AMERICAN HEALTH CONSULTANTS®

SPORTS MEDICINE REPORTS™

NEWSLETTER & ELECTRONIC PUBLISHERS FOUNDATION EDITORIAL EXCELLENCE AWARD WINNER

The essential guide to developments in sports medicine and orthopaedics

American Health Consultants Home Page—http://www.ahcpub.com

CME for Physicians—http://www.cmeweb.com

ACL Injury in Female Athletes: Differences in Etiology, Prevention, and Treatment

By James R. Slauterbeck, MD, David E. Hassinger, MD, and Dan M. Hardy, PhD

Females tear their ACLs 3-10 times more frequently than males participating in similar athletic events. The reasons for this disparity are not known and are probably due to several causative factors. Extrinsic factors relate to those outside the body such as training and conditioning. Intrinsic factors within the body include intercondylar notch configuration, ligamentous laxity, anatomic alignment, femoral anteversion, genu valgum, and finally hormonal differences. The cross-sectional area of the female ACL normalized by body weight is smaller than that of the male ACL. Thus, the same tensile force may be sufficiently large enough to rupture the female ACL but not large enough to rupture the male ACL.

In female athletes, the tensile loads on the ACL may reach higher levels than in males. The dynamic resistance to translation is termed the sagittal plane shear stiffness, and is due to maximal co-contraction of quadriceps and hamstrings muscles around the knee.[1] Co-contraction of muscle groups occurs during running, cutting, and landing. Because women have less sagittal plane stiffness than men, activities producing high shear forces will place a greater percentage of the force on the ACL.

According to Wolff's Law, the increased load on the female ACL should invoke a remodeling response to increase its strength. Tissue remodeling occurs continuously in both normal and injured tissues. Indeed, a cyclic tensile load on the ACL in culture results in increased collagen synthesis.[2] However, increasing estrogen concentration in tissue culture decreases ACL collagen synthesis[3] and has shown a decreased load to failure in rabbit ACLs.[4] Also, an increase in a matrix degredadive enzyme, MMP3, without a concomitant increase in its inhibitor, TIMP-1, has been reported.[5] Collectively, these factors decrease the ability of the female ACL to remodel over time with elevated stress levels.

VOLUME 4 • NUMBER 10 • OCTOBER 2002 • PAGES 73-84

INSIDE

Prophylactic treatment recommendations for female athletes are being considered based on inconclusive data from both animal and human studies. Some physicians are already recommending control of the menstrual cycle for injury prevention without sound science to support treatment. We do not support this approach but rather are investigating if a correlation between gender, ligament remodeling, and ACL strength exists. If so, perhaps a medication could be formulated that shifts the remodeling process in favor of ACL repair. Clearly, no one factor has been shown to be the cause for the gender disparity of ACL injury. We submit that a multi-factorial integrated approach combining biomechanical, neuromuscular, and molecular theories is required to address the gender-based disparity of ACL injury in humans.

Males and females demonstrate different neuromuscular responses to landing from a height. Females respond with greater dynamic knee valgus, such that the knees may actually collapse together and touch. Neuromuscular-based training programs have been implemented to limit knee valgus during jumping and landing and have been successful in decreasing ACL injuries. These training programs use plyometric techniques to change muscular firing strategies in athletes.[6]

Regarding operative treatment of ACL deficient knees, most controversy today centers around graft choice and fixation options. When autograft is chosen, the primary choices are hamstring and patellar tendon. Clinical results are slightly better with patellar tendon graft with 93% of patients returning to their same level of sports activity vs. 88% in hamstring patients.[7] There is also slightly increased laxity in hamstring graft patients as measured with KT-2000 arthrometry. Hamstring graft patients had 3 mm or less side-to-side difference in 83% vs. 93% for patellar tendon graft in one large randomized, prospective study.[7] The hamstring muscle group is an agonist to ACL function by acting as a dynamic constraint resisting anterior translation of the tibia on the femur. Their harvest for graft may impair this stabilizing role during the recovery period, although a growing body of evidence supports regrowth of the hamstring tendons over time.

Patellofemoral pain after patellar tendon autograft occurs in up to half of patients. Although there may be less graft site morbidity with hamstring autograft, longer incorporation time remains problematic, although initial fixation methods are improving. Allograft reconstructions are selected primarily because of their lack of graft site morbidity. The main risk with allograft reconstruction is the possibility of disease transmission. The HIV transmission risk has been estimated at 1 in 1.7 million.[8] Functional results are somewhat similar to autograft with good-to-excellent results in 70-90% and laxity testing of 3 mm or less in 71%.[9]

A final controversy in ACL surgery involves fixation choice. The fixation needs to be able to withstand forces seen by the ACL during the rehabilitation period until adequate graft interface healing has occurred. These forces are approximately 500 N and can involve 125,000-250,000 cycles.[10] There are many options available (26 in 1 review). Femoral fixation with a post provides greater than 1000 N of fixation strength and several tibial fixation systems produce similar results. Traditional interference screw fixation gives up to 640 N of fixation strength.[11] All of these are viable options at physiologic loads.

I recommend patella tendon autograft as my graft of choice because I believe it is important to keep the muscles that counter anterior tibial translation strong during the early rehabilitation process. I accept that some athletes may have a small amount of nondebilitating anterior knee pain but will have less anterior tibial excursion. I will consider hamstring grafts for female athletes with exaggerated Q-angles or significant preinjury anterior knee pain. Finally, I avoid allografts in young athletes,

Sports Medicine Reports,™ ISSN 1524-0991, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.
VICE PRESIDENT/GROUP PUBLISHER: Donald R. Johnston.
EDITORIAL GROUP HEAD: Glen Harris.
MANAGING EDITOR: Robin Mason.
ASSOCIATE MANAGING EDITOR: Neill Larmore.
SENIOR COPY EDITOR: Robert Kimball.
MARKETING PRODUCT MANAGER: Schandale Kornegay.
GST Registration Number: R128870672.
Periodical postage pending at Atlanta, GA.
POSTMASTER: Send address changes to ***Sports Medicine Reports***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $37. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

THOMSON
AMERICAN HEALTH CONSULTANTS

Questions & Comments

Please call **Robin Mason,** Managing Editor, at (404) 262-5517; or e-mail: robin.mason@ahcpub.com or **Neill Larmore,** Associate Managing Editor, at (404) 262-5480; or e-mail: neill.larmore@ahcpub.com between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Subscriber Information

Customer Service: 1-800-688-2421.
Customer Service E-Mail Address: customerservice@ahcpub.com
Editorial E-Mail Address: neill.larmore@ahcpub.com
World-Wide Web: http://www.ahcpub.com

Subscription Prices

United States
$269 per year (Student/Resident rate: $108).
Multiple Copies
1-9 additional copies: $197 each. 10-20 copies: $175 each.
Canada
Add GST and $30 shipping.
Elsewhere
Add $30 shipping.

Accreditation

American Health Consultants (AHC) designates this continuing medical education (CME) activity for up to 25 hours of category 1 credit toward the AMA Physician's Recognition Award.

Each physician should claim only those hours of credit that he/she actually spent in the educational activity.
This CME activity was planned and produced in accordance with the ACCME Essentials.
AHC is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

Statement of Financial Disclosure

In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Diduch serves as a consultant to DePuy and Mitek, serves on the speaker's bureau of Mitek, and does research for Smith & Nephew. Dr. Cole serves as a consultant to Mitek and Genzyme, serves on the speaker's bureau of Oratec, and does research for Oratec and Mitek. Dr. Gunther does research for Linvatec. Dr. Schenck does research for Howmedica. Dr. Colman, Dr. Griffin, Dr. Holmes, Dr. Miller, Dr. Perrin, Dr. Safran, Dr. St. Pierre, and Dr. Slauterbeck report no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

reserving these for older athletes with limited exercise goals or a need to return to sedentary type work fast. ■

Dr. Hassinger is a PGY-V Resident in the Department of Orthopedic Surgery at the Texas Tech University Medical Center. Dr. Hardy has a Joint Appointment as an Associate Professor in the Cell and Molecular Biology and Department of Orthopedic Surgery at the Texas Tech University Medical Center, Lubbock, Tex.

References

1. Wojtys EM, et al. *J Bone Joint Surg Am.* 2002;84-A: 10-16.
2. Ohta S, et al. *Lab Invest*. 1998;78:79-87.
3. Liu SH, et al. *Am J Sports Med.* 1997;25:704-709.
4. Slauterbeck JR, et al. *J Ortho Res.* 1999;17:405-408.
5. Slauterbeck JR, Hardy DM. *Am J Med Sci.* 2001;322: 196-199.
6. Hewett TE. *Sports Med.* 2000;29:313-327.
7. O'Neill DB, et al. *J Bone Joint Surg Am.* 1996;78(6): 803-813.
8. Buck BE, et al. *Clin Orthop.* 1989;240:129-136.
9. Noyes FR, et al. *J Bone Joint Surg Am.* 1990;72(8): 1125-1136.
10. Rodeo SA, et al. *J Bone Joint Surg Am.* 1993;75(12): 1795-1803.
11. Pena F, et al. *Am J Sports Med.* 1996;24(3):329-334.

ACL Reconstruction Fixation Update

By COL Patrick St. Pierre, MD

ALTHOUGH ACL RECONSTRUCTION IS COMMONLY performed for symptomatic patients, graft selection, fixation method, initial graft tension, and speed of rehabilitation remain topics of debate. This update will review the current methods of ligament fixation and discuss the pros and cons of each technique.

Ideal graft fixation allows for anatomic graft placement with sufficient strength to allow accelerated rehabilitation during graft incorporation. Ideally, the fixation would enhance the incorporation of the graft to speed its development into becoming as close to the native ACL as possible. The strength required for activities of daily living is estimated to be 454 N based on the failure load of a normal ACL.[1] Fixation techniques have been traditionally measured against this benchmark.

For ACL reconstruction using bone-patellar tendon-bone graft, the gold standard of fixation has been the interference fit screw. This technique is effective with the longest follow-up of current fixation methods. Load to failure has been reported as between 235 ± 124 N and 845.8 ± 188.5 N.[2] Most studies have demonstrated values > 500 N and differences in testing techniques probably account for the variability. Screw length, graft-tunnel gapping, and screw divergence have been studied, and generally a 20 mm screw with < 20° divergence and minimal gap size is the acceptable standard.

The development of bioabsorbable materials has led to the use of absorbable screws made of aliphatic polyesters such as PGA and PLA. Using a bioabsorbable material precludes the need to remove the screw in the case of a revision and allows better MR imaging postoperatively. Biomechanical testing has shown similar fixation strength and stiffness when compared with titanium screws in both single load to failure and cyclic loading.[3] However, as these screws are absorbed they may fragment or leave behind fibrous tissue rather than bone and this can create problems for revision.

Screws made with calcium phosphates have recently been introduced. Like bioabsorbable screws, they do not hinder revision or MR imaging. The Biocryl screw (Mitek Worldwide, Westwood, Mass) is made with a composite of resorbable L-PLA and the osteoconductive bioceramic, *B*-tricalcium phosphate (TCP). TCP has been shown to enhance vascular ingress and calcium deposition, without the formation of an intermediary connective tissue layer.[4] This suggests that the screws should bond to surrounding bone and be replaced with bone rather than fibrous tissue as they dissolve.

Use of an interference screw technique in the femur can lead to complications such as graft laceration, posterior wall blowout, and screw-graft divergence. Errors in graft preparation may produce small bone plugs, or graft-tunnel mismatch that may leave insufficient bone within the tibial tunnel. Graft protectors and adequate visualization usually prevents inadvertent graft laceration. An Endobutton (Smith & Nephew, Andover, Mass) device may be used for insufficient bone plugs, graft tunnel mismatch, or posterior wall blowout. This suspensory type of fixation provides adequate strength for femoral tunnel fixation. However, because it does not provide aperture fixation it may allow "windshield-wiper" graft motion in the tunnel. The development of tunnel expansion has been shown, however a long-term deleterious effect has not been demonstrated.[5]

Another method of femoral fixation for bone-tendon-bone constructs is the RigidFix system (Mitek Worldwide, Westwood, Mass). This system uses bioabsorbable cross pins to secure the bone plug within the femoral tunnel. The advantage of this system is that it allows

100% circumferential healing, provides aperture fixation, and does not interfere with revision surgery or postoperative imaging by MRI. McKernan has shown the pullout strength to range between 600-800 N. This technique is also useful in cases of posterior wall blowout because it doesn't rely on the posterior wall for fixation.

Fixation of soft-tissue grafts such as hamstring tendons or a free quadriceps tendon graft introduces other issues and questions concerning graft fixation. The Endobutton provides adequate fixation strength in an anatomic position, but again does not provide aperture fixation. There is concern that the more distal the fixation from the joint the greater the potential for graft stretch, motion, and tunnel widening. Transfixion pin systems such as the Trans-fix pin (Arthrex, Tampa, Fla) and the Bone-Mulch screw (Arthrotek, Inc, Ontario, Canada) provide for stronger fixation (> 500 N) somewhat closer to the joint. These devices are metal and may interfere with MRI but are usually proximal enough to allow evaluation of the joint. They may require removal for revision surgery. The Mitek RigidFix (Mitek Worldwide, Westwood, Mass) transfixes the graft with 2 absorbable pins much closer to the joint and provides the same advantages as it does for bone-tendon-bone grafts. Finally, soft-tissue interference screws have been produced with less aggressive threads to minimize damage to the grafts. These screws appear to provide adequate fixation strength in the femur, but some studies have questioned their reliability in the tibia.[6]

Tibial tunnel fixation remains the weakest link for soft-tissue graft reconstructions. Compaction of the tibial tunnel by serial dilation, rather than extraction drilling, may produce denser cancellous bone for stronger interference fit fixation. Another method of interference fixation is provided by the Intra-fix system by Mitek Worldwide. This system uses a sheath that separates the 4 tendon strands and provides uniform compression against the tunnel walls when the interference screw is placed in a moly-bolt fashion. Pullout strength of up to 700 N has been reported in company tests. More traditional methods include the use of sutures around a post (573 ± 109 N), fixation with a low-profile screw and soft tissue washer (821 ± 219 N), and belt-buckle double staples (705 ± 174 N). The strongest ultimate failure load (905 ± 291 N) reported is with the Washer Loc (Arthrotek, Biomet, Inc, Warsaw, Ind) washer plate device that is placed at the distal end of the tibial tunnel. These fixation methods do not provide aperture fixation and leave prominent hardware that may need to be removed if symptomatic.[6]

ACL reconstruction methods have developed rapidly over the past 20 years. Fixation devices that enhance tendon healing to bone and increase strength of fixation will continue to improve surgical methods to restore ACL stability. ■

Dr. St. Pierre is Assistant Professor, Uniformed Services University, Orthopedic Co-Director, Primary Care Sports Med Fellowship, DeWitt Army Community Hospital, Ft. Belvoir, Va.

References

1. Noyes FR, et al. *J Bone Joint Surg Am.* 1984;66-A: 344-352.
2. Kurosaka M, et al. *Am J Sports Med.* 1987;15:225-229.
3. Weiler A, et al. *Am J Sports Med.* 1998;26:119-128.
4. Block JE, Thorn MR. *Tissue International.* 2000; 234-238.
5. L'Insalata JC, et al. *Knee Surg Sports Traum Arthro.* 1997;5:234-238.
6. Magen HE, et al. *Am J Sports Med.* 1999;27:35-43.

Meniscal Repair Innovations—Are They Better?

By David R. Diduch, MS, MD

Preserving the meniscus is a well-established hallmark of knee surgery to prevent arthrosis. The recent explosion of all-inside meniscal repair devices has made repair more attainable to even the general orthopaedic surgeon. This is a good thing. However, with this plethora of implants comes the difficult task of determining which are better as there is a dearth of literature regarding each device.

All meniscal repair innovations must stand up against the gold standard, which remains inside-out suture repair. Alternating vertical sutures on the superior and inferior surfaces are the strongest constructs mechanically. These have produced healing rates of 60-80% with isolated repairs, and roughly 90% with repairs in conjunction with ACL reconstruction. The problem has been with the morbidity associated with the additional posterior incisions and the inherent risks to the neurovascular structures, not to mention the extra manpower needed to perform this type of repair.

All-inside meniscal repair has undergone an evolution of sorts. The first generation involved cumbersome suture hooks passed in the back of the knee through cannulas with arthroscopic knot tying. While successful, the

difficulty in the technique prevented its widespread acceptance. This evolved into the suture anchor concept from the front with the T-Fix (Smith & Nephew, Andover, Mass). This required 2 separate anchors placed across the tear with an arthroscopic knot pusher to tie a knot between them. The problem was the inability to tension the knot adequately to compress the tear. However, we learned that it was safe to cross the tear with a puncturing device and anchor this on the periphery of the meniscus. This led to an explosion of all-inside repair devices.

The third generation of all-inside repair involved various absorbable implants to include arrows, darts, screws, fasteners, and other devices that anchored on the periphery and had some type of head to compress the tear. The meniscal arrow (Bionx, Blue Bell, Pa) was probably the most popular as it was basically the first such device. The common concern with all of these is risk of articular cartilage abrasion due to the rigid implant. If inserted obliquely, the tip may abut the tibial surface and drive the head into the femur. In addition, there were various reports of breakage, migration, extrusion from the joint, and transient pain until resorbed.[1,2] Compounding the problem was that they were so easy to put in that surgeons may have begun to change their indications for repair. However, the success rate with these all-inside devices has been reasonably good with short-term follow-up.[3,4]

These problems with chondral abrasion and implant-related morbidity have led to development of the fourth generation of implants. Two new devices incorporate a combination of suture, slip knot, and a peripheral anchor. The fast T-Fix (Smith & Nephew, Andover, Mass) involves 2 of the T-Fix anchors on a single inserter. The anchors are separately placed at the rim of the meniscus through the tear and then a slip knot is tensioned across the tear. The Rapid-Loc meniscal repair device (Mitek Worldwide, Westwood, Mass) involves a single backstop that is deployed on the rim of the meniscus connected by a segment of suture to a slip knot that cinches down an absorbable top hat on the surface of the meniscus to compress the tear. Given the lack of a rigid implant, both of these constructs share the potential ability to deform and move with the meniscus with weight bearing activities and decrease chondral abrasion. Indeed, chondral abrasion scores were lower for company-sponsored studies for the Rapid-Loc in an animal model compared to arrows and other devices.

However, distinct differences exist between these 2 implants. The fast T-Fix requires a sharp inserter to be extended well beyond the meniscus periphery so that the backstop can be deployed, potentially placing the neurovascular structures at risk. If an additional depth stop is not applied to the device, it actually penetrates 22 mm when buried to the hub. In a cadaver study (submitted for publication), we found that these were correctly inserted only 63% of the time by experienced surgeons. The Rapid-Loc in a similar study (submitted for publication) was correctly inserted 85% of the time. Problems with the remaining devices were minor and of questionable clinical significance. This device has a depth stop limiter of only 13 mm. The backstop is deployed further into the periphery using a blunt, flexible spring, which is much safer to the neurovascular structures. The ability to tension the repair is quite remarkable; in fact, the surgeon can even over tension the device if not careful. I have had occasion to rearthroscope patients with this device and have found in each case the meniscal tissue grows over the surface of the implant and I have seen no evidence of chondral abrasion. Even though we just published a paper with the arrows having good clinical success,[3] I switched to the Rapid-Loc device over a year ago given its easy and safe insertion, ability to adjust compression of the tear, and diminished risk of chondral abrasion. Although it is too early to tell for either of these devices, I feel the clinical healing rate thus far is excellent.

These new all-inside meniscal repair techniques offer distinct advantages over existing all-inside methods, including the ability to adjust tension on the repair and a flexible construct for weight-bearing forces. Good comparative and prospective studies are needed in this rapidly growing area of orthopaedics. Until then, the safest recommendation is to use these devices when the ACL is reconstructed and the healing environment is optimal, perhaps reserving inside out repairs for isolated meniscal tears. ■

References

1. Anderson K, et al. *Arthroscopy.* 2000;16(7):749-753.
2. Ross G, et al. *Arthroscopy.* 2000;16(7):754-756.
3. Gill SS, Diduch DR. *Arthroscopy.* 2002;18(6):569-577.
4. Jones HP, et al. *Arthroscopy.* 2002;18(1):64-69.

Osteochondritis Dissecans (OCD): Current Concepts

By Robert C. Schenck, Jr., MD

MUCH LIKE THE TREATMENT OF ANY DEFECT IN THE articular surface, surgical management of osteochondritis dissecans (OCD) lesions has tremendous

challenges to create a stable, hyaline surface. OCD (from the Latin "to separate") is commonly seen in the knee, ankle, and elbow, but has been described in virtually every anatomic site. The pathophysiology is different depending upon location (contrast talar OCD vs knee) and age of presentation. Furthermore, the literature is replete with many differing types of articular injuries categorized under OCD and can be confusing when studying the topic. The focus of this discussion will be on OCD of the knee and the treatment options currently available.

OCD of the knee has varying presentations but can be categorized as either juvenile (open physes) or adult onset (closed physes). Trauma in conjunction with an underlying developmental abnormality of the epiphysis is considered to be the most common mechanism for juvenile OCD. Classically, juvenile OCD presents in the lateral aspect of the medial femoral condyle (85%). Radiographic evaluation of the painful knee in the adolescent (in addition to a careful clinical examination of the hip and spine) involves a tunnel view of the knee whereby the medial and lateral edges of the condyles can be viewed more clearly than in a standard AP radiograph. By using magnetic resonance imaging the presence of OCD separation and loose bodies can be further evaluated. Adult onset OCD presents with similar radiographic findings but has much less healing potential than in a patient with open physes.[1,2]

With the presence of open growth plates, the initial management of the stable juvenile OCD lesion involves immobilization and protected weight bearing.[2] Due to the relative vascularity and repair potential of the child/adolescent, potential for healing with such management is good. The use of arthroscopy and drilling of OCD lesions in those youngsters failing conservative treatment has been shown to be successful.[3] Kocher and associates reported on 23 patients with a ***stable*** OCD lesion of the knee treated with transarticular drilling to heal both clinically and radiographically on average at 4.4 months. They questioned the technique of retrograde drilling, noting the difficulty in accuracy of pin placement. In addition, they also questioned the length of conservative treatment prior to proceeding with surgery, but reaffirmed the long held adage of the younger the patient, the better the healing noted.

In contrast, the ***unstable*** OCD lesion requires a more aggressive approach, either arthroscopic or open. There are long-term clinical data that patients do poorly with simple removal of the OCD fragment.[1,2] Most authors recommend that the clinician should make every effort to repair the unstable OCD lesion with one of a variety of fixation techniques described. The early use of internal fixation devices prompted the development of biodegradable screws and pins to create a stable construct, with compression of the unstable OCD lesion to promote optimal healing. For this reason, screw fixation may be considered optimal over simple pin fixation. The use of differing pitched headless screws allows for internal fixation of the fragment without the need for hardware removal.

An interesting recent advance is the use of osteochondral plug transfer to internally fix an unstable OCD lesion. In 2 separate reports, Berlet and Yoshizumi report on their techniques for fixation and grafting of an OCD lesion about the knee.[4,5] Such a technique (COR®, Mitek Worldwide, Westwood, Mass) using smaller diameter plugs can function to both stabilize the lesion as well as graft across the lesion into healthy bone. Careful attention to surgical technique is required to insure reduction of the OCD lesion as well as avoiding breakage of the osteochondral plug while performing the transfer. Crossing a large OCD lesion can be problematic, especially in the presence of a sclerotic base. Although osteochondral plug transfer doesn't necessarily provide compression of the unstable OCD lesion, in essence the placement of a biologic "bony" pin has tremendous advantages over metal or biodegradable fixation devices as it functions to both fix and bone graft the unstable fragment.

Lastly, the clinician should give consideration to fixation of the free-floating, large OCD fragment as the chondrocytes on the fragment remain viable, bathed in synovial fluid. Such fragments, when large and involving the weight-bearing surface, should be given an attempt at internal fixation. The fragment frequently has slight overgrowth and may require some trimming, but then is reducible and can be internally fixed with good potential for healing. Predrilling the bed to allow for vascular ingrowth in combination with bone grafting, compression fixation, and/or osteochondral plugs can provide an excellent salvage for an otherwise challenging orthopaedic problem.

This leads to the difficult problem of the large empty articular defect due to a chronic OCD lesion. Such clinical scenarios have historically functioned poorly with chronic pain, instability, and degenerative change. These lesions require consideration of transplantation of osteochondral allografts or autografts vs. consideration for autologous chondrocyte implantation. Treatment options must take into consideration the common finding of a large bony defect that in most instances must be simultaneously addressed. Allograft osteoarticular substitution has the advantage of a 1-stage procedure treating both the bony and articular defects. Disadvantages include the risk of disease transmission, availability of transplanta-

tion tissues, and the long-term viability and incorporation of bone and hyaline surfaces. Osteochondral plug transfer is a consideration, but has size and donor site limitations, and is best reserved for smaller lesions between 2 and 4 cm^2 in size. Cell transplantation technologies have gained tremendous popularity due to the availability and the autologous nature of the tissue source. The need to perform a 2-stage procedure (both for bone grafting of the defect site, and simultaneous harvest of hyaline tissue for chondrocyte replication) and cost are relative disadvantages for this technique. Regardless of the treatment option, patient education with hyaline repair is critical for any successful result.

In summary, OCD of the knee requires thoughtful treatment with options dependent upon age and presentation. Failure of initial conservative treatment in those patients presenting with open physes and a stable OCD lesion requires drilling techniques. Aggressive treatment to save the OCD fragment is advocated with the knowledge of poor clinical results with simple excision of the involved osteoarticular segment. Future treatment is still dependent upon early recognition of an OCD lesion to allow for appropriate treatment. The presence of an empty articular defect requires articular grafting. Depending upon lesion size, this involves allo- or autograft osteochondral transplantation vs. bone grafting and chondrocyte implantation. OCD of the knee is a complex orthopaedic problem and requires a careful approach for successful treatment. ■

References

1. Schenck RC, Goodnight JM. *J Bone Joint Surg Am.* 1996;78(3):439-456.
2. Cahill B. *J Am Acad Orthop Surg.* 1995;3:237-247.
3. Kocher MS, et al. *Am J Sports Med.* 2001;29(5): 562-566.
4. Berlet GC, et al. *Arthroscopy.* 1999;15:312-316.
5. Yoshizumi Y, et al. *Am J Sports Med.* 2002;30(3): 441-445.

Current Status of Autologous Chondrocyte Implantation

By Brian Cole, MD, and Shane Nho, MS

In the late 1980s, Lars Peterson, MD, initiated the use of cultured chondrocytes implanted beneath a periosteal patch as a treatment for chondral injuries. Animal studies demonstrating hyaline-like repair and encouraging early clinical results led to the widespread implementation of autologous chondrocyte implantation (ACI) in the United States and Europe with clinical and basic science studies supporting the long-term efficacy and durability of ACI. However, there are a number of scientists investigating alternative methods of enhancing the biological repair and the surgical technique using ACI.

ACI Clinical Outcomes

Mid-term ACI results have reported approximately 85% improvement of femoral lesions and osteochondritis dissecans (OCD).[1,2] Chondral defects of the patella and tibia have been known to be difficult areas to repair; thus, the results have been much less predictable. Minas compared the clinical outcomes of patients in 3 different groups: simple (mean size, 4.30 cm^2), complex (6.75 cm^2), and salvage (11.66 cm^2) groups at 24 months.[3] The patients of complex and salvage groups usually required additional procedures to correct alignment or ligament insufficiency. Patients in the simple and complex group demonstrated high functional improvements, but the patients in the salvage group had the highest satisfaction rating of 90% compared to 50% in the simple group and 80% in the complex group.

Vasara and associates[4] performed second-look arthroscopy with electromechanical indenter testing 1 year following ACI of the knee. Fifteen of 29 patients rated their knee as good or excellent by the Brittberg score, but 20 patients had follow-up scores greater than baseline scores. Arthroscopy demonstrated lesions filled with repair tissue with generally good integration with the surrounding cartilage, and periosteal hypertrophy was evident on several occasions. The average indenter stiffness of the implantation site was roughly 65% of the surrounding normal cartilage. The OCD lesions tended to be lower at 42% than the traumatic lesions at 72%. Vasara et al concluded that the indentation analysis did not correlate with clinical evaluation at 1 year because the tissue healing and remodeling process is not yet complete.

Innovations in ACI

Despite the success of ACI, there is considerable interest in improving and expanding this new technology. A suitable substitute for the periosteal patch is one modification that has received significant attention. Regarding the current periosteal patch, there are concerns of periosteal hypertrophy, delamination, dedifferentiation of chondrocytes, donor site morbidity, and uneven distribution of chondrocytes beneath the patch.

Collagen membrane and hyaluronan scaffolds appear to be the most promising and have already been implanted in human subjects.

Different variations of the collagen matrix scaffold are being investigated by a number of groups. Mahroof et al[5] have implanted the chondral lesions (mean, 2.88 cm^2) of 34 patients with a porcine collagen type I/III membrane and autologous cells. With an average follow-up of 19 months, 68% of patients have good or excellent Brittberg ratings and improvements in Lysholm scores. Arthroscopy demonstrated good implant integration with surrounding normal cartilage, and 70% of biopsies confirmed the presence of hyaline cartilage. Bentley et al[6] implanted the chondral defects (mean, 4.35 cm^2) of 125 patients with autologous cells using either traditional periosteum (26%) or porcine collagen membrane (74%). At 1 year patients reported 89% good or excellent ICRS ratings and second-look arthroscopy of 61 patients revealed 82% ICRS grade 1 or 2 repair. Granrath et al[7] reported that patients implanted with collagen fleece scaffold coated with autologous cells demonstrate good clinical results and well-restored joint surface by MRI. Second-look arthroscopy reveals no scaffold hypertrophy or ossification of the graft, and biopsies confirmed collagen-like repair similar to adjacent cartilage with regard to microscopic, biomechanical, and viscoelastic patterns. Other collagen-based scaffolds that are under consideration include collagen tri-layer matrix, three-dimensional collagen sponge, and chitosan blended collagen scaffold.

Hyaluronic acid based polymer (Hyaff-11, Fidia Advanced Biopolymers, Italy) is a biodegradable, 3-dimensional biologic scaffold. Facchini et al[8] conducted studies to determine the ability of this biomaterial to support the growth of human chondrocytes. Proteoglycan and collagen type II production were noted with time and chondrocytes completely colonized the scaffold. Nehrer et al[9] reported the preliminary results of the human experience with the hyaluronan matrix (Hyalograft C, Fidia Advanced Biopolymers, Italy). Twenty-three patients with a mean defect size of 6.2 cm^2 in the femoral condyles and patella were implanted. After 6 months, the average VAS-Scale decreased to 16.4 (nearly no pain) from a preoperative score of 77.9 (severe pain). This technique requires a smaller incision with fibrin glue fixation. It is thought that the 3-dimensional matrix should be able to provide a more uniform distribution of chondrocytes in the chondral defect. Preliminary studies are also being conducted on agarose gel, calcium phosphate cement, polylactide and polyglycolide sponge, 3D polysaccharide scaffold, polyethylene glycol terephthalate-polybutylene terephthalate block copolymer scaffold, polyurethane scaffold, perforated polyurethane prosthesis, biphase hydrogel beads, and cartilage-like biomaterial.

In addition to the biologic scaffold, there are a number of institutions that are conducting research involving chondrocyte culture techniques, cryopreservation of chondrocytes, periosteum evaluation, growth factor augmentation, and the use of stem cells. The next generation of ACI should use a biologic scaffold that is able to transport and sustain chondroctyes without adverse reactions. A 3-dimensional matrix may provide more uniform chondrocyte distribution in the defect and relative ease of surgical implantation that may permit the orthopaedic surgeon to perform the procedure with an arthroscopic or arthroscopically-assisted approach. Purification of chondrocyte culture techniques and augmentation with growth factors may prevent dedifferentiation of chondrocytes, thereby facilitating the production of hyaline cartilage. The early term clinical results of collagen and hyaluronan scaffolds are promising and seem to at least parallel traditional ACI outcomes.

Further scientific and clinical studies are necessary to determine which modifications to ACI may yield the best possible results. A focus on decreased processing costs, biologic carriers, and less invasive techniques is likely to dominate these future efforts. ■

Shane Nho is a Fourth Year Medical Student at Rush Medical College in Chicago, Ill.

References

1. Peterson L, et al. *Am J Sports Med.* 2002;30:2-12.
2. Gillogly S, et al. *J Orthop Sports Phys Ther.* 1998;28: 241-251.
3. Minas T. Clinical experience of autologous chondrocyte implantation for the severely injured knee. In: *4th International Cartilage Repair Society Symposium*. Toronto, Canada; 2002:65.
4. Vasara A, et al. Arthroscopic indentation analysis and clinical follow-up one year after autologous chondrocyte transplantation. In: *4th International Cartilage Repair Society Symposium*. Toronto, Canada; 2002:58.
5. Mahroof S, et al. Autolgous chondrocyte transplantation: Histological evaluation one year following surgery. In: *4th International Cartilage Repair Society Symposium*. Toronto, Canada; 2002:64.
6. Bentley G, et al. Autologous chondrocyte implantation in the young adult knee: Clinical, arthroscopic, and histological results of 125 patients at 18 month follow-

up. In: *4th International Cartilage Repair Society Symposium*. Toronto, Canada; 2002:71.
7. Granrath M, et al. Minimal invasive autologous chondrocyte transplantation using a collagen scaffold. In: *4th International Cartilage Repair Society Symposium*. Toronto, Canada; 2002:60.
8. Facchini A, et al. Human chondrocyte grown onto hyaluronic acid-based polymer scaffold undergo a redifferentiation process. In: *4th International Cartilage Repair Society Symposium*. Toronto, Canada; 2002:107.
9. Nehrer S, et al. Preliminary results of matrix-assisted chondrocyte transplantation using a hyaluronan matrix. In: *4th International Cartilage Repair Society Symposium*. Toronto, Canada; 2002:57.

PCL Reconstruction Update

By Mark D. Miller, MD

Reconstruction of the posterior cruciate ligament (PCL) continues to be a subject of much debate within sports medicine. Despite the evolution of various surgical techniques, we are still not as successful in reconstructing the PCL as we are at reconstructing the ACL. This is probably due to a variety of factors that we are only beginning to understand. Perhaps the most basic reason is that PCL injuries are far less common. The average sports medicine surgeon may see only a handful of these injuries each year, and may see an equal number of ACL injuries in a month or even a week. The old adage "Practice makes Perfect" certainly applies.

Another major factor is the recognition of the importance of other structures that may be injured at the time of PCL injury. Perhaps the most important of these structures is the posterolateral corner (PLC). We now recognize that PCL injuries with more than 10-12 mm of posterior displacement commonly have associated PLC injuries. Reconstruction of the PCL should not be attempted without combined PLC reconstruction. A variety of techniques for PLC reconstruction have been described and primary repair of injured structures with augmentation when necessary is recommended.[1]

Another factor that continues to evolve is controversy regarding the best technique for PCL reconstruction. Recent biomechanical studies have suggested that the traditional arthroscopic trans-tibial technique may subject the graft to excessive bending, abrasion, and even failure.[2] Because of these concerns, the tibial inlay technique has been developed. This technique avoids the so-called "killer turn" at the back of the knee. It does require a posterior approach, but the safety of this approach has been demonstrated in a recent cadaveric study.[3]

The tibial inlay technique is perhaps best carried out when the patient is positioned in the lateral decubitus position with the injured leg up. The leg is externally rotated at the hip for patella tendon graft harvest, arthroscopy, debridement of the PCL stump, and femoral tunnel placement. The guide wire for the femoral tunnel is placed in the anterolateral portion of the PCL origin, at approximately the 10:30 or 11:00 position, 8 mm from the articular surface. It is overdrilled with a 10- or 11-mm drill and the back edge is rasped. The leg is positioned on a Mayo stand and a posterior approach is made in the flexion crease overlying the popliteal fossa. The key to the approach is to incise the fascia and mobilize the medial head of the gastrocnemius. Retracting this muscle laterally protects the neurovascular structures and allows direct access to the back of the tibia. A trough is made in the PCL fossa, and the graft bone plug is fixed with spiked, soft tissue washer plus a low-profile, bicortical screw placed from posterior to anterior. This provides secure fixation of the graft. The graft is delivered into the knee through a posterior arthrotomy and retrieved with a bent wire that is placed from the femoral tunnel into the back of the knee. After the knee is cycled, the graft is fixed in the femoral tunnel with an interference screw and back-up screw and washer fixation.

Another controversial issue centers on whether 2 femoral tunnels should be used. This 2-bundle technique has been shown biomechanically to result in better graft stability in both extension (which would be expected) and also in flexion.[4] The unknown factor is whether these biomechanical differences will affect clinical results.

There are extremely limited published reports of PCL reconstruction in the literature. Fanelli has published good results with trans-tibial PCL reconstruction.[5] Unfortunately, like a lot of these studies, his population was mixed and included many cases of combined PLC reconstructions. Cooper has presented results using the tibial inlay technique with side-to-side differences on stress radiographs of approximately 3 mm (compared to 10-15 preoperatively).[6] Jung and associates recently reported their 2-year follow-up results of PCL inlay reconstructions done in Korea. Average posterior displacement on stress radiography improved from 10.8 mm to 3.4 mm in this study with 90% of patients reporting a satisfactory outcome.[7]

Although we are encouraged by these reports, PCL reconstruction, even with the inlay technique, is not as successful as ACL reconstruction. The theoretical improvement offered by 2-bundle femoral reconstructions may not justify the additional technical difficulty and potential complications of this new technique. Better grafts, improved techniques, and long-term results may change the way that we perform PCL reconstruction in the future. ■

References

1. Miller MD, et al. Posterior cruciate ligament: Current concepts. Instr Course Lect. Rosemont, IL: AAOS; 2002;51:347-351.
2. Markolf KL, et al. *J Bone Joint Surg Am.* 2002;84-A: 518-524.
3. Miller MD, et al. *J Knee Surg.* In Press, Summer 2002.
4. Griffin JR, et al. *J Knee Surg.* 2002;15(2):114-120.
5. Fanelli GC, et al. *Arthroscopy.* 1996;12(5):521-530.
6. Cooper DE. Primary PCL reconstruction with the tibial inlay technique. AOSSM Proceedings, June 2001, Keystone, CO.
7. Jung Y-B, et al. Reconstruction of the posterior cruciate ligament by the modified tibial inlay method. Paper #9, Proceedings of the 2002 Annual Meeting of the AAOS, Feb. 2002, Dallas, TX, 3:602

Current Concepts in Patellar Instability

By Marc R. Safran, MD

Recent interest in patellar instability has focused on the role of the medial patellofemoral ligament (MPFL), a well-defined structure in more than 90% of cadaver knees. Biomechanical studies suggest it is a prime static stabilizer to prevent patellar dislocation, providing 41-80% of the restraint to lateral displacement, with the greatest contribution in the first 15° of knee flexion.[1] The MPFL is in layer II of the medial knee soft tissues and runs from its femoral attachment just distal to the adductor tubercle and postero-superior to the medial epicondyle, to the upper two-thirds of the medial patellar margin. In some series, the MPFL attaches to the underside of the VMO instead of the patella. The MPFL is 5-6 cm in length, becoming narrower and thinner as it approaches its femoral attachment.

Until recently, the MPFL has been overlooked in the pathophysiology of patellar instability. It has been commonly thought that lateral patellar dislocation was associated with tears of the medial retinaculum and/or the VMO; however, recent research reveals these structures are not injured, and the MPFL is the essential lesion with patellar dislocation.[2] The injury to the MPFL can occur anywhere along its course—midsubstance, off its femoral attachment, or from its patellar attachment—and can be injured in more than one location with a single patellar dislocation.

Many other factors are felt to play a role in recurrent patellar instability, including trochlear dysplasia, increased Q-angle, and excessive genu valgum. The Q-angle gives a static determination of one component of the vector of pull of the extensor mechanism and is best measured with the knee in 90° of flexion. Those with recurrent patellar dislocation and an increased Q-angle may be considered for an operation medializing the tibial tubercle to decrease this displacing vector of lateral pull. The Hauser procedure (simple medialization of the tibial tubercle) has an obligatory posteriorization of the tubercle due to the triangular shape of the tibia. This posteriorization increases the forces on the patellofemoral joint and usually results in arthritis. Alternatively, Fulkerson developed a tibial tubercle osteotomy that provides for anteromedialization.[3] This oblique osteotomy goes from anteromedial to posterolateral so that the tubercle is slid anteriorly and medially (AMZ Tracker, Mitek Worldwide, Westwood, Mass). The osteotomy is usually 7-10 cm long to allow a large contact surface to reduce the risk of non-union. The osteotomy is internally fixed by 2 low profile screws to reduce postoperative symptoms related to their subcutaneous position.

The recurrence of acute patellar dislocations has been reported to be 15-44%. Maenpaa and Lehto reported a prospective randomized trial of treatment of patellar dislocation and found the recurrence rate was approximately 3 times greater in the group treated with early range of motion.[4] A way to consistently predict who will have a recurrence is important, as is a way to reduce the likelihood of recurrence. In a prospective natural history study of 125 first-time patellar dislocators, Fithian showed that 17% had a recurrence of dislocation or subluxation within 2-5 years, while 9% had a dislocation of the contralateral patella (unpublished data). The predictors for recurrence included younger age at the time of initial dislocation, while the risk of dislocating the contralateral patella was increased in those with a family history of patellar problems and hip dysplasia.

A few authors in the 1990s recommended primary repair of the MPFL after initial dislocation for young,

athletic individuals who some authors feel are at higher risk of recurrent dislocation. Several small, noncontrolled studies have shown MPFL repair to be successful in preventing recurrent patellar instability. However, 2 recent prospective, controlled studies were unable to find a reduction in recurrence of patellar instability for first-time patellar dislocation when comparing those treated surgically (including MPFL repair) and those treated nonoperatively.

At this point, surgery can only be recommended for acute, first-time patellar dislocations if there is an associated osteochondral fracture that requires removal or internal fixation; repairing the MPFL at its site of injury should also be considered at that time. Acute repair of an avulsion from the patella may be managed with suture anchors or bony tunnels, while repair of an avulsion from the femoral attachment is usually accomplished using a low profile screw with a spiked soft tissue washer or suture anchors. Midsubstance injuries may be repaired primarily; however, the strength of the repair is of question and many would recommend augmentation of the MPFL. It is critical when performing an MPFL repair or reconstruction not to overconstrain the patellofemoral joint thereby limiting motion.

For recurrent dislocations, addressing the cause of recurrence is critical. A lateral release does not address the cause of recurrence and is generally not recommended in the management of patellar instability. As the essential lesion in patellar instability, the MPFL generally warrants repair. Although at this time repair of the MPFL for the first-time dislocation is not indicated, exceptions may be repair of an MPFL tear when operating for an acute osteochondral lesion. However, more study is needed to further define who may benefit from early surgery. ■

References

1. Tuxoe JI, et al. *Knee Surg Sports Traumatol Arthrosc.* 2002;10:138-140.
2. Nomura E, et al. *Knee.* 2002;9:139-143.
3. Fulkerson JP, et al. *Am J Sports Med.* 1990;18: 490-496.
4. Maenpaa H, Lehto MU. *Am J Sports Med.* 1997;25: 213-217.

CME Questions

21. Reasons for an increased incidence of ACL tears in females include all of the following *except*:
a. hormonal differences, especially involving estrogen.
b. neuromuscular differences, especially decreased co-contraction of quads and hamstrings.
c. greater dynamic knee valgus on landing.
d. quadriceps to hamstring muscle imbalance.

22. Aperture fixation is felt to diminish which problem with ACL fixation?
a. Graft motion and tunnel widening
b. Initial graft fixation strength
c. Subsequent MRI imaging
d. Hardware in the way of revision

23. An important advantage to the fourth generation meniscal repair devices which combine a peripheral anchor and a suture construct is:
a. increased chondral risk of abrasion.
b. diminished risk of tethering neurovascular structures.
c. the ability to tension the repair to compress the tear.
d. that it can be put in faster.

24. Treatment of OCD of the knee:
a. involves initial early aggressive surgical management.
b. is best followed by serial bone scans.
c. is dependent upon age and presentation of the patient.
d. is more straightforward in the juvenile patient.

25. Which chondral defect location has the least clinical follow-up following autologous chondrocyte implantation?
a. Patella
b. Tibia
c. Femoral condyle
d. Trochlea

26. PCL injuries with major instability commonly have what associated injury that must also be addressed?
a. Posterolateral corner injury
b. Medial meniscocapsular injury
c. Lateral meniscus tear
d. Patellar dislocation

27. Surgery for the individual with a first-time patellar dislocation is indicated when:
a. there is a tear of the medial patellofemoral ligament from its femoral origin.
b. the patient is a young girl with ligamentous laxity.
c. there is an operative osteochondral fracture.
d. the patient has an increased Q-angle.
e. All of the above

Readers are Invited. . .

Readers are invited to submit questions or comments on material seen in or relevant to *Sports Medicine Reports*. Send your questions to: Neill Larmore, *Sports Medicine Reports*, c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. For subscription information, you can reach the editors and customer service personnel for *Sports Medicine Reports* via the internet by sending e-mail to neill.larmore@ahcpub.com. We look forward to hearing from you. ■

In Future Issues:

Is Arthroscopy Effective for Arthritis?

PHARMACOLOGY WATCH

Forgot Your Ginkgo? Forget About It, Study Shows

The $15 billion dietary supplement industry took a bruising in the last month with reports that some of the most popular over-the-counter treatments are little more than expensive placebo. Ginkgo, the commonly used memory enhancing agent, was evaluated in 230 men and women older than the age of 60 who had normal memory and were in good health. Patients were randomly assigned to receive ginkgo 40 mg 3 times a day or matching placebo for 6 weeks. Neuropsychological tests were administered at the end of the study, which revealed no significant differences between treatment groups on any of the outcome measures including verbal and nonverbal learning and memory, attention and concentration, naming and expressive language, self-reported memory, and companion scoring. The study concluded that ginkgo did not facilitate learning memory tension or concentration in adults older than the age of 60 (*JAMA*. 2002;288:835-840). In a separate study from The Netherlands, 652 adults older than age 60 were given a multivitamin/mineral supplement, 200 mg of vitamin E, both, or placebo in a study to evaluate whether the supplements would reduce the incidence and severity of acute respiratory tract infections. Patients were followed for nearly 1.5 years. No difference was found among any of the groups with regard to incidence or severity of acute respiratory infections, except for the finding of worsening severity of disease in the vitamin E group (19 days illness with vitamin E vs 14 days illness with placebo; $P = 0.2$). (*JAMA*. 2002;288:715-721.)

On the other hand, a homocysteine-lowering therapy with a combination of B vitamins effectively improves clinical outcomes after percutaneous coronary interventions. Folic acid, vitamin B_{12}, and vitamin B_6 were tested in a randomized, double-blind, placebo-controlled trial involving more than 550 patients in Switzerland who had undergone successful angioplasty. The participants received a combination of folic acid 1 mg/d, vitamin B_{12} 400 µ/d, and vitamin B_6 10 mg/d, or placebo. The main outcome measure was the composite outcome of major adverse events including death, nonfatal myocardial infarction, and the need for repeat revascularization evaluated at 6 months and 1 year. The composite end point was significantly lower at 1 year in the vitamin-treated patients (15.4%) compared to the placebo group (22.8%) (RR, 0.68; 95% CI, 0.48-0.96; $P = .03$) primarily due to reduce rate of revascularization. (*JAMA*. 2002;288:973-979).

Celebrex OK for Asthma Patients

Celecoxib (Celebrex®) may be safe to use in patients with a history of aspirin-induced asthma. Patients with known aspirin sensitivity, or aspirin-exacerbated respiratory disease (AERD), are generally unable to take aspirin or any NSAID. In a study from San Diego, 60 patients with AERD were challenged with celecoxib, a COX-2 inhibitor, or placebo over 48

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. Telephone: (404) 262-5517. E-mail: robin.mason@ahcpub.com. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.

hours. During the study period, none of the 60 patients experienced any symptoms or changes in nasal examinations or declines in FEV_1. The following day, all 60 patients were exposed to aspirin and all showed sensitivity. The study concluded that inhibition of COX-1 is the critical initiating event in respiratory reactions in patients with AERD (*Arthritis Rheum*. 2002;46:2201-2206).

Losartan Not Superior to Captopril

The angiotensin II receptor blocker losartan is not superior to the ace inhibitor captopril after complicated acute myocardial infarction. The large OPTIMAAL trial (Optimal Trial in Myocardial Infarction with the Angiotensin II Antagonist Losartan) looked at 5477 patients in 7 European countries with confirmed acute myocardial infarction and heart failure. Patients were randomly assigned and titrated to target dose of losartan 50 mg once daily or captopril 50 mg 3 times daily. The primary end point was all-cause mortality. During a mean follow-up of 2.7 years, there were 499 (18%) deaths in losartan group and 447 (16%) in the captopril group (RR 1.13; 95% CI, 0.99-1.28; $P = 0.07$). Because of this nonsignificant trend in total mortality in favor of captopril, the study suggests that losartan cannot be generally recommended in this population. It is noted however that losartan was better tolerated than captopril, and associated with significantly fewer discontinuations (*Lancet*. 2002;360:752-760).

Alfa-Interferon Could Help Fight West Nile

The number of West Nile virus cases is mounting in the United States, Canada, and Mexico where 37 deaths have been attributed to the virus, now the first case has been reported in California, and other cases are the result of organ donation from infected donor. Researchers are hoping that alfa-interferon may be of help. The drug has been effective against St. Louis encephalitis, a similar virus, and is the drug of choice for treatment of hepatitis C. Researchers are enrolling patients in the New York area where the virus first appeared 3 years ago. Although infection with the mosquito-borne virus rarely causes serious illness (< 1%), the elderly and chronically ill are particularly prone to encephalitis. alfa-interferon will be given for 2 weeks and should be started within the first few days of illness, prior to the onset of encephalitis. Research is also progressing on 3 West Nile virus vaccines, which should be in human trials by 2003.

Sertraline Effective Against Depression

Depression is common in patients with coronary artery disease and represents a significant independent risk factor for both first myocardial infarction and cardiovascular mortality. A new study shows that the selective serotonin reuptake inhibitor sertraline is safe and effective for treating major depression in patients with recent myocardial infarction or unstable angina. A total of 369 patients on 3 continents with major depressive disorder were enrolled and randomized to sertraline 50-200 mg/d or placebo in a double-blind fashion for 24 weeks. The main outcome was change in left ventricular ejection fraction (LVEF) while other outcomes included surrogate cardiac measures and cardiovascular adverse events. Sertraline had no significant effect on LVEF, and also did not increase ventricular premature complex runs, QTc intervals, or other cardiac measures. The incidence of severe cardiovascular adverse events was 14.5% with sertraline and 22.4% with placebo. Depression scores were better in the sertraline group. The authors conclude that sertraline is safe and effective for trading depression in patients with recent MI or unstable angina (*JAMA*. 2002;288:701-709).

FDA Actions

Procter & Gamble has announced that it expects an over-the-counter form of omeprazole (Prilosec) to be available by early 2003. The company has received an approval letter from the FDA but needs to clarify language on the package label so that consumers will clearly understand how to use the drug. Procter & Gamble is planning a study to make sure consumers understand the drug labeling, a process which will take several months. The FDA has approved fluoxetine (Prozac) for the treatment of panic disorder. The indication was previously only granted to paroxetine (Paxil) and sertraline (Zoloft), and it has been heavily promoted by the manufacturers of these drugs. Fluoxetine is also recently approved for long-term treatment of bulimia. The drug has been been available as a generic for more than a year, and as such represents a lower cost alternative for patients with these conditions. ■