet and shoulder pads should not be removed.
- d. The helmet and shoulder pads should be removed.

10. Rupture of the subscapularis tendon is best identified by which of the following clinical findings?

- a. Weakness on external rotation
- b. A positive Napoleon test
- c. A positive Jobe's test
- d. A positive lift-off test

11. SLAP repairs using a mini-Revo suture repair for the labrum is:

- a. successful at functionally returning throwing athletes to their sport approximately 1% of the time.
- b. successful at functionally returning throwing athletes to their sport approximately 20% of the time.
- c. successful at functionally returning throwing athletes to their sport approximately 75% of the time.
- d. successful at functionally returning throwing athletes to their sport approximately all of the time.

12. All-inside meniscal repair using the Mitek fixation device:

- a. has no risk of loosening, migration, or cartilage damage with insertion.
- b. has no risk of migration or cartilage damage, but may loosen, even intra-operatively.
- c. has a risk of loosening (including intra-operatively), migration, and cartilage damage.
- d. was successful in 90% of all patients evaluated at 2-year follow-up.

13. In vivo, Caspase inhibitors can reduce chondrocyte death following injury due to:

- a. drill holes in the articular surface.
- b. direct impact loading of the articular surface.
- c. following repetitive injury.
- d. All of the above

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In Future Issues:

Hamstring Muscle Atrophy Following Tendon Harvesting

PHARMACOLOGY WATCH



No Shortage in Sight for Tetanus-Diphtheria Vaccine

The number of vaccine shortages has been unprecedented in the last year, but at least one vaccine, tetanus-diphtheria (Td), is back in full production. The Centers for Disease Control and Prevention (CDC) has announced that they are removing restrictions on the Td booster. Despite the fact that there is only one manufacturer of the vaccine, supplies are large enough to resume routine vaccination. The news is also good for childhood vaccines that have been in short supply, including MMR, varicella, and PCV-7 (pneumococcal) vaccine. All are expected to be in full supply by the end of the year.

Cholesterol-Lowering Therapy OK for Seniors

What to do with the 75-year-old patient with a cholesterol of 300, but no history of heart disease? Primary prevention studies have shown a benefit for treatment of younger patients, but there have been few studies of primary prevention studies in the elderly. Now data from the Cardiovascular Health Study of patients age 65 or older suggest that cholesterol-lowering therapy is useful in older patients as well. After nearly 7.5 years of follow-up, elderly patients with elevated cholesterol levels clearly benefited from cholesterol-lowering treatment. Compared with no drug therapy, statin use was associated with a decreased risk of cardiovascular events (multivariate hazard ratio [HR], 0.44; 95% CI, 0.27-0.71) and all-cause mortality (HR, 0.56; 95% CI, 0.36-0.8). This translates into a relative risk reduction of 56% of incident cardiovascular events and a 44% reduction in all-cause mortality. This was a prospective study, as pointed out in an accompanying editorial; however, it does add to the body of medical literature that suggests that the recent National Cholesterol Education Program (NCEP) guidelines should apply to those aged 65 or older (*Arch Intern Med.* 2002;162:1395-1400; editorial 1329-1331).

Beta-Blockers and CABG Patients

Preoperative beta-blockers have been shown to reduce operative complications and mortality in noncardiac surgery, and now 2 studies confirm the importance of beta blockade in patients undergoing coronary artery bypass grafting (CABG). In a large observational analysis of more than 600,000 patients undergoing CABG, preoperative beta-blocker therapy was associated with a small but consistent survival benefit in all patients except those with a preoperative left ventricular ejection fraction of less than 30% (*JAMA.* 2002;287:2221-2227). The most common postoperative complication of CABG is atrial fibrillation. A recent meta-analysis compares beta-blockers, sotalol, amiodarone, and biatrial pacing to prevent atrial fibrillation after heart surgery. All 4 modalities were effective (odds ratio compared to placebo—beta-blockers 0.39, sotalol 0.35, amiodarone 0.48, biatrial pacing 0.46). Each of the 4 drug modalities also significantly reduced length of stay. Significantly, beta-blockers, which are safe and easily administered were as effective as other treatment modalities (*Circulation.* 2002;106:75-80).

Asthma Sufferers: Use Clarithromycin

Asthmatics with evidence of infection with *Mycoplasma pneumoniae* or *Chlamydia pneumoniae* ben-

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efit from a 6-week course of the macrolide antibiotic clarithromycin, according to a new study. In 55 patients with stable asthma in the Denver community, 31 were found to have evidence of mycoplasma or chlamydia infections by PCR and culture. All 55 patients were randomly assigned to treatment with either placebo or clarithromycin 500 mg p.o. b.i.d. 6 weeks. Patients who were PCR-positive and received clarithromycin were found to have a significant improvement in FEV₁ (2.50 pretreatment, 2.69 post-treatment; $P = 0.05$), while those who were PCR negative and those who did not receive antibiotic showed no change (*Chest*. 2002; 121:1782-1788). In a related study, Turkish researchers administered azithromycin 250 mg twice weekly to a group of 11 asthmatics for 8 weeks. No change in FEV₁ was noted, but patients had a marked reduction in bronchial hyperresponsiveness as measured by histamine challenge tests. These patients were not evaluated for evidence of infection prior to initiating therapy (*J Asthma*. 2002;39:181-185).

Good News: Antibiotic Use in Children Down

Meanwhile, efforts by the CDC and others to curb the use of antibiotics in children seem to have paid off. Researchers compared antibiotic prescription rates from 1999-2000 to data from 1989-1990. The number of prescriptions per 1000 individuals age 15 and younger decreased from 838 to 503 a decade later ($P < 0.001$). Prescriptions per 1000 office visits also fell during the same period of time (*JAMA*. 2002;287:3096-3102).

Linezolid Successful in Treatment of MRSA

Methicillin-resistant *Staphylococcus aureus* (MRSA), the bane of hospitals coast-to-coast, is effectively treated with linezolid. Previously vancomycin has been the standard of care for treating MRSA. A new study compares linezolid with vancomycin in 460 patients with known or suspected MRSA infections. Patients were treated with either linezolid 600 mg twice daily ($n = 240$) or vancomycin 1 g twice daily ($n = 220$) for 7-28 days. Clinical cure rates and microbiological success rates were similar for both groups, and both regimens were well tolerated with similar rates of adverse events. It is suggestive that linezolid is a reasonable alternative to vancomycin for MRSA infections and adds the additional option of oral therapy (*Clin Infect Dis*. 2002;34:1481-1490). The study is timely, as the CDC has reported the first isolate of fully vancomycin resistant *S aureus* in a Michigan man. Several cases of intermediate vancomycin-resistant staph have been reported, but

this represents the first case of full resistance (*Morb Mortal Wkly Rep MMWR*. 2002;51:565-567).

SSRIs Relieve Dizziness in Psychiatric Patients

General internists and family practitioners will be delighted to learn that selective serotonin reuptake inhibitors (SSRIs) have been shown to effectively relieve dizziness in patients with psychiatric symptoms, a common office complaint. A group of 60 patients at University of Pennsylvania with psychogenic dizziness, dizziness due to a neurologic condition (with psychiatric symptoms), or idiopathic dizziness were treated with an SSRI for at least 20 weeks. Two thirds of patients had been treated previously with either meclizine or a benzodiazepine. Twenty-five percent of the patients did not tolerate SSRIs. Of those who finished at least 20 weeks of therapy, 84% improved substantially with no difference between patients with major psychiatric disorders and those with lesser psychiatric symptoms. Patients with peripheral vestibular conditions and migraine also improved with SSRIs (*Arch Otolaryngol Head Neck Surg*. 2002;128:554-560).

DEET-Based Mosquito Repellents Just in Time for Vacation

Just in time for summer vacation, the *New England Journal of Medicine* has published a report showing that DEET-based mosquito repellents are superior to non-DEET-based repellants. DEET is the most common compound found in commercial insect repellents. Recently, several botanical repellents have come on the market as well as 3 repellent-impregnated wristbands. These were tested against DEET containing repellents as well as one other chemical repellent containing IR3535. The worst performers were the wristbands, which offered no protection. The IR 3535-based repellents offer minimal protection while the soybean oil-based botanical repellents work for an average of 95 minutes. In comparison, the formulation containing 23.8% DEET offers complete protection for more than 300 minutes (*N Engl J Med*. 2002;347:13-18).

FDA Actions

Risedronate (Actonel), P&G Pharmaceuticals' bisphosphonate for the treatment of osteoporosis, has been approved in a 35 mg once-a-week form. The drug has been available as a 5-mg daily tablet. As with other bisphosphonates, the drug needs to be taken 30 minutes before meals, and patients must remain upright for at least 30 minutes following administration. ■