Efficacy of Dextrose Prolotherapy in Elite Male Kicking-Sport Athletes With Chronic Groin Pain

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ABSTRACT. Topol GA, Reeves KD, Hassanein KM. Efficacy of dextrose prolotherapy in elite male kicking-sport athletes with chronic groin pain. Arch Phys Med Rehabil 2005;86: 697-702.

Objective: To determine the efficacy of simple dextrose prolotherapy in elite kicking-sport athletes with chronic groin pain from osteitis pubis and/or adductor tendinopathy.

Design: Consecutive case series.

Setting: Orthopedic and trauma institute in Argentina.

Participants: Twenty-two rugby and 2 soccer players with chronic groin pain that prevented full sports participation and who were nonresponsive both to therapy and to a graded reintroduction into sports activity.

Intervention: Monthly injection of 12.5% dextrose and 0.5% lidocaine into the thigh adductor origins, suprapubic abdominal insertions, and symphysis pubis, depending on palpation tenderness. Injections were given until complete resolution of pain or lack of improvement for 2 consecutive treatments.

Main Outcome Measures: Visual analog scale (VAS) for pain with sports and the Nirschl Pain Phase Scale (NPPS), a measure of functional impairment from pain.

Results: The final data collection point was 6 to 32 months after treatment (mean, 17mo). A mean of 2.8 treatments were given. The mean reduction in pain during sports, as measured by the VAS, improved from 6.3± 1.4 to I.0±2.4 (P<.001), and the mean reduction in NPPS score improved from 5.3±0.7 to 0.8t 1.9 (P<_001). Twenty of 24 patients had no pain and 22 of 24 were unrestricted with sports at final data collection.

Conclusions: Dextrose prolotherapy showed marked efficacy for chronic groin pain in this group of elite rugby and soccer athletes.

Key **Words:** Athletic injuries; Glucose; Groin; Growth substances; Osteitis; Rehabilitation; Sports medicine; Tendinitis; Tendons.

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T HIS ARTICLE WAS WRITTEN to introduce a different treatment approach to a common clinical condition. Groin pain is a very common problem in kicking sports. Among male soccer players, the incidence of groin pain is estimated at 10%

to 18% per year. The most common causes of chronic groin pain in athletes are adductor strain and osteitis pubis. Osteitis pubis is the most common pain condition involving the symphysis pubis, is often self-limited in symptom duration, and occurs most commonly in men during their thirties and forties. Pain may be in the pubic area, 1 or both groins, or in the lower abdomen, and it may be exacerbated by exercise or specific movements such as running, kicking, or pivoting on 1 leg; it may also occur when just walking. The usual treatment for muscular or enthesis-related groin pain typically includes use of modalities until the range of motion is less inhibited, then a restoration of range, followed by strengthening and endurance efforts, and finally a return to full sport. There is some indication that active training returns more athletes to being able to participate in their sport than passive modalities[ ] Unrestricted sports participation may be delayed up to 6 months for chronic adductor sprain and strain, and time to complete resolution of symptoms may exceed 1 year in osteitis pubis .[3] Failure to return to the prior level of sports function may be as high as 25%:[o]

It has become the prevalent opinion in basic science literature that the pathology of sprain and strain is primarily an "-osis," rather than an "-his" (a degenerative process rather than a change induced by inflammation), with connective tissue degenerative change in the presence of a paucity of leukocytes.[ ] This explains the generally short-lived results from corticosterojd injection used for chronic sprain and strain.[ ] Leadbetter[7] coined the term *connective tissue insufficiency* to describe the loss of tissue strength related to degenerative change, which results in loading and stimulation of relatively fixed-length pain mechanoreceptors.

Prolotherapy is a treatment technique involving the injection of growth factors or growth-factor–production stimulants to promote growth and repair of normal cells and tissue. Growth factors are complex polypeptides that initiate multiplication (proliferation) of new cells or reparative changes in current cells. The most common form of prolotherapy is the wide-spread use of erythrocyte growth factor injected into patients with chronic anemia.[8] Other methods of elevating growth factors include injection of human blood, which contains a variety of growth factors,[5] injection of recombinant growth factors,[9] or injection of plasmids (nonviral deoxyribonucleic acid particles)[10] or viruses[ ] that are programmed to produce growth factors. Human cells also begin to produce growth factors within minutes to several hours after exposure to an extracellular D-glucose (dextrose) concentration of as little as 0.6% (normal cellular glucose concentration is 0.1·4[12] These growth factors include platelet-derived growth factor,[13] trans-forming growth factor beta,[ ] epidermal growth factor,[15] basic fibroblast growth factor.[16] insulin-like growth factor.[17] and connective tissue growth factor.[14] These growth factors have also been identified as key stimulants of tendon, ligament. and cartilage (not bone) repair and growth.[18] Recent human double-blind studies of intra-articular 10% dextrose injection have confirmed that dextrose is clinically beneficial in the treatment of large[19] and small joint[20] osteoarthritis, and a 3-year follow-up study on anterior cruciate ligament (ACL) laxity has

shown that simple dextrose injection tightens and strengthens loose ACLs.[2] in addition to a simple dextrose effect on growth factors, other proliferation effects of injection are thought to occur: both disruption of cells by needle trauma and use of dextrose in a concentration over 10% result in a brief inflammatory reaction with expected elevation of growth factor levels through the inflammatory cascade.[22]

The concentration of dextrose used in our study was 12.5%. Dextrose concentrations of 10% to 20% are used routinely in peripheral and central hyperalimentation solutions. Inadvertent infiltration of hypertonic dextrose into soft tissue is common on a daily basis, and yet a MEDLINE search from 1966 to 2004 yielded no reports of tissue necrosis from such infiltration. This, and the experience of over 50 years of hypertonic dextrose injection into soft tissues in nearly all entheses in the human body in the performance of prolotherapy, speaks against the likelihood of any safety concerns with hypertonic dextrose injection into connective tissue areas.

Prolotherapy has the potential to add to the natural repair process and to treat multiple causes of groin pain. In the presence of groin pain, for example, injection of the adductor attachments to the pelvis, injection of conjoint tendons on the pelvic rim, and injection of the symphysis pubis can treat adductor tendinosis, osteitis pubis, and even groin disruption (injury to the external oblique aponeurosis and conjoined ten-don on the suprapubic region).

Our hypothesis was that chronic, overuse-related, and performance-limiting groin pain in elite kicking-sport (predominantly rugby) athletes can be treated effectively using dextrose prolotherapy, despite failure of nonsurgical treatment for a minimum of 6 months.

METHODS

Most patients were ref erred by the orthopedic surgeon and team physician of the Rosario Rugby Union and were primarily on city teams that supplied the national team of Argentina. 'Twenty-two patients were rugby players and 2 were regional soccer players. All subjects were men. The average age was 25 years. All patients had chronic pain that blocked full performance in sports and occurred even with activities of daily living.

Patients had experienced groin pain for a mean of 15.5 months (range, 6—60mo) and physical examination showed that all had evidence of both osteitis pubis and adductor tendinosis. Two patients had received corticosteroid injections in the symphysis pubis without lasting benefit. In all patients enrolled, pain over the symphysis pubis was noted with manual compression while contracting abdominal muscles in partial sit-up or with adductor contraction. Pain over the adductor insertions was also noted with palpation over the insertion and with adductor isometric contraction at various angles. All patients were checked for a true leg-length discrepancy or foot abnormality such as excessive pronation positioning that could predispose to osteitis pubis. Neither leg-length discrepancies nor foot abnormalities were found in this group.

Patients provided a history of previous physical therapy (PT) treatments. If this did not include ultrasound application, electrogalvanic stimulation, trigger point pressure on tendon inset tions, stretching, and strengthening, a therapy course was provided that included the treatment modalities not previously received. Fifteen of the 24 patients had already had the specified PT. At the conclusion of 10 sessions of therapy, no patient experienced an improvement of more than 10% and pain recurred to the same level when patients attempted to perform athletic activity. If pain levels were such that the patients believed they were still unable to perform at a high level in their sport, they were offered prolotherapy. A pretreatment

visual analog scale (VAS) for pain with exercise was administered, and each subject was asked to fill out the Nirschl Pain Phase Scale (NPPS) to determine his functional impairment level (appendix 1).[23]

The solution used was a combination of 12.5% dextrose and 0.5% lidocaine. It was prepared by mixing 8mL of 1% preservative- and epinephrine-free lidocaine with 8mL of 25% dextrose solution in a 20mI. syringe. Overlying hair and skin areas were prepared with liberal use of povidone iodine.

The injection order is shown in figure 1 (right side). The symphysis pubis was injected first with 2mL of solution using a 23-gauge needle at a depth of 2 to 4cm (point 1 on fig 1). One milliliter was then injected in each of points 2 to 4 along the pubic rim on either side of the symphysis pubis in I-cm intervals, covering the pectineus origin and pyramidalis insertion and external oblique insertions. For points 2 through 4, the superior pelvic rim was contacted with the needle, the needle was directed off the edge to confirm location at the top of the rim, and then the needle was redirected back onto bone for the injection. Redirection of the needle was attempted only after withdrawing the needle to a nearly subcutaneous position to avoid having the needle follow the same tract on readvancement.

A total of 4mL (in 1-mL aliquots) was then injected along each ischiopubic sinus (points 5— 8), covering attachments of the adductors (fig 1, left side). Laterally to medially these injections touched the adductor magnus, gracilis, adductor brevis, adductor longus origins, and the insertion for the rectus abdominis on the pubic tubercle. In addition, the obturator externus origin was likely affected by solution spread effect due to its proximity to the adductor attachments.

Injection sites 5 through 8 were addressed by having each patient extend his opposite leg. The leg to be injected was flexed and externally rotated with the foot against the opposite leg as in fig 2. (Female injection in the same area is depicted in figure 2 for clearer illustration.)

For injection into the ischiopubic minus, the needle entry was in a caudocephalad direction to ensure a better sense of distance from the midline. The line of needle insertion points was vertical rather than angled to ensure that bone contact occurred rather than the needle falling off bone medially at first insertion. The depth of injection was similar for each ischiopubic ramus injection site and the typical distance off midline for entry in ischiopubic minus injections was about 4cm. Due to tissue depth. it was sometimes necessary to use 2 fingers, I on each side of the needle, to indent the soft tissue to allow needle contact with hone. However, this was done without skin traction to avoid altering mediolateral orientation.

Confirmation that the painful areas were injected was done by numbness on palpation. Five minutes after injection, patients were checked to ensure that isometric contractions of the abdominals and stretching and/or isometric contractions of the adductors were no longer painful. If contraction was still painful. additional solution was infiltrated in the area of residual pain. If pain continued, palpation was repeated for any residual tender spots. Both legs were injected in tender locations if both were symptomatic. and at follow-up patients commonly had only 1 symptomatic side.

Subjects were told not to jog or run for the first week after the first treatment; from days 7 to 14 they could jog as tolerated (usually not more than 6—8krnld at a speed of ==5min/km); and from days 14 to 21 they were allowed to increase distance and speed as tolerated. Forceful kicking was to be avoided for 21 days. Patients were educated not to do anything that would result in more than mild discomfort. These patients were not allowed to take nonsteriodal anti-inflammatory drugs (NSAIDs), primarily so that they would have a better pain
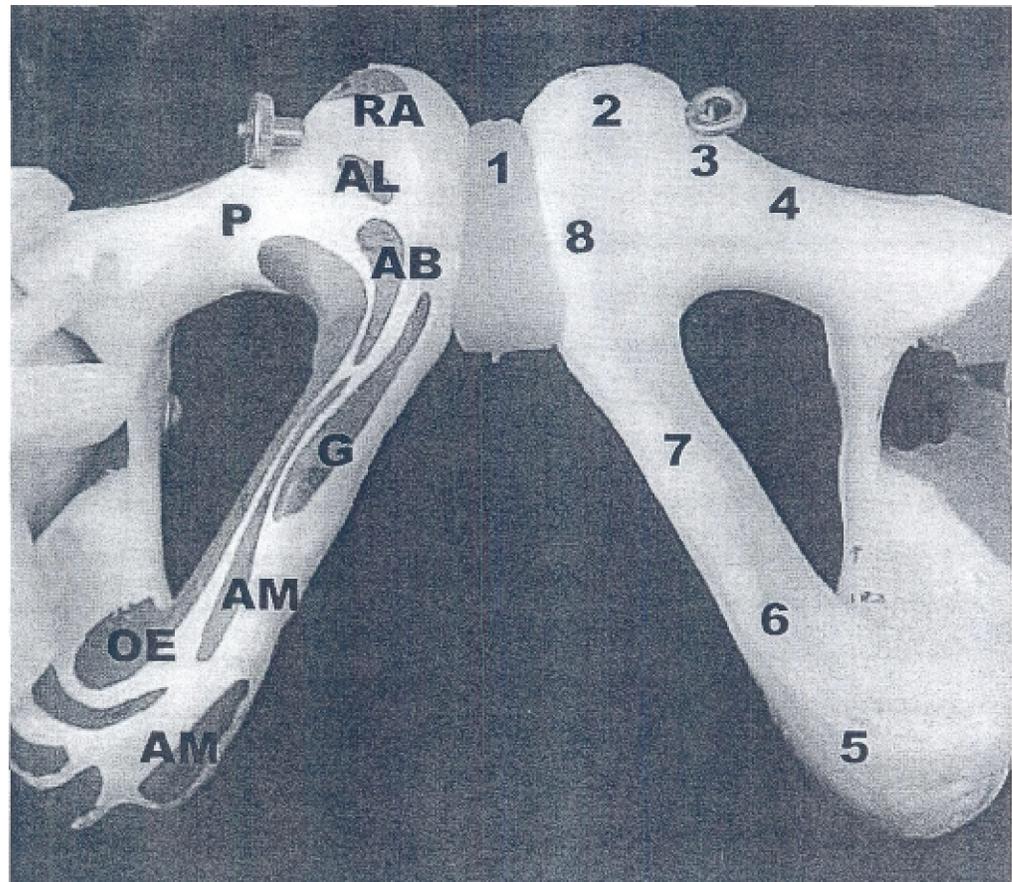
Fig 1. Injection order and muscle attachments injected in the treatment of chronic groin pain. Abbreviations: AS, adductor brevis; AL, adductor longus; AM, adductor magnus; G, gracilis; OE, obturator externus; P, pectineus origin; RA, rectus abdominus.

gauge to determine if they could tolerate the amount of exercise being introduced. Typical prolotherapy recommendations suggest that NSAIDs and narcotics he avoided because they interfere with normal inflammatory soft tissue signals that aid in healing soft tissue. NSAIDs are not contraindicated if the proliferant mechanism of action is noninflammatory. In our study, the dextrose concentration exceeded 10% (12.5% was used), which was expected to create some inflammatory stimulation for healing as well, and NSAID avoidance was still recommended.

Acetaminophen was allowed, but only a few patients took it. The only exercise that patients were Instructed to do was adductor and abdominal muscle stretching and strengthening, as tolerated. if there was pain with isometric contraction at the mid range, they were instructed to perform contractions at angles that were pain free. Subjects were then seen at 4-week intervals and given a repeat injection of 12.5% dextrose if they still had pain with activity or if they had pain with stretching or isometric contractions of the abdominals or adductors. After the second and any subsequent injections, they were told to abstain from physical activities for only 3 days and then to participate in practices and game situations as tolerated.

Treatment was stopped if the patient reported complete resolution of symptoms on the VAS and the NPPS, palpation of the adductor and abdominal tendons in the pubic and suprapubic area was pain free, and isometric contraction of the abdominal and adductor muscle groups was pain free. Treatment was also stopped if the subject did not report improvement after 2 consecutive prolotherapy treatments. Follow-up data were ob-

tanned on all patients 1 month after the first injection. A long-term data follow-up point was obtained on all patients 6 months after the last patient completed his injections. This data point varied from 6 to 32 months (mean. 17mo) after the final injection.

Procedures followed were in accordance with ethical standards outlined in the Helsinki Declaration revision of 1983 and institutional review approval was obtained from the Science and Research Committee of the Provincial Hospital of Rosario, Argentina. The statistical analysis software used was SPSS, version 7.5." A preliminary test for the significance of both variables (sports pain, NPPS score) was performed simultaneously using the Hotelling T^2 method. Because the Hotelling test showed significant differences between pretreatment and posttreatment values in multivariate analysis, we ran individual paired t tests for each variable. Bonferroni adjustment for 2 variables confirmed significance of the P values.

RESULTS

Ten subjects needed 2 treatments, 7 subjects needed 3 treatments, 4 required 4 treatments, and I each required 1, 5, and 6 treatments. The average number of treatments received per patient was 2.8. No patients dropped out. Discomfort with injection and after injection was minimal, with soreness and stiffness typically lasting for several days. Subjects did not need narcotic analgesia and were able to avoid taking NSAIDs. Hotelling multivariate T^2 analysis of mean difference before and after treatment was highly statistically significant at P less

not

than .001. Individual paired t tests showed statistically significant reductions from the baseline for each variable (table I).

Figure 3 shows the VAS sports pain ratings before treatment. 1 month after treatment, and at long-term follow-up evaluation; figure 4 shows NPPS scores before treatment, 1 month after treatment, and at long-terra follow-up evaluation. The improvements reached at 1 month after treatment were well sustained, despite participation in sports in an unrestricted manner. Of particular interest is that 20 patients had no pain with sports at an average follow-up time of 17.2 months and that 22 of 24 patients were playing at full capacity. "Those who needed 1 to 2 treatments returned to full sports participation by 6 weeks.

Fig 3. VAS for sports pain before treatment, 1 month after first injection, and at final data collection (range, 6–32mo; average, 17.2mo).

Those who needed more than 2 treatments were fully participatory in sports by 3 months, except for the 2 nonresponders. Each of the 2 nonresponders received a magnetic resonance imaging (MRI) scan of the pelvis, which showed no pathology other than osteitis pubis.

DISCUSSION

Groin pain in athletes is complex because of the frequent presence of 2 or more injuries and a rather extensive differential diagnosis. These patients did not have a relatively acute presentation of lower abdominal pain, so aneurysm, appendicitis. diverticulosis, and inflammatory bowel disease were not seriously considered. They also did not have recent-onset groin pain or any urinary symptoms: thus. urinary tract infection, lymphadenitis, prostatitis. scrotal and testicular abnormalities, and nephrolithiasis were not considered likely. Internal snapping hip syndrome was
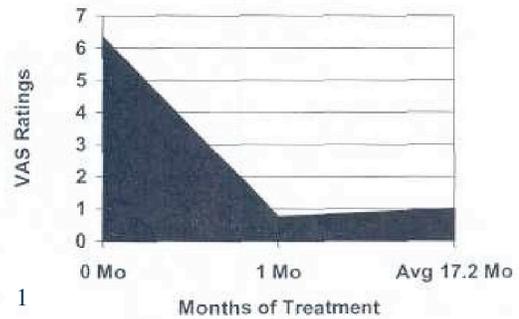
evidenced historically. Other causes of groin and pubic area pain include hip synovitis, slipped capital femoral epiphysis. avascular necrosis of femoral head. osteoarthritis, stress fracture of the femur or pelvis, avulsion fracture, sports hernia, ilioinguinal neuralgia. Reiter's syndrome, and rare (in athletes) subclinical infection of the pubic ssymphysis.3 [4,24][25] However, these patients had no systemic signs or symptoms and, after anesthesia to the entheses, they showed pain-free adduction and pain-free abdominal flexion against resistance and could hop without pain. A preinjection sedimentation rate was not obtained in this study and is a reasonable consideration to further rule out rare infection of the symphysis pubis.

Alternative injection treatments merit attention. Although there has been only 1 study of corticosteroid injection, it appeared successful in helping patients return to athletics and showed some sustaining benefit. That study was quite small

Table 1: Variables Before Treatment and After Treatment (At Long-Term Follow-Up Evaluation)

Variables	Pretreatment*	Posttreatment'	Mean Difference Before to After Treatment	SEM Difference	95% CI for the Mean Difference	Pr
VAS rating for sports pain	6.311.4	1.012.4	-5.3	0.5	-6.3 to -	<.001
NPPS score	5.310.7	0.8-1.9	-4.5	0.3	-5.1 to -	<.001

NOTE. Individual paired t tests for mean difference between pretreatment and posttreatment values in patients with chronic groin pain.
Abbreviations: CI, confidence interval; SEM, standard error of mean.
*Values are mean ± standard deviation.
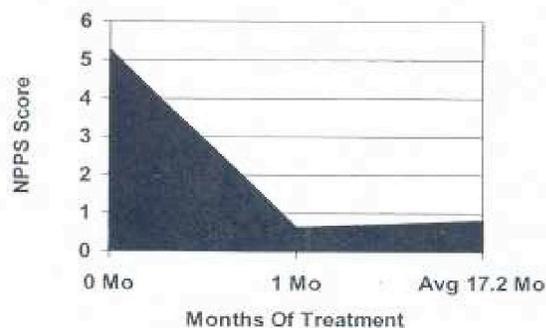tSignificance of the mean difference between pre- and posttreatment.

Fig 4. NPPS before treatment, 1 month after first injection, and at final data collection.

(9 patients), and a larger-scale replication study has not been reported. If our understanding of pathology that "-osis" rather than "-itis" is the primary pathology in chronic sprain and strain, it may be that growth induction treatment methods merit consideration as the treatment of choice. Surgical options, such as symphyseal curettage for osteitis pubis, have been per-formed in athletes with chronic groin pain, but outcomes have not been entirely predictable or sustained and surgical considerations should typically follow a conservative approach except in cases of significant groin disruption.[3;28]

Growth factor stimulation as a potential mechanism for clinical benefit cannot be confirmed, because growth factor levels were not measured in this study. The effect of dextrose injection in this study was not compared with injection of saline or lidocaine. For a true placebo comparison, it would likely be necessary for the placebo arm of the test to avoid any tendon or ligament contact because *mere* contact can create a growth response. Cell membrane disruption caused by a needle will result in leakage of proinflammatory lipids from cell membranes, and thus a growth factor response. In addition, needle contact can result in microbleeding. Blood contains a number of growth factors, as shown by Taylor et al,[29] who created a growth response in normal rabbit patellar tendon by simple blood injection, and Edwards and Calandruccio[5] showed marked benefit in extensor tendinosis with a single nontraumatic injection of blood. Yelland et al[30] also showed that needling alone may be beneficial in patients with chronic low hack pain. Patients injected with dextrose appeared to fare somewhat better than patients injected with saline, but this difference was not significant and both groups experienced significant and sustained benefit. Their study conclusions were hampered by lack of inclusion of several key nociceptors in the injection field. In an effort to show the effect of dextrose in the absence of needle trauma, initial double-blind studies on dextrose proliferant injection were designed to involve minimal (finger osteoarthritis) or no (knee arthritis and ACL laxity) bony contact.[19-21] The benefit of needle trauma may he proportional to the amount of needle trauma, as suggested by Alta)/ et al,[3'] who achieved an excel-lent response in extensor tendinosis in humans by needling the common extensor enthesis 50 times or more with an 18-gauge needle. The need for injection with dextrose proliferant versus traumatic needling may depend therefore on the amount of needling feasible at the site in question.

A lack of understanding of needling effect has led to a misunderstanding of what a placebo study in prolotherapy really consists of, and funding limitations affect the ability of investigators to perform a 3-arm study—that is, dextrose plus

needle contact versus saline plus needle contact versus subcutaneous injection of saline without ligament or tendon contact. Investigators should also consider that results in I enthesis should be applied only with caution to other entheses, because Chun et a1[3`] have clearly shown that even ligaments about the same joint respond differently to growth factors.

In our study, subjects served as reasonable, typical treatment controls, because all had failed conservative measures, several had also received steroid injections, and pain interference with sports participation was chronic. The needle trauma was necessarily minimal due to lack of sedation and injection in the periperineal area.

Use of diagnostic musculoskeletal ultrasound or soft tissue modified MRI scanners may also help in future studies by determining the objective presence of tendinosis and showing its resolution.

CONCLUSIONS

Dextrose injection prolotherapy at 1-month intervals was highly clinically effective in the treatment of chronic groin pain in these rugby and soccer athletes. Correct diagnosis and proper treatment is of paramount importance in musculoskeletal medicine. The treatment method we describe offers the potential advantage of simultaneous treatment of many potential nociceptive contributors to chronic groin pain. This pilot study suggests a new clinical frontier for physiatrists and other musculoskeletal physicians; however, larger controlled trials are needed to confirm our findings.

APPENDIX: NPPS SCORING OF **ATHLETIC** OVERUSE INJURIES

Phase 0. No stiffness or soreness after activity.

Phase I. Stiffness o[r] mild soreness after activity. Pain is usually gone within 24 hours.

Phase 2. Stiffness or mild soreness before activity that is relieved by warm-up. Symptoms are not present during activity but return afterward, lasting up to 48 hours.

Phase 3. Stiffness or mild soreness before specific sport or occupational activity. Pain is partially relieved by warm-up. It is minimally present during activity but does not cause the athlete to alter activity.

Phase 4. Similar to phase 3 pain but more intense, causing the athlete to alter performance of the activity. Mild pain occurs with activities of daily living hut does not cause a major change in them.

Phase 5. Significant (moderate or greater) pain before, during, and after activity, causing alteration of activity. Pain occurs with activities of daily living but does not cause a major change in them.

Phase 6. Pain that persists even with complete rest. Pain disrupts simple activities of daily living and prohibits doing household chores.

Phase 7. Pain that also disrupts sleep consistently. Pain is aching in nature and intensifies with activity.

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Supplier

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