

BioMechanics

by K. Dean Reeves, MD, Brad Fullerton, MD, Gaston Topol, MD, and Greg Bancroft

SPORTS MEDICINE



Study seeks treatment to keep athletes in the game

Osgood-Schlatter disease (OSD) is one of the most common sports-limiting orthopedic conditions that adolescent athletes will encounter.¹ It involves damage to the epiphysis of the tibial tuberosity and to the attachment of the patellar tendon to the tuberosity.

Price et al found an incidence of OSD of one in 20 athletes aged 11 to 13 for each season of each year studied.² The recognized criteria for an OSD diagnosis include pain, tenderness, and swelling of the tibial tuberosity.³ Pain reproduction in most patients occurs on extension of the knee against resistance.⁴ Single leg stance with the knee in flexion reproduces pain over the tibial tuberosity. Typically, local tenderness is aggravated by kneeling, running, cycling, and climbing or descending stairs.⁴

The condition was originally—and incorrectly—termed an epiphysitis because of a few white blood cells found on biopsy. In reality, it is a predominantly degenerative condition and better termed an “osis” rather than an “itis,” which

explains why arthritis medications offer no long-term benefit to OSD patients.⁵

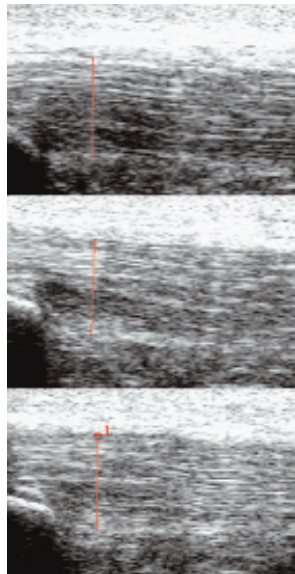


Figure 1. High-resolution ultrasound images indicating the healing process. The top image is prior to injection. The other images are two (middle) and eight (bottom) months after injection.

OSD causes significant intermittent pain, interferes with sports choices and participation for an average of 18 months, and wreaks havoc with young boys' and girls' self-esteem at a critical point in their development. It also leads to chronic pain and limitations in a substantial number of athletes, seriously damaging or altering careers, or causing participants to drop sport altogether. Despite a mandate by the Joint Commission on Accreditation of Healthcare Organizations to adequately address pain,⁶ these young adolescents are typically informed that their condition is “benign” and that they will “outgrow it.” Treatment for the pain, other than minimizing it via activity modification, is not available. The term “benign” is a gross oversimplification that shows no empathy for these young athletes. The only prospective scientific literature available indicates that current methods

The effects of Osgood-Schlatter disease can extend beyond resolution of pain to a patient's sports career.

are very limited and will not fix this condition.

We are beginning a placebo-controlled international study of a treatment for OSD involving injection of 12.5% dextrose to repair the patellar tendon connection with the tibial tuberosity. Injection, however simple, may be considered invasive by some sports medicine professionals. But we believe the condition of OSD merits an attempt at cure and will describe a treatment method that is inexpensive, minimally uncomfortable, and similar in safety to acupuncture.

Typical exam and treatment

OSD is thought to be caused by a traction effect of the patellar tendon on the tibial tuberosity.¹ If, during an adolescent growth spurt, the lengthening of the quadriceps lags behind the lengthening of the femur, extra tensile force is applied to the patellar tendon at its insertion point on a tibial tuberosity that has not achieved skeletal maturity. This stress is accentuated by repetitive contractions of the quadriceps during sports activity. OSD can also be caused by a major traumatic event, such as a fall or blunt trauma to the tibial tuberosity.¹

Magnetic resonance imaging has clarified the stages of OSD.³ The early stage shows edema about the tibial tuberosity. The progressive stage involves first a small tear in the cartilage, then a widening of the tear, and then the separation of a portion of the cartilage from underlying structures. The only follow-up MRI study³ in the literature included 40 knees with 11 of them showing complete avulsion (separation) of the cartilage piece from underlying bone. But the percentage of OSD cases that proceed to full avulsion is not precisely known. Mital et al demonstrated that in all knees with complete avulsion of the cartilage a small fluid pocket (bursa) separated the ossicle from the tibial tuberosity.⁷

Patients are typically told by their treating practitioner that the condition is symptomatic for only 12 to 18 months, as long as the cartilage doesn't rupture, and that skeletal maturity brings relief from symptoms for most patients.⁸ Treatment, as a rule, includes suspension of sporting activity and a variety of remedies such as an infrapatellar strap, ice, massage, and NSAIDs.³ A conservative treatment regimen of rest and suspension of sports activity, though often recommended, has shown limited evidence of improving outcomes. There may be some benefit to use of an infrapatellar strap to limit symptoms, but again, no evidence of long-term efficacy.³ There are no reported prospective interventional studies.⁹

Hamstring flexibility exercises and judicious quad strengthening are typically recommended. Short-arc hamstring strengthen-

ing has been mentioned, but never studied. Immobilization of the knee in a splint is not used except for resistant cases, and then only for a short duration. Steroid injection is generally not recommended.¹⁰ Often athletes are forced to drop one or more of their sports; the literature has no good data on the frequency with which this occurs.

Short- and long-term effects

We consider true success to be a return to full power, full effectiveness, and full aggressiveness of play, unrestricted by fear of the injury worsening. No study now available on Medline suggests anything close to true success with current OSD treatment. If success is defined, it is usually as "return to training" or "return to play." Earlier literature often did not describe therapeutic exercises to avoid disuse and to correct associated hamstring tightness or weakness. In a 1985 study, though subjects were prescribed two months' rest from any activity causing pain, pain often led them to cease training entirely for 3.2 months on average. Time to return to full training was 7.3 months on average.¹¹

Current approaches appear to be a little better. For example, Hirano in 2002 described an average time of return to training of 6.3 weeks.³ However, even with current treatment approaches, the short-term effect of OSD in more symptomatic cases is to block the athlete from participating in one or more of the sports with greater jumping or patellar contact components.

Earlier conservative approaches led to a failure rate for return to full sport within three years of more than 10%.⁷ Only two studies have looked at long-term follow-up.

Krause et al¹² asked patients previously diagnosed with OSD on whom they'd gathered retrospective data whether they were still limited in activity. At an average of nine years after OSD diagnosis, 60% of 62 respondents still had pain or discomfort with kneeling, 24% claimed to be limited in activities other than kneeling by chronic anterior knee pain, and 18% stated their pain was still over the tibial tubercle. They were not asked about current engagement in sport or whether the diagnosis had caused them to drop certain sports. Nor were they asked whether they felt had lost scholarships or forfeited a chance at a career in sport due to OSD. Thus, this study likely underestimated the long-term effects of the condition in terms of forcing changes in the lives of these young people.

Ross and Villard¹ studied 25 Air Force Academy students whose OSD had been diagnosed on average 7.6 years previously and compared them to 25 matched controls. The investigators

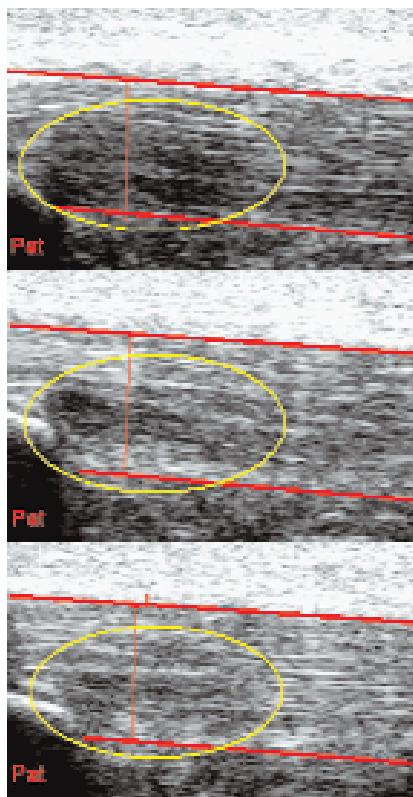


Figure 2. In this image, the tendon is outlined, the patella indicated, and a major area of tendon degeneration circled.

found that 88% of those with a history of OSD reported anterior knee pain with sporting activity. In addition, subjects with a history of OSD scored significantly ($P < 0.00001$) lower on both the activities of daily living and sports activity scales of the Knee Outcome Survey. Although all cadets were participating fully in their required athletic and military training activities, subjects with a history of OSD experienced greater limitations in running, jumping, cutting, or pivoting.

There are, of course, those who are quite experienced and particularly talented in OSD treatment and would predict better long-term results, but their results have not been reported in the peer-reviewed literature.

Based on current literature and observations, OSD has important short-term effects on aggressiveness of practice and of play, may cause disuse weakness of the quadriceps, and results in loss of participation in some sports during critical skill development periods. Functionally important long-term effects include chronic anterior knee pain with at least mild limitation of activity in the majority of athletes, chronic discomfort with kneeling in the majority of athletes, and lower function on a scale of ADLs.

We cannot comment about the frequency and severity of self-esteem effects of OSD or on the number of athletes who ultimately drop out of sport entirely, because these issues have not been included in outcome measure analysis.

Case report

Greg Bancroft has an undergraduate degree in physical education and has served as a coach in the Kansas City area in various sports for many years, primarily at junior high and high school levels. Bancroft's son Philip, when he was 11, began to complain of severe knee pain at the outset of basketball practice sessions. After one practice the pain became so severe that Philip stayed home from school the next day and needed help to walk down the stairs of his home. The diagnosis confirmed OSD. Philip was given a typical stretching and modalities program. He also took oral supplements (selenium and vitamin E) and used a neoprene sleeve on the affected limb.

Despite state-of-the-art treatment, for 18 months the on-and-off pain was significant enough that he did not run with the same speed or play with same aggressiveness, especially in basketball and football. OSD affected his practice time as there were drills he could not do. He found he could play baseball without as much trouble but both basketball and football were substantially affected, as the constant running and the chance of contact against the touch-sensitive knee is high in these sports.

The greatest damage may have been to his confidence. He not only had to deal with pain and the fear of pain, but he also had to compete with other athletes for positions and playing time. He was operating, according to his dad's evaluation, at about 80% of his actual capability.

Bancroft said of his son's experience that though he did play and earn significant playing time, he lost confidence as well as status among his peers and coaches during this time.

Because there is not yet a treatment available that enhances or

speeds up tissue repair, limiting activity until healing is usually part of the OSD treatment. Even athletes who can afford to see a sports physician for a diagnosis and who are prescribed appropriate strengthening/stretching exercises and relative rest are often asked to drop a sport or limit their primary sport for significant periods of time.

"These pubescent kids are already dealing with insecurity and now they are dealing with a pain they did nothing to create," Bancroft said.

"This adolescent period is critical not only for physical development but also for psychosocial development. OSD is a major adverse factor affecting these athletes' psychosocial health," Bancroft said.

Study rationale

Though they are different types of connective tissue, cartilage (chondrocyte) and tendon (fibroblasts) cells have one useful and important characteristic in common: Both begin to grow and repair themselves when exposed to specific complex proteins called growth factors. The GFs that cause this to happen for both cell types are very similar. GFs that stimulate both chondrocytes and fibroblasts, for example, include platelet-derived growth factor (PDGF), transforming growth factor beta (TGF- β), basic fibroblast growth factor (bFGF), insulin-like growth factor (IGF), and connective tissue growth factor (CTGF).¹³ These agents are specific to particular kinds of cells and do not affect bone, which has its own set of specialized proteins. They will not cause bone spurs or other abnormal structures to grow.

When anyone, adolescent or adult, experiences an acute injury to ligament, tendon, or cartilage, the body goes through three stages in an attempt to heal the injury:⁵ inflammation, which helps signal repair cells; proliferation, during which repair cells begin to multiply and produce new material for repair; and remodeling, during which new tissue is laid down in an organized fashion. However, repair is almost always less than perfect, and with repeated events the cumulative injury increases to the point of more tissue disruption and pain.

Prolotherapy is defined as "the injection of growth factors or growth factor production stimulants to produce normal cells or tissue."¹⁴ It can also be described as reconstructive injection. The injection can be either growth factors produced outside the body and then injected or a solution that stimulates production of growth factors within the body.¹⁴ Research with a single growth factor has been frustrating because it does not imitate the body's own healing method. The body produces multiple growth factors at the same time, which is particularly important since each of these growth factors has a different function and they work together as a team. It is exciting and particularly pertinent that exposing chondrocytes and fibroblasts to elevated glucose concentration results in the production of all the growth factors listed above (PDGF, TGF- β , bFGF, IGF, and CTGF). Glucose is fuel for all body cells and injected glucose is not left behind once it serves the function of stimulating the GF production, making its use for this purpose inexpensive and "natural." The concentration of glucose

surrounding a cell that's needed to turn on GF production by chondrocyte and fibroblast cells in a test tube is approximately 0.5%.¹⁵ That level cannot be reached by oral intake.

In clinical practice the concentrations of dextrose (glucose in solution) injected are higher, allowing for a dilution effect and keeping the blood glucose level elevated for several hours while local cells absorb the extra dextrose. Growth is stimulated without inflammation by dextrose up to 10% concentration. In some clinical situations, the practitioner may want to use the inflammatory cascade to produce more vigorous growth and so may increase dextrose concentration above 10% or add another inflammatory component, such as sodium morrhuate (a fatty acid derivative) or phenol, to the solution.

This adolescent period is critical for physical and psychosocial development.

Studies in humans have thus far demonstrated safety and symptomatic benefit from dextrose injection in severe large joint (knee) and small joint (finger) arthritis.^{16,17}

The ability to tighten loose ACL ligaments by simple knee injection has been demonstrated in a pilot study in humans.¹⁸ Elite kicking-sport athletes with chronic adductor or abdominal strain or osteitis pubis appear to respond dramatically with simple dextrose injection in affected attachment sites.¹⁹

High-resolution ultrasound imaging is a relatively new addition to the practitioner's armamentarium. Lazzara²⁰ recently published the first case study using pre- and post-treatment CT and high-resolution ultrasound to demonstrate healing of a complete Achilles tendon rupture in a soccer athlete. High-resolution ultrasound imaging of the patellar tendon and its attachment is expected to objectively demonstrate post-treatment changes in OSD patients.

An example of patellar tendon healing is shown in Figures 1 and 2. The athlete whose ultrasound results are depicted is a 40-year-old male cyclist who had been unable to train seriously for more than a year due to "jumper's knee" with degeneration of the patellar tendon as it attaches to the lower patella (knee cap). On just one occasion 0.5-mL amounts of 15% dextrose and 0.125% sodium morrhuate were injected directly into the athlete's patellar tendon at 0.5- to 1-cm intervals in four locations.

Figure 1 shows serial high-resolution ultrasound before injection, two months after injection, and eight months after injection. The athlete returned to full-time cycling by three months after injection. The ultrasound images are longitudinal along the tendon. They start at the patella (on the left) and go about 2 cm down the tendon. In Figure 2 the tendon is outlined in red, yellow circles outline the area of degeneration, and the patella is labeled (Pat). The dark area in the first images of both figures represent areas of fiber separation and thinning to the point that it appears as though there is a dark hole in the tendon. The reader will observe that in the later images, taken with the same

intensity and at the same depth, not only is the dark area lightening, but the entire tendon is becoming more densely populated with linear fibers and thus appears more organized and lighter on the ultrasound. The National Institutes of Health are working on standardizing the reading of high-intensity ultrasound images and these methods will be used in the current OSD study design.

Study design

Research will be conducted at sites in Kansas City, KS; Austin, TX; and Rosario, Argentina.

Recruitment. Subjects will be recruited via contacts with rugby and soccer clubs and through coaches, pediatricians, sports medicine physicians and surgeons, physical therapists, and athletic trainers. This is a study of athletes and only those who play on an organized team with a coach will be accepted. We expect subjects to have had discomfort during or after sport intermittently for three months or more, and standard treatment approaches are to be taken before study enrollment. Specifically at least a one-month period of minimized sports activity will be requested, along with at least a one-month attempt at exercises to include hamstring stretching and mild quadriceps strength maintenance exercises in extension. Because we are hoping to have a number of athletes young enough to truly heal OSD, we are accepting only nine to 15-year-old girls and 10 to 17-year-old boys. Subjects outside this age group will be treated in open label fashion in a separate data collection effort.

Examination. To rule out jumper's knee or chondromalacia (which respond to prolotherapy as well but are not being studied here), patients must point to the tibial tuberosity to describe where their pain is and not also at the patella. A single leg squat test must reproduce their pain. No other symptom or condition should be causing pain with sport.

Treatment. A tiny (27 gauge) needle will be used to inject those in the experimental group with 0.5 mL of 12.5% dextrose in 1% lidocaine at a depth of 0.5 cm and at intervals of 0.5 cm along the area of pain over the tuberosity and in the tendon. Both patients and participating practitioners will be blinded; the solution will consist of either 12.5% dextrose in 1% lidocaine (active injection) or 1% lidocaine without dextrose (control injection). Those injected will repeat a single leg squat to confirm that solution was injected in all areas responsible for their pain.

Because injection itself is often of therapeutic benefit, another control group will receive exercise only, which of course will be unblinded. Subjects will be assigned randomly to exercise, lidocaine injection, or dextrose injection groups. Those in the injection groups will receive injections at zero, one, and two months; at three months the blinded portion of the study will stop. Those who received lidocaine only and those who received exercise only will be offered dextrose injection open label for months three, four, and five. Those who received dextrose will be offered PRN dextrose if their OSD symptoms are not completely resolved.

Data collection. A visual analog scale (VAS) for sports-related pain (either during or after sport) will be obtained as well as a

Nirschl Pain Phase Scale (a measure of functional impairment from pain). Double blind data will be gathered at zero, one, and two months and open label data will be gathered after that, since all subjects will receive active treatment by three months. Twelve-month follow-up data will be gathered on all subjects as well.

In addition, a subgroup of patients will have their tendon and tuberosity status followed by high-intensity ultrasound imaging to objectively demonstrate changes that occur with dextrose injection. Pretreatment imaging will be compared with images taken three and six months post-treatment onset.

Summary

OSD has been a defined condition since 1903, and is a degenerative condition (osis) rather than an inflammatory condition (itis). It is common in adolescents and is best treated before a tear occurs in the cartilage. There are no reported prospective interventional studies. Current treatment is helpful but does not prevent substantial short-term physical and psychological effects and significant long-term alteration in sports careers. Requiring that an athlete endure this condition until maturity is not optimum for many reasons. Tendons and cartilage both respond to dextrose-stimulated growth factors. A double blind study is soon to begin comparing dextrose, lidocaine injection, and exercise alone for athletes with OSD. The goal for this study will be to cure OSD prior to cartilage separation. High-intensity ultrasound monitoring of subjects' progress will be useful to objectively demonstrate healing. ■

K. Dean Reeves, MD, FAAPM&R, is a clinical associate professor of physical medicine and rehabilitation at the University of Kansas Medical Center in Kansas City. Brad Fullerton, MD, has a private physical medicine and rehabilitation practice in Austin, TX. Gaston Topol, MD, is team physiatrist for the Rosario Rugby Union in Rosario, Argentina. Greg Bancroft, BS Phys Ed, is a coach in the Greater Kansas City Area.

References

1. Ross MD, Villard D. Disability levels of college-aged men with a history of Osgood-Schlatter disease. *J Strength Cond Res* 2003;17(4):659-663.
2. Price RJ, Hawkins RD, Hulse MA, Hodson A. The Football Association medical research programme: an audit of injuries in academy youth football. *Br J Sports Med* 2004;38(4):466-471.
3. Hirano A, Fukubayashi T, Ishii T, Ochiai N. Magnetic resonance imaging of Osgood-Schlatter disease: the course of the disease. *Skeletal Radiol* 2002;31(6):334-342.
4. Hussain A, Hagroo GA. Osgood-Schlatter disease. *Sports Exerc Inj* 1996;2:202-206.
5. Kader D, Saxena A, Movin T, Maffulli N. Achilles tendinopathy: some aspects of basic science and clinical management. *Br J Sports Med* 2002;36(4):239-249.
6. Phillips D. JCAHO pain management standards are unveiled. Joint Commission on Accreditation of Healthcare Organizations. *JAMA* 2000;284(4):428-429.
7. Mital MA, Matza RA, Cohen J. The so-called unresolved Osgood-Schlatter lesions. *J Bone Joint Surg* 1980;62-A(5):732-739.
8. Ishida K, Kuroda R, Sato K, et al. Infrapatellar bursal osteochondromatosis associated with unresolved Osgood-Schlatter disease. *J Bone Joint Surg* 2005;87-A(12):2780-2783.
9. Bloom OJ, Mackler L, Barbee J. What is the best treatment for Osgood-Schlatter disease? *J Fam Pract* 2004;53(2):153-156.
10. Duri ZA, Patel DV, Aichroth PM. The immature athlete. *Clin Sports Med* 2002;21(3):461-482.
11. Kujala UM, Kvist M, Heinonen O. Osgood-Schlatter's disease in adolescent athletes. Retrospective study of incidence and duration. *Am J Sports Med* 1985;13(4):236-241.
12. Krause BL, Williams JP, Catterall A. Natural history of Osgood-Schlatter disease. *J Pediatr Orthop* 1990;10(1):65-68.
13. Reeves KD. Sweet Relief: prolotherapy targets sprains and strains. *Biomechanics* 2004;10(9):24-35.
14. Reeves KD. Prolotherapy: basic science, clinical studies, and technique. In: Lennard TA, ed. *Pain procedures in clinical practice*, 2nd ed. Philadelphia: Hanley & Belfus, 2000:172-190.
15. Ohgi S, Johnson PW. Glucose modulates growth of gingival fibroblasts and periodontal ligament cells: correlation with expression of basic fibroblast growth factor. *J Periodontal Res (Denmark)* 1996;31(8):579-588.
16. Reeves KD, Hassanein K. Randomized prospective double-blind placebo-controlled study of dextrose prolotherapy for knee osteoarthritis with or without ACL laxity. *Altern Ther Health Med* 2000;6(2):37-46.
17. Reeves KD, Hassanein K. Randomized prospective placebo controlled double blind study of dextrose prolotherapy for osteoarthritic thumbs and finger (DIP, PIP, and trapezio-metacarpal joints): evidence of clinical efficacy. *J Altern Complement Med* 2000;6(4):311-320.
18. Reeves KD, Hassanein KM. Long-term effects of dextrose prolotherapy for anterior cruciate ligament laxity: a prospective and consecutive patient study. *Altern Ther Health Med* 2003;9(3):58-62.
19. Topol GA, Reeves KD, Hassanein K. Efficacy of dextrose prolotherapy in elite male kicking-sport athletes with chronic groin pain. *Arch Phys Med Rehabil* 2005;86(4):697-702.
20. Lazzara MA. The non-surgical repair of a complete Achilles tendon rupture by prolotherapy: biological reconstruction. A case report. *J Orthop Med* 2005;27(3):128-132.