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Device for Zone-II Flexor Tendon Repair

A Multicenter, Randomized, Blinded, Clinical Trial

By Brian W. Su, MD, Michael Solomons, MD, Andrew Barrow, MD, Matschediso E. Senoge, MD, Marco Gilberti, MD, Lawrence Lubbers, MD, Edward Diao, MD, H. Matthew Quitkin, MD, and Melvin P. Rosenwasser, MD

Investigation performed at Columbia University Medical Center, New York, NY, Groote Schuur Hospital, Cape Town, Johannesburg General Hospital, Johannesburg, and King Edward VIII Hospital, Durban, South Africa

Background: The stainless-steel Teno Fix tendon-repair device has improved biomechanical characteristics compared with those of suture repair, and it was well tolerated in a canine model. The purpose of this study was to compare the Teno Fix with suture repair in a clinical setting.

Methods: Sixty-seven patients with isolated zone-II flexor tendon injury were randomized to be treated with a Teno Fix or a four-stranded cruciate suture repair. There were eighty-five injured digits: thirty-four were treated with the Teno Fix, and fifty-one served as controls. A modified Kleinert rehabilitation technique was employed, with active flexion starting at four weeks postoperatively. Patients were followed for six months by blinded observers who determined the range of motion, Disabilities of the Arm, Shoulder, and Hand (DASH) score, pinch and grip strength, and pain score on a verbal scale and assessed swelling and neurologic recovery. Adverse outcomes, including device migration and rupture, were monitored at frequent intervals.

Results: Nine of the fifty-one suture repairs ruptured, whereas none of the Teno Fix repairs ruptured (p < 0.01). Five of the nine ruptures were caused by resistive motion against medical advice. There were no differences between the two groups in terms of range of motion, DASH score, pinch and grip strength, pain, swelling, or neurologic recovery. The Teno Fix group had slightly slower resolution of pain and swelling compared with the control group. Of the patients who were available for follow-up at six months, sixteen of the twenty-four treated with a Teno Fix repair and nineteen of the twenty-seven treated with a control repair had a good or excellent result. One Teno Fix device migrated and extruded secondary to a wound infection. Of all eighty-five digits that were operated on, four were thought to have tendons of inadequate size to accommodate the device and nine were deemed to have inadequate exposure to allow placement of the anchors.

Conclusions: The Teno Fix is safe and effective for flexor tendon repair if the tendon size and exposure are sufficient. Tendon repairs with the Teno Fix have lower rupture rates and similar functional outcomes when compared with conventional repair, particularly in patients who are noncompliant with the rehabilitation protocol.

Level of Evidence: Therapeutic Level I. See Instructions to Authors for a complete description of levels of evidence.

In 1960, Verdan suggested that gentle passive mobilization at four weeks could rupture fresh adhesions and improve the end result of flexor tendon repairs. In the 1970s, Kleinert et al. and Lister et al. reported the results of flexor tendon repair with the Bunnell suture technique followed by immediate active extension and passive flexion with Young’s rubber-band contraption to prevent active flexion and rupture. Subsequent studies shaped the now widely accepted belief that the tendon should be mobilized with either passive or active flexion soon after repair to prevent contractures and the need for tenolysis.

Modern four or six-stranded repairs and the addition of circumferential sutures have increased the tensile strength of repairs, suggesting that they are adequate to sustain forces of early active mobilization. However, several investigators have proposed that measurement of forces in tendons without prior trauma does not account for increases in work of flexion from postoperative edema and adhesion formation. Underestimation of forces after trauma and patients’ noncompliance with instructions to avoid resistive active motion during

A video supplement to this article is available from the Video Journal of Orthopaedics. A video clip is available at the JBJS web site, www.jbjs.org. The Video Journal of Orthopaedics can be contacted at (805) 962-3410, web site: www.vjortho.com.
may explain rupture rates of up to 46% in patients treated with early-active-motion protocols. In addition to rupture, gapping with adhesion formation and diminished tendon glide and function may result from early mobilization.

While many of the proposed suture configurations result in high tensile strength, they are technically demanding, require excessive tendon manipulation, and increase the work of flexion. Strickland’s repair requirements were based on the concept of sufficient strength throughout the healing period to permit early motion stress, minimal interference with vascularity, minimal gapping, a smooth juncture at the tendon ends, secure knots, and easy placement of sutures in the tendon. Another criterion may be ease of application and reproducibility of the repair technique across a range of surgeons. The Teno Fix device (Ortheon Medical, Winter Park, Florida) was developed for zone-II flexor tendon repairs to meet these ideal repair requirements.

We previously demonstrated that the Teno Fix device withstands greater force and energy at a 2-mm gap than does a 4-0 four-stranded cruciate repair. In addition, we showed that the device was well tolerated in a canine model, with successful repairs progressing with normal tendon-healing as documented histologically. The purpose of the present prospective, blinded, randomized clinical study was to evaluate the safety and effectiveness of the Teno Fix device compared with the locked four-stranded cruciate suture repair.

**Materials and Methods**

Patients with flexor tendon injury, seen at one of three separate centers over a one-year period, were randomized to be managed with either a locked four-stranded cruciate repair (control group) or a Teno Fix repair. A separate blocked randomization procedure, based on random numbers generated by the SAS statistical package (SAS Institute, Cary, North Carolina), was used to assign the patients at each center to one of the two treatment groups. Each series of assignments was blocked in groups of eight, so that, of every eight surgical procedures, four were Teno Fix repairs and four were control repairs. Single and multiple-digit injuries were subdivided into two stratifications and randomized separately to ensure an approximately equal number of repaired digits in each treatment group. Digits that were eligible for the study were those that had a laceration of the flexor digitorum profundus tendon, with or without a concomitant injury of the flexor digitorum superficialis, in zone II of the index, long, ring, and/or small fingers that had occurred within the fourteen days prior to the study. Fourteen days was used as the cutoff, as studies have demonstrated no differences in outcome between tendons repaired immediately after injury and those repaired up to four weeks after injury. Randomization was performed after it had been determined that the inclusion criteria had been met but before the patient was taken to the operating room. Ethics committee/institutional review board approval was obtained at each site prior to the initiation of the trial and was in accordance with the Food and Drug Administration’s good clinical practices guidelines and the declaration of Helsinki ethical principles for medical research involving human subjects. All patients enrolled in the study signed an informed-consent form and were willing to return for the required postoperative follow-up visits.

**Fig. 1**

Schematic of the Teno Fix device.

**Fig. 2**

A longitudinal tenotomy is performed halfway through each tendon, starting 1.0 cm from the cut edge. The arrows denote the beginning and end of the tenotomy.
All patients were at least eighteen years of age at the time of the repair. Exclusion criteria included known pregnancy, diabetes mellitus, an autoimmune disorder, documented acquired immunodeficiency syndrome, chronic infection, or another condition or use of a medication that could affect postoperative wound-healing. To avoid complications related to the wound site or that could confound outcome measurements, patients were excluded if they had a history of keloid formation, a lack of adequate cutaneous coverage at the repair site, a concomitant fracture, an amputated digit, arthritis of the hand, prior hand trauma, a congenital hand defect, or another condition that would affect comparative measurements in the contralateral hand. Patients with a crush injury were also excluded, as were those with prior sensory impairment in digits of either hand. However, patients with digital nerve injuries associated with the trauma that had caused the flexor tendon injury were eligible. Patients with known sensitivity or allergy to the metals contained in the ASTM F138-00 stainless steel (chromium, nickel, copper, cobalt, and/or iron) used to manufacture the Teno Fix device were excluded from the study.

At each of the three sites, one experienced senior surgeon who was adept at standard four-stranded cruciate repairs performed both the control and the Teno Fix repairs. All procedures were performed with use of either axillary or Bier block anesthesia and with a similar surgical technique. Tendons were approached through a modified Bruner incision with windowing of the tendon sheath. Once exposed, all tendons were subjectively evaluated to determine if their size and the exposure were adequate for implantation of the Teno Fix device. Specific criteria included a tendon that was wide enough for approximately 1 mm of tendon to remain on each side of the anchor following implantation; also, it had to be possible to expose at least 10 mm of tendon from the severed end of each injured segment. The tendons that had been preoperatively randomized to be repaired with the Teno Fix device but did not meet the intraoperative criteria for implantation were switched into the control group and were followed as members of that group.

The Teno Fix device is composed of two intratendinous, stainless-steel anchors (a coil around a core) joined by a single multifilament 2-0 stainless-steel suture (Fig. 1). Each anchor is 2.2 mm in diameter and 4.0 mm in length, and the suture is 0.3 mm in diameter. After exposure, a longitudinal intratendinous split is made through half of the tendon substance. This incision starts 1.0 cm from the cut edge and is extended proximally several millimeters away from that edge to accommodate the obturator tip and delivery tube (Fig. 2). After ensuring that the delivery tube is sitting comfortably within the tendon substance, the anchors are twisted into the tendon (Figs. 3-A and 3-B). The anchor engages the tendon substance by capturing fibers between the core and the corkscrew-like coil. A straight needle with a 2-0 multifilament...
stainless-steel suture and an attached stop-bead is threaded into one of the cannulated anchors and is pulled through the center of the tendon’s cut end until the end of the stop-bead comes into contact with the anchor. The needle is then threaded through the center of the opposite tendon segment and anchor. The needle is delivered through the proximal anchor.

The operative technique for the cruciate suture repair has been previously described. All cruciate repairs were performed with a single 4-0 or 3-0 monofilament polypropylene (Prolene; Ethicon, Somerville, New Jersey) suture, depending on tendon size.

Both the control and the Teno Fix repairs were finished with a single epitendinous 6-0 monofilament nylon suture (Ethilon; Ethicon) in a running circumferential configuration.

Concomitant injury to the flexor digitorum superficia- lis tendon did not preclude the digit from being included in the study and did not affect randomization. In digits with a proximal zone-II injury with transection of the flexor digi-
torum superficialis tendon, the flexor digitorum superficialis tendon was repaired with an interrupted suture technique. In other cases, the decision was made to repair only the flexor digitorum profundus tendon and to leave the distal flexor digitorum superficialis tendon stump as a gliding bed for the tendonorrhaphy and to maintain the vascular supply to the flexor digitorum profundus tendon. Except for jagged injuries, lacerated digital nerves were isolated and were repaired with 8-0 or 9-0 monofilament nylon (Ethilon) under loupe magnification. The flexor sheath was replaced over the tendon but was not closed. Repairs under the A2 or A4 pulley that impeded gliding led to pulley narrowing. After the procedure, the hand was immobilized in a dorsal plaster splint with the wrist in 30° of flexion, the metacarpophalangeal joints in 60° of flexion, and the interphalangeal joints in 0° of flexion.

Rehabilitation was started on the first postoperative day with a passive flexion and active extension protocol. The Kleinert method was utilized for the first three weeks of rehabilitation. Starting at four weeks, an active flexion protocol that was a modification to the Coventry-Kleinert regimen was implemented. The protocol required patients to exercise the injured digit or digits with the prescribed regimen five times a day, with the goals of achieving 25% of flexion during the fourth week, 50% of flexion during the fifth week, and 100% of flexion during the sixth week. Each patient was seen by a therapist twice a week for the first twelve weeks and then once at six months. Each visit included visual inspection and physical examination of the repaired digit or digits, assessment for signs of wound dehiscence or infection of the wound or surrounding area, a pain rating, and a review of home exercise regimens and limitations of activity. In addition, complications such as tendon rupture (as reported by the patient and confirmed through physical examination), triggering, and flexion contractures were monitored weekly. Pain was rated with use of a verbal scale ranging from 0 to 10, with 10 being the “worst pain imaginable.” Verbal reports of pain show good correlation with the visual analogue pain scale described by Huskisson. Other outcome measures were assessed at one or two days postoperatively and at three, six, twelve, and twenty-six weeks.

Fig. 5
The tendon ends are pulled together until the tendon is approximated and tensioned. A stop-bead is then crimped onto the suture.

Fig. 6
The final repair prior to the completion of the circumferential suture. The arrow denotes the area of tendon approximation.
The mobility of the distal interphalangeal and proximal interphalangeal joints were evaluated with use of Strickland’s revised score at twelve and twenty-four weeks. This score is calculated as: \(\left(\frac{\text{[proximal interphalangeal + distal interphalangeal flexion]} - \text{[proximal interphalangeal + distal interphalangeal extension deficit]}}{175}\right) \times 100\). Repairs are then classified as excellent (75% to 100%), good (50% to 74%), fair (25% to 49%), or poor (<25%). The number and percentage of repairs within each group were used for statistical analysis.

Grip strength and pinch strength were measured at twelve and twenty-four weeks with use of a Jamar hydraulic grip dynamometer and a Jamar hydraulic pinch gauge (Sammons Preston Rolyan, Bolingbrook, Illinois), respectively. Grip strength was measured according to the recommendations by the American Society for Surgery of the Hand, with the elbow in 90° of flexion and the wrist in the neutral position. Tip pinch was measured with the thumb and injured digit in a tip-pinching position. Both grip and tip-pinching strength were calculated as a percentage of the strength of the contralateral, uninjured hand. Swelling (an increase in the circumference of the injured digit relative to the contralateral, uninjured digit) was measured in millimeters with use of a finger-circumference gauge (Sammons Preston Rolyan) placed over the approximate area of repair at three, six, twelve, and twenty-four weeks postoperatively.

Functional outcome was assessed with use of the validated Disabilities of the Arm, Shoulder and Hand (DASH) questionnaire. This survey contains thirty questions on activities of daily living and pain and is intended to be used to evaluate disability and symptoms in patients with a single disorder or multiple disorders of the upper limb at one point or many points in time. A higher score on the DASH reflects greater disability, with 100 representing the highest level of disability. The baseline DASH score was calculated on the first postoperative day to estimate the patient’s preinjury level of disability and was compared with the DASH scores at six, twelve, and twenty-four weeks postoperatively.

**Statistical Methods**

All analyses were based on the repair that was performed on the injured digit rather than on the group to which it had been initially randomized. Differences between the control and treatment groups with respect to swelling, grip strength, pinch strength, and DASH score were analyzed with a repeated one-way analysis of variance; a post hoc least-significant-difference method was used when significance was found. The percentage of patients within range-of-motion and demographic categories was analyzed with a chi-square test or Fisher exact test when expected values were less than five. All statistical testing was done with the SAS statistical package (SAS Institute). The level of significance for all tests was \(p \leq 0.05\).

**Results**

Sixty-seven patients with a total of eighty-five injured digits met the inclusion criteria; forty-one digits were initially randomized to the Teno Fix repair group and forty-four, to
the control group. However, seven digits that had been randomized to the Teno Fix group were switched into the control group because there was inadequate surgical exposure to implant the device. Ultimately, thirty-four digits were repaired with the Teno Fix device and fifty-one, with the control technique. With the exception of one patient, all patients had involvement of only one or two digits. All injuries were associated with a concomitant injury to the flexor digitorum superficialis tendon, but only one patient had a repair of that tendon. Specific characteristics of the patients, including hand dominance, mechanism of injury, involved digit or digits, and presence of digital nerve injury are summarized in Table I. Sixty (90%) of the sixty-seven patients were available for follow-up at twelve weeks, and fifty-two (78%) were available at six months. One patient (the one who had the repair of the flexor digitorum superficialis tendon) in the control group died from a cerebrovascular event four weeks postoperatively.

Nine (18%) of the fifty-one tendons that were repaired with the cruciate technique ruptured, whereas none of the tendons repaired with the Teno Fix device ruptured (p < 0.01). The cause and course of all ruptures are presented in the Appendix. With the exception of those in two patients (Cases 4 and 6; see Appendix), all ruptures occurred within six weeks after the primary repair. One patient (Case 4; see Appendix) missed all of the visits between the sixth and twelfth weeks after the operation, and the repair may have ruptured earlier than the twelve-week visit. Three ruptures (Cases 7, 8, and 9; see Appendix) occurred in patients who had two digital injuries, but the other repair remained unruptured. Two ruptures (Cases 1 and 9; see Appendix) occurred after a wound infection. Five of the nine ruptures occurred while the patient was being noncompliant with therapy by prematurely using the hand for active or resisted flexion earlier than healing dictated. Three of the nine ruptures occurred during the active-motion

### TABLE II Outcome Measures

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Teno Fix</th>
<th>Control</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of op.* (min)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single digit</td>
<td>91 ± 23</td>
<td>86 ± 34</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Multiple digits</td>
<td>164 ± 53</td>
<td>148 ± 52</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Ruptures (no. of digits)</td>
<td>0/34 (0%)</td>
<td>9/51 (18%)</td>
<td>P = 0.01†</td>
</tr>
<tr>
<td>Infections (no. of patients)</td>
<td>3/29 (10%)</td>
<td>4/38 (11%)</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Swelling* (% of circumference of uninjured digit)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 wk</td>
<td>115 ± 11</td>
<td>115 ± 9</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>6 wk</td>
<td>116 ± 10</td>
<td>109 ± 7</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>12 wk</td>
<td>110 ± 7</td>
<td>106 ± 7</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>6 mo</td>
<td>107 ± 7</td>
<td>103 ± 6</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Pain* (verbal scale) (points)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 day</td>
<td>2.9 ± 2.5</td>
<td>2.7 ± 1.8</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>3 wk</td>
<td>1.4 ± 2.6</td>
<td>0.9 ± 1.5</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>6 wk</td>
<td>1.6 ± 2.3</td>
<td>0.8 ± 1.2</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>12 wk</td>
<td>0.6 ± 0.9</td>
<td>0.5 ± 0.9</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>6 mo</td>
<td>0.6 ± 1.6</td>
<td>0.4 ± 1.2</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Strickland’s revised score at 6 mo (no. of digits)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>7 (29%)</td>
<td>8 (30%)</td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>9 (38%)</td>
<td>11 (41%)</td>
<td></td>
</tr>
<tr>
<td>Fair</td>
<td>5 (21%)</td>
<td>5 (19%)</td>
<td></td>
</tr>
<tr>
<td>Poor</td>
<td>3 (13%)</td>
<td>3 (11%)</td>
<td></td>
</tr>
<tr>
<td>Excellent/good</td>
<td>16 (67%)</td>
<td>19 (70%)</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Fair/poor</td>
<td>8 (33%)</td>
<td>8 (30%)</td>
<td></td>
</tr>
<tr>
<td>Grip strength at 6 mo* (% of that of uninjured hand)</td>
<td>88 ± 38</td>
<td>84 ± 20</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Pinch strength at 6 mo* (% of that of uninjured digit)</td>
<td>81 ± 32</td>
<td>78 ± 42</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>Mean DASH score* (points)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Baseline</td>
<td>1.3 ± 4.7</td>
<td>0.8 ± 2.2</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>6 wk</td>
<td>27.2 ± 22.7</td>
<td>22.7 ± 19.8</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>12 wk</td>
<td>7.4 ± 8.6</td>
<td>8.1 ± 13.8</td>
<td>P &gt; 0.05</td>
</tr>
<tr>
<td>6 mo</td>
<td>2.5 ± 3.8</td>
<td>2.0 ± 4.2</td>
<td>P &gt; 0.05</td>
</tr>
</tbody>
</table>

*The values are given as the mean and standard deviation. †A significant difference.
phase of rehabilitation of patients who were compliant with therapy. Seven of the ruptured repairs were treated with suture repair or tendon-grafting. Intraoperative findings revealed that five of those repairs had failed by suture rake-out and one, by suture breakage. The failure mode was not recorded for the seventh repair. None of the ruptures for which the failure mode was recorded were due to failure at the knot. Regardless of the final outcome of the repair of a rupture, all ruptured digits were excluded from the final range-of-motion measurements.

Pain and swelling decreased six weeks after the Teno Fix repairs and three weeks after the control repairs; both decreased over time over six months (Table II). There was no significant difference in the percentage of digits with an excellent or good result, based on Strickland’s revised score, at twelve weeks between the Teno Fix group (44%; twelve of twenty-seven digits) and the control group (59%; seventeen of twenty-nine digits). This percentage was increased at six months in both the Teno Fix group (67%; sixteen of twenty-four) and the control group (70%; nineteen of twenty-seven), and again there was no difference between the groups (p > 0.05) (Table II). Grip and pinch strength relative to that of the contralateral hand or digit increased over time, to approximately 80% of that on the contralateral side at six months, with no significant differences between the two groups at any time-point (Table II). At six months, the mean functional DASH scores (and standard deviation) for the Teno Fix and control groups were 2.5 ± 3.8 and 2.0 ± 4.2 points, respectively (p > 0.05), which approached baseline preinjury scores (Table II). There were no significant differences in the DASH scores between the two groups at baseline or at six, twelve, or twenty-four weeks.

In the Teno Fix group, a nerve laceration was repaired in fourteen digits, and at twelve weeks eleven of them were available for testing of neurologic recovery with the Semmes-Weinstein monofilaments. In the cruciate-repair group, a nerve laceration was repaired in twenty-eight digits, and at twelve weeks twenty-three were available for testing. The majority of the patients in the series had diminished protective sensation (purple monofilament) or better neurologic function, regardless of whether the digital nerve had never been injured or had been transected and repaired. With the numbers available, the proportion of patients with a digital nerve repair who had diminished protective sensation or better neurologic function did not differ significantly between the Teno Fix and control groups, and there were no differences in the remaining outcome measures between the patients who had had a digital nerve repair and those who had not.

An infection developed in three patients in the Teno Fix group and four patients in the control group; details of those cases are summarized in the Appendix. The infection in one patient (Case 10; see Appendix) led to extrusion of the Teno Fix device. Four digits (three ring fingers and one small finger) were deemed to have inadequate exposure, to have tendons that were too small to accommodate the tendon anchors for all randomized digits. Nine (11%) of the digits (one index finger, two long fingers, two ring fingers, and four small fingers) were deemed to have inadequate exposure or an injury too distal in zone II for placement of both anchors. Of the forty-one digits that had been initially randomized to be treated with a Teno Fix repair, seven were reassigned intraoperatively to be managed with a cruciate repair because the surgical exposure was perceived to be inadequate for implantation of the Teno Fix. Three of the digits for which it was decided intraoperatively that it was necessary to change to a control repair were in patients who did not complete the study and were lost to follow-up. Another of the repairs (of the index finger in Case 9; see Appendix) ruptured at 1.5 weeks, in a patient who was noncompliant with therapy. In a subset analysis, there were no significant differences between the outcomes of the remaining three digits that were switched into the control group and those of the digits that had been originally randomized to the control group.

Discussion

Since the advent of primary repair of flexor tendon lacerations in Bunnell’s “no man’s land,” there has been an abundance of biomechanical and animal studies on flexor tendon repair. The aim of those studies was to reduce gapping and rupture secondary to forces encountered during rehabilitation. Clinical studies of flexor tendon repair have focused less on comparing repair techniques and more on methods of rehabilitation (Table III). With the exception of studies by Savage and Risitano, who used a six-stranded technique,

fected at the time of presentation and was treated with irrigation and antibiotics for eleven days until the infection resolved clinically. At nine days after the primary repair with the Teno Fix device, Staphylococcus aureus cellulitis developed in the wound and was treated with antibiotics. The infection resolved three weeks postoperatively. At four weeks postoperatively, a flexion contracture of the proximal interphalangeal joint developed, and the ring finger was splinted in extension. At eleven weeks postoperatively, a pressure area developed on the volar aspect of the proximal interphalangeal joint, presumably from a tight-fitting dorsal extension splint. At twelve weeks, despite the flexion contracture, the range of motion was categorized as good. At sixteen weeks, a small piece of the Teno Fix suture became visible over the volar sore. The patient was taken to the operating room, where an intact repair site surrounded by dense adhesions and an extruded Teno Fix device were found. The device was removed. Pus drained from the wound three days later, and the skin was surgically debrided. Antibiotics were administered, and the infection resolved twelve days later. This patient ended up with a poor result. At the end of the study, no other Teno Fix devices had migrated or had been removed after a primary repair.

Regardless of the initial randomization, all digits were subjectively evaluated to determine the feasibility of placement of the Teno Fix device. Four digits (three ring fingers and one small finger) were deemed, on the basis of visual inspection, to have tendons that were too small to accommodate the tendon anchors for all randomized digits. Nine (11%) of the digits (one index finger, two long fingers, two ring fingers, and four small fingers) were deemed to have inadequate exposure or an injury too distal in zone II for placement of both anchors. Of the forty-one digits that had been initially randomized to be treated with a Teno Fix repair, seven were reassigned intraoperatively to be managed with a cruciate repair because the surgical exposure was perceived to be inadequate for implantation of the Teno Fix. Three of the digits for which it was decided intraoperatively that it was necessary to change to a control repair were in patients who did not complete the study and were lost to follow-up. Another of the repairs (of the index finger in Case 9; see Appendix) ruptured at 1.5 weeks, in a patient who was noncompliant with therapy. In a subset analysis, there were no significant differences between the outcomes of the remaining three digits that were switched into the control group and those of the digits that had been originally randomized to the control group.

Discussion

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and Becker et al., who used a beveled tendon technique, all of the clinical investigations that we reviewed were of two-stranded core repairs. Of the studies on rehabilitation techniques, few involved more than one cohort within the same population, which makes it difficult to draw conclusions on the advantages of one technique over another. Comparisons are also difficult because the results of flexor tendon repairs are influenced by many factors, such as patient age, cause and severity of injury, case selection, preoperative delay, postoperative rehabilitation, methods of measurements, and technique of repair. To our knowledge, we performed the first randomized, blinded study in which more than one repair technique was investigated in a series of patients treated with the same rehabilitation protocol.

While some authors have advocated early active flexion over passive flexion, others have reported high proportions of excellent and good results of protocols involving passive flexion with either the Kleinert or the Duran-Houser technique. We elected to use the Kleinert technique because it is the gold standard worldwide. Others who have used the Kleinert method of rehabilitation have reported rates of good to excellent results ranging between 49% (nineteen of thirty-nine) and 85% (twenty-two of twenty-six). The rates of good to excellent results in the present study (67% in the Teno Fix repair)

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### TABLE III Clinical Studies on Zone II Flexor Tendon Repair

<table>
<thead>
<tr>
<th>Study</th>
<th>Repair</th>
<th>Mobilization*</th>
<th>Mean Duration of Follow-up (mo)</th>
<th>Rate of Exc./Good Results (%)</th>
<th>Rupture Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duran and Houser, 1975†</td>
<td>Modified Bunnell (two-strand)</td>
<td>Duran Houser</td>
<td>NA</td>
<td>74†</td>
<td>16</td>
</tr>
<tr>
<td>Lister et al., 1977‡</td>
<td>Modified Bunnell (two-strand)</td>
<td>Kleinert</td>
<td>5.3</td>
<td>75</td>
<td>7</td>
</tr>
<tr>
<td>Becker et al., 1979</td>
<td>Becker repair (beveled ends secured by three sutures on each side)</td>
<td>Active</td>
<td>2</td>
<td>70</td>
<td>10</td>
</tr>
<tr>
<td>Strickland and Glogovac, 1980‡</td>
<td>Modified Bunnell or modified Kessler (two-strand)</td>
<td>Immobilized</td>
<td>5.1</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Strickland, 1985‡</td>
<td>Modified Bunnell or modified Kessler (two-strand)</td>
<td>Duran Houser</td>
<td>NA</td>
<td>56</td>
<td>4</td>
</tr>
<tr>
<td>Gault, 1987†</td>
<td>Kessler (two-strand)</td>
<td>Kleinert</td>
<td>26.4</td>
<td>72</td>
<td>4†</td>
</tr>
<tr>
<td>Singer and Maloon, 1988‡</td>
<td>Kessler-Mason-Allen (two-strand)</td>
<td>Kleinert</td>
<td>10</td>
<td>49</td>
<td>3†</td>
</tr>
<tr>
<td>Chow et al., 1988‡</td>
<td>Modified Kessler or Tajima (two-strand)</td>
<td>Kleinert with Duran Houser component</td>
<td>6 (minimum)</td>
<td>98</td>
<td>4</td>
</tr>
<tr>
<td>Small et al., 1989‡</td>
<td>Kessler (two-strand)</td>
<td>Active</td>
<td>6 (minimum)</td>
<td>75</td>
<td>9</td>
</tr>
<tr>
<td>Cullen et al., 1989‡</td>
<td>Modified Kessler (two-strand)</td>
<td>Active</td>
<td>10.2</td>
<td>78</td>
<td>7</td>
</tr>
<tr>
<td>Savage and Ristitano, 1989‡</td>
<td>Savage (six-strand)</td>
<td>Active</td>
<td>3 (minimum)</td>
<td>70</td>
<td>4</td>
</tr>
<tr>
<td>May et al., 1992‡</td>
<td>Kessler (two-strand)</td>
<td>Kleinert</td>
<td>12</td>
<td>72</td>
<td>4</td>
</tr>
<tr>
<td>Silfverskiold and May, 1994‡</td>
<td>Kessler (two-strand)</td>
<td>Modified active**</td>
<td>6</td>
<td>100</td>
<td>4</td>
</tr>
<tr>
<td>Bainbridge et al., 1994‡</td>
<td>Modified Kessler (two-strand)</td>
<td>Kleinert</td>
<td>2.5 (minimum)</td>
<td>54</td>
<td>4</td>
</tr>
<tr>
<td>Elliot et al., 1994‡</td>
<td>Modified Kessler (two-strand)</td>
<td>Active</td>
<td>6.1</td>
<td>79</td>
<td>5</td>
</tr>
<tr>
<td>Baktir et al., 1996‡</td>
<td>Kessler (two-strand)</td>
<td>Kleinert</td>
<td>12</td>
<td>78</td>
<td>5</td>
</tr>
<tr>
<td>Peck et al., 1998‡</td>
<td>Modified Kessler (two-strand)</td>
<td>Kleinert</td>
<td>3</td>
<td>85</td>
<td>8</td>
</tr>
<tr>
<td>Kitsis et al., 1998‡</td>
<td>Kessler (two-strand)</td>
<td>Active</td>
<td>12</td>
<td>89</td>
<td>6</td>
</tr>
<tr>
<td>Harris et al., 1999‡</td>
<td>Kessler (two-strand)</td>
<td>Active</td>
<td>7.5</td>
<td>NA</td>
<td>4</td>
</tr>
</tbody>
</table>

*Active = active flexion and extension, Kleinert = passive flexion and active extension, Duran Houser = passive flexion and passive extension, and Immobilized = immobilization for three weeks. †Average percentage of the range of motion, compared with the contralateral side, based on distal interphalangeal, proximal interphalangeal, and metacarpophalangeal motion. ‡Includes injuries in other zones. §Passive flexion with active extension with the addition of increased passive flexion. **Active flexion after full passive flexion.
Device for Zone-II Flexor Tendon Repair

The range-of-motion results in this study with those in other reports may be of limited value because of differences in patient compliance with the rehabilitation protocol and in the rehabilitation regimens themselves. In addition, the method used to score the range of motion is a confounding factor between studies, which share only the categorization of results into excellent, good, fair, or poor categories. Other investigators have commented that many uncontrolled variables make it extremely difficult to meaningfully compare results between different centers. Notably, Singer and Maloon studied a cohort of patients that was similar to ours in terms of socioeconomic variables and found that, at ten months, only 49% of digits in which a zone-II injury had been repaired with a two-stranded suture technique had a good or excellent outcome.

We did not anticipate differences between our two study groups with respect to range of motion, as the same rehabilitation protocol was used in both groups. As other investigators have reported, the Kleinert technique potentiated flexion deformities early on, as a result of the flexed position of the interphalangeal joints from the rubber band traction. We employed an established method of passive extension exercises and extension splinting at night starting at nine weeks after the surgery. This increased the number of good to excellent results between the twelve and twenty-four-week time-points in both groups.

Clinical studies of patients treated with flexor tendon repair and various rehabilitation protocols have demonstrated rupture rates ranging from 2% to 46% (Table III). While the trade-off for the benefits of aggressive mobilization may be an increased risk of gapping and rupture, there has been no clearly defined increase in rupture rates with the progression from early passive to early active mobilization. We agree with other authors that it is likely that variations in patient population, rather than the method of mobilization, produces the variations in rupture rates among studies. The 18% rate of ruptures of the four-stranded cruciate repairs in our study is within the range for historic controls but is higher than the typical rate of between 4% and 10%. We think that a randomized trial is an ideal method for controlling for patient characteristics. Two ruptures (Cases 1 and 9; see Appendix) in our study likely occurred because of infection, which may have disrupted the fixation of the suture to the tendon substance. As has been reported by others, the majority of the ruptures occurred when the patients were noncompliant with therapy by prematurely using the hand for active or resistive flexion earlier than the protocol dictated. None of the thirty-four digits with the Teno Fix repair ruptured. To our knowledge, no other clinical study has demonstrated a 0% rupture rate with zone-II repair. Notably, Savage and Risitano reported a 4% rupture rate following use of a six-stranded suture configuration in twenty-three zone-II repairs. Almost all of the ruptures in our study occurred within the first six weeks after the primary repair, a finding that is in agreement with those in other studies that we reviewed. Assuming that the control and study groups were equally matched cohorts, it is likely that the Teno Fix device increased the threshold for rupture during the active-motion phase of therapy or when the patient used the hand prematurely.

We are not aware of any previous studies in which a validated hand and upper-extremity questionnaire was used to evaluate functional outcome following flexor tendon repair. We found no differences in the DASH scores between the two groups at any time-point in our study. There was a reduction in disability from the six-week to the three-month time-point, and function approached the baseline level at six months following the repair. This finding was supported by grip and pinch-strength measurements. Grip strength at six months (88% of that on the contralateral side in the Teno Fix group and 84% in the control group) was similar to that reported by others who measured grip strength at one year. Finally, with the numbers available, our analysis showed that the Teno Fix device did not interfere with recovery of digital nerve function compared with that following the control repairs.

As anticipated, the patients in both groups reported the greatest pain on the first postoperative day. The pain rapidly
decreased after the three-week time-point in the control group and after the six-week time-point in the Teno Fix group. Overall, the pain ratings were relatively low because of a lack of concomitant injuries and the assessment of pain at rest rather than during movement. Digital swelling followed a similar pattern, with the Teno Fix group having slightly more swelling than the control group at most time points. The surgeons performing the repairs noted that the exposure needed to implant the Teno Fix anchors was greater than that needed for the cruciate repairs. This might explain the prolonged increase in swelling and pain after the Teno Fix repairs.

In vitro studies have suggested that stainless-steel sutures have high resistive loads to failure. However, they are not typically used in flexor tendon repair, probably because of the difficulty in handling them and in knot-tying. The Teno Fix device was designed to take advantage of the properties of stainless-steel sutures while providing a knotless anchoring device, thus preventing both suture and knot-related failures. Gordon et al. developed a flat, stiff, stainless-steel device that was biomechanically superior to two and six-stranded suture repairs; however, they did not perform clinical studies to demonstrate efficacy or equivalence. The Teno Fix device did not limit interphalangeal joint flexion, as evidenced on radiographs and by clinical examinations (Fig. 7). Olivier et al. reported the results following use of a stainless-steel device anchored on the exterior of the tendon surface; the device had to be removed from 29% of patients secondary to local irritation. Foreign material placed on the outside of tendons was shown to cause adhesions in a canine study. In our study of a canine model, we observed that the Teno Fix device remains embedded in the tendon substance with little reaction on the tendon surface in successful primary repairs. Similarities between the ranges of motion in the two groups in the present clinical study suggest that the device does not increase extratendinous adhesions when compared with suture repair. The single strand of braided stainless-steel suture that crosses the repair site did not lead to clinically reported triggering, and none of the patients complained of a foreign-body sensation or bulkiness along the volar aspect of the digit.

There was no significant difference in the duration of surgery between the two groups, and all three surgeons reported that they had easily mastered the technique of implanting the Teno Fix device. An advantage of the device was the ability to use the proximal anchor with a stop-bead and suture attached as a tendon passer to retrieve the flexor digitorum profundus and flexor digitorum superficialis tendons from the palm and to redirect them through the fibro-osseous sheath. This technique has been previously employed with the two-stranded modified Kessler repair. The Teno Fix device is currently available in one size and, as a result, mandates that tendon size and exposure be adequate for placement of both anchors while pulley anatomy is respected. Throughout the study, techniques for negotiating repairs of distal zone-II injuries in which the repair site lay under the A4 pulley were developed. The repair sequence requires retrieval of the distal stump out of the sheath to allow anchor placement with delivery of the tendon through the pulley with use of the wire suture of the device. This is followed by crimping at the proximal end of the repair and windowing the pulley to complete the repair.

The results of this study showed that, compared with a conventional repair, the Teno Fix repair has a lower rupture rate and a similar outcome in patients treated with a conservative rehabilitation protocol. The Teno Fix repair may be particularly useful in noncompliant patients by raising the threshold for rupture early after the repair. We are presently studying this device in the setting of a more aggressive, early-active-motion protocol, where gap-associated adhesions may emphasize differences in the range of motion while maintaining a low rupture rate.

Appendix

Tables presenting the details on all tendon repair ruptures and the course of all infections that occurred in the series are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

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In support of their research or preparation of this manuscript, one or more of the authors received grants or outside funding from Orthene Medical, Winter Park, Florida. In addition, one or more of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity (Orthene Medical). No commercial entity paid or directed, or agreed to pay or direct, any bene-
fits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.C.01483

References

Tissue-Engineered Osteochondral Constructs in the Shape of an Articular Condyle

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Investigation performed at the Departments of Anatomy and Cell Biology, Bioengineering, and Orthodontics, University of Illinois at Chicago, Chicago, Illinois

Background: An entire articular condyle engineered from stem cells may provide an alternative therapeutic approach to total joint replacement. This study describes our continuing effort to optimize the chondrogenic and osteogenic differentiation from mesenchymal stem cells toward engineering articular condyles in vivo.

Methods: Primary rat bone-marrow mesenchymal stem cells were induced to differentiate into chondrogenic and osteogenic lineages in vitro and were suspended in polyethylene glycol-based hydrogel. The hydrogel cell suspensions, each at a density of $20 \times 10^6$ cells/mL, were stratified into two separate layers that were molded into the shape and dimensions of an adult human cadaveric mandibular condyle by sequential photopolymerization. The osteochondral constructs fabricated in vitro were implanted in the dorsum of immunodeficient mice for twelve weeks.

Results: De novo formation of articular condyles in the shape and dimensions of the adult human mandibular condyle occurred after a twelve-week period of in vivo implantation. Histological evaluation demonstrated two stratified layers of cartilaginous and osseous tissues, and yet there was mutual infiltration of cartilage-like and bone-like tissues into each other’s territories. The cartilaginous portion was stained intensively to safranin O and expressed immunolocalized type-II collagen. Chondrocytes adjacent to the tissue-engineered osteochondral junction were enlarged and expressed type-X collagen, typical of hypertrophic chondrocytes. The osseous portion contained bone trabeculae-like structures and expressed immunolocalized type-I collagen, osteopontin, and osteonectin.

Conclusions: A cell encapsulation density of 20 million cells/mL with in vivo incubation for twelve weeks yields further tissue maturation and phenotypic growth of both cartilage-like and bone-like tissues in the tissue-engineered articular condyle.

Clinical Relevance: Tissue engineering of an entire condyle with chondral and osseous components derived from a single population of adult stem cells, as described in the present study, may have therapeutic implications in total joint replacement.

The prevalence of synovial joint degeneration has motivated tremendous advances in the field of bone and cartilage tissue engineering in the past decade. Despite ongoing applications of cell and tissue-based therapies, such as mosaicplasty and chondrocyte transplantation for the treatment of articular cartilage defects, prosthetic replacement of the entire articular condyle continues to be the predominant practice for total joint replacement. Alternative therapeutic approaches for large osteochondral defects and condylar replacement, including autografts, allografts, and xenografts, are also used to replace small synovial joints, such as the phalanges and the temporomandibular joint. Collectively, prosthetic implants and grafting procedures share certain deficiencies, such as implant dislocation, wear, suboptimal biocompatibility, donor site limitation and morbidity, immunological challenge, and potential pathogen transmission. An entire articular condyle derived from adult stem cells should overcome most of the deficiencies associated with the current prosthetic and grafting approaches.

Adult mesenchymal stem cells are capable of differentiating into all connective tissue cell lineages, including cartilaginous and osseous phenotypes. For the purpose of bone and cartilage tissue engineering, adult mesenchymal stem cells have an advantage over embryonic stem cells or differentiated osteoblasts and chondrocytes because of the shorter differentiation journey that they may have toward their natural derivatives such as bone and cartilage. Since mesenchymal stem cells can be harvested readily by needle aspiration, donor site morbidity may be reduced compared with that associated with procedures for harvesting autologous bone grafts. Although mature os-
teoblasts can also be harvested in the same fashion, mesenchymal stem cells are more expandable ex vivo than are mature osteoblasts. The isolated mesenchymal stem cells can be reliably induced to differentiate into bone-forming and cartilage-forming cells after exposure to well-established osteogenic and chondrogenic supplements in cell culture, respectively.

Our previous work has demonstrated, with use of different outcome measurements, the feasibility of tissue engineering of an entire articular condyle with stratified cartilaginous and osseous components from a single population of adult mesenchymal stem cells. However, in our previous work, we used a cell encapsulation density of 5 million cells/mL for each of the chondrogenic and osteogenic components and up to four and eight weeks of in vivo implantation. Although this cell encapsulation density led to in vivo chondrogenesis and osteogenesis, the level of tissue formation needed to be improved. As argued in our previous work, because cell densities at given stages of natural synovial joint development are unknown, cell encapsulation densities need to be explored in tissue-engineered articular condyles. Accordingly, the present study was designed to tissue engineer articular condyles with both cartilaginous and osseous components from a single population of adult stem cells in the shape and dimensions of an adult human cadaveric mandibular condyle by increasing the cell encapsulation density to 20 million cells/mL followed by an extended twelve-week period of in vivo implantation in immunodeficient mice.

Materials and Methods
Isolation and In Vitro Cultivation of Mesenchymal Stem Cells

Bone marrow-derived mesenchymal stem cells were harvested from two to four-month-old (200 to 250-g) male Sprague-Dawley rats (Harlan, Indianapolis, Indiana). Following CO₂ asphyxiation of the rats, the tibiae and femora were dissected under aerobic conditions. The whole bone marrow plugs were flushed out with use of a 10-ml syringe with Dulbecco modified Eagle medium-low glucose (DMEM-LG; Sigma, St. Louis, Missouri) supplemented with 10% fetal bovine serum and antibiotic-antimycotic solution (transforming growth factor-β1; RDI, Flanders, New Jersey), whereas osteogenic medium contained 100 nm dexamethasone, 10 mM β-glycerophosphate, and 0.05 mM ascorbic acid-2-phosphate (Sigma). Monolayer mesenchymal stem-cell cultures for control constructs were grown for the same period in a basic culture medium consisting of Dulbecco modified Eagle medium, fetal bovine serum, and antibiotic-antimycotic solution but without any chondrogenesis or osteogenesis-inducing supplements. All cultures were incubated in 95% air and 5% CO₂ at 37°C with medium changes every three to four days.

Preparation of Polyethylene Glycol-Based Hydrogel-Photoinitiator Solution

Polyethylene glycol diacrylate (MW 3400; Shearwater Polymers, Huntsville, Alabama) was dissolved in sterile phosphate-buffered saline solution supplemented with 100 U/mL penicillin and 100 µg/mL streptomycin (Gibco) to a final solution of 10% weight per volume. A photoinitiator, 2-hydroxy-1-[4-(hydroxysyloxy) phenyl]-2-methyl-1-propanone (Ciba, Tarrytown, New York), was added to the polyethylene glycol diacrylate solution to obtain a final photoinitiator concentration of 0.05% weight per volume.

Fabrication of Osteochondral Constructs

After a one-week incubation in medium with either chondrogenesis-inducing or osteogenesis-inducing supplements, mesenchymal stem cell-derived chondrogenic and osteogenic cells were trypsinized, counted, and resuspended in polyethylene glycol diacrylate polymer-photoinitiator solution at a density of 20 × 10⁶ cells/mL. A 150-µl aliquot of cell-polymer suspension with mesenchymal stem cell-derived chondrogenic cells was loaded into a hollow bivalved polysiloxane negative mold that had been previously fabricated from a positive replica of an adult human cadaveric mandibular condyle (Fig. 1, A and B). The chondrogenic layer was photopolymerized by a long-wave, 365-nm ultraviolet lamp (Glowmark, Upper Saddle River, New Jersey) at an intensity of approximately 4 mW/cm² for five minutes. A cell-polymer suspension containing mesenchymal stem cell-derived osteogenic cells (approximately 600 µl) was then loaded to occupy the remainder of the mold followed by the same photopolymerization protocol. The polymerized osteochondral constructs were then removed from the mold, washed twice with phosphate-buffered saline solution and implanted in the subcutaneous pockets in the dorsum of SCID (severe combined immunodeficient strain) mice (Harlan), which had been prepared by blunt dissection under general anesthesia with an intraperitoneal injection of 100 mg/kg ketamine and 5 mg/kg xylazine. A total of six fabricated osteochondral constructs and five control constructs were implanted in three immunodeficient mice. Among the five control constructs, three constructs encapsulated mesenchymal stem cells grown in basic medium without either chondrogenesis or osteogenesis-inducing supplements, and two control hydrogel constructs were cell-free.
Histological and Immunohistochemical Phenotyping of Tissue-Engineered Osteochondral Constructs

After a twelve-week period of in vivo implantation in the dorsum of the immunodeficient mice, harvested experimental osteochondral constructs and control hydrogel constructs were fixed in 10% formalin overnight, decalcified in 0.5-M EDTA solution, and embedded in paraffin with use of standard histological procedures. Sequential sections were stained with either hematoxylin and eosin or safranin O-fast green (Sigma). Serial consecutive sections adjacent to those used for histological examination were deparaffinized, washed in phosphate-buffered saline solution, and digested for thirty minutes at room temperature with bovine testicular hyaluronidase (1600 U/mL) in sodium acetate buffer, pH 5.5, with 150 mM of sodium chloride. Sections were treated with 5% bovine serum albumin for twenty minutes at room temperature to block nonspecific reactions. All antibodies for immunohistochemical analysis were obtained from Developmental Studies Hybridoma Bank (University of Iowa, Iowa City, Iowa). Type-I, II, and X collagens were immunolocalized with monoclonal antibodies to type-I collagen (SP1.D8; 1:2)\(^{18}\), type-II collagen (II-116B3; 1:2)\(^{19}\), and type-X collagen (X-AC9; 1:2)\(^{20}\), respectively. Osteopontin and osteonectin were immunolocalized with monoclonal antibodies to osteopontin (MPIIIB10; 1:2)\(^{21}\) and to osteonectin (AON-10; 1:4)\(^{22}\). After overnight incubation with the primary antibody in a humidity chamber, sections were rinsed with phosphate-buffered saline solution and incubated with immunoglobulin G anti-mouse secondary antibody (1:500; Antibodies Incorporated, Davis, California) for thirty minutes. Sections were then incubated with streptavidin-horseradish peroxidase conjugate for thirty minutes in a humidity chamber. After washing in phosphate-buffered saline solution, the double-linking procedure with the secondary antibody was repeated. Slides were developed with diaminobenzidine solution and were counterstained with Mayer hematoxylin for three to five minutes. Counterstained slides were dehydrated in graded ethanol and cleared in xylene. The same procedures were performed for negative controls except for the omission of the primary antibody. In addition, all histological and immunohistochemical characterization procedures were performed for positive-control normal rat mandibular condyles obtained from adult Sprague-Dawley rats (Harlan) that were age-matched to those from which the mesenchymal stem cells were originally harvested.

Results

Gross Examination of Tissue-Engineered Articular Condyles

Following twelve weeks of in vivo implantation in the dorsum of immunodeficient mice, osteochondral constructs in the shape and dimensions of real-sized adult human mandibular condyle formed de novo (Fig. 1). The tissue-engineered articular condyles measured 18 mm long by 9 mm wide by 11 mm high (Fig. 1, C), proportionally analogous to...
the original adult human cadaveric mandibular condyle and the acrylic positive replica of the mandibular condyle. The constructs were firm and unyielding upon physical manipulation and demonstrated multiple areas of calcification upon radiographic examination (Fig. 1, D). The chondrogenic and osteogenic layers of the tissue-engineered osteochondral constructs were inseparable with no observable seam at the interface, signifying positive material integration between the two stratified hydrogel layers.

Histogenesis of Chondral and Osseous Tissues and Immunohistochemical Phenotyping

The chondrogenic and osteogenic layers of the tissue-engineered articular condyles demonstrated distinctive histological characteristics (Fig. 2). Histological examination of the interface between the top polyethylene glycol-based hydrogel layer encapsulating the chondrogenic cells derived from mesenchymal stem cells and the bottom polyethylene glycol-based hydrogel layer encapsulating the osteogenic cells derived from mesenchymal stem cells revealed distinctive phenotype-specific characteristics of cartilage-like and bone-like tissues, respectively (Fig. 2, A and B). The chondrogenic and osteogenic portions of the tissue-engineered articular constructs largely remained in their respective layers (Fig. 2, A and B). However, there was mutual infiltration of the cartilaginous and osseous components into each other’s territory (Figs. 2, A and B; 3, A; and 4, A, C, and D), especially in comparison with our previous work of four-week and eight-week periods of in vivo

Fig. 2

Histologic and immunohistochemical characterization of a tissue-engineered articular condyle. A: A representative hematoxylin and eosin-stained section of the osteochondral interface of the tissue-engineered articular condyle. The upper third of the photomicrograph represents the chondrogenic portion of the tissue-engineered articular condyle and is characterized by relatively large chondrocyte-like cells housed in lacuna-like structures. The lower portion (approximately two-thirds) of the photomicrograph represents the osteogenic component of the tissue-engineered articular condyle characterized by bone trabeculae-like structures occupied by few cells and sparsely distributed between large clusters of cells. B: Representative positive safranin-O red staining of the chondral portion of the tissue-engineered articular condyle indicating a high concentration of cartilage-specific glycosaminoglycans in the extracellular matrix. In contrast, the osseous portion of the tissue-engineered articular condyle showed negative reaction to safranin-O staining. C: A hematoxylin and eosin-stained section of the osteochondral interface of a normal mandibular condyle from an age-matched rat. Note the rudimentary morphological resemblance of the osteochondral interface between the tissue-engineered articular condyle (A) and the normal mandibular condyle (C). D: Safranin-O red staining of the cartilaginous part of a normal mandibular condyle from an age-matched rat resembles the positive safranin-O red staining of the chondral portion of the tissue-engineered articular condyle (B).
incubation. This mutual infiltration of cartilage-like and bone-like tissues may resemble, to a rudimentary degree, the normal osteochondral interface of the mandibular condyles in an age-matched normal rat (Fig. 2, C and D).

The chondrogenic layer consisted of chondrocyte-like cells in lacunae and surrounded by an abundant intercellular matrix that showed intense reactions to cartilage-specific safranin-O staining. Type-II collagen was immunolocalized throughout the chondrogenic portion (Fig. 3, A). Sparse areas of positive reaction to safranin O and immunolocalized type-II collagen were also observed within the osteogenic layer near the osteochondral interface (Figs. 2, B and 3, A). The deep chondrogenic layer adjacent to the tissue-engineered osteochondral junction consisted of cells with a hypertrophic appearance (Fig. 2, A and B) and expressed type-X collagen (Fig. 3, B), characteristic of the extracellular matrix of hypertrophic and degenerating chondrocytes. Type-II collagen immunolocalization within the cartilaginous portion and at the osteochondral interface in a normal mandibular condyle from an age-matched rat (Fig. 3, C) showed rudimentary morphological resemblance to type-II collagen immunolocalization observed in tissue-engineered condyle constructs (Fig. 3, A). Control constructs encapsulating mesenchymal stem cells that were not preconditioned with chondrogenesis-inducing or osteogenesis-inducing supplements lacked the osteochondral organization, and they were mostly negative to immunolocalization of chondrogenic and osteogenic markers (Fig. 3, D). Histological examination of the control (cell-free) polyethylene glycol diacrylate hydrogel scaffolds revealed the intact borders of the hydrogel material, the absence of infiltration of the hydrogel by the host cells, and a lack of immunolocalization of chondrogenic or osteogenic markers (Fig. 4, B).

The osseous portion of the tissue-engineered articular condyle showed bone trabeculae-like structures that were occupied by cells both on the surface and in the center that were embedded within abundant extracellular matrix (Figs. 2, A and B; 3, A; and 4). Type-I collagen, osteopontin, and osteonectin were immunolocalized in this osteogenic layer of the tissue-engineered construct.
engineered osteochondral constructs, whereas the chondrogenic layer lacked positive immunolocalization of these bone markers (Fig. 4, A, C, and D). The osseous portion of the tissue-engineered articular condyle showed negative reaction to safranin O (Fig. 2, B) and a lack of immunolocalization of type-II collagen (Fig. 3, A).

**Discussion**

The present study is a necessary extension of our previous work, as we increased the encapsulation density of adult stem-cell-derived tissue-forming cells in osteochondral constructs from 5 million to 20 million cells/mL, with an extended in vivo implantation period of twelve weeks. Because increasing the in vivo cultivation period alone from four weeks to eight weeks without increasing the initial cell density (5 million cells/mL) failed to enhance the maturation level of the tissue-engineered structures, we believe that the greater encapsulation density (20 million cells/mL), in addition to the longer in vivo implantation period (twelve weeks), probably accounts for the advanced tissue maturation stage of the engineered bone-like and cartilage-like tissues seen in the present study. This observation is in agreement with similar cell-based tissue-engineering investigations. For example, increased maturation of tissue-engineered cartilage is observed upon seeding greater densities of isolated chondrocytes. Moreover, clustering of marrow stromal cells, as observed in the present study of clustering of mesenchymal stem cell-derived chondrocytes and osteoblasts, enhances their differentiation toward the osteogenic lineage.

The results of the present study substantiate the findings in our previous reports on the feasibility of de novo formation of osteochondral constructs in the shape of a small human articular condyle with two stratified layers of chondrogenic and osteogenic histogenesis from a single population of bone marrow-derived chondrogenic and osteogenic cells encapsulated in a hydrogel scaffold. The exposure of mesenchymal stem cell cultures to the media containing chondrogenesis-inducing and osteogenesis-inducing supplements for one week prior to in vivo implantation is aligned with our previous work and the work done by others. This short

![Fig. 4](image-url) Immuno histochemical characterization of the osteogenic portion in the tissue-engineered articular condyle. A: Positive immunohistochemical localization of type-I collagen is seen at the osteochondral interface and within the osseous portion of the tissue-engineered articular condyle. B: Representative acellular control construct showing negative reaction to type-I collagen antibody and the intact border of the hydrogel surrounded by the host fibrous-tissue capsule. There is a lack of host cell invasion into the tissue-engineered osteochondral construct. C and D: Positive immunolocalization of osteopontin and osteonectin, respectively, is evident within the (lower) osseous portion of the tissue-engineered articular condyle. By contrast, the (upper) chondral portion of the tissue-engineered articular condyle lacked the expression of osteopontin and osteonectin (C and D, respectively).
ex vivo manipulation period may facilitate eventual therapeutic applications. The presence of abundant matrix biosynthesis and immunolocalization of chondrogenic and osteogenic markers in corresponding layers of the tissue-engineered articular condyles indicates continuing phenotypic differentiation of chondrogenic and osteogenic cells from a single population of mesenchymal stem cells. The morphological appearance of the tissue-engineered osteochondral interface and the expression of cartilaginous and osseous markers within the corresponding chondrogenic and osteogenic layers rudimentarily resembles that of a native articular condyle.

Specifically, mutual infiltration of tissue-engineered cartilaginous and osseous tissues offers encouraging morphological evidence of interactions between mesenchymal stem cell-derived chondrogenic and osteogenic cells stratified in two hydrogel layers. The appearance of hypertrophic chondrocyte-like cells with immunolocalization of type-X collagen in the deep region of the chondrogenic layer likely indicates a transformation from chondrocyte hypertrophy to osteogenic phenotype. In support of this assumption is the continuing expression, although sparse and less intense, of chondrogenic markers such as type-II collagen and safranin O within the osteogenic portion of the tissue-engineered osteochondral construct, pointing to a phenotypic transition at the osteochondral interface. The nature of scattered tissue formation in the osteogenic layer, evident from both radiographic and histological images, appears to suggest that in the absence of directional cues that are embedded in cells during development, mesenchymal stem cell-derived osteogenic cells demonstrate that cell-to-cell contact may be necessary for continuing cell differentiation and matrix synthesis. In addition, longer in vivo cultivation and the application of mechanical stresses may accelerate tissue maturation.

Although previous approaches to the engineering of osteochondral constructs with use of isolated mature chondrocytes and osteoblasts have yielded important data, upon which the present study was based, the current work on tissue-engineering of articular condyles with both cartilaginous and osseous components from a single population of adult mesenchymal stem cells may represent another step toward the eventual goal of an alternative total joint replacement therapy. The design of osteochondral constructs in the shape and dimensions of a human articular condyle is likely a key parameter since cell survival and viability are increasingly challenging for large three-dimensional scaffolds used for bone and cartilage tissue engineering. The stratified fabrication of the osteochondral constructs from a single hydrogel system in the present study has the potential to promote physical integration between their cartilaginous and osseous components and to minimize the potential ingrowth of host fibrous tissue between the chondrogenic and osteogenic components after in vivo implantation. An empirical concern coupled with seeding cells in prefabricated three-dimensional scaffolds is the tendency for the seeded cells and the synthesized extracellular matrix to localize toward the outer surface of the scaffold, where most cells are initially seeded. The present work has adopted several approaches to encapsulate mesenchymal stem cell-derived chondrogenic and osteogenic cells in the aqueous phase of the polyethylene glycol-based hydrogel, thus maximizing the possibility of homogeneous cell distribution in the hydrogel and encouraging de novo tissue formation from within the photopolymerized constructs. The ease of fabrication and the ability to mold the photopolymerizable hydrogel systems into given proportions are advantages toward their potential applications for tissue engineering of osteochondral constructs.

Despite the advantages described above, a potential concern associated with polyethylene glycol-based hydrogel is the degradation rate. Increasing efforts are being made to investigate the enhancement of the degradation rate of the polyethylene glycol-based hydrogel system by the addition of degradable linkages to the macromere backbone such as polyester and phosphate groups. Our experience with in vivo implantation of the chondrogenic and osteogenic cells derived from rat mesenchymal stem cells encapsulated in a polyethylene glycol diacrylate hydrogel has revealed a positive relationship between the hydrogel degradation and the period of in vivo implantation. Nonetheless, the experimental divergence in our approach with ex vivo incubation of mesenchymal stem cells with chondrogenesis-inducing and osteogenesis-inducing supplements prior to the hydrogel encapsulation, the environmental differences between in vivo and in vitro incubation, and the extended implantation periods may have contributed to the differences observed in the degradation behavior of polyethylene glycol diacrylate relative to that seen in other studies. The ultimate goal of the present approach is to tissue engineer autologous articular condyles ex vivo that are structurally and functionally sound to serve as replacements for missing or degenerated articular condyles. However, a number of challenging issues need to be addressed before reaching this ambitious goal. Larger animal models are probably necessary to test the feasibility of in vivo implantation of tissue-engineered articular condyles derived from autologous mesenchymal stem cells. In addition, the tissue maturation and the mechanical strength of the tissue-engineered articular condyles should be attained ex vivo before in vivo implantation.

Zonal organization of articular cartilage is of structural and functional importance. Thus, tissue-engineered articular cartilage may need to incorporate appropriate molecular cues to recapitulate the developmental process of normal articular cartilage. The present selection of a photopolymerizable hydrogel system may facilitate this goal. A recent study has shown successful fabrication of a multilayered articular cartilage construct with zonal organization by encapsulating bovine chondrocytes from corresponding zones of the femoral articular cartilage. Encapsulating growth factors for the in vivo modulation of chondrogenesis and osteogenesis may be necessary for further differentiation and phenotypic maintenance of mesenchymal stem cell-differentiated chondrogenic and osteogenic cells in an in vivo environment. The most challenging task appears to be functional enablement of tissue-engineered articular condyles to withstand the mechanical loads that are experienced by normal articular condyles.
Increasing evidence of the potential enhancement of the extracellular matrix properties of both bone and cartilage by mechanical modulation is recognized as functional tissue engineering, a field that currently studies the responses of progenitor cells to mechanical stresses with an ultimate goal of enhancing the maturation and mechanical strength of tissue-engineered structures. Much additional work is warranted along several fronts before the present approach can be used for therapeutic applications.

**References**


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In support of their research or preparation of this manuscript, one or more of the authors received grants or outside funding from the National Institutes of Health (grants R01DE13964 and R01DE15391), the National Institute of Dental and Craniofacial Research, and the National Institute of Biomedical Imaging and Bioengineering (R01EB02332). None of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.02104


Use of a Distraction Plate for Distal Radial Fractures with Metaphyseal and Diaphyseal Comminution

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Background: Distal radial fractures with extensive comminution involving the metaphyseal-diaphyseal junction present a major treatment dilemma. Of particular difficulty are those fractures involving the articular surface. One approach is to apply a dorsal 3.5-mm plate extra-articularly from the radius to the third metacarpal, stabilizing the diaphysis and maintaining distraction across the radiocarpal joint.

Methods: Twenty-two patients treated with a distraction plate for a comminuted distal radial fracture were included in the study. With use of three limited incisions, a 3.5-mm ASIF plate was applied in distraction dorsally from the radial diaphysis, bypassing the comminuted segment, to the long-finger metacarpal, where it was fixed distally. The articular surface was anatomically reduced and was secured with Kirschner wires or screws. Eleven of the twenty-two fractures were treated with bone-grafting. The plate was removed after fracture consolidation (at an average of 124 days), and wrist motion was initiated. All patients were followed prospectively with use of radiographs, physical examination, and DASH (Disabilities of the Arm, Shoulder and Hand) scores.

Results: All fractures united by an average of 110 days. Radiographs showed an average palmar tilt of 4.6° and an average ulnar variance of neutral (0°), whereas loss of radial length averaged 2 mm. Flexion and extension averaged 57° and 65°, respectively, and pronation and supination averaged 77° and 76°, respectively. The average DASH scores were 34 points at six months, 15 points at one year, and 11.5 points at the time of final follow-up (at an average of 24.8 months). According to the Gartland-Werley rating system, fourteen patients had an excellent result, six had a good result, and two had a fair result. Grip strength and the range of motion of the wrist at one year correlated inversely with the proximal extent of fracture comminution into the diaphysis. The duration of plate immobilization did not correlate with the range of motion of the wrist or with the DASH score at one year.

Conclusions: The use of a distraction plate combined with reduction of the articular surface and bone-grafting when needed can be an effective technique for treatment of fractures of the distal end of the radius with extensive metaphyseal and diaphyseal comminution. A functional range of motion with minimal disability can be achieved despite a prolonged period of fixation with a distraction plate across the wrist joint.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

The management of high-energy fractures of the distal part of the radius involving both an intra-articular component and metaphyseal comminution with diaphyseal extension remains challenging. External fixation, which neutralizes compressive forces on the articular segment, may not provide sufficient stability and immobilization to allow healing of the metaphysis to the diaphysis proximally. Similarly, open reduction and internal fixation does not provide sufficient stability to maintain the reduction of the lunate and scaphoid fossae of the distal part of the radius. Hybrid options may include fixation of the diaphyseal fracture with a compression plate as well as external fixation of the articular surface or a combination of multiple plates.

Since 1998, we have treated high-energy injuries of the distal part of the radius with a fourteen or sixteen-hole dorsal 3.5-mm ASIF plate. The plate extends from the long-finger metacarpal to the radial diaphysis proximal to the comminuted fracture segment and is inserted through three small
incisions. The plate provides optimal fixation of the comminuted diaphyseal segment of the radius while simultaneously permitting distraction across the impacted articular segment. The implant passes extra-articularly, beneath the extensor tendons, across the radiocarpal and midcarpal articulation. Distraction may be applied prior to screw placement, thereby neutralizing the impacted segment. The plate is removed once fracture union has been achieved. The purpose of this study was to report the radiographic and functional outcomes of treatment with this technique.

Materials and Methods

From 1998 to 2002, selected high-energy distal radial fractures were treated with open reduction and internal fixation with application of a 3.5-mm plate (Synthes, Paoli, Pennsylvania) in distraction across the wrist joint. The indication for the use of this technique was a high-energy fracture of the distal part of the radius that demonstrated proximal extension involving the radial diaphysis at least 4 cm proximal to the radiocarpal articulation. The patients were followed prospectively, according to internal review board protocol, at six months, at one year, and at the time of final follow-up, at an average of 24.8 months. Demographic data, including age, gender, handedness, and mechanism of injury, as well as operative findings, including the fracture pattern, associated injuries, and soft-tissue disruption, were recorded. Preoperative radiographs (anteroposterior, lateral, and oblique) were evaluated to identify the number of articular fragments and the extent of comminution, and the fracture was classified with the AO system. Specific attention was paid to the proximal extent of the comminution as measured along the ulnar border of the radius to a line drawn perpendicular to the ulnar head and rounded to the nearest centimeter. Data regarding the treatment course, including subsequent procedures, duration that the implant was left in place, and complications, were collected.

Outcomes were assessed with physician-directed outcome tools at six months and one year and with subjective, patient-oriented questionnaires at six months, one year, and the time of final follow-up (at an average of 24.8 months). Objective findings including deformity, tenderness, grip strength, and range of motion were assessed by the treating surgeons. The subjective outcome tool was the Disabilities of the Arm, Shoulder and Hand (DASH) instrument. This instrument quantifies disabilities related to the upper extremity with a score ranging from 0 points (no disability) to 100 points (maximum disability). In addition, the results were rated with use of the Gartland and Werley demerit scoring system, which evaluates residual deformity, pain and limitation of motion, objective loss of motion, and complications (both arthritic and neurological). A score of 0, 1, or 2 points indicates an excellent result; 3 to 8 points, a good result; 9 to 20 points, a fair result; and ≥21 points, a poor result. Anteroposterior, lateral, and oblique radiographs of each wrist were analyzed to evaluate radiocarpal joint congruity, radial length, palmar tilt, and capitolunate angle at each postoperative visit and at the time of final follow-up.

Complications, including implant failure, infection, soft-tissue compromise, digital stiffness, and delayed union, were recorded. These complications were categorized as related to the primary injury, the index operative procedure (plate fixation), or plate removal.

Demographic Data (Table I)

Between 1998 and 2002, twenty-six patients underwent surgical treatment for a comminuted distal radial fracture that extended from the distal part of the radius to involve the diaphysis proximally. Twenty-two patients were followed for a minimum of one year. One of the twenty-six patients died as a result of injuries sustained in the accident, two patients sustained a severe closed head injury and were not able to provide subjective follow-up data, and one patient was lost to follow-up following plate removal. Data derived from physical examinations, radiographs, and DASH questionnaires were prospectively collected for twenty-two patients at six months and one year. Eighteen of those twenty-two patients were evaluated at a minimum of two years (average, 27.6 months; range, twenty-four to seventy-five months) with administration of the DASH questionnaire. Of the four patients who were not evaluated at two years, one had died as a result of illness unrelated to the original injury, one could not be contacted despite many attempts, one was unable to return for follow-up after one year.

<table>
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<th>TABLE I Characteristics of the Patients*</th>
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<td>Mean age (range) (yr)</td>
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<td>Mean duration of internal fixation (range) (days)</td>
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*The values are given as the number of patients with the percentage in parentheses unless otherwise indicated.
because of an inability to travel long distances, and one (a ninety-two-year-old patient) had become debilitated and confined to bed rest as a result of unrelated comorbidities, including a stroke. The one-year DASH scores were considered the “final” scores for those patients. The final subjective follow-up for all twenty-two patients was conducted at an average of 24.8 months.

The mechanism of injury was a motor-vehicle accident for sixteen patients, a fall for one, a crush injury for three, a gunshot wound for one, and a table saw injury for one. Nine patients had an open fracture. Four of those patients were treated initially with irrigation and débridement as well as external fixation; two, with irrigation and débridement as well as a dorsal plate; and three, with irrigation and débridement as well as manipulation and splinting. Three closed fractures were treated with external fixation prior to referral to our institution. Radiographs following preliminary internal or external fixation revealed persistent shortening and unacceptable alignment. The remaining ten patients underwent closed manipulation and splinting. Radiographs of all patients demonstrated inadequate reduction of the metaphyseal-diaphyseal junction of the radius with loss of radial length and/or radiocarpal and/or distal radioulnar joint incongruity.

Of the nine open fractures, two required a forearm flap for soft-tissue coverage and one was treated with split-thickness skin-grafting. These procedures were carried out several days after osteosynthesis, with a vacuum-assisted closure device covering the wound in the interim. For the remaining six open fractures, wound closure was performed after irrigation and débridement.

Four of the twenty-two patients had median nerve symptoms prior to the surgery and underwent a carpal tunnel release. Two of the carpal tunnel releases were performed during the initial procedure (external fixation) and two were performed before the distraction plate was applied. No vascular injuries were found in these patients.

Thirteen patients were considered to have sustained polytrauma and had associated orthopaedic or visceral injuries, including cardiac contusion, abdominal injuries, and burns. Six patients sustained a pelvic or lower-extremity long-bone fracture. Two patients sustained a concomitant fracture of the ipsilateral radial head, and one of them had an associated dislocation of the elbow. One patient had bilateral wrist fracture, and the contralateral side was treated with open reduction and internal fixation without a distraction plate. One patient had an extra-articular fracture of the proximal metacarpal of the ipsilateral thumb, and another patient had a fracture of the proximal phalanx of the ipsilateral index finger, which was treated with pinning.

Surgical Technique

The procedure is performed under tourniquet control with the patient lying supine on a radiolucent table. A 4-cm incision is made dorsally over the midpart of the shaft of the long-finger metacarpal, and the extensor tendon mechanism is retracted. A second, 4 to 6-cm incision is made at the dorsal radial aspect of the radius at least 4 cm proximal to the most proximal extent of the comminuted segment (Fig. 1). A twelve, fourteen, or sixteen-hole dorsal plate (3.5-mm ASIF compression plate; Synthes) is then passed from distal to proximal, with use of the plane between the extensor tendons (fourth compartment) and the periosteum and joint capsule. When necessary, reduction of the articular surface and/or placement of bone graft can be accomplished through this third incision.
and care is taken to ensure that the plate does not impinge on either the extensor pollicis longus or the digital extensor tendon as it is passed proximally under the tendons. This incision also permits placement of allograft bone in the metaphyseal defect as needed. The plate is fixed to the long-finger metacarpal, with care taken to drill the holes in the midline of the metacarpal, thereby avoiding subsequent rotatory displacement of the hand relative to the forearm.

Next, traction is applied, under fluoroscopic guidance, to obtain radial length. The plate is then clamped to the radial shaft proximally with use of a serrated bone-holding clamp while traction is applied. In an effort to prevent the tendency for pronation of the distal fragment, the hand is maintained in 60° of supination before the serrated clamp is used to hold the proximal plate to the diaphysis. Full rotation of the forearm is confirmed with the clamp holding the proximal portion of the plate to the radial shaft prior to final placement of the proximal screws to ensure that there is no rotational malalignment. The wrist is then assessed radiographically for radial length and congruity of the distal radioulnar joint. The digits are assessed clinically for full passive flexion to avoid extrinsic extensor tightness, and the forearm is assessed for full rotation. Diaphyseal fragments are then reduced and are fixed to the shaft with interfragmentary screws when possible. Finally, the articular surface of the radius is reduced. The lunate fossa is elevated with use of the same incision that had been employed to facilitate passage of the plate under the extensor pollicis longus tendon. Allograft bone is then placed in the metaphyseal void to support the articular surface when necessary, unless there is a contraindication to this procedure, such as an open fracture with contamination, prior surgery with potential contamination of the fracture, or a soft-tissue defect that precludes primary wound closure.

When possible, a 3.5-mm screw is then inserted through the plate and under the lunate fossa to serve as a direct buttress to prevent subsequent collapse. When distal fragments are too small for screw fixation, 0.45 or 0.62-in (11.4 or 15.75-mm) Kirschner wires are inserted under fluoroscopic guidance after reduction of the articular surface through the small dorsal incision used for exposure of the extensor pollicis longus tendon. Pins are inserted percutaneously through either the radial styloid or the intermediate column of the wrist, depending on the need for stability of the articular fragments. The radial styloid is reduced percutaneously with use of a tenaculum clamp and then is pinned with either 0.45 or 0.62-in Kirschner wires. The tips of the pins are left outside of the skin and are protected by bending them back on themselves.

Once the radius is stabilized, the distal radioulnar joint is assessed for stability. Instability should be suspected when a patient has a large displaced ulnar styloid fracture or a displaced ulnar head fracture, and it is confirmed by a finding of >8 mm of palmar-dorsal translation of the ulna relative to the
radius’. In cases of instability of the distal radioulnar joint, the forearm is maintained in a sugar-tong splint in 60° of supination for three weeks following stabilization, after which immobilization is discontinued and a gentle range of motion is initiated. No immobilization is utilized if the distal radioulnar joint is stable. The percutaneous pins are removed at six weeks postoperatively (Figs. 2-A through 2-G).

Digital range of motion is initiated on the second postoperative day under the supervision of an occupational therapist. An upper-extremity exercise program including active and passive range-of-motion exercises of the digits, pronation-supination exercises of the forearm, and range-of-motion exercises of the elbow is carried out under the guidance of an occupational therapist throughout the duration of internal fixation. Patients are permitted to perform activities of daily living, but lifting is restricted to 5 lb (2.3 kg). Patients are also allowed to return to work with the plate in place, while maintaining light-duty precautions. Patients with lower-extremity injuries are permitted to use a platform walker. The distraction plate is removed with use of regional (axillary block) anesthesia as outpatient surgery after verification of fracture union on posteroanterior, lateral, and oblique radiographs. Range-of-motion exercises of the wrist and digits are initiated immediately and no splinting is utilized following hardware removal.

Bone-Grafting
Eleven of the twenty-two patients underwent bone-grafting. Three patients with an open fracture and a large osseous defect required delayed insertion of corticocancellous structural autograft. The graft was placed during a secondary procedure after soft-tissue closure and digital motion had been obtained, at an average of four weeks after the index procedure. The grafting was performed through a dorsal incision that extended the previous incision over the Lister tubercle, with mobilization of the extensor pollicis longus tendon to gain access to the plate and adjacent bone defect. The graft was placed under the plate and fixed to the shaft as well as to the metaphysis with interfragmentary screws. A single screw was also placed through the plate and into the graft to maintain its stability. The other eight patients underwent placement of cancellous allograft at the time of the initial surgery, through
the incision based over the Lister tubercle, after distraction was applied.

Statistical analysis was performed with use of SAS statistical software (SAS Institute, Cary, North Carolina). Spearman correlations were used to evaluate outcomes with respect to the number of articular fragments, the proximal extent of the comminution into the radial diaphysis, and the duration of internal fixation. Significance was set at $p \leq 0.05$.

Results
A table summarizing the clinical data is available in the Appendix.

Time to Union
All fractures united by an average of 110 days, as determined with clinical examination and on posteroanterior, lateral, and oblique radiographs made at six weeks (baseline) and at four to eight-week intervals thereafter. Hardware removal was scheduled to be performed, on an elective basis, approximately two to three weeks after union was confirmed radiographically. The average time from application to removal of the plate was 124 days (range, sixty-eight to 240 days).

Radiographic Results
Final radiographic results were graded at a minimum of one year postoperatively (a minimum of six months after plate removal) on the basis of standard posteroanterior, lateral, and oblique views. The average loss of radial length was 2 mm as compared with the contralateral extremity on final radiographs. The mean palmar tilt was 4.6°, and only one of the twenty-two patients had radiographic evidence of dorsal tilt (5°). The capitolunate angle was neutral in twenty-one patients. One patient demonstrated dorsal angulation of the lunate with a 15° volar angulation of the capitate. The remaining twenty-one patients showed collinear alignment of the carpus with the distal part of the radius. A congruous radiocarpal joint (a step-off of <2 mm) was restored in twenty-one of the twenty-two wrists, as measured on radiographs after plate removal. The average ulnar variance was 0 mm (neutral) with a congruent distal radioulnar joint noted in

Fig. 2-E
Radiographs made at four months after the injury. Note the maintenance of radial length and palmar tilt as well as union of the fracture with bridging of the bone defect.
eighteen of twenty-one patients. (One patient had had a distal ulnar resection.)

Physical Examination
Physical examination consisted of assessment of the range of motion and grip strength. At six months, flexion and extension averaged 35° and 45°, respectively, and pronation and supination averaged 69° and 72°, respectively. The mean grip strength was 41% of that on the contralateral side. At one year, flexion and extension averaged 57° and 65°, pronation and supination averaged 77° and 76°, and grip strength averaged 69% of that on the contralateral side.

Complications
An infection developed at the surgical site in three patients, all of whom had a Grade-III A’ open fracture. It is noteworthy that two of the three patients had undergone previous open reduction and internal fixation with a dorsal plate prior to referral to our institution. The infections were treated with irrigation and débridement followed by antibiotic therapy. It was not necessary to remove the hardware prior to union in any patient. There were no cases of osteomyelitis or extensor tendon rupture. Rehabilitation, including digital motion, was performed without incident throughout the duration that the bridging plate was in place and after it had been removed. Three patients reported an extensor lag of approximately 15° in the long finger while the implant was in place. At the time of final follow-up, the extensor lag was <10° and caused no functional impairment in all three patients. There were no complications related to implant removal. Specifically, there was no refracture, tendon rupture, loss of reduction, or loss of length. No patients reported digital stiffness.

DASH Outcome Questionnaire
The average DASH score was 33.8 points at six months, 15.4
points at one year, and 11.5 points at the time of final follow-up (at an average of 24.8 months). The DASH scores at the time of final follow-up included those determined at one year for the four patients who were unable to complete the questionnaire after one year.

Gartland and Werley Ratings
On the basis of the rating system of Gartland and Werley, at one year postoperatively fourteen results were rated as excellent, six were rated as good, and two were rated as fair.

Return to Work
Patients were allowed to return to work with the implant in place, with light-duty restrictions, after the soft-tissue wounds had healed and pain was well controlled. Fifteen patients were able to return to their previous jobs at an average of 6.4 weeks postoperatively, whereas two patients were unable to return. Five patients were not working prior to the injury.

Clinical Correlations
Regression analysis revealed that, with the numbers available, there was no significant correlation between the duration of the internal fixation with the plate and wrist flexion-extension or forearm pronation-supination at six months or one year. Only a trend was noted for less pronation with an increased duration of plate fixation (p = 0.13). There was a significant relationship between the extent of the fracture and wrist motion. An increased extent of proximal comminution was associated with a significant decrease in wrist extension at six months (p < 0.03), a trend for a decrease in wrist flexion at six months (p < 0.07), a significant decrease in forearm pronation at one year (p < 0.05), and a trend for a decrease in wrist flexion at one year (p < 0.06). There was also a significant correlation between a longer duration of plate fixation and decreased grip strength at one year (p < 0.05) as well as a significant correlation between a greater extent of proximal comminution and less grip strength at six months (p < 0.02) and at one year (p < 0.01).

The DASH scores at six months correlated significantly with the duration of plate fixation, with higher scores seen with shorter durations of fixation (p < 0.02). However, with the numbers available, there was no correlation between the duration of internal fixation and the DASH scores at one year (p = 0.09). Similarly, there was no correlation between the number of articular fragments and the DASH scores at six months (p = 0.11) or one year (p = 0.77). As would be expected, the DASH scores correlated inversely with flexion (p = 0.001), extension (p = 0.002), and supination (p < 0.01) at one year.

Discussion
The stabilization of highly comminuted metaphyseal-diaphyseal fractures of the distal part of the radius remains a major orthopaedic challenge as a result of both biological and biomechanical considerations. Weber and Szabo noted that highly comminuted fractures of the distal part of the radius were associated with a 52% to 63% complication rate when treated with external fixation alone. They concluded that these fractures were difficult to manage, complications should be anticipated, and alternative treatment should be considered. One of the primary reasons why these fractures are difficult to manage lies in the different biological and mechanical considerations that must be taken into account when treating intra-articular fractures with proximal extension. Articular fractures may be managed with external or internal fixation with thin, low-profile plates. Diaphyseal fractures in the forearm are best treated with rigid plates that can allow compression across cortical interfaces, maintain axial length, and...
permit an immediate range of motion. These plates are rigid and resist fatigue failure, but they are difficult to contour and they provide limited options for screw placement, which makes them relatively poor choices for multifragmentary articular fractures. There is no standard treatment for fractures that involve both the diaphysis and the metaphysis of the distal part of the radius. Surgical options essentially focus on treating them as two separate fractures with application of one implant to stabilize the diaphyseal segment and a second to treat the articular segment.

The technique of extended plate fixation of the wrist and forearm has several potential advantages. High-energy fractures with extensive comminution often require fixation for a prolonged period of time in order to achieve union. Prolonged immobilization with external fixation is often not possible because of pin-track infection or loosening leading to loss of reduction. Eleven of the twenty-two patients in our series had bone loss requiring grafting, and nine fractures were open and thus required soft-tissue management. The use of the distraction plate permitted the soft-tissue envelope to mature while maintaining radial length, allowing incorporation of the bone graft, and retaining congruity of the radiocarpal and radioulnar joints.

We believe that the dorsal ulnar position of this plate gives it an advantage over conventional external fixation, which relies on maintaining the length of the ulnar column of the radius (metaphyseal bone underlying the lunate fossa) from a radially based axis. With plate fixation on the long-finger metacarpal, the distraction moment is centralized with the added advantage of stabilizing the lunate fossa of the distal part of the radius. In addition, the implant serves simultaneously as a distraction device and a dorsal buttress to the fracture. Radial length is maximized and radiocarpal alignment and palmar tilt are maintained. Carpal alignment and the alignment of the carpus with respect to the distal part of the radius have been demonstrated to be an important determinant of functional outcome after distal radial fracture. This alignment was accomplished in our patients and may account for the satisfactory range of motion and functional results.

We believe that another advantage of the dorsal distraction-plate fixation technique is that it permits the patients to use the upper extremity for moderate or light activities while the comminuted segments heal. Thirteen of the twenty-two patients had sustained polytrauma, and six of them had pelvic or lower-extremity fractures. The stability of the implant permitted those patients to use a platform walker to assist in transfers during physical activity and to perform personal hygiene. Furthermore, fifteen of seventeen patients who had been working before the injury were able to return to work during their treatment.

There are two distinct concerns with the use of this technique. First, there is the potential for stiffness of the wrist. The patients in this series all had substantial comminution, which would have necessitated some protective immobilization regardless of the fixation technique that was employed. The average time that the plate remained in place was 124 days in our study. Many investigators have evaluated the effect of immobilization on outcome following fractures of the distal part of the radius. The majority have indicated that early motion results in earlier restoration of function but not significant differences in function at the time of one-year follow-up. Kaempffe et al. documented that the outcome was adversely affected by a longer duration of distraction with an external fixator. Other authors have documented no difference between results when they compared early motion with immobilization by external fixation or a cast. In those studies as well as in the current one, it is difficult to distinguish the effect of the severity of the fracture and the associated soft-tissue injuries from the effect of the duration of the immobilization. Our study suggests that a functional range of motion can be regained within the first year after the injury despite up to six months of plate fixation across the wrist joint. In addition, regression analysis showed no relationship between the duration of fixation and the range of motion. There was, however, a relationship between fracture severity (the proximal extent of the comminution) and loss of both flexion and pronation. Taken together, these findings suggest that the implant can remain in place across the wrist joint until union occurs without risking any more loss of motion than can be expected on the basis of the severe nature of the injury.

The other concern regarding this technique is the potential for delayed union of the radius. Metaphyseal fractures of the radius tend to heal by collapse, which facilitates union but often results in loss of motion and symptomatic distal radioulnar incongruity. The use of a more rigid method of maintaining the reduction may prevent the collapse that would otherwise permit union. The average amount of shortening seen in our series was only 2 mm, and neutral ulnar variance was restored. However, all fractures healed by an average of 110 days. It should be noted that eleven of the twenty-two patients underwent adjunctive bone-grafting, which not only facilitates union but also may prevent collapse of the fracture.

No hardware failures occurred in this series, and there were no cases of extensor tendon injury or tenosynovitis as have been previously reported with use of a conventional dorsal plate. However, three patients did note an extensor lag of the long finger of at least 15° while the distraction plate was in place. This was most likely secondary to the bulk of the 3.5-mm plate lying adjacent to and underneath the common digital extensor tendon. Furthermore, the extensor lag improved to <10° at the time of final follow-up, and none of these patients complained of functional impairment.

The technique described here is not new. In a case report, Burke and Singer described the use of an “internal distraction plate” for treatment of comminuted, displaced distal radial fractures. Their technique and indications were similar to those in our series. In addition, Becton et al. described this technique as well as a specially designed plate (Biomet, Warsaw, Indiana) for use for Colles fractures. Their results suggested that this technique may be useful in elderly patients with metaphyseal bending fractures. We found their plate to...
be too short to bypass the zone of injury in the current series of patients, but we recognize that this device can be useful for less comminuted fractures.

In conclusion, a dorsal wrist-forearm distraction plate is useful in the management of severely comminuted fractures of the distal part of the radius in which there is proximal extension into the diaphysis and inadequate bone distally to support conventional plate fixation. This plate serves the same role as an external fixator in a multiply injured patient by maintaining fracture reduction by fixed distraction. However, with the fixation device buried below the skin, the problems with pin-track infection are circumvented. Furthermore, the rigidity of the construct allows greater patient activity, assists with patient transfers, and allows limited weight-bearing, which may not be possible with external fixation. Despite the long-term internal fixation across the wrist joint, the range of motion and DASH scores were acceptable at the time of final follow-up. Additional studies should be performed to compare this technique with nonbridging internal fixation and external fixation.

Appendix

A table summarizing the clinical data is available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

References

Diagnostic Accuracy of a New Clinical Test (the Thessaly Test) for Early Detection of Meniscal Tears

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Background: Clinical tests used for the detection of meniscal tears in the knee do not present acceptable diagnostic sensitivity and specificity values. Diagnostic accuracy is improved by arthroscopic evaluation or magnetic resonance imaging studies. The objective of this study was to evaluate the diagnostic accuracy of a new dynamic clinical examination test for the detection of meniscal tears.

Methods: Two hundred and thirteen symptomatic patients with knee injuries who were examined clinically, had magnetic resonance imaging studies performed, and underwent arthroscopic surgery and 197 asymptomatic volunteers who were examined clinically and had magnetic resonance imaging studies done of their normal knees were included in this study. For clinical examination, the medial and lateral joint-line tenderness test, the McMurray test, the Apley compression and distraction test, the Thessaly test at 5° of knee flexion, and the Thessaly test at 20° of knee flexion were used. For all clinical tests, the sensitivity, specificity, false-positive, false-negative, and diagnostic accuracy rates were calculated and compared with the arthroscopic and magnetic resonance imaging data for the test subjects and the magnetic resonance imaging data for the control population.

Results: The Thessaly test at 20° of knee flexion had a high diagnostic accuracy rate of 94% in the detection of tears of the medial meniscus and 96% in the detection of tears of the lateral meniscus, and it had a low rate of false-positive and false-negative recordings. Other traditional clinical examination tests, with the exception of joint-line tenderness, which presented a diagnostic accuracy rate of 89% in the detection of lateral meniscal tears, showed inferior rates.

Conclusions: The Thessaly test at 20° of knee flexion can be used effectively as a first-line clinical screening test for meniscal tears, reducing the need for and the cost of modern magnetic resonance imaging methods.

Level of Evidence: Diagnostic Level I. See Instructions to Authors for a complete description of levels of evidence.

Meniscal injuries are very common among professional and amateur athletes and are one of the most common indications for knee surgery. The evaluation of such injuries is not always easy, especially in the setting of primary health care. The diagnosis can be made accurately in 75% of such knees on the basis of the history alone, whereas the specific clinical tests that have been used for the detection of such injuries do not have high sensitivity and specificity values.

In order to improve diagnostic accuracy, arthroscopic evaluation of the knee joint had been initially proposed. For both orthopaedic surgeons and primary health-care physicians, magnetic resonance imaging has currently become the most widely used noninvasive imaging method for detecting meniscal injuries, with a reported diagnostic accuracy of as high as 98%. However, the cost of magnetic resonance imaging scans is high, and the wide use of the method is restricted to certain health-care systems in different countries.

In this study, we present the diagnostic accuracy of a new dynamic clinical test for the detection of meniscal injuries, which can be easily performed by physicians in the outpatient setting.
Materials and Methods

Patients

Between January 2001 and December 2002, 780 patients with symptoms relating to the knee joint were examined in the sports injuries outpatient clinic of our department. From this pool of patients, all adults with a knee injury who had an initial diagnosis of a meniscal tear made on the basis of the history and the mechanism of injury were included in this study. Exclusion criteria were multiple knee injuries, a history of knee surgery, early clinical and radiographic signs of osteoarthritis, articular cartilage injuries, neurological and musculoskeletal degenerative disorders, and disorders of the synovium. All patients with abnormal findings on conventional radiographs were also excluded from the study. We did not evaluate acutely injured knees (those seen less than four weeks after the injury) as such knees are very painful and resist clinical examination and a diagnostic approach based on either magnetic resonance imaging or arthroscopy was thought to be more appropriate.

Two hundred and thirteen adult patients (213 knees) (group A), with an average age of 29.4 years (range, eighteen to fifty-five years), were identified, signed a consent form, and were studied prospectively. There were 157 men and fifty-six women. A diagnostic magnetic resonance imaging scan of the knee was performed on all patients. Afterward, all patients in group A underwent therapeutic arthroscopic surgery and the findings were recorded.

For the purpose of the study, another group of 197 volunteers (197 knees) (group B) was also recruited from the outpatient clinics. These subjects (the healthy controls) had no knee symptoms or history of knee disorders. They had attended the outpatient clinics for the treatment of lumbar spine and shoulder disorders, and a diagnostic magnetic resonance imaging scan of either the lumbar spine or the shoulder was indicated for all of them. Following consultation and the signing of a consent form, all patients agreed to undergo a knee examination and to have an additional magnetic resonance imaging scan of the healthy knee. The patients in the two groups were similar with regard to age, gender, body weight, and the knee being tested (Table I).

Clinical Evaluation

All patients in both groups had a thorough clinical examination performed by two experienced examiners (T.K. and M.H., specialists in orthopaedic surgery) and a separate examination done by two inexperienced examiners (A.H.Z. and V.Z., residents). They recorded and evaluated the results of five tests: the medial and lateral joint-line tenderness test, the McMurray test (applying mild valgus or varus compressive stress while the knee is progressively extended and the tibia is rotated), the Apley compression and distraction test, the Thessaly test at 5° of flexion, and the Thessaly test at 20° of flexion. The examiners were all blinded with regard to the results of the magnetic resonance imaging scans. In the case of disagreement between the examiners, a reevaluation of the patient was performed and a common decision was made.

The Thessaly test is a dynamic reproduction of load transmission in the knee joint and is performed at 5° and 20° of flexion (Figs. 1-A through 1-E). It was named in honor of the county, or prefecture, in our country, which has a continuous, uninterrupted ten-thousand-year history. The examiner supports the patient by holding his or her outstretched hands while the patient stands flatfooted on the floor. The patient then rotates his or her knee and body, internally and externally, three times, keeping the knee in slight flexion (5°). Then the same procedure is carried out with the knee flexed at
Patients with suspected meniscal tears experience medial or lateral joint-line discomfort and may have a sense of locking or catching. The theory behind the test is that, with this maneuver, the knee with a meniscal tear is subjected to excessive loading conditions and almost certainly will have the same symptoms that the patient reported. The test is always performed first on the normal knee so that the patient may be trained, especially with regard to how to keep the knee in 5° and then in 20° of flexion and how to recognize, by comparison, a possible positive result in the symptomatic knee.

**Magnetic Resonance Imaging Studies**

Magnetic resonance imaging scans were performed on a 1.0-T scanner (Intera NT; Philips Medical Systems, Best, The Netherlands) with use of a quadrature knee coil. The magnetic resonance sequences acquired for each patient included a sagittal fat-suppressed intermediate-weighted (repetition time, 2400 msec; echo time, 15 msec) turbo spin-echo sequence (section thickness, 4 mm; field of view, 140 × 160 mm; matrix, 256 × 304; echo train length, five) and a coronal T1-weighted (repetition time, 550 msec; echo time, 15 msec) spin-echo sequence (section thickness, 4 mm; field of view, 140 × 160 mm; matrix, 198 × 304). The acquisition times were seven minutes and thirty-six seconds and five minutes and thirty-five seconds, respectively. Magnetic resonance imaging scans were evaluated independently by one experienced musculoskeletal radiologist (A.H.K.) and one research fellow in musculoskeletal radiology. Both of them were blinded with regard to the results of the clinical tests. In cases of disagreement, a consensus was reached. A meniscal tear was diagnosed when a signal abnormality reached the articular surface of the meniscus in at least two adjacent images or when the abnormal signal reached the articular surface of the meniscus in one image of both sequences. The meniscal tears were classified, according to the systems of Mesgarzadeh et al.13 and De Smet et al.14, into four groups: horizontal or oblique partial-thickness tears, radial tears, vertical or complex full-thickness tears, and tears with displaced meniscal fragments.
Diagnostic Accuracy of a New Clinical Test (the Thessaly Test) for Early Detection of Meniscal Tears

Statistical Analysis
Sensitivity, specificity, false-positive, false-negative, and diagnostic accuracy values were calculated for all clinical tests. The chi square test was used to determine whether the findings on the imaging studies for the symptomatic patients and asymptomatic controls were significantly different. A p value of <0.05 was considered to be significant.

Before the study was begun, an error analysis of the clinical evaluation was conducted on twenty patients. The four examiners, who later examined the two groups of patients, showed an initial interobserver and intraobserver agreement of 95% for all clinical tests.

Ethical Aspects
The study design was approved by both the National Ethical and the Hospital Scientific Committees. All patients in both groups were fully informed and signed a consent form for participation in the study.

Results
Magnetic Resonance Imaging and Arthroscopic Findings
The findings on magnetic resonance imaging in group A included medial meniscus tears in 130 patients, lateral meniscus tears in thirty-seven patients, a combination of anterior cruciate ligament and meniscal tears in twenty patients, isolated anterior cruciate ligament tears in fifteen patients, and miscellaneous lesions (chondral lesions, plicae, or cysts) in eleven patients. Arthroscopic findings in the same group of patients were in agreement with those of the magnetic resonance images in all patients except two. Arthroscopy initially failed to visualize two nondisplaced horizontal tears of the posterior horn of the medial meniscus. Arthroscopic surgery was then performed for the treatment of all patients on the basis of the magnetic resonance imaging findings.

The findings on magnetic resonance imaging in group B included a normal appearance of all knee structures in 188 patients and medial meniscus tears in nine patients (4.6%). The tears in the asymptomatic patients were located in the posterior horn of the medial meniscus and consisted of five nondisplaced, horizontal partial-thickness tears and four oblique partial-thickness (incomplete) tears. These types of meniscal tears do not represent Grade-I or II meniscal degenerative changes. A significant difference was detected between groups A and B with regard to the presence of meniscal tears (chi-square test, p < 0.001).

Evaluation of Clinical Diagnostic Tests
The values for the diagnostic parameters for all clinical examination tests, with magnetic resonance imaging used as the...
method to determine the disorder, are shown in Table II. The true-positive, true-negative, false-positive, and false-negative recordings for the Thessaly test with the knee at 20° of flexion are shown in Table III. The Thessaly test at 20° of flexion showed high values for diagnostic accuracy, with an accuracy level of 94% in the diagnosis of medial meniscal tears and 96% in the diagnosis of lateral meniscal tears. In knees with a combination of an anterior cruciate ligament and meniscal tear, the diagnostic accuracy of the Thessaly test for meniscal tears reached the level of 90%. Identical values were produced when arthroscopy was used for the determination of the disorder.

The rates of false-positive and false-negative results, expressed as a percentage, for all clinical tests are also shown in Table II. When the Thessaly test at 20° of flexion was used to identify medial meniscal tears, false-negative results were recorded for seven knees in group A and eight knees in group B. When the test was used to identify lateral meniscal tears, false-negative results were recorded for three knees in group A. Magnetic resonance imaging analysis of the knees with false-negative recordings showed partial-thickness medial meniscal tears and nondisplaced horizontal tears of the lateral meniscus. The rest of the clinical examination tests showed inferior diagnostic accuracy values and a higher number of false-negative and false-positive recordings, with the exception of the joint-line tenderness test, which showed an acceptable accuracy value at the level of 89% in identifying lateral meniscal tears (Table II).

All isolated medial meniscal tears found on magnetic resonance imaging produced medial joint-line tenderness, and all isolated lateral meniscal tears found on magnetic resonance imaging produced lateral joint-line tenderness. When the Thessaly test was performed at 20° of flexion, seven (3.3%) of the patients in group A had a clinically impor-

### TABLE II Values for Diagnostic Parameters of the Clinical Examination Tests

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<th>Test</th>
<th>Diagnosis</th>
<th>Combined Injury of Anterior Cruciate Ligament and Meniscus</th>
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<tr>
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<td>Injury of Medial Meniscus</td>
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</tbody>
</table>

The true-positive, true-negative, false-positive, and false-negative recordings for the Thessaly test with the knee at 20° of flexion are shown in Table III. The Thessaly test at 20° of flexion showed high values for diagnostic accuracy, with an accuracy level of 94% in the diagnosis of medial meniscal tears and 96% in the diagnosis of lateral meniscal tears. In knees with a combination of an anterior cruciate ligament and meniscal tear, the diagnostic accuracy of the Thessaly test for meniscal tears reached the level of 90%. Identical values were produced when arthroscopy was used for the determination of the disorder. The rates of false-positive and false-negative results, expressed as a percentage, for all clinical tests are also shown in Table II. When the Thessaly test at 20° of flexion was used to identify medial meniscal tears, false-negative results were recorded for seven knees in group A and eight knees in group B. When the
Discussion

Meniscal tears occur as a result of injury or degeneration of the substance of the meniscus. Most patients report an acute onset of sharp pain following a twisting injury with the knee flexed and the foot planted on the ground\(^1,2,10\). The pain typically subsides after a period of time, and the patient usually reports pain and discomfort in the affected part of the joint. Recurrent effusions are common and, occasionally, a locking sensation is felt. Physical examination of the knee with a torn meniscus reveals joint-line tenderness with a palpable click or snap. The range of motion may be limited secondary to displacement of a meniscal tear.

Several provocative maneuvers or tests have been described to elicit symptoms from a torn meniscus. They can be divided into two groups\(^1,10\). In the first group are those tests that depend on palpation to elicit tenderness or clicks, such as the Bragard, McMurray, and Steinmann second test\(^1,10\). In the Bragard test, the examiner palpates the joint line and demonstrates that external tibial rotation and knee extension increases the tenderness across the joint line. The McMurray test demonstrates a palpable click at the joint line\(^12\). Medially, this is demonstrated with external tibial rotation and passive motion from flexion to extension. Laterally, it is demonstrated with the tibia in internal rotation and passive motion from flexion to extension. The Steinmann second test demonstrates joint-line tenderness that moves posteriorly with knee flexion and anteriorly with knee extension.

In the second group are the tests that depend on pain with rotation\(^1,10\). The Apley test forces the tibiofemoral surfaces together in flexion to elicit pain. This is believed to confirm a meniscal tear. The Apley test is also performed with the knee surfaces distracted. If this test elicits less discomfort than the compression test, it favors the finding of a meniscal tear over that of a fixed articular cartilage disorder. The Bohler test is performed with varus stress and compression to demonstrate a medial tear and with valgus stress and compression to diagnose a lateral tear. Duck walking increases the compressive forces on the posterior horns of the torn menisci and causes pain. The Helfet test is a failure of the knee to externally rotate normally with extension and is seen when the knee is locked. The Steinmann first test is done with the knee flexed to 90°, and sudden external rotation of the tibia is applied to test the medial meniscus. The result is pain along the medial joint line. Internal tibial rotation is used for lateral meniscal tears. The Merke test is the first Steinmann test with the patient in the weight-bearing position. Internal rotation of the body produces external rotation of the tibia and medial joint-line pain when the medial meniscus is torn. The opposite occurs when the lateral meniscus is torn. Although the Merke test is a dynamic test, it differs from the Thessaly test because of the fact that it is performed at 90° of knee flexion with partial bipedal weight-bearing. To the best of our knowledge, no clinical examination test similar to the Thessaly test has been reported in the literature.

The McMurray test is the most widely used test, and it is found to be positive in 58% of knees with a torn meniscus\(^10\). Others believe that joint-line tenderness is the most accurate clinical sign of meniscal tears, as it is present in 77% to 85% of such cases\(^11,18,19\). Despite the wide use\(^1,10\) of these tests, their sensitivity and specificity and diagnostic accuracy are low\(^1\). Moreover, the reports describing them in the literature are old and very few of the tests have been studied to determine how their diagnostic accuracy compares with that of arthroscopy or magnetic resonance imaging\(^1,11,19-26\). In the later studies, the sensitivity and specificity of the clinical tests, mainly the McMurray test, rarely exceed the level of 80%. These tests have a high rate of false-positive findings, and their diagnostic accuracy does not improve with the examiner’s experience; therefore, it seems that all have a limited value in current clinical practice. The joint-line tenderness sign only can be safely used for the detection of lateral meniscal tears\(^1\). Thus, in order to improve diagnostic accuracy in the detection of meniscal tears, arthroscopic evaluation was initially proposed\(^1\). This procedure has a cost and subjects the patient to the risks of a

### TABLE III Recordings of the Thessaly Test at 20° of Knee Flexion*

<table>
<thead>
<tr>
<th></th>
<th>Positive</th>
<th>Negative</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Medial meniscal injury</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>124 (a)</td>
<td>9 (b)</td>
<td>133 (a + b)</td>
</tr>
<tr>
<td>Negative</td>
<td>15 (c)</td>
<td>262 (d)</td>
<td>277 (c + d)</td>
</tr>
<tr>
<td>Total</td>
<td>139 (a + c)</td>
<td>271 (b + d)</td>
<td>410</td>
</tr>
<tr>
<td><strong>Lateral meniscal injury</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive</td>
<td>34 (a)</td>
<td>15 (b)</td>
<td>49 (a + b)</td>
</tr>
<tr>
<td>Negative</td>
<td>3 (c)</td>
<td>358 (d)</td>
<td>361 (c + d)</td>
</tr>
<tr>
<td>Total</td>
<td>37 (a + c)</td>
<td>373 (b + d)</td>
<td>410</td>
</tr>
</tbody>
</table>

*True-positive (a), false-positive (b), false-negative (c), and true-negative (d) recordings.*
surgical procedure. More recently, despite the substantial cost, magnetic resonance imaging scans have been widely used as a screening tool for meniscal tears. On the basis of the high predictive value of negative findings on magnetic resonance imaging studies, it has been suggested that magnetic resonance imaging can be used in order to exclude patients from unnecessary arthroscopy.\(^\text{11,14,27,28}\)

For the last three years in our department, we have used this new clinical test for the early and accurate detection of meniscal tears. It has been developed by one of us (T.K.) to reproduce the exact dynamic mechanisms that cause meniscal injuries in humans. It can be inferred that the dynamic (monopodal weight-bearing) internal and external rotation of the knee at 20° of flexion squeezes apart the fragments of the meniscus and causes pain arising from the outer intact part of the meniscal substance, which is innervated.\(^\text{29,30}\) Because the meniscal load is increased substantially with this maneuver, we believe that even small tears can be detected with this test.

In order to evaluate the diagnostic accuracy of the Thessaly test, a control group of subjects with healthy asymptomatic knees was used.\(^\text{11,12}\) We did not use symptomatic knees with no suspected meniscal abnormality or the asymptomatic contralateral knee of the patients in group A as controls because studies have shown that such knees are associated with a high prevalence of meniscal tears (perhaps because of over-stressing of the noninjured knee or because of lifestyle risk factors), which introduces bias.\(^\text{31,32}\) This clinical examination maneuver with the knee at 20° of flexion was tested against both arthroscopy and magnetic resonance imaging and demonstrated high sensitivity and specificity rates and a diagnostic accuracy of 94% for tears of the medial meniscus and 96% for tears of the lateral meniscus, which are comparable with the accuracy rates reported for magnetic resonance imaging.\(^\text{11,14,27}\)

The same maneuver at slight flexion (5°) did not show equivalent accuracy rates. The other clinical diagnostic tests reviewed showed low accuracy rates, and we do not recommend them.

All clinical tests showed a high rate of interobserver and intraobserver agreement. This can be explained by the fact that an error analysis of the clinical evaluations was performed prior to the initiation of the study. The joint-line tenderness sign (for the lateral meniscus only) showed an acceptable, albeit lower than previously reported, accuracy rate of 89%\(^\text{11}\). In our study, the presence of a disorder of the anterior cruciate ligament rendered the clinical examination tests less effective in the diagnosis of a meniscal abnormality, which is comparable with the findings in other reports.\(^\text{31,32}\) In our study, the findings of arthroscopy and magnetic resonance imaging were found to be in agreement with respect to the diagnosis of meniscal tears in the vast majority of the knees. Arthroscopic evaluation failed to diagnose two meniscal tears, and magnetic resonance imaging studies demonstrated a meniscal abnormality in 4.6% of the asymptomatic patients, which is lower than the rates reported in other studies.\(^\text{31,32}\) A possible explanation is that our control group (group B) comprised volunteers who did not have any knee problems at all, whereas the control groups in other studies have consisted of the asymptomatic knee in patients with a symptomatic knee.\(^\text{32}\)

The Thessaly test at 20° of knee flexion has low rates of false-negative and false-positive results. This allows it to be used safely as a first-line screening test\(^\text{13}\) for the diagnosis of both medial and lateral meniscal tears. This test has recently changed our everyday clinical practice. We use its results for the selection of patients who need arthroscopic meniscal surgery. We continue to use magnetic resonance imaging scans as a second-line screening test for those patients in whom the history, mechanism of injury, and clinical examination indicate the existence of a disorder other than a meniscal injury. This diagnostic approach has allowed us to decrease substantially the cost of diagnostic imaging as fewer magnetic resonance imaging studies are necessary.\(^\text{11,14,27}\)

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The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.02338

References

Our hypothesis in this study was that the classification system and treatment protocol would be prognostic of overall patient outcome. The purpose of this study was to report the intermediate to long-term clinical and radiographic results of this treatment protocol for calcaneal fracture malunions.

Materials and Methods

Patients

Between 1991 and 2001, ninety-four calcaneal malunions in eighty-seven patients were managed by the senior author (R.W.S.) at our institution. All patients had been initially managed at an outside institution; twenty-four malunions in twenty-three patients had had previous attempts at operative fixation of the fracture elsewhere and were excluded. Four patients (four feet) died and twenty patients (twenty-one feet) were lost to follow-up, leaving forty-five feet (64%) with a malunion after nonoperative treatment of a calcaneal fracture in forty patients who were available for follow-up evaluation at an average of 5.3 years (range, twenty-four to 151 months). All patients had been followed for a minimum of two years. Five feet had a type-I malunion; thirty, a type-II malunion; and ten, a type-III malunion. Five patients had a bilateral malunion; one of them had a type-II and a type-III malunion, three had a type-II malunion bilaterally, and one had a type-III malunion bilaterally.

The average patient age was 46.8 years (range, twenty-four to seventy-four years). There were thirty-one men and nine women. Twenty-four (60%) of the forty patients were smokers. While the cessation of smoking was encouraged and patients were informed of the risks, many disregarded the advice. Despite this, and with informed consent obtained, smoking was not a contraindication to surgery in our series. Additionally, nineteen (48%) of the forty patients were involved in Workers’ Compensation claims. The average interval between the fracture and the surgery was 16.4 months (range, two to 117 months), but several patients were treated two or three months after the injury. Several patients with polytrauma were transferred to our institution without definitive treatment of the calcaneal fractures. These patients all had substantial deformity with displacement of the subtalar joint, lateral wall explosion, peroneal tendon impingement, and varus malalignment of the hindfoot. At two or three months, the fracture had already consolidated to such a degree that open reduction and internal fixation was not feasible. Because the patients were convalescing from other injuries, we performed the operation at that time to minimize the rehabilitation period.

All patients in the study group were managed according to a standard treatment protocol based on the classification system for calcaneal malunions described by Stephens and Sanders. In addition to standard radiographs, axial and semi-coronal computerized tomography scans were made to determine the type of malunion. Type-I malunions include a large lateral wall exostosis without subtalar arthrosis or hindfoot malalignment. Type-II malunions exhibit both a large lateral wall exostosis as well as subtalar arthrosis. Hindfoot malalignment is minimal if present at all. Type-III malunions include a large lateral wall exostosis, subtalar arthrosis, and >10° of hindfoot malalignment (typically varus).

Fig. 1

Intraoperative photograph showing excision of the lateral wall exostosis. Note the use of retractors to avoid violation of the talofibular joint.
Intermediate to Long-Term Results of a Treatment Protocol for Calcaneal Fracture Malunions

BY MICHAEL P. CLARE, MD, WILLIAM E. LEE III, PhD, AND ROY W. SANDERS, MD

Investigation performed at The Florida Orthopaedic Institute, Tampa, Florida

Background: Nonoperative management of displaced intra-articular calcaneal fractures may result in malunion affecting the function of both the ankle and the subtalar joint. The purpose of this study was to report the intermediate to long-term results of a treatment protocol for calcaneal fracture malunions.

Methods: Seventy feet (sixty-four patients) with a malunion after nonoperative management of a displaced intra-articular calcaneal fracture were evaluated. On the basis of the classification system of Stephens and Sanders, type-I malunions were treated with a lateral wall exostectomy and peroneal tenolysis; type-II malunions, with a lateral wall exostectomy, peroneal tenolysis, and subtalar bone-block arthrodesis; and type-III malunions, with a lateral wall exostectomy, peroneal tenolysis, subtalar bone-block arthrodesis, and a calcaneal osteotomy. The patients were evaluated clinically and radiographically at a minimum of twenty-four months following surgery.

Results: Forty-five feet in forty patients were available for follow-up evaluation at a minimum of two years, with an average duration of follow-up of 5.3 years. Thirty-seven (93%) of the forty feet that had an arthrodesis achieved union. Statistical analysis revealed no significant difference among the types of malunion with respect to the Maryland foot score, the American Orthopaedic Foot and Ankle Society (AOFAS) ankle and hindfoot score, or the Short Form-36 (SF-36) health survey subscales, which was likely due to sample size discrepancies. Forty-two (93%) of the forty-five feet were aligned in neutral or slight valgus hindfoot alignment, and all forty-five were plantigrade. Twenty-nine (64%) of the forty-five feet had mild residual pain, and nineteen of them had pain in the lateral aspect of the ankle. Radiographically, talocalcaneal height was significantly greater for the type-III malunion group relative to the type-I and type-II malunion groups (p = 0.021).

Conclusions: This treatment protocol proved to be effective in relieving pain, reestablishing a plantigrade foot, and improving patient function. Because of the difficulty we encountered in restoring the calcaneal height and the talocalcaneal relationship in this group of patients with a symptomatic calcaneal fracture malunion, we believe that patients with a displaced intra-articular calcaneal fracture may benefit from acute operative treatment.

Level of Evidence: Therapeutic Level III. See Instructions to Authors for a complete description of levels of evidence.
neal malunions. Our hypothesis in this study was that the classification system and treatment protocol would be prognostic of overall patient outcome. The purpose of this study was to report the intermediate to long-term clinical and radiographic results of this treatment protocol for calcaneal fracture malunions.

**Materials and Methods**

**Patients**

Between 1991 and 2001, ninety-four calcaneal malunions in eighty-seven patients were managed by the senior author (R.W.S.) at our institution. All patients had been initially managed at an outside institution; twenty-four malunions in twenty-three patients had had previous attempts at operative fixation of the fracture elsewhere and were excluded. Four patients (four feet) died and twenty patients (twenty-one feet) were lost to follow-up, leaving forty-five feet (64%) with a malunion after nonoperative treatment of a calcaneal fracture in forty patients who were available for follow-up evaluation at an average of 5.3 years (range, twenty-four to 151 months). All patients had been followed for a minimum of two years. Five feet had a type-I malunion; thirty, a type-II malunion; and ten, a type-III malunion. Five patients had a bilateral malunion; one of them had a type-II and a type-III malunion, three had a type-II malunion bilaterally, and one had a type-III malunion bilaterally.

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All patients in the study group were managed according to a standard treatment protocol based on the classification system for calcaneal malunions described by Stephens and Sanders. In addition to standard radiographs, axial and coronal computerized tomography scans were made to determine the type of malunion. Type-I malunions include a large lateral wall exostosis without subtalar arthrosis or hindfoot malalignment. This exostosis can extend to the calcaneocuboid joint, locking its motion, and can also impinge on the undersurface of the fibula as well as trap or displace the peroneal tendons. Type-II malunions exhibit both a large lateral wall exostosis as well as subtalar arthrosis. Hindfoot malalignment is minimal if present at all. Type-III malunions include a large lateral wall exostosis, subtalar arthrosis, and >10° of hindfoot malalignment (typically varus).
Treatment was specific to the type of malunion. Type-I malunions had a lateral wall exostectomy and peroneal tenolysis; type-II malunions were treated with a lateral wall exostectomy, peroneal tenolysis, and subtalar bone-block arthrodesis; and type-III malunions had a lateral wall exostectomy, peroneal tenolysis, subtalar bone-block arthrodesis, and a Dwyer-type calcaneal osteotomy to correct the hindfoot malalignment.

Surgical Technique
The patient is placed in the lateral decubitus position on a beanbag, with the normal leg down and in front of the injured extremity. A thigh tourniquet is placed. After preparation and draping, the leg is exsanguinated with use of an Esmarch bandage. The tourniquet is inflated to 350 mm Hg. A standard lateral extensile approach to the calcaneus is used, and a full-thickness subperiosteal flap is raised. The vertical limb of the incision should be made just anterior to the Achilles tendon, and thus posterior to the sural nerve, allowing the nerve to be elevated with the full-thickness flap posteriorly. Care must be taken, however, to avoid violation of the nerve at the terminal portion of the horizontal limb of the incision. Three 1.6-mm Kirschner wires are placed, one in the distal part of the fibula, one in the talar neck, and the third in the cuboid, for retraction of the peroneal tendons and the subperiosteal flap.

In all three types of calcaneal malunions, the lateral wall exostosis must be resected. Attention is first directed to the lateral wall of the calcaneus, which is carefully freed of all adjacent soft tissue as far distally as the calcaneocuboid articulation. A Hohmann retractor is placed on the plantar aspect of the calcaneus, another is placed at the anterior process of the calcaneus, and a thin-bladed AO osteotomy saw (Synthes USA, Paoli, Pennsylvania) is used to perform the exostectomy. Starting posteriorly, the saw blade is angled slightly medially relative to the longitudinal axis of the calcaneus, leaving more residual bone plantarly, and thus providing decompression of the area of impingement in the subfibular region (Fig. 1). Care is taken throughout the exostectomy to avoid violation of the talofibular joint. The exostectomy is continued to the level of the calcaneocuboid joint, as the residual overhang of the lateral wall often results in an osseous block to motion of this joint. Both the overhang as well as the lateral fourth of the distal aspect of the calcaneus should be removed, as we have found that the articulation of this lateral portion with the cuboid is almost always arthritic. The exostectomy is completed distally with an osteotome, to avoid saw-blade damage to the cuboid, and the fragment is removed en bloc (Fig. 2). The excised lateral wall fragment should be maintained as a single fragment, if possible, for later use as a bone-block autograft in type-II and III malunions.

In type-II and III calcaneal malunions, attention is next directed to the subtalar joint. Whether the joint is deemed to be arthritic preoperatively (as determined by a computerized tomography scan, subtalar joint injections, or plain radiographs) or as determined by direct visualization intraoperatively, once it is diagnosed as such, a subtalar arthrodesis is undertaken. A lamina spreader is placed within the joint, and a sharp periosteal elevator or osteotome is used to débride the remaining articular surface, leaving the underlying subchondral bone intact. The inferior talar as well as the superior calcaneal osseous surfaces are prepared with a 2.5-mm drill-bit, creating multiple perforations within the subchondral bone.
for vascular ingrowth. With the lamina spreader fully expanded within the subtalar joint posteriorly, a lateral fluoroscopic image is acquired to verify how much height needs to be obtained. The talar head should align anatomically with the navicular, thus indicating restoration of the medial column, the normal angle of talar declination, and the talocalcaneal angle. Once alignment is confirmed radiographically, the dimensions of the defect can be measured with a ruler, thereby allowing the autograft bone block to be contoured to match the defect. If the joint is excessively tight medially, lamina spreaders are placed both in the sinus tarsi and the posterior facet of the subtalar joint and are sequentially spread to progressively distract the joint. A femoral distractor placed medially is not used because it is, in our experience, cumbersome and not as effective as direct intra-articular distraction. The surgeon should avoid incising the deltoid ligament from inside the subtalar joint as this will render the joint unstable, and overdistraction with the graft may result.

The previously excised lateral wall fragment is then placed within the joint as an autograft bone block (Fig. 3). This bone can be folded over on itself to obtain more height if needed, but it should fill the subtalar joint, as the height of the lateral calcaneus (and hence the graft) is usually equal to the width of the posterior facet. Additional cancellous allograft chips may be placed in the debrided sinus tarsi to assist fusion.

If a subtalar arthrodesis alone is needed (a type-II malunion), then fixation is placed at this point. With the subtalar joint held in neutral to slight valgus alignment, two terminally threaded 3.2-mm guide-pins are placed percutaneously from the posterior-planter edge of the calcaneus and advanced across the subtalar joint perpendicular to the plane of the posterior facet and into the talar dome. The guide-pins are angled in a divergent fashion into the talar dome for increased stability. Care should be taken to avoid placing a pin in the lateral aspect of the ankle joint. Fluoroscopic anteroposterior and mortise images of the ankle and an axial radiograph of the calcaneus should be made to verify correct pin placement and hindfoot alignment. A third guide-pin may be placed from the plantar margin of the anterior process of the calcaneus into the distal aspect of the talar neck and head for more stable fixation. Care should be taken to avoid violation of the talonavicular joint. Large-fragment partially-threaded (7.3 or 8.0-mm) cannulated screws are then placed in lag mode for definitive fixation (Fig. 4).

In patients with a type-III malunion, correction of axial malalignment is also necessary. Because rotation of the midfoot in the coronal plane about an anteroposterior axis (pronation-supination) will not correct a malpositioned calcaneal tuberosity healed in varus or valgus, a calcaneal osteotomy is performed prior to placement of the fixation for the subtalar arthrodesis (Fig. 5). For varus malalignment, a Dwyer lateral closing-wedge osteotomy is performed posterior to the posterior facet; a medial displacement calcaneal osteotomy with rotation is used for the patients with valgus malalignment. Once the osteotomy is completed, the guide-pins are inserted in the manner described above. In this way, both the osteotomy and the fusion can be compressed simultaneously. If bone is removed during the closing-wedge osteotomy, it can be used as graft material as well.

Once the bone work is completed, attention should be turned to the peroneal tendons. The Kirschner wires are removed, and the tendons are examined for dislocation. In many ankles with obvious preoperative tendon subluxation, removal of the exostosis allows the tendons to fall back behind the fibula, and no further treatment is needed. However, the peroneal tendon sheath should still be entered distally with a Freer elevator to evaluate sheath stenosis proximally. If stenosis is found, the sheath must be incised over a length of 2 to 3 cm along the undersurface of the subperiosteal flap so that a tenolysis can be performed. If peroneal tendon dislocation is identified, reconstruction of the superior peroneal retinaculum is performed through a small separate incision in the flap23.
At the conclusion of the procedure, a deep drain is placed exiting at the proximal tip of the vertical limb of the incision and the subperiosteal flap is closed in layered fashion. Interrupted 0-Vicryl sutures (polyglactin; Ethicon, Johnson and Johnson, Rutherford, New Jersey) are passed in the deep layers of the subperiosteal flap, angling such that the flap is advanced to the apex of the incision. The sutures are temporarily clamped until all deep sutures have been placed. Once completed, the sutures are hand-tied sequentially, starting at the proximal and distal ends and working toward the apex of the incision. The subcuticular layer is closed in a similar fashion with interrupted 2-0 Vicryl. The skin layer is closed with...
3-0 nylon suture with use of the modified Allgöwer-Donati technique, again starting at the ends and progressing toward the apex. Postoperatively, patients with type-I malunions are kept non-weight-bearing until the incision has healed, and physical therapy with early range-of-motion activities and gait training with full weight-bearing is initiated thereafter, usually by three weeks. Patients with type-II and type-III malunions are kept non-weight-bearing with the leg in a cast for twelve weeks (with cast changes every four to six weeks). This is followed by progression of weight-bearing and the initiation of physical therapy once radiographic evidence of union of the subtalar fusion mass is confirmed.

**Assessment**

Patients who were available for follow-up were assessed clinically with use of the Maryland foot score, the American Orthopaedic Foot and Ankle Society (AOFAS) ankle and hindfoot score, and the Short Form-36 (SF-36) health survey. For patients with a type-II or type-III malunion, modifications were made to the Maryland foot and AOFAS scores by eliminating the subtalar joint motion score because all patients in these groups underwent a subtalar arthrodesis; thus, the maximum achievable score was 99 for the Maryland foot scoring system and 94 for the AOFAS scoring system. Passive range of motion of the ankle, standing hindfoot align-

---

**TABLE I Postoperative Data**

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Overall Average</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>P Value</th>
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</thead>
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<td>71.4</td>
<td>79.4</td>
<td>83.1</td>
<td>0.37</td>
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<td>68.2</td>
<td>74.2</td>
<td>76.1</td>
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</tr>
<tr>
<td>Range of motion of ankle</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Dorsiflexion</td>
<td>11.7°</td>
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<td>12.1°</td>
<td>7.5°</td>
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<td>32.0°</td>
<td>30.6°</td>
<td>28.8°</td>
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<td>Radiographic measures</td>
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<tr>
<td>Lateral talocalcaneal angle</td>
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<td>30.0°</td>
<td>32.6°</td>
<td>32.0°</td>
<td>0.71</td>
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<tr>
<td>Talar declination angle</td>
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<td>13.8°</td>
<td>15.3°</td>
<td>13.5°</td>
<td>0.56</td>
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<tr>
<td>Calcaneal pitch angle</td>
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<td>16.4°</td>
<td>17.3°</td>
<td>19.4°</td>
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<tr>
<td>Talocalcaneal height (mm)</td>
<td>71.4</td>
<td>66.2</td>
<td>70.9</td>
<td>76.2</td>
<td>0.021</td>
</tr>
</tbody>
</table>

Radiographic measurements included the lateral talocalcaneal angle (A), talar declination angle (B), calcaneal pitch angle (C), and talocalcaneal height (D).
ment, the presence of residual subfibular impingement, and tenderness to palpation in the ankle and hindfoot were also assessed.

Patients were also evaluated with weight-bearing anteroposterior, lateral, and mortise radiographs of the ankle; weight-bearing anteroposterior and lateral radiographs of the foot; and axial radiographs of the calcaneus. In type-II and type-III malunions, union was defined as radiographic evidence of osseous trabeculae crossing the arthrodesis site.

Radiographic assessment also included measuring the lateral talocalcaneal angle (the angle subtended by the lines bisecting the longitudinal axes of the talus and the calcaneus), the talar declination angle (the angle formed by the intersection of perpendicular lines from the longitudinal axis of the talus and the plane of support), the calcaneal pitch angle (the angle subtended by lines bisecting the longitudinal axis of the calcaneus and the plane of support), and talocalcaneal height (the length in millimeters from the superiormost portion of the talar dome to the plantarmost portion of the calcaneal tuberosity on the weight-bearing lateral radiograph) (Fig. 6).

Patients were grouped according to the type of malunion, and the clinical and radiographic results were compared with use of one-way analysis-of-variance testing. The clinical and radiographic outcomes for the patients with a Workers’ Compensation claim and those without a Workers’ Compensation claim were also compared with use of paired t testing, where \( p < 0.05 \) was considered to represent a significant difference.

Results (Table I)

Thirty-seven (93%) of forty type-II and type-III malunions that had an arthrodesis achieved initial union; all three nonunions underwent revision arthrodesis and successfully united. Eleven (24%) of forty-five feet had delayed wound healing; only one superficial wound progressed to a deep infection. Eight of the eleven incisions with delayed wound-healing were in patients who smoked; with the numbers available, no significant correlation between smoking and delayed wound-healing was detected \((p = 0.11)\), although there was a strong trend toward significance. All three nonunions occurred in patients who smoked. Again, with the numbers available, only a trend toward significance was seen \((p = 0.25)\).

On follow-up evaluation, the overall average Maryland foot score was 79.1, while the average AOFAS ankle and hindfoot score was 73.8. The average Maryland foot and AOFAS scores were 71.4 and 68.2, respectively, for the type-I malunion group; 79.4 and 74.2 for the type-II malunion group; and 83.1 and 76.1 for the type-III malunion group. With the numbers available, no significant differences in the Maryland foot and the AOFAS ankle and hindfoot scores were detected among the three malunion groups at the 95% confidence level.

Statistical analysis also revealed no significant difference...
in the SF-36 health survey subscale scores among the three malunion groups at the 95% confidence level. Three subscale scores (general health, mental health, and mental component summary), however, exhibited trends toward significance among the three malunion types.

The average overall range of motion of the ankle was dorsiflexion to 11.7° and plantar flexion to 28.8°. The average dorsiflexion and plantar flexion of the ankle were 21.0° and 32.0°, respectively, for the type-I malunion group; 12.1° and 30.6° for the type-II malunion group; and 7.5° and 28.8° for the type-III malunion group. Statistical analysis revealed significantly greater ankle dorsiflexion in the type-I malunion group relative to the type-II and type-III malunion groups (p = 0.0014). With the numbers available, no significant difference in ankle plantar flexion was found among the three malunion groups at the 95% confidence level.

Forty-two (93%) of the forty-five feet with a malunion were aligned in neutral or neutral to slight valgus, and all were plantigrade. Twenty-nine (64%) of the forty-five feet still caused the patient mild pain; in nineteen (66%) of them, the pain was in the lateral aspect of the ankle. Of the eight feet with a malunion that required peroneal pulley reconstruction (six feet) or deepening of the fibular groove (two feet), none had recurrent instability of the peroneal tendons. Six of the eight patients returned for follow-up evaluation, and none reported residual pain along the peroneal tendons.

Radiographically, the overall average talocalcaneal angle was 32.2°, the overall average talar declination angle was 14.7°, the overall average calcaneal pitch angle was 17.6°, and the overall average talocalcaneal height was 71.4 mm. For the type-I malunion group, the average talocalcaneal angle was 30.0°, the average talar declination angle was 13.8°, the average calcaneal pitch angle was 16.4°, and the average talocalcaneal height was 66.2 mm. For the type-II malunion group, the average talocalcaneal angle was 32.6°, the average talar declination angle was 15.3°, the average calcaneal pitch angle was 17.3°, and the average talocalcaneal height was 70.9 mm. For the type-III malunion group, the average talocalcaneal angle was 32.0°, the average talar declination angle was 13.5°, the average calcaneal pitch angle was 19.4°, and the average talocalcaneal height was 76.2 mm. Statistical analysis revealed that the type-III malunion group had significantly greater talocalcaneal height relative to the type-I and type-II malunion groups (p = 0.021) (Figs. 7-A, 7-B, and 7-C). With the numbers available, no significant difference was detected at the 95% confidence level among the three malunion groups with respect to the lateral talocalcaneal angle, talar declination angle, and calcaneal pitch angle.

All but one of the nineteen patients involved in Workers’ Compensation claims returned to gainful employment at an average of nine months following surgery; however, they all required job retraining, usually to a sedentary job. Statistical analysis revealed that the patients in the Workers’ Compensation group had significantly lower outcome scores in all but one of the SF-36 subscales (p < 0.01 to 0.03) compared with those who were not involved in a Workers’ Compensation claim. With the numbers available, no significant difference was detected between the patients who had a Workers’ Compensation claim and those who did not have one with respect to the Maryland foot or AOFAS scores, ankle dorsiflexion or plantar flexion, lateral talocalcaneal angle, talar declination angle, calcaneal pitch angle, or talocalcaneal height.

Discussion

The management of displaced intra-articular calcaneal fractures remains a challenge. It appears that, on the basis of the work of many investigators, operative management by a surgeon experienced in the treatment of these fractures offers the best results. With an anatomic reduction, the patient should expect to wear normal shoes, exhibit a normal gait,
and experience a pain-free existence for an extended period of time unless posttraumatic arthritis develops. Thereafter, a straightforward in situ subtalar arthrodesis should offer lasting pain relief. Initial nonoperative management of these fractures more often than not results in an extremely painful malunion, affecting the function of the ankle, subtalar, and calcaneocuboid joints and leading to prolonged disability and difficulty wearing normal shoes.

Isbister was the first, as far as we know, to describe calcaneofibular abutment as a cause of pain in malunited calcaneal fractures. Braly et al. evaluated lateral decompression without subtalar arthrodesis as a treatment alternative for malunited calcaneal fractures. Included in their series was a subgroup of eleven patients with both a malunited calcaneal fracture and subtalar joint involvement (analogous to our type-II malunions). Using an isolated lateral calcaneal excision as an alternative to late subtalar arthrodesis, they reported satisfactory results in nine of the eleven patients at an average follow-up of twenty-eight months. Thus, the importance of adequate decompression of the subfibular impingement cannot be overemphasized.

Conversely, Carr et al. reported the results of a series of sixteen feet in thirteen patients who had undergone an isolated subtalar distraction bone-block arthrodesis through a longitudinal posterolateral incision (the Gallie incision), with use of fully threaded 6.5-mm screws in a non-lag mode. Because the operation as described was limited to a straight posterior incision, it was not possible to narrow the lateral wall, minimize fibular impingement, release the calcaneocuboid joint, or reposition subluxed or dislocated peroneal tendons. The principal goals of this approach were the restoration of talocalcaneal height and improvement in the lateral talocalcaneal angle, indicating restoration of the talocalcaneal relationship. By restoring talocalcaneal height, the long axis of the talus was made more vertical relative to the plane of support, thus relieving tibial impingement on the talar neck anteriorly and improving ankle dorsiflexion. The study was noted to be preliminary, as only eleven feet in eight patients had been followed for a minimum of one year.

In using this technique, Sanders et al., Myers and Quill, and Bednarz et al. noted problems with varus malalignment. Because only a fixed amount of joint distraction is possible with use of a medially based distractor before the deltoid ligament is maximally distracted, any further joint distraction thereafter occurs laterally, resulting in a varus deformity of the hindfoot. While it is possible to perform a calcaneal osteotomy to correct this intraoperatively, it has been our experience that the correct position of the osteotomy is difficult to ascertain and results in a zigzag deformity. Because of this concern, extreme care is taken with our technique to either limit the height of the bone block laterally to only equal the width of the medially distracted joint or to shape the graft to allow for the differential opening by narrowing the lateral width of the block if the medial side is overdistected. While this could, in theory, limit the amount of height obtained, our results (a mean talocalcaneal angle of 32°) are not significantly different from those obtained by Carr et al. (a mean talocalcaneal angle of 36°).

Our series was remarkable for the high number of successful subtalar fusions. We believe that this is specifically due to the use of titanium-alloy large-fragment (7.3 or 8.0-mm) cannulated screws placed in lag mode. There were no implant failures in this series and only three nonunions. While stainless-steel screws are acceptable, we prefer titanium implants as they exhibit a modulus of elasticity closer to that of bone, which theoretically lessens the potential of implant failure. Additionally, in the event that postoperative computerized tomography or magnetic resonance imaging scans are necessary to assess osseous alignment or arthrodesis healing, the compatibility of titanium eliminates the scatter that accompanies stainless-steel implants.

We believe that the use of fully threaded 6.5-mm stainless-steel cancellous lag screws (a core diameter of 3.2 mm) as described by Carr et al. presents several potential disadvantages in this clinical scenario. These screws are, by definition, placed in a non-lag mode; thus, limited compression forces are placed across the arthrodesis site. The smaller core diameter and screw size may be of insufficient strength to counteract the bending forces at the interfaces of the arthrodesis, which could result in implant failure and nonunion of the subtalar arthrodesis. In this instance, fractured screws within the dome of the talus are extremely difficult to remove.

We have found that if structural bone graft is placed, height will not be lost with the use of a large-fragment screw in lag mode, unless fracture of the graft occurs. We have also found that the use of 3.2-mm guide-pins is advantageous in allowing the surgeon to assess the positioning in the anteroposterior and lateral radiographs of the ankle and the axial radiograph of the calcaneus prior to final seating of these cannulated screws. Additionally, should the patient require implant removal, percutaneous extraction can be facilitated by using the guide-wire to locate the screw head.

With respect to the correction of pronation, the deformity in the overwhelming majority of calcaneal malunions is limited to the hindfoot. Our technique uses a lateral extensile incision, allowing us to address the lateral wall abnormality. This lateral wall almost invariably overhangs the cuboid anteriorly, preventing the Chopart joint from moving freely. Because we respect the lateral wall, and because we remove the lateral fourth of the anterior process of the calcaneus at the level of the calcaneocuboid joint, we not only remove the arthritic and malpositioned anterolateral corner of the calcaneus but we also free the cuboid from the osseous block caused by the malunion. As a result, we have not encountered problems with supination-pronation in our series.

Romash reported the results of a complex calcaneal osteotomy through the primary fracture line combined with a subtalar arthrodesis for the treatment of calcaneal malunion in a small series of ten patients. An Ollier incision was performed to obtain exposure of the entire sinus tarsi. The technique allowed for good correction of calcaneal height and...
narrowing of the heel, and satisfactory results were achieved in nine of the ten patients. The limitations of this technique included the inability to address the calcaneocuboid joint or peroneal tendons or to perform a secondary calcaneal osteotomy for hindfoot malalignment if needed.

The extensile lateral approach to the calcaneus was used in this study because of the limitations of both the Gallie and Ollier approaches as discussed above. Using the extensile approach, we were able to complete the removal of the lateral wall expansion along its entire length, including the overhang often seen at the calcaneocuboid joint. Excellent exposure of the peroneal tendons was also possible. In addition to allowing easy exposure and arthrodesis of the subtalar joint, this approach allowed for the inclusion of a Dwyer-type osteotomy if needed. The theoretical limitation of this approach is incomplete restoration of height in type-III malunions, but this was not an issue in our series; in fact, the feet with type-III malunion in our study had a significantly greater height restoration than did those with type-II malunion.

Concerns about wound closure with use of this technique are reasonable. However, because these deformities are corrected late, there is no acute edema of the flap and vascular compromise does not appear to be an important risk factor. Resection of the residual lateral wall expansion also effectively decompresses the flap, allowing restoration of calcaneal height without adversely affecting the ability to close the flap. In the vast majority of patients, the height restoration is not so extreme as to prevent wound closure. If this becomes an issue intraoperatively, the vertical limb of the incision could be extended proximally to allow the flap to shift and rotate downward, with the proximal wound being left open to granulate, although this was not required in any of the feet in this study. In the present series, delayed wound healing was defined as any patient in the perioperative period who exhibited residual drainage, underwent dressing changes or whirlpool treatments, or received oral antibiotics. Delayed wound-healing occurred in eleven (24%) of the forty-five feet, which is comparable with that reported by Carr et al.15 (31.2%) and Myerson and Quill19 (14.3%). Only one foot had a deep infection, and no foot needed a free tissue transfer.

Approximately two-thirds of the patients in the current study continued to have mild pain, many of whom (66%) reported pain in the lateral side of the ankle. Residual pain on the lateral side of the ankle is postulated to be a result of compensatory stresses in the ankle joint, particularly in the coronal plane of motion. With a fused subtalar joint, inversion-eversion stresses are transferred to the ankle joint, especially the lateral ligamentous structures of the ankle.15 Such pain in the type-I malunions could be the result of subtalar joint stiffness, again leading to transfer of compensatory stresses to the ankle.

In this study, clinical outcome was measured with the modified Maryland foot and AOFAS ankle and hindfoot scoring systems as well as the SF-36 health survey. Only forty of sixty-four patients returned for follow-up evaluation at an average of 5.3 years, which is indicative of a typically transient patient population. With the numbers available, we were unable to demonstrate that the treatment protocol had prognostic significance, likely because of large discrepancies in sample sizes among the three malunion types. Conversely, the ankles with a type-I malunion had significantly greater ankle dorsiflexion compared with those with a type-II or a type-III malunion. Although radiographically counterintuitive, these findings may reflect differences in the severity of the initial injury, whereby those with a type-I malunion may have sustained a relatively lower-energy injury resulting in less overall ankle and hindfoot stiffness. Although only trends were identified statistically, smoking appeared to be an important risk factor in both of the complications seen in this series: nonunion at the site of the arthrodesis and wound problems.

Finally, nonoperative treatment of a displaced intra-articular calcaneal fracture has been advocated as acceptable in order to minimize the associated operative risks, including wound complications and infection. The technical challenges associated with operative treatment of malunion, however, are such that the patient must be informed that it is a salvage operation, and it will never restore the hindfoot in the way that an acute fracture reduction can. We believe that operative treatment of acute, displaced intra-articular calcaneal fractures by experienced fracture surgeons in appropriate surgical candidates allows not only reduction of the articular joint surface and anterior process region, but it also allows a more accurate restoration of talocalcaneal height and overall hindfoot alignment. This should lead to a better overall clinical outcome and greater long-term patient benefit, even in the event that posttraumatic arthritis of the subtalar joint develops over time.

On the basis of the results of this study, this treatment protocol was found to be a reliable means of salvage for patients with malunion of a calcaneal fracture. The protocol is effective in relieving pain, reestablishing a stable plantigrade foot, and improving overall patient function. Patients may note mild persistent pain, however, particularly in the lateral side of the ankle. Patients who smoke must be counseled that cessation of smoking will decrease the risk of complications. Most patients involved in a Workers’ Compensation claim can expect to return to work following treatment, albeit at a different job. Because of the difficulty in restoring the talocalcaneal relationship following a calcaneal fracture malunion, patients with a displaced calcaneal fracture may derive better long-term results from acute operative treatment.
The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.C.01603

References


Interscalene Regional Anesthesia for Shoulder Surgery

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Background: Despite a trend toward the use of regional anesthesia for orthopaedic procedures, there has been resistance to the use of interscalene regional block for shoulder surgery because of concerns about failed blocks and potential complications.

Methods: We retrospectively reviewed the cases of 568 consecutive patients who had shoulder surgery under interscalene regional block in a tertiary-care, university-based practice with an anesthesiology residency program. The blocks were performed by a group of anesthesiologists who were dedicated to the concept of regional anesthesia in their practice. Complete anesthetic and orthopaedic records were available for 547 patients. The surgical procedure, planned type of anesthesia, occurrence of block failure, and the presence of complications were noted.

Results: Of the 547 patients, 295 underwent an arthroscopic procedure and 252 (including eighty who had an arthroplasty) underwent an open procedure. General anesthesia was the initial planned choice for sixty-nine patients because of the complexity or duration of the procedure, the anatomic location, or patient insistence. Thirty-four of the sixty-nine patients also received an interscalene regional block. Interscalene regional block alone was planned for 478 patients. A total of 462 patients (97%) had a successful block whereas sixteen required general anesthesia because the block was inadequate. The success of the block was independent of the type or length of the surgery. No patient had a seizure, pneumothorax, cardiac event, or other major complication. Twelve (2.3%) of the 512 patients who had a block had minor complications, which included sensory neuropathy in eleven patients and a complex regional pain syndrome that resolved at three months in one patient. For ten of the eleven patients, the neuropathy had resolved by six months.

Conclusions: Interscalene regional block provides effective anesthesia for most types of shoulder surgery, including arthroplasty and fracture fixation. When administered by an anesthesiologist committed to and skilled in the technique, the block has an excellent rate of success and is associated with a relatively low complication rate.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.
medical center with an anesthesiology residency program. Complete anesthetic and orthopaedic records were available for 547 patients. Intraoperative anesthetic records were obtained from the anesthesia information management system (CompuRecord; Philips, Andover, Massachusetts). All postoperative records, including physician notes on patient follow-up visits, were obtained from the senior author (E.L.F.). The surgical procedure and planned type of anesthesia, i.e., general anesthesia alone or isolated interscalene block, or both, were recorded. The exclusion criteria for interscalene regional block included coagulopathy and patient refusal. In patients for whom interscalene regional block was the planned sole anesthetic agent, any reason for conversion to general anesthesia was considered a block failure.

After an intravenous line was inserted and monitors were placed, the patients were sedated according to the individual preference of the attending anesthesiologist. The patients received ≤4 mg midazolam with or without 100 µg fentanyl. A nerve stimulator technique with use of Stimuplex needles and stimulators (B. Braun Medical, Bethlehem, Pennsylvania) was employed in all patients. After sterile preparation of the arm, the interscalene groove was identified and stimulation of ≤0.4 mA of the deltoid, triceps, or biceps muscles or forearm was accepted as evidence of the necessary proximity of the needle to the nerve. Either 40 mL of 0.5% bupivacaine or 20 mL of 0.5% bupivacaine with 20 mL of 1.5% mepivacaine, both with or without epinephrine 1:200,000, was then injected at the discretion of the anesthesiologist.

The need for intraoperative administration of propofol, fentanyl, or midazolam as well as the rate and amount of those medications were noted. Midazolam and propofol were used to provide amnesia and sedation, primarily at the request of the patient. Fentanyl was given to alleviate any pain due to the positioning. An additional field block, containing a 50:50 mixture of 1% lidocaine with epinephrine and 0.25% bupivacaine, was given to all patients receiving interscalene block alone. This was administered with a 22-gauge needle by the surgeon after the sterile preparation and draping but before the incision. It was placed in the supraclavicular region and in the axillary region to block the suprascapular nerves in all patients undergoing arthroscopy, or to provide a distal incisional block in all patients undergoing total shoulder arthroplasty, as these nerves are routinely missed by the interscalene regional block. The amount given was recorded for each patient, and the average amount given overall was calculated. All operations, with the exception of latissimus-teres major tendon transfers and scapulothoracic arthroscopies, were performed with the patient in the beach-chair position. Interscalene regional block with the patient in the lateral position, while technically possible, is not very comfortable for the patient. Not only is the traction on the involved arm painful but lying motionless for long periods on the nonanesthetized shoulder can be uncomfortable. Depending upon the body habitus of the patient and the evaluation of the airway, it is possible to administer sedation to allow the patient to tolerate the position, but, most frequently, we combine a light general anesthetic with the interscalene regional block if we use the lateral position.

Surgical and anesthesia times were recorded. Procedure length was defined as the total operative time from the incision to the skin closure. Anesthesia time included the procedure length as well as the time from the arrival of the patient in the operating room to the beginning of the procedure and then from the end of the procedure to the departure of the patient from the operating room. If the blocks were performed in the holding area, the anesthesia automatic record keeper (a computerized system that automatically enters the vital signs and the hemodynamic and ventilatory parameters into the patient’s anesthetic record rather than having them entered manually) was timed to reflect the starting time of anesthesia, as patient care was being delivered. The difference between the procedure length and the anesthesia time was then calculated and termed “nonsurgical time.” The nonsurgical time for the patients who received interscalene regional block alone and those managed with general anesthesia was compared. The preoperative and postoperative nonsurgical times were not separately analyzed.

Problems during the administration of the block were recorded on the anesthesia information management system. Acute complications included any signs of local anesthetic intoxication, blood aspiration, cardiac events, respiratory distress, pneumothorax, or hematoma. Nonacute complications were noted from the records of the postoperative anesthesia care unit and orthopaedic office records and included any postoperative evidence of motor or sensory deficits, paresthesias, dysesthesias, and any pain or pain syndrome unrelated to the site of surgery. Patients were evaluated for resolution of symptoms at two weeks, six weeks, three months, six months, and then at twelve-month intervals.

Statistical Methods
The anesthesia information management system was used to analyze data. Paired Student t tests were performed with significance defined as p < 0.05 for further data analysis.

Results
Of the 568 consecutive patients who had shoulder surgery performed by the senior surgeon, 547 had complete anesthetic and orthopaedic records. The mean age (and standard deviation) of the patients was 53 ± 18.4 years (range, eight to 100 years). The mean weight was 79 ± 19.7 kg (range, 24 to 175 kg). Two hundred and ninety-five patients (54%) had arthroscopic shoulder surgery, and 252 patients (46%), including eighty who had a total shoulder arthroplasty, had open shoulder surgery (Fig. 1). Interscalene block alone was planned for 478 patients. General anesthesia was planned as the primary anesthetic agent for sixty-nine patients because of the expected length, complexity, or location of the procedure (i.e., posterior procedures or clavicular or sternoclavicular procedures medial to the blocked area and procedures requiring harvest of iliac crest bone or tensor fascia lata for grafting) or because of pa-
Patient insistence (Fig. 2). Of the sixty-nine patients, thirty-four also received interscalene regional block prior to general anesthesia to aid in postoperative pain control. Of the 478 patients who were to have been managed with interscalene regional block alone, 462 (97%) had a successful block and sixteen (3%) had block failure requiring the conversion to general anesthesia. Overall, eighty-five patients received general anesthesia and 512 patients received an interscalene regional block.

Of the sixteen patients with a block failure, nine had an unsuccessful result because the interscalene regional block was not achieved and three had an incomplete block (see Appendix). In addition, two patients could not tolerate the block placement, and one patient could not tolerate the positioning and the length of the procedure and thus adjunctive general anesthesia was induced midway through the operation. In the remaining patient, local anesthetic tinged with blood was aspirated after injection of 20 mL of 1.5% mepivacaine. The patient exhibited no signs of central nervous system toxicity and had no signs of seizure activity during a five-minute period of observation, but the interscalene regional block was aborted and general anesthesia was induced.

Prior to the start of the surgical procedure, all 462 patients receiving interscalene regional block alone were given an additional field block averaging 7.7 mL of a mixture of 0.25% bupivacaine and 1% lidocaine with epinephrine. Of those patients, 397 received propofol at an average rate of 37.5 µg/kg/min and 455 received an average of 1.7 mg of midazolam. In addition, 319 of the 455 patients received an average of 44.5 µg of fentanyl during the procedure. For the sixty-nine patients managed with general anesthesia alone, the average
dose of midazolam was 1.83 mg and the average dose of fentanyl was 360 µg.

For the patients who received interscalene regional block alone, the average procedure length was 157 minutes, the average anesthesia length was 211 minutes, and the average nonsurgical time was fifty-four minutes. For the patients managed with general anesthesia alone, the average procedure length was 174 minutes, the average anesthesia time was 255 minutes, and the average nonsurgical time was eighty-one minutes. This difference between nonsurgical times for interscalene regional block alone and general anesthesia alone was found to be significant (p < 0.02). With the numbers available, no difference was detected between procedure lengths when patients who had general anesthesia were compared with those who had an interscalene regional block (p = 0.09).

No patient had an acute complication; however, twelve (2.3%) of the 512 patients who received an interscalene regional block had a nonacute complication (Table I). All symptoms of the nonacute complications appeared within fourteen days after the surgical procedure and were reported by the patients at the two-week postoperative follow-up visit. Eight of the twelve complications occurred in patients who had open surgical procedures, whereas four developed in patients who had arthroscopy. Therefore, the complication rate was 1.4% for those receiving an interscalene regional block for arthroscopy and 3.2% for those who had open shoulder surgery.

None of the patients had any clinical motor weakness. The most serious complication, complex regional pain syndrome, occurred in a patient who underwent a total shoulder arthroplasty to treat a chronic anterior shoulder dislocation. Exploration of the brachial plexus and isolation of the axillary nerve was required. In eleven patients, the symptoms spontaneously resolved by an average of nine weeks (range, two weeks to six months). Only one patient did not have complete resolution of the paresthesias in the ring and little fingers. The symptoms were mild enough that the patient did not want any additional investigation or treatment. One patient had transient facial numbness, which was thought to be due to the positioning of the face mask used to secure the head during the operation. There were no complications of general anesthesia.

**Discussion**

This study confirms the finding that interscalene regional block is an effective anesthetic technique for both arthroscopic and open surgical procedures of the shoulder. The rate of successful blocks was 97%, the rate of short-term complications was 2.3%, and no patient had permanent disabling neurologic sequelae or seizures. Thus, we think that the advantages of interscalene regional block far outweigh the disadvantages of the technique. We believe that the ability to have a successful regional anesthesia program requires commitment and depends upon cooperation between the surgeons and the

<table>
<thead>
<tr>
<th>Case</th>
<th>Gender, Age</th>
<th>Procedure</th>
<th>Deficit</th>
<th>Outcome</th>
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<tr>
<td>1</td>
<td>F, 30</td>
<td>Arthroscopic subacromial decompression and distal clavicle resection</td>
<td>Paresthesias of the thumb, index, and long finger</td>
<td>Resolved by 6 wk</td>
</tr>
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<td>2</td>
<td>F, 72</td>
<td>Open rotator cuff repair and acromioplasty</td>
<td>Paresthesias of the index finger</td>
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<td>3</td>
<td>M, 36</td>
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<td>4</td>
<td>F, 77</td>
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<td>Paresthesias of the ring and little finger</td>
<td>Persistent</td>
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<td>5</td>
<td>F, 45</td>
<td>Open revision posterior capsulorraphy, inferior capsular shift, and labral reconstruction</td>
<td>Paresthesias of the ring and little finger</td>
<td>Resolved by 24 wk</td>
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<td>6</td>
<td>F, 30</td>
<td>Open partial resection of scapula and open posterior capsulorraphy</td>
<td>Paresthesias of the ring and little finger</td>
<td>Resolved by 12 wk</td>
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<td>7</td>
<td>M, 48</td>
<td>Revision arthroscopic subacromial decompression and distal clavicle resection</td>
<td>Paresthesias of the ring and little finger</td>
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<td>8</td>
<td>F, 46</td>
<td>Arthroscopic subacromial decompression and distal clavicle resection</td>
<td>Paresthesias of the thumb, small, and ring finger</td>
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<td>9</td>
<td>F, 58</td>
<td>Total shoulder arthroplasty</td>
<td>Paresthesias of the thumb, index, and long finger</td>
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<td>10</td>
<td>M, 48</td>
<td>Open reduction and internal fixation of glenoid fracture</td>
<td>Paresthesias of the thumb, index, and long finger</td>
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<td>11</td>
<td>F, 60</td>
<td>Brachial plexus exploration, total shoulder arthroplasty, and Bankart repair</td>
<td>Complex regional pain syndrome</td>
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<td>12</td>
<td>M, 33</td>
<td>Arthroscopic subacromial decompression, biceps tenodesis, labral augmentation, and posterior thermal capsulorraphy</td>
<td>Postoperative neck numbness</td>
<td>Resolved by 2 wk</td>
</tr>
</tbody>
</table>
anesthesiologists. We introduce our patients to the concept of the interscalene regional block at the office of the senior surgeon during the surgical scheduling visit, when the risks and benefits of the anesthetic options are discussed. If it is presented as an advantageous method that avoids airway manipulations and postoperative nausea and vomiting and offers postoperative analgesia, there is a high degree of patient acceptance. We explain that there will be light sedation during the block placement, which will continue, as the patient desires, intraoperatively. Our anesthesiology residents receive extensive training in interscalene regional block and are supervised by a cadre of attending anesthesiologists who are committed to the use of regional anesthesia. Surgeons, too, must understand the anatomic limitations of the block and the necessity to supplement blocks, and they should not consider this cooperative effort to be a sign of block failure.

Our findings are consistent with those in multiple other studies, yet the orthopaedic literature continues to challenge the use of interscalene regional block. Many of these conflicting studies are from community hospitals rather than university-based hospitals. In particular, Weber and Jain reported on a retrospective review of 218 patients who had had shoulder surgery under interscalene regional block at a free-standing surgery center and a community hospital. They reported a block failure rate of 13% (twenty-eight patients) and a complication rate of 4% (eight patients). The complications in their study were more acute than those in our study and included four patients who had respiratory distress due to phrenic nerve injuries, one patient who had a grand mal seizure, one who had cardiovascular collapse, and two who had temporary nerve injuries that persisted at six weeks. Therefore, their reluctance to offer interscalene regional block is understandable. Although our complication rate was 2.3% (twelve of 512 patients), it consisted primarily of sensory neuropathies, which resolved by an average of nine weeks. In addition, our block failure rate was only 3% (sixteen of 478 patients).

Several studies have warned against the use of interscalene regional block because of a high complication rate. The possible complications, including cardiac arrest, grand mal seizures, high spinal blocks, hematoa, pneumothorax, phrenic nerve palsy, and respiratory distress, and the rates of occurrence of these complications have been well described. The experience of our anesthesia team may have contributed to our lower complication rate as they are dedicated to the concept of regional anesthesia and practice it on a daily basis. In addition, the anesthetic techniques they use have been continually refined to improve outcomes and reduce risks.

Of our ten patients who had postoperative paresthesias, five had symptoms on the ulnar side. These complications could possibly have been due to the use of an arm holder and/or the positioning of the limb during surgery. The ulnar nerve is anatomically derived from the lower cervical roots and is blocked by the interscalene regional block only 40% of the time. Ulnar neuropathies due to positioning are known to occur more frequently than median nerve symptoms, primarily because of the superficial path that the ulnar nerve takes near the elbow.

Conflicting results have also been reported with regard to nonsurgical operating-room times for those receiving interscalene regional block compared with those managed with general anesthesia. We found, as have several others, that these times are less for those receiving an interscalene regional block. The difference in the nonsurgical times for our patients managed with interscalene regional block and those who had general anesthesia was twenty-seven minutes. Although we did not examine recovery room times, several studies have described a shorter stay in the recovery room after interscalene regional block and our experience is that many of our patients who have an interscalene regional block do not even need this phase of the recovery process.

One limitation of this retrospective study is that the intravenous sedation, which is necessary to ensure patient comfort in the sitting position for extended periods of time, was not standardized. Other investigators have considered the need for intravenous narcotics on arrival in the recovery room to be an indication of block failure. However, the majority of these patients had both general anesthesia and an interscalene regional block. Thus, intraoperative identification of block failure was not possible. As the majority of our patients received interscalene regional block alone, block failure was immediately evident. Thus, administration of a combination of intravenous medications was performed to achieve relief of positional discomfort and any patient anxiety or restlessness. We believe that this is an adjunct to a successful block, not a solution for an unsuccessful block.

In conclusion, interscalene regional block can provide effective anesthesia for most types of shoulder surgery, including arthroplasty and fracture fixation. We showed that interscalene regional block, when administered by an anesthesiologist committed to and skilled in the technique, has a high degree of success and a low rate of complications.

Appendix

A table listing all block failures is available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).
The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.02003

References


Efficacy of Surgical Preparation Solutions in Foot and Ankle Surgery

BY ROGER V. OSTRANDER, MD, MICHAEL J. BOTTE, MD, AND MICHAEL E. BRAGE, MD

Investigation performed at the Department of Orthopaedics, University of California, San Diego, San Diego, California

Background: Previous studies have demonstrated higher infection rates following orthopaedic procedures on the foot and ankle as compared with procedures involving other areas of the body. Previous studies also have documented the difficulty of eliminating bacteria from the forefoot prior to surgery. The purpose of the present study was to evaluate the efficacy of three different surgical skin-preparation solutions in eliminating potential bacterial pathogens from the foot.

Methods: A prospective study was undertaken to evaluate 125 consecutive patients undergoing surgery of the foot and ankle. Each lower extremity was prepared with one of three randomly selected solutions: DuraPrep (0.7% iodine and 74% isopropyl alcohol), Techni-Care (3.0% chloroxylenol), or ChloraPrep (2% chlorhexidine gluconate and 70% isopropyl alcohol). After preparation, quantitative culture specimens were obtained from three locations: the hallux nailfold (the hallux site), the web spaces between the second and third and between the fourth and fifth digits (the toe site), and the anterior part of the tibia (the control site).

Results: In the Techni-Care group, bacteria grew on culture of specimens obtained from 95% of the hallux sites, 98% of the toe sites, and 35% of the control sites. In the DuraPrep group, bacteria grew on culture of specimens obtained from 65% of the hallux sites, 45% of the toe sites, and 23% of the control sites. In the ChloraPrep group, bacteria grew on culture of specimens from 30% of the hallux sites, 23% of the toe sites, and 10% of the control sites. ChloraPrep was the most effective agent for eliminating bacteria from the halluces and the toes (p < 0.0001).

Conclusions: The use of effective preoperative preparation solution is an important step in limiting surgical wound contamination and preventing infection, particularly in foot and ankle surgery. Of the three solutions tested in the present study, the combination of chlorhexidine and alcohol (ChloraPrep) was most effective for eliminating bacteria from the forefoot prior to surgery.

Level of Evidence: Therapeutic Level I. See Instructions to Authors for a complete description of levels of evidence.
consistent order throughout the study period. The preparation was performed by well-trained members of the operating-room staff who were not involved in the study. No home cleansing or disinfection protocols were utilized prior to surgery. Forty patients were included in each of the three surgical preparation groups (see Appendix). Overall, the patient population was healthy. In the DuraPrep group, four patients had rheumatoid arthritis, one patient had diabetes mellitus, one patient had renal failure, and two patients had liver disease. In the TechniCare group, two patients had rheumatoid arthritis, two patients had liver disease, and one patient had renal insufficiency. In the ChloraPrep group, two patients had rheumatoid arthritis, one patient had end-stage renal disease, and one patient had undergone a renal transplantation.

Culture specimens were obtained in an identical fashion from five additional subjects (the Pre-Prep Group) immediately before surgical preparation. This was done to quantitate the normal amount of skin bacteria present prior to treatment with an antibacterial surgical scrub.

All patients received a preoperative dose of an antibiotic (1 g of intravenously administered cefazolin) within one hour before the surgical start time. After preparation and draping were complete, quantitative culture specimens were obtained from three locations on the foot and ankle. Separate cotton-tipped applicators were used at each of the three locations to obtain the culture specimens. The first specimen was taken from the anterior part of the tibia, 12 cm proximal to the ankle joint. This site was used as the control site because we are not aware of any documented problems with regard to the elimination of skin bacteria or with regard to high rates of postoperative infection in this region. The second specimen was taken along the hallucal nail fold, which subsequently was referred to as the hallux site. The third specimen was taken from the web spaces between the second and third and between the fourth and fifth digits, which subsequently was referred to as the toe site. The swabs were placed into Amies transport media (Becton Dickinson, Franklin Lakes, New Jersey) and were sent immediately to the microbiology laboratory for quantitative aerobic and anaerobic culture.

The culture swabs were placed into 1 mL of brain-heart infusion broth and were vortexed. Next, 0.025 mL of the specimen broth was inoculated onto rabbit blood agar, colistin-nalidixic acid agar, and eosin-methylene blue agar and into thioglycolate broth (for aerobic culture) or Schaedler broth (for anaerobic culture). All culture media were supplied by Beckton Dickinson (Sparks, Maryland). The aerobic specimens were incubated in 5% carbon dioxide atmosphere at 35°C. The plates were read at twenty-four and forty-eight hours before a final report was issued. The anaerobic plates were incubated in an anaerobic chamber at 35°C. The plates were read daily, and a final report was issued at seven days. The colony count on each plate was determined and multiplied by 40 to calculate the number of colony-forming units per mL. All plates were read and counted manually by a laboratory technician who was not involved in the study. If any growth was detected, the sample was considered positive. Colony-forming units are referred to as “colonies” for simplicity. The term “bacterial isolate” is used to refer to a bacterial strain, including different strains of the same bacterial species.

The present study was reviewed and approved by our institutional review board.

**TABLE I Positive Culture Rates**

<table>
<thead>
<tr>
<th>Culture Site</th>
<th>Hallux</th>
<th>Toe</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Techni-Care</td>
<td>95%</td>
<td>98%</td>
<td>35%</td>
</tr>
<tr>
<td>DuraPrep</td>
<td>65%</td>
<td>45%</td>
<td>23%</td>
</tr>
<tr>
<td>ChloraPrep</td>
<td>30%</td>
<td>23%</td>
<td>10%</td>
</tr>
<tr>
<td>Pre-Prep</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

In Foot and Ankle Surgery
Statistical Analysis
Data were analyzed with use of two-way analysis of variance with position (control, hallux, or toe site) and treatment (ChloraPrep, DuraPrep, or Techni-Care) as grouping variables. Data were first screened for normality to justify the use of parametric statistics. As a result of the high skew, data were log-transformed, which dramatically decreased skew and kurtosis values to normal levels. Post hoc tests for comparisons between groups were performed with use of the Fisher protected least-squares-difference test.

Chi-square analysis was used to evaluate the difference in culture rates between the study groups and the different culture locations.

Results
In the Pre-Prep group, bacteria grew on culture of specimens obtained from 100% of the hallux sites, 100% of the toe sites, and 100% of the control sites. In the Techni-Care group, bacteria grew on culture of specimens obtained from 95% (thirty-eight) of the hallux sites (with eighty-three total bacterial isolates and 145,500 total colonies), 98% (thirty-nine) of the toe sites (with eighty-five total bacterial isolates and 188,360 total colonies), and 35% (fourteen) of the control sites (with twenty total bacterial isolates and 6000 total colonies) (Fig. 1, Table I). In the DuraPrep group, bacteria grew on culture of specimens obtained from 65% (twenty-six) of the hallux sites (with forty-eight total bacterial isolates and 49,400 total colonies), 45% (eighteen) of the toe sites (with twenty-seven total bacterial isolates and 27,480 total colonies), and 23% (nine) of the control sites (with eleven total bacterial isolates and 4960 total colonies). In the ChloraPrep group, bacteria grew on culture of specimens obtained from 30% (twelve) of the hallux sites (with eighteen total bacterial isolates and 10,200 total colonies), 23% (nine) of the toe sites (with thirteen total bacterial isolates and 10,880 total colonies), and 10% (four) of the control sites (with four total bacterial isolates and 160 total colonies).

The positive culture rate associated with the hallux site in the ChloraPrep group was significantly lower than that in the DuraPrep group (p < 0.01), which was significantly lower than that in the Techni-Care group (p < 0.001). The positive culture rate associated with the toe site in the ChloraPrep group was significantly lower than that in the DuraPrep group (p < 0.05), which was significantly lower than that in the Techni-Care group (p < 0.001). The positive culture rate associated with the control site in the ChloraPrep group was not significantly different from that in the DuraPrep group (p < 0.2), but it was significantly lower than that in the Techni-Care group (p < 0.01). The positive culture rate associated with the control site in the DuraPrep group was not significantly different from that in the Techni-Care group (p < 1.0).

On the average, 4544 colonies were identified per culture in the Pre-Prep group, compared with 177 in the ChloraPrep group, 682 in the DuraPrep group, and 2833 in the Techni-Care group. All three treatment preparations were significantly different from one another with regard to the mean number of colonies per culture. ChloraPrep was associated with fewer bacterial colonies than DuraPrep (p < 0.0001), which was associated with fewer colonies than Techni-Care (p < 0.0001). With the numbers available, the Techni-Care group was the only group that was not significantly different from the Pre-Prep group (p < 0.09).

On the average, 4544 colonies were identified per positive culture in the Pre-Prep group, compared with 850 in the ChloraPrep group, 1544 in the DuraPrep group, and 3736 in the Techni-Care group. With the numbers available, the mean number of colonies per positive culture in the ChloraPrep group was not significantly different from that in the DuraPrep group (p < 0.2). The ChloraPrep group had significantly fewer colonies per positive culture than did the Techni-Care group (p < 0.0003) and the Pre-Prep group (p < 0.0004). The DuraPrep group also had significantly fewer colonies per positive culture than did the Techni-Care group (p < 0.0003) and the Pre-Prep group (p < 0.002). With the numbers available, the Techni-Care group was the only group that was not significantly different from the Pre-Prep group (p < 0.4).

With regard to the presence of residual bacteria after surgical preparation, there were highly significant differences among the different culture locations. In general, more bacteria were isolated from the hallux site compared with the control site (p < 0.0001) and more bacteria were isolated from the toe site compared with the control site (p < 0.0001). However, there was no significant difference between the toe site and hallux site (p > 0.05). With regard to specific solutions, ChloraPrep was the only solution that resulted in a positive culture rate at the toe site that was not significantly different, with the numbers available, from that at the control site (p < 0.2).

Of the 360 culture specimens that were obtained, 169 were positive for at least one organism. In many cases, multiple organisms grew on culture. Many potential aerobic and anaerobic pathogens were found (Fig. 2). Overall, 206 different bacterial isolates were identified, and, of these, 145 were identified as Staphylococcus epidermidis.

A postoperative infection developed in three patients, including two (5%) of the forty patients in the Techni-Care group and one (2.5%) of the forty patients in the ChloraPrep group. There were no infections in the DuraPrep group. With the numbers available, there was no significant difference among the three groups with regard to the postoperative infection rate (p < 1.0). In the Techni-Care group, one patient had development of a polymicrobial infection after open reduction and internal fixation of a calcaneal fracture. Cultures were positive for Pseudomonas, Staphylococcus epidermidis, Enterococcus, and Enterobacter. Staphylococcus epidermidis had grown on culture of post-preparation specimens, but the other organisms had not. The second patient in the Techni-Care group had development of an atypical mycobacterium infection after excision of a Morton neuroma. We had not tested for mycobacteria on cultures of the post-preparation specimens. One patient in the ChloraPrep group had development of a polymicrobial infection after excision of a large lipoma from the lateral aspect of the heel. A portion of the large tissue flap underwent necrosis, with
subsequent development of infection. Cultures of the post-preparation specimens had been negative.

**Discussion**

The findings of the present study are in agreement with those of previous studies that have shown that it is difficult to eliminate skin flora from the forefoot. The foot provides a unique environment for the growth of numerous bacterial species. The skin surrounding the foot has many characteristics that differentiate it from other sites of the body. The lack of pilosebaceous units, the absence of apocrine sweat glands, and the wearing of occlusive footwear provide a unique habitat for microbes. In addition, the presence of the nail, hyponychium, and nailfold provides a physical barrier to cleansing. In a previous study, we found that potential bacterial wound pathogens grew on culture of specimens from 80% of halluces and 72% of toes following preparation with one of two randomly selected povidone-iodine-based antibacterial scrubs. Neither of these preparations contained alcohol. Wolf et al. studied an iodine-based scrub and paint and reported that bacteria grew on culture of specimens obtained from 98% of halluces and 83% of toes. The findings of the current study suggest that the combination of iodine and alcohol is more effective than iodine alone.

The combination of chlorhexidine and alcohol was the most effective solution tested in the present study. The efficacy of chlorhexidine has been documented in a number of other studies. In a direct comparison of chlorhexidine, povidone-iodine, and chloroxylenol, Aly and Maibach found that chlorhexidine was significantly more effective for reducing bacterial counts from the hands. With use of a dog model, Stubbs et al. found that chlorhexidine performed significantly better than chloroxylenol as a preoperative skin-preparation solution ($p < 0.0001$). Paulson evaluated five surgical hand-scrub preparations and found that the two chlorhexidine products achieved a significant reduction in microorganism counts ($p < 0.001$), with better residual effects, than either the iodine or chloroxylenol products did. The properties that make chlorhexidine effective include its strong affinity for binding to skin, its high level of antibacterial activity, and its prolonged residual effects. In addition, its rapid activity has been found to surpass that of both povidone-iodine and chloroxylenol-containing solutions.

There are numerous possibilities for further research. Different preparation techniques or solution combinations could be studied. However, one needs to consider the logistics of, and the surgeon's compliance with, the institution of more complicated protocols. Hort and DeOrio evaluated the use of a chlorhexidine home wash followed by preoperative preparation with iodine alone or iodine followed by alcohol. They found no significant difference between the two techniques. Brooks et al. reported that scrubbing of the toe clefts combined with the use of a standard preparation reduced the recolonization of bacteria in this area. Isolating the forefoot with an antibacterial-impregnated barrier may be a useful adjunct during procedures performed on the ankle, although this needs further study.

To our knowledge, this is the first study in which quantitative cultures have been used to document the efficacy of surgical scrub solutions in patients undergoing foot and ankle surgery.
surgery. On the basis of these data, we can make assumptions regarding the ability of a surgical scrub solution to limit infection, although this effect is unproven. An ideal study would directly evaluate infection rates. Given the frequency of postoperative infection, such a study would require a much larger patient population to demonstrate a significant effect. There were three postoperative infections in the present study, including two in the Techni-Care group and one in the ChloraPrep group. The infection in the ChloraPrep group and one of the two infections in the Techni-Care group occurred following surgery over the lateral aspect of the calcaneus. Both of these infections developed as the result of wound-healing problems, which are well-known complications associated with surgery in this region given the thin soft-tissue envelope and tenuous blood supply. We are not aware of any studies that have specifically evaluated the ability of a surgical scrub solution to reduce infection rates in patients undergoing foot and ankle surgery.

Another limitation of the present study is the fact that we did not obtain culture specimens from the foot of each patient prior to surgical preparation. It is possible that some individuals have a higher baseline bacterial load than others do. Culture specimens were obtained from five patients prior to surgical preparation. Cultures of specimens from all five patients demonstrated a substantial resident bacterial population.

For the purpose of the present study, we believed that using cotton-tipped swabs to sample the skin for bacterial culture, in the setting of a concomitant surgical procedure, was valid. Skin biopsy may be more accurate, but it is invasive and is associated with potential complications. Cotton-tipped swabs have been used to sample the skin on the foot and ankle in other similar studies in the literature.

Performing a second set of cultures at a later point in time might have been useful. However, selecting a consistent time-interval to repeat the cultures would have been difficult because some procedures were completed in minutes whereas others lasted two to three hours. We believe that immediate cultures are most important in the clinical setting. If the surgical preparation solution is unable to reduce the bacterial load initially, then subsequent recolonization is irrelevant. Studies evaluating the pharmacokinetics of povidone-iodine and chloroxylenol have demonstrated good activity for more than three hours. Similar research evaluating chlorhexidine has shown excellent activity for more than six hours.

All of the procedures in the present study lasted three hours or less.

In conclusion, given the higher rates of postoperative infection following foot and ankle surgery, every effort should be made to reduce the risk of infection in patients undergoing such procedures. The foot has a large resident microbial population and a unique anatomy, which make it difficult to eliminate skin bacteria preoperatively. In the present study, the combination of chlorhexidine and alcohol (ChloraPrep) was the most effective solution for eliminating potential wound contaminants from the forefoot prior to surgery.

Appendix

Tables presenting clinical data on all 120 patients are available with the electronic versions of this article, on our website at jbjs.org (go to the article citation and click on "Supplementary Material") and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

NOTE: The authors thank Richard L. Lieber, PhD, for his statistical analysis and review.

| Reference |
|--------------------------|---------------------------------|--------------------------|

doi:10.2106/JBJS.D.01977
Preoperative Skin Preparation of the Foot and Ankle: Bristles and Alcohol Are Better

By David J. Keblish, MD, David Zurakowski, PhD, Michael G. Wilson, MD, and Christopher P. Chiodo, MD

Investigation performed at the Brigham Foot and Ankle Center, Faulkner Hospital, Boston, Massachusetts

Background: The most efficient way to prepare the skin for foot and ankle surgery is unknown. In recent studies, >70% of aerobic bacterial cultures of specimens taken from the nail folds following skin preparation with povidone-iodine were positive. The goal of the current study was to determine the effect of isopropyl alcohol on the eradication of bacteria from the nails and skin of the normal foot and ankle. In addition, the effect of using a bristled brush rather than sponges to scrub the foot was investigated.

Methods: Four skin-preparation techniques were studied in two sets of twenty-five volunteers. In phase I of the study, the right foot and ankle of each member of the first set of volunteers was prepared with method 1, which consisted of a two-stage povidone-iodine scrub and paint with use of soft sponges. The left foot and ankle was prepared with method 2, which consisted of method 1 as well as an additional prewash with 70% isopropyl alcohol. In phase II, the right foot and ankle of each member of the second set of volunteers was prepared with method 3, which consisted of a povidone-iodine scrub and paint with use of a bristled brush to scrub the foot. The left side was prepared with method 4, which consisted of an alcohol scrub and paint with use of a bristled brush to scrub the foot. At the end of the preparation process, specimens for aerobic bacterial cultures were obtained from the hallucal nail fold, interdigital web spaces, and anterior aspect of the ankle. Cultures were interpreted as positive or negative, and the results were also assessed quantitatively.

Results: The rates of positive cultures of the nail-fold specimens were 76% and 80% after methods 1 and 2 (soft sponges) and 76% and 12% after methods 3 and 4 (bristled brush). The reduction in the percentage of positive cultures with method 4 was highly significant (p < 0.001). Cultures of the specimens from the web spaces showed a significant difference in the rates of positive results between methods 1 and 2 (36% and 8%, p < 0.05) but no significant difference between methods 3 and 4 (12% and 0%, p = 0.25). The rates of positive cultures of specimens from the anterior aspect of the ankle were consistently low (≤4% for all methods). Quantitative analysis of positive cultures demonstrated significant reductions (p < 0.01) in heavy growth when bristled brushes had been used, both with povidone-iodine and isopropyl alcohol.

Conclusions: The use of isopropyl alcohol and the use of a bristled brush both have beneficial effects on the skin-preparation process before foot and ankle surgery. In the current investigation, the most effective technique was the use of isopropyl alcohol in conjunction with scrubbing with a bristled brush. Merely washing the foot with alcohol-soaked sponges provided limited benefit to the web spaces only.

Level of Evidence: Therapeutic Level I. See Instructions to Authors for a complete description of levels of evidence.
Materials and Methods

Two separate sets of twenty-five healthy adult volunteers underwent simulated preoperative skin preparation of both feet and both ankles. Exclusion criteria included a history of onychomycosis, paronychia, nail deformity, diabetes, recent antibiotic use, and recent nail polish use. The investigation was approved by our institutional review board.

Skin Preparation Methods and Planned Comparisons

Four skin-preparation methods were investigated: (1) a standard povidone-iodine scrub and paint with use of soft sponges, (2) a prewash with isopropyl alcohol followed by a standard povidone-iodine scrub and paint with use of soft sponges, (3) a povidone-iodine scrub and paint with use of a bristled brush to scrub the foot, and (4) an alcohol-only scrub and paint with use of a bristled brush to scrub the foot.

The study was designed to answer three questions. First, does the use of an alcohol prewash provide additional benefit to a standard povidone-iodine skin preparation (comparison of methods 1 and 2)? Second, does the use of bristles to scrub the skin provide added benefit (comparison of methods 1 and 3)? Finally, is there any difference between the efficacy of skin preparation with povidone-iodine alone and one with alcohol alone (comparison of methods 3 and 4)?

Phase I

The goal of the first phase of the study was to investigate whether a prewash with isopropyl alcohol prior to a standard skin preparation with povidone-iodine would further reduce the amount of residual skin flora. Twenty-five volunteers were enrolled in this phase of the study. A two-stage povidone-iodine skin preparation of the right foot and ankle was performed on each volunteer. First, the skin was scrubbed for five minutes with a diluted povidone-iodine solution (Triad 10% povidone-iodine; Triad Disposables, Brookfield, Wisconsin). After being wiped clean with a sterile towel, the skin was painted with nondiluted povidone-iodine solution. The scrub and paint solutions were applied with foam sponges and paint sticks supplied in the commercial surgical skin-preparation kit (Medline Industries, Mundelein, Illinois) used at our institution. The web spaces were “flossed” in a manner similar to that described by Brooks et al. This constituted method 1 in our study.

The identical process was then performed on the left foot and ankle of each volunteer, with the addition of a three-minute prewash with 70% isopropyl alcohol (McKesson General Medical, Richmond, Virginia). The alcohol was applied with sterile gauze, and the web spaces were again flossed. The foot and ankle were allowed to dry before the povidone-iodine component of the process was started. The combined alcohol prewash and povidone-iodine skin preparation constituted method 2.

One investigator performed all of the skin preparations. All solutions were allowed to dry at each step of the process. Subsequently, a second investigator used swabs to obtain three specimens for aerobic culture, one from the medial hallucal nail fold, one from the interdigital web spaces (with a single swab), and one from the anterior aspect of the ankle of both lower extremities of each volunteer. The swabs were immediately plated on blood agar Petri dishes and incubated at 35°C to 37°C. The second investigator was blinded with regard to which extremity had undergone the alcohol prewash.

After forty-eight hours, all cultures were inspected for bacterial growth. The presence of one or more colony-forming units (CFUs) on the agar streak line was considered to indicate a positive culture. All negative plates were re-evaluated after an additional twenty-four hours of incubation before being discarded. Cultures were first designated as either positive or negative. Positive results were then further interpreted quantitatively by counting the number of CFUs on each plate. As observed during pilot sampling, bacterial growth occurred in one of two distinct patterns. There was either an agar streak with a few sparse colonies (<20 CFUs) or a streak line covered with CFUs that were too numerous to count. Bacterial load was considered to be light if <20 CFUs were present and heavy if there were ≥20 CFUs. Gram staining and coagulase testing were used to analyze the positive cultures.

Phase II

The purpose of the second phase of the study was to investigate whether the mechanical nature of the device used to scrub the foot would affect the efficacy of the skin preparation process. Additionally, the efficacy of an alcohol-only preparation was examined.

A second set of twenty-five volunteers was enrolled in this phase of the study. A two-stage povidone-iodine skin preparation as described above was performed on the right foot and ankle of each volunteer. However, instead of using a sponge to scrub the foot, the investigator used a sterile disposable surgical scrub brush with plastic bristles on one side and a foam sponge on the other side (Becton, Dickinson, Franklin Lakes, New Jersey). The foam portion of the brush was saturated with povidone-iodine solution at the outset to allow a generous application to all skin surfaces. The bristled side was used to scrub the entire foot and ankle, including the nails and web spaces, and the foam side was used to floss between the toes. This constituted method 3 of our investigation.

Subsequently, the left foot and ankle of each volunteer were prepared as described above with use of a bristled brush and alcohol only. This constituted method 4 of the investigation.

As in phase I, the skin preparation was performed by one investigator and all preparation solutions were allowed to dry at each step of the preparation process. Specimens for cultures were again obtained from the hallucal nail fold, interdigital web spaces, and anterior aspect of the ankle. Incubation and interpretation of the cultures were performed in the same fashion as in phase I.

The rationale for using only alcohol in method 4 of the investigation was as follows. In phase I, “horizontal” comparisons between methods 1 and 2 (povidone-iodine alone and povidone-iodine with an alcohol prewash, respectively) allowed the effect of the alcohol prewash to be isolated and
In phase I, two variables, scrubbing with a bristled brush and use of an alcohol-only preparation, were introduced. The use of “vertical” comparisons between phases I and II allowed two questions to be simultaneously investigated. First, through comparison of methods 1 and 3, the effect of scrubbing with a bristled brush on the results of the standard povidone-iodine skin-preparation process could be isolated and quantified. Second, with the presumption that the use of a bristled brush could have an effect on reducing skin bacteria, it was possible to make a comparison between skin preparation with a bristled scrub brush and povidone-iodine (method 3) and skin preparation with a bristled scrub brush and alcohol only (method 4).

**Statistical Analysis**
A power analysis (nQuery Advisor, version 5.0; Statistical Solutions, Boston, Massachusetts) indicated that a sample size of twenty-five patients in each group (a total of fifty patients in the study) would provide 80% power to detect a significant difference, between methods and groups, with regard to the percentages of positive cultures of specimens from the nail folds, web spaces, and anterior aspects of the ankles. Comparisons within phase I and within phase II were analyzed with the nonparametric McNemar test for related samples. The efficacy of scrubbing with a bristled brush was assessed by using a Fisher exact test for binary proportions to compare phases I and II. With use of heavy growth on culture as a primary outcome measure, logistic regression was applied to determine the estimated odds of heavy growth as a result of using or not using bristles. The 95% confidence interval was constructed around the odds ratio with use of the exact likelihood method. Two-tailed values of p < 0.05 were considered to be significant. The SPSS statistical package (version 12.0; SPSS, Chicago, Illinois) was used for data analysis.

**Results**
The rates of positive cultures (nonquantitative data) for all three swabbed sites are summarized in Table 1 and reported below. Comparisons between groups are shown in Figure 1.

**Hallucal Nail Folds**
In phase I, cultures were positive for 76% and 80% of the nail-fold samples after methods 1 and 2, respectively. This difference was not significant (p = 0.99). In phase II, cultures were positive for 76% and 12% of the nail-fold samples after methods 3 and 4, respectively. This difference was highly significant (p < 0.001). There was no significant difference between methods 1 and 3 with regard to the rates of positive cultures from the nail folds. However, the rate of positive cultures after method 2 (80%) was significantly higher (p < 0.001) than that after method 4 (12%).

**Web Spaces**
In phase I, the rate of positive cultures after method 1 (36%) was significantly higher (p < 0.05) than that after method 2 (8%). In phase II, there was no significant difference in the rates between methods 3 and 4 (12% and 0%, respectively, p = 0.25). Comparison of the rates of positive cultures of the web-space specimens between methods 1 and 3 showed a reduction from 36% to 12%, although this trend was not significant (p = 0.09).

**Anterior Aspect of the Ankle**
In phase I, none of the twenty-five volunteers had a positive culture after either skin-preparation method. In phase II, there was a single positive culture, after method 4, but the rate after that method was not significantly different from the rates after the other methods (p = 0.99).

**Quantitative Analysis**
Quantitative analysis of the positive cultures revealed significant reductions in the number of colony-forming units in the cultures of the nail-fold specimens after a bristled brush had been used. The rate of heavy growth (>20 CFUs) in cultures of nail-fold specimens obtained after method 3 (povidone-iodine preparation with scrubbing with a bristled brush) was significantly lower than that in cultures of nail-fold specimens obtained after method 1 (povidone-iodine preparation without use of a bristled brush) (28% compared with 72%, p < 0.01; Table II). In addition, logistic regression analysis indicated that the odds of heavy growth after use of povidone-iodine without scrubbing with a bristled brush were more than six times higher than that after use of the solution in conjunction with scrubbing with a bristled brush (odds ratio = 6.6, 95% confidence interval =

### Table 1: Rates of Positive Cultures

<table>
<thead>
<tr>
<th>Skin Preparation Method (N = 25 Each)</th>
<th>% (No.) of Positive Cultures*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nail Fold</td>
</tr>
<tr>
<td>Povidone-iodine without scrubbing with bristled brush</td>
<td>76 (19)</td>
</tr>
<tr>
<td>Povidone-iodine without scrubbing with bristled brush and with alcohol prewash</td>
<td>80 (20)</td>
</tr>
<tr>
<td>Povidone-iodine with scrubbing with bristled brush</td>
<td>76 (19)</td>
</tr>
<tr>
<td>Alcohol only with scrubbing with bristled brush</td>
<td>12 (3)†</td>
</tr>
</tbody>
</table>

*The data represent the presence of any growth (light or heavy). †The value represents a significant reduction (p < 0.05).
TABLE II Rates of Heavy Bacterial Growth

<table>
<thead>
<tr>
<th>Skin Preparation Method (N = 25 Each)</th>
<th>% (No.) of Cultures with Heavy Growth*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Nail Fold</td>
</tr>
<tr>
<td>Povidone-iodine without scrubbing with bristled brush</td>
<td>72 (18)</td>
</tr>
<tr>
<td>Povidone-iodine without scrubbing with bristled brush and with alcohol prewash</td>
<td>72 (18)</td>
</tr>
<tr>
<td>Povidone-iodine with scrubbing with bristled brush</td>
<td>28 (7)†</td>
</tr>
<tr>
<td>Alcohol only with scrubbing with bristled brush</td>
<td>4 (1)†</td>
</tr>
</tbody>
</table>

*Heavy growth was considered to be >20 CFUs. †The reductions in heavy growth in cultures of the nail-fold specimens following preparation with the methods that included scrubbing with a bristled brush were significant compared with the values following the methods without scrubbing with a bristled brush (p < 0.01).

2.0 to 22.1, p < 0.01). This implies, by reciprocating the odds ratio, that the use of the bristled brush decreases the risk of heavy bacterial growth by an estimated 85% (95% confidence interval = 50% to 95%).

Similarly, the rate of heavy growth in the cultures of the nail-fold specimens obtained after a standard povidone-iodine preparation with a brushless alcohol prewash (method 2) was significantly higher than that after the alcohol-only preparation combined with scrubbing with the bristled brush (method 4) (72% compared with 4%, p < 0.001). On the basis of the results of logistic regression, the odds of heavy bacterial growth following skin preparation with method 2 were estimated to be nearly thirty times higher than that following method 4 (odds ratio = 29.6, 95% confidence interval = 5.5 to 160, p < 0.001). This implies that the use of bristles cuts the risk of heavy bacterial growth by an estimated 97% and anywhere from 82% to 99%.

Finally, 80% (forty) of the fifty positive cultures in phase I (no bristles) showed heavy growth compared with only 35% (nine) of the twenty-six positive cultures in phase II (bristles). This difference was highly significant according to the Fisher exact test (p < 0.001). The estimated odds that a positive

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**Figure 1. Effect of Skin Preparation Method on Positive Cultures**

Histogram comparing rates of positive cultures according to the method of skin preparation and the site from which the specimen was obtained. The reduction in the rate of positive cultures of nail-fold specimens after preparation with a bristled brush and alcohol only was highly significant (p < 0.001). The reduction in the rate of positive cultures of web-space specimens after preparation with povidone-iodine and an alcohol prewash was also significant (p < 0.05) when compared with the rate following preparation with povidone-iodine alone.
culture would show heavy growth was seven times higher in phase I than in phase II (odds ratio = 7.6, 95% confidence interval = 2.6 to 21.9).

Bacterial Analysis

Bacterial analysis was limited to the presence or absence of growth, the volume of colonies per plate, and minimal identification of species. Coagulase-negative staphylococcal species were the most common bacteria grown on culture after all of the methods (seventy of the seventy-six positive cultures contained coagulase-negative Staphylococcus), followed by Bacillus species (eight of the positive cultures), and Staphylococcus aureus (six of the positive cultures). More than one bacterial species were identified in seven positive cultures, only Bacillus species grew in three cultures, and only Staphylococcus aureus grew in three cultures.

Discussion

Eradicating bacteria from the skin and nails prior to foot and ankle surgery is particularly challenging. Ostrander et al. examined fifty consecutive patients who had undergone either a single-stage or a two-stage povidone-iodine skin preparation. They found that the nail fold remained heavily contaminated, with a 76% rate of positive cultures after the single-stage preparations and an 80% rate after the two-stage preparations. The rates of positive cultures after the two methods were 68% and 76%, respectively, for specimens from the web spaces and 16% and 28%, respectively, for those from the anterior aspect of the ankle. None of the reported differences were significant. Similarly, Zacharias et al. reported a 75% rate of positive cultures of specimens from the web spaces following skin preparation with povidone-iodine solution.

Hort and DeOrio investigated whether a prewash with isopropyl alcohol added any benefit to a povidone-iodine skin preparation. They found that 35% of cultures of specimens from the nail beds were positive after the povidone-iodine preparation and 57% were positive in the group that had the supplemental alcohol wash. While this difference was not significant, the authors speculated that the increased prevalence of positive cultures in the group that had received the alcohol prewash may have been a result of the defatting action of the alcohol and its damage to mucosal cells, which in turn may have resulted in the liberation of bacteria that were then capable of growing on culture.

The current investigation differs from the above studies for several reasons. First, we examined the efficacy of an alcohol-only preparation. In addition, we investigated the effect of a more mechanical preparation involving use of a bristled brush. Finally, we performed quantitative analysis of positive bacterial cultures, which, to our knowledge, has never been done previously in a study of preoperative skin preparation of the foot and ankle. Culture results have been reported as positive or negative only, and that is an important consideration when interpreting the data from those studies. It is extremely difficult, if not theoretically impossible, to completely eradicate all bacteria from the skin and nails of the feet without injuring soft tissues. Thus, differences between skin-preparation techniques may not be detected unless quantitative culture analysis is performed.

The results of the cultures performed after all four preparation techniques investigated in our study confirmed that the nail fold is the most heavily contaminated anatomic location of the foot and ankle. The 76% rate of positive cultures of specimens from the hallucal nail fold following our two-stage preparation with povidone-iodine (method 1) was similar to that reported by others. The addition of an alcohol prewash had no significant effect on this rate, even when the cultures were analyzed quantitatively. However, when the alcohol was applied with a bristled brush (method 4), it reduced the rate of positive cultures of the hallucal nail-fold specimens to 12%. We did find a beneficial effect of using an alcohol prewash in the web spaces, where the rate of bacterial colonization was significantly reduced from 36% after method 1 to 8% after method 2 (p < 0.05). When analyzed quantitatively, the rate of heavy bacterial growth in the cultures of the web-space specimens was found to be reduced from 12% to 4%, although this trend was not significant.

The use of isopropyl alcohol as a skin preparation agent has both advantages and disadvantages. As a bactericidal agent, it is extremely effective. It interferes with cellular metabolism and causes cell lysis through its ability to denature proteins. Furthermore, its cost is low, it is widely available, and it has a rapid onset of action. Alcohol also has a broad spectrum of action: it is effective against bacterial, fungal, and viral organisms (including vancomycin-resistant Entercoccus, Mycobacterium tuberculosis, hepatitis-B virus, herpes simplex virus, and human immunodeficiency virus) and . We also speculate that an additional advantage of alcohol is its low surface tension (21.79 dyn/cm). This may allow it to penetrate the irregular contours of the dermis and epidermis more efficiently.

The most often cited disadvantage of isopropyl alcohol is its flammability and . However, most operating room fires occur around the airway, head, and face, where the three components of the “fire triangle”—heat, fuel, and oxygen—may coexist. The risk of fire during foot and ankle surgery can be further diminished by avoiding pooling of the alcohol beneath the drapes and by allowing the alcohol to dry before beginning the procedure (and especially before using electrocautery). A second disadvantage of alcohol is that it is both clear and colorless. It should therefore be applied methodically to avoid missing any regions of skin.

With the exception of Brooks et al., authors who have previously investigated the optimal preoperative preparation of the foot and ankle have focused on the effect of changing the bactericidal solution. In the current study, we sought to determine whether there was any benefit to modifying the mechanical nature of the scrub portion of the skin preparation process. Brooks et al. demonstrated that additional scrubbing between the toes with a gauze swab soaked in antibiotic significantly (p = 0.048) reduced bacterial recoloniza-
tion by the end of surgery. The use of bristles has previously been shown to enhance bacterial kill on the hands.14

Bacteria reside in the desquamating, cornified layers of the superficial epithelium of the skin as well as in the glandular ducts and depths of the hair follicles.15 When topically applied in a nonmechanical fashion, disinfectants may not be able to penetrate these areas. We therefore speculate that scrubbing with a bristled brush aids in exfoliation and introduces the disinfectant to the deeper contours of the skin, improving bacterial kill. Ironically, while most surgeons continue to scrub their own hands with a bristled brush, preoperative scrubbing of a patient’s foot with a bristled brush is not a widespread clinical practice.1-5

In phase II of our study, we compared the effect of bristled brushes with that of soft sponges for scrubbing the foot. Our quantitative results revealed the most dramatic differences when a bristled brush had been used, both in conjunction with povidone-iodine and in conjunction with isopropyl alcohol. When we reviewed the combined data pertaining to all three sites from which culture specimens had been obtained following preparation with povidone-iodine, we found an overall reduction in the rate of cultures with heavy bacterial growth from 84% when method 1 (povidone-iodine without scrubbing with a bristled brush) had been used to 28% when method 3 (povidone-iodine with scrubbing with a bristled brush) had been used (p < 0.001). The rate of cultures with heavy growth in the cultures of the nail-fold specimens was reduced from 72% to 28% (p < 0.01) (Fig. 2). The rate of heavy growth in the cultures of the web-space specimens was reduced from 12% to 0%, although this trend was not significant. Similarly, comparison of the combined data (for all three sites) pertaining to method 2 (alcohol prewash without scrubbing with a bristled brush) with the combined data pertaining to method 4 (alcohol only with scrubbing with a bristled brush) showed the rate of cultures with heavy growth to be reduced from 76% to 8% (p < 0.001). The rate of cultures of the nail-fold specimens that had heavy growth was reduced from 72% to 4% (p < 0.001) (Fig. 2).

Perhaps the most dramatic finding in this study was the marked reduction in the rate of positive cultures of nail-fold specimens to 12% after the use of method 4 (alcohol only and scrubbing with a bristled brush). This result was highly significant when compared both with the rate after method 3 (76%) and that after method 2 (80%) (p < 0.001). We believe that this reflects the combined advantages of alcohol and scrubbing with a bristled brush. When interpreted in light of the fact that use of alcohol and a bristled brush had no effect on cultures of the specimens from the anterior aspect of the ankle, it would appear that the utility of alcohol and scrubbing with a bristled brush are inversely proportional to the accessibility of the surgical preparation site.

The current investigation demonstrated that both mechanical and chemical factors affect the efficacy of skin preparation before foot and ankle surgery. We acknowledge that we examined the rate of positive cultures following simulated skin preparation processes. Whether the differences detected in our study will have an effect on the actual prevalence of infection will require a larger, prospective clinical investigation.
Nevertheless, we agree with previous authors\textsuperscript{2,3} who have recommended that the toes be covered whenever possible during foot and ankle surgery. We strongly recommend that alcohol and scrubbing with a bristled brush be incorporated into the skin preparation process before forefoot surgery.

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The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.02695

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LONG THORACIC NERVE: ANATOMY AND FUNCTIONAL ASSESSMENT

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Background: The anatomy and function of the long thoracic nerve are not fully understood. The purposes of this study were to clarify the anatomy of the long thoracic nerve and to propose a clinical test to assess the function of the upper division of the long thoracic nerve.

Methods: The long thoracic nerve and the serratus anterior muscle were studied in fifteen fresh cadavera. Six patients had an operation to treat a brachial plexus injury, and the long thoracic nerve was electrically stimulated. The resulting shoulder motion was then observed.

Results: The long thoracic nerve was formed by branches arising from the C5, C6, and C7 nerve roots. The C5 and C6 branches joined beneath the scalenus medius muscle to form the upper division of the long thoracic nerve, which was located 1 cm posteriorly and superiorly to the upper trunk origin. The union of the upper division with the branch from C7 occurred caudally, in the axillary region. Two branches from the upper division of the long thoracic nerve to the upper portion of the serratus anterior muscle were consistently identified. After electrical stimulation of the upper division branches, shoulder protraction was observed.

Conclusions and Clinical Relevance: In the supraclavicular region, the long thoracic nerve has a trajectory parallel to the brachial plexus, which is contrary to the schematic representation in most textbooks. The upper division of the long thoracic nerve can be assessed by the shoulder protraction test.

Materials and Methods

Anatomic Studies: Fifteen fresh cadavera were used. The serratus anterior muscle was dissected, the portions were separated, and their origins and insertions were investigated. The brachial plexus was dissected, and the long thoracic nerve origin trajectory and branches were studied. The long thoracic nerve diameter was measured in digitized photographs with use of the ImageJ 1.32j software (United States National Institutes of Health).

Clinical Studies: Six patients with C5 and C6 brachial plexus injuries, who had a mean age of twenty-four years (range, twenty-one to twenty-eight years), had an operation at an average of four months (range, two to six months) after the injury. The upper division of the long thoracic nerve and its branches were dissected from caudad to cephalad up to the C5 and C6 nerve roots. The upper division of the long thoracic nerve and its branches to the upper portion of the serratus anterior muscle were then each electrically stimulated, and the result-
ing movement was observed. To prevent stimulus diffusion to the distal part of the brachial plexus, each branch of the upper portion of the serratus anterior muscle was dissected from the origin to the muscle entrance. After dissection, the branches were suspended by silicon loops to avoid electrical stimulus dispersion on the surrounding muscles, and a low-intensity electrical stimulus was applied close to the nerve-muscle junction. On three occasions, the branch stemming from C7 (i.e., the lower division of the long thoracic nerve) was dissected and stimulated, and the elicited shoulder motion was observed.

The surgical protocol of retrograde dissection of the long thoracic nerve and electrical stimulation of the emerging branches has been used by us in a previous study. The approach allows the surgeon, in difficult situations, to locate the upper roots of the brachial plexus and begin the dissection in healthy tissues. The brachial plexus is approached from its posterior aspect, and major vessels are avoided. Moreover, when the electrical stimulation of the branches from the long thoracic nerve elicits muscle contraction, the pertinent roots are likely to be in continuity with the cord and suitable for grafting.

The surgical protocol of the current study was approved by the local ethics committee, and informed consent was obtained from each of the patients.

**Results**

**Anatomical Findings**

**Serratus Anterior Muscle**

On the basis of the muscle fiber origin, direction, and insertion, the serratus anterior muscle was divided into three major portions (Fig. 1). These portions were separated from each other by connective tissue. The upper portion was cylindrical in shape, originated from the first and second ribs, and, after a slight ascending trajectory, inserted into the superior medial border of the scapula. The intermediate portion was very thin and originated from the lateral and anterior aspects of the second, third, and fourth ribs. Its muscle fibers presented a divergent trajectory, having a final transverse arrangement to insert on the medial border of the scapula. The lower portion was the largest and the longest one, originating from the third to the eighth rib. The muscle fibers formed a convergent trajectory to the lower scapular angle.

**Long Thoracic Nerve**

One branch from the C5 nerve root and another from the C6 nerve root united behind the scalenus medius muscle to form the upper division of the long thoracic nerve (Fig. 2), which emerged from the scalenus medius about 1 cm posteriorly and superiorly to the upper trunk origin. At this point, two branches to the upper portion of the serratus anterior muscle.

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**Fig. 1**

Anatomic and schematic representation of the serratus anterior muscle, showing the long thoracic nerve (Lt) and the nerve branches to the lower serratus digitations (Sb) and the upper portion (U), intermediate portion (I), and lower portion (L) of the serratus anterior muscle. The lower portion is the largest portion followed by the upper portion.
were consistently identified. In ten dissections, a third, smaller branch was noted. Additional branches to the upper portion of the serratus anterior muscle arising directly from the C5 nerve root (four dissections) or from the C5 contribution to the long thoracic nerve (four dissections) were identified in eight dissections (Fig. 3). In a single dissection, a branch from the C4 nerve root joined the C5 branch to the upper division of the long thoracic nerve. The average diameter of the upper division of the long thoracic nerve was 1.5 mm (range, 1.2 to 1.8 mm). At the root of the axilla, on the surface of the upper portion of the serratus anterior muscle, a branch originating from the C7 nerve root, which ultimately comprises the lower division of the long thoracic nerve, joined the upper division (Fig. 4). This branch ran over the scalenus medius muscle. After the union of the upper and lower divisions, one or two additional branches to the upper portion and a single branch to the intermediate portion of the serratus anterior muscle were noted. From the second to the fifth rib, no other branch originated from the long thoracic nerve. The five lower digitations of the serratus anterior muscle each received a separate nerve branch (Fig. 1).

Surgical Findings
In all six patients, the C5 and C6 nerve roots were ruptured extraforaminally and the C7 nerve root was preserved. When the upper division of the long thoracic nerve was stimulated electrically, the shoulder moved anteriorly. Shoulder protraction was also noted after stimulation of each branch of the upper division of the long thoracic nerve to the upper portion of the serratus anterior muscle. Upon stimulation of the lower division of the long thoracic nerve (i.e., the branch stemming
from C7), muscle contraction on the lateral thoracic wall was demonstrated but shoulder protraction did not occur.

Shoulder Protraction Test
Shoulder girdle or scapular forward motion around the chest wall is defined as shoulder girdle or scapular protraction. On the basis of the anatomical findings and the observations on direct electrical stimulation during surgery, a test was designed to investigate the integrity of the upper division of the long thoracic nerve. In the supine position, the patient is asked to move the shoulder forward (i.e., protraction), separating it from the bed. Next, the examiner’s hand is placed...
over the anterior region of the shoulder and active shoulder forward motion is resisted (Fig. 5).

Discussion

We demonstrated that the long thoracic nerve is formed by an upper portion stemming from the C5 and C6 nerve roots and a lower portion stemming from the C7 nerve root. The union of these portions occurs in the axilla. In the supraclavicular region, the upper division of the long thoracic nerve runs parallel to the brachial plexus close to the suprascapular nerve. Electrical stimulation of the upper division of the long thoracic nerve and its branches produces shoulder protraction. Therefore, the upper division of the long thoracic nerve is tested by asking the patient to perform forward shoulder motion (i.e., the shoulder protraction test).

Our anatomical findings are in agreement with those of Hovelacque. In one of fifteen dissections, we demonstrated a branch from the C4 nerve root; however, we could not identify a branch from the C8 nerve root to the long thoracic nerve. This is probably because of our limited series. Horwitz and Tocantins, in a study of 100 dissections, found branches to the long thoracic nerve arising from C4 or C8 in eight dissections. They also found that the branch originating from C7 was absent in eight dissections. However, Herrinhan, quoted by Hovelacque, found the C7 contribution to be absent in only one of fifty-five cases. Herrinhan, after intraneural dissection, observed that the upper serratus fibers were innervated by C5; the intermediate fibers, by C5 and C6; and the lower fibers, by C7. All of the above-mentioned authors described the upper division of the long thoracic nerve as running close to the suprascapular nerve just as we found in the present study. This is not in agreement with the current textbook descriptions of the long thoracic nerve, in which the nerve is represented as being formed around the lateral border of the scalenus anterior muscle and descending perpendicularly to the brachial plexus trunks.

The present anatomical studies separated three portions of the serratus anterior muscle, which is in conformity with observations in previous reports. Our anatomical and surgical findings indicated that the upper portion is responsible for scapular protraction, and the lower portion, with its fan shape, is the most important for scapular stabilization. In contrast to our findings, Gregg et al. believed that the upper portion is responsible for scapular rotation (i.e., the glenoid cavity is rotated superiorly), whereas the middle portion is involved in scapular protraction. In this regard, when the long thoracic nerve is injured in the axilla, the lower portion of the serratus anterior is denervated and scapular winging is observed. Therefore, the upper portion does not provide scapular stabilization. On the other hand, when the lower portion is partially removed, as in a free serratus transfer, scapular stability is preserved. It is possible that only two or three lower serratus digitations are needed to provide scapular stabilization. Additional studies including electromyographic evaluation during active motion would be helpful to clarify further the function of the different portions of the serratus anterior muscle.

In a brachial plexus traction injury, the lesions are located either in the supraclavicular region (i.e., an extraforaminal root rupture) or at the spinal cord (i.e., a root avulsion). The functional preservation of muscles innervated by branches coming directly from the roots, such as the long thoracic nerve, is highly suggestive of extraforaminal root rupture. With a complete brachial plexus palsy, the classical maneuver to elicit scapular winging and to test the long thoracic nerve function is not feasible. The shoulder protraction test is more appropriate to assess such injuries. The serratus anterior muscle has been consistently reported to be responsible for scapular protraction. Other muscles, such as the pectoralis major and minor, participate to a lesser extent in shoulder protraction. In fact, controversy continues. Some authors have stated that the pectoralis minor, but not the pectoralis major, acts in scapular protraction in conjunction with the serratus anterior muscle. Others have believed that the pectoralis minor is an antagonist of the serratus anterior muscle. Of importance is the fact that, in complete brachial plexus injuries, these muscles are denervated and do not contribute to shoulder protraction. Conversely, the function of the trapezius and levator scapulae muscles is preserved in brachial plexus lesions, but inactivity during protraction has been demonstrated electromyographically.

In conclusion, in total brachial plexus palsy, preservation of shoulder protraction should be considered an indication of an extraforaminal rupture of the C5 nerve root.

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Results of Unicompartmental Knee Arthroplasty at a Minimum of Ten Years of Follow-up

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Background: There is a renewed interest in unicompartmental knee arthroplasty. The present report describes the minimum ten-year results associated with a unicompartmental knee arthroplasty design that is in current use.

Methods: Sixty-two consecutive unicompartmental knee arthroplasties that were performed with cemented modular Miller-Galante implants in fifty-one patients were studied prospectively both clinically and radiographically. All patients had isolated unicompartmental disease without patellofemoral symptoms. No patient was lost to follow-up. Thirteen patients (thirteen knees) died after less than ten years of follow-up, leaving thirty-eight patients (forty-nine knees) with a minimum of ten years of follow-up. The average duration of follow-up was twelve years.

Results: The mean Hospital for Special Surgery knee score improved from 55 points preoperatively to 92 points at the time of the final follow-up. Thirty-nine knees (80%) had an excellent result, six (12%) had a good result, and four (8%) had a fair result. At the time of the final follow-up, thirty-nine knees (80%) had flexion to at least 120°. Two patients (two knees) with well-fixed components underwent revision to total knee arthroplasty, at seven and eleven years, because of progression of patellofemoral arthritis. At the time of the final follow-up, no component was loose radiographically and there was no evidence of periprosthetic osteolysis. Radiographic evidence of progressive loss of joint space was observed in the opposite compartment of nine knees (18%) and in the patellofemoral space of seven knees (14%). Kaplan-Meier analysis revealed a survival rate of 98.0% ± 2.0% at ten years and of 95.7% ± 4.3% at thirteen years, with revision or radiographic loosening as the end point. The survival rate was 100% at thirteen years with aseptic loosening as the end point.

Conclusions: After a minimum duration of follow-up of ten years, this cemented modular unicompartmental knee design was associated with excellent clinical and radiographic results. Although the ten-year survival rate was excellent, radiographic signs of progression of osteoarthritis in the other compartments continued at a slow rate. With appropriate indications and technique, this unicompartmental knee design can yield excellent results into the beginning of the second decade of use.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.
In contrast, in 2000 and 2001, 33,900 unicompartmental knee arthroplasties were performed, comprising 6% of all knee arthroplasties performed\textsuperscript{17}.

The present report describes the ten to thirteen-year results associated with a unicompartmental knee system that is in current use.

**Materials and Methods**

Between June 1987 and June 1993, the senior authors (J.O.G., M.B.S., and A.G.R.) performed 517 knee arthroplasties, of which sixty-two (12%) were unicompartmental knee arthroplasties. All procedures were performed through a standard medial parapatellar approach that included patellar eversion.

Patients were deemed to be candidates for unicompartmental knee arthroplasty rather than total knee replacement on the basis of the criteria of Kozinn and Scott\textsuperscript{16}: a diagnosis of unicompartmental osteoarthritis or osteonecrosis, radiographic evidence of preservation of the opposite compartment, and only mild radiographic signs of deterioration of the patellofemoral joint. The inclusion criteria were a range of motion of at least 90° with a flexion contracture of <15°, minimal pain at rest, a relatively sedentary lifestyle, a weight of <275 lb (124.7 kg), and an age of more than fifty years. The exclusion criteria were inflammatory arthritis, hemochromatosis, chondrocalcinosis, hemophilia, patellofemoral joint symptoms, a positive patellar grind test, and symptomatic knee instability.

The patients included thirty-four women and seventeen men with an average age of sixty-eight years (range, fifty-one to eighty-four years). The average weight was 176 lb (79.8 kg) (range, 115 to 270 lb [52.2 to 122.5 kg]). Eleven patients weighed 200 lb (90.7 kg) or more. The diagnosis was osteoarthritis in fifty-three knees (85%) and osteonecrosis in nine knees (15%). Fifty-nine arthroplasties (95%) involved the medial compartment, and three (5%) involved the lateral compartment. Equal numbers of right and left knee arthroplasties were performed. Fifty knees had undergone previous arthroscopy, and two had had a previous proximal tibial osteotomy.

Thirty-seven patients underwent a single unicompartmental knee arthroplasty, ten underwent a sequential bilateral unicompartmental knee arthroplasty, and one had a staged bilateral procedure. The three remaining patients had sequential unicompartmental knee arthroplasty and contralateral tricompartmental knee arthroplasty.

No patient was lost to follow-up. Thirteen patients (thirteen knees) died after less than ten years of follow-up as a result of causes that were unrelated to the arthroplasty. Thus, thirty-eight patients (forty-nine knees) had a minimum of ten years of follow-up. The preoperative diagnosis was osteoarthritis for forty-six of these forty-nine knees and osteonecrosis for three. The average duration of follow-up for these forty-nine knees was twelve years (range, ten to thirteen years).

The Miller-Galante unicompartmental knee system (Zimmer, Warsaw, Indiana) was used in all patients (Fig. 1). The system consisted of a cobalt-chromium alloy femoral component, a titanium alloy tibial tray, and an ultra-high molecular weight polyethylene insert. The femoral components were available in five sizes, and the polyethylene inserts were available in four thicknesses. The thinnest tibial component that was used had a total thickness of 8 mm, of which 5.7 mm comprised the polyethylene liner and 2.3 mm comprised the tibial baseplate. The system was designed to be used with cement fixation. To provide enhanced fixation, the fixation surface of the femoral component had two pegs and the fixation surface of the tibial component had two pegs and a fin. In addition, the fixation surface of the tibial component was precoated with polymethylmethacrylate. The shape of the tibial articulating surface was essentially flat to allow for unconstrained motion of the femur on the tibia. The surgical instrumentation included an extramedullary cutting jig for the femur and an extramedullary cutting attachment for the tibial component.

The intramedullary femoral guide was set to remove 6 mm of bone both distally and posteriorly. The femoral component replaced the resected bone millimeter for millimeter. The femoral component was aligned in the coronal plane so that its long axis was perpendicular to the tibial component and therefore parallel to the long axis of the tibia (Fig. 2). The component was sized to be congruent with the curvature of the anterior part of the femur (Fig. 3).

The tibia was cut perpendicular to its long axis. In varus knees, the medial collateral ligament was released from the tibial plateau approximately 1 cm from the joint line from the patellar tendon to the posteromedial corner of the tibia. This 1-cm release of the medial collateral ligament was not done to correct deformity but instead was done for exposure. An appropriate polyethylene liner thickness allowed 2 mm of joint motion.
laxity in both full extension and flexion. This distance was tested with use of a calibrated spacer.

Chondral damage of the articular surfaces of the patellofemoral and opposite compartments was graded at the time of surgery according to the method of Outerbridge. Patients with Outerbridge Grade-3 or 4 lesions were considered to be unsuitable for unicompartmental knee arthroplasty and were managed with tricompartmental knee replacement. (This was the case for two patients who were not included in this series.) At the time of surgery, Outerbridge Grade-1 or 2 changes were seen in the patellofemoral compartment in forty-eight knees (77%) and in the opposite compartment in twenty knees (32%).

All patients were evaluated prospectively. Postoperative knee function was evaluated by independent observers (clinical nurses and fellows) with use of the Hospital for Special Surgery knee score before surgery and at yearly intervals after surgery. Radiographic analysis included measurement of the mechanical axis, measurement of the femorotibial axis, and assessment of the degree of correction. On standing anteroposterior radiographs, we measured the varus or valgus tilt of the prosthesis with respect to the longitudinal tibial axis. On lateral radiographs, we measured the posterior slope of the tibial component with respect to the longitudinal tibial axis and the flexion or extension of the femoral component with respect to the longitudinal femoral axis. The cement interfaces were evaluated for the presence and extent of radiolucent lines in each of ten zones. A radiolucent line was considered to be progressive if it increased in size or if it progressed from one zone to an adjacent zone over time. Sequential radiographs were reviewed for evidence of component subsidence, or change in position. Definite loos-
ening was defined as a change in position (subsidence) of >2 mm or an angular change of >3° relative to the surrounding bone as seen on sequential radiographs, with use of the early radiographs as a baseline.

In addition to evaluating the components, we evaluated arthritic progression in the opposite compartment and the patellofemoral joint on standing radiographs. Radiographic changes were defined as Grade 1 (evidence of radiographic changes such as osteophytes, but with no measurable loss of joint space), Grade 2 (≤25% loss of joint space), Grade 3 (≤50% loss of joint space), or Grade 4 (>50% loss of joint space).

Kaplan-Meier survivorship analysis of all sixty-two knees was performed with revision for any reason and with revision or radiographic signs of loosening as the end points.

Results
Clinical Results
The average Hospital for Special Surgery knee score improved from 55 points (range, 30 to 79 points) preoperatively to 92 points (range, 60 to 100 points) at the time of the final follow-up. Thirty-nine knees (80%) had an excellent result (85 to 100 points), six (12%) had a good result (70 to 84 points), and four (8%) had a fair result (60 to 69 points). Two of the four patients who had a fair result (with scores of 63 and 60 points) underwent conversion to total knee replacement. The other two patients who had a fair result (with scores of 65 and 67 points) had limited walking ability secondary to severe cardiopulmonary disease at the time of the latest follow-up and subsequently died of causes that were unrelated to the arthroplasty. All living patients who had the unicompartmental replacement in place at the time of the final follow-up had an excellent result (thirty-nine knees, 87%) or a good result (six knees, 13%).

Patients reported no pain in twenty-nine knees (59%), slight pain in seventeen knees (35%), moderate pain in two knees (4%), and severe pain prior to revision in one knee (2%). Twenty-nine patients (76%) did not limp, six patients (16%) had a slight limp, two patients (5%) had a moderate limp, and one patient was unable to walk. At the time of the latest follow-up, thirty patients (79%) used no assistive devices, six patients (16%) used a cane for walking long distances, one patient used a cane full time, and one patient was unable to walk because of severe cardiopulmonary disease.

The average arc of knee flexion was 118° (range, 85° to 135°) preoperatively and 121° (range, 100° to 140°) at the time of the final follow-up. Thirty-nine knees (80%) had at least 120° of flexion at the time of the latest follow-up.

At the time of surgery, the anterior cruciate ligament was found to be intact in all patients but one. This patient had a Hospital for Special Surgery knee score of 100 points at the time of the latest follow-up, 153 months postoperatively. Two patients who had had a previous proximal tibial osteotomy had Hospital for Special Surgery knee scores of 95 and 81 points at the time of the final follow-up.

In the group of knees that were treated with medial compartment arthroplasty, the average preoperative deformity was 8° of varus (range, 3° of varus to 14° of varus) from the mechanical axis. The average postoperative alignment was 2° of varus (range, 2° of valgus to 10° of varus), for an average correction of 6°. Ten (17%) of the fifty-nine knees that were treated with medial unicompartmental arthroplasty were not corrected to within 5° of the neutral mechanical axis (range, 5° of varus to 10° of varus).

Conversion to Total Knee Arthroplasty
Two knees, with Hospital for Special Surgery scores of 63 and 60 points, underwent conversion to total knee replacement because of progressive patellofemoral arthritis. One of these knees was in a fifty-eight-year-old woman who had had a medial unicompartmental knee arthroplasty for the treatment of osteoarthritis. At the time of the index arthroplasty, the patellofemoral articulation demonstrated Outerbridge Grade-2 chondrosis. Heterotopic ossification in the quadriceps tendon developed postoperatively, and anterior knee pain subsequently developed five years postoperatively. By seven years postoperatively, the patient had increasing pain anteriorly as well as evidence of osteophytes around the patellofemoral joint. At eighty-seven months, she underwent total knee arthroplasty.

The second patient who required total knee replacement was a fifty-one-year-old woman who had undergone sequential bilateral medial unicompartmental knee arthroplasty for the treatment of osteoarthritis. At the time of the index arthroplasty, there was no evidence of degenerative changes in the lateral compartment of the right knee and the patellofemoral joint exhibited a large area of Outerbridge Grade-2 involvement. Approximately 120 months later, degeneration of the patellofemoral compartment was evident radiographically and the patient had anterior knee pain that was refractory to conservative measures. She underwent total knee arthroplasty at 127 months.

In both cases, the unicompartmental knee arthroplasty was converted to a straightforward tricompartmental knee replacement without the need for blocks, wedges, or augmentation. At the time of the revision operation, the unicompartmental components in both knees were found to be well fixed intraoperatively.

Technical Complications
Technical complications included three intraoperative tibial plateau fractures and one avulsion of the medial collateral ligament. One of the fractures was unrecognized at the time of surgery but was noted as a displaced marginal medial tibial plateau fracture on the first postoperative radiograph. The patient was managed nonoperatively with restricted weight-bearing until the fracture healed. At the time of the latest evaluation, ten years postoperatively, the Hospital for Special Surgery score was 88 points and radiographic evaluation revealed a stable tibial component. The knee had a mechanical axis of 1° of valgus and an anatomic axis of 7° of valgus. Radiographs revealed a 2-mm radiolucent line where the fracture intersected the cement mantle of the tibial component at its...
outer edge. The radiolucent line had not progressed since forty-four months postoperatively.

The second intraoperative fracture involved the medial tibial plateau and was fixed with a 6.5-mm screw. The fracture healed without adverse sequelae. At the time of the last follow-up, the patient was pain-free and the Hospital for Special Surgery knee score was 82 points. The relatively low overall score was attributed to severe peripheral neuropathy that was unrelated to the arthroplasty.

The third tibial plateau fracture was observed on the six-week postoperative radiographs of a patient who had undergone bilateral unicompartmental knee arthroplasty. On the lateral radiograph, the well-fixed tibial component had changed position as a result of rotation and/or subsidence of the fracture fragment. The tibial component, which had had 9° of posterior slope on the initial postoperative radiograph, was now noted to have 0° of posterior slope. The tibial component remained well fixed, and the fracture healed uneventfully. At 129 months postoperatively, the knee score was 96 points.

A fourth patient required stapling of the medial collateral ligament after it was avulsed during exposure of the medial part of the tibia. This knee remained clinically stable, and the knee score was 91 points at 161 months postoperatively.

One patient had only 80° of flexion at three weeks postoperatively and underwent manipulation under anesthesia to 145°. At the time of the most recent follow-up, 120 months postoperatively, the range of motion was 0° to 140°. Another patient had pain in the popliteal region and a 10° flexion contracture that persisted until eight months postoperatively. Radiographs revealed a piece of retained cement in the posterior aspect of the knee; the cement particle was removed arthroscopically. The patient reported relief of pain, and the Hospital for Special Surgery knee score was 100 points at 148 months postoperatively.

Other Complications

Two patients had a symptomatic deep venous thrombosis in the calf. The thromboses were confirmed with Doppler ultrasound at one and two weeks. Both patients were managed with Coumadin (warfarin) for three months.

Radiographic Results

At the time of the final radiographic evaluation, no component showed evidence of definite loosening and no knee had evidence of osteolysis. Three knees had a complete tibial radiolucent line. All complete and partial radiolucent lines were <2 mm in thickness. The three knees that had a complete tibial radiolucent line were followed for 11.2, 12.4, and 14.2 years. At the time of the final follow-up, the Hospital for Special Surgery knee scores for these three knees were 83, 83, and 100 points. There were no complete femoral radiolucent lines.

Partial tibial radiolucent lines were observed in at least one zone in nineteen of the forty-nine knees. In the majority (sixteen) of these knees, the tibial radiolucent lines were at the cement-bone interface. In four knees, the lines appeared to be progressive initially but did not progress after three years of follow-up. Seven knees showed partial femoral radiolucent lines. In contrast to the tibial radiolucent lines, which occurred at the cement-bone interface, the majority of the partial femoral radiolucent lines occurred at the cement-prosthesis interface. None of the femoral radiolucent lines was progressive.

Overall, twenty-three (47%) of the forty-nine knees had at least one partial radiolucent line around either the tibial or the femoral component. In the subgroup of eleven knees in patients who weighed >200 lb (90.7 kg), seven (64%) had at least one partial radiolucent line around either the tibial or the femoral component. None of the lines was complete or progressive.

Of the forty-nine knees that had at least ten years of follow-up, forty knees (82%) had some radiographic evidence of deterioration of the opposite compartment or the patellofemoral compartment at the time of the final evaluation and nine knees (18%) did not. However, only fourteen (29%) of the forty-nine knees had measurable loss of joint space: five had a loss of patellofemoral joint space only; seven had a loss of tibiofemoral joint space only; and two had a loss of both patellofemoral and tibiofemoral joint space.

Nineteen knees (39%) had Grade-1 radiographic changes (no loss of joint space) in the opposite compartment, six knees (12%) had Grade-2 changes (≤25% loss of joint space), and three knees had Grade-3 changes (≤50% loss of joint space). The three knees with Grade-3 changes in the opposite compartment had Hospital for Special Surgery knee scores of 92, 93, and 100 points at the time of the latest follow-up (at 156, 144, and 152 months, respectively).

Thirteen knees (27%) had Grade-1 radiographic changes in the patellofemoral joint, one knee had Grade-2 changes, three knees had Grade-3 changes, and four knees had Grade-4 changes. Two of the three knees with Grade-3 radiographic changes underwent revision to a tricompartmental knee arthroplasty, as described earlier. The four knees with Grade-4 radiographic changes (three of which had had a medial arthroplasty and one of which had had a lateral arthroplasty) demonstrated severe patellofemoral joint-space loss secondary to impingement with the femoral component. In all four knees, the subchondral erosion of the patella was not observed radiographically until the time of the latest follow-up evaluation and in all cases it was preceded by progressive patellofemoral joint-space loss on serial radiographs. The average duration of follow-up for these four knees was 151 months, and the average Hospital for Special Surgery knee score was 93 points (range, 89 to 96 points).

Survivorship

Kaplan-Meier analysis of all sixty-two knees revealed a ten-year survival rate of 98.0% (95% confidence interval, 96.0% to 100%) with revision for any reason or radiographic loosening as the end point (Fig. 4), a thirteen-year survival rate of 95.7% (95% confidence interval, 91.4% to 100%) with revision or ra-
diagnostic loosening as the end point, and a thirteen-year survival rate of 100% with definite aseptic loosening of either component as the end point.

Discussion

The present study of sixty-two cemented modular unicompartmental knee replacements demonstrated excellent clinical and radiographic results after ten to thirteen years of follow-up. The results of the present study compare favorably with the reported results associated with total knee replacement and with contemporary designs of unicompartmental knee implants.

The survival rate in the present study was 96% after thirteen years of follow-up. The revision rate of 4% is comparable with the rates in other studies. Notably, there were no radiographic signs of definite loosening of any component. The 47% prevalence of nonprogressive partial radiolucent lines in the present series is lower than the prevalences reported in other studies. Also, the 6% prevalence of complete tibial radiolucent lines in this series is lower than that reported in other studies. Thus far, these radiolucent lines have not led to failure or poor clinical scores.

At the time of the latest follow-up, 18% of the knees had progressive loss of joint space in the opposite compartment and 14% of the knees had progressive loss of joint space in the patellofemoral compartment. Degeneration in the opposite compartment is a common cause of failure after unicompartmental arthroplasty. Some authors have suggested that overcorrection of joint deformity results in the transfer of increased forces to the uninvolved compartment and accelerates degeneration. We believe that the overall undercorrection reported in the present series may be responsible for the low rate of degeneration of the opposite compartment. We do not recommend formal medial collateral ligament release because we believe that it will result in overcorrection of the varus deformity. Many authors have suggested that the presence of extensive disease, such as an area of eburnated bone in the patellofemoral joint or contralateral compartment at the time of the index procedure, is the primary factor that predisposes these compartments to further degeneration. We believe that the stringent selection criteria used in the present study (i.e., not more than Grade-2 chondrosis in the other compartments) is probably responsible for our excellent results.

Recently, Hernigou and Deschamps documented patellar impingement radiographically in twenty-eight (28%) of ninety-nine knees at an average of fourteen years after unicompartmental knee arthroplasty. In that study, impingement of the patella on the femoral component was associated with anterior placement of the femoral component and resulted in patellofemoral symptoms in the most severe cases. In the present series, impingement was documented radiographically in four knees; all four patients had an excellent clinical score without patellofemoral symptoms after an average duration of follow-up of thirteen years. The impingement occurred secondarily to progressive joint-space narrowing as observed on sequential radiographs and, in all four knees, it was not observed until the time of the latest radiographic evaluation.

Alignment of the femoral component in the sagittal plane is important in order to avoid patellar impingement. As shown in Figure 3, the femoral component should be congruent...
The rate of perioperative fracture in this series was high (three of forty-nine). These three fractures were technique-related and occurred in association with the first thirteen procedures performed in this series. At the time of those procedures, we did not predrill the fixation pins for the tibial alignment guide. Since that time, we have predrilled the holes and tibial fracture has not occurred.

The mean flexion at the time of the final follow-up was 121°, with 80% of the knees having at least 120° of flexion. This excellent range of motion slightly exceeds that reported in most studies of total knee replacement.22-25,38

Tibial aseptic loosening and accelerated polyethylene wear are two of the most common causes of failure of unicompartmental knee arthroplasty.3,7,15,28,39-41. However, these complications were not seen in the present series despite the use of a thin (5.7-mm) polyethylene liner in more than half of the knees, the use of a tibial component with a relatively flat articular surface, and intentional undercorrection of the preoperative angular deformity. We believe that undercorrection of the preoperative angular deformity precludes overstressing the compartment and thus minimizes polyethylene wear.26,34

The metal backing of the tibial component was intended to provide more uniform stresses in the proximal part of the tibia and to protect the cancellous bone. Its use required minimal tibial bone resection and did not adversely affect conversion to total knee arthroplasty.5,12,16,21. Total knee replacement can be performed readily after a failed unicompartmental knee arthroplasty if an appreciably small amount of bone was resected during the original implantation and if the holes for fixation with cement do not deeply invade the condylar bone stock.29. In the two knees in the present study that underwent conversion to total knee arthroplasty, a standard posterior-stabilized and a standard posterior cruciate-retaining total knee replacement were used without blocks, wedges, or bone grafts. Furthermore, excessive tibial resection was not needed, as demonstrated by our use of 10 and 12-mm tibial components in these two knees.

Although this unicompartmental design was associated with excellent clinical and radiographic results after a minimum duration of follow-up of ten years, we urge its use only in properly selected patients.

Results of Unicompartmental Knee Arthroplasty at a Minimum of Ten Years of Follow-up

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In support of their research or preparation of this manuscript, one or more of the authors received grants or outside funding from Zimmer. In addition, one or more of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity (Zimmer). Also, a commercial entity (Zimmer) paid or directed, or agreed to pay or direct, benefits to a research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.C.00568

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Ilizarov Hip Reconstruction for the Late Sequelae of Infantile Hip Infection

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Background: The late sequelae of infantile hip infection include absence of the femoral head and neck, proximal migration of the femur, lower-extremity length discrepancy, abnormal gait, and pain. The Ilizarov hip reconstruction includes an acute valgus and extension osteotomy at the proximal part of the femur combined with gradual distraction for realignment and lengthening at a second, more distal, femoral osteotomy. The purpose of this study was to determine whether this technique can successfully treat the sequelae of infantile hip infection.

Methods: We performed a retrospective review of a series of eight consecutive patients with a Type-IV or V hip deformity, according to the classification system of Hunka et al., after an infantile hip infection. The patients’ mean age at surgery was 11.2 years. All hips were unstable, with a mean of 3.8 cm of proximal migration. A mean valgus angular correction of 44° and a mean extension angular correction of 19° were created with the proximal osteotomies. Distal femoral lengthening averaged 5.7 cm, and distal femoral varus angular correction averaged 10°. The mean time in the Ilizarov frame was 4.7 months. Outcomes were evaluated clinically and radiographically. The clinical evaluation included gait analysis and the use of a modified Harris hip score.

Results: At the time of follow-up, at a mean of five years, the mean lower-extremity length discrepancy had improved from 4.6 cm preoperatively to 0.7 cm. The mean modified Harris hip score had improved from 51 points to 73 points (p = 0.007). All extremities were well aligned, with a mean pelvic mechanical axis angle of 89°. The mean deviation of the mechanical axis was 2 mm in a lateral direction. The mean stance-time asymmetry improved from 16% to 5.4% (p = 0.0037), and the mean ground-reaction force (second peak) improved from 102% of body weight to 122% of body weight (p = 0.0005).

Conclusions: The Ilizarov hip reconstruction can successfully correct a Trendelenburg gait and simultaneously restore knee alignment and correct lower-extremity length discrepancy. When the procedure is performed on a young patient, remodeling of the proximal osteotomy site and development of lower-extremity length discrepancy should be expected and the procedure may need to be repeated.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

The sequelae of infantile septic arthritis and osteomyelitis of the hip are diverse and can include premature closure of the triradiate cartilage, acetabular dysplasia, lower-extremity length discrepancy, premature or asymmetrical closure of the capital femoral physis, necrosis of the articular cartilage, osteonecrosis, pseudarthrosis of the femoral neck, and complete destruction of the femoral head and neck. Children with late sequelae of neonatal hip infection often present with the clinical problems of pain, a Trendelenburg gait, lower-extremity length discrepancy, and hip instability, all related to absence of part or all of the femoral head and neck and proximal migration of the femur.

Reconstructive procedures for this difficult problem have not been satisfactory. Most authors have reported poor results with the current reconstructive procedures, including trochanteric arthroplasty, hip arthrodesis, pelvic osteotomy, and femoral osteotomy. A proximal femoral subtrochanteric osteotomy (pelvic support osteotomy) also has been described. Support is achieved by means of a valgus osteotomy of the proximal part of the femur that places the superior end of the femur against the lateral aspect of the pelvis. In addition, the valgus angulation improves hip biomechanics by increasing the mechanical efficiency of the abductor muscles. This approach also has shortcomings, however. The optimal extent of angulation is difficult to achieve. If the angle is too small, the hip biomechan-
Ilizarov combined the pelvic support osteotomy with a second, separate distal femoral varus lengthening osteotomy (Figs. 1-A through 1-E). Furthermore, he emphasized the importance of not only valgus but also extension at the proximal osteotomy site. This procedure is called the Ilizarov hip reconstruction. The purpose of the present study was to evaluate the results of this technique for the treatment of the sequelae of infantile hip infection.

Materials and Methods

A retrospective review of the cases of eight consecutive patients with late sequelae of infantile hip infection was conducted. The two senior authors (D.P. and J.E.H.) performed all of the procedures. Five of the eight patients returned for a physical examination and gait analysis for the purpose of this study. The others could not return because of travel and logistical issues. They were interviewed by telephone, and data on the range of motion of the hip were obtained from their local physicians or physical therapists, who had performed a physical examination. Standardized radiography and physical examination were performed for all patients, and hip scoring was also done for seven patients. The outcomes were evaluated on anteroposterior standing radiographs of both lower extremities and 91-cm anteroposterior and lateral radiographs of the femur. Clinical assessment included a history, physical examination, gait analysis, and the use of a modified Harris hip score.

Hips were classified according to the system described by Hunka et al. Type I indicates no or slight femoral head changes; Type IIa, deformity of the femoral head with an intact physis; Type IIb, deformity of the femoral head with premature physeal closure; Type III, pseudarthrosis of the femoral neck; Type IVa, complete destruction of the capital femoral epiphysis with a stable neck fragment; Type IVb, complete destruction of the capital femoral epiphysis with an unstable small neck fragment; and Type V, complete destruction of the head and neck to the intertrochanteric line with dislocation of the hip.

Preoperatively, an anteroposterior radiograph of the pelvis, an anteroposterior standing radiograph (teleorontgenogram) of both lower extremities, a single-limb stance
anteroposterior radiograph of each lower extremity, an an-
teroposterior standing radiograph of the affected side, and a
maximum-adduction cross-legged anteroposterior radiograph
of the pelvis (made with the patient supine with the lower ex-
tremities adducted and the involved hip flexed and adducted
over the top of the uninvolved hip) were made. Proximal
migration was calculated as the difference between the dis-
tance from a transverse line through the sacroiliac joints to the
tip of the greater trochanter on both sides. Lower-extremity
length discrepancy was calculated from the teleoroentgeno-
gram. The pelvic mechanical axis angle comprised a horizon-
tal pelvic line and a mechanical axis line that was extended
proximally from the ankle joint center through the knee joint
center.

Pain and functional outcomes were analyzed with use of
a modified Harris hip score that includes only the subjective
part of the original score. This modification also incorporates
“shoe lift” (substituted for “cane”) into the “support” category
because of its clinical relevance to our patient group (see Ap-
pendix). The initial score was for patients with hip arthritis,
but we found the remainder of the scoring system to be rele-
vant. A score of 0 to 50 points indicates a poor result; 51 to 60
points, a fair result; 61 to 70 points, a good result; and 71 to 79
points, an excellent result.

Gait Analysis
Gait analysis was conducted with our previously described
method. Two strain-gauge force-platforms (AMTI; Advanced
Medical Technologies, Watertown, Massachusetts) were ar-
ranged end to end in the frontal plane and were offset in the
sagittal plane in the middle of a walkway that was 30 ft (9.1 m)
long and 4.5 ft (1.4 m) wide. Data were gathered from the
force-plates at a frequency of 1000 Hz. An analog-to-digital
converter connected to an IBM-compatible computer was
used to collect amplified force data, and the ground-reaction
force vectors were analyzed with use of AMTI software.

The variables measured were stance-time asymmetry
and the second peak of the ground-reaction force. Both of
these parameters have been shown to correspond well to limb-
length differences of >2 cm in the absence of pain and muscle

Fig. 1-D Determination of the distal osteotomy level and the degree of varus cor-
rection required according to the intersection between the proximal and distal
mechanical axis lines. The proximal mechanical axis is a line perpendicular to the
horizontal line of the pelvis that passes through the proximal femoral osteotomy
site. The distal mechanical axis line is a line from the center of the ankle that
passes through the center of the knee. Fig. 1-E Schematic diagram of a radiograph
made at the end of distraction, showing both the proximal and the distal osteotomy.
Note the lengthening and the varus correction with the distal osteotomy to achieve
equal lower-extremity lengths and a 90° pelvic mechanical axis.
weakness\textsuperscript{18,19}. Stance-time asymmetry was expressed as the percentage of stance-time reduction on the short side as compared with the stance time on the long side. The second-peak ground-reaction-force vector was expressed as a percentage of body weight. Normalization of these parameters in our study signified successful equalization of the limb lengths, absence of pain, and adequate muscle strength for stabilization during walking. There is no stance-time asymmetry in a normal gait. Five of the eight patients underwent this gait analysis.

\textbf{Surgical Planning}

The Ilizarov hip reconstruction involves a proximal femoral osteotomy for valgus angulation and extension and a distal femoral osteotomy for lengthening and limb realignment. The level of the proximal femoral osteotomy is determined from the maximum-adduction anteroposterior cross-legged radiograph of the pelvis. For this view, the affected lower extremity and hip are maximally adducted over the normal side, a maneuver that requires some flexion of the affected side. The osteotomy is performed at the level at which the femoral shaft crosses the ischium. This osteotomy level is similar to the one proposed by Schanz, as reported by Hass\textsuperscript{6}. The amount of valgus angulation to be achieved with the proximal osteotomy is determined by adding 15\degree to the femoropelvic abduction measured on the anteroposterior standing radiograph of the affected side rather than on the maximum-adduction anteroposterior radiograph of the pelvis (Figs. 1-A, 1-B, and 1-C). The overcorrection of 15\degree is based on experience and is used to compensate for fatigue of the abductor muscles. Extension at the proximal osteotomy site is equal to the amount of fixed flexion deformity of the hip. Finally, internal rotation at the osteotomy site is determined, at the time of surgery, as the amount of external rotation of the hip that occurs with maximum adduction of the hip. As the hip is maximally adducted, external rotation of the femur occurs. This amount of external rotation of the hip is corrected with internal rotation at the proximal femoral osteotomy site.

The goal of the distal femoral osteotomy is to lengthen and realign the lower extremity (Figs. 1-D and 1-E). A perpendicular line from a horizontal pelvic line that passes through the proximal osteotomy site should ultimately pass through the center of the knee and the center of the ankle. The distal femoral osteotomy is needed to achieve this. The level of the distal femoral osteotomy is determined on the basis of the amount of valgus angulation of the proximal femoral osteotomy. A paper tracing of the planned correction was performed. A line perpendicular to the top of the pelvis is drawn through the region of the apex of angulation of the proximal osteotomy and is extended distally (Fig. 1-D). A distal line is drawn from the center of the ankle through the center of the knee joint and is extended proximally. The intersection of these two lines is the level of the second center of rotation of angulation, which corresponds to the level of the hinges controlling varus at the distal osteotomy site. The level of the distal femoral osteotomy is either at this level or slightly more distal. In the latter situation, the distal part of the femur will translate medially with varus angulation. The magnitude of the varus alignment of the distal osteotomy is equal to the magnitude of the angulation measured between the intersecting distal and proximal axis lines on the preoperative drawing, as described above.

\textbf{Surgical Technique}

Preoperatively, an Ilizarov external fixation frame is constructed with two rings connected by a hinge at the anticipated level of the distal femoral osteotomy. The magnitude of varus angulation of the distal osteotomy is fixed in the hinges. A femoral arch is connected parallel to the proximal ends of the two rings, and the frame is sterilized before surgery.

The patient is positioned on a radiolucent operating table with sheets placed under the sacrum to maintain a level pelvis and to avoid any rotation. With use of an image intensifier, a 1.8-mm Ilizarov wire, and a surgical marking pen, a line is marked across the inferior edge of the two sacroiliac joints. This is called the horizontal line of the pelvis.

The involved extremity is then maximally adducted and is crossed over the contralateral extremity. The involved hip flexes and adducts over the uninvolved hip. This places the proximal part of the femur in an adducted and flexed position. In this position, the femur externally rotates because maximal adduction of the hip results in some flexion and external rotation. This is also a unique function of the pathological anatomy in this region. This rotation must be taken into consideration during pin placement.

The proximal part of the femur is now in the position that it will assume after the proximal osteotomy. This is the pelvic support position. The surgeon should observe that the proximal part of the femur cannot adduct farther. This is important to eliminate the Trendelenburg gait. The first proximal pin is then inserted. Because the proximal part of the femur is in its post-osteotomy position, it has moved relative to the overlying skin and subcutaneous tissues, such that a pin placed in this position will enter the skin over the underlying bone without tethering or displacing the skin after the osteotomy. A 6-mm threaded half-pin is inserted parallel to the horizontal line of the pelvis from the lateral side and parallel to the floor. The pin is connected to a free femoral arch. The arch is kept perpendicular to the floor with the extremity crossed, automatically imparting extension to the osteotomy. For more or less extension, the arch can be tilted in a posterior or anterior direction, respectively.

A second 6-mm threaded half-pin is then inserted anterolaterally into the proximal fragment, parallel to the same femoral arch. The femoral arch is then fixed to the proximal part of the femur at the correct angle. The extremity is then uncrossed and is placed parallel to the other extremity with the patella facing forward, or anteriorly. The skin at the proximal end of the thigh is now tented over the proximal two pins. This corrects after the proximal osteotomy.

In the supracondylar region of the distal part of the femur, a 1.8-mm Ilizarov wire is inserted parallel to the knee joint line. It is fixed and tensioned to the distal ring of the
preconstructed frame. A 6-mm threaded half-pin is inserted from the posteromedial direction on the distal ring. A second half-pin is inserted from the proximal ring on the lateral side. The proximal femoral osteotomy is then performed. Through a 1-cm lateral incision, multiple drill holes are made with a 4.8-mm drill bit at the planned osteotomy level. An osteotome is then used to complete the osteotomy. All procedures are performed under fluoroscopic guidance.

After the proximal femoral osteotomy is completed, the distal femoral fragment is rotated until the distal wire is parallel to the first half-pin that was inserted. The distal fragment is then displaced medially by manipulating the arches before connecting them. Finally, the extremity is abducted to make the distal arch parallel to the proximal arch. When the surgeon does this, the proximal arch is also flexed to effect the extension correction. Two threaded rods with a conical washer at each end are connected between the two arches. It is very important not to lose contact between the femoral segments during the medial translation. If contact is lost, the osteotomy site will be unstable. One more 6-mm threaded half-pin is inserted from a posterolateral direction into the distal segment, and another half-pin is inserted from the distal arch.

If there is any residual tenting of the skin by the proximal pins, a third small pin is inserted temporarily to allow removal and reinsertion of each of the proximal pins to eliminate skin tenting. The pin is removed, a new incision is made at the level of the pin, and the pin is reinserted in the previously drilled and tapped bone hole. This is preferable to creating the long deep scars that result from pin site releases.

The distal femoral osteotomy is then performed at the planned level in the same percutaneous manner as described above. Next, the distal femoral wire is removed. A third 6-mm threaded half-pin is added proximally and distally in larger children and in adults.
Rotary instability of the knee is associated with this condition in some patients, who demonstrate a tendency for the knee to subluxate during lengthening. If this is recognized preoperatively, extension of the external fixation to the tibia with knee hinges should be considered. The knee hinges should be located at the intersection of the Blumensaat line and the posterior cortex of the femur. Two tibial half-pins are connected to a single half-ring suspended from the hinges with threaded rods.

**Statistical Analysis**
Statistical analysis was conducted with use of the StatView package of programs (SAS Institute, Cary, North Carolina). The significance of the findings was evaluated with a paired t test for comparison of all paired variables, and regression analysis was conducted. A p value of <0.05 was considered significant.

**Results**
Clinical and radiographic data are summarized in the Appendix.

All patients had a Type-IV or V hip, according to the classification system of Hunka et al. There were two Type-IVa, two Type-IVb, and four Type-V deformities. The patients’ mean age at surgery was 11.2 years (range, 7.8 to 14.2 years). All hips were unstable preoperatively, with a positive push-pull sign. Proximal migration was diagnosed and quantified with a physical examination, on the basis of a push-pull sign, and with observation of a limb-length discrepancy on standing radiographs made with blocks placed under the lower extremity. The standing anteroposterior radiographs of both lower extremities revealed that the mean proximal migration was 3.8 cm (range, 1 to 5.5 cm). The proximal osteotomy was performed at a mean of 7.2 cm (range, 5.5 to 9.2 cm) distal to the tip of the greater trochanter. The mean valgus angulation...
created by the osteotomy was 44° (range, 16° to 70°), and the mean extension angulation created by the osteotomy was 19° (range, –5° to 30°). The mean varus angulation correction with the distal femoral osteotomy was 10° (range, 0° to 23°), and the mean lengthening was 5.7 cm (range, 4.4 to 7 cm). The mean time in the Ilizarov frame was 4.7 months (range, three to seven months). The mean duration of follow-up was five years (range, 1.9 to 9.8 years).

Knee flexion averaged 130° (range, 125° to 135°) preoperatively and 121° (range, 70° to 135°) at the time of follow-up. The decrease in knee flexion probably can be explained by tightening of the quadriceps muscle associated with the femoral lengthening. Hip flexion averaged 94° (range, 30° to 130°) preoperatively and 70° (range, 40° to 105°) at the time of follow-up. The mean hip flexion contracture decreased from 14° (range, 0° to 30°) preoperatively to 9° (range, 0° to 20°) at the time of follow-up. Internal rotation of the hip in extension increased from a mean of 10° (range, –20° to 30°) preoperatively to a mean of 25° (range, 5° to 35°) at the time of follow-up. External rotation of the hip in extension averaged 40° (range, 5° to 90°) preoperatively and 41° (range, 10° to 90°) at the time of follow-up. The mean hip abduction increased from 28° (range, 0° to 70°) preoperatively to 35° (range, 30° to 40°) at the time of follow-up, whereas hip adduction averaged 28° (range, 0° to 50°) preoperatively and 23° (range, 5° to 45°) at the time of follow-up. The decrease in hip flexion, increase in hip extension, and increase in hip abduction can be explained by the direction of the proximal femoral osteotomy.

The mean lower-extremity length discrepancy improved from 4.6 cm (range, 0.6 to 6.4 cm) preoperatively to 0.8 cm (range, 0 to 1.2 cm) at the time of follow-up. The mean modified Harris hip score improved from 51 points (range, 21 to 67 points) to 73 points (range, 64 to 79 points) (p = 0.007). All extremities were well aligned. At the time of follow-up, the mean pelvic mechanical axis was 89° (range, 84° to 94°) and the mean deviation of the mechanical axis was 2 mm in a lateral direction (range, 16 mm in a medial direction to 23 mm in a lateral direction). The pelvic drop associated with trunk lean (the Trendelenburg sign) was eliminated in six patients and reduced in two.

Fig. 2-F Radiograph made after completion of the distraction, showing 55° of valgus at the proximal femoral osteotomy site and 7 cm of lengthening, with varus realignment at the distal femoral osteotomy site. Fig. 2-G Standing anteroposterior radiograph, made two years postoperatively, when the patient was fourteen years of age, showing normal alignment of the extremity with a 91° pelvic mechanical axis. Fig. 2-H Clinical photograph showing that no Trendelenburg sign is present during single-limb stance.
Five patients underwent gait analysis both preoperatively and postoperatively, at a mean of 1.2 years (range, one to two years) after frame removal (Table I). The mean stance-time asymmetry (measured in milliseconds and shown as the percent difference compared with the contralateral side) improved from 16% to 5.4% (p = 0.0037). The mean ground-reaction force (second peak) improved from 102% to 122% of body weight (normal, 112% to 131% of body weight) (p = 0.0005). The parameters of stance-time asymmetry and second-peak ground-reaction-force vector were normalized.

**TABLE I Gait Analysis Data**

<table>
<thead>
<tr>
<th>Case</th>
<th>Stance-Time Asymmetry (Preoperative)</th>
<th>Stance-Time Asymmetry (Postoperative)</th>
<th>Second-Peak Ground-Reaction-Force Vector (Preoperative)</th>
<th>Second-Peak Ground-Reaction-Force Vector (Postoperative)</th>
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<td>6</td>
<td>102</td>
<td>122</td>
</tr>
<tr>
<td>P Value</td>
<td>0.0037</td>
<td>0.0005</td>
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<td></td>
</tr>
</tbody>
</table>

*Normal is 112% to 131% of body weight.

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Fig. 2-I Clinical photograph showing maximum hip flexion. Fig. 2-J Clinical photograph showing the range of internal rotation. Fig. 2-K Clinical photograph showing the range of external rotation.
The patient had 3.8 cm of length discrepancy and a Trendelenburg gait decreased from 4.8 cm to 1.0 cm. At the age of fourteen years, the lower-extremity length discrepancy had decreased from 4.9 cm to 1 cm. At thirteen years of age, the proximal femoral osteotomy site had remodelled, the Trendelenburg gait had returned, and the lower-extremity length discrepancy had increased to 3.1 cm. As a result, the Ilizarov hip reconstruction was repeated. The second patient had undergone the initial surgery at 7.8 years of age, and the lower-extremity length discrepancy had decreased from 4.8 cm to 1.0 cm. At the age of fourteen years, the patient had 3.8 cm of length discrepancy and a Trendelenburg gait and the proximal osteotomy site had remodelled. The Ilizarov hip reconstruction was repeated. Both patients had an almost normal gait at skeletal maturity.

Three patients had undergone previous femoral lengthening without a proximal osteotomy (Figs. 2-A through 2-C). At the time of the previous femoral lengthening in each of those patients, a hinged hip-distraction external fixator was attached to the Ilizarov frame to prevent the femur from migrating proximally. Two pins were placed in the pelvis. This construct allowed hip flexion and extension while stabilizing the hip articulation. No other patients had undergone relevant surgery previously.

Nine complications occurred in six patients (Table II). Three patients had pin-track infections, which responded to oral antibiotics. Knee stiffness occurred in two patients, with flexion decreased to 20° in both, and was treated with surgical soft-tissue release. At the time of follow-up, both patients had regained a full range of flexion (130° and 135°). Premature consolidation occurred in two patients and was treated with repeat osteotomy. One patient had proximal migration of the femur, which was treated with a revision of the proximal femoral osteotomy with a greater degree of valgus angulation. Another patient had knee subluxation, which was treated with extension of the frame across the knee. No neurologic injuries or fractures were present after frame removal.

**Discussion**

As outlined by Hass, the proximal femoral subtrochanteric osteotomy (pelvic support osteotomy) as a treatment for instability of the hip has a long history in orthopaedic surgery. With early procedures, the resulting increased stability of the hip was due to actual support of the pelvis on the osteotomized proximal part of the femur. In this type of reconstruction, the hip joint is not directly approached. Milch expanded the concept and popularized the pelvic support osteotomy in the United States during the mid-twentieth century. He advocated subtrochanteric valgus osteotomy to improve hip mechanics but cautioned against excessive valgus. Excessive valgus at the osteotomy site leads to abutment of the proximal part of the femur against the pelvis and even to pelvic tilt when the patient tries to bring the involved extremity into a neutral abduction-adduction position. This is not desirable because it limits abduction and results in pain. Thus, there were two competing goals. Although excessive subtrochanteric valgus improved hip stability, it also caused valgus malalignment of the knee and abutment of the proximal part of the femur against the pelvis as the patient attempted to bring the hip into neutral abduction-adduction. The compromise is less abduction than would be ideal to stabilize the hip and eliminate the Trendelenburg gait.

The optimal level for a pelvic support osteotomy has been controversial. Although some authors have recommended a proximal osteotomy with insertion of the lesser trochanter into the acetabulum, others have preferred a longer proximal segment. We favor a more distal osteotomy, similar to that recommended by Schanz, as reported by Hass. The specific area of weight-bearing is not absolute. Although it likely varies with the level of the osteotomy, the aim is to achieve a soft-tissue interpositional weight-bearing surface between the apex of the proximal femoral osteotomy and the pelvis. With

<table>
<thead>
<tr>
<th>Case</th>
<th>Complication</th>
<th>Treatment</th>
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<tr>
<td>1</td>
<td>Superficial pin infection</td>
<td>Oral antibiotic</td>
</tr>
<tr>
<td></td>
<td>Knee stiffness, flexion to 20°</td>
<td>Soft-tissue release</td>
</tr>
<tr>
<td>2</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>Premature consolidation</td>
<td>Repeat osteotomy</td>
</tr>
<tr>
<td>4</td>
<td>Premature consolidation</td>
<td>Repeat osteotomy</td>
</tr>
<tr>
<td></td>
<td>Knee stiffness</td>
<td>Soft-tissue release</td>
</tr>
<tr>
<td>5</td>
<td>Superficial pin infection</td>
<td>Oral antibiotic</td>
</tr>
<tr>
<td>6</td>
<td>Proximal migration of femur</td>
<td>Increase of valgus at proximal osteotomy site</td>
</tr>
<tr>
<td></td>
<td>Knee subluxation</td>
<td>Extension of frame across knee</td>
</tr>
<tr>
<td>7</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>8</td>
<td>Superficial pin infection</td>
<td>Oral antibiotic</td>
</tr>
</tbody>
</table>
a distal osteotomy, this weight-bearing probably occurs at the inferior aspect of the pelvis, near the ischial tuberosity.

Surgical reconstruction of the hip for the treatment of late sequelae of infantile and early childhood hip infection has generally not yielded satisfactory results, leading several authors to conclude that reconstruction should not be attempted\(^1\). One of these reconstructive options was a greater trochanteric arthroplasty\(^1\), with the greater trochanter redirected into the acetabulum to substitute for the absent femoral head. The expectation was that the apophyseal cartilage would remodel to the shape of the acetabulum. However, the subsequent progressive subluxation that was encountered in most patients necessitated additional procedures, such as femoral osteotomy, pelvic osteotomy, and acetabuloplasty, to maintain coverage and containment\(^1\). Satisfactory results were unusual, even after multiple operations. Hip stiffness was common, and abductor insufficiency was typical.

Choi et al.\(^7\) reported poor results after treatment of late sequelae of neonatal hip infection. They used a variety of procedures, including Pemberton osteotomy, trochanteric arthroplasty, arthrodesis, epiphysiodesis of the contralateral extremity, and lengthening of the ipsilateral tibia. Satisfactory results were achieved in only four of thirteen hips with a Choi type-4 deformity, which is comparable with the Hunka Type-IV and V deformities treated in our study.

Wopperer et al.\(^1\) reviewed the results of nine hips in eight patients who had had infantile hip infection and had not undergone any reconstructive procedure on the hip joint. On the basis of their long-term observations of this group of patients, the authors concluded that, after hip joint infection, neither reconstructive efforts designed to relocate an inadequate femoral head to address persistent dislocation nor transfer of the greater trochanteric epiphysis into the acetabulum yielded results comparable with those of nonoperative treatment. They recommended only contralateral distal femoral epiphysiodesis in adolescence to minimize the lower-extremity length discrepancy; they did not recommend proximal tibial or fibular epiphysiodesis.

Fabry and Meire\(^3\) reviewed the cases of seventeen patients with absence of the femoral head and neck from a group of twenty-nine children with sequelae of septic arthritis of the hip. Eleven patients had undergone reconstructive surgery, including Salter osteotomy, greater trochanteric arthroplasty, femoral osteotomy, and Chiari osteotomy. Only two of the seventeen patients had a satisfactory result, and the authors concluded that late reconstructive surgery is difficult and unpredictable. They did not address the issue of lower-extremity length discrepancy.

Betz et al.\(^1\) reported the results of a multicenter long-term follow-up study of thirty-two hips in twenty-eight patients who had had septic arthritis of the hip during infancy or childhood. They concluded that patients who had undergone hip reconstruction functioned more poorly than did those who had not. They advised against reconstructive surgery of the hip joint but did advocate femoral osteotomy to reposition the extremity into a more functional position; they also recommended treatment of the lower-extremity length discrepancy.

Cheng et al.\(^2\) used a new technique involving placement of pedicled vascularized iliac crest graft to replace the destroyed femoral neck and head. They reviewed their experience with eight hips in seven children with Choi type-4B sequelae of septic arthritis (equivalent to a Hunka Type-V deformity). Three of the eight hips had excellent substitution of the femoral head and neck. Lower-extremity length discrepancy was not addressed, and there were symptoms related to this discrepancy at the time of final follow-up. Cheng et al. speculated that this hip reconstruction would restore hip stability to a degree that would allow subsequent distraction lengthening to be performed without causing dislocation.

In other reports\(^2,22\), Cheng et al. reviewed the results of femoral lengthening in four patients with a Choi type-4B deformity due to septic arthritis of the hip. Three of them had previously undergone reconstruction with a pedicled vascularized iliac crest graft. A mean of 9 cm of lengthening was achieved, all hips remained stable, and there was no substantial loss of motion of the hip or knee.

Ilizarov hip reconstruction is a combination of the pelvic support osteotomy and a second, distal femoral osteotomy to correct lower-extremity length discrepancy and to realign the extremity. The proximal femoral osteotomy was designed to eliminate hip adduction. If the hip cannot adduct, the Trendelenburg sign and gait cannot occur because the pelvis cannot drop. Elimination of hip adduction requires overcorrection with the valgus osteotomy—by 15°, according to previous experience. This places the extremity in a fixed abduction position relative to the pelvis, and this was one of the problems with the previous pelvic support osteotomies as they led to problems with the knee joint. To address this problem, Ilizarov introduced a second femoral osteotomy, which was performed more distally, to realign the knee joint and to correct the lower-extremity length discrepancy\(^21,22\). It solved two of the problems that had not been previously addressed. Furthermore, Ilizarov emphasized extension of the proximal femoral osteotomy to correct the fixed flexion deformity of the hip and to permit locking of the hip joint. The biomechanics of the hip are substantially improved by these corrections. The valgus alignment of the proximal part of the femur positions the greater trochanter and the abductor muscle insertion laterally and distally. The lateralization increases the length of the abductor lever arm, while the distal shift tensions the previously redundant muscle. The valgus alignment also creates a fulcrum at the medial end of the pelvic support. The lower the level of the proximal osteotomy, the more medial the fulcrum. Medialization of the fulcrum decreases the abductor force needed to balance the weight of the body in single-limb stance. The net effect is a marked improvement in the function of the hip abductor mechanism. Extension of the osteotomy contributes to this by stabilizing the hip in the sagittal plane during single-limb stance. If any fixed flexion deformity is present, the pelvis unlocks itself from the “pelvic support” and the fulcrum is lost,
destabilizing the hip and the abductor lever arm. Finally, equalization of the lower-extremity length discrepancy is also important to improve gait mechanics. With a lower-extremity length discrepancy and without use of a shoe lift, the pelvis is tilted. This alters the abductor lever arm and leaves room for adduction of the femur on the pelvis in single-limb stance. Therefore, without equalization of lower-extremity length, pelvic drop cannot be prevented.

A Trendelenburg gait is one of the hallmarks of this condition. Younger children often do not manifest a pelvic drop during gait because of their lighter weight and shorter stride length. As they become adolescents and their height, lower-extremity length, and weight increase, the pelvic drop becomes more apparent. With time, this is associated with increased pain and fatigue while walking, especially toward the end of the day. We found the Ilizarov hip reconstruction to be very effective in eliminating the Trendelenburg gait and sign in these patients. No other treatment method, except for arthrodesis, has been able to address this aspect of the problem successfully. In contrast to arthrodesis, the Ilizarov hip reconstruction preserves an acceptable, painless range of motion of the hip, at least early on. If the patient presents with a painful stiff hip, which was not typical in our series, arthrodesis may be a better option. Ilizarov hip reconstruction is best suited for a patient with an unstable hip that is mobile and associated with a lower-extremity length discrepancy and a Trendelenburg gait. Hip arthrodesis may be avoided in these patients, which is beneficial because that procedure has been associated with pathologic conditions of the ipsilateral knee, contralateral hip, and back.

Two patients in this study underwent the index procedure at a young age. Both had a proximal femoral osteotomy just distal to the level of the lesser trochanter (a high osteotomy). In both patients, the proximal femoral valgus osteotomy site completely remodeled, demonstrating no evidence of the pelvic support within one or two years after the operation. Three other patients had undergone lengthening without a pelvic support osteotomy at a similar young age (six to ten years old). In all three patients, a pelvic support osteotomy was subsequently combined with distal femoral lengthening when they were near skeletal maturity, without subsequent remodeling of the valgus alignment. On the basis of those results, it appears that pelvic support osteotomy is not ideal for young children. Although the procedure is not contraindicated in these young patients, one should expect to have to repeat the pelvic support osteotomy at or near skeletal maturity. Because the amount of lower-extremity length discrepancy requires two lengthenings, or one lengthening and an epiphysiodesis, the pelvic support osteotomy should be reserved for the second lengthening in most cases. The femur can be lengthened at a younger age with extension of the external fixation to the pelvis (Fig. 2-C). Extension of the external fixation to the tibia should also be considered if rotatory subluxation of the tibia is identified.

Ilizarov hip reconstruction is most suitable for skeletally mature adolescents and for young adults. Older adults may be best treated with total hip replacement. An Ilizarov hip reconstruction probably can be converted to a total hip replacement in later life if needed. Schiltenwolf et al. reviewed the results of their long-term follow-up study of twenty-four patients who had undergone subtrochanteric valgus osteotomy without femoral head resection for the treatment of a painful congenitally dislocated hip. Pain relief and improvements in gait and hip abduction and extension were maintained in most patients. Four of the patients underwent total hip replacement without difficulty. If necessary, the proximal femoral deformity can be straightened with an osteotomy and use of a long-stem prosthesis.

This study had limitations. The number of patients was small because of the rarity of this condition, and the follow-up was intermediate-term. Also, although the Harris hip score that was used to evaluate pain and function had been modified to fit this patient population, the modification has not been validated and it has limitations with regard to functional outcome assessment.

In conclusion, the Ilizarov hip reconstruction is a very good option for the treatment of the late sequelae of infantile hip infection in adolescents. It greatly reduces the lower-extremity length discrepancy resulting from this condition while preserving hip motion and improving hip biomechanics. Because all other alternatives for treatment yield relatively unsatisfactory and unpredictable results, Ilizarov hip reconstruction should be considered a promising choice for the management of late sequelae of infantile hip infection.

Appendix

Tables presenting the modified Harris hip score and the clinical and radiographic results for the individual patients are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).
References

Surgical Treatment of Pigmented Villonodular Synovitis of the Hip

BY LAURENT VASTEL, MD, PATRICK LAMBERT, MD, GONZAGUE DE PINIEUX, MD, OLIVIER CHARROIS, MD, MARCEL KERBOULL, MD, AND JEAN-PIERRE COURPIED, MD

Investigation performed at Cochin University Hospital, Paris, France

Background: Pigmented villonodular synovitis of the hip is a rare disease. Synovectomy is generally accepted as the only surgical treatment for the disorder, but there have been few studies with a sufficient sample size and duration of follow-up to allow the evaluation of long-term outcomes. The aim of this study was to determine the long-term outcome of the treatment in sixteen patients.

Methods: Sixteen patients (nine men and seven women), with a mean age of 35.5 years at the time of surgery, were treated between 1970 and 1996. Complete synovectomy was performed in all patients; in addition, three had a cup arthroplasty, four had a total hip arthroplasty, and one had a monopolar arthroplasty. Clinical and radiographic outcomes were evaluated retrospectively at a mean of 16.7 years postoperatively. Only one patient was followed for less than eight years.

Results: Nine patients needed repeat surgery, but only one had recurrent synovitis, as detected with pathological examination fourteen years after treatment with synovectomy and cup arthroplasty. Secondary osteoarthritis developed in all eight patients who had been treated with synovectomy alone, and four of them required a total hip arthroplasty within the follow-up period.

Conclusions: These results support earlier data indicating that osteoarthritis consistently develops in patients with pigmented villonodular synovitis of the hip. Complete synovectomy seems to be effective in preventing recurrence of the synovitis, but it does not appear to prevent the development of secondary osteoarthritis.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

Pigmented villonodular synovitis of the hip is a relatively uncommon disease. Myers and Masi estimated that the worldwide incidence of the disease, at any site in the body, is 1.8 per million per year, with the hip involved in 15% of cases. We are aware of only two published series that included more than ten cases. The cellular proliferation characteristic of pigmented villonodular synovitis is consistent with either inflammation or neoplasia. The pathogenesis has not been elucidated since Jaffé et al. first described the disease in 1941, although recent studies have demonstrated clonal chromosomal abnormalities, findings that support a neoplastic mechanism. The insidious onset of pain and limitation of the range of motion are the most common presenting features of pigmented villonodular synovitis of the hip, which typically show cortical erosions in the acetabulum, femoral neck, and margins of the femoral head, which are often seen as cyst-like structures on anteroposterior radiographs (Fig. 1). Magnetic resonance imaging is currently the best diagnostic investigation. It typically shows an intra-articular effusion, low signal intensity on both T1 and T2-weighted images due to hemosiderin deposition and thick fibrous tissue, synovial hyperplasia, bone erosions, and preservation of bone density and joint space width (Fig. 2).

Synovectomy is generally accepted as the appropriate surgical treatment for pigmented villonodular synovitis, and it can be performed through an open approach or arthroscopically. There have been few case series that have included a sufficient number of patients and duration of follow-up to allow an evaluation of long-term outcomes, including the recurrence rates after surgery (see Appendix). Data on long-term recurrence rates and other outcomes would help to determine the best treatment for this tumor-like condition, which is characterized by a slow rate of progression. The aim of this study was to analyze the effects on disease progression in patients with pigmented villonodular synovitis of the hip treated with open synovectomy alone or combined with reconstructive surgery.

Materials and Methods

Patients

We retrospectively reviewed the cases of sixteen patients (nine men and seven women) in whom pigmented vil-
Pigmented villonodular synovitis had been treated with total synovectomy of the hip at our orthopaedic department from 1970 to 1996. The clinical history, treatment modalities, radiographic and pathological findings, and status before and after surgery were abstracted from the medical records of each patient. The Merle d’Aubigné-Postel score was used to evaluate functional improvements, and the Kellgren-Lawrence grading scale was used to assess the degree of osteoarthritis.

The mean age of the patients at the time of surgery was 35.5 years (range, twenty-three to sixty-one years). The left hip was affected in nine patients and the right, in seven. None of the patients had pigmented villonodular synovitis involving other joints or a known family history of pigmented villonodular synovitis.

**Treatment Modalities**

All sixteen patients were treated with a total synovectomy of the affected hip through a lateral approach with a trochanteric osteotomy, which allowed good visualization of the acetabulum after anterior dislocation of the hip. In patients scheduled to be treated with femoral head preservation rather than total hip arthroplasty, a modified trochanteric osteotomy was performed with preservation of the deepest fibers of the gluteus medius tendon and the piriformis muscle left attached to the femur in order to protect the medial circumflex artery. With this technique, after capsulotomy and section of the round ligament, there is enough space between the pelvis and femur to allow dislocation of the head and achievement of sufficient exposure of the acetabulum.

Arthroplasty was performed in eight patients. In four of them, osteoarthritis with joint space destruction and severe functional impairment prompted implantation of a Charnley-type total hip prosthesis (with cementing of both components). In three patients, a cup arthroplasty (Stryker France, Lyon, France) was used. One patient was managed with a monopolar arthroplasty because of a fracture of the femoral neck without acetabular abnormalities. The remaining eight patients were treated with synovectomy alone: six of them had this more conservative treatment because they had only a minor degree of degenerative arthritis, and the other two patients, who had grade-3 osteoarthritis according to the system of Kellgren and Lawrence, were treated with synovectomy alone because of their young age.

Postoperative care consisted of suction drainage for three days, prophylactic antibiotic therapy for two days, and pharmacological thromboprophylaxis during the six to eight weeks of toe-touch weight-bearing that followed the surgical procedure.

Pathological examination of operative specimens was performed routinely. None of the patients received chemical synovectomy, radiation synovectomy, or external radiation therapy.

**Clinical and Radiographic Features Before Treatment (Table I)**

In one male patient with pigmented villonodular synovitis confined to the femoral neck, a femoral neck fracture at the age of sixty-one years led to the diagnosis. Hip pain was the main presenting symptom in all other patients. Brief episodes of severe pain usually occurred during the first few years. The...
The mean Merle d’Aubigné-Postel score for hip pain prior to the surgery was 3.9 points (3, 4, or 5 points). None of the patients were impaired with regard to their ability to walk. Restriction of flexion or fixed external rotation of the hip related to secondary osteoarthritis was noted in three patients. Moderate instability (a score of 4 or 5 points) due to pain was a consistent finding. The mean global Merle d’Aubigné-Postel score was 13.6 points (range, 10 to 15 points). Moderate swelling over the anterior aspect of the hip was visible and palpable in two patients.

Radiographic findings included the typical features of pigmented villonodular synovitis (Fig. 1): cysts in fourteen patients, eleven of whom had them only in non-weight-bearing zones; femoral neck erosions in five patients; and joint space narrowing in eleven patients, including four with nearly complete obliteration of the joint space.

The three most recently treated patients were evaluated with computed arthrotomography and magnetic resonance imaging, in addition to standard radiography, and those studies provided the primary evidence of the diagnosis. The radiographic features were consistent with erosive coxarthrosis in two patients, who had superolateral osteophytes and joint space narrowing, and with an inflammatory arthropathy of the hip in four patients. The diagnosis of pigmented villonodular synovitis in these six patients was suspected intraoperatively and was confirmed histologically. One patient in whom the diagnosis was made on the basis of a histological examination of a biopsy specimen refused surgical treatment for three years. Excluding the patient who had a femoral neck fracture, the mean time from the onset of symptoms to the diagnosis was 5.7 years (range, ten months to ten years). The patients with radiographic findings suggesting hip osteoar-

### Table I: Study Group

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Gender</th>
<th>Duration of Symptoms (yr)</th>
<th>Preop. Radiographic Findings*</th>
<th>Biopsy</th>
<th>Type of Index Op.†</th>
<th>Recurrence</th>
<th>Time between 1st and 2nd Op. (yr)</th>
<th>Type of 2nd op.</th>
<th>Duration of Follow-up (yr)</th>
<th>Progression of Osteoarthritis (follow-up grade)</th>
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<tr>
<td>1</td>
<td>23</td>
<td>M</td>
<td>4</td>
<td>1</td>
<td>N</td>
<td>Synovectomy</td>
<td>N</td>
<td>18</td>
<td>4</td>
<td>18</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>59</td>
<td>F</td>
<td>4</td>
<td>4</td>
<td>Y</td>
<td>Synovectomy + total hip arthroplasty</td>
<td>N</td>
<td>24</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>43</td>
<td>M</td>
<td>1</td>
<td>4</td>
<td>N</td>
<td>Synovectomy + cup arthroplasty</td>
<td>Y (at 14 yr postop.; treated with synovectomy)</td>
<td>14</td>
<td>Total hip arthroplasty</td>
<td>17</td>
<td></td>
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<tr>
<td>4</td>
<td>61</td>
<td>M</td>
<td>Fracture of fem. neck</td>
<td>N</td>
<td>Monopolar arthroplasty</td>
<td>N</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>5</td>
<td>28</td>
<td>F</td>
<td>5</td>
<td>4</td>
<td>N</td>
<td>Synovectomy + total hip arthroplasty</td>
<td>N</td>
<td>11</td>
<td>Revision</td>
<td>21</td>
<td></td>
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<tr>
<td>6</td>
<td>24</td>
<td>F</td>
<td>5</td>
<td>2</td>
<td>N</td>
<td>Synovectomy + cup arthroplasty</td>
<td>N</td>
<td>11</td>
<td>Total hip arthroplasty</td>
<td>24</td>
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<tr>
<td>7</td>
<td>44</td>
<td>M</td>
<td>10</td>
<td>4</td>
<td>N</td>
<td>Synovectomy + total hip arthroplasty</td>
<td>N</td>
<td>14</td>
<td>Revision</td>
<td>20</td>
<td></td>
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<td>24</td>
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<td></td>
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<td>9</td>
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<td>3</td>
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<td>Synovectomy</td>
<td>N</td>
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<td>Total hip arthroplasty</td>
<td>11</td>
<td></td>
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<tr>
<td>10</td>
<td>41</td>
<td>M</td>
<td>5</td>
<td>3</td>
<td>N</td>
<td>Synovectomy + total hip arthroplasty</td>
<td>N</td>
<td>16</td>
<td>Total hip arthroplasty</td>
<td>28</td>
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<tr>
<td>11</td>
<td>34</td>
<td>M</td>
<td>6</td>
<td>2</td>
<td>Y</td>
<td>Synovectomy</td>
<td>N</td>
<td>16</td>
<td>Total hip arthroplasty</td>
<td>28</td>
<td></td>
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<tr>
<td>12</td>
<td>31</td>
<td>F</td>
<td>7</td>
<td>3</td>
<td>N</td>
<td>Synovectomy + cup arthroplasty</td>
<td>N</td>
<td>9</td>
<td>Total hip arthroplasty</td>
<td>25</td>
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<td>8</td>
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<tr>
<td>14</td>
<td>28</td>
<td>F</td>
<td>8</td>
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<td>Synovectomy</td>
<td>N</td>
<td>14</td>
<td>2</td>
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<td>Synovectomy</td>
<td>N</td>
<td>11</td>
<td>Total hip arthroplasty</td>
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<td></td>
</tr>
</tbody>
</table>

*1 = normal, 2 = changes but no joint space narrowing, 3 = joint space narrowing, and 4 = joint space collapse. †The patients who had more than one operation had them performed simultaneously.
thritis had the longest intervals between symptom onset and diagnosis.

Results
Pathological Results
Histological examination showed proliferation of synovial cells and histiocytes with multinucleate giant cells in both nodular and villous areas in all specimens. Hemosiderin granules were found in eleven of the sixteen patients. No differences were noted between the primary and the recurrent lesions in the one patient who had recurrent disease. Pathological examination of the recurrent lesion showed cellular proliferation of pigmented villonodular synovitis with fibrous tissue infiltration. Multinucleate giant cells were regularly scattered throughout the lesion. The mitotic rate was six mitoses per ten high-power fields (magnification, ×400). No cytological atypia or malignant change was identified.

Clinical and Radiographic Results (Table I)
The mean duration of follow-up was 16.7 years (range, one to twenty-eight years); the patient treated with the unipolar arthroplasty was lost to follow-up after one year. None of the eight patients who did not undergo arthroplasty had clinical or radiographic evidence of recurrent pigmented villonodular synovitis. However, secondary osteoarthritis developed in all eight patients. It manifested as worsening mechanical pain and joint space narrowing, sclerosis, and osteophytosis on radiographs. Total hip arthroplasty was required in four of those eight patients, nine to sixteen years after the synovectomy (Fig. 3). None of the patients had the development of femoral head osteonecrosis related to the transtrochanteric approach. Histological examination of specimens from the femoral head and capsule that had been removed during the arthroplasties showed no evidence of recurrent pigmented villonodular synovitis. At the time of this report, none of the other four patients who had had a synovectomy alone had undergone additional surgery, but they had radiographic evidence of osteoarthritis.

All three patients treated with a cup arthroplasty had mechanical cup failure with migration requiring total hip arthroplasty nine to fourteen years after the synovectomy. The outcomes after the total hip arthroplasties were good. One of the three patients, who underwent the total hip arthroplasty at fourteen years after the synovectomy, was found, at the time of surgery, to have recurrent or persistent pigmented villonodular synovitis, which had not caused bone cysts. Of the four patients who had undergone total hip arthroplasty at the time of the synovectomy, two required revision arthroplasty, after eleven and fourteen years, because of aseptic loosening of the acetabular component. No histological evidence of recurrent pigmented villonodular synovitis was found in either patient. Of the fifteen patients followed for longer than two years, nine required a second operation, which provided material for pathological examination.

Discussion
Most published series of patients with pigmented villonodular synovitis, of which we are aware, included a small number of patients with a short duration of follow-up. The diagnosis has been facilitated in recent years by advances in magnetic resonance imaging and arthroscopic biopsies for histological confirmation. However, the long-term outcomes after surgical synovectomy for pigmented villonodular synovitis of the hip are not well known. In an extensive review of the literature, we identified 150 well-documented cases of pigmented villonodular synovitis of the hip (see Appendix).

In the present study, the mean age of the patients at the time of diagnosis was 35.5 years (range, twenty-three to sixty-one years). Similarly, in the largest study of pigmented villonodular synovitis of the hip of which we are aware, Cotten et al. found that their fifty-eight patients had a mean age of thirty-eight years at diagnosis. Schwartz et al. reported a mean age of 36.9 years at diagnosis in a series of twenty patients, and Gitelis et al. noted a mean age of 34.8 years for sixty-four patients identified in a literature review. Women were more often affected than men in most studies, with a female-to-male ratio of 2:1, although Jaffé et al. reported a slight male predominance. The symptom duration before diagnosis in the present study ranged from ten months to ten years (excluding the patient who had a femoral neck fracture), with a mean of 5.7 years. This finding is consistent with those in earlier studies, including a recent meta-analysis by Gonzalez Della Valle et al., in which the mean symptom duration was four years. We believe that this lag in diagnosis is evidence of the slow rate of progression of pigmented villonodular synovitis.

One patient in our study was found to have an asymptomatic recurrence (or persistence) of the synovitis fourteen years after the synovectomy. Thus, data from case series with short follow-up should be considered with caution.

The symptom duration before the diagnosis was longer for two of our patients who had radiographic changes consis-
tomy, total hip arthroplasty is performed at the time of synovec-
tomy in our sixteen patients, recurrence may be less common when
with grade-2 or 3 arthritis against osteoarthritic progression. Three of the four patients
were grade-0 or 1 arthritis at the time of treatment with synovec-
tomy and notable osteoarthritis developed in all four patients who
had had grade-0 or 1 arthritis at the time of treatment with synovec-
tomy alone, although only one had undergone arthro-
plasty during the follow-up period. Synovectomy seemed to
provide relief of symptoms for many years before manifesta-
tions of secondary osteoarthritis developed, but osteoarthritic
progression seemed relatively similar in all patients. Advances in
magnetic resonance imaging (Fig. 2) will likely decrease the
interval between the initial evaluation and treatment, thereby
reducing the proportion of patients who have severe osteoar-
thritis at the time of diagnosis of pigmented villonodular syno-
vitis. In addition, magnetic resonance imaging provides
more information on the extent of the synovitis, thus facilitat-
ing surgical planning. Finally, magnetic resonance imaging is
valuable for monitoring the patients after surgery. As it has
been established that pigmented villonodular synovitis pro-
gresses slowly and open synovectomy failed to protect the hip
from progression of osteoarthritis in our study, arthroscopic
synovectomy might deserve consideration for patients with
limited and very slowly progressive pigmented villonodular
synovitis. However, the long-term outcomes of such treatment
need to be evaluated.

Appendix

A table presenting details of 150 well-documented cases of
pigmented villonodular synovitis of the hip is available
with the electronic versions of this article, on our web site at
jibs.org (go to the article citation and click on “Supplementary
Material”) and on our quarterly CD-ROM (call our subscrip-
tion department, at 781-449-9780, to order the CD-ROM).

The authors did not receive grants or outside funding in support of their
research or preparation of this manuscript. They did not receive pay-
ments or other benefits or a commitment or agreement to provide such
benefits from a commercial entity. No commercial entity paid or
directed, or agreed to pay or direct, any benefits to any research fund,
organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.C.01297

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Surgical Treatment of Pigmented Villonodular Synovitis of the Hip


Complications of Fluoroscopically Guided Extraforaminal Cervical Nerve Blocks

An Analysis of 1036 Injections

By Daniel J. Ma, MS III, Louis A. Gilula, MD, and K. Daniel Riew, MD

Background: A number of serious complications associated with fluoroscopically guided extraforaminal cervical nerve blocks have been reported in the literature. The purpose of the present study was to determine the rate of complications associated with these blocks and to determine whether needle positioning during the procedure affected the prevalence of complications at one institution.

Methods: Between October 1999 and June 2003, we performed 1036 fluoroscopically guided extraforaminal cervical nerve blocks in 844 patients. Plain radiographs documenting the procedure were made as part of the standard quality-assurance protocol. An independent observer who was uninvolved with the procedures reviewed a prospectively kept database on all patients. We subsequently reviewed the patient records to identify complications.

Results: There were no catastrophic complications such as vessel damage, paralysis, or death. Overall, fourteen patients (1.66%) had a minor complication in association with the procedure. With the numbers available, the rate of complications associated with deep injection (798 blocks) was not significantly different from that associated with shallow injection (238 blocks) (1.89% compared with 0.84%). However, the rate of complications associated with anterior placement of the needle tip (thirty-three blocks) was higher than that associated with ideal placement of the needle tip (904 blocks) (6.06% compared with 1.55%) (p = 0.04).

Conclusions: No catastrophic complications occurred in this series of 1036 nerve blocks. We found that the medial-lateral needle depth as seen on frontal-view radiographs was not associated with complications, although the anterior positioning of the needle as seen on lateral-view radiographs was associated with minor complications. Our results suggest that, with our technique, cervical nerve blocks are relatively safe procedures.

Level of Evidence: Therapeutic Level III. See Instructions to Authors for a complete description of levels of evidence.

Fluoroscopically guided extraforaminal cervical nerve blocks are a noninvasive alternative to surgical treatment. In addition, they have been reported to be of value in helping to determine the pain-generating level preoperatively. Fluoroscopic guidance was added as a means of avoiding needle misplacement associated with blind cervical nerve blocks.

As with any nerve block, minor complications such as headache, temporary pain, nausea, numbness, and weakness have been associated with the procedure. Alarming reports have also been recent case reports of fatal spinal cord infarction, injection into an anterior radicular artery, and puncture of the epidural sac of the nerve root sleeve. In addition, there has been concern regarding potential injury to the vertebral artery. The potential for these and other catastrophic complications, and the associated potential for litigation, have anecdotally prompted some groups to advocate protocols that maintain shallow needle position.
Materials and Methods

All patients who received a fluoroscopically guided extraradicular cervical nerve block at our institution between October 1999 and June 2003 were included in the present retrospective study. One thousand and thirty-six injections were performed on 844 patients, for an average of 1.23 injections per patient. The average age of the patients at the time of injection was forty-seven years. Fifty-four percent of the patients were women, and 46% were men. The large majority of patients had symptoms related to either disc herniation or foraminal stenosis and had been referred by a single orthopaedic spine surgeon (K.D.R.). Blocks were performed either for verification of a pathological nerve root level or to prevent or delay the need for surgery. The injections were performed by or under the direction of three attending radiologists in our radiology department. All three radiologists used a standardized technique, which was verified prospectively by the senior radiologist (L.A.G.) by means of a quality-assurance review of all of the injections.

Before the procedure, each patient completed a form indicating the distribution pattern of pain as well as the severity of pain on a scale from 0 to 10. For the procedure, the patient was placed in the lateral decubitus position with the side of interest elevated. C-arm fluoroscopy was used to place a 25-gauge needle into the extraradicular area of the level of interest. The needle was inserted to slide along the anterior surface of the articular pillar (lateral mass) and was kept as posterior as possible in order to avoid the vertebral artery. To ascertain that the needle tip was not located in a vascular structure, myelographic contrast material (iohexol) (Omnipaque 180 or 300; Amersham Health, Princeton, New Jersey) was injected prior to the injection of the anesthetic and medication mixture. Once the needle was adequately positioned, 1 mL of Celestone Soluspan (betamethasone sodium phosphate and betamethasone acetate; Schering-Plough, Chatsworth, Georgia) with 0.5 mL of preservative-free 2% lidocaine or Xylocaine, or 0.5 mL of methylprednisolone acetate suspension (DepoMedrol 80 mg/mL; Pharmacia-Upjohn, Kalamazoo, Michigan) with 0.5 mL of 2% preservative-free Xylocaine and 0.5 mL Omnipaque 180 or 300, for a total volume of 1.5 mL, was injected. DepoMedrol was used later in the study period as Celestone became unavailable commercially. Images were made during and after injection to verify needle tip placement.

A duplicate fluoroscopic record of each procedure was obtained prospectively as part of our standard quality-assurance protocol. Every patient was observed for ten to twenty minutes after the injection and was given a follow-up form regarding pain. Immediate pain relief and complications were recorded in the dictated radiographic report. Patients were instructed to contact the referring doctor if delayed complications occurred. An independent observer (D.J.M.) who had not been involved in the procedures reviewed a prospectively kept database on all patients who had undergone cervical nerve blocks during the study period. Radiographs were reviewed, and the needle position in both the frontal and lateral views was noted and labeled. Uncertainties about needle position were resolved by means of a consensus between the independent reviewer and the radiologist (L.A.G.).

On the frontal view, needle depth was measured with use of the lateral mass as a marker. Needle tips that were peripheral to the lateral border of the lateral mass were labeled as being in Zone 1. Needle tips overlying the lateral mass but lateral to the midline were labeled as being in Zone 2. Needle tips overlying the medial half of the lateral mass but within the...

Fig. 1
Frontal view of a cervical spine model, demonstrating the boundaries of the various frontal zones. (See the text for a description of Zones 1 through 4.)
mass were labeled as being in Zone 3. Needle tips medial to the lateral mass were labeled as being in Zone 4 (Fig. 1). Needle tips that were on the boundary between zones were labeled as being within the deeper zone.

On the lateral view, ideal needle placement (defined as placement directly on the anterior edge of the lateral mass) was labeled as Zone A. Needle positions that were within two needle-tip diameters anterior to Zone A were labeled as Zone B. Positions further anterior than Zone B were labeled as Zone C (Fig. 2). Radiographs with inadequate lateral views were labeled U. Radiographs were labeled inadequate if the lateral masses did not overlap by at least 50%.

A thorough review of a list of complications concurrently recorded by the radiology department as well as of all procedure reports was performed to identify which procedures were associated with complications. These complications were matched to the needle position within the radiographic image. Institutional review board approval was obtained for this retrospective study.

**Results**

No catastrophic complications such as death, paralysis, stroke, spinal cord injury, vertebral artery injury, or infection were recorded. Seventeen injections (1.64%) were associated with complications, most of which were minor and transient (Tables I and II). Two patients with complications had multiple injections: one had had two simultaneous injections, and the other had had three. Thus, a total of fourteen patients (1.66%) had a complication in association with the procedure. Ninety-nine injections were excluded because of an inadequate lateral fluoroscopic record. None of these injections were associated with any reported complications, and all were excluded only because of the inability to analyze the radiographs.

The prevalence of minor complications according to needle position is summarized in Table I. The complications that were encountered are summarized in Table II. Three patients had symptoms that probably were linked to uncontrolled diabetes, concomitant neurological findings, or alcohol consumption, but we included them for completeness. One patient who had transient global amnesia, dizziness, and nausea was admitted to the hospital overnight and had a thorough neurological workup, which revealed negative findings. The dizziness had resolved by two weeks.

In addition to the fourteen patients who had complications, two patients received the injection at the wrong level.
and one patient received a facet block instead of a nerve block. While the wrong-level injections and the facet injection did not produce complications, they do nevertheless represent complications of the procedure. For the purposes of statistical analysis, however, we did not consider these procedural errors as complications.

Chi-square tests were performed to determine whether there were any significant differences in the rate of complications associated with differences in needle placement. Analysis of needle tip depth on the frontal view revealed no significant difference, with the numbers available, between the rate of complications associated with deep injections (Zones 3 and 4; 798 blocks) and that associated with superficial injections (Zones 1 and 2; 238 blocks) (p = 0.31). Analysis of needle placement on the lateral view, however, demonstrated a significant result. Specifically, the rate of complications associated with skewed (anterior) placement of the needle tip (Zone C; thirty-three blocks) was significantly higher than that associated with ideal or near-ideal placement of the needle tip (Zones A and B; 904 blocks) (p = 0.04).

Discussion

Several small series have established the efficacy of fluoroscopically guided extraforaminal cervical nerve blocks. The complications associated with this procedure, however, have only been mentioned in passing in those articles as well as in isolated case reports. To our knowledge, the present study represents the largest reported series of such blocks to date as well as the only study that has focused on the complications of such blocks.

Several articles have described catastrophic complications that have occurred in association with fluoroscopically guided extraforaminal cervical nerve blocks. Intravascular penetration has always been the primary concern related to this procedure. Furman et al. attempted to address this concern by detailing the prevalence of intravascular penetration associated with transforaminal procedures. However, none of their 337 patients experienced symptoms associated with intravascular contrast medium because the needle was immediately repositioned if any contrast medium was found to pass intravascularly. Our study confirmed this finding. The risks of intravascular injection can be minimized by injecting contrast medium before performing the nerve block. We observed none of the catastrophic complications that have been associated with intravascular penetration, and we have modified our injection procedure to avoid intravascular injection by adding

<table>
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<th>Complication</th>
<th>Number of Patients with Complications</th>
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<tr>
<td>Headache/dizziness</td>
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<tr>
<td>Transient neurologic deficits (pain or weakness)</td>
<td>6</td>
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<tr>
<td>Hypersensitivity reaction</td>
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**Fig. 3-A** Oblique radiograph demonstrating the needle tip and contrast medium projecting over the posterior aspect of the extraforaminal area.

**Fig. 3-B** Lateral radiograph of the same patient. What appeared to be an adequate needle tip position on the oblique radiograph is actually an anteriorly placed needle tip position on the true lateral radiograph.
contrast medium to the final injectate. Another method for preventing intravascular injection is to attach the needle to a thin-walled, short lymphangiographic tube (MX453; Medex, Dalton, Ohio) through which contrast medium can be injected. Another syringe containing the injectate can then be attached to the free end of the connecting tube to inject the medication, thereby eliminating the need to retouch the needle to instill the injectate.

The International Spine Injection Society and Windsor et al. recommend frontal and oblique radiographic views for verification of needle tip position. The importance of lateral views was not stressed. It has been our experience, however, that an apparently adequate needle position as seen on the oblique view does not necessarily translate into an adequate needle position on the lateral view. In order to prevent damage to the vertebral artery, we routinely keep the needle close to the anterior surface of the lateral mass, a position that can only be ascertained on a true lateral view. This is relevant because we also found that anteriorly positioned needles were associated with a higher complication rate than more posteriorly positioned needles were.

As with any study, the present study is not without flaws. This was a retrospective study and therefore is constrained by the limitations of such analyses. As is the case with all retrospective studies, we cannot be certain if there were any unreported complications that occurred. Our standard policy was to inform the patient of the potential known or probable complications of the procedure, including all of the complications that we have analyzed. All patients were observed in the radiology department postoperatively in order to identify any immediate complications, which were duly recorded. Upon discharge, the patients were given specific instructions about how to contact the radiology department in order to notify us of any late complications. In addition, all patients were instructed to contact the referring doctor, both to notify him or her of the results of the injection as well as to report any complications. Despite all of these precautions, we believe that it is quite probable that a certain number of patients may have suffered a minor complication without informing the physicians or that the referring doctor may have neglected to inform the radiologist. However, problems such as death, stroke, and paralysis are not subtle findings and cannot be ignored or self-treated by the patient. We believe that it is highly unlikely that these catastrophic events could have occurred without our knowledge. As stated previously, all patients were requested to fill out a post-injection questionnaire regarding the immediate and one-week results. While we did not specifically use the questionnaire to detect complications, we believe it provided the patients with an additional means of informing their referring doctors of any complications.

Another shortcoming of our study is that the static fluoroscopic image that we utilized to analyze the position of the needle recorded only where the needle was at the time that the image was made. However, we took specific precautions to prevent accidental movement of the needle during the procedure. All of the injections were performed under fluoroscopic control, and the needle was repositioned correctly if any movement was detected on the fluoroscopic image. Also, a post-injection image was made to verify the position of the needle tip. Therefore, we believe that the spot image that was recorded reasonably reflects the actual location of the injection. As with any technique-dependent procedure, our results will not be universally reproducible. Nevertheless, we believe that, in competent hands, our results will be reproducible at other institutions as there were no apparent differences with regard to complication rates among the three radiologists at our institution.

In conclusion, case reports on complications can be unnecessarily alarming in that they most often do not provide the prevalence of such complications. We undertook the present study on nerve blocks that had been performed at a single institution to put such complications into perspective. There were no catastrophic complications, and the rate of minor complications was low. We believe that the risk of complications can be further minimized by positioning the needle as posteriorly as possible, hugging the anterior wall of the lateral mass. Our results suggest that, in experienced hands, the described technique for cervical nerve root blocks has an acceptable safety profile.

NOTE: The authors thank Dr. Thomas Pilgrim for his assistance with the statistical analysis.

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The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.02139

References


Impact of Educational Intervention on Confidence and Competence in the Performance of a Simple Surgical Task

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Investigation performed at the Department of Orthopaedics and Sports Medicine, University of Washington Medical Center, Seattle, Washington

Background: Many complex new procedures involve a learning curve, and patients treated by individuals who are new to a procedure may have more complications than those treated by a practitioner who has performed the intervention more frequently. Still, at some point on the learning curve, each individual must decide that he or she is qualified to perform a procedure, presumably on the basis of his or her level of confidence, background, education, and skill. To evaluate the interrelationship of these factors, we designed a study in which we assessed the performance of a simulated knee joint injection.

Methods: Ninety-three practitioners attending a continuing medical education session on knee injection were randomized to receive skills instruction through the use of a printed manual, a video, or hands-on instruction; each performed one injection before and after instruction. The participants completed pre-instruction and post-instruction questionnaires gauging confidence and also provided self-assessments of their performances of injections before and after instruction. Self-assessments were compared with objective performance standards measured by custom-designed knee models with electronic sensors that detected correct needle placement.

Results: Before instruction, the participants’ confidence was significantly but inversely related to competent performance ($r = -0.253, p = 0.02$); that is, greater confidence correlated with poorer performance. Both men and physician-practitioners displayed higher pre-instruction confidence ($p < 0.01$), which was not correlated with better performance. After instruction, performance improved significantly in all three training groups ($p < 0.001$), with no significant differences in efficacy detected among the three groups ($p = 0.99$). After instruction, confidence correlated with objective competence in all groups ($r = 0.24, p = 0.04$); however, this correlation was weaker than the correlation between the participants’ confidence and their self-assessment of performance ($r = 0.72, p = 0.001$).

Conclusions: Even low-intensity forms of instruction improve individuals’ confidence, competence, and self-assessment of their skill in performing the fairly straightforward psychomotor task of simulated knee injection. However, men and physicians disproportionately overestimated their skills both before and after training, a finding that worsened as confidence increased. The inverse relationship between confidence and competence that we observed before the educational intervention as well as the demographic differences that we noted should raise questions about how complex new procedures should be introduced and when self-trained practitioners should begin to perform them.

Level of Evidence: Therapeutic Level I. See Instructions to Authors for a complete description of levels of evidence.
sive for most interventions. However, at some point on the learning curve, each individual must decide that he or she is qualified to perform a procedure. Since there is no certification process for individual orthopaedic procedures, this decision must be made by individual surgeons, who presumably base it on their level of confidence, background, education, and skill.

Minimally invasive procedures are being developed and disseminated at a rapid rate in orthopaedic surgery, and most surgeons will need to learn these procedures in a milieu other than traditional residency training. As a result, understanding how one arrives at the decision that one is ready to perform a particular task and determining whether that choice is reasonable and safe are important subjects for research. We are not aware of any previously published work on these topics. Moreover, relatively little is known about the efficacy of different methods used in medical education to teach psychomotor tasks, and, while confidence with particular tasks has been studied to a limited degree, the relationship between an individual’s perception of his or her psychomotor skills and objective measures of competence has hardly been explored.

In this study, in which practitioners performed a simulated knee joint injection on an anatomic model, which we considered to be a simple surgical task, the following hypotheses were tested:

1. There is a relationship between an individual’s confidence in his or her ability to perform a task and his or her ability to perform the task competently.
2. Psychomotor skills education improves the correlation between confidence and competence.
3. Demographic variables are associated with differences in the confidence-competence relationship.

Materials and Methods
Participants and Study Sites
All participants at an approved continuing medical education course on outpatient management of musculoskeletal disorders, taught by orthopaedic surgeons, were invited to participate in this study, which took place over the course of an afternoon laboratory session on knee joint injections. Of 134 attendees of the course, ninety-three licensed practitioners whose practice included knee joint injections, or would perhaps include them in the future, agreed to participate. The education and practice backgrounds of the practitioners varied, but included forty-three allopathic physicians (Medical Doctors), three osteopathic physicians (Doctors of Osteopathy), thirty-five advanced registered nurse-practitioners, and twelve physicians’ assistants.

This study was reviewed and granted a certificate of exemption by the human subjects division of the medical center’s institutional review board.

Study Intake, Baseline Questionnaires, and Pretest
All study participants attended a fifteen-minute illustrated presentation on the indications for knee joint injection and aspiration, the risks of the procedure, sterile technique, anatomic landmarks, needle position, and needle insertion through the superolateral approach. Participants were asked to complete a background questionnaire that elicited information concerning their type of practice (internal medicine, family practice, or other), number of years in practice since completion of training, gender, age, number of knee injections/aspirations performed in the last year, formal training in this procedure, and preferred approach to knee injection (superolateral, superomedial, anteromedial, anterolateral, or other). Each practitioner was asked to rate his or her confidence about performing the following tasks: measuring blood pressure, performing bone marrow biopsy, and injecting a knee joint through the superolateral approach. A 10-point Likert scale, ranging from “not confident” (1 point) to “very confident” (10 points), was used for self-assessment of confidence. In the population that we studied, measuring blood pressure is considered to be a basic skill that all practitioners should be confident about performing, and it was used as a positive control in this study. In contrast, few if any of the practitioners attending this course would perform bone marrow biopsy as part of routine practice, and we expected relatively low levels of confidence with regard to this task; this was the negative control on the confidence questionnaire. This approach has been used in other studies on the confidence of medical practitioners.

Next, all study subjects were asked to mark the relevant anatomic landmarks (superior pole of the patella and lateral border of the patella), simulate a sterile skin preparation, and perform a knee joint injection with use of superolateral needle placement on a custom-built anatomic knee model (Sawbones, Pacific Research Laboratories, Vashon, Washington). The models have several layers of foam “tissues” that are designed to simulate the feel of injecting a human limb, and they incorporate an electrical conductive system that provides audio feedback when the needle is positioned in the knee joint. The models were created to specifications designed to simulate a moderate knee-joint effusion, with the suprapatellar pouch extending 1 cm proximal to the superior pole of the patella. The models were constructed in this way so as not to make the task overly challenging, in view of a recent study that demonstrated the difficulty of reliably achieving intra-articular needle placement in knees without joint effusions.

An overlay apparatus made for each model allowed trained preceptors to readily grade the accuracy of needle placement in a reproducible manner. The preceptors graded each injection attempt on a 10-point scale that included several elements: simulating sterile skin preparation (1 point), marking anatomic landmarks that define the injection site (1 point each for being within 5 mm of the superior pole and the lateral border of the patella), inserting the needle at the correct angle (1 point if it was within 30° of being perpendicular to the thigh and 30° of being parallel to the floor), gaining entry to the knee with as few repeat attempts as possible (3 points for zero or one redirect, 1 point for two or three redirects, and no points for four or more attempts), and gaining entry to the
knee in as short a time as possible after the needle was inserted (3 points if entry was gained within ten seconds, 1 point if it was gained in eleven to twenty seconds, and no points if it was gained in more than twenty seconds). The participants were not informed that they were being timed during this exercise.

After performing the pre-instruction injection, each participant was asked to rate his or her own performance with use of a 10-point Likert scale, anchored with “unsatisfactory” (1 point) and “very skillful” (10 points).

### Randomization and Study Educational Intervention

Next, a table of random numbers was used to randomly assign participants to one of three study groups. The participants in each study group then received further instruction on knee joint injection through the superolateral approach in one of three ways: Group I was given a printed guide demonstrating the superolateral technique of knee joint injection, Group II watched a CD-ROM video demonstrating the superolateral technique of knee joint injection, and Group III received hands-on instruction by a trained tutor.

The printed guide included descriptions as well as illustrations (line drawings and photographs) of the relevant anatomy and of the recommended needle placement and insertion; it also briefly reviewed the alternative approaches and how to perform a sterile skin preparation properly. Practitioners assigned to this group were allowed to spend as much time as they wanted reviewing the guide, and they were permitted to refer to it during the study (although not while they were actually performing the injection). The CD-ROM video covered the same material and used the same static illustrations, but it also included an audio component describing the procedure and it depicted a knee joint injection through the superolateral approach carried out in real time. Participants who were randomized to receive hands-on instruction spent five to ten minutes with a trained preceptor (a fellow in adult reconstruction, a rheumatologist, or an orthopaedic surgeon) and then had the opportunity to perform supervised practice injections, with feedback from the instructor, until each participant indicated that he or she was comfortable enough with the technique to demonstrate an injection for testing purposes to a preceptor other than the one who provided the hands-on instruction.

### Table I: Association of Demographic Variables with Confidence and Competence Before Instruction

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean Score for Confidence (and Standard Deviation) on 10-Point Likert Scale</th>
<th>Mean Score for Performance (and Standard Deviation) on 10-Point Objectively Graded Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred approach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superolateral</td>
<td>4.88 ± 2.33</td>
<td>6.83 ± 2.70</td>
</tr>
<tr>
<td>Other</td>
<td>3.92 ± 2.92</td>
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<td>NS</td>
</tr>
<tr>
<td>Years of practice</td>
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<td></td>
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<td>≤ 5</td>
<td>3.72 ± 2.67</td>
<td>6.69 ± 2.54</td>
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<td>4.43 ± 2.90</td>
<td>5.93 ± 2.64</td>
</tr>
<tr>
<td>P value*</td>
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<td>NS</td>
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<td>Age</td>
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<td>&gt; 46 yr</td>
<td>4.20 ± 3.17</td>
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<tr>
<td>≤ 46 yr</td>
<td>3.95 ± 2.41</td>
<td>6.70 ± 2.69</td>
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<td>P value*</td>
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<td>NS</td>
</tr>
<tr>
<td>No. of injections performed in last yr</td>
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<td></td>
</tr>
<tr>
<td>≥ 3</td>
<td>6.57 ± 2.18</td>
<td>5.81 ± 2.58</td>
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<tr>
<td>&lt; 3</td>
<td>3.17 ± 2.40</td>
<td>6.59 ± 2.81</td>
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<tr>
<td>P value*</td>
<td>&lt;0.01</td>
<td>NS</td>
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<tr>
<td>Gender</td>
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<td>Male</td>
<td>6.32 ± 2.68</td>
<td>6.62 ± 2.58</td>
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<tr>
<td>Female</td>
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<td>5.86 ± 2.81</td>
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<tr>
<td>P value*</td>
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<td>NS</td>
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<td>Type of practitioner</td>
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<td>Physician</td>
<td>5.32 ± 2.59</td>
<td>6.36 ± 2.76</td>
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<tr>
<td>Non-physician</td>
<td>2.78 ± 2.43</td>
<td>6.40 ± 2.63</td>
</tr>
<tr>
<td>P value*</td>
<td>&lt;0.01</td>
<td>NS</td>
</tr>
</tbody>
</table>

*NS = not significant (p > 0.1).
Impact of Educational Intervention on Confidence and Competence in the Performance of a Simple Surgical Task

Post-Test and Outcomes Assessment

Following instruction with one of the three described methods, each practitioner was asked to rate again his or her confidence about injecting a knee joint through the superolateral approach. The same 10-point Likert scale was used for self-assessment of confidence, with 1 point representing “not confident” and 10 points representing “very confident.” Participants then were asked, for a second time, to simulate a sterile skin preparation and to perform a knee joint injection with superolateral needle placement on the custom-built anatomic knee model, and this second effort was graded by trained preceptors using the same 10-point scale as they used to grade the first injection. To avoid bias, preceptors who performed the hands-on instruction were not permitted to grade their own students on the second (post-instruction) knee injection. Following the post-instruction injection, each participant was asked to rate his or her own performance on a 10-point Likert scale in which 1 point represented “unsatisfactory” and 10 points represented “very skillful.”

Statistical Methods

Comparisons between groups were made by the study biostatistician using one-way analysis of variance with post hoc comparisons, t tests, and Pearson correlation coefficients as appropriate to the comparison of interest. All analytic procedures were conducted with use of SPSS version-10.1 software (SPSS, Chicago, Illinois). Significance was set at the p < 0.05 level for all comparisons.

Results

Baseline Comparisons

Before instruction, the practitioners reported a mean confidence level of 9.88 of 10 points on the Likert scale for measuring blood pressure, 4.04 for knee joint injection, and 1.62 for bone marrow biopsy; this framed the knee joint injection task as intermediate between very familiar and unfamiliar and tended to validate the use of the Likert-scale confidence instrument.

Before instruction, there were no significant differences in confidence or skill between any of the following groups of practitioners: those who listed a preference for a superolateral approach and those who preferred another approach for the knee injection, those with five or fewer years of practice experience and those with six or more years of experience, and those older than the median age of forty-six years and those younger than that age (Table I). Practitioners who reported performing three or more injections in the previous year were significantly more confident than those who performed two or fewer injections (6.57 compared with 3.17 points on the 10-point scale, p < 0.01), although there was no significant difference in the results of the objective pre-instruction performance assessments between these two groups (5.81 compared with 6.59 points, p > 0.1). It is worth noting that only five practitioners estimated that they had performed more than ten injections in the year before they attended the course, so there was no opportunity to perform a significant correlation analysis with a larger number of cases. Nevertheless, the results of the objective pre-instruction performance assessments between these two groups (5.81 compared with 6.59 points, p > 0.1).

Fig. 1

A significant but inverse relationship was identified between practitioner confidence (x axis) and objectively graded performance of simulated knee joint injections (y axis) before the practitioners received formal instruction (r = −0.253, p = 0.02); that is, increased confidence was associated with poorer objective performance on the pre-instruction knee injection test. The number of points on each icon indicates the number of observations at that x-y point. Circles represent a frequency count of 1, and each line radiating from the circle represents an additional observation, so that 2, 3, 4, 5, 6, or more points indicates frequencies of 2, 3, 4, 5, 6, or more observations, respectively, at that x-y point.

Fig. 2

After formal instruction, a significant positive correlation was observed between confidence (x axis) and objectively graded performance of simulated knee joint injections (y axis) (r = 0.24, p = 0.04). The number of points on each icon indicates the number of observations at that x-y point. Circles represent a frequency count of 1, and each line radiating from the circle represents an additional observation, so that 2, 3, 4, 5, 6, or more points indicates frequencies of 2, 3, 4, 5, 6, or more observations, respectively, at that x-y point.
evaluate true high-volume practitioners with respect to this issue. Before instruction, there were no significant differences in performance or confidence among the individuals randomized to the three educational intervention groups, which tended to validate the randomization.

Before instruction, male participants were significantly more confident (6.32 of 10 points on the Likert scale) than female participants (2.95 of 10 points) (p < 0.01). However, before instruction, there was no significant difference between the objective performances of the men and the women (6.62 and 5.86 points, respectively; p > 0.05). Also, before instruction, physicians were more confident than non-physicians (5.32 and 2.78 points, respectively; p < 0.01), but no significant difference in the objective performance was observed between physicians and non-physicians (p > 0.1) (Table I).

Confidence before instruction was significantly and inversely correlated with objective performance before instruction (r = −0.253, p = 0.02); that is, greater confidence was associated with poorer objective performance on the pre-instruction knee-injection test (Fig. 1). However, confidence before instruction was strongly and directly correlated with the participants’ assessment of their own performance of the pre-instruction joint injection (r = 0.42, p = 0.001); that is, confidence was associated with overestimation of self-assessed performance of this simple psychomotor task.

### After Formal Instruction

After participants underwent formal training in knee joint injection with use of one of the three educational interventions, the confidence-performance link changed from the inverse relationship observed before the instruction to a direct (positive) correlation (r = 0.24, p = 0.04; Fig. 2). However, this correlation was not nearly as strong as that observed between participants’ confidence after instruction and participants’ self-assessment of post-instruction performance (r = 0.72, p = 0.001). These findings suggest that both before and after instruction, increased levels of confidence among these practitioners were correlated with overestimation of their own skills at knee joint injection.

After instruction, physicians continued to self-report higher confidence scores than non-physicians (8.22 compared with 6.98 points, p < 0.01), a difference that was not associated

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean Score for Confidence (and Standard Deviation) on 10-Point Likert Scale</th>
<th>Mean Score for Performance (and Standard Deviation) on 10-Point Objectively Graded Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred approach</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Superolateral</td>
<td>8.08 ± 1.05</td>
<td>8.50 ± 2.22</td>
</tr>
<tr>
<td>Other</td>
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<td>7.89 ± 2.54</td>
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<td>P value*</td>
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<td>NS</td>
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<td>Years of practice</td>
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<td>≤5</td>
<td>7.76 ± 1.94</td>
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<td>&gt;5</td>
<td>7.50 ± 1.89</td>
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<td>P value*</td>
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<td>Age</td>
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<td>&gt;46 yr</td>
<td>7.57 ± 2.12</td>
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<td>7.53 ± 1.69</td>
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<td>7.73 ± 2.71</td>
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<td>Female</td>
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<td>Physician</td>
<td>8.22 ± 1.43</td>
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<td>6.98 ± 2.08</td>
<td>8.18 ± 2.34</td>
</tr>
<tr>
<td>P value*</td>
<td>&lt; 0.01</td>
<td>NS</td>
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</table>

*NS = not significant (p > 0.1).
with better performance on the post-instruction objectively scored knee joint injection test by the physicians (8.00 points for the physicians and 8.18 points for the non-physicians, $p > 0.05$). After instruction, female study participants were significantly more confident than male participants (8.77 compared with 6.98 points, $p < 0.01$) and also had higher objective scores for performance (8.88 compared with 7.73 points, $p < 0.05$; Table II).

The other demographic and practice-related factors that were studied, including age, years in practice, the performance of three or more injections (compared with two or fewer) over the past year, and preferred approach for the knee joint injection, were not significantly correlated with either confidence or performance after instruction, with the numbers available (Table II).

Objective measures of performance improved significantly across all groups after instruction ($p < 0.001$). However, with the numbers available, hands-on teaching—the most labor-intensive mode of instruction—did not improve performance of this relatively simple task significantly more than did the less labor-intensive techniques. The mean objective competence score (and standard deviation) on the 10-point scale improved from 6.16 to 8.07 ± 2.61 points after instruction with the brochure, from 6.63 to 8.12 ± 2.45 points after the instruction with the CD-ROM video, and from 6.17 to 8.14 ± 2.29 points after the hands-on instruction. The difference among these groups was not significant, either before or after instruction, with the numbers available ($p = 0.99$).

Discussion

This study demonstrated that even low-labor-intensity forms of didactic instruction achieved significant improvements in the confidence and competence with which practitioners performed simulated knee joint injections as well as the accuracy with which they assessed their own skills ($p < 0.01$). For teaching this relatively simple psychomotor task, hands-on instruction—a more resource-intensive educational intervention—was not significantly more effective than a printed technique guide or a CD-ROM tutorial; it is likely that this was because most practitioners scored near the top of the scale (indicating satisfactory performance) after spending time reviewing a printed technique guide. It seems possible that more complex psychomotor tasks will require higher-intensity interventions to bring practitioners to an acceptable level of proficiency. Outlining the level of resource intensity required for teaching different skills is a topic that needs further study.

One academic orthopaedist opined that “surgical education has not shown much progress in the past few hundred years.”22 While this may be an overstatement, it is true that orthopaedic education as an area of scientific inquiry is in its infancy. To our knowledge, there is no published body of work investigating the relationship between practitioner confidence and competence, the effects (if any) of demographic differences on the efficiency of mastering particular surgical psychomotor skills, and the required level of resource intensity of an educational intervention needed to teach a psychomotor task of a given level of complexity. Yet, few would suggest that these topics are not important and worthy of serious inquiry.

There is evidence to suggest that the knee joint is more difficult to inject reliably than had previously been thought16. Determining whether the models used in the present study replicated the experience of injections performed in the clinical setting was not critical to our message, although the investigators (who were all fellowship-trained orthopaedic surgeons or rheumatologists) found that the models simulated a joint injection from the superolateral approach quite well. We used custom-manufactured knee-joint simulators to provide a reproducible, standardized, and easily evaluated model for testing a simple surgical task and for correlating participants’ confidence with their performance of maneuvers that had been demonstrated to them. One might question whether the overconfidence observed in this study of primary care practitioners can be extrapolated to either surgery residents or practicing surgeons; to know for certain will require analogous studies of those populations. That said, there seems little reason to believe that primary care practitioners would be more likely than orthopaedic surgeons to be overconfident regarding a psychomotor task. Finally, having attendees at a continuing medical education course serve as study subjects effectively prevented the inclusion of control subjects who had received no instruction but were permitted multiple attempts at injecting the models to see whether repetition alone increased confidence or competence. However, the experimental design tested the three most common means that practitioners employ to acquire new skills (self-study with a printed guide or a video, and preceptored hands-on learning), perhaps offsetting this potential limitation to some degree. While this work is preliminary, it is our hope that the findings will generate interest in and further study of the relationships between confidence and skill as well as the associations between learners’ backgrounds and their confidence in educational venues where new skills are acquired.

The literature contains limited information on the surgical learning curve, and the work that has been done has mainly been in other specialties10-13. Optimizing the learning curve is critical to a specialty’s ability to deliver consistently good results to patients, particularly in an environment where new procedures are being introduced and disseminated at a rapid rate. Our ability to facilitate surgical education is at least partly contingent on our understanding of potential barriers to learning or differences among learners that affect the process that are not obvious or intuitive. This report identifies, at least in a preliminary manner, three such elements: one demographic (gender), one emotional (pre-instruction confidence level), and one social (educational background). To our knowledge, this line of inquiry has not been made in the context of even a simple surgical task before, so both the study approach and the preliminary findings should be of interest to orthopaedic educators.

Although all three educational interventions that we studied effectively changed the inverse relationship between practi-
tioner confidence and objective skill that had been demonstrated before the instruction, the fact that a significant inverse relationship was observed between the confidence and competence of practitioners—that is, the finding that they were relatively naive regarding the task under study—is quite troubling. Also troubling is the observation that, even after instruction, the fact that a significant inverse relationship between confidence and actual skill at performing a task before receiving instruction—raise questions about how new, more complex procedures are introduced and how or when self-trained practitioners begin to perform them. Such deleterious confidence-competence relationships have an adverse effect on the learning curves of new, less-invasive orthopaedic surgical procedures is not known, but the high rates of complications observed in patients cared for by practitioners who are early on those learning curves offer strong incentive for surgical educators to find out.

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The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. A commercial entity (Zimmer, Inc.) paid or directed, or agreed to pay or direct, benefits to a research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.
Development of the QuickDASH: Comparison of Three Item-Reduction Approaches

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Background: The purpose of this study was to develop a short, reliable, and valid measure of physical function and symptoms related to upper-limb musculoskeletal disorders by shortening the full, thirty-item DASH (Disabilities of the Arm, Shoulder and Hand) Outcome Measure.

Methods: Three item-reduction techniques were used on the cross-sectional field-testing data derived from a study of 407 patients with various upper-limb conditions. These techniques were the concept-retention method, the equi-discriminative item-total correlation, and the item response theory (Rasch modeling). Three eleven-item scales were created. Data from a longitudinal cohort study in which the DASH questionnaire was administered to 200 patients with shoulder and wrist/hand disorders were then used to assess the reliability (Cronbach alpha and test-retest reliability) and validity (cross-sectional and longitudinal construct) of the three scales. Results were compared with those derived with the full DASH.

Results: The three versions were comparable with regard to their measurement properties. All had a Cronbach alpha of $\geq 0.92$ and an intraclass correlation coefficient of $\geq 0.94$. Evidence of construct validity was established ($r \geq 0.64$ with single-item indices of pain and function). The concept-retention method, the most subjective of the approaches to item reduction, ranked highest in terms of its similarity to the original DASH.

Conclusions: The concept-retention version is named the QuickDASH. It contains eleven items and is similar with regard to scores and properties to the full DASH. A comparison of item-reduction approaches suggested that the retention of clinically sensible and important content produced a comparable, if not slightly better, instrument than did more statistically driven approaches.

Clinical Relevance: The QuickDASH is a more efficient version of the DASH outcome measure that appears to retain its measurement properties.

Patient-based questionnaires are well-accepted means with which to quantify a patient’s perception of the impact of a disorder. Shorter questionnaires are attractive as they save time, are easier to use, and minimize the burden on the respondent and therefore minimize missing data. However, they often sacrifice measurement properties (internal consistency and test-retest reliability) for their brevity. An ideal scale would be one that was as short as possible while retaining the necessary measurement properties.

The Disabilities of the Arm, Shoulder and Hand Outcome Measure (DASH) is a thirty-item questionnaire that quantifies physical function and symptoms in persons with any or multiple musculoskeletal disorders of the upper limb. Direct comparisons with other, more joint-specific or disease-specific measures have shown the DASH to have comparable or almost comparable reliability and validity. A major advantage of the DASH is that it can be used for any upper-extremity evaluation and therefore offers more versatility for clinical and research applications.

Shortening the DASH is attractive and sensible provided that its measurement properties are maintained. The thirty-item DASH has been shown in multiple studies to have a high Cronbach alpha (0.97), suggesting the possibility of item re-

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The purpose of this study was to develop a valid, reliable eleven-item version of the DASH on the basis of a comparison of these three approaches to item reduction.

**Materials and Methods**

**Data**

Two datasets were used for the item-reduction process. The first was the field-testing data that had been used to create the thirty-item DASH, and the second was data gathered in a cohort study used to test the reliability and validity of the DASH. Each will be briefly described below and in Table I.

**Field-Testing Data**

The DASH was created by pooling items from thirteen different questionnaires that addressed the health-related quality of life of persons with an upper-limb problem. Through a process of eliminating overlap, a set of seventy-eight items was selected and was fielded in a cross-sectional study of 407 persons with varying upper-extremity problems from twenty-one different sites. In a second sample, the importance and difficulty of the seventy-eight items were rated by a sample of seventy-six persons from two of the twenty-one sites. The mean age (and standard deviation) in both of these samples was 45 ± 16 years; the percentages of women were 51% and 61%. Equidiscriminative item-total correlations were used along with patient ratings of difficulty and importance to form the final thirty-item DASH. The mean DASH score (and standard deviation) was 37.9 ± 22.0 points.

**Cohort Data**

The measurement properties of the DASH were evaluated in a prospective cohort study of 200 persons who completed a questionnaire package twice, at intervals three to five days apart, before treatment and twice, at four and twelve weeks, after treatment for a shoulder or wrist/hand problem. This study focused on four diagnostic groups: rotator cuff tendinopathies, shoulder osteoarthritis, carpal tunnel syndrome, and wrist/hand tendinopathies. Other measures used as comparators for the assessment of construct validity included visual analogue scales of the patients’ perception of their problem, pain severity, function, and ability to work as well as questions about work status and their ability to cope with symptoms or limitations. The mean age of this sample was 53.6 ± 14.2 years, and 57% (113) of the 200 individuals were female. The mean DASH score in this sample was 43.9 ± 22.9 points. Table I summarizes the data on the two samples.
In the current study, the field-testing data were used for item reduction and the cohort data were used to evaluate the measurement properties of the three versions of the QuickDASH created by the three item-reduction approaches\(^{2,12,13}\). Each of the original studies had been reviewed by the research ethics board at each clinical site, and the participants had consented to be in the study with the knowledge that the data would be used for ongoing testing of the DASH questionnaire.

**Application of Three Item-Reduction Approaches to the DASH**

**Concept-Retention Approach**

The intent of the concept-retention approach was to create a short version with items selected from the key domains identified in the theoretical framework of the DASH\(^1\). To achieve this, items in the DASH were sorted according to the domain that they represented. Data from the field-testing study were used to rank the importance and difficulty of each of the items as well as the correlation that each had with the total score. This information was combined to identify the highest-ranking item in each of the sixteen domains\(^9,10,15\). Five domains had to be eliminated to achieve our target of an eleven-item questionnaire. Sexual functioning was dropped as a result of the high percentage of missing values, probably due to poor acceptability, during clinical use of the DASH\(^1\). Self-image was furthest from the core concepts of physical function and symptoms and therefore was also eliminated. Family care was eliminated by combining it with social activities. Finally, since inter-item correlations among stiffness, pain, and weakness were all \(-0.60\) (polychoric correlations), only pain, the most universally experienced of the three symptoms and the most salient presenting feature for patients, was used. The number of domains now numbered eleven, and the top item in each domain became part of the short, concept-retention version, which was approved by the Upper Extremity Collaborative Group, who originally developed the DASH.

**Equidiscriminative Item-Total Correlation Approach**

The second item-reduction approach was the equidiscriminative item-total correlation method\(^1\). This was the statistical approach that contributed to the development of the DASH from a larger pool of items\(^8,12,14\), and we followed the same process. Three variables were created, representing the 25th, 50th, and 75th percentile values for the distribution of the thirty-item DASH scores in the field-testing sample. Individuals were assigned a “yes” or “no” for each of these variables depending on whether or not their score on the thirty-item DASH was higher or lower than the particular percentile value. Each dichotomous variable was then correlated with each of the items in the DASH. A higher correlation identified items associated with a higher DASH score (yes/no to above the 75th percentile), midrange, or lower (yes/no to above the 25th percentile) score. The four items with the highest correlations with each dichotomous marker were selected because they represented the items most likely to be sensitive and discriminating to that score level. If the same item was in the top-four list for two of the score ranges, it was dropped from the list of the higher score group, and the next ranked item from that group was substituted into that list. Finally, the item with the lowest correlation of the twelve was dropped to bring the total to our target of eleven items.

**Rasch Approach**

A single-parameter partial credit Rasch model\(^9,10,15\) was used to create the third short version of the DASH with use of Bigsteps software (version 2.6)\(^7\). Items are weighted according to their level of difficulty along a linear logistic function. Adjustments are made to allow for multiple rather than dichotomous response options (partial credit model). If an item fits this linear function, the mean square error term for the item will rest between 0.7 and 1.3, or the related Z statistic will be <2. In item reduction, Rasch methodology can be used to delete these misfitting items as well as to minimize overlap in the level of difficulty represented in the scale. Items were deleted when their infit and/or outfit statistic was >2, indicating noise in how that item was scored relative to other items across individuals. Priority was given to the infit Z statistics because they are sensitive to errors near the person's ability, as opposed to outfit statistics, which are more sensitive to errors in items further from the person’s ability. Highly negative (less than \(-2\)) standardized infit statistics suggest redundancy in items. We used this factor only as a second line of reduction. Although it is not done with most Rasch approaches to scale development, we set an a priori target of eleven items. The first run included all thirty DASH items. Misfitting items (infit and outfit Z statistics of >2) were dropped manually, with the item with the largest infit statistic dropped first and the program rerun. Iterations continued until eleven items remained, ideally with no misfitting items and a good range of logit (weighting) values (\(-2\) to +2) and good steps between the logit values (\(-0.15\) logits). Rasch modeling was used only for item selection; Rasch weights and scores were not used as a final scoring because of the complexities of applying these partial credit weights in a clinical situation. A simple summative score was used across the Rasch-selected items.

**Testing of the Measurement Properties of the Resultant Questionnaires**

The three eleven-item QuickDASH versions resulting from the three approaches to item reduction were evaluated independently. Testing was done with use of the prospective cohort data. The results were then compared with each other and with the results of the DASH outcome measure.

**Item Level**

The proportion of the sample falling into each of the response categories, including “missing,” was calculated. Items with >40% in one category were considered to be at risk for poor discrimination in this sample\(^1\). Mean item difficulties, item-to-total correlations, and Cronbach alpha coefficients were calculated\(^9\).
Domains. On the other hand, the Rasch version of the QuickDASH would have the advantage of covering all of the relevant item reduction. For example, the concept-retention QuickDASH would have certain strengths based solely on its approach to item reduction. We recognize a priori that each item-reduction method would have certain strengths based solely on its approach to item reduction. For example, the concept-retention QuickDASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the questionnaire could be closest to interval level in measurement but would be expected to have items with skewed distribution because of its effort to capture the full spectrum of disability. Finally, the version derived with the equidiscriminative item-total correlation method would probably have items with the highest correlation with each other and with the total score, giving it an advantage with regard to traditional psychometric markers such as the Cronbach alpha as well as homogeneity in the distribution of responses to items. The different advantages meant that we had to set clear a priori rules for deciding which version we would endorse. The final decision was to be based on three criteria: (1) fewest items with >40% in one response category, (2) a Cronbach alpha of >0.90, and (3) highest correlation with the full DASH and measurement properties most similar to those of the full DASH.

Results

Creation of Three Versions of the QuickDASH

Concept-Retention Approach

The final eleven items derived with the conceptual approach to item reduction are shown in the Appendix as well as in Figure 1. As described above, the best item was selected from eleven of the sixteen original domains of the theoretical framework of the DASH. The domains that were dropped were weakness, stiffness, family care, sexual activity, and self-image.

Equidiscriminative Item-Total Correlation Approach

The four items with the highest correlation to the dichotomous indicators of having a DASH score higher or lower than each of the 25th, 50th, and 75th percentiles are shown in Figure 1 and in the Appendix. Several items appeared in more than one list. These included pushing open a heavy door, doing heavy household chores, gardening/yard work, carrying heavy objects, and recreational activities with force through the arm. These were retained in the lowest percentile column and were replaced with the next highest ranked item in the higher percentile column. After all twelve items (four in each column) were selected, the one with the lowest item-total correlation (doing usual work; r = 0.58) was dropped to achieve the final target of eleven items.

Rasch Approach

Five iterations of Rasch modeling were used, with misfitting items dropped at each step. The first item to be eliminated was self-image (infit Z = 9.9) followed by weakness and tingling (infit Z = -6). Writing was deleted as well because of a less extreme misfit (infit Z = 2.4). Sexual function was also dropped at this stage because of a high rate of missing values (115 of 395 observations were missing). The next four steps deleted additional items. Fortunately, the fit improved as the item count neared the target of eleven. The final items are shown in Figure 1 and the Appendix, which listed the retained items, their weight, and the standardized infit and outfit statistics. Two items, using a key and doing usual work, became margin-

A Priori Decision Rules

We recognized a priori that each item-reduction method would have certain strengths based solely on its approach to item reduction. For example, the concept-retention QuickDASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the DASH would have the advantage of covering all of the relevant domains.

Scale Level

Distribution

Univariate analyses, including the mean, median, standard deviation, 25th and 75th percentiles, and full range of scores, were used to describe the distribution of scores for each of the QuickDASH versions.

Convergent Construct Validity

Correlations (Pearson product moment) were calculated between each of the QuickDASH versions and the visual analogue scores for ability to function in daily activities, rating of problem, pain severity, and ability to work. Correlations were 0.64 to 0.80, as were expected and which were consistent with the previous testing of the DASH. Higher correlations would not be expected because of the use of single-item scales (higher measurement error).

Known-Groups Validity

Two constructs to which the DASH is known to be sensitive were used to test the ability of the three QuickDASH versions to differentiate between people who are more severely affected from those who are not as severely affected. The first was the ability to work versus the inability to work as a result of the upper-limb problem. The second was the ability to do all that one wanted to do versus being limited in some way. Unpaired t tests were used to compare QuickDASH scores to determine whether there were significant differences in the scores across groups. The magnitude of the difference was also compared across QuickDASH versions.

Responsiveness

Standardized response means, defined as the mean change score divided by the standard deviation of the change, were used as a summary statistic of responsiveness. Responsiveness was calculated on the basis of the patients expected to improve (therefore everyone in the cohort study) and those who actually indicated that their problem was decreased on an 11-point transitional scale (a scale of 0 to 10, with >6 considered to indicate improvement). Relative efficiency was assessed by creating a ratio of the square of the standardized response mean for each QuickDASH over the square of the standardized response mean for the thirty-item DASH. If the relative efficiency was greater than one, that version of the QuickDASH was considered to be more “efficient” (more signal, less noise) than the full DASH for measuring change in that sample. The relative efficiency provides a ratio that can be related to the relative sample size needed to observe that level of effect size if one used the instrument in the denominator rather than the one in the numerator.

A Priori Decision Rules

We recognized a priori that each item-reduction method would have certain strengths based solely on its approach to item reduction. For example, the concept-retention QuickDASH would have the advantage of covering all of the relevant domains. On the other hand, the Rasch version of the QuickDASH would have the advantage of covering all of the relevant domains.
ally misfitting (infit and outfit Z > 2) in this final model, but they were retained because no other substitution of a similarly weighted item had a better fit and because of their consistent fit in previous iterations.

**Summary of Items Across Different Versions of the QuickDASH**

Only two items were shared across all three methodological approaches: doing heavy household chores and carrying a shopping bag (Fig. 1). The equidiscriminative item-total correlation version of the QuickDASH and the Rasch version had the greatest overlap, with five items shared only between them and two items common to all three versions. The questionnaire derived with the concept-retention approach had the most unique items (five), which probably reflects the focus on unique domains in each item.

**Results of Item-Level Analysis**

Details of the item-level analysis are available in the Appendix. There were very few items to which more than one or two patients failed to respond. Recreational activities with force taken through the arm and doing yard work had the highest frequency of missing responses, with 6% (twelve) of the 200 patients not responding to those questions. Light recreation, managing transportation needs, using a key, and using a knife were the only items to which >40% of the sample responded with one response category ("no difficulty"). On the concept-retention version of the QuickDASH, the response to the item regarding severity of numbness and tingling was given as "none" by 39.5% of the respondents, and that item had the lowest item-to-total correlation (r = 0.46), suggesting that it could be different than the other items. Pain severity did not have this problem. The distributions were most disparate between the items in the Rasch version of the QuickDASH. This finding is consistent with Rasch analyses, which seek items across the score range and hence with opposite distributions. Equidiscriminative item-total correlation tends to favor similar, more normal distributions where the greatest variance is found, leading to a higher correlation. The Cronbach alpha coefficient was ≥0.92 for each version (0.92 for the concept-retention version, 0.95 for the equidiscriminative item-total correlation version, and 0.95 for the Rasch version), and item-to-total correlations were also satisfactory in all versions.
Results of Scale-Level Analysis Distribution of Scores
The mean and median scores for the concept-retention and equidiscriminative item-total correlation versions of the QuickDASH were similar in magnitude to the scores for the DASH, whereas those for the Rasch version tended to be lower (mean scores [and standard deviation], 45.3 ± 23.2 points for the concept-retention version, 45.6 ± 26.2 points for the equidiscriminative item-total correlation version, and 37.9 ± 25.1 points for the Rasch version; see Appendix). Correlations between the QuickDASH and the DASH were extremely high (Pearson product-moment correlation, r ≥ 0.97), which speaks to the comparability of scores between the full DASH and QuickDASH versions. Correlations among the three versions of the QuickDASH were also extremely high (Pearson product-moment correlation, r ≥ 0.94). The distribution of the concept-retention version was closest to that of the DASH.

Construct Validity: Correlational Convergent and Known-Groups
Only the concept-retention version of the QuickDASH maintained the levels of correlation expected with the target constructs for pain and for rating of the overall problem. All versions had satisfactory correlations with the ability to function and the ability to work. These correlations, especially those of the concept-based QuickDASH, were also comparable with those of the DASH. Each version of the QuickDASH was able to discriminate (p < 0.0001) between the known groups of being able to do everything one needs to do (or not)

| TABLE II Construct Validity, Responsiveness, and Test-Retest Reliability for Three Versions of QuickDASH with Reference to Full DASH Results* for Comparison* |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
|                                 | Concept-Retention               | Equidiscriminative              | Rasch Item-Total                | Full DASH                       |
| Convergent construct validity (Pearson correlation) |                                 |                                 |                                 |                                 |
| Overall problem                 | 0.70                            | 0.64                            | 0.65                            | 0.71                            |
| Overall pain                    | 0.73                            | 0.64                            | 0.65                            | 0.72                            |
| Ability to function             | 0.80                            | 0.74                            | 0.78                            | 0.79                            |
| Ability to work                 | 0.76                            | 0.72                            | 0.73                            | 0.77                            |
| Known-groups validity (mean scores for subgroups)† |                                 |                                 |                                 |                                 |
| Able to do all one needs to do  | 25.4                            | 24.1                            | 20.6                            | 23.6                            |
| Unable to do all one needs to do| 48.6                            | 49.0                            | 41.1                            | 47.1                            |
| Known-groups validity (mean scores for subgroups)† |                                 |                                 |                                 |                                 |
| Able to work                    | 27.5                            | 26.4                            | 20.1                            | 26.8                            |
| Unable to work due to arm       | 52.6                            | 53.1                            | 45.3                            | 47.1                            |

**Responsiveness** (standardized response mean†)

| Observed change (n = 171) | 13.4/16.9 = 0.79 | 13.1/18.9 = 0.69 | 12.5/18.2 = 0.64 | 13.2/16.9 = 0.78 |
| Change in those rating problem as better (n = 121) | 17.3/16.7 = 1.03 | 17.1/18.8 = 0.91 | 16.0/18.0 = 0.89 | 17.3/16.4 = 1.05 |
| Ability to function            | 0.96                            | 0.75                            | 0.72                            | 1.0                            |
| Ability to work                | 0.91                            | 0.76                            | 0.68                            | 1.0                            |
| Ability to work due to arm     | 1.02                            | 0.70                            | 0.74                            | 1.0                            |

**Relative efficiency§ (compared with full DASH)

| Observed change | 1.03                            | 0.78                            | 0.67                            | 1.0                            |
| Change in those rating problem as better | 0.96                            | 0.75                            | 0.72                            | 1.0                            |
| Ability to function            | 0.91                            | 0.76                            | 0.68                            | 1.0                            |
| Ability to work due to arm     | 1.02                            | 0.70                            | 0.74                            | 1.0                            |

**Correlations with change (transitional index)

| Change in problem overall     | 0.39                            | 0.37                            | 0.32                            | 0.40                            |
| Change in ability to function | 0.35                            | 0.26                            | 0.25                            | 0.32                            |
| Test-retest reliability (Shrout and Fleiss 2,1 intraclass correlation coefficient) | 0.94                            | 0.96                            | 0.97                            | 0.96                            |

*All correlations are Pearson product-moment correlations and were significant at p = 0.05. †Known-group differences were analyzed with an unpaired t statistic and were significant at p = 0.05. ‡Standardized response mean (SRM) = mean change/standard deviation of that change. §Relative efficiency = SRM²QuickDASH/SRM²DASH*
Reliability and Responsiveness

Test-retest reliability was excellent for all three versions of the QuickDASH and was fairly consistent with that of the DASH (intraclass correlation coefficient = 0.94 to 0.97). Analysis of responsiveness revealed that the concept-retention version of the QuickDASH was most similar to the DASH, with higher standardized response means than were found for the other versions. This translated into a high relative efficiency of this version (0.96), offering a statistical advantage over the other versions (relative efficiency, 0.72 and 0.75), which required larger sample sizes to detect the same change in patient state. This advantage of the concept-retention version was retained after stratification by proximal versus distal disorders. Responsiveness was also assessed by examining the correlation with responses to the transitional scales rating the change in the overall problem and the change in function. The correlations were all low to moderate and were similar to the DASH correlations. The concept-retention version again was ranked first and was closest to the DASH.

Decision on Which Version of the QuickDASH to Adopt

Each version of the QuickDASH was highly correlated with the DASH. In terms of the criteria set before the analysis, the equidiscriminative item-total correlation and concept-retention approaches both had one item each with >40% responses in one category and the Rasch approach had three. The Rasch version would be expected to have more such items because, with that approach, items with extreme scores are selected in order to cover the spectrum of disability and to ensure that items are available across the range of disability in the sample. This often provides an advantage in a fairly well or a very ill group. The other two approaches were more correlationally based, which favors items in the midrange and with a broader distribution of responses. Thus, these versions would be expected to have fewer items with extreme response distributions.

All versions had a Cronbach alpha of >0.90 and acceptable test-retest reliability (intraclass correlation coefficient of 0.94). The construct validity and responsiveness of the concept-retention QuickDASH were closest to those of the thirty-item DASH, although by rank more than by magnitude.

The descriptive and psychometric results for all three versions were sent to ten members of the Upper Extremity Collaborative Group. The group members, blinded to the item-reduction approach, independently judged which version to recommend on the basis of the criteria described above. There was unanimous support for the concept-retention version.

Discussion

Short, psychometrically sound measures offer clinicians and researchers more efficient ways of quantifying patient outcomes while retaining the validity and reliability of the longer versions. Such instruments offer the advantage of providing the same quality of information with less burden for the patient completing it and easier scoring for the clinician or researcher. In this study, we developed the QuickDASH, an eleven-item questionnaire that addresses symptoms and physical function in people with any or multiple disorders involving the upper limb. We demonstrated strong measurement properties with use of this shortened scale. The QuickDASH demonstrated reliability, validity, and responsiveness when it was used for patients with either a proximal or a distal disorder of the upper extremity. It provides a summative score on a 100-point scale, with 100 indicating the most disability. Scores are obtained by summing circled responses, dividing the total by the number of items completed, subtracting one, and then multiplying that figure by 25. Only one missing item (>10% of the items) can be tolerated; the QuickDASH score cannot be calculated if two or more items are missing. The QuickDASH is comparable with the full DASH (r = 0.98), and its construct validity and responsiveness suggest that the QuickDASH scores should give views of disability and symptoms that are relatively similar to those provided by the full DASH.

Additional comparisons should be made. For direct comparisons of two datasets with DASH and QuickDASH scores, clinical researchers may wish to extract the QuickDASH items from the full DASH data to have the greatest confidence. The high correlation between the QuickDASH and DASH suggests highly comparable scores; however, an exact match between the numeric scores of long and shorter scales is not guaranteed (i.e., 45 points on the DASH may not equal 45 points on a QuickDASH), but they are likely to be close. The optional modules (sports/performing arts and work) are retained as optional; they have not changed from the original DASH.

In this study, we compared three approaches toward item reduction. The resultant scales differed in content, but at a group level they were similar in terms of their measurement properties and relationship to other measures. The three scales were so similar in performance that the results were unlikely to reflect clinically important differences in performance. The version that ultimately was selected was concept-based. As described above, items for this version were selected by our core development group with the goal of retaining the key concepts outlined in the conceptual framework of the DASH. An added benefit of this decision is the retention of the key elements of our framework, which were domains deemed to be clinically relevant to clinicians and are the important issues for patients.

The similarity of the measurement properties despite differences in item content could reflect the high inter-item correlations in the full thirty-item DASH. The thirty-item version has a very high Cronbach alpha (0.97), which to some
suggests redundancy across items. The various approaches to item reduction reflected this high inter-item correlation, in their similar performances with regard to numeric scores, construct validity, and correlation with the full DASH.

The concept-retention QuickDASH, which was the most subjective version, had the strongest ranking in terms of measurement properties, which are often assumed to depend on solid psychometric foundations for a measure. This finding might be counterintuitive to those who believe that psychometric approaches produce a good, or better, psychometric measure. On the other hand, it lends support to the hypothesis that greater clinical sensibility in a measure translates into greater validity.

Our study was limited by the fact that we had to extract the QuickDASH versions from longer questionnaires for the psychometric testing of the resultant scale. Although we have no clear understanding about whether this affected response patterns, we cannot be certain that it did not. To avoid this limitation, we would have had to have performed three independent studies, one for each version of the QuickDASH. This would have been impractical from a sample-size point of view, and it would have meant the loss of the ability to perform concurrent comparisons in the same sample.

Another limitation of the study is the method used for the Rasch approach. The Rasch model focuses on one parameter, item difficulty. Other item-response-theory models offer up to three parameters or are nonparametric, which also allows the response options to have broader or narrower scales of meaning between items. These models become more complex to interpret in a clinical setting and almost necessitate the use of computer interfaces for data collection or analysis. The second weakness in our use of the Rasch approach was the a priori decision to target eleven items. We retained two items that had been fitting on previous iterations but were borderline misfitting items on the eleven-item iteration. There were no alternative items with which to replace those items and provide a better fit. In a purely Rasch approach, one might decide to stop at another level and have a better fit.

In conclusion, on the basis of these findings, we anticipate that the new eleven-item QuickDASH (see Appendix) will work very well in groups of patients (in research studies, case series, and program evaluations involving groups of patients) and has the potential to work well in the more demanding role of monitoring care of individual patients in a clinical setting. Congruent findings from evaluations of the QuickDASH on its own, rather than as extracted from the full DASH, will increase our confidence in its measurement properties. On the basis of our current findings, the QuickDASH appears to perform comparably with the DASH, with little loss of reliability, validity, or responsiveness.

Appendix

Tables providing details of the item reduction, details of the item-level analysis, and the distribution of the scores for all three methods as well as the eleven-item QuickDASH outcome measure are available with the electronic versions of this article, on our web site at jbj.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

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In support of their research or preparation of this manuscript, one or more of the authors received grants or outside funding from the Institute for Work and Health, the American Academy of Orthopaedic Surgeons, the American Society of Surgery of the Hand, Canadian Institutes of Health Research, and the National Institutes of Health (Grants K24 AR02123 and P60 AR47782). None of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.02060

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Development of the QuickDASH: Comparison of Three Item-Reduction Approaches


Early Quadriceps Strength Loss After Total Knee Arthroplasty

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Investigation performed at the University of Delaware, Newark, Delaware, and the University of Florida, Gainesville, Florida

Background: While total knee arthroplasty reduces pain and provides a functional range of motion of the knee, quadriceps weakness and reduced functional capacity typically are still present one year after surgery. The purpose of the present investigation was to determine the role of failure of voluntary muscle activation and muscle atrophy in the early loss of quadriceps strength after surgery.

Methods: Twenty patients with unilateral knee osteoarthritis were tested an average of ten days before and twenty-seven days after primary total knee arthroplasty. Quadriceps strength and voluntary muscle activation were measured with use of a burst-superimposition technique in which a supramaximal burst of electrical stimulation is superimposed on a maximum voluntary isometric contraction. Maximal quadriceps cross-sectional area was assessed with use of magnetic resonance imaging.

Results: Postoperatively, quadriceps strength was decreased by 62%, voluntary activation was decreased by 17%, and maximal cross-sectional area was decreased by 10% in comparison with the preoperative values; these differences were significant (p < 0.01). Collectively, failure of voluntary muscle activation and atrophy explained 85% of the loss of quadriceps strength (p < 0.001). Multiple linear regression analysis revealed that failure of voluntary activation contributed nearly twice as much as atrophy did to the loss of quadriceps strength. The severity of knee pain with muscle contraction did not change significantly compared with the preoperative level (p = 0.31). Changes in knee pain during strength-testing did not account for a significant amount of the change in voluntary activation (p = 0.14).

Conclusions: Patients who are managed with total knee arthroplasty have profound impairment of quadriceps strength one month after surgery. This impairment is predominantly due to failure of voluntary muscle activation, and it is also influenced, to a lesser degree, by muscle atrophy. Knee pain with muscle contraction played a surprisingly small role in the reduction of muscle activation.

Level of Evidence: Prognostic Level I. See Instructions to Authors for a complete description of levels of evidence.
the motor units that are recruited\textsuperscript{12}. The results of preliminary studies have confirmed that reduction in muscle activation contributes substantially to early postoperative weakness\textsuperscript{10,11}, but the contribution of a loss in muscle cross-sectional area to a loss in strength is unknown.

Understanding how atrophy and the failure of voluntary muscle activation contribute to quadriceps weakness following total knee arthroplasty is important when directing postoperative care. The purpose of the present study was to determine the role of failure of voluntary muscle activation and muscle atrophy in the early loss of quadriceps strength after surgery. We hypothesized that (1) voluntary activation, maximal cross-sectional area, and strength of the involved quadriceps muscle decrease substantially after surgery, (2) changes in voluntary activation and cross-sectional area account for a majority of the loss of strength, (3) the change in muscle activation accounts for more of the loss of quadriceps strength than does the change in muscular cross-sectional area, and (4) a worsening of knee pain compared with the preoperative level accounts for a considerable portion of the worsening of voluntary activation after surgery.

Materials and Methods

Subjects

This prospective study included a total of twenty subjects (eight women and twelve men) who were scheduled to undergo primary unilateral total knee arthroplasty for the treatment of knee osteoarthritis. All subjects underwent tri-compartamental total knee arthroplasty with cement fixation through a medial parapatellar surgical approach. All of the operations were performed by experienced surgeons who extended the proximal incision into the quadriceps tendon. Potential subjects were excluded from the study if they were considered to be morbidly obese (that is, if they had a body-mass index [calculated as the weight in kg divided by the height in meters squared] of >40) or if they had been diagnosed with uncontrolled blood pressure, diabetes mellitus, neoplasms, or neurological disorders (e.g., Parkinson disease or stroke). Subjects who had substantial impairment in any of the other lower-extremity joints were also excluded. The average age was 62 ± 8 years (range, fifty-two to eighty-two years), and the average body-mass index was 31 ± 5 kg/m\textsuperscript{2} (range, 22 to 40 kg/m\textsuperscript{2}).

Postoperatively, all subjects underwent standardized in-patient and home-therapy protocols before testing and were functioning clinically as expected. The average maximal active knee flexion was 119° ± 13° (range, 95° to 141°) before surgery and 95° ± 14° (range, 75° to 121°) at the time of the follow-up test. The study was approved by the Human Subjects Review Board at the University of Delaware, and all subjects signed an informed consent form before participation.

Measurement of Quadriceps Strength and Voluntary Activation

Knee extensor strength and voluntary activation were assessed in all patients at an average of 10 ± 4 days (range, three to sixteen days) before and 27 ± 2 days (range, twenty-three to thirty-two days) after surgery. Measurement of maximal voluntary isometric contraction of the quadriceps muscle was assessed with use of a burst-superimposition technique, which was described in detail in a previous publication\textsuperscript{11}. Subjects were seated in a dynamometer with the knee flexed to 75°. All

![Fig. 1](image-url)  
A sample of quadriceps force production during a burst-superimposition test of a subject who was tested four weeks after total knee arthroplasty. CAR = central activation ratio.
subjects were able to achieve 75° of knee flexion without additional discomfort. Seat adjustments and transducer settings were recorded to allow for an identical setup for subsequent postoperative testing.

Each subject performed two submaximal contractions (perceived to be 50% to 75% of maximal effort) and one maximal voluntary contraction lasting two to three seconds each in order to warm-up the muscle and to gain familiarity with the testing procedure. After three minutes of rest, the subject was instructed to contract the quadriceps muscle maximally for approximately three seconds. Approximately two seconds into the contraction, a stimulator delivered a supramaximal burst of electrical stimulation through two electrodes that had been placed on the motor points of the quadriceps.

If maximal voluntary force output was achieved and no augmentation of force was observed in association with the stimulation (that is, there was optimal muscle recruitment), then the testing session was concluded for that limb. If force augmentation was present during the application of the electrical stimulus, the test was repeated. Three minutes of rest were provided between contractions in an effort to minimize fatigue. A maximum of three trials was recorded. The trial with the highest volitional force achieved during the three attempts was used for analysis.

The extent of voluntary activation of the quadriceps muscle was quantified with use of the central activation ratio described by Kent-Braun and Le Blanc\(^\text{12}\). The central activation ratio is calculated by dividing the maximal volitional force by the maximal force produced by the combination of volitional effort and the superimposed burst (Fig. 1). A central activation ratio of 1.0 indicates complete activation of the muscle, with no augmentation of the maximal volitional force being observed during the electrical stimulation.

**Measurement of Knee Pain**

A numeric rating scale was used to quantify knee pain during burst-superimposition testing. Subjects were asked to verbally rate the pain in and around the knee during the burst-superimposition test on a scale from 0 to 10, with 0 representing no pain and 10 representing the worst pain imaginable. The knee pain rating that was assigned during the attempt that produced the greatest force was used for analysis.

**Health-Status Questionnaires**

Health-status questionnaires were completed by all subjects at the time of the strength assessment and included the Medical Outcomes Survey Short Form 36 (SF-36)\(^\text{13}\) and the Activities of Daily Living Scale of the Knee Outcome Survey\(^\text{14}\). The Activities of Daily Living Scale of the Knee Outcome Survey is a fourteen-item scale designed to assess how knee symptoms and knee condition affect the ability to perform daily functions. Scores are presented as a percentage of the maximal

![Illustration showing the mean percent changes (and standard errors) in quadriceps strength, voluntary muscle activation, and maximal cross-sectional area, normalized to the initial condition. NMVIC = normalized force of maximal voluntary isometric contraction (calculated as the units of force, in Newtons, divided by body-mass index [weight in kg divided by the height in meters squared]). CAR = central activation ratio (with a value of 1.0 representing complete activation). CSA = maximal cross-sectional area (in centimeters squared).]
score, with 100% representing full perceived knee function during activities of daily living.

**Magnetic Resonance Imaging**

Each subject underwent magnetic resonance imaging of the quadriceps muscle an average of 2 ± 2 days after both the preoperative and postoperative strength assessments. Three-dimensional images were acquired with a spoiled gradient-echo sequence (flip angle, 30°) with use of a body coil in a 1.5-T magnet (General Electric Medical Systems, Milwaukee, Wisconsin). Images were acquired with an encoding matrix of 256 × 256 × 28, a field of view of 24 cm, a pulse-repetition time of 31 ms, and an echo time of 10 ms. Seven-millimeter slices were acquired along the entire length of the thigh with use of chemically selective fat suppression to enhance the definition between muscles. The cross-sectional area of each individual knee extensor muscle was determined with use of a validated, custom-designed, interactive computer program that allows for correction of partial volume-filling effects. Nonmuscular regions, such as subcutaneous fat, were excluded from these measurements. The sum total of each of the four muscles of the quadriceps provided an anatomical maximal cross-sectional area for each slice. The slice with the largest combined cross-sectional area was used for analysis. All cross-sectional area measurements were performed by one person who had a high intratester reliability for determining the maximum cross-sectional area, with an intraclass correlation coefficient (ICC [2,1]) of 0.97 (95% confidence interval, 0.94 to 0.99).

**Data Management and Statistical Methods**

All statistical analyses were performed with SPSS for Windows (Version 11.5.1; SPSS, Chicago, Illinois). The contribution of changes in voluntary activation and atrophy to the change in quadriceps strength was analyzed with use of multiple linear regression analysis. The influence of knee pain during strength-testing on voluntary activation of the quadriceps was analyzed with use of linear regression analysis. The level of alpha was set at 0.05 for all regression analyses. Differences in the mean values between the preoperative and postoperative conditions were compared with use of paired t tests, with a Bonferroni correction for multiple corrections. An adjusted alpha level of 0.007 (determined by dividing the original alpha by the number of comparisons [i.e., 0.05/7]) was used to determine significance for all statistical tests performed to compare means.

**Results**

The average score on the Activities of Daily Living Scale of the Knee Outcome Survey was 50% ± 20% before surgery and 54% ± 17% one month after surgery (p = 0.33). Preoperatively, the average physical component and mental com-
ponent summary scores of the SF-36 were 34 ± 11 and 58 ± 8, respectively. The postoperative physical component summary score (31 ± 9) was not significantly different from the preoperative score (p = 0.42), whereas the postoperative mental component summary score (52 ± 11) approached a significant decrease compared with the preoperative score (p = 0.03).

The quadriceps muscle of the involved limb was significantly weaker after surgery than it had been before surgery; specifically, the average normalized strength of the involved quadriceps muscle was decreased by 62% compared with the preoperative value (p < 0.001) (Fig. 2). In addition, the average voluntary muscle activation of the involved quadriceps was decreased by 17% compared with the preoperative value (p = 0.002) and the maximal cross-sectional area of the involved quadriceps was decreased by 10% compared with the preoperative value (p = 0.004).

Multiple regression analysis revealed that the percent change in voluntary muscle activation and the percent change in maximal cross-sectional area explained 85% of the relative change in quadriceps strength ($r^2 = 0.85$, $p < 0.001$) (Fig. 3). The relative contribution of the percent change in the central activation ratio was nearly twice the relative contribution of the percent change in maximal cross-sectional area in the regression equation that was used to predict the loss of quadriceps strength after total knee arthroplasty.

The postoperative score for knee pain with muscle contraction was not significantly different from the preoperative score (average, 3.6 ± 3.9 compared with 2.4 ± 3.0; $p = 0.31$). Knee pain with muscle contraction explained a small but significant portion of the variance in voluntary activation of the quadriceps at the time of the preoperative assessment ($r^2 = 0.29$, $p = 0.015$), but it did not have a significant effect at the time of the postoperative assessment ($r^2 = 0.20$, $p = 0.05$). The change in knee pain during muscle contraction between the preoperative and postoperative tests did not account for a significant amount of the change in voluntary muscle activation ($r^2 = 0.12$, $p = 0.14$) (Fig. 4). Half of the subjects reported no knee pain during the quadriceps strength test preoperatively, and the same proportion reported no knee pain during the same test postoperatively.

Discussion

We found that patients who had undergone total knee arthroplasty experienced a profound loss of quadriceps strength, marked failure of voluntary muscle activation, and a decrease in quadriceps cross-sectional area when evaluated one month after surgery. The loss of strength was largely explained by a combination of failure of voluntary muscle activation and atrophy. Failure of voluntary muscle activation explained much more of the strength loss than atrophy did;
however, the increased activation failure after total knee arthroplasty was not explained by increased pain.

The loss of >62% of the preoperative quadriceps strength was dramatic and closely matched the 60% loss of strength that we reported previously in a similar study involving a different group of patients. Not only was the change in strength after surgery pronounced, but the preoperative quadriceps strength also appears to have been below normal. The preoperative quadriceps force production reported in the present study (18.1 N of force/body-mass index) was 25% less than the force production reported for healthy older adults who were tested previously in our laboratory (24.2 N of force/body-mass index). Failure of voluntary muscle activation is likely to have contributed to the low preoperative quadriceps force production. The subjects in the present study had an average central activation ratio of 0.867 at the time of preoperative testing, whereas healthy older adults with no known knee abnormalities have been reported to have an average central activation ratio of 0.955. Two recent studies involving the use of electrical burst-superimposition strength-testing showed that patients with less advanced knee osteoarthritis (grade 2 or 3 according to the scale of Kellgren and Lawrence) did not have such a low level of voluntary muscle activation (as indicated by central activation ratios of 0.928 and 0.964). Individuals who undergo total knee arthroplasty represent a population of patients who clearly have substantial deficits in voluntary muscle activation.

Not only was there considerable failure of voluntary muscle activation before surgery, but the degree to which it worsened was remarkable. In contrast, it has been previously reported that patients who had undergone anterior cruciate ligament reconstruction did not exhibit abnormal voluntary activation of the quadriceps muscle eight weeks after surgery. Suter et al. reported an unexpected lack of worsening of voluntary muscle activation at six weeks in patients who had undergone arthroscopic surgery for the treatment of anterior knee pain. A large reduction in voluntary activation following total knee arthroplasty bodes poorly for the recovery of strength as patients with large activation deficits have been reported to have negligible improvement in strength even after intensive rehabilitation.

Some improvement in voluntary muscle activation is expected during the subsequent recovery period, a point that was not addressed in this investigation. In fact, Berth et al., in a long-term follow-up study of patients managed with total knee arthroplasty, demonstrated that voluntary activation of the quadriceps improves over time. Specifically, the level of voluntary activation of the quadriceps improved from 76% preoperatively to 85% at the time of the thirty-three-month follow-up. While this improvement was substantial, the intervention of total knee arthroplasty did not result in resolution of activation impairments as the level of voluntary activation of the quadriceps remained much less than that in healthy controls at both testing times.

A relatively small cross-sectional area of the quadriceps at the time of the preoperative assessment also appears to have contributed to the overall reduction in knee extensor strength. The preoperative maximal cross-sectional area in the present study was much lower than the typical cross-sectional areas found in healthy older adults and was slightly lower than the value found in individuals with less advanced osteoarthritis. The change in maximal cross-sectional area was smaller than expected as the average knee extensor strength decreased to less than half of preoperative strength. To our knowledge, the only other investigation that has assessed acute changes in quadriceps cross-sectional area associated with total knee arthroplasty also demonstrated only a small amount of atrophy (a 5% reduction) compared with the preoperative assessment.

Unexpectedly, the change in knee pain did not account for a significant amount of the large reduction in voluntary activation of the quadriceps muscle. A similar moderate relationship between knee pain and muscle activation has been reported in previous investigations of patients managed with total knee arthroplasty. Most of the activation failure does not appear to be due to knee pain during muscle contraction in this patient population. Assuming that muscle activation will improve as perioperative knee pain subsides, therefore, may not be valid.

In the present study, patients who had been managed with total knee arthroplasty had profound impairment in terms of quadriceps force-producing ability one month after surgery. Both failure of voluntary muscle activation and atrophy contributed to the strength loss; however, the major factor appeared to be failure of voluntary activation. Since activation failure was not strongly related to knee pain after surgery, pain control alone may be insufficient to prevent loss of strength. It appears that efforts that are taken specifically to address deficits in voluntary muscle activation in the early postoperative period may improve the outcome in terms of quadriceps strength. Exploring the use of exercise programs that encourage high-intensity muscle contractions and interventions that facilitate activation (e.g., biofeedback and neuromuscular electrical stimulation) appears to be warranted to counter the large deficit in quadriceps strength following total knee arthroplasty.

NOTE: The authors thank Glenn Walter, PhD, and Supriya Shidore, BPT, for their assistance in the analysis of the magnetic resonance images.
Institutes of Health (R01HD041055-01, T32 HD07490) and the Foundation for Physical Therapy through the Promotion of Doctoral Studies program. None of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.01992

References


Function of Skin Grafts in Children Following Acquired Amputation of the Lower Extremity

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Background: Investigators have recommended aggressive use of skin-grafting in order to preserve length and proximal joint function following an acquired amputation in children. However, there is little objective evidence to either support or refute that recommendation.

Methods: We performed a retrospective review of the cases of all children for whom a skin graft had been applied to the residual limb following an acquired lower-extremity amputation at our Limb Deficiency Clinic between 1984 and 2002. Skin graft dysfunction, defined as breakdown, contracture, and/or pain, was considered to be clinically relevant if it required the child to discontinue use of the prosthesis for any period of time or if it required revision surgery to facilitate continued prosthetic fitting.

Results: Twenty-three children (mean age at amputation, 4.4 years) with a total of thirty-one acquired lower-extremity amputations had been treated with skin-grafting. At a mean of 6.3 years after the operation, sixteen (52%) of the thirty-one extremities had had no episodes of skin graft dysfunction. The remaining fifteen extremities (48%) had had clinically relevant skin graft dysfunction (breakdown in thirteen and contracture and pain in one extremity each). Nine of the ten extensive skin grafts underwent clinically relevant breakdown, as did thirteen of the twenty-four grafts that were located distally on the residual limb. Subsequent surgical revision of the residual limb because of inadequate function of the skin graft was performed on seven extremities (23%), with revision to a more proximal limb-segment level required in five.

Conclusions: Focal skin-grafting (involving ≤25% of the surface area) of partial-thickness soft-tissue defects in order to optimize the length of the residual limb at the time of an amputation is an effective option for children with an acquired lower-extremity amputation. Limited skin-grafting (involving 26% to 50% of the surface area) is more likely to result in skin graft breakdown, particularly when it is done distally. Extensive skin-grafting, while technically possible, frequently requires revision and rarely results in an optimally functioning limb. Alternative treatment strategies should be considered for extremities that would require extensive, distal skin-grafting.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.
issues, the possibility of unpredictable growth remaining, and the potential for subsequent performance of an epiphysiodesis or limb-lengthening to facilitate prosthetic management. Often, the goals of optimal length and soft-tissue coverage are at odds with each other. When faced with a deficient soft-tissue envelope, the orthopaedic surgeon may utilize rotational flaps, skin-grafting, and/or free tissue transfers to achieve coverage of the residual limb. The use of skin grafts to optimize the length of the residual limb has been debated for many years. Most investigators have recommended the use of skin-grafting in order to preserve length and proximal joint function. Skin grafting on the residual limbs of children will mature and withstand the shearing or frictional forces of socket contact. Denuding of a short transtibial residual limb is no indication to proceed with higher amputation in a child. Instead, skin grafting should be carried out. Despite the conflicting opinions, a computer-based review of the English-language literature revealed only one study of the function of skin grafts on the residual limb in a pediatric population. Published in 1980, this study revealed recurrent breakdown of the skin graft on ten (29%) of thirty-five extremities, with surgical revision because of “unacceptable graft durability” required in six (17%) of the thirty-five extremities. The goal of the current study was to evaluate the function of skin grafts on the residual limbs of children who had had an acquired lower-extremity amputation and prosthetic fitting with use of current surgical and prosthetic techniques.

Materials and Methods

The study was reviewed and approved by our institution’s research review committee. A computer-based search was performed to identify all patients with an acquired amputation of the lower extremity who had been treated in our pediatric Limb Deficiency Clinic between 1984 and 2002. All children who had had application of a skin graft to the residual limb and for whom prosthetic fitting had been attempted were selected for further analysis. The medical records were reviewed to determine the nature of the index skin-grafting procedure, the extent and location of the skin graft on the residual limb, and the subsequent clinical course. The extent of the skin-grafting on the portion of the residual limb that was contained within the prosthetic socket was determined by estimating the limb-segment surface area covered by the graft. The skin grafts were classified as focal (involving ≤25% of the surface area of the limb segment), limited (involving between 26% and 50% of the surface area of the limb segment), or extensive (involving ≥51% of the surface area of the limb segment). The location of the skin graft on the residual limb was described as proximal (located on the proximal 50% of the limb segment) or distal (located on the distal 50% of the limb segment, including the end of the residual limb), or both, and as anterior, posterior, medial, and/or lateral. Breakdown of the skin graft, contracture of the skin graft, or pain associated with the skin graft was considered to be clinically relevant if it required the child to discontinue use of the prosthesis for any period of time or if it required revision surgery to facilitate continued prosthetic fitting. Disruption of prosthetic wear due to skin graft problems was categorized as episodic or continuous on the basis of the frequency and duration of the time spent not wearing the prosthesis.

Surgical revision, when feasible, was offered to all patients who had a substantial disruption in prosthetic management. Not all families agreed to the revision surgery, for a variety of psychosocial reasons. In such cases, continued prosthetic management was generally attempted.

Statistical analysis of continuous data was descriptive, with the mean and range of values reported for the selected variables.

Results

Twenty-three children with a total of thirty-one affected lower extremities met the inclusion criteria and formed the cohort of the study (see Appendix). The mean age at the time of the index amputation was 4.4 years (range, 1.3 to 16.6 years). At the time of the initial amputation, eighteen children were five years of age or less, four were between six and ten years of age, and one was older than sixteen years of age. The mean age at the time of the most recent follow-up was 11.4 years (range, 5.1 to 21.9 years). Thus, the mean duration of follow-up was 6.3 years (range, 1.2 to 18.3 years). Trauma was the cause of fourteen amputations (twelve unilateral amputations and one bilateral amputation), with a lawn-mower accident leading to ten amputations (all unilateral), a motor-vehicle accident accounting for one (unilateral), and an automobile-pedestrian accident resulting in three (one unilateral amputation and one bilateral amputation). Infection (meningococcemia) was the cause of thirteen amputations (one unilateral amputation and six bilateral amputations), and burn-related injury accounted for four (two unilateral amputations and one bilateral amputation).

Six extremities had been amputated above the knee; two, through the knee; sixteen, below the knee; five, through the ankle (Syme or Boyd procedure); and two, at the midfoot level (Chopart procedure). Split-thickness skin-grafting was performed on twenty-nine extremities and full-thickness skin-grafting, on two. The extent of the skin-grafting on the residual limb was categorized as focal for eight extremities, limited for thirteen, and extensive for ten.

The mean time from the skin-grafting of the residual limb to the initial prosthetic fitting was five months (range, two to fifteen months). In all cases, the prosthetic socket was fabricated to minimize direct and indirect loading of the skin graft area. Deviations from standard prosthetic prescriptions, in order to accommodate for the skin graft area, included application of a silicone-gel liner or a plastic insert for eleven extremities, modifications of the socket design for three, and auxiliary proximal suspension for thirteen.

During the period of study, sixteen (52%) of the thirty-one extremities had no episodes of skin graft dysfunction (breakdown, contracture, or pain) that required the child to...
discontinue use of the prosthesis. The remaining fifteen extremities (48%) had clinically relevant skin graft dysfunction, with breakdown in thirteen extremities (42%) and contracture and pain in one extremity each. The disruption of prosthetic wear due to skin graft breakdown was episodic for nine extremities (29%) and continuous for four (13%). In the group that had episodic disruption of prosthetic wear, the mean time until the first clinically relevant breakdown of the skin graft was one year (range, 0.25 to two years) and the mean frequency of clinically relevant skin breakdown was 0.5 episode per year (range, 0.1 to two episodes per year). In all four extremities with continuous disruption of prosthetic wear due to skin breakdown, the clinically relevant breakdown occurred within one month after the initial prosthetic fitting.

None of the eight extremities with a focal skin graft had clinically relevant breakdown, contracture, or pain. Four of the thirteen extremities with a limited skin graft had episodic breakdown, and all four of those skin grafts were located distally. One extremity with a limited skin graft, located distally and posteriorly, had substantial pain. Nine of the ten extremities with an extensive skin graft had clinically relevant breakdown. The skin graft breakdown was continuous for four of the extremities and episodic for five, and all nine skin grafts were located distally. A flexion contracture of the knee developed in one extremity with extensive skin-grafting.

None of the seven extremities with only a proximal skin graft had clinically relevant breakdown, contracture, or pain, whereas thirteen of the twenty-four extremities with a distal skin graft had clinically relevant breakdown. Seven of the extremities with a distal skin graft were end-bearing. Of those seven extremities, five (the one with a through-the-knee amputation, two of the four with a through-the-ankle amputation, and the two with a midfoot-level amputation) had clinically relevant skin graft breakdown (four extremities) or pain (one extremity). The remaining seventeen extremities with a distal skin graft were non-end-bearing. Of those seventeen extremities, nine (three of the four with an above-the-knee amputation and six of the thirteen with a below-the-knee amputation) had clinically relevant skin graft breakdown.

Twenty-four (77%) of the thirty-one extremities had no subsequent surgery for problems related to the skin graft. Surgical revision was performed on seven extremities (23%): because of breakdown in five, because of contracture in one, and because of pain in one. Five of these extremities had revision of the amputation to a more proximal limb-segment level to improve prosthetic management and function. The decision to perform revision surgery was quite difficult for families in which the child had sustained the original injury in a lawn-mower accident. The prospect of additional surgery was often associated with guilt related to the mechanism of the initial injury (usually a family member driving the lawn mower).

Discussion

The soft-tissue envelope of the portion of the residual limb that is contained within the socket of a prosthesis is subjected to thermal and mechanical loading. Circumferential coverage of the residual limb segment by the socket blocks normal heat exchange through the skin, resulting in increased surface temperature and trapping of perspiration. This may result in maceration and breakdown of an otherwise normal soft-tissue envelope. Loading in compression, distraction, and shear modes may also lead to soft-tissue breakdown of the residual limb. Finally, use of a suction socket exposes the residual limb to prolonged negative pressure, which disrupts the normal electrical gradient across the skin and may make it more susceptible to breakdown.

Skin grafts on the residual limbs of children with acquired amputations are generally thought to perform poorly on the residual limbs of adults following an acquired amputation. Most authors have recommended aggressive use of split-thickness grafts to achieve soft-tissue coverage in order to maintain the length of the residual limb and improve prosthetic management and function. The decision-making regarding amputation of the lower extremity, whether performed in an adult or a child, prioritizes the preservation of proximal joints whenever possible.

The rationale for this approach is based on energetics studies of walking by adults who have had an amputation. Those studies showed that the more proximal the level of amputation, the greater the energy cost associated with normal walking. Although we are not aware of any comprehensive studies of the impact of modern prosthetic design technologies on the energetics of gait in the twenty-five years since those investigations, the conclusions are widely thought to remain valid and have been applied both to children with
congenital lower-extremity amputations and to those with acquired amputations. In the current study, thirteen of the twenty-four distal skin grafts, which had been placed to maximize the length of the residual limb, had clinically relevant breakdown. The energy cost of walking following an amputation at an inappropriate level, related to an extremely short residual limb segment or breakdown of the soft-tissue envelope, has not been determined.

An additional priority in the surgical decision-making for amputation of the lower extremity in children is to avoid transdiaphyseal amputation and instead perform a disarticulation whenever appropriate (i.e., whenever the contemplated disarticulation level is distal to the contemplated transdiaphyseal amputation level). Transdiaphyseal amputations are associated with a risk of skeletal overgrowth during the growing years, and the limb cannot be fit with an end-bearing or distally suspending prosthesis. Disarticulations, particularly when combined with an appropriately timed epiphysiodesis, can result in a residual limb that is end-bearing and distally suspended, with the mechanical joint centers aligned at a level that is symmetric with the biologic joints of the contralateral extremity. In the current study, there was clinically relevant dysfunction of the skin graft following five of the seven disarticulations that resulted in an end-bearing residual limb that required soft-tissue grafting to achieve coverage distally. Skin grafts may not tolerate the loading under such conditions.

The current study suggests that focal skin-grafting (involving ≤25% of the surface area) of partial-thickness defects in order to optimize the length of the residual limb at the time of amputation is an effective option for children with an acquired lower-extremity amputation. Limited skin grafts (involving 26% to 50% of the surface area) are more likely to break down, particularly when they are placed distally. More extensive skin-grafting procedures (involving ≥51% of the surface area) or coverage of full-thickness soft-tissue defects with split-thickness skin grafts applied directly over bone, although technically possible, frequently require revision and rarely result in an optimally functioning limb. In such cases, alternative treatment strategies such as free tissue transfer, assisted secondary wound-healing, or selection of a more proximal amputation level (with an intact soft-tissue envelope) and subsequent limb-lengthening, if necessary, should be considered.

Appendix
A table presenting details on all study patients is available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.01832

References


Background: Demineralized bone matrix and recombinant human bone morphogenetic protein-2 or 7 (BMP-2 or BMP-7)-containing collagenous matrix have been shown to induce new bone formation in orthotopic and heterotopic sites. We examined the ability of subcutaneous implants of collagen combined with adenoviral vector containing the BMP-2 gene (AdBMP-2) to induce bone formation in rats. We also evaluated whether targeting the AdBMP-2 vector through an alternative receptor pathway, fibroblast growth factor (FGF), would increase the vector's potency.

Methods: In a time-course study, rat subcutaneous sites were implanted with (1) AdBMP-2 in rat-bone-derived collagen or (2) rat-bone-derived collagen alone. Samples were collected three, seven, fourteen, or thirty-five days after treatment. In a dose-response study, bone induction by AdBMP-2 in collagen (AdBMP-2/collagen) or by AdBMP-2 and FGF2 Fab' anti-adenovirus knob protein antibody in collagen (FGF2-AdBMP-2/collagen) was tested at fourteen days. Viral vector doses of 1 × 10^9 PN (viral particle number), 3 × 10^9 PN, 1 × 10^10 PN, 3 × 10^10 PN, or 1 × 10^11 PN per implant were used. Equal amounts of collagen (25 mg) were used to formulate all implants. Explanted tissues were evaluated histologically to determine bone formation, specific activity of alkaline phosphatase, and calcium content.

Results: AdBMP-2/collagen implants induced robust bone formation. New bone was formed by the fourteenth day after implantation. In contrast, little or no bone was induced by the implant containing collagen alone. FGF2-AdBMP-2/collagen implants stimulated significantly more bone formation (p < 0.05) than did AdBMP-2/collagen implants, regardless of the dose of viral particles.

Conclusions: Local delivery of AdBMP-2 in a collagen matrix rapidly induces bone formation, and targeting the virus through FGF receptors enhances the osteogenic potential of AdBMP-2.

Clinical Relevance: Local delivery of BMP genes in matrices offers an attractive therapeutic approach to bone repair. The potential of sustaining BMP production at the implant site may be desirable to provide a long-lasting osteogenic signal to delayed unions and fracture nonunions. Moreover, gene delivery within a matrix retains the vector at the site and also provides a scaffold for the influx of osteoprogenitor cells. Lower effective vector doses achieved by the FGF2-AdBMP-2 conjugate may be desirable in order to minimize the adenovirus dose and the adenovirus-elicited inflammation in patients while maximizing gene expression.

The current clinical standard of care for nonhealing fractures is autogenous or allogeneic bone-grafting. While these grafts have been successful in improving bone function, both types have distinct clinical disadvantages. Harvesting of autogenous graft from an injured patient is accompanied by substantial morbidity, whereas allogeneic grafts have a lower osteogenic potential than autografts and present an inherent risk of disease transmission.

Cell and growth-factor-based treatments to induce bone regeneration are the two main alternative methods of bone repair currently under investigation. Bone-marrow-derived stem cells that are concentrated and adhered to biocompatible implants have been shown to promote spinal fusion. This method has great appeal because of the plasticity of the cells and hence their potential to contribute to multiple aspects of tissue regeneration. However, cell therapy is somewhat impractical because of the morbidity at the donor site as well as a requisite cell-processing step.

Growth-factor-based therapy for bone repair has shown initial clinical promise for spinal fusion. The use of bone growth factors such as bone morphogenetic protein (BMP) enables treatment with a known and consistent dose of the osteoinductive protein. Growth factors, however, have short half-lives, which, for some patients, may necessitate multiple doses to achieve bone-healing. In contrast, delivery of genes encoding growth factors by means of vectors that drive sustained gene expression can result in persistent production of growth factor protein at the site. Bone formation by stem, mesenchymal, and muscle cells transduced ex vivo with adenovirus encoding BMP-2 or BMP-7, followed by implantation
of the transduced cells on bone-compatible matrices, has been demonstrated at heterotopic sites and in bone defects 8-13. Our approach to gene therapy for tissue regeneration utilizes a carrier matrix to immobilize therapeutic gene vectors at the treatment site. This delivery modality was first described by Bonadio et al. 14, to our knowledge. Repair cells such as macrophages, fibroblasts, and progenitor cells migrate into the implant, internalize the gene vector, and locally express the transgene protein. Because the gene vector is associated with the matrix, dissemination of the vector away from the injured site is slow and unlikely 15. As a gene therapy, this is a practical alternative to ex vivo viral transduction in autologous or allogeneic cells, since the former requires a surgical procedure to obtain the cells and the latter has the potential to transmit disease. Moreover, in contrast to conventional, allograft, or allogeneic cell-based therapies, there is minimal to no risk of transmission of infectious disease. In this study, we evaluated the osteogenic potential of implants consisting of adenoviral vector containing the BMP-2 gene (AdBMP-2) in collagen to induce new bone formation at ectopic sites.

We hypothesized that AdBMP-2 is osteoinductive and that its potency can be enhanced by targeting the vector to cells with the use of fibroblast growth factor-2 (FGF2). To test this hypothesis, we evaluated bone formation induced by AdBMP-2 and by FGF2-AdBMP-2, delivered in a non-osteocnductive collagen matrix into an ectopic site.

Materials and Methods
Experimental Design
A subcutaneous axillary tissue pocket was created bilaterally with blunt dissection in rats. The rats used in the time-course study either received AdBMP-2 (1 × 10^9 particle number [PN]) in allogeneic rat-bone-derived collagen (25 mg) or received the collagen alone (25 mg). Six rats (twelve replicate treatments) from each treatment group were killed at three, seven, fourteen, and thirty-five days postoperatively. The rats used in the dose-response study were treated with implants consisting of either AdBMP-2 in allogeneic rat-bone-derived collagen (25 mg) or with FGF2 and AdBMP-2, at viral vector doses of 1 × 10^9 PN (viral particle number), 3 × 10^9 PN, 1 × 10^10 PN, 3 × 10^10 PN, or 1 × 10^11 PN, in the same collagen (25 mg). The tissues were collected fourteen days after implantation. For both studies, one implant from each rat was harvested for histological evaluation, whereas the contralateral implant was processed for alkaline phosphatase and calcium quantification. The study protocols, housing, and care of the animals were approved by the Institutional Animal Care and Use Committee of Selective Genetics.

Surgical Procedure
Outbred Long-Evans rats (Charles River Breeding Laboratories, Wilmington, Massachusetts), four to five weeks old and weighing 120 to 150 g, were anesthetized with a mixture of ketamine (60 mg/kg) and xylazine (8 mg/kg) by intraperitoneal injection. Artificial tears ointment was placed in each of the animals’ eyes. The area from the neck to the hindlimb regions of all animals was shaved free of hair. The surgical area was scrubbed with Betadine (povidone-iodine) solution and then was rinsed with 70% ethanol. Animals were transferred individually, just prior to each surgery, from their cages to the surgical suite. Under sterile conditions, two longitudinal full-thickness incisions, approximately 0.8 × 1.0 cm in length, were made on either side of the sternal midline, proximal to the axillary regions. The skin at each incision was lifted. A pathway to the axillary region was created with use of blunt scissors. The test implants, approximately 150 µL in volume, were placed into the bluntly dissected pockets, and the incisions were closed with 9-mm wound staples. Following completion of the surgical procedure, the animals were placed on a heating pad, observed at least every ten minutes until recovery, then returned to their cages (three rats per cage), and given food and water ad libitum. Three, seven, fourteen, and thirty-five days after application of the test material, the animals were killed with a lethal injection of pentobarbital (60 mg/kg), and the subcutaneous implants were removed for histological and biochemical analyses.

Bone Collagen Preparation
Bone collagen was prepared from rat long bones as previously described 16-19. Briefly, bone from the tibia and femur of rats approximately six months of age was delipidated by chloroform extraction, ground, and sieved to obtain granules of between 75 and 240 µm in diameter. After demineralization of the bone granules by treatment with hydrochloric acid (0.6N), noncollagenous proteins were removed by treatment with guanidine hydrochloride (4M). The resulting collagen granules were then ethanol-washed, dried, and stored at ambient temperature until use.

Adenovirus Preparation
AdBMP-2 is an adenoviral vector encoding human BMP-2. The adenoviral vector is a human Ad5 serotype, engineered to be replication-deficient by deletion of the E1 and E3 domains. The BMP-2 cDNA (catalogue number 40345) was originally obtained from American Type Culture Collection (ATCC, Manassas, Virginia). The cDNA was subcloned into shuttle CMV (cytomegalovirus) (Qbiogene, Carlsbad, California), then recombined with pAdEasy-1 (Qbiogene) to generate AdBMP-2. Purified lots of AdBMP-2 were prepared and quantified as previously described 20. Briefly, the 293 cell line (ATCC) was infected with AdBMP-2 (fifty viral particles per cell) and was cultured for seventy-two hours. The crude viral material was purified over cesium chloride gradients to obtain purified lots of AdBMP-2. AdBMP-2 doses are described in viral particle number (PN). Particle concentration was determined by ascertaining the content of DNA by measuring its binding to PicoGreen and comparing it with that of a known reference stock (PicoGreen assay kits; Molecular Probes, Eugene, Oregon). Plaque-forming units (PFU) were determined by plaque formation by infected 293 cells. The PN:PFU ratio of the AdBMP-2 used in this study was 12:1.
Fig. 1
Time course of AdBMP-2-mediated subcutaneous bone formation. The photomicrographs show subcutaneously placed implants, consisting of either AdBMP-2 ($1 \times 10^{10}$ PN) in rat bone collagen (25 mg) (Panels A through D) or rat bone collagen alone (25 mg) (Panel E), that were explanted on day 3 (Panel A), day 7 (Panel B), day 14 (Panel C), or day 35 (Panels D and E) after treatment. Rat bone collagen (Coll), chondrocytes (Ch), osteoblasts (Ob), blood cells (BC), osteocytes (Oc), medullary cavity (MC), and osteoclasts (OCl) are visible (toluidine blue, original magnification ×400).
FGF2-Adenovirus Conjugation
Adenoviral vectors were retargeted for entry through FGF receptors as previously described. Briefly, a 155-amino-acid form of FGF2 containing an accessible cysteine residue was produced with use of a bacterial expression system. Monovalent fragments of a mouse monoclonal neutralizing anti-knob antibody (Fab') were prepared by papain digestion, and the free sulfhydryl group on the anti-knob Fab' was activated with Ellman reagent. The activated Fab' was then conjugated to FGF2 and chromatographically purified.

Adenovirus was complexed to FGF2-Fab' by incubation in a minimal volume at ambient temperature for thirty minutes as previously described. The calculated FGF2-Fab' conjugate: knob fiber monomer ratio used in all experiments was 10:1.

In Vitro Bioactivity of AdBMP-2-Transduced C2C12 Cells
C2C12 cells (ATCC catalogue number CRL 1772) were plated at 2 × 10^4 cells per well in a forty-eight-well cluster plate in complete culture medium (Dulbecco modified Eagle medium [DMEM] high glucose [catalogue number 1230-054; Invitrogen, San Diego, California] containing 10% fetal bovine serum, glutamine [catalogue number F2442; Sigma Chemical, St. Louis, Missouri], 2mM L-glutamine [catalogue number 25030-081; Invitrogen], 50 µg/mL gentamicin reagent [catalogue number 10131-035; Invitrogen], 0.1mM non-essential amino acids [catalogue number 11140-050; Invitrogen], and 1mM minimum essential medium sodium pyruvate [catalogue number 11360-070; Invitrogen]) and were incubated overnight at 37°C and 5% CO2. Wells were then aspirated, and 500 µL of fresh culture medium was added, after which 200 µL of AdBMP-2 or FGF2-AdBMP-2 at a concentration of 750 or 7500 PN/cell was added to each well. At forty-eight hours, the medium was aspirated and was replaced with fresh culture medium. Three days later, the medium was aspirated, cells were rinsed once with phosphate-buffered saline solution, and 200 µL of buffer (20mM Tris, 1mM MgCl2; pH 9.8) was added to each well. Plates were freeze/thawed by cycling three times at −20°C and ambient temperature. Alkaline phosphatase activity from the solubilized cell lysate was then measured with use of a previously reported chemiluminescent procedure. Briefly, 2-µL aliquots of cell lysates were placed in a white, opaque ninety-six-well plate, and 100 µL of the alkaline phosphate substrate/enhancer, disodium 2-chloro-5-(4-methoxyspiro[1,2-dioxetane-3,2’-(5’chloro)-tricyclo[3.3.1.13,7]decan]-4-yl)-1-phenyl phosphate obtained from a kit (CDP-Star substrate; Tropix, Applied Biosystems, Bedford, Massachusetts) was added to each well and was incubated for approximately sixty seconds. Alkaline phosphatase activity was determined by measuring the sample emission at 460 nm and comparing this value with that of a known alkaline phosphatase standard. As a measure of cell quantity, separate aliquots of cell lysates were assayed for total protein content by the BCA Protein Assay (Reagent A number 23221 and Reagent B number 23224; Pierce Chemical, Rock-
ford, Illinois). Cell bioactivity in response to vector transduction units was described as alkaline phosphatase activity, normalized per cell number.

**Implant Formulation**

Each implant was formulated by adding 125 µL of either AdBMP-2 or FGF2-AdBMP-2 in 2.5% (w/v) glycerol and 25mM NaCl in 20mM Tris, pH 8.0 (GTS [glycerol-Tris-saline]) or GTS alone to microfuge tubes containing dry granules of rat bone collagen (25 mg). The tubes were vortex-mixed at a low speed for up to thirty seconds to completely hydrate the granules, incubated for thirty minutes at ambient temperature, and then stored at 4°C for up to one hour prior to implantation. Retention of viral particles on the collagen granules was determined by measuring bound virus from the granules after their disruption by collagenase. Subsequently, collagenase buffer was analyzed with high-performance liquid chromatography for the presence of virus. Analysis of multiple lots of AdBMP-2/collagen confirmed that between 90% and 95% of the virus was bound to the collagen granules.

**Tissue-Processing for Histological Analysis**

The implants, along with a small border of normal subcutaneous tissue, were excised for histological analysis at three, seven, fourteen, or thirty-five days after treatment. The implants were preserved and demineralized in Bouin fixative (LabChem, Pittsburgh, Pennsylvania) for forty-eight hours, washed with deionized water, and then transferred to 70% ethanol. After the specimens were embedded in paraffin, sections of approximately 4 µm in thickness were placed on slides, deparaffinized, and then stained with toluidine blue (Fisher, Tustin, California).

**Histological Scoring of Bone Formation**

Newly formed bone was quantified by scoring histological samples with a discrete scale of arbitrary units ranging from 0 (no cartilage or bone) to 4 (90% to 100% of the area occupied by bone and cartilage). Data are reported as the mean and standard error of scores from three independent scorers.

**Tissue Homogenization**

Implants were excised, along with a small subcutaneous tissue border, from the treatment site at three, seven, fourteen, or thirty-five days after treatment. The implants were clearly separable from the surrounding tissue by a thin fibrous capsule. Excised tissues were weighed, placed in 1 mL of lysis buffer (150mM NaCl, 3mM NaHCO₃; pH 7.4), and homogenized with use of the FastPrep system (Qbiogene). Soluble and insoluble homogenate fractions were separated. Soluble fractions were immediately assayed for alkaline phosphatase activity.

**Determination of Alkaline Phosphatase Activity and Calcium Content**

Alkaline phosphatase activity from the soluble homogenate fraction was measured as described in the above section on the...
in vitro transduction bioassay method.

Calcium levels were determined as follows. Insoluble tissue homogenate fractions were incubated with 0.5N HCl for four to seventy-two hours at 4°C, while rocking, followed by complexing of the hydrolysate with the chromogen, o-cresolphthalein (Sigma). Calcium was quantified by measuring light absorbance of the samples at OD 550 with a reference at OD650 nm. Calcium content was normalized to wet weight of the tissue.

**Statistical Analysis**
All results are expressed as the mean and standard error. Student t tests were performed to determine significant differences in alkaline phosphatase activity and calcium levels between two treatment groups. Mann-Whitney rank-sum tests were used to determine significant differences in discrete histological bone scores between two treatment groups. The level of significance was p < 0.05.

**Results**

**Time Course of Bone Formation**
A dBMP-2 (1 × 10^9 PN)/collagen or collagen matrix alone was implanted in subcutaneous sites of rats. AdBMP-2/collagen implants evaluated on day 3 consisted predominantly of the implanted collagen matrix with few mesenchymal cells and some fibrin clots surrounding the collagen matrix (Fig. 1, Panel A). By day 7, chondrocytes and proteoglycan-rich cartilage were abundant, as evidenced by metachromatic staining of hyaline chondrocytes (Fig. 1, Panel B). By day 14, newly forming bone was evident. Osteoblasts secreting new osteoid were surrounded by resorbing collagen matrix, and new bone was replacing the matrix (Fig. 1, Panel C). Hematopoiesis was evident in cavities filled with red and white blood cells and was surrounded by remodeling bone (osteoclastic resorption). By day 35, mature bone was present throughout the majority of all sites treated with an AdBMP-2/collagen implant, and the matrix was completely resorbed (Fig. 1, Panel D).

In contrast to the AdBMP-2/collagen-treated sites, the collagen-treated tissues contained no histologically evident bone up to thirty-five days after treatment (Fig. 1, Panel E). By day 35, most of these sites contained soft, non-mineralized tissue and largely resorbed collagen matrix.

Alkaline phosphatase-specific activity was measured to quantify the rate of bone formation within the implants. Alkaline phosphatase was detected at the AdBMP-2/collagen-treated sites beginning on day 7, and it peaked on day 14 (Fig. 2). In contrast, alkaline phosphatase levels at the sites that had been treated with collagen alone were negligible through day 35.

Calcium levels within the excised implants were determined as a measure of mineral deposition within the implanted tissue. Negligible amounts of calcium were apparent three and seven days after treatment with the AdBMP-2/collagen implants (Fig. 3). An increase in the calcium level was apparent by day 14, and it peaked by day 35. In contrast, calcium was not present through day 14 at the sites treated with collagen alone. By day 35, the calcium levels in the sites treated with collagen alone had increased to the levels at the AdBMP-2/collagen-treated sites.

**Fig. 4**
Alkaline phosphatase activity of AdBMP-2 or FGF2-AdBMP-2-transduced C2C12 cells in vitro in response to increasing vector doses. Alkaline phosphatase activity, normalized to total protein, was quantified in lysates of cells transduced with 0, 750, or 7500 PN per cell. The asterisks denote a significant difference between treatment groups (p < 0.05, powered at 0.5) at the designated time point.
Effect of FGF2 Targeting on AdBMP-2 Osteoinductive Potency

First, to determine if FGF2-AdBMP-2 was a more potent osteogenetic agent than non-FGF2-targeted AdBMP-2, C2C12 myoblast precursor cells were transduced in vitro with the FGF2-targeted or non-targeted AdBMP-2 at 0, 750, or 7500 PN per cell. Cells transduced with FGF2-AdBMP-2 at both vector doses (750 and 7500 PN) exhibited significantly greater alkaline phosphatase activity per cell than did cells transduced with non-targeted AdBMP-2 (Fig. 4). Importantly, lysates of non-transduced cells and cells transduced with FGF2 either conjugated with or not conjugated with AdBMP-2 all
contained equivalent total protein, indicating no effect of the adenovirus transduction or the FGF on total protein synthesis.

Next, to determine if FGF2-AdBMP-2 could stimulate increased bone formation compared with that stimulated by AdBMP-2 in vivo, we measured bone formation fourteen days after subcutaneous implantation of FGF2-AdBMP-2/collagen or AdBMP-2/collagen. As determined with histological quantification, peak bone formation at the sites treated with AdBMP-2/collagen occurred at a viral vector dose of $1 \times 10^{10}$ PN per implant (Fig. 5). In contrast, peak bone formation at the sites treated with FGF2-AdBMP-2/collagen occurred at $1 \times 10^{9}$ PN per implant and was significantly higher ($p < 0.01$) than bone formation induced by the same vector dose of AdBMP-2/collagen (Fig. 5). At this dose, negligible bone or cartilage was visible within AdBMP-2/collagen-treated tissue. In contrast, newly forming bone and some cartilage were prominent throughout the FGF2-AdBMP-2-treated tissue, as evidenced by the presence of osteoblasts along the edges of the bone collagen matrix, hypertrophying chondrocytes, and osteocytes within lacunae.

The relative levels of alkaline phosphatase within FGF2-AdBMP-2/collagen and AdBMP-2/collagen-treated tissues were comparable with the patterns of bone formation observed histologically (Fig. 6). Alkaline phosphatase levels in the AdBMP-2/collagen-treated tissues peaked between $3 \times 10^9$ PN and $1 \times 10^{10}$ PN, whereas the peak alkaline phosphatase activity in the FGF2-AdBMP-2-treated tissues peaked between $1 \times 10^9$ PN and $3 \times 10^9$ PN. Negligible alkaline phosphatase activity was present among sites treated with FGF2 conjugated to adenovirus (FGF2-AdLuc) encoding luciferase or to collagen alone.

A similar relative pattern of calcium deposition was observed among these tissues (Fig. 7). AdBMP-2/collagen implants elicited maximal calcium deposition at vector doses between $3 \times 10^9$ PN and $1 \times 10^{10}$ PN. In contrast, FGF2-AdBMP-2 stimulated maximal calcium secretion at vector doses between $1 \times 10^9$ and $3 \times 10^9$ PN. Calcium was undetectable in tissues treated with FGF2-AdLuc or collagen alone.

**Discussion**

The aim of this study was to assess the bone-forming potential of collagen matrix combined with AdBMP-2 in rat subcutaneous implants. The histological and biochemical data support our hypothesis that AdBMP-2 is osteoinductive and that its potency can be enhanced by targeting the vector to cells by means of FGF2. Specifically, AdBMP-2/collagen implants induced a robust amount of rapidly forming bone. Because collagen alone induced no bone formation in this site, we can conclude that AdBMP-2 is osteoinductive. Furthermore, we demonstrated that targeting AdBMP-2 to cell-surface FGF receptors enhanced the vector’s osteoinductive potency.

Previous studies by us and other investigators have shown that enhancement of adenoviral transgene expression depends on linkage of FGF2 to the adenovirus, since free FGF2 does not affect transduction of unmodified adenoviral vectors. Moreover, we previously showed that the mechanism of FGF2-mediated enhancement of adenoviral transgene expression is due, at least in part, to increased entry of the virus into the cell and of DNA into the nucleus, leading to increased transgene protein expression. It is likely that the increased BMP-2 production observed following the FGF2-AdBMP-2 treatment was due to an increased number of transduced cells as well as to an increased amount of transgene protein produced per cell. It is unlikely that the FGF2 conjugated to AdBMP2 that we used in these studies stimulated cell
proliferation in the subcutaneous implant, since in vitro transduction assays showed the number of osteoprogenitor cells transduced with FGF2-AdBMP-2 to be equal to that transduced with unmodified AdBMP-2.

Bone formation in response to increasing vector doses exhibited a bell-shaped pattern, with a sharp increase at mid-dose followed by a substantial decline at higher doses. It is unlikely that this was due to neutralizing antibodies to the adenovirus, as clinical evaluations of several adenovirus gene therapies delivered at increasing doses or with repeat administration of a constant dose showed no change in therapy-related efficacy, despite measurable neutralizing antibodies to the adenovirus. Moreover, those studies showed no dose-limiting toxicity, suggesting that higher doses of adenovirus can be tolerated by humans. It is possible that the inhibition observed in the subcutaneous model that we described may have been due to these cells’ insufficiency in processing high adenovirus doses, to which they became relatively unresponsive.

Measurements of calcium in the AdBMP-2/collagen implants correlated with histologically evident bone formation at all of the examined time points. Likewise, an absence of calcium three, seven, and fourteen days after implantation of collagen matrix alone was consistent with the absence of histological evidence of new bone formation. In contrast, a high calcium content was measured in the implants obtained on day 35, although disorganized collagen, rather than bone, was apparent histologically in these samples. Dystrophic calcification has previously been reported to occur, weeks after implantation, in response to collagen placed in soft tissues.

The safety of AdBMP-2 in humans must be established if the therapy is to be considered for clinical use. Three major elements of treatment with this nonintegrating, transient virus need to be considered: (1) adenovirus-induced cellular and humoral immune responses, (2) local or systemic pathologic responses to the BMP-2 transgene protein, and (3) the replicative potential of the adenovirus.

One important safety issue is nonspecific vector tropism to all tissue types whose cells express the Coxsackie adenovirus receptor. In this study, we addressed this issue by employing an FGF-conjugated adenoviral vector that is internalized only by cells expressing FGF receptors. Since such cells are found most abundantly in regenerating tissues, our approach largely mitigates unwanted viral vector tropism.

Viral vectors can be localized to the injured tissue by immobilization of the vector on the carrier matrix. Separate studies in our laboratory demonstrated maintenance of adenovirus carrying a platelet-derived growth factor transgene (AdPDGF) at the dermal site of application. In two of six animals, minimal virus (50 copies/mg of tissue) was detected in the regional lymph nodes and none was detected in any other organs. We believe that this was largely due to carrier-directed persistence of the vector at the implantation site.

Delivery of viral vectors on carrier matrices may also dictate the rate and duration of transgene expression, and it is important to control both parameters in patient populations with variable bone-forming capacity. A single treatment with a matrix-immobilized gene has the potential for exact temporal as well as spatial control of growth-factor expression. The characteristics and quantity of biomaterial used to deliver the genes influence their biolocalization. In vitro data from our laboratory demonstrated differences in adenoviral release on the basis of the ratio of collagen matrix to vector used. Others have reported the influence of collagen-glycosaminoglycan cross-linking and pH on vector association and transgene expression of the released vector. Our current research interests include evaluation of the influence of biomaterial physiochemical properties on the duration of gene expression.

An additional benefit of carrier-mediated transgene delivery is its practical application in the clinical setting. For example, a solution of AdBMP-2 can be readily combined with a granular carrier matrix such as demineralized bone matrix in a closed system that efficiently mixes the components while minimizing operator exposure to the treatment. This procedure requires no more than thirty minutes.

In conclusion, we have shown that AdBMP-2 delivered on a biocompatible and biodegradable collagenous matrix supports robust and rapid new bone formation in rats. Furthermore, enhanced osteoinductivity was observed within sites treated with FGF2-AdBMP-2. Following further development and preclinical evaluations, localized delivery of a matrix-immobilized BMP-2 gene to a site of bone injury has the potential to be a safe, effective, and biologically controllable clinical alternative when new bone formation is needed.
References


DECREASED ORTHOTIC EFFECTIVENESS IN OVERWEIGHT PATIENTS WITH ADOLESCENT IDIOPATHIC SCOLIOSIS

BY PATRICK J. O’NEILL, MD, LORI A. KAROL, MD, MICHAEL K. SHINDLE, BA, EMILY E. ELERSON, RN, KARLYNN M. BRINTZENHOFEZOC, DSW, DONALD E. KATZ, BS, CO, KEVIN W. FARMER, MD, AND PAUL D. SPONSELLER, MD

Investigation performed at the Departments of Orthopaedic Surgery at The Johns Hopkins Hospital, Baltimore, Maryland, and Texas Scottish Rite Hospital for Children, Dallas, Texas

Background: Many studies have demonstrated that orthotic treatment is effective for the prevention of curve progression in patients with adolescent idiopathic scoliosis. However, the effect of being overweight on the outcome of orthotic treatment has not been reported. The purpose of the present study was to determine whether orthotic treatment of adolescent idiopathic scoliosis is less successful for patients who are overweight than it is for those who are not overweight.

Methods: A ten-year multicenter retrospective review of patients in whom adolescent idiopathic scoliosis had been treated with a Boston or a custom-molded thoracolumbosacral orthosis was performed. The inclusion criteria were no previous treatment, skeletal immaturity (a Risser sign of 0, 1, or 2), a curve of 25° to 40° at the time of orthotic initiation, and follow-up to skeletal maturity. Patients were divided into two groups according to body habitus, with overweight patients defined as those with a body mass index in the eighty-fifth percentile or greater. Curve progression was compared between the two groups. Successful orthotic treatment was defined as no more than a 5° increase in the primary curve from the start of orthotic wear to skeletal maturity. Absolute curve progression to 45° or greater also was considered to be an adverse outcome.

Results: Two hundred and seventy-six consecutive patients from two institutions were analyzed, and thirty-one patients were considered to be overweight. The mean curve progression was 9.6° ± 7.3° for the patients who were overweight, compared with 3.6° ± 9.4° for those who were not overweight (p < 0.01). Overweight patients were 3.1 times more likely to have an unsuccessful result than those who were not overweight. Curve progression to 45° or greater occurred in fourteen (45%) of the thirty-one patients who were overweight, compared with sixty-nine (28%) of the 245 patients who were not overweight.

Conclusions: The results of the present study suggest that overweight patients with adolescent idiopathic scoliosis will have greater curve progression and less successful results following orthotic treatment than those who are not overweight. The ability of an orthosis to transmit corrective forces to the spine through the ribs and soft tissue may be compromised in overweight patients. This factor should be taken into consideration when making treatment decisions. Additional study is warranted to determine a threshold effect.

Level of Evidence: Therapeutic Level III. See Instructions to Authors for a complete description of levels of evidence.

Although it remains a controversial topic, orthotic treatment of adolescent idiopathic scoliosis is the only nonoperative method that has been shown to potentially decrease curve progression. The Milwaukee orthosis was first introduced as a nonoperative treatment for idiopathic scoliosis in 1945 and became the standard with which other designs were compared. However, because of poor compliance, Watts et al. developed a smaller and more manageable orthosis in 1977, commonly referred to as a thoracolumbosacral orthosis or underarm orthosis. Since then, many studies have demonstrated the effectiveness of using a thoracolumbosacral orthosis for the prevention of curve progression in
patients with adolescent idiopathic scoliosis.  

Orthotic management is generally indicated for skeletally immature patients (patients with a Risser sign of 0, 1, or 2) who present with a curve of 50° to 45° or for those in whom an initial curve of 25° demonstrates ≥5° of progression. Regardless of their adherence to an orthotic regimen, not all patients benefit equally from orthotic management because many factors have been shown to increase the likelihood of curve progression, including measures of immaturity (such as a lower Risser sign, younger age, and premenarchal status). Curve properties (such as initial magnitude, pattern, flexibility, amount of side-bending correction, and amount of initial correction in the orthosis) and curve characteristics (such as initial magnitude, pattern, flexibility, amount of side-bending correction) are independently related to curve progression. Patients who were overweight were then compared with patients who were not overweight with regard to curve progression, the rate of surgery, and the rate of orthotic success (defined as no dition, only patients who were followed to skeletal maturity (as indicated by <6 mm of growth over six months, a Risser sign of 5, and a menstrual status of two years postmenarche [for female patients]) were included. Patients were asked to wear the orthosis for at least eighteen hours per day until discontinuance at Risser sign 4 or 5 or until a threshold for discussion of surgical options (a curve of ≥45°) was reached.

Information obtained from the records of each patient included gender, age, menarchal status, height, weight, Risser sign, initial curve magnitude (as determined with the Cobb method), final curve magnitude, curve type and location, and number of hours per day that the patient reported wearing the orthosis at each visit until weaning began. A single investigator at each institution (E.E.E. or P.D.S.) measured all radiographs. For patients with more than one curve, the one with the largest Cobb angle was designated as the primary or major curve and was used for analysis. For patients who underwent surgery, the last curve measurement before surgery was recorded. The percentage of curve correction in the initial orthosis was recorded. Patients were assessed radiographically by the orthopaedist and the orthotist at each center (L.A.K., D.E.K., and P.D.S.) within one month after initial procurement. A posteroanterior radiograph of the entire spine was made with the patient standing while wearing the orthosis, with a source-to-film distance of 152 cm. An orthotist (D.E.K.) inspected each orthosis at the time of the first post-fitting visit. Modifications were made unless the orthotist thought that no further improvements were possible. Modifications included pad addition or adjustment, increasing relief on the concave side, making the upper trim line higher, or remaking the brace if necessary. The number of hours of orthotic wear was determined by recording the number of hours per day that each patient reported wearing the orthosis at each visit and then averaging these values over the life of orthotic wear, starting from initiation until weaning from the orthosis began.

Patients were grouped according to body habitus and percentile of body mass index. Body mass index was determined by dividing the weight in kilograms by the square of the height in meters (weight [kg]/height [m]²). Patients in the eighty-fourth percentile or less were not considered to be overweight whereas those in the eighty-fifth percentile or greater were considered to be overweight, as is standard in the pediatric literature. Data were obtained from standardized reference tables for children in the United States. The formula log y = 0.011x – 0.177 was used to correct for the decrease in height due to the curvature, where y is the loss in height (in centimeters) caused by a curve of magnitude x (in degrees). This correction resulted in three patients being moved from the overweight group to the not overweight group.

Statistical Methods

Correlational analysis was performed to determine which factors were independently related to curve progression. Patients who were overweight were then compared with patients who were not overweight with regard to curve progression, the rate of surgery, and the rate of orthotic success (defined as no

Materials and Methods

The present retrospective study included 320 patients with adolescent idiopathic scoliosis who were managed with either a Boston or custom-molded thoracolumbosacral orthosis at two large referral centers between 1991 and 2001. Patients who were managed with nighttime bending orthoses such as the Charleston or Providence orthoses were not included in this study. The inclusion criteria required the patient to be eleven years of age or older at the time of clinical onset; to have adolescent idiopathic scoliosis; to have a Risser sign of 0, 1, or 2; to have a major curve between 25° and 40°; and not to have undergone prior treatment. We included all patients for whom either a Boston or custom-molded thoracolumbosacral orthosis had been prescribed and then excluded those with insufficient data, those who had a Risser sign of 3 or higher at the time of orthotic prescription, and those who had had previous treatment.
patients were female. The mean age at the start of orthotic management was 12.8 ± 1.3 years (range, eleven to seventeen years), the mean number of hours in the orthosis was 14.3 ± 5.5 hours per day, the mean age at the time of weaning was 14.9 ± 1.4 years, and the mean time between the initiation of orthotic treatment and the final measurement was 2.1 ± 1.1 years. The mean initial curve magnitude was 32° ± 4.4°, and the mean progression over the course of brace treatment was 4.3° ± 9.3° (range, −20° to 47°) for the entire sample. With regard to outcome, 135 patients (49%) had a successful outcome (the curve did not progress >5°), eighty-three patients (30%) had an unsuccessful outcome (the curve progressed >5° and the final curve was ≥45°), and fifty-eight patients (21%) had an intermediate outcome (the curve progressed >5° but the final curve was <45°).

The factors that were significantly correlated (p < 0.05) with increased curve progression were a lower mean number of hours in the orthosis per day (r = −0.265), a lower Risser sign (r = −0.262), being overweight (r = 0.203), male gender (r = 0.151), and a younger age when orthotic treatment was initiated (r = −0.118) (Table I). These factors were included in a multiple regression analysis to determine their interaction on curve progression. The regression analysis showed that 18% of the curve progression could be explained by mean hours in the orthosis per day, Risser sign, being overweight, and gender (p < 0.01). The remaining 82% of curve progression was explained by variables that were unknown or were not included in this study. In other words, knowing the gender, overweight status, Risser sign, and the number of hours of orthosis wear increases the ability to predict the outcome for a patient by 18%. The weighting of each factor on curve progression, in decreasing order, was hours of wear, Risser sign, being overweight, and gender (Table II).

When the patients who were overweight were compared with those who were not overweight, the two groups were similar in terms of the mean hours of orthotic wear and the mean initial curve magnitude (Table III). There was a significant difference between the groups with regard to the mean age when the orthosis was started and the mean Risser sign (p < 0.05). The mean curve progression was 9.6° ± 7.3° for the patients who were overweight, compared with 3.6° ± 9.4° for those who were not overweight (p < 0.01). The mean in-orthosis correction was 26% ± 21.5% (with a mean initial curve magnitude of 33.3° and a mean in-orthosis correction to 24.7°) for the patients who were overweight, compared with 41% ± 20.1% (with a mean initial curve magnitude of 32.2°

Table I: Factors Related to Curve Progression*

<table>
<thead>
<tr>
<th>Category</th>
<th>R Value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean hours in brace per day</td>
<td>−0.265</td>
</tr>
<tr>
<td>Risser sign</td>
<td>−0.262</td>
</tr>
<tr>
<td>Overweight</td>
<td>0.203</td>
</tr>
<tr>
<td>Gender</td>
<td>0.151</td>
</tr>
<tr>
<td>Age when orthosis initiated</td>
<td>−0.118</td>
</tr>
</tbody>
</table>

* p < 0.05. †Pearson’s product moment correlation coefficient.

Table II: Multiple Regression Analysis of Factors Influencing Curve Progression

<table>
<thead>
<tr>
<th>Category</th>
<th>Beta*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean hours in orthosis per day</td>
<td>−0.256</td>
</tr>
<tr>
<td>Risser sign</td>
<td>−0.241</td>
</tr>
<tr>
<td>Overweight</td>
<td>0.153</td>
</tr>
<tr>
<td>Gender</td>
<td>0.144</td>
</tr>
</tbody>
</table>

*Standard partial regression coefficient.

Table III: Patient Characteristics

<table>
<thead>
<tr>
<th>Orthotic Wear* (hr)</th>
<th>Initial Curve Magnitude* (deg)</th>
<th>Age When Orthosis Started* † (yr)</th>
<th>Risser Sign* †</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not overweight (n = 245)</td>
<td>14.3 ± 5.5</td>
<td>32.2 ± 4.3</td>
<td>12.9 ± 1.3</td>
</tr>
<tr>
<td>Overweight (n = 31)</td>
<td>14.0 ± 5.6</td>
<td>33.3 ± 4.5</td>
<td>12.3 ± 1.2</td>
</tr>
</tbody>
</table>

*The values are given as the mean and the standard deviation. †p < 0.05.
and a mean in-orthosis correction to 19.1° for those who were not overweight (p < 0.01). The rate of success (as indicated by a curve that did not progress >5°) was 26% (eight of thirty-one) for the patients who were overweight, compared with 52% (127 of 245) for the patients who were not overweight (p < 0.01). The rate of curve progression to 245° was 45% (fourteen of thirty-one) for the patients who were overweight, compared with 28% (sixty-nine of 245) for the patients who were not overweight (p < 0.05) (Table IV). On the basis of the odds ratio, orthotic treatment was 3.1 times more likely to be unsuccessful for patients who were overweight than for those who were not overweight.

### Discussion

Many studies have documented the apparent effectiveness of an orthosis in altering the natural history of curve progression in patients with adolescent idiopathic scoliosis. However, it would be ideal to prescribe an orthosis to only those patients who would benefit. Lonstein and Winter demonstrated that patients with a Risser sign of 0 or 1 are three times more likely to experience curve progression than are patients with a Risser sign of 2 to 5 and that curves of ≥30° are three times more likely to progress than are smaller curves. A prospective study conducted by the Scoliosis Research Society demonstrated that eighty-five (66%) of 129 skeletally immature female patients with untreated idiopathic curves between 25° and 35° experienced >5° of curve progression. Thus, most authors agree that orthoses are indicated for skeletally immature patients with a mean initial curve magnitude of 32.2° and a mean in-orthosis correction to 19.1° for those who were not overweight (41%, based on a mean initial curve magnitude of 32.2° and a mean in-orthosis correction to 19.1°) was 58% greater than the mean curve correction for patients who were overweight (26%, based on a mean initial curve magnitude of 33.3° and a mean in-orthosis correction to 24.7°). The mean curve correction for overweight patients (26%) was substantially below the values reported in previous studies that have demonstrated mean in-orthosis corrections, for all patients, in the range of 36% to 62%.

A successful outcome depends on the ability of an orthosis to exert forces of sufficient magnitude to create and maintain curve correction. Previous studies have documented the importance of the forces generated by the orthosis. Chase et al. demonstrated that, in patients with similar curve types, increased force through the compression pads resulted in improved correction of the scoliotic curve. Wong et al. reported that the Cobb angle was strongly correlated with both pad pressure and strap tension. Overweight patients have more soft-tissue thickness and surface area through which the corrective forces of the pads and straps are transmitted. This may dissipate the forces to the spine, resulting in less curve correction.

There may be other explanations for why orthotic treatment is less effective for patients who are overweight. The orthosis may have a poorer overall fit for overweight patients, leading to shifting and discomfort. However, there was little difference in the rate of compliance reported for each group (mean, 14.0 hours for patients who were overweight compared with 14.3 hours for those who were not). Patients with increased body mass may have greater loading of the spinal column and, as a result, greater compression force on the curve. The hormonal effects associated with obesity may be a causative factor. Increasing insulin resistance and hyperinsulinemia are correlated with increasing body mass index. Insulin resistance during puberty may increase the growth process by amplifying the effects of growth hormone and insulin-like growth factor-1. Also, increased peripheral adipose tissue leads to increased estrogen levels, which may influence growth.

The outcome of orthotic treatment can be measured in terms of whether curve progression (usually defined as progression of >5°) is successfully halted or whether the curve reaches a set threshold at which surgery is commonly offered. In the present study, the curve was successfully halted in 135 (49%) of the 276 patients whereas it reached a surgical threshold in eighty-three (30%). These values compare well with the

| TABLE IV Comparison of Patients Who Were Overweight with Those Who Were Not Overweight |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| **Mean Progression**† (deg)     | **Mean Correction**† (%)        | **Success Rate†**               | **Progression** of >5°†         | **Progression** of >45°†        |
| Not Overweight                  | 3.6 ± 9.4                       | 41 ± 20.1                       | 52% (127 of 245)                | 48% (118 of 245)                |
| Overweight                      | 9.6 ± 7.3                       | 26 ± 21.5                       | 26% (8 of 31)                   | 74% (23 of 31)                  |

*The data are given as the mean and the standard deviation. †p < 0.01. ‡p < 0.05.
values in previous studies as well as with the natural history of this condition\(^{4,9,10,11,14,16,20,22}\). However, in the group of thirty-one patients who were overweight, the curve was successfully halted in only eight patients (26%) whereas it progressed to ≥45° in fourteen (45%). In the remaining nine overweight patients (29%), the curve progressed by >5° but the final magnitude was <45°, representing an intermediate outcome.

The present study had several limitations. It was not a prospective study. Several factors that have been reported to affect curve progression were not studied. The number of hours of orthotic wear was determined on the basis of self-reports and not objective measurements.

To our knowledge, the present report describes the first study in which body habitus has been found to be a predictive factor in the orthotic treatment of adolescent idiopathic scoliosis. This factor should be taken into account when making treatment decisions. Additional study is warranted, particularly to determine if there is a threshold body type for which orthotic management becomes less effective. As more and more children are becoming overweight\(^{40}\), the effects of being overweight on the outcome of orthotic treatment of adolescent idiopathic scoliosis is increasingly important. ■

Note: The authors thank Mike Reiter, Carolyn Finck, Marlene Harris, and Lana Bailey for their help in the study.

References


Revision of Unstable Capitellocondylar (Unlinked) Total Elbow Replacement

By David Ring, MD, Mininder Kocher, MD, Mark Koris, MD, and Thomas S. Thornhill, MD

Background: Instability is a recognized complication associated with unlinked total elbow implants. The best form of treatment of this problem is uncertain as very little has been written about it.

Methods: Twelve patients underwent operative treatment of instability at the site of a capitellocondylar unlinked total elbow replacement, and the results were reviewed retrospectively. The study group included ten women and two men with an average age of fifty-eight years. Ten patients had rheumatoid arthritis. Three elbows underwent conversion to a semiconstrained hinged prosthesis. In the other nine elbows, an attempt was made to continue with an unlinked prosthesis: three had reconstruction of one or both collateral ligaments, four had component revision, and two had both ligament reconstruction and component revision.

Results: After an average duration of follow-up of six years (range, two to fifteen years) only three patients had retained a functioning unlinked prosthesis. Of the remaining nine patients, three had had a conversion to a semiconstrained arthroplasty at the time of the index procedure, four had had a conversion to a semiconstrained prosthesis at the time of a salvage procedure, one had had a resection arthroplasty, and one had a painfully dislocated elbow and had declined revision. Thus, seven elbows eventually underwent conversion to a semiconstrained prosthesis; these conversion procedures were technically difficult, with perforation of the humerus occurring in six patients and perforation of the ulna occurring in four. After all procedures, the average elbow flexion was 132° and the average flexion contracture was 25°. According to the Mayo Elbow Performance Index, there were four excellent results, three good results, three fair results, and one poor result.

Conclusions: Revision of an unlinked total elbow prosthesis to a linked total elbow prosthesis is difficult, but it restores elbow function. Although the present series documents the unpredictability of attempts to salvage an unstable unlinked prosthesis, it seems reasonable to attempt at least one soft-tissue procedure before converting to a linked prosthesis.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

One drawback of total elbow arthroplasty with use of an unlinked implant is the potential for subluxation or dislocation of the elbow1-16, leading some authors to recommend routine postoperative cast immobilization after this procedure17. While most reports on total elbow arthroplasty involving unlinked implants have described at least one patient with postoperative instability, there has been little discussion of how to treat this problem. In the present report, we review the results of treatment of unstable capitellocondylar total elbow implants at our institution.

Materials and Methods

Twenty-two patients who had a reoperation or revision at the site of a capitellocondylar total elbow arthroplasty between 1975 and 1995 were identified through a search of a total joint registry and were studied prior to the requirement for approval of the institutional review board at our institution. Twelve (55%) of these twenty-two patients had repeat surgery for the treatment of instability. Eleven of the twelve patients had had the initial total elbow arthroplasty at our institution; these eleven procedures represented 3.2% of the 349 primary capitellocondylar total elbow replacements that had been performed at our institution during this time-period. The medical records of the twelve patients who had repeat surgery for the treatment of instability were reviewed retrospectively.

The study group included ten women and two men with an average age of fifty-eight years (range, forty-five to eighty-seven years). Ten patients had rheumatoid arthritis, one had posttraumatic arthritis after a fracture-dislocation of the el-
bow, and one had an ununited fracture of the distal part of the humerus. Four patients had had prior radial head excision and synovectomy, and one patient had had a prior fascial interposition arthroplasty.

The average interval between the initial total elbow arthroplasty and the index procedure was four months (range, one week to eleven months). Three patients underwent conversion to a semiconstrained hinged (linked) prosthesis. In the remaining nine patients, an attempt was made to continue with an unlinked prosthesis: three had reconstruction of one or both collateral ligaments (two had repair of the medial collateral ligament and one had repair of both the medial and lateral collateral ligaments), four had component revision (two had placement of a thicker polyethylene insert, one had exchange of the humeral and ulnar components, and one had exchange of the humeral component only), and two had both component revision and ligament reconstruction (one had placement of a larger polyethylene insert and reconstruction of the lateral collateral ligament and one had repositioning of the humeral component with repair of both the lateral and the medial collateral ligament).

All surviving patients were evaluated clinically and radiographically, and the Mayo Elbow Performance Score was calculated.

Results (see Appendix)
Complications and Repeat Operations

Among the nine patients in whom an attempt was made to continue with an unlinked, resurfacing total elbow replacement, six had persistent instability after the index operation. One of these six patients refused additional surgery, one had a resection arthroplasty, and three had a revision arthroplasty with a semiconstrained total elbow implant (Figs. 1-A, 1-B, and 1-C). The sixth patient had a second reoperation involving an exchange of the humeral component; this procedure also failed to restore stability, and the elbow eventually underwent conversion to a semiconstrained total elbow implant. Other complications of the index procedure included a transient ulnar neuropathy (one patient) and a small wound separation that healed with dressing changes (one patient).

A stable capitellocondylar total elbow replacement was achieved in only three of the twelve patients. Of the remaining nine patients, seven ultimately had a semiconstrained total elbow replacement, one had dislocation of a capitellocondylar replacement and declined additional treatment, and one had a resection arthroplasty.

Removal and exchange of the recently inserted total elbow components proved to be very challenging. Six of the seven elbows that eventually underwent conversion to a semiconstrained total elbow implant had perforation of both the humerus and the ulna (four patients) or perforation and fracture of the humerus (two patients). These perforations are not surprising given the osteoporotic bone in these older patients, most of whom had rheumatoid arthritis. Furthermore, difficulties with reaming are often encountered as remnants of the original polymethylmethacrylate may direct reamers and other devices away from the hard cement and toward the osteoporotic bone. Six patients had a total of ten procedures subsequent to the index reoperation, including three procedures that were performed for revision of a semi-
constrained total elbow replacement and one tendon transfer procedure that was performed to address a permanent radial nerve palsy that was sustained at the time of a repeat revision procedure.

The patients were evaluated both clinically and radiographically on a periodic basis as part of the maintenance of an ongoing total joint arthroplasty registry. One patient died two years after undergoing a conversion to a semiconstrained total elbow arthroplasty. The eleven surviving patients were evaluated an average of seven years (range, two to fifteen years) after the index operation. The average elbow flexion was 132° (range, 90° to 145°), with an average flexion contracture of 25° (range, 0° to 90°). One patient had restriction of supination to 45°; all other patients had full or nearly full forearm rotation. Six patients had no pain, two had mild pain, two had moderate pain, and one (the patient with a dislocated elbow who refused additional treatment) had severe pain. Evaluation with use of the Mayo Elbow Performance Score revealed four excellent results, three good results, three fair results, and one poor result.

**Discussion**

The failure of total elbow arthroplasty with use of hinged designs led to the development of unlinked designs that depend on the geometry of the prosthesis, the surrounding capsuloligamentous structures, and static and dynamic muscular contributions to stability. Newer hinged designs with some laxity in the hinge—so-called semiconstrained total elbow implants—have decreased the need for soft-tissue stability and thereby have expanded the indications for total elbow arthroplasty to patients with ligament attenuation and bone loss. Total elbow arthroplasty with use of unlinked implants remains an option for patients with inflammatory arthritis, and good long-term results have been reported. A major drawback of unlinked prostheses has been the potential for elbow instability.

As revision of a newly implanted prosthesis can be very difficult—particularly because many of the patients receiving total elbow arthroplasty have poor-quality metaphyseal bone—it is desirable to try to maintain these components by...
reconstructing or retensioning the soft-tissue envelope. Three elbows in the present series were converted directly to a semi-constrained prosthesis, including both of those with posttraumatic problems. Four additional elbows eventually underwent conversion to a semiconstrained total elbow replacement. The conversion procedures proved to be technically difficult, with cement and prosthesis removal leading to humeral or ulnar perforation with or without fracture in six of the seven patients. In spite of these difficulties, a functioning elbow was restored in all patients although the functional result was rated as unsatisfactory for two patients.

Retensioning of the soft-tissue envelope by increasing the valgus angle of the humeral component, the size of the polyethylene insert, or the rotation of the components was successful in only one of four patients. Reconstruction of one or both collateral ligaments with or without component revision was successful in three of five patients. The patients in the present series were managed over an eleven-year period starting in 1975. Since that time, our understanding of the collateral ligament complexes of the elbow has improved and better techniques for their reconstruction with tendon grafts have been developed. It is possible that better results would be achieved with use of current techniques. In particular, it is now recognized that the lateral collateral ligament may be more important than the medial collateral ligament to elbow stability, particularly in this setting, and that reconstruction of the lateral collateral ligament with a tendon graft as described by Nestor and colleagues may be a useful technique.

This approach is important given the difficulties associated with revision to a semiconstrained prosthesis. Although this series documents the unpredictability of attempts to salvage an unlinked prosthesis that is unstable, it seems reasonable to attempt at least one soft-tissue procedure before undertaking the complex and risky removal of a freshly-mented unlinked prosthesis from poor-quality bone. In particular, attention should be paid to maintaining or restoring an adequate lateral collateral ligament complex by firmly reattaching it to the lateral epicondyle with use of sutures through drill-holes in bone or by reconstructing the ligament with a tendon graft.

Appendix

A table presenting the clinical details for all patients is available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

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The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.02449

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Polyethylene Wear After Total Elbow Arthroplasty

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Investigation performed at the Department of Orthopedic Surgery, Mayo Clinic, Rochester, Minnesota

Background: Articular wear is considered to be a possible long-term complication of the use of stemmed, coupled elbow replacements with the capacity to correct deformity and restore function. There have been no reports on this topic, to our knowledge.

Methods: A review of the results of 919 replacements with the semiconstrained linked Coonrad-Morrey total elbow implant, performed between 1981 and 2000, revealed that twelve patients (1.3%) had undergone an isolated exchange of the articular bushings as a result of polyethylene wear. The status of these patients was assessed clinically and radiographically.

Results: The mean age of the twelve patients at the time of the initial total elbow replacement was forty-four years compared with a mean age of sixty-two years in the overall group (p < 0.001). Seven of the twelve patients had post-traumatic arthritis, and five had rheumatoid arthritis. Nine patients had extensive deformity. The group consisted of seven women and five men, and ten patients had involvement of the right dominant elbow. The mean age at the bushing revision was fifty-two years, and the bushings were revised at an average of 7.9 years after implantation. All twelve patients reported pain, and five reported crepitus or a squeaking sound. None had extensive osteolysis. The mean duration of follow-up after the bushing exchange was sixty-five months. The mean arc of motion improved from 89° before the surgery to 109° after it. Three of the twelve patients underwent an additional articular revision at fifty-three, fifty-four, and 136 months after the initial bushing exchange. At the time of final follow-up, all twelve patients had functioning elbows.

Conclusions: Isolated bushing exchange can be a successful revision procedure in patients with a semiconstrained linked total elbow prosthesis. Younger patients with a posttraumatic condition and/or severe pre-existing deformity are at greater risk for the development of excessive bushing wear. Patients should be cautioned against exceeding the recommended activity and lifting restrictions.

Level of Evidence: Therapeutic Level IV. See Instructions to Authors for a complete description of levels of evidence.

The success of total elbow arthroplasty has become more established and accepted in the last decade. Indications have also expanded to include the full spectrum of traumatic conditions, including distal humeral nonunion, instability, ankylosis, established arthritis, and acute intra-articular, comminuted fracture in selected older patients. To our knowledge, wear of the polyethylene articulating surface has not been previously described as a mode of failure of total elbow arthroplasty since loosening and implant dislocation have tended to occur before articular wear. With improved longevity of the total elbow replacement and better function resulting in increased use of the limb, polyethylene wear and its consequences now occur and should be studied. We are not aware of any specific reports on this topic, which is not typically considered when complications are being discussed.

To address this issue, we reviewed our experience with reoperations to exchange worn bushings in the semiconstrained linked Coonrad-Morrey total elbow replacement (Zimmer, Warsaw, Indiana). Our aim was to document the prevalence of isolated bushing exchange due to wear problems, factors predisposing to bushing wear, diagnostic features, and results of the revision surgery.

Materials and Methods

Database

Through a search of the Mayo Clinic total joint database, we identified 919 Coonrad-Morrey semiconstrained total elbow arthroplasties that had been done at our institution from October 1981 through December 2000. The majority of the procedures were performed because of rheumatoid arthritis (377; 41%) or trauma-related conditions (310; 34%). The latter category included posttraumatic elbow arthritis, distal...
humeral nonunion, acute distal humeral intra-articular frac-
ture, chronic instability, and ankylosis6,7. The remaining 232
procedures were revision total elbow arthroplasties: sixty were
revisions of Coonrad-Morrey prostheses that had been im-
planted at our institution, forty-eight were revisions of other
designs that had been inserted at our institution, and 124 were
revisions of various designs that had been implanted else-
where. Of the 919 elbows, ten (1%) were lost to follow-up and
sixty-two were followed for less than one year. Thus, data ob-
tained after at least one year of follow-up were available for
847 elbows (92%).

Study Group
Of the 919 elbows, twelve (1.3%) in twelve patients underwent
exchange of the articular bushings between 1989 and 2000
(see Appendix). Patients who underwent revision because of
loosening were excluded from the study regardless of the sta-
tus of the bushings. An additional six patients were diagnosed
as having bushing wear on the basis of an asymmetric anterior-
posterior orientation of the ulnar component within the hu-
meral yoke, but these patients did not have a revision.

Demographic data were obtained through a review of
the patients’ charts. Predisposing factors such as hand domi-
nance, body weight, occupation, and amount of deformity
seen radiographically were specifically assessed to identify po-
tential influences on bushing wear.

The presence of pain, the range of motion, and the func-
tional assessment were recorded to determine elbow function.
This information allowed calculation of the Mayo Elbow Per-
formance Score (MEPS) both before and after bushing ex-
change (see Appendix). The results were graded as excellent,
good, fair, or poor according to this system10.

Radiographic assessment was conducted before the to-
tal elbow replacement to identify deformity and after replace-
ment to identify signs of bushing wear, osteolysis, and the
status of the implant. Anteroposterior plain radiographs of
each elbow in full extension that were made following the in-
dex total elbow arthroplasty and at the time of the bushing
exchange were compared to measure the extent of the bush-
ing wear. The prosthesis was designed with 7° to 10° of varus-
valgus laxity. The criteria for the assessment of wear were
previously described by Ramsey et al.2. A line is drawn paral-
lel to the yoke of the humeral component, and another line is
drawn parallel to the medial or lateral surface of the articular
surface of the ulnar component. An angle of intersection of
>7° between these two lines indicates alteration of the bush-
ning due to wear or plastic deformation (Fig. 1). An angle of
≥10° is considered to indicate mild-to-moderate bushing
wear. In addition, the presence of humeral or ulnar implant-
bone lucency and osteolysis were recorded at the time of the
bushing exchange.

Surgical Technique
The previous skin incision is used to explore the elbow, and
the ulnar nerve is palpated. If the patient has ulnar nerve
symptoms, the nerve is explored and decompressed. If the
nerve is not symptomatic, it is identified proximally at the me-
dial aspect of the triceps and is protected throughout the pro-
cedure. If the distal part of the humerus has been resected or is
absent, the triceps is left attached to the ulna, the pseudocap-
sule is entered medially and laterally, the articulation is disengaged, and the humerus and ulna are separated. If the condyles are intact, the triceps is again reflected from the ulna according to a previously described technique\(^1\). At this juncture, the anterior aspects of the medial and lateral epicondyles are removed to an extent sufficient to allow the implant locking pin to be removed both medially and laterally (Fig. 2). The posterior aspects of the condyles are left intact. The medial and lateral bushings are removed from the humerus, and the bushing is removed from the ulna. The soft tissue is assessed, and a thorough débridement is carried out. If the wear is sufficient to have resulted in impingement of the metallic ulnar component on the metallic humeral component, then black synovitis is the predominant feature.

After débridement, the implant is inspected for the integrity of the fixation and orientation. In this series, no patient was thought to have sufficient malorientation to justify revision of either implant. If there has been resorption or osteolysis at the distal aspect of the humerus or the proximal aspect of the ulna, the interface is thoroughly cleaned and is filled with methylmethacrylate. Fresh bushings are then inserted in the ulnar and humeral components, and the implant is coupled with use of the pin-within-pin snap-fit articulation. If the preoperative assessment and intraoperative evaluation indicated a fixed angular deformity that cannot be corrected passively, then the soft tissue is released to allow correction of the deformity. Thus, an extensive flexor release from the humerus is carried out for the treatment of varus deformity. Similarly, an aggressive extensor tendon release, including the distal fibers of the brachioradialis, is performed to treat a fixed valgus deformity. The triceps is reattached with use of a cruciate and transverse drill pattern as previously described\(^1\).

\[\text{Statistical Analysis}\]

A chi-square test was used to determine significant differences between two sets of discrete data. Differences that had less than 0.05 probability of occurring from chance were considered significant.

\[\text{Results}\]

\[\text{Initial Clinical Characteristics}\]

Seven female and five male patients (twelve elbows) underwent bushing exchange. Five had rheumatoid arthritis and seven had posttraumatic arthritis. Ten patients had involvement of the right, dominant elbow. In the overall sample, the patients with posttraumatic arthritis had a higher prevalence of bushing wear (seven of 294; 2.4%) than did those with rheumatoid arthritis (five of 377; 1.4%) (\(p = 0.14\), chi-square test). There were no isolated bushing exchanges following any of the 232 index revision total elbow replacements. The index primary total joint replacements in the twelve patients who subsequently had a bushing exchange were performed between 1982 and 1994, when the patients were an average of forty-four years old (range, thirty to fifty-nine years). This compares with a mean age of sixty-two years in the 907 patients who did not have isolated bushing exchange in the overall sample of 919 patients (\(p < 0.001\)). Of the twelve patients who underwent bushing exchange, six had a sedentary occupation (homemaker or a desk job), four had a moderately active occupation (nurse and sales agent), and two had a strenuous occupation (contractor and lumberjack). The mean body weight of the twelve patients was 77 kg (range, 54 to 96 kg).

Prior to the arthroplasty, radiographic assessment revealed a markedly distorted joint in nine patients, with severe rheumatoid arthritis in four, marked varus or valgus defo-
mity of ≥10° in nine, and gross dissociation of the ulna from the humerus (a flail elbow with complete loss of the distal humeral condyles) in four (Figs. 3-A and 3-B). Nine of the elbows had absence of one or both distal humeral condyles.

Initial Outcome
All twelve patients had had an excellent or good result immediately following the index elbow arthroplasty. Postoperative anteroposterior radiographs revealed that the articulation was at the limits of the designed angular tolerance in nine of the twelve patients. One patient had a fracture of the medial condyle during the index surgery, which was fixed with a screw.

Failure of the index total elbow arthroplasty occurred at a mean age of fifty-two years (range, thirty-seven to sixty-eight years). The period between the index arthroplasty and the bushing exchange averaged 7.9 years (range, forty-eight to 156 months).

Prior to the bushing exchange, all twelve patients had pain and five had crepitus or squeaking sounds with any movement of the affected elbow. Pain was graded as mild in two patients, moderate in seven, and severe in three. The mean total arc of motion was 89° (range, 60° to 130°). The average extension loss was 32° (range, 0° to 55°), and the average flexion was 121° (range, 105° to 140°). The mean amount of pronation and supination were 64° (range, 30° to 90°) and 59° (range, 20° to 90°), respectively. No patient had any symptoms of functional instability. The Mayo Elbow Performance Score (MEPS) averaged 48 points (30 to 65 points), with two elbows graded as fair and ten graded as poor.

Radiographic Assessment
Plain anteroposterior radiographs of the elbow in full extension made just prior to bushing exchange all showed obvious asymmetry of ≥10° at the yoke as described above. Osteolysis, defined as localized osseous resorption, was assessed immediately after the primary total elbow arthroplasty and at the time of the bushing revision. It was identified in the distal part of the humerus in four patients, and some resorption of the proximal part of the ulna was recorded in three.
Bushing Exchange
Marked synovial discoloration due to titanium particulate debris was found at the time of surgery in four patients. Two patients had a moderate amount of discoloration, four had a small amount, and two had no appreciable synovial discoloration. In no instance did the osteolytic process appear to compromise fixation or function. The humeral and ulnar bushings were replaced in all patients.

Clinical Outcome
Initially, the isolated bushing exchange was technically successful in all twelve patients (Figs. 4-A through 4-E). There were no wound complications or deep infections. Clinically, eight patients had no pain, one had mild pain, one had moderate pain, and two had severe pain following the revision surgery. None had instability symptoms. The mean MEPS was 86 points (range, 50 to 100 points), with eight elbows graded as excellent; one, as good; one, as fair; and two, as poor. The mean arc of flexion after the bushing exchange improved to 109° (range, 70° to 130°) with a mean extension loss of 21° (range, 0° to 50°) and a mean flexion of 130° (100° to 145°).

Pronation and supination, which were essentially unchanged from the preoperative values, averaged 69° (range, 50° to 90°) and 63° (range, 20° to 90°), respectively.

All patients were assessed at an average of sixty-five months (range, twenty-four to 136 months) after the revision. At this time, three patients were examined by us, five were in-
Three patients underwent a second bushing exchange procedure because of clinical and radiographic evidence of wear of the previously exchanged bushings at fifty-three, fifty-four, and 136 months after the initial bushing exchange. Of the three patients, two had a sedentary occupation and one, a moderately strenuous occupation. All had had a marked initial deformity. All three patients had a successful second bushing exchange, with a “good” MEPS at fifteen, eighteen, and fifty-one months. Hence, at the time of final follow-up, all twelve patients had a functioning elbow replacement.

Two patients had a poor result, due to persistent pain from ulnar nerve neuropathy, following the bushing exchange. In one of these patients, the symptoms had been present before the revision procedure and did not resolve or change after the nerve was decompressed at the time of the bushing replacement. In the other patient, ulnar neuritis developed after the revision surgery. In both cases, clinically adequate ulnar nerve transposition had been performed at the time of the primary total elbow arthroplasty and the nerve had been reexplored at the revision operation and noted to have been decompressed. These residual symptoms substantially compromised the overall functional outcome for these two individuals.

Discussion

Despite the increased longevity of semiconstrained linked total elbow prostheses and the use of these implants to treat an increasingly complex array of pathological conditions, only twelve (1.3%) of 919 such implants inserted at our institution over a twenty-year period required a reoperation specifically for replacement of worn articular bushings. A higher bushing revision rate was associated with a younger patient age and showed a trend toward an association with traumatic conditions.

While the low prevalence of clinically relevant wear requiring revision is encouraging, the small numbers in this study make analysis difficult. This experience does not docu-
ment the overall wear rate of this device during the study period because six additional patients with radiographically documented worn bushings were found in the database. Furthermore, since stress radiographs were not routinely made, the absolute wear rate cannot be determined from this study. On the basis of the data available, neither increased patient weight nor hand dominance in relation to the involved elbow was found to predispose the bushings to wear. We do not have sufficiently accurate data to definitely correlate strenuous or very active lifestyles or occupations with bushing wear.

It is possible that the feature with the greatest prognostic importance is severe preoperative deformity at the time of the index total elbow arthroplasty. Nine of the twelve patients had extensive or high-grade deformity or loss of at least one humeral condyle at the time of the primary total elbow arthroplasty. In addition, all three elbows that required a second bushing exchange procedure had had marked initial deformity with both angular and translatory loss of the humeral relationship to the ulna.

In all patients, the angular deformity exceeded the tolerance of the articular design. Yet, it is these very problems that
can be addressed only with this type of coupled implant. Substantial malrotation of components at the time of insertion, even without deformity, can also contribute to increased bushing wear although this problem was not specifically recognized in any of the patients in the present series. The insight documented herein is that correcting deformity comes at a price of a potential increased rate of bushing wear. Our current practice, therefore, is to extensively release soft-tissue contractures to eliminate preoperative deformity. We are more willing to resect bone in order to lessen soft-tissue tension that can result in an imbalance that differentially loads the polyethylene.

When a patient has radiographic evidence of wear but no symptoms following the arthroplasty, the process is discussed with the patient. Typically, we simply follow the patient radiographically since, in our experience, the wear debris does not cause fixation-compromising osteolysis. Instability was not a symptom in this group of patients. If a patient has pain or mechanical squeaking, then revision is offered.

Osteolysis that presumably developed in reaction to debris from the worn bushing was not extensive in any of these patients. This finding is in contrast to the situation with hip and knee replacements, in which polyethylene wear causes periarticular osteolysis that can lead to fixation failure. This difference is presumably due to the much smaller absolute volume of wear debris generated by the smaller articular surfaces at the elbow. However, osteolysis can develop and progress in the presence of loose cemented total elbow implants. This has been attributed to small-fragment debris, generated from micromotion, that accelerates osteolysis as a result of third-body abrasion (Fig. 5). A reaction of this type and extent is specifically associated with a loose cemented stem, and it is very important to recognize that polyethylene wear is not its principal cause. Although the reaction has been attributed to bushing wear, its extent and location readily distinguish it as one primarily due to loosening and not directly related to a worn bushing.

Isolated bushing exchange is a successful procedure in the particular situation of isolated bushing wear. The procedure is not extensive, and morbidity is minimal when compared with that associated with the index total elbow arthroplasty. Yet, the issue of articular wear is likely to receive more attention with the rapid increase in the number of total elbow arthroplasties performed worldwide, improved longevity of the implant, expanded indications, and increased patient activity. Attempts to mitigate the problem of bushing wear, such as by increasing the thickness of the polyethylene bushings and using cross-linked polyethylene, are being investigated. Most importantly, the results of our study emphasize the need to perform soft-tissue release and to attempt to balance elbow alignment at the time of total elbow arthroplasties. This is especially the case in patients with severe long-standing deformity.

In summary, the prevalence of isolated wear of polyethylene bushings as a complication and an isolated cause of revision of total elbow arthroplasty was low in our practice, although wear was associated with severe pre-existing deformity in younger patients. Our data revealed that osteolysis is not extensive in patients with worn bushings and well-fixed implants. Isolated bushing exchange is a reliable and effective revision procedure in the majority of instances.

Appendix

Tables presenting details on all twelve patients and the Mayo Elbow Performance Score are available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

References

Human Periprosthetic Tissues Implanted in Severe Combined Immunodeficient Mice Respond to Gene Transfer of a Cytokine Inhibitor

BY SHANG-YOU YANG, MD, SAM NASSER, MD, DAVID C. MARKEL, MD, PAUL D. ROBBINS, PhD, AND PAUL H. WOOLEY, PhD

Investigation performed at the Department of Orthopaedic Surgery, Wayne State University, Detroit, Michigan, and the Department of Molecular Genetics and Biochemistry, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

Background: Periprosthetic tissue formation and local inflammation that are associated with wear debris contribute to the pathogenesis of aseptic loosening of a prosthesis. This study evaluated a retrovirus-mediated gene therapy with use of a novel xenograft-based animal model.

Methods: Human periprosthetic tissues obtained from patients during revision arthroplasty performed because of aseptic loosening of a prosthetic joint were transplanted into the left quadriceps and paravertebral muscles of severe combined immunodeficient (SCID) mice. The engrafted tissues were recovered seven, fifteen, or thirty days after implantation for histological and molecular analyses. The periprosthetic tissues were incubated with retroviruses encoding for human interleukin-1 receptor antagonist (hIL-1Ra) or bacteria β-galactosidase (LacZ) at 37°C for three hours prior to implantation to evaluate their responses to gene modification.

Results: The human periprosthetic tissues were well accepted in SCID mice for up to thirty days, with angiogenesis occurring in the majority of the implanted tissue sections. The histological appearance was consistent between the recovered graft tissue and the original donor tissue. Strong expression of interleukin-1, tumor necrosis factor, and interleukin-6 was detected in the xenografts with use of immunohistochemical stains. Histological analysis revealed that interleukin-1 receptor antagonist gene modification significantly decreased the total number of inflammatory cells (p < 0.01) in engrafted human tissue containing implant wear debris. Real-time reverse transcription-polymerase chain reaction and immunohistochemical staining showed declining expression levels of interleukin-1 and tumor necrosis factor following interleukin-1 receptor antagonist gene transfer in comparison with LacZ-transduced or virus-free controls.

Conclusions: Human periprosthetic tissue can survive in the SCID mouse host for up to thirty days and responds to the interleukin-1 receptor antagonist gene transfer with the amelioration of inflammation.

Clinical Relevance: The human periprosthetic tissue-SCID mouse chimera has been characterized in this study as a useful model to explore the properties of human periprosthetic tissue in vivo, laying the foundation for potential clinical application of gene therapy in aseptic loosening.

Total joint replacement is a common and effective procedure for the treatment of end-stage arthritis. It is estimated that over 500,000 such procedures are performed each year in the United States, but periprosthetic osteolysis and aseptic loosening often develop within ten to twenty years, making aseptic loosening the single most common long-term complication of this procedure. Many studies have suggested that particulate wear debris from prosthetic components contributes to the pathogenesis of aseptic loosening. A layer of connective tissue (the periprosthetic pseudomembrane) is usually present at the implant-bone interface of the loose implant. This tissue is vascularized granulomatous tissue containing mainly macrophages, fibrocytes, foreign-body-type giant cells, and numerous wear debris particles. Wear debris activates and stimulates macrophages and other inflammatory cells to release inflammatory cytokines, such as interleukin-1, tumor ne-
crosis factor, interleukin-6, and other mediators\(^5\), which in turn lead to osteoclastogenesis and periprosthetic bone resorption\(^12\)–\(^14\). We examined the central hypothesis that local inflammation induced by particulate wear debris is responsible for osteolysis-associated aseptic loosening in total joint arthroplasty and that gene therapy directed against proinflammatory cytokines in periprosthetic tissue may prevent or retard the loosening process. It has been well documented that interleukin-1 receptor antagonist protein (IL-1Ra or IRAP) inhibits the biological activities of interleukin-1 by occupying the type-I interleukin-1 receptor without eliciting a signal transduction response, therefore blocking the interleukin-1-induced inflammation cascade\(^15\)–\(^18\). We and others have reported that blocking the major proinflammatory cytokines (interleukin-1 and tumor necrosis factor) effectively ameliorated wear debris-induced local inflammation and subsequent bone resorption in animal models\(^17\)–\(^19\), suggesting a potential therapeutic approach. Moreover, virus-mediated gene transfer has been utilized as a promising alternate delivery of cytokine inhibitors, with potential advantages in site-specific therapy and in the avoidance of adverse effects of systemic administration\(^20\)–\(^22\).

In order to extend these findings and investigate how cytokine blockade through gene therapy can influence the pathological process of a failing prosthesis and human periprosthetic tissue, a novel model utilizing human tissue was developed. Severe combined immunodeficient (SCID) mice do not reject xenografts because of a lack of functional T and B lymphocytes\(^22\)–\(^24\), which provides a means to study gene transfer effects in vivo on human periprosthetic tissue. The two separate objectives of this study were to validate the SCID-human periprosthetic tissue chimera model and to examine the in vivo human periprosthetic tissue responses to virus-mediated gene therapy directed against the proinflammatory cytokine interleukin-1.

### Materials and Methods

**Animals and Materials**

Forty female severe combined immunodeficient (SCID) mice (CB17-Prkdc\(^scid\); Jackson Laboratory, Bar Harbor, Maine) that were three to four weeks old were quarantined in a pathogen-free environment for at least one week before experimentation. Immunohistochemistry staining kits, polyclonal antibodies against human interleukin-1, tumor necrosis factor, and interleukin-6 were obtained from Santa Cruz Biotechnology (Santa Cruz, California). Monoclonal antibodies against mouse CD68 and against human CD68 were purchased from R and D Systems (Minneapolis, Minnesota). These reagents exhibited no cross-reactivity between the relevant species (mouse and human) in our study. Real-time polymerase chain reaction reagents were all obtained from PerkinElmer (Norwalk, Connecticut). All other chemicals were analytical grade.

**Transplantation of Human Periprosthetic Tissue-Bone Pieces into SCID Mice**

The study was approved by the institutional review board at Wayne State University, and informed consent was obtained from all patients. The institutional animal investigation committee approved all of the experimental procedures on animals. Human periprosthetic tissue was obtained from osteolytic areas adjacent to hip and knee implants that had developed aseptic loosening (Table I). Within thirty minutes after removal, the periprosthetic tissue was rinsed in sterile warm saline solution and was diced into tissue cubes of \(<5\) mm\(^3\). The SCID mice were anesthetized with a mixture of xylazine (7.5 mg/kg) and ketamine (90 mg/kg). Under sterile conditions, one segment (4 to 5 mm\(^3\)) of human periprosthetic tissue was surgically embedded into the left quadriceps and another was grafted into the paravertebral muscles of each SCID mouse, while similar pieces of tissue were snap-frozen and stored at –80°C to serve as preimplantation controls. Since periprosthetic tissue usually appeared heterogeneous in composition, attention was paid to avoid obvious fibrotic or fatty tissue. On the basis of previous experience\(^5\), it was expected that the granulomatous tissue for implantation would contain debris particles and associated inflammatory cells. The mice were killed at seven, fifteen, and thirty days following surgery, and the human xenografts (along with adjacent mouse tissues) were harvested for histological assessment and molecular and protein analyses. Fourteen SCID mice were implanted with xenografts from two individual patients (Table I, Cases 1 and 2) in this phase of the study.

**Viral Vectors and Virus-Mediated Gene Transduction**

A retrovirus encoding for human interleukin-1 receptor antagonist protein (DFG-IRAP-neo) was used to investigate the influence of a transgene product directed against interleukin-1 in comparison with a control viral vector (a retrovirus coding for β-galactosidase [MFG-LacZ]), and virus-free controls. Fresh human periprosthetic tissues were diced into 4 to 5-mm\(^3\) pieces and divided into three groups. Tissue segments in Groups 1

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Duration of Implantation (yr)</th>
<th>Underlying Disease</th>
<th>Prosthetic Joint</th>
<th>Reason for Revision</th>
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<td>10</td>
<td>Pseudogout arthritis</td>
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</table>
and 2 were incubated in Dulbecco’s modified Eagle medium (DMEM; Gibco, Carlsbad, California) containing DFG-IRAP-neo or MFG-LacZ, respectively, at a titer of $1 \times 10^7$ colony-forming units at 37°C for three hours, whereas tissue segments in Group 3 were incubated in Dulbecco’s modified Eagle medium without viral vectors (virus-free control) for the same length of time and at the same temperature. Then, the human tissues were immediately transplanted into SCID mouse hosts as described above. Each mouse received two pieces of gene-transferred periprosthetic tissue (on the back and on the left thigh), and three animals were assigned to each group. Mouse serum was collected at day 0, 2, and 7 after surgery for transgene expression. Mice were killed seven days after surgery for tissue assessment. The experiment was repeated two more times (Table I, Cases 3, 4, and 5) to assure reproducibility, and a total of twenty-six SCID mice were used for this part of the study.

**Detection of Transgene Production**

To confirm the successful transduction and expression, conventional polymerase chain reaction was performed on DNA iso-

---

**Fig. 1**

Representative photomicrographs of hematoxylin and eosin-stained human periprosthetic tissue sections prior to transplantation (A) and thirty days after intramuscular transplantation into an SCID mouse (B) (×100).

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**Fig. 2**

Immunohistochemical detection of human proinflammatory cytokines on human periprosthetic tissues engrafted in SCID mice for thirty days (×200). Cytokine-expressing cells are stained dark brown with specific antibodies against human interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF). Hematoxylin counterstains the nuclei of cells blue.
lated from xenografts with primers specific for the reporter neo gene (a vector marker of DFG-IRAP-neo) or the LacZ gene as described previously. The polymerase chain reaction was conducted for thirty-five cycles with use of a thermal cycler (Perkin-Elmer), with each cycle consisting of denaturation at 94°C for one minute, annealing at 60°C for one minute, and extension at 72°C for one minute. Amplified neo or LacZ polymerase chain reaction products were visualized under ultraviolet light after electrophoresis on 1.8% agarose gels containing ethidium bromide. The production of human interleukin-1 receptor antagonist protein subsequent to the integration of the transgene was determined with use of enzyme-linked immunosorbent assay (ELISA) with anti-human interleukin-1 receptor antagonist antibodies that do not cross-react with murine interleukin-1 receptor antagonist.

**Histological Evaluation and Image Analysis**

Mouse tissues containing human xenografts were fixed, dehydrated, and embedded in paraffin. A solution of 12% EDTA was used for five days to decalcify the adjacent bone. Five-micrometer sections were cut, mounted, and stained with hematoxylin and eosin. After staining, the slides were permanently bonded with coverslips. A minimum of four separate sections per specimen were evaluated in a blinded fashion with use of the Image-Pro Plus analysis software package (Media Cybernetics, Silver Spring, Maryland). The total number of cells (based upon nuclei count) was expressed as cells per mm². All data were exported to an Excel spreadsheet (Microsoft, Redmond, Washington), and the mean cellular tissue densities were calculated.

Immunohistochemical stains were used to localize human interleukin-1β, tumor necrosis factor, and interleukin-6 expression in the xenograft. Antibodies for human and mouse CD68 were also applied to frozen sections of xenografts to identify host macrophage invasion. Briefly, cryosections of tissues were fixed in acetone and blocked with 1.5% normal goat se-

![Image](image_url)
rum before being incubated with primary antibodies overnight in a moisturized chamber at 4°C. Biotin-conjugated secondary antibody and avidin-biotin enzyme reagent were applied to sections followed by color development in 3,3′-diaminobenzidine tetrahydrochloride. Hematoxylin was applied for a counterstain. In negative control sections, the primary antibody was replaced with nonimmune sera. Digital images from at least two different fields of each tissue section (to include both the xenograft and the adjacent host tissue) were captured and analyzed with use of the Image-Pro Plus software package. The level of expression and localization of these proteins was evaluated in six different fields and was expressed as integrated optical density (a unit generated by the software that normalizes the optical density with the positive stained area).

**Real-Time Quantitative Polymerase Chain Reaction for Gene Expression**

The expression of proinflammatory cytokines interleukin-1β, tumor necrosis factor, and interleukin-6 was determined by real-time quantitative polymerase chain reaction with use of the ABI Prism 7700 sequence detector (PE-Applied Biosystems, Foster City, California) as described previously. Briefly, the human xenografts were carefully separated from surrounding mouse muscles and were homogenized on ice with use of a Polytron (PT-MR2100; Kinematica, Lucerne, Switzerland) operated at three bursts of fifteen seconds. A fraction of the homogenate was processed for RNA-DNA extraction with use of a commercial kit (Tel-Test, Friendswood, Texas) in accordance with the manufacturer’s instructions. Complementary DNA (cDNA) was reverse transcribed from 0.5 µg of total RNA before being incubated with primary antibodies overnight in a moisturized chamber at 4°C. Biotin-conjugated secondary antibody and avidin-biotin enzyme reagent were applied to sections followed by color development in 3,3′-diaminobenzidine tetrahydrochloride. Hematoxylin was applied for a counterstain. In negative control sections, the primary antibody was replaced with nonimmune sera. Digital images from at least two different fields of each tissue section (to include both the xenograft and the adjacent host tissue) were captured and analyzed with use of the Image-Pro Plus software package. The level of expression and localization of these proteins was evaluated in six different fields and was expressed as integrated optical density (a unit generated by the software that normalizes the optical density with the positive stained area).

**Fig. 4**

A: Agarose gels to show xenogeneic gene incorporation. The product of conventional polymerase chain reaction with specific primers for neo gene. Lane 1 contains a DNA ladder (size markers), lanes 2 to 5 contain DNA from tissues transduced with DFG-IRAP-neo. Lanes 6 and 7 are DNA extracted from xenograft tissue infected with MFG-LacZ. The correct size of the polymerase chain reaction product amplified with the specific primers for neo is 295 base pairs. B: Polymerase chain reaction product with primers for LacZ. Lane 1 shows a DNA ladder. A positive product band was identified in DNA extracted from MFG-LacZ-transduced tissue (lanes 4 and 5), whereas DNA from virus-free tissue (lanes 2 and 3) and DFG-IRAP-neo transduced xenografts (lanes 6 and 7) remained negative.

**Fig. 5**

Typical photomicrographs of transplanted periprosthetic tissues stained with hematoxylin and eosin seven days following xenogeneic gene transfer (×100). A: The virus-free control. B: The LacZ gene transduced. C: The interleukin-1 receptor antagonist gene transduced. Note the cellularity at regions containing wear debris particles. The inserts illustrate the wear debris in the xenografts (×400).
RNA in 40 mL of a reaction mixture containing 1× polymerase chain reaction buffer, 500 mM each of deoxynucleotide triphosphates (dNTP), 0.5 U/µL of ribonuclease inhibitor, 2.5 mM of random hexamers, 5.5 mM of MgCl2, and 1.25 U/µL of reverse transcriptase (PerkinElmer), with use of a DNA thermal cycler (PerkinElmer) at 25°C for ten minutes, 48°C for five minutes, and followed by 95°C for five minutes. For real-time polymerase chain reaction, 2 µL of cDNA was added into a final volume of 25 µL of a reaction mixture containing 12.5 µL of 2× SYBR Green PCR Master Mix (5 mM of MgCl2; 200 mM each of dATP, dCTP, and dGTP; 400 mM of dUTP; 1.25 U AmpliTaq Gold DNA polymerase; and 0.5 U of AmpErase uracil N-glycosylase), and 0.5 µL each of 0.4-µM target primer pairs. The polymerase chain reactions were set in MicroAmp optical ninety-six-well reaction plates with MicroAmp optical caps (PE-Applied Biosystems) and amplified in the ABI Prism 7700 Sequence Detector for forty cycles (at 95°C for fifteen seconds and at 60°C for one minute). The fluorescent signals were recorded dynamically. The values of the threshold cycle (Ct) at which a substantial increase in reporter-dye signals was first detected were normalized against expression of a housekeeping gene (18S), and the target gene copies were calculated by regression analysis against the standard curve. The primer pairs for target genes were constructed by Sigma-Genosys (Woodlands, Texas) and are listed as follows: human interleukin-1 beta, 5′-CTGTCTCCTGGTGTTGAAAGA-3′ and 5′-TCCTTCAGACACCCTCAACC-3′; human tumor necrosis factor, 5′-TGTCTCCAGAGCCCTAGTTTGAATTCTT-3′; human interleukin-6, 5′-GAGGTGCCCATGCTACATTT-3′ and 5′-GAGGTGCCCATGCTACATT-3′. Selected reaction mixtures after real-time polymerase chain reaction were electrophoresed on 1.8% agarose gels containing ethidium bromide to verify the amplification of the correct target gene.

Statistical Analysis

Power analysis was used to estimate the number of mouse samples required for the current study. A software package,
Human Periprosthetic Tissues Implanted in Mice Respond to Gene Transfer of a Cytokine Inhibitor

Acceptance of Xenografts in SCID Mice

The embedded human periprosthetic tissue survived in SCID mouse hosts for up to thirty days. No infection or tissue rejection reactions were appreciable at the time of tissue harvest. Histological evaluation indicated that human periprosthetic tissue attached firmly to surrounding host muscles, with a morphology very similar to the original tissue before implantation. The viability of the cells within the xenograft was confirmed by the intact nature of the cell boundaries, the normal granulation of the cellular cytoplasm, and the normal size and staining characteristics of the nucleus. Figure 1 shows typical photomicrographs of human xenograft embedded in the SCID mouse quadriceps. Wear debris particles, including polyethylene and metals, were found in most implanted tissues, surrounded by extensive cellular infiltrates. The general morphology of the periprosthetic tissues was consistent between the engrafted tissue and the original tissue before implantation (Fig. 1).

Immunohistochemical probes for human interleukin-1β, tumor necrosis factor, and interleukin-6 applied to xenografts retrieved from SCID hosts revealed strong expression of proinflammatory cytokines, similar in severity to the tissue before transplantation (Fig. 2). Immunohistochemical stains with anti-human and anti-mouse CD68 showed that the majority of macrophages in the transplanted tissue were of human origin (Fig. 3). In addition, increased vascularity was noted in the xenografts at fifteen and especially at thirty days following transplantation (data omitted).

Virus-Mediated Gene Transfer and Transgene Production

Transduction and subsequent transgene expression of the xenografts was determined with use of conventional polymerase chain reaction with primers specific for the neo gene (a vector marker of DFG-IRAP-neo) or the LacZ gene. A positive band corresponding to the neo polymerase chain reaction product was observed in DNA extracted from xenografts transduced with DFG-IRAP-neo, while DNA extracted from human tissue infected with MFG-LacZ was consistently negative (Fig. 4, A). LacZ incorporation was confirmed in a similar manner by positive polymerase chain reactions (Fig. 4, B), while X-gal staining for LacZ-transduced xenografts revealed that approximately 10% of the cells were stained positive (data not shown). ELISA showed that the therapeutic transgene product, interleukin-1 receptor antagonist, averaged 314.1 ± 5.7 pg/mg in xenografts transduced with DFG-IRAP-neo in comparison with 43.2 ± 3.4 pg/mg in human xenografts without gene transfer at the time that the mice were killed. There was no detection of human interleukin-1 receptor antagonist in the mouse sera after xenograft transplantation.

Amelioration of Inflammation by Gene Transfer

Interleukin-1 receptor antagonist gene transfer dramatically decreased the total inflammatory cell accumulation around the debris in engrafted human tissue in comparison with LacZ-transduced or virus-free controls. Figure 5 illustrates the histological appearance of human xenografts receiving gene transduction. Whereas the LacZ gene transferred and the virus-free control tissues maintained inflammatory characteristics, including inflammatory cell aggregation around debris and increased vascularity (Fig. 5, A and B, respectively), interleukin-1 receptor antagonist transgene production significantly reduced cellular density in the xenografts (p < 0.01) (Fig. 5, C, and Fig. 6), especially in the areas associated with wear debris deposit (Fig. 5, inserts). Real-time polymerase chain reaction to examine changes in mRNA expression of cytokines following interleukin-1 receptor antagonist gene transfer showed declining expression levels of interleukin-1β (p < 0.05) and tumor necrosis factor compared with virus-free control tissues, although changes in cell density after inhibition of tumor necrosis factor expression did not reach significance (p = 0.12) (Fig. 7). Image analysis to quantify the expression of proinflammatory cytokines on immunohistochemically stained sections showed that interleukin-1 receptor antagonist gene modification significantly diminished expression of tumor necrosis factor and interleukin-
1β (p < 0.05), although no significant change was detected for interleukin-6 expression (Fig. 8). The gene transfer experiment was repeated three times with implantation of periprosthetic tissue derived from three individual patients. Interleukin-1 receptor antagonist gene transfer showed very similar amelioration effects for all of the periprosthetic tissue embedded.

Discussion

A severe combined immunodeficient (SCID) mouse in a litter of otherwise normal mice was observed by Bosma et al. in 1983, and subsequent backcrosses established the now well-known SCID mouse. SCID mice fail to develop mature T and B lymphocytes because of an inability to carry out functional rearrangements of the elements encoding the immunoglobulin and T-cell receptor genes. SCID mice accept allogeneic and xenogeneic grafts, making them an ideal model for cell and tissue-transfer experiments. Recent work has demonstrated that rheumatoid synovial implants in SCID mice can serve as an in vivo model of human rheumatoid arthritis. However, to the best of our knowledge, there has been no report of an SCID mouse model being used to investigate the pathological mechanisms of implanted periprosthetic tissue. We report in the present study that human periprosthetic tissues may be successfully engrafted and well accepted in SCID mice for up to thirty days without loss of tissue morphology. In addition, wear debris-associated inflammatory cell composition and proinflammatory cytokine expression were well preserved. Although many studies have been conducted with use of implanted xenografts (usually arthritic synovium) subcutaneously or under the renal capsule, we embedded human periprosthetic tissue intramuscularly. The advantages of intramuscular transplantation include the plentiful blood supply at the implantation site and less tissue damage due to the surgery. At fifteen and thirty days after transplantation, neovascularization was observed in the transplanted tissue.

On the basis of the observation that SCID mice may have a residual nonspecific immune system (consisting of natural killer cells and macrophages), Sandhu et al. developed a protocol for engraftment of human peripheral blood lymphocytes and transplantation of human tissues into SCID mice utilizing pretreatment of the mice to deplete host mouse macrophages and natural killer cells prior to transplantation.

In our experiments, we stained the xenografts immunohistochemically to distinguish macrophages of host and graft origin. There were only a few mouse CD68-positive cells scattered in the human tissue at the boundaries of the receiving sites. The majority of cells in the implanted tissue were of human origin, consistent with the findings in the SCID-human rheumatoid arthritis model.

Since the generation of particulate wear debris is inevitable during the movement of a prosthetic joint, blockade of debris-associated inflammation may be an effective strategy to treat or retard the process of the loosening. In comparison with the traditional drug delivery system, gene transfer-mediated delivery of therapeutic proteins directly into the joints offers the following potential advantages: (1) targeted delivery to periprosthetic tissues at the site of inflammation without the need for unnecessary high systemic doses, (2) sustained expression of the protein and avoidance of the peaks and troughs frequently seen following systemic drug administration, and (3) an opportunity to regulate intracellular signaling pathways directly. Indeed, in vivo or ex vivo anti-inflammatory cytokine gene therapy has shown efficacy in ameliorating joint disease in a number of animal models of inflammatory arthritis.

Interleukin-1 appears to be one of the most predominant cytokines in periprosthetic tissue retrieved from patients who had aseptic loosening. It is a pyrogentic cytokine that can act directly as an osteoclast-activating factor or indirectly through a stimulatory effect on the production and activation of other potent mediators of osteolysis. Interleukin-1 receptor antagonist blocks the interleukin-1-induced inflammation cascade by occupying the type-I interleukin-1 receptor without eliciting a signal transduction response. Recombinant interleukin-1 receptor antagonist is now available as a drug to treat rheumatoid arthritis. It is administered by daily subcutaneous injection, a process frequently associated with injection site reactions. Its clinical effectiveness is reduced by the short half-life of the protein in plasma, and it is unclear how much interleukin-1 receptor antagonist actually accumulates in the joints. Local transfer of the gene expressing the short half-life protein appears to be a more effective and safer alternative. Previously, using retroviral vectors encoding for human interleukin-1 receptor antagonist, we successfully transduced the therapeutic gene using in vivo murine models of inflammation and osteolysis, and the gene modification effectively ameliorated orthopaedic biomaterial particle-induced inflammation and bone resorption. In the current study, we extended our previous findings by investigating the human periprosthetic tissue responses to anti-inflammatory cytokine gene therapy. Our data demonstrated that human periprosthetic xenografts responded to the interleukin-1 receptor antagonist gene transfer. Tumor necrosis factor and interleukin-1β expression at both the mRNA and protein levels were decreased in response to interleukin-1 receptor antagonist transgene production, and a reduction of inflammatory cell accumulation in the xenografts was observed. This finding supports the concept that interleukin-1β and tumor necrosis factor play pivotal roles in periprosthetic inflammation. Further study is required to explore the fate of the inflammatory cells following gene therapy and to determine whether their reduction reflects increased apoptosis or cell trafficking away from the tissue.

The limitations of retroviral vector transduction include the observation that retroviruses only infect dividing cells and have the tendency to mutate. Tumorigenicity has also been reported in clinical trials with use of retroviral vectors. It is apparent that gene therapy is still in its infancy, and extensive investigations are required to advance the potential of gene therapy for the treatment of diseases in humans. Among the important concerns recently discussed by Baum et al., the most prominent were the absence of a “perfect” vector, dissemination of the vector beyond the target tissue, and compli-
cations due to host immune responses. However, we did not detect any transgene protein production in mouse sera in this study, and we have not observed transgene expression in major organs distant to the injection site during our previous studies. As for the concern of whether the vector-mediated transgene expression is adequate to elicit the desired therapeutic effect, 10% of the xenograft cells were transduced with transgene (LacZ) and appeared positive for X-gal stain in the current study, indicating a reasonable efficacy of retroviral vector infection. This transduction efficacy was sufficient to result in adequate interleukin-1 receptor antagonist expression to diminish wear debris-associated inflammation.

Overall, this study shows that human periprosthetic tissue successfully survived in the SCID mouse host and responded to viral vector-mediated gene modification. The data validate this experimental approach as a useful preclinical model to examine potential therapeutic agents for asptic loosening and to analyze the expression of a transgene over time in engrafted human periprosthetic tissue. The findings also show that interleukin-1 receptor antagonist transgene production effectively diminished the debris-associated inflammatory cell accumulation and reduced the expression of proinflammatory cytokines.

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Traumatic Spondylopelvic Dissociation
A Report of Two Cases

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Traumatic spondylopelvic dissociation is an extremely rare injury resulting in mechanical dissociation of the pelvis from the spine. Similar mechanical dysfunction can occur in association with lumbosacral fracture-dislocation or bilateral sacroiliac joint dislocation. However, traumatic spondylopelvic dissociation is a distinct injury pattern, characterized by a transverse sacral fracture in conjunction with bilateral sacroiliac fracture-dislocation, that requires a unique approach to overall patient management and surgical stabilization. Options for the surgical treatment of spondylopelvic dissociation are limited as the sacrum may not provide structural support or stability for internal fixation. Our patients were informed that data concerning the cases would be submitted for publication.

Case Reports

Case 1. A nineteen-year-old woman who was wearing a helmet while riding as a passenger on a motorcycle was ejected at high speed, struck a tree, and subsequently was run over by an eighteen-wheel tractor-trailer. She initially presented to an outside hospital with a Glasgow Coma Score of 15 but was unable to move either lower extremity. She was intubated because of respiratory distress, and a chest tube was inserted bilaterally for the treatment of pneumothorax. A diagnostic peritoneal lavage was positive, and the patient underwent exploratory laparotomy. She had multiple musculoskeletal injuries, including spondylopelvic dissociation with highly comminuted sacral fractures that had both vertical and transverse components (Fig. 1-A), a closed fracture of the proximal part of the right femoral shaft, a comminuted fracture of the left acetabulum, open midshaft fractures of the left tibia and fibula, left metacarpal fractures, and degloving injuries of both feet. The open fractures of the left tibia and fibula were irrigated and debrided in the operating room and then were stabilized with external fixation. A traction pin was placed in the distal part of each femur. The patient then underwent bilateral internal iliac artery embolization. Acute respiratory distress syndrome developed on the day of the injury. Because of increasing intra-abdominal pressure and concern about an abdominal compartment syndrome, the patient was returned to the operating room for abdominal decompression.

On the first day after the injury, the patient was transferred to our tertiary-care academic hospital for further management. At the time of arrival, she continued to have...
substantial pulmonary difficulties that prevented a return to the operating room. On the sixth day of hospitalization, the patient had improved enough to undergo adjustment of the external fixator in the left tibia, repeat irrigation and débridement of the left tibia and foot, and wound closures. A bedside tracheostomy was performed on the tenth day.

The patient’s condition improved over the next several days, and, on the sixteenth day after the injury, she underwent stabilization of the spondylopelvic dissociation. Because of the neurologic deficits in the lower extremity, immediate exploration of the nerve roots within the sacral fracture was considered. However, given the extensive trauma to the soft tissues in the sacral area and the high likelihood of disruption of the lower sacral roots, a decision was made to defer exploration of the neural elements. The treatment plan was to restore alignment and to stabilize the spondylopelvic dissociation with internal fixation while leaving the sacral fracture and the tissues overlying the traumatized sacral region undisturbed. The reason for avoiding further disruption of the sacral soft tissue was so that the sacral skin could be closely monitored and potentially used as an operative site in the event of a nonunion of the sacrum. Additionally, in an attempt to preserve lumbar spine motion, the lumbar segment was not fused.

To accomplish these goals, the spinous processes and laminae at the L3, L4, and L5 levels were exposed through a limited midline incision, and the posterior superior iliac spine was exposed bilaterally through two small, separate incisions. Pedicle screws (ISOLA instrumentation; DePuy Acromed, Raynham, Massachusetts) were placed bilaterally at L3, L4, and L5, with avoidance of the facet joints. Two iliac bolts were placed in each posterior superior iliac spine to create Galveston-like iliac fixation. An attempt was made to recess these bolts as much as possible. The iliac bolts and the pedicle screws were interconnected with I-rods. These I-rods were bent to restore sacral inclination with the eyelets positioned to accommodate the distal iliac bolts. A slotted connector was added to each I-rod for attachment of the proximal iliac bolt at each posterior superior iliac spine, and the I-rods were tunneled from the iliac incisions below the fascia into the lumbar wound. Slotted connectors for the pedicle screws were then added to the rod in the lumbar wound. All screws and bolts were then attached and tightened to secure the hardware, and the rods were interconnected with multiple transverse connectors (Figs. 1-B and 1-C).

On the eighteenth hospital day, the fracture of the right femur was treated with internal fixation with use of an in-

Fig. 1-B
Anteroposterior (Fig. 1-B) and lateral (Fig. 1-C) radiographs made after operative fixation with use of a modified Galveston technique.

Fig. 1-C
tramedullary rod. The fracture of the left acetabulum was treated nonoperatively with traction. The patient remained in the intensive-care unit for forty-five days. Over the course of that time, she lost 35 lb (15.9 kg) (20% of her body weight) despite efforts to keep her in an anabolic state. She began to move all four extremities, although she still had bilateral lower extremity deficits in the distributions of the L4, L5, and S1 nerve roots. An iliac decubitus ulcer with wound dehiscence began to develop approximately one month postoperatively. It was successfully treated with wet-to-dry dressing changes. By six weeks, the patient had been weaned from the ventilator. She required supportive acute hospitalization for two months and was then discharged to an acute rehabilitation unit. The spinal hardware was removed electively seven months postoperatively, after plain radiographs and a computerized tomographic scan of the pelvis suggested stable healing of the sacral fractures.

At the time of the most recent follow-up examination, five years and two months after the injury, the patient was able to walk without an assistive device. The left-sided neurologic deficits had resolved, and the patient had no obvious motor deficiencies; however, she continued to have right-sided sensory deficits in the distributions of the L4, L5, and S1 nerve roots as well as bowel and bladder dysfunction. The range of motion of the lumbar spine was estimated to be 55° in flexion (measured by having the patient bend forward with her knees straight), 20° in extension (measured by having the patient bend backward over the examiner’s hand when placed over the posterior superior iliac spine), and 15° on lateral bending (measured by having the patient lean to each side after stabilization of the iliac crest). Overall, the patient was satisfied with the outcome, and she had returned to school.

CASE 2. A twenty-one-year-old man who worked as a radio tower installer fell approximately 100 ft (30.5 m) before landing on the roof of a building. At the time of presentation to our institution, he had an initial Glasgow Coma Score of 15 and was rapidly intubated in the trauma bay before undergoing a thorough neurologic examination. A chest tube was inserted bilaterally for the treatment of pneumothorax. The patient had multiple musculoskeletal injuries, including spondylopelvic dissociation (Fig. 2-A), a highly comminuted sacral fracture with vertical and transverse components, an L5 burst fracture, a bilateral intra-articular distal radial fracture, a bilateral scaphoid fracture, a fracture-dislocation of the right elbow with a fracture of the radial head and a tear of the medial collateral ligament, closed fractures of the right tibia and fibula, Grade-IIIB open fractures of the left tibia and fibula, closed fractures of the right calcaneus and talus, Grade-IIIB open fractures of the left calcaneus and cuboid, and a dislocation of the left talonavicular joint.

The patient underwent embolization of the right internal iliac artery and then was taken to the operating room for multiple orthopaedic procedures: irrigation and débridement and external fixation of the open fracture of the left tibia, irrigation and débridement of the open fracture of the left calcaneus, closed reduction of the dislocation of the left talonavicular joint, intramedullary rodding of the closed fracture of the right calcaneus, splinting of the wrist fractures, and closed reduction of the fracture-dislocation of the right elbow. The patient remained intubated. On the third day after the injury, the patient underwent open reduction and internal fixation of both scaphoid fractures, both intra-articular distal radial fractures, and the right radial head fracture. The patient was then weaned from the ventilator and extubated. After extubation, a detailed neurologic examination revealed motor and sensory deficits in the distribution of the L3, L4, and L5 nerve roots in the right lower extremity and complete paralysis of the left lower extremity.

On the eighth day after the injury, the patient underwent stabilization of the spondylopelvic dissociation. The technique was identical to that used for the previous patient (Case 1), except that the lumbar fixation included L2 instead of L3.
of L5 because of the L5 burst fracture (Figs. 2-B and 2-C). Once again, the region overlying the traumatized sacral region was left undisturbed and no attempt at fusion was made.

On the fourteenth day after the injury, the patient underwent open reduction and internal fixation of the right calcaneal fracture along with primary subtalar fusion, open reduction and internal fixation of the right talar fracture, closed reduction and pinning of the right navicular fracture, closed reduction and pinning of the left talonavicular joint, and irrigation and débridement of the open left calcaneal fracture. He required supportive acute hospitalization for one month and was then discharged to an acute rehabilitation unit. During the period of acute hospitalization, the patient lost 20 lb (9.1 kg) (12% of his body weight).

Over the course of acute hospitalization, iliac decubiti developed and necessitated surgical débridement and closure. Hardware removal was performed eight months after surgical stabilization, once radiographs and a computerized tomographic scan of the pelvis suggested stable healing of the sacral and L5 fractures.

At the time of the most recent follow-up examination, six years after the injury, the patient was able to walk without an assistive device. He had no motor deficits in either lower extremity but had some paresthesias in the left lower extremity. He continued to have bowel and bladder dysfunction, but with some improvement. The range of motion of the lumbar spine was estimated to be 50° in flexion, 25° in extension, and 10° on lateral bending to each side. Overall, the patient was satisfied with the outcome and had returned to sedentary work with his previous employer.

Discussion

While there have been a number of case series on fracture-dislocations involving the lumbosacral and sacroiliac joints, there have been only a few case reports on traumatic spondylopelvic dissociation. Nork et al. described the largest series of such debilitating injuries in their review of thirteen U-shaped sacral fractures that had been treated with iliosacral screw fixation. However, such fractures differ slightly from traumatic spondylopelvic dissociations. Traumatic spondylopelvic dissociation results in mechanical dissociation of the pelvis from the spine as the result of a highly comminuted sacral fracture with severe instability in the cephalad direction. This extremely high-energy fracture pattern is associated with extensive soft-tissue damage, hemorrhage, and orthopaedic and visceral injury. It is presumed that reports on the treatment of traumatic spondylopelvic dissociation are rare because of a high associated mortality rate. However, ad-
vancements in the emergency management system as well as improvements in trauma transport and resuscitation have resulted in the need to develop treatment strategies for these rare injuries.

The lack of sites for sacral fixation is the primary challenge when treating the gross instability associated with traumatic spondylopelvic dissociation. Previous investigators have used a combination of pedicle screws, sacroiliac screws, plates, percutaneous fixation, and Harrington rods with varying degrees of success. The technique that we described is a modification of Galveston iliac fixation. Originally, the Galveston technique was accomplished by inserting angled rods into the iliac wings. Our modification of this technique allowed spanning fixation from the lumbar spine directly to each ilium with the use of screws and rods. Placing two iliac screws per ilium, instead of one, and connecting them both to the distal rods allows for a greater degree of stability and an improved ability to mobilize the patient. In both of our patients, all hardware remained well fixed until the time of removal.

The mechanism of injury in our two patients was a direct blow to the posterior part of the sacrum. In both cases, the skin overlying the sacral region remained intact but was extremely confused. The surgical approach that we used avoided direct exposure of the comminuted sacrum as well as additional injury to the traumatized soft tissues. As noted in other reports, traumatic spondylopelvic dissociation is likely to be associated with neurologic injury. The rationale for our approach to the treatment of the neurologic injury was provided in the description of the case of the first patient (Case 1). Whether sacral nerve root exploration would have benefited these patients is unknown, but surgical exploration remains a consideration. We believe that treatment in this regard must be tailored to the individual patient and remains a matter of judgment.

Restoration of spondylopelvic alignment at the time of surgical stabilization is important. The assessment of coronal alignment with use of intraoperative radiographic imaging is relatively straightforward. The assessment of sagittal alignment is more difficult and therefore requires more consideration. The surgeon is essentially trying to restore the lumbosacral angle or the sacral inclination. If the vertical plane is considered to be the normal sagittal plumb line for the spine, normal sacral inclination is approximately 45°. The sagittal relationship of the spine to the sacrum and the ilium should be reviewed preoperatively in order to avoid difficulty in assessing it intraoperatively. Difficulty may arise from the loss of visual clues secondary to the sacral comminution. We recommend that sagittal alignment be assessed with use of fluoroscopy at the time of patient positioning. This alignment should then be reconfirmed before fixation of the hardware. The two-point iliac fixation creates excellent rotational stability for maintaining this alignment.

In an attempt to preserve lumbar motion, we took measures to avoid facet injury and chose not to fuse the lumbar spine. The rationale for this approach was to compensate for any spondylopelvic malalignment and to minimize future disc degeneration cephalad to the fused segments in these young patients. Both patients had preservation of some lumbar motion, but it remained limited.

These multiply traumatized patients exhibited substantial catabolic weight loss despite what was considered at the time to be an adequate nutritional resuscitation. As noted previously, the combination of tissue damage, fracture, and decubiti places these patients at a very high risk for infection and underscores the need for aggressive nutritional resuscitation. A manifestation of the weight loss, which was a direct consideration in these patients, was skin breakdown overlying the iliac screws. These screws, which were resected at the time of surgery, became more prominent secondary to weight loss, and ulceration at the sites of the screws necessitated surgical treatment. This problem may have been avoided if more aggressive preventative measures had been instituted before the breakdown.

In summary, traumatic spondylopelvic dissociation is a rare high-energy injury that requires surgical stabilization. A modification of the Galveston technique provides stable fixation while sparing the traumatized sacral area.

References


Treatment of U-Shaped Bone Ankylosis of the Knee with the Ilizarov Method

A Case Report

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Ossseous ankylosis following thermal burns is an uncommon but disabling problem. There are two different types of bone ankylosis. The first type is due to extra-articular bridging heterotopic ossification with preservation of the underlying joint. This type typically responds to physical therapy and other treatment modalities, including surgical excision. The second type of bone ankylosis is intra-articular and occurs most commonly at the interphalangeal joints, resulting in serious functional and cosmetic problems.

There are several alternatives for treatment, including arthrodesis, osteotomy, arthroplasty, and amputation. However, treatment is always very difficult and the outcomes can be discouraging.

We present the case of a patient who had intra-articular bone ankylosis of the right knee joint in full flexion that was treated with the Ilizarov method. To our knowledge, this is the first time that such a case, in terms of both the clinical presentation and the method with which it was treated, has been reported in the literature. Our patient was informed that data from the case would be submitted for publication.

Case Report

A forty-seven-year-old woman presented with a 160° fixed flexion deformity of the right knee that was very disabling. She had sustained a third-degree thermal burn involving the right lower extremity when she was seven years old. There was circumferential scarring of the skin about the knee, and the right thigh appeared to be adhered to the leg. She required the use of crutches for mobility. A lateral radiograph showed that the right femur and tibia were almost parallel to each other and the knee was ankylosed (Fig. 1). We recommended treatment with an osteotomy at the apex of the deformity in the knee followed by gradual distraction of the leg with use of the Ilizarov method. At surgery, two proximal 5/8 rings were applied to the femur and two distal 5/8 rings were applied to the tibia. The femoral and tibial components were joined with lateral and medial hinges at the center of the apex of the deformity. Two distraction rods were applied, medially and laterally, between the ends of the distal femoral and proximal tibial rings. After the application of the frame, an osteotomy was performed (Fig. 2).

After ten days, gradual distraction was started at a rate of 3.0 mm/day, divided into two 1.0-mm increments and two
0.5-mm increments as tolerated. During the distraction period, passive stretching of the triceps surae was applied by a physiotherapist and family members. We connected a canvas strap around the patient’s foot to the front of the frame to assist with ankle dorsiflexion. During the middle of the distraction period, severe pain and hyperesthesias developed over the dorsal aspect of the ankle and the foot without any motor loss. The rate of distraction was decreased to 1.5 to 2.0 mm/day. As the hyperesthesias and severe pain decreased, the rate of distraction was increased again to 3.0 mm/day. When the deformity was corrected to 60° of flexion, the 5/8 rings were changed to half-rings at a second operation (Fig. 3), in order to provide a more stable frame and more powerful distraction.

Full extension was achieved with new bone formation at the distraction site after three and a half months. Radiographs made at eight months demonstrated stable bone consolidation at the distraction site, and the frame was removed. The patient used a long leg brace for immobilization of the limb for two months to protect the distraction site. After completion of the treatment, the range of motion of the hip was 90° of flexion, 0° of extension, 60° of abduction, 45° of lateral rotation, and 30° of medial rotation. There was 0° of dorsiflexion and 20° of plantar flexion at the ankle. At the latest follow-up visit, twenty-six months after the first surgery, the range of motion of the ankle had improved to 10° of dorsiflexion and 30° of plantar flexion (Fig. 4). The neurovascular examination revealed normal findings. The patient returned to a more normal lifestyle and used a cane to walk.

Discussion

Intra-articular bone ankylosis is a severely disabling deformity when the position of the joint is unacceptable. The knee is not a common location for this type of bone ankylosis. The optimal position for a knee arthrodesis is 0° to 15° of flexion, 5° to 8° of valgus, and 10° of external rotation. Herzenberg et al. emphasized that knee flexion contractures of ≥30° alter gait adversely by overstressing the quadriceps, and they believed that surgical correction may be a reasonable treatment alternative.

Several methods have been proposed to treat moderate contractures or ankylosis of the knee. Herzenberg et al. treated fourteen knees with severe flexion contracture (in ten patients) with gradual mechanical distraction by using either the Ilizarov circular external fixator or an Orthofix monolateral external fixator. They emphasized that the average total arc of motion remained essentially unchanged between the preoperative and follow-up examinations; however, the functional position of the arc improved substantially. Calhoun et al. used the Ilizarov fixator to correct chronic burn deformities of the foot and ankle. They classified the contractures as “simple” or “complex” on the basis of associated deformities and musculoskeletal function. They reported that obtaining and subsequently maintaining correction of complex deformities with varus or valgus angulation, bone abnormality, or muscle loss was more difficult. Naranja et al. reported on thirty-seven knees without any preoperative motion that underwent a total knee arthroplasty. They stressed that treatment of an ankylosed or fused knee with total knee arthroplasty is possible but the results may be compromised and there is an increased
rate of complications. Their total complication rate was 57%, and a satisfactory outcome was obtained in only ten patients (27%). Therefore, one must consider this option with caution.

There may be several options for the treatment of severe bone ankylosis in an unacceptable position; these include osteotomy with or without shortening, osteotomy following gradual distraction with use of an external fixator, and amputation followed by application of an orthosis. We believe that only two of these options—amputation or gradual correction—
of the deformity followed by arthrodesis with the knee in an acceptable position—were possible for our patient who had severe bone deformity. We chose the second method and planned a two-stage approach. Our treatment relied on the principle of tension-stress described by Ilizarov. With use of the Ilizarov method, we achieved both osseous union and acceptable realignment of the limb.

We believe that important factors in the successful treatment of this severe deformity included the use of a circular external fixator; the adjustment of the rate of distraction during the correction period; and the exchange of the first frame, composed of two 5/8 rings, with a second one, composed of two half-rings. In conclusion, we believe that osteotomy and gradual distraction with a circular external fixator can be an effective method, and it appears to be a unique alternative to amputation, for the reconstruction of a knee with u-shaped bone ankylosis.

References

Dislocation of Rotating Hinge Knee Prostheses

A Report of Four Cases

By William G. Ward, MD, David Haight, MD, Paul Ritchie, MD, Stan Gordon, BS, and Jeffrey J. Eckardt, MD

Investigation performed at the Department of Orthopaedic Surgery, Wake Forest University Baptist Medical Center, Winston-Salem, North Carolina, and the University of California-Los Angeles Medical Center, Los Angeles, California

The rotating hinge knee mechanism was designed to provide a stable total knee reconstruction when the intrinsic stability of the knee has been lost as a result of severe soft-tissue compromise. It is not recommended for routine total knee arthroplasty because it has been associated with high rates of revision. Rotating hinge knee designs have a transversely (horizontally) oriented hinge axis for flexion-extension motion and a vertically oriented post-in-channel axis for internal and external rotation (Fig. 1). The post-in-channel design also allows distraction up to the limits imposed by soft-tissue tension. As a result, component dislocation due to distraction disengagement is prevented only by the restraint of the soft-tissue envelope. Once distraction occurs, the degree of tilting of the central rotational stem within the channel directly reflects the intrinsic stability of the component design. The amount of distraction required for implant dislocation is directly related to the length, degree of taper, and tolerance of the stem in the cylinder (Fig. 1). To our knowledge, only one design (Link America, Pine Brook, New Jersey) possesses an antisubluxation feature that

![Fig. 1](image_url)

Line diagrams illustrating the minimal varus-valgus toggle and hence the excellent stability provided by designs that employ a long (7-cm) vertical, cylindrical rotational stem within a cylindrical channel compared with the excessive toggle under similar conditions (2.5 cm) of joint distraction, permitted in designs that have a substantial taper of the post-in-cylinder design (7.5°).
specifically prevents implant distraction. There have been few reports in the literature with regard to the clinical stability afforded by these rotating hinge knee prostheses, and we are aware of no reports comparing the clinical stability provided by the various rotating hinge knee mechanisms. We therefore conducted a retrospective review to assess the prevalence of instability and dislocation in a consecutive series of rotating hinge total knee prostheses of various designs, and we identified four dislocations.

**Materials and Methods**

The records on all patients in whom a rotating hinge knee endoprosthesis (Fig. 2) had been implanted by two senior surgeons (W.G.W. and J.J.E.) were reviewed to determine the clinical results, including the occurrence of dislocation. We limited our statistical analysis to patients who had been followed for a minimum of two years or until dislocation (whichever occurred first).

Of the initial 275 consecutive rotating hinge knee reconstructions (214 primary and sixty-one revision) performed by us in 240 patients, 185 reconstructions (132 primary and fifty-three revision) in 152 patients had been followed for a minimum of two years or until dislocation. The eighty-two men and seventy women had an average age of 28.2 years (median, twenty-two years; range, five to ninety-one years) at the time of the index arthroplasty. The duration of follow-up averaged 74.4 months (range, twenty-four to 194 months) in these patients, except for two of the four patients with dislocation. One of those two patients died, as a result of progression of an underlying malignant disease, 1.4 months following dislocation and one underwent an above-the-knee amputation, as a result of a recalcitrant deep infection of the knee, 11.5 months following dislocation. The rotating hinge prosthesis was indicated for 172 reconstructions (128 primary reconstructions and forty-four revision reconstructions) in 140 patients because the arthroplasty followed a tumor resection and there were no remaining cruciate or collateral ligaments (Fig. 2). It was indicated for thirteen total knee arthroplasties (four primary reconstructions and nine revision reconstructions) in twelve patients because arthritic deformity (coupled with fracture in six patients) had created substantial bone and soft-tissue deficiency. There were 136 distal femoral replacements, twenty-eight proximal tibial replacements, fifteen total femoral replacements, and six standard rotating hinge total knee replacements. All implants were custom or modular prostheses that incorporated the following rotating hinge knee designs: Kinematic II Rotating Hinge Knee (Howmedica, Rutherford, New Jersey), Noiles Rotating Hinge Knee (Techmedica-Intermedics/Sulzermedica, Austin, Texas), Endo-Model Rotational Knee (Link America), Lacey Knee-Segmental Oncology System (S.O.S.) Rotating Hinge Knee (Dow Corning Wright/Wright Medical Technology, Arlington, Tennessee), S-ROM Noiles Modular Rotating Hinged Knee (Joint Medical Products/Johnson and Johnson, Stamford, Connecticut), and Finn Rotating Hinge Knee (Biomet, Warsaw, Indiana) (Figs. 3-A and 3-B). The stem length, stem taper, and minimal amount of measured distraction for dislocation with each implant are shown in Table I. With use of the Fisher exact test, we compared the prevalence of dislocation in patients with a short and/or tapered central rotational stem with that in patients with a long and/or straight central rotational stem.

**Case Reports**

There were four dislocations (Table I), three of which occurred within the first three months following implantation. Case 1. The first dislocation, of a custom total femoral reconstruction (Howmedica), occurred at the time of a simultaneous hip dislocation one month after total femoral resection and endoprosthetic reconstruction to treat a dedifferentiated osteosarcoma in a seventy-five-year-old man. The hip dislocation probably allowed the prosthetic femur to subluxate...
proximally a sufficient distance for the knee mechanism to disengage.

CASE 2. The second dislocation, involving a custom distal femoral reconstruction (Techmedica-Intermedics), occurred eight months after implantation following a distal femoral resection to treat osteosarcoma in a forty-eight-year-old man. This patient had a contralateral below-the-knee amputation performed many years earlier to treat a metachronous osteosarcoma. The dislocation occurred when he fell in the shower while not wearing his prosthetic contralateral leg and while attempting to balance on his recently reconstructed leg.

CASE 3. The third dislocation involved a S-ROM Noiles modular rotating hinge revision total knee prosthesis (Joint Medical Products/Johnson and Johnson) that had been implanted as part of the sixth revision total knee arthroplasty in a sixty-eight-year-old man who had a loose fixed-hinge Guepar (Groupe d’utilisation et d’experimentation des prostheses articulares [Guepar, Paris, France]; Howmedica, Rutherford, New Jersey) total knee prosthesis. He had had severe soft-tissue laxity, and a 31-mm tibial tray had been utilized to regain adequate soft-tissue tension. Following this revision, he had symptomatic instability of the knee in flexion, which was most apparent to him when he was climbing in and out of bed. Anterior and posterior drawer stress radiographs in 90° of flexion were ob-

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**Fig. 2**
Anteroposterior radiograph of a typical modular distal femoral tumor endoprosthesis with a rotating hinge knee design.

**Fig. 3-A**
Lateral radiograph of the knee, made while the leg was suspended over the side of the radiology table, shows tilting of the polyethylene tray/post component.
tained with the leg suspended over the side of the radiology table, confirming the distraction of the central rotational stem, which allowed the stem to tilt when a gentle anterior or posterior force was applied to the proximal aspect of the tibia (Fig. 3-A). Three months after implantation, the polyethylene post fractured at the inferior tip of the central reinforcing post, causing a dislocation (Fig. 3-B) that required revision. A subsequent revision was performed to insert a custom tibial tray containing a full-length central metallic reinforcing post. However, a postoperative deep periprosthetic infection ultimately resulted in an above-the-knee amputation.

CASE 4. The fourth dislocation occurred following a staged revision, with a Biomet modular Finn rotating hinge distal femoral replacement, of a total knee prosthesis in a sixty-eight-year-old man who had had multiple previous total knee revisions and two previous infections at the site of the total knee arthroplasty. The joint line had been lowered approximately 1 cm at the latest revision. The knee dislocated two weeks postoperatively as the patient was swinging his leg into bed from a seated position on the side of the bed. The rotational stem disengaged from the cylindrical rotational channel. Following open reduction, the limb was placed into a full extension brace for eight weeks. The soft tissues tightened sufficiently to prevent further instability over the subsequent two years. The range of motion at the time of the latest follow-up was from full extension to 115° of flexion.

In our previous biomechanical analysis of rotating hinge knee prostheses, we determined the amount of distraction required for dislocation of each design. In the present study, there were dislocations of two (1.1%) of 179 endoprostheses with designs that require ≥3.9 cm of joint distraction to dislocate, as determined in our previous study. Conversely, two of five endoprostheses that require ≤3.3 cm of distraction to dislocate dislocated (p < 0.01, Fisher exact test, Table I). Reconstructions with the Endo-Model Rotational Knee (Link America) were excluded from the calculations because the implant has an antisubluxation design feature.

Discussion

Mild distraction of the knee joint often occurs in patients who have had endoprosthetic reconstruction following tumor resection. These patients have usually undergone resection of all cruciate and collateral ligaments as well as much of or all of the knee capsule. Essentially all of these patients have an imbalance between the flexion and extension gaps because they have only the skin, the neurovascular bundle, the extensor mechanism, and the implant to maintain balance. Any rotational stem can be easily dislocated from the tibial component by simply lifting the distal aspect of the femur at the time of surgery after everting the extensor mechanism with the knee flexed 90°, as there is no capsule and there are no collateral ligaments. The resultant lack of soft-tissue restraint often allows mild distraction of the knee joint, especially when these patients sit with the knees flexed and the legs dangling off the side of a table or when they are climbing in and out of bed. This flexion laxity is primarily resisted only by the tension on the extensor mechanism. Only two of the patients in the overall series (neither of whom had dislocation) lacked functional extensor mechanisms. Troubling instability can result if the intrinsic design of the implant allows excessive tilting under mild joint distraction. Thus, it is important for rotating hinge knee prostheses to provide adequate stability under conditions of mild-to-moderate distraction.
unless soft-tissue tension and balance are somehow otherwise restored. If a surgeon attempts to address the instability of a multiply ligament-deficient knee, especially one with an imbalance between the flexion and extension gaps, by utilizing a rotating hinge implant, the situation is probably best addressed with use of a prosthetic design that has a long, minimally tapered central rotational stem that requires a longer distraction distance to dislocate.

Although the duration of follow-up was short for some patients, most commonly because of early death from underlying malignant disease, the dislocations reported herein occurred within one year after implantation in all patients. None of the eighty-eight patients excluded from the study because of a shorter interval of follow-up had had a dislocation.

We believe that rotating hinge knee designs that have a short stem or a notably tapered stem geometry in the central post-in-channel component may not provide adequate stability, especially in patients with soft-tissue compromise, to allow for distraction of the knee joint. Such implants, by themselves, cannot restore stability in these patients. We recommend avoiding such designs in patients with flexion-extension gap imbalance or laxity unless an antisubluxation device is used. The findings of this study suggest that a rotating hinge mechanism that has a cylindrical or nearly cylindrical, long (≥25 cm) metallic rotational post be used to restore knee stability in patients with severe bone and/or soft-tissue compromise. Further clinical evaluation is indicated to verify this recommendation.

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The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They choose not to provide The Journal and its readers with any information concerning any relationship that may exist between any commercial party and any material in the Work, which relationship may represent a conflict of interest.

doi:10.2106/JBJS.00837pp

References


Viscosupplementation Pseudotumor

A Case Report

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Use of intra-articular viscosupplementation has increased dramatically in recent years. Associated complications have been reported. Complications associated specifically with Hylan G-F 20, commercially available as Synvisc (Wyeth-Ayerst Pharmaceuticals, Philadelphia, Pennsylvania), have included both transient and, rarely, prolonged inflammatory reactions. We report an unusual complication of intra-articular injection of Hylan G-F 20: the formation of a soft-tissue mass that was initially diagnosed as a sarcoma by expert pathologists. The patient consented to the publication of the details of the case and helped confirm their accuracy.

Case Report

Histopathologic slides of tissue obtained with an excisional biopsy of a soft-tissue mass were sent to the musculoskeletal pathologist at our institution from a community hospital. The accompanying clinical history documented an expanding painful mass, of two months’ duration, in the posterolateral aspect of the left knee of a thirty-six-year-old woman with adult-

Fig. 1-A
Coronal gradient-echo magnetic resonance image (repetition time, 450 msec; echo time, 9.4 msec) of the left knee (lateral is to the right, and medial is to the left), demonstrating a nonspecific hyperintense multilobulated mass lateral to the iliobibial band in the subcutaneous tissues. The black arrow demonstrates high signal intensity from diffuse edema, and the white arrow indicates some of the hyperintense lobules of the mass.
onset diabetes and hypertension. The accompanying report on
the magnetic resonance imaging findings noted a nonspecific
soft-tissue mass (Figs. 1-A and 1-B). The pathologist at
the community hospital, who sent the slides, suspected a diagnosis
of myxoid sarcoma but requested a second opinion.

Histologically, the tissue showed a cellular infiltrate within
a myxoid ground substance that appeared to dissect through sur-
rounding fibrous connective tissue (Figs. 2-A, 2-B, and 2-C). This
pattern was thought to represent aggressive growth. The cells
showed mild to moderate degrees of nuclear atypia. Occasional
nuclei with an open chromatin pattern and small but readily dis-
cernible nucleoli were also present. Rare mitotic figures were
identified. The interpretation by our pathologist, communicated
to the community hospital, was a low-grade fibromyxoid sar-
coma. The key element in this interpretation was the dissection of
myxomatous material between collagen bundles.

The patient was referred to our clinic for further evalua-
tion, where additional historical information was ascertained.
Approximately six weeks prior to the clinical presentation
with the enlarging mass, the patient had completed a course of
three weekly injections of Hylan G-F 20 (nine and seven days
apart) for the treatment of osteoarthritis of the left knee. The
Hylan G-F 20 was administered with a medial parapatellar in-
jection with the knee flexed to 45°. Generalized knee swelling,
warmth, and mild erythema developed between the first two
injections. The knee inflammation persisted, and erythema
and swelling in the leg, swelling in the foot, paresthesias of the
dorsum of the foot, and a small posterolateral knee lump that
subsequently began to enlarge developed between the second
and third injections. These symptoms eventually prompted
the evaluation that led to the excisional biopsy.

On physical examination, the excisional biopsy wound
was found to have dehisced and was draining serous fluid.
There was no palpable mass, but there was diffuse swelling lat-
eral to the left knee.

A new magnetic resonance imaging scan, acquired nine
weeks after the first scan, demonstrated extensive fluid-filled
cysts with surrounding inflammation encompassing the poste-
rior and lateral aspects of the knee. Contrast-medium-enhanced
computed tomography of the chest, abdomen, and pelvis showed
no metastatic disease.

We proposed exploration of the still-open wound for re-
peat biopsy and secondary wound closure. At surgery, myx-
omatous material was identified deep to the previous surgical
field in multiple cyst-like spaces. No discrete mass was found.
The peroneal nerve was surrounded by fibrous tissue. The cys-
tic material was resected en bloc, and the surrounding tissues
were extensively biopsied.

Histologic examination of these specimens revealed fibro-
inflammatory tissue with little myxoid material (Figs. 3-A
and 3-B). The bulk of the tissue exhibited fibrosis, chronic
nongranulomatous inflammation, and small reactive vascular
channels.

On the basis of the operative findings and a review of
the first biopsy slides in light of the newly discovered history
of viscosupplementation injections, the musculoskeletal pa-
Photomicrographs of tissue obtained with an excisional biopsy of a mass lateral to the left knee, demonstrating myxoid tissue dissecting between collagen bundles (arrow in Fig. 2-A), mild-to-moderate nuclear atypia including variably sized pyknotic nuclei (arrows in Fig. 2-B), and increased mitotic figure frequency with three or four noted per ten high-power fields (arrow in Fig. 2-C) (hematoxylin and eosin, ×40 for Fig. 2-A and ×1000 for Figs. 2-B and 2-C).
thologists interpreted the lesion as being reactive, inflammatory tissue rather than a malignant tumor.

One year after the final resection of the cysts, the patient had a healed wound but advanced symptomatic osteoarthritis of the knee. No recurrence was palpable. Repeat magnetic resonance imaging demonstrated resolution of the cystic inflammation without a recurrent mass.

Discussion

Because of the temporal sequence, we suspect that the mass in our patient was an atypical inflammatory response to a course of viscosupplementation therapy. The patient had generalized knee warmth and erythema during the course of the injections, beginning after the first injection. Such reactions to viscosupplementation are common. The reported prevalence of acute inflammatory reactions to a first course of treatment with Hylan G-F 20 has ranged from 2% to 27%.

Most reactions involve mild pain at the injection site or generalized knee inflammation that typically resolves spontaneously over days or weeks. Nonetheless, persistent inflammatory reactions lasting many months have been reported. Some documented reactions have even included chronic granulomatous inflammation. We are not aware of any reports of a mass associated with viscosupplementation. The anatomical explanation of how an anteromedial intra-articular injection can lead to a posterolateral cystic mass is not clear.

The histologic features of the cystic mass are also not easily explained. Most troubling initially was the combination of mitotic figures and nuclear atypia with dissection of myxomatous material between collagen bundles. While it is well recognized that the histologic appearance of an inflammatory, reactive process can mimic that of a malignant tumor, such interpretations usually depend on specific exclusion of an infiltrative growth pattern. The initial diagnosis of a low-grade malignant tumor was based on the appearance of dissecting myxomatous material infiltrating through collagen bundles, but this interpretation was subsequently questioned when the pathologists learned of the temporally related injections.

Among the interpretations that were offered as the magnetic resonance images were reviewed by multiple musculoskeletal imaging experts was that the cystic mass may have arisen from a ruptured popliteal cyst in this patient with advanced osteoarthritis and a complex medial meniscal tear. Lateral popliteal cysts, involving the popliteus bursa, are less common than enlargements of the medial semimembranosus bursa originally described by Baker in 1877. However, both dissection and rupture of such lateral popliteal cysts have been reported. Lateral cysts have been found to rupture into the subcutaneous tissues around the fibular head, cause peroneal nerve dysfunction, and even extend further into the anterior compartment. Medial and directly posterior popliteal cyst ruptures are frequently associated with swelling and erythema of the leg and foot. This condition has been named the “pseudo-thrombophlebitic syndrome.” Such a pattern is consistent with the swelling of the foot and leg that our patient recalled from the time that she noticed the mass. Ruptured popliteal cysts can temporarily maintain an intra-articular communication, exposing the periaricular tissue to additional insult from any generalized intra-articular inflammation.
Photomicrographs of tissue obtained with the second excisional biopsy, demonstrating bland inflammatory fibrovascular tissue, including typical granulation tissue, with numerous small vascular channels (arrow in Fig. 3-A) and areas of normal subcutaneous adipose tissue ("a" in Fig. 3-B) surrounded by mature scar-like collagenous matrix ("c" in Fig. 3-B) (hematoxylin and eosin, ×40 for Fig. 3-A and ×250 for Fig. 3-B).
Axial gradient-echo magnetic resonance images (repetition time, 450 msec; echo time, 9.4 msec) of the left knee (lateral is to the right, and medial is to the left), made before the first excisional biopsy. These images are at the level of the joint line (Fig. 4-A) and a few millimeters distal to it (Fig. 4-B), and they demonstrate a small volume of residual hyperintense signal in the region of the popliteal bursa (arrows with white dot), with the multilobulated mass and subcutaneous edema lateral to the lateral head of the gastrocnemius muscle and tracking anteriorly (multiple arrows). The point adjacent to the anterolateral margin of the lateral head of the gastrocnemius appears to provide a potential conduit for dissection to the posterolateral subcutaneous tissues, from a ruptured lateral popliteal cyst.
We therefore concluded that a lateral popliteal cyst was a part of a generalized intra-articular inflammatory reaction to viscosupplementation; this cyst ruptured, exposing the posterolateral periarticular tissues to dissecting volumes of inflammatory synovial fluid, resulting in an inflammatory mass.

In summary, we report a large cystic mass with sarcomalike pathologic features in temporal association with a course of intra-articular viscosupplementation with Hylan G-F 20. As with any intervention, the risks and benefits of intra-articular viscosupplementation must be weighed carefully. Perhaps more important is awareness of this possible complication to avoid the potential for drastic mismanagement.

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References

Posterolateral Rotatory Instability of the Elbow in Association with Lateral Epicondylitis

A Report of Three Cases

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Lateral stability of the elbow depends on the integrity of the lateral collateral ligament and secondary soft-tissue restraints. Posterolateral rotatory subluxation of the elbow has been recognized in association with elbow trauma, surgery for epicondylitis, and congenital cubitus varus deformity. While abnormal signal changes on magnetic resonance imaging have been shown to include the lateral collateral ligament in patients with tennis elbow, we are aware of no reports of elbow instability detected in patients in whom epicondylitis had been managed nonoperatively.

We describe the cases of three middle-aged women who presented with atraumatic lateral epicondylitis and subsequently had clinical findings consistent with posterolateral rotatory instability of the elbow. Two of the patients had a visible synovial fistula and magnetic resonance imaging studies indicative of insufficiency of the lateral collateral ligament. All three patients eventually underwent an examination of the elbow under anesthesia, which confirmed the posterolateral rotatory subluxation. All were treated with débridement and reconstruction of the common extensor tendon origin and the lateral collateral ligament. The potential role of corticosteroid injections in the pathogenesis of combined lateral epicondylitis and rotatory instability of the elbow is discussed. Each patient was informed that data concerning her case would be submitted for publication.

Case Reports

Case 1. A fifty-one-year-old, healthy, right-hand-dominant female administrative assistant presented with pain in the lateral aspect of the left elbow of unknown cause. She reported no elbow trauma, unusual musculoskeletal pain, or prior use of fluoroquinolone antibiotics (which has been reported to be associated with degenerative tendon conditions). A diagnosis of tennis elbow was made by the treating hand surgeon on the basis of tenderness over the lateral epicondyle that was exacerbated by wrist extension against resistance. Conservative treatment measures, including the use of a forearm counterforce strap and a wrist splint, were initiated. Two corticosteroid injections, consisting of approximately 40 mg of triamcinolone acetonide, were administered three months apart into the area of maximum point tenderness. Each injection provided nearly complete relief of symptoms for four to six weeks.

The patient sought a second opinion one year following the development of the symptoms. At this time, she described pain and swelling localized to the lateral aspect of the left elbow in addition to a sensation of elbow joint laxity with loading. Examination revealed a tender fluctuant mass extending for a distance of two fingerbreadths distal to the lateral epicondyle. The overlying tissue appeared to be mildly atrophic and less pigmented than the surrounding skin. Subtle posterior subluxation of the radial head was palpable with a lateral pivot-shift maneuver, which was performed by applying a valgus stress and axial load to the partially flexed elbow with the forearm fully supinated.

The findings on plain radiographs of the left elbow were unremarkable. However, magnetic resonance imaging revealed rupture of the lateral collateral ligament with retraction of a large portion of the common extensor tendon origin and a 2 by 2.5-cm synovial fistula projecting into the subcutaneous tissues (Fig. 1-A).

The patient elected to proceed with surgical treatment. The results of preoperative laboratory studies, including a complete blood-cell count and measurements of the serum uric acid level, erythrocyte sedimentation rate, and C-reactive protein level, were normal. A joint fluid analysis demonstrated features of a noninflammatory synovial effusion. Cultures were negative.

With the patient under axillary block anesthesia, the lateral epicondyle and the common extensor tendon origin were exposed through a curvilinear incision. A large defect in the common extensor tendon origin was appreciated distal to the lateral epicondyle (Fig. 1-B). Gross posterolateral and varus
instability was demonstrated with application of stress to the joint. A capsulotomy anterior to the lateral collateral ligament was performed, revealing a bare epicondyle anteriorly and attenuated tissue posteriorly. The capsular tissue was thinned and expanded.

The remaining attachments of the common extensor tendon origin and the lateral collateral ligament were elevated sharply from the lateral epicondyle and debrided back to healthy-appearing tissue. The lateral collateral ligament was reconstructed with a free palmaris longus tendon graft harvested from the ipsilateral forearm (Fig. 1-C). The joint capsule was closed beneath the graft as well as possible, and remnants of the endogenous collateral ligament were sewn to the tendon graft construct proximally. Extensions of the common extensor origin were then reattached to the lateral epicondyle with use of a bone anchor and number-2 braided polyester suture. Because of the poor quality of the capsular tissue and the partially deficient extensor origin, an anconeus muscle pedicle flap was rotated for coverage of the tendon graft and the inferior margin of the radiohumeral joint to prevent recurrence of the synovial fistula. Restoration of elbow joint stability was confirmed fluoroscopically with varus and lateral pivot-shift testing.

Postoperatively, the elbow was immobilized in 60° of flexion with the forearm fully pronated. Active elbow-motion exercises with a 30° extension-block splint were encouraged at approximately two weeks postoperatively. Forearm-rotation exercises were initiated at five weeks, and the use of the splint was discontinued at six weeks. Unrestricted use of the extremity was permitted at four months following the surgery. When she was last examined, two years postoperatively, the patient reported no residual elbow pain or sensation of joint laxity. With the exception of a loss of 5° of terminal extension, the patient had full elbow and forearm motion and no clinical or radiographic evidence of recurrent joint instability.

CASE 2. A forty-nine-year-old, healthy, right-hand-dominant female nurse presented with pain in the lateral aspect of the right elbow, which she related to pushing up from the ground with her hands to stand. She reported that she had not had previous elbow surgery or relevant trauma and that she had not used fluoroquinolone antibiotics preceding the onset of the symptoms. A diagnosis of tennis elbow was made by her treating physician on the basis of the history and the pain localized to the lateral epicondyle. Physical therapy was prescribed, and over a fifteen-month interval four separate corticosteroid injections were administered into the region of maximum point tenderness. Each injection, consisting of approximately 40 mg of triamcinolone acetonide, markedly but only temporarily relieved the symptoms.

Shortly following the fourth injection, prominent swelling corresponding to the common extensor origin. The lateral pivot-shift test elicited sensations of both pain and apprehension. Baseline radiographs of the elbow revealed unremarkable findings, whereas magnetic resonance imaging demonstrated disruption of the lateral collateral ligament and the common extensor tendon origin with a synovial fistula extending through the soft-tissue defect.

The elbow joint was aspirated, and the fluid analysis revealed features of a noninflammatory synovial effusion. Cultures were negative. The results of preoperative serological studies, including a complete blood-cell count and measurements of the uric acid level, erythrocyte sedimentation rate, and C-reactive protein level, were normal.

At surgery, the common extensor origin was found to be torn and retracted with the tendon edge positioned approximately 3 cm distal to the epicondyle. Pathological laxity of the elbow was demonstrated with application of posterolateral rotatory stress under fluoroscopy. The synovial fistula was entered, and the lateral collateral ligament was found to be partially disrupted and attenuated. Both varus laxity and pos-
terolateral rotatory subluxation of the elbow were confirmed by direct visualization. Small chondral defects were detected in the radial head and capitellum, but joint congruity had been preserved.

The deficient lateral collateral ligament was reconstructed with a palmaris longus tendon autograft. Capsular tissue was then attached to the undersurface of the tendon graft, and the remaining collateral ligament origin was sewn to the graft construct proximally. The extensor tendon origin was débrided and was repaired to the lateral epicondyle with one suture.

**Fig. 1-B**

Intraoperative photograph depicting a torn and retracted common extensor tendon origin (arrow). This was visible on incision of the skin.

**Fig. 1-C**

Intraoperative photograph showing reconstruction of the lateral collateral ligament (white arrowhead at the humeral tunnels) and the reflected anconeus muscle (black arrowhead).
anchor. The anconeus muscle was advanced proximally and anteriorly to cover the graft and the inferior part of the radiohumeral joint. A rehabilitation program identical to the program described for Case 1 was prescribed.

Histological analysis revealed features of myxoid alteration, fibroblast proliferation, and neovascularization in the torn tendon edge. At the latest clinical examination, nine months after the surgery, the patient reported that she had no residual elbow pain. She had full elbow extension as well as elbow flexion and forearm rotation that were symmetrical with those on the contralateral side. There was a painless palpable click directly over the ligament reconstruction site with elbow flexion but no clinical or radiographic evidence of recurrent elbow joint instability.

CASE 3. A forty-five-year-old, right-hand-dominant female administrator presented with pain in the lateral aspect of the left elbow that had developed while she was constructing a shed in her yard. Conservative measures for the treatment of tennis elbow, including nonsteroidal anti-inflammatory medication and a counterforce strap, were prescribed by her primary care physician. Initial records documented tenderness over the lateral epicondyle.

The patient was referred for orthopaedic evaluation two months later. She reported no medical problems, previous use of fluoroquinolone antibiotics, or previously recognized elbow injury. On physical examination, point tenderness over the lateral epicondyle was elicited in addition to lateral elbow pain with resisted wrist extension. There was no appreciable joint instability with lateral pivot-shift testing. Two separate corticosteroid injections, consisting of approximately 15 mg of triamcinolone acetonide, were administered over a six-month interval; each injection resulted in partial pain relief for several months.

Ten months following the initial onset of symptoms, the patient reported recurrent and more pronounced pain in the left elbow. The pain was localized laterally and was reproducible with full elbow extension, resisted wrist extension, and finger pressure over the lateral epicondyle. Radiographs of the joint revealed unremarkable findings, whereas magnetic resonance imaging demonstrated extensive partial tearing of the common extensor tendon origin, a small joint effusion (synovitis), and degenerative cysts in the capitellum. Although the lateral collateral ligament appeared intact, the entire structure was not well visualized.

The patient decided to undergo surgery to débride the common extensor tendon origin. She was informed of the possibility of detecting lateral instability intraoperatively and that this might alter the surgical plan to include ligament reconstruction. The results of laboratory studies, including a complete blood-cell count and measurement of the erythrocyte sedimentation rate, were normal.

Fluoroscopic imaging of the left elbow with the patient under general anesthesia revealed frank posterolateral rotatory instability (Fig. 2). No instability of the asymptomatic right elbow was detected. The common extensor tendon origin was
approached by elevating the inferior border of extensor carpi radialis longus muscle. Abundant amorphous tissue was visualized at the origins of the extensor carpi radialis brevis muscle and the lateral collateral ligament, and there was definite instability of the elbow joint. Degenerative tissue was debrided, and pathological laxity of the lateral collateral ligament was appreciated with application of varus and lateral pivot-shift testing. The ligament was reconstructed with use of a palmaris longus tendon autograft. Capsular tissue was then secured to the undersurface of the tendon graft, and the origins of the common extensor tendon and endogenous lateral collateral ligament were reattached to the lateral epicondyle with use of one suture anchor. As adequate soft tissue was available for joint coverage, the anconeous muscle was not transferred. Stability was confirmed by direct visualization and with fluoroscopic imaging.

The splinting and rehabilitation protocols were similar to those used for the other two patients. Tissue obtained at the time of surgery demonstrated features of fibroblast proliferation and neovascularization. At the latest clinical examination, eight months after the surgery, the patient reported resolution of the elbow pain. Full and symmetrical elbow and forearm motions were demonstrated. There was painless palpable crepitus over the radiohumeral joint with stress testing but no clinical or radiographic evidence of recurrent joint instability.

Discussion

Posterolateral rotatory instability of the elbow typically results from a traumatic event involving a combination of axial compressive, external rotatory, and valgus forces, such as occurs when a person falls on an outstretched hand3. This pattern of instability has been recognized following failed surgery for tennis elbow and has been attributed to iatrogenic injury to the lateral collateral ligament4. While lateral ligament insufficiency has also been detected by magnetic resonance imaging in patients in whom tennis elbow had been managed conservatively, and by direct visualization during primary surgery for tennis elbow, concurrent rotatory instability has not been previously reported, to our knowledge5,6.

At present, there is little clinical information to guide the choice of corticosteroid preparation or method or the number of injections that can be safely administered for the treatment of tennis elbow5. Although a steroid injection may alleviate the pain associated with tennis elbow, the effects are usually transitory4. In addition, animal data support caution regarding the nonjudicious use of local corticosteroids. An intratendinous injection results in collagen necrosis followed by a decrease in tensile strength17-20. An injection into an injured ligament impairs healing and adversely affects the failure load of the tissue21-24. A reduction in the structural properties of severed rabbit ligaments has been shown to persist for three weeks or more following a single corticosteroid injection24,26.

We postulate that the degenerative changes in the extensor tendon origin associated with lateral epicondylitis can also involve the underlying lateral collateral ligament. The epicondylar attachments of the extensor carpi radialis brevis, the extensor digitorum communis, and the lateral collateral ligament are confluent25. Repeated corticosteroid injections into the tendon and ligament origins may contribute to weakening and ultimate failure of these structures. Early joint-loading following an injection may further compromise the lateral soft-tissue restraints of the elbow. Seemingly minor previous trauma to the elbow could conceivably be an additional factor in tendon and ligament deficiency.

Posterolateral rotatory subluxation of the elbow should be considered in the differential diagnosis of either persistent or recurrent symptoms of tennis elbow, especially in patients with mechanical elbow symptoms and/or a recognized synovial fistula. Magnetic resonance imaging and stress radiographs may be helpful for identifying subtle cases of instability26-34. We currently advocate intraoperative evaluation for lateral instability of the elbow joint following surgical treatment of lateral epicondylitis. When lateral elbow instability is identified, debridement and repair of degenerative extensor tendon tissue with reconstruction of the lateral collateral ligament may be indicated. Supplemental coverage of the radiohumeral joint, when required, can be achieved with a local anconeous muscle transfer. Additional clinical series with longer follow-up are necessary to determine the efficacy of this surgical approach.

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DOI:10.2106/JBJS.D.02293
Acute Paraspinal Compartment Syndrome

A Case Report

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Acute compartment syndrome is the condition of raised pressure within an enclosed compartment, such that the perfusion and the function of the tissues within are compromised, resulting in ischemia and eventually necrosis. Although, in theory, it can occur in any compartment, it is most commonly seen in the lower limb. We describe a rare case of acute compartment syndrome in the paraspinal muscles that responded well to surgical decompression. Our patient was informed that data concerning this case would be submitted for publication.

Case Report

A thirty-five-year-old man on the third day of a skiing holiday presented to the emergency department because of severe, unrelenting pain in the right lumbosacral paraspinal area, radiating across the abdomen to the groin. The pain had been present for four hours and had begun spontaneously with no history of trauma. In retrospect, the patient had experienced similar but milder pains during previous ski trips and during long-distance running. There was associated numbness in the right lumbosacral area.

Positive findings on physical examination were bilateral paraspinal muscle rigidity associated with swelling, marked tenderness, and loss of the lumbar lordosis. There was dense loss of sensation in the paraspinal area to the midaxillary line and altered sensation extending anteriorly to the midline. Reduced abdominal muscle tone on the right side, resulting in asymmetry, was also noted. Active movement of the spine was minimal and exacerbated the pain. The patient had mild tenderness of the abdomen with absent bowel sounds.

The initial differential diagnosis included a renal stone, a herniated disc, discitis, and a retroperitoneal abnormality. A urine specimen was dark in appearance, and analysis revealed 3+ myoglobinuria. Blood chemistry studies showed elevation of aspartate aminotransferase (804 IU/L; normal, 17 to 59 IU/L), alanine aminotransferase (141 IU/L; normal, 21 to 72 IU/L), lactate dehydrogenase (3823 IU/L; normal, 313 to 618 IU/L), myoglobin (7961 ng/mL; normal, <116.4 ng/mL), and creatine kinase (48,550 IU/L; normal, 55 to 70 IU/L). Other blood parameters were within normal limits. A spiral computerized tomography study excluded an abnormality of the urinary tract. Swelling of the paraspinal muscles and a paralytic ileus were noted. Angiography showed no evidence of arterial occlusion. The pain was controlled with opioids, and it was elected to continue treatment with intravenous rehydration although a definitive diagnosis had not been made.

Twelve hours after presentation, the patient had little improvement. A magnetic resonance imaging scan revealed a marked increase in signal within the medial and lateral right paraspinal muscles as well as the left medial paraspinal muscle (Fig. 1). An increased signal was also noted within the soft tissues adjacent to the spinous processes and posterior to the paraspinal muscles. There was asymmetry of the paraspinal muscles, with the right side notably larger than the left. Some fluid was also noted in the right retroperitoneal region. The possibility of acute compartment syndrome was considered, and pressures were measured with a transducer (Intra-Compartmental Pressure Monitor; Stryker, Kalamazoo, Michigan). The needle was inserted into the paraspinal muscle compartment at the level of maximal tenderness (approximately L2). Pressure in the paraspinal muscle was 44 mm Hg on the right side and 26 mm Hg (normal, 3.1 to 10.8 mm Hg) on the left side.

By this time, the serum creatine kinase level had increased to 59,863 IU/L. The diagnosis of acute compartment syndrome of both paraspinal muscle groups with rhabdomyolysis was confirmed.

The patient underwent bilateral fasciotomy of the lumbar paraspinous muscle through a midline incision, from the level of the first lumbar vertebra to the first sacral vertebra. At the time of surgery, the deeper muscles were pale but soon turned pink, bled, and responded to stimulation following decompression. Intraoperatively, the pressures returned to normal (<10 mm Hg).

Postoperatively, the patient had notable improvement with respect to pain and, by the following day, he was able to walk with crutches. The serum creatine kinase level decreased to 4600 IU/L over the next five days. There were no postoperative complications apart from a wound seroma that resolved following six aspirations. Within four weeks, the patient had returned to sports with no further back pain. The numbness and reduced abdominal muscle tone resolved after three months.
Discussion

A natomic cadaver studies have demonstrated a well-defined closed paraspinal space comprised of the erector spinae muscle enclosed by the posterior and middle lamellae of the thoracolumbar fascia. The fascial envelope is anatomically and physiologically similar to other muscle compartments known to be susceptible to compartment syndrome.

Physiological studies have measured compartment pressures within the paraspinal muscle groups. Normal compartment pressure has been reported to be between 3.1 and 10.8 mm Hg when measured in the prone position, and the pressure at which subjects have muscle fatigue during exercise has been reported as 14 mm Hg. Pressures have been reported to vary with posture, and they are particularly high when standing with the knees in flexion, which simulates the skiing stance.

Chronic compartment syndrome of the paraspinal muscles has been recognized as an uncommon cause of back pain. Acute paraspinal compartment syndrome, conversely, is very rare. It appears to have three causes: direct trauma to the paraspinal muscles; occlusion of the blood supply to the paraspinal muscles during aortic abdominal aneurysm repair, followed by a reperfusion injury; or atraumatic acute compartment syndrome.

A closer analysis of the cases of the three other patients who had atraumatic acute compartment syndrome revealed that they had many features in common that have not previously been recognized. These features include bilateral lumbar paraspinal muscle spasm with loss of lordosis and marked tenderness as well as reduced or absent bowel sounds. The laboratory investigations showed myoglobinuria, normal acute phase inflammatory markers, and elevated levels of aspartate aminotransferase, alanine aminotransferase, myoglobin, and serum creatine kinase. Interestingly, two of the patients also had associated numbness involving the cutaneous nerves traversing the paraspinal muscle compartment—a relatively late sign in compartment syndrome of the leg. In addition, our patient had a motor disturbance with a reduction of abdominal muscle tone.

All four patients, including ours, who had atraumatic acute compartment syndrome were initially managed with fluid resuscitation and opioids, since the diagnosis was unclear. Of the three patients in whom the diagnosis was confirmed during hospitalization, two had no improvement in the clinical condition and surgical intervention was undertaken. It is of note that both of these patients went on to make a full recovery without recurrence of the previous pain, even on exertion. Both patients who were managed nonop-
eratively reported at the follow-up examination that they had pain with exercise. Our impression is that once the diagnosis of compartment syndrome has been confirmed with elevated intracompartmental pressures, and there is evidence of rhabdomyolysis, surgical intervention is indicated.

Surgeons need to be aware of the existence of acute paraspinal compartment syndrome to aid in its early identification. There should be a low threshold for measuring paraspinal compartment pressures, particularly in patients with severe back pain who present with paraspinal muscle rigidity and increased levels of serum creatine kinase, when other diagnoses have been excluded.

Appendix

A table presenting the clinical and laboratory features of the four patients who had atraumatic acute paraspinal compartment syndrome is available with the electronic versions of this article, on our web site at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

doi:10.2106/JBJS.D.02133

References

Aprotinin is a naturally occurring serine protease inhibitor that has been shown to reduce blood loss in cardiothoracic and liver surgery\(^1\). Aprotinin is nonspecific and inhibits several proteases, such as trypsin, chymotrypsin, cathepsin, elastase, kallikrein, plasmin, protein C, thrombin, and urokinase. Consequently, it has a variety of effects on several organ systems and the mechanism by which it reduces blood loss is not fully understood.

It has been postulated that aprotinin reduces bleeding through its effects on fibrinolytic pathways, coagulation pathways, the inflammatory response, and platelet function. It inhibits fibrinolysis, turnover of coagulation factors, and inflammatory cytokine release. In addition, by preserving the adhesive glycoproteins on the platelet membrane, it promotes platelet adhesion\(^6\). Taken together, these effects contribute to the pro-hemostatic function of aprotinin.

Orthopaedic surgery, which is associated with large amounts of blood loss that lead to increased morbidity and mortality, often requires blood transfusions. Transfusions increase the risk of transmission of infectious agents, such as human immunodeficiency virus, cytomegalovirus, hepatitis-C virus, hepatitis-B virus, and others, from the infected donor blood as well as the risk of postoperative infections through the suppression of the immune system\(^11,13\). Hemolytic reactions induced by transfusion may be fatal. Therefore, it is crucial to minimize both bleeding and the amount of transfused blood.

In 1993, the United States Food and Drug Administration approved the use of aprotinin in coronary artery bypass surgery, which provoked an interest in the potential use of this drug in other types of surgery. Several clinical trials are being carried out to investigate the role of aprotinin in orthopaedics. Evidence-based medicine, a relatively new discipline that provides tools for evaluating the medical literature to make decisions in clinical practice, is gaining popularity in orthopaedic surgery\(^14,16\). In this review, we utilized evidence-based-medicine principles to critically appraise the best studies demonstrating that aprotinin reduces blood loss as well as transfusion requirements during hip, knee, and spine surgery.

Materials and Methods
To find all clinical trials addressing the role of aprotinin in orthopaedic surgery, we searched OVID/Medline, PubMed, EMBASE, Web of Science, Cochrane Database of Systematic Reviews, and Cochrane Central Register of Controlled Trials
from their earliest records until the time of the review (April 2004). To ensure that no relevant studies were missed, we first conducted an unrestricted search of the databases using combinations of keywords: aprotinin and orthopaedic surgery, aprotinin and spine surgery, aprotinin and pelvic surgery, aprotinin and knee surgery, and aprotinin and hip surgery. We then restricted our results to clinical trials and systematic reviews with the keywords clinical trial, randomized controlled trial, and review. Also, the references of pertinent articles in the literature as well as textbooks were manually screened for additional studies.

Only randomized clinical trials with the end points of aprotinin effects on blood loss and/or transfusion requirements were included in the review. Studies with other primary end points such as the effects of aprotinin on coagulation pathways, platelet function, lactate level, and prevalence of deep venous thrombosis, although interesting and often of high quality, were not included in the present review. Nonrandomized prospective studies, retrospective studies, case series, and case reports were also excluded. Studies in languages other than English were excluded as well because of a language barrier.

The levels of evidence were assigned according to The Journal of Bone and Joint Surgery guidelines for studies investigating the results of treatment (see Instructions to Authors).

Since we included only clinical randomized trials in our review, all of them were assigned either Level I or Level II. As a result of the lack of explicit criteria differentiating Level-I from Level-II studies (high versus poor-quality randomized trials), we used the “Users’ Guides to the Medical Literature” to distinguish between the two levels. In almost all cases, we based this distinction on the study size because the trials were similar with regard to other aspects of their design (randomization, blinding, and inclusion of a properly matched control group). Consequently, large studies (arbitrarily defined as including more than twenty patients in both the experimental and the control groups) were assigned Level I, and smaller studies were assigned Level II. In one study, the authors failed to specify whether the trial was blinded, so even though the study met the other criteria, it was assigned Level II.

Finally, a grade of recommendation on the use of aprotinin in orthopaedic surgery was determined according to the guidelines of the Oxford Centre for Evidence-Based Medicine (www.cebm.net) (Table I).

Results
An exhaustive search of the databases identified twenty clinical trials. (A few additional studies were found in references, but they were not in English and therefore were not included.) To our knowledge, no systematic reviews dealing specifically and exclusively with the use of aprotinin in orthopaedic surgery have been published to date. No Cochrane reviews, which are high-quality evidence-based reviews, were found except for one, by Henry et al., on the use of antifibrinolytics to minimize perioperative allogeneic blood transfusion. This review included only three studies on the use of aprotinin in orthopaedic surgery, among eighty-six studies on the effects of a variety of antifibrinolytics on several types of surgery (identified by electronic searches of Medline and EMBASE to May 1998 and December 1997, respectively). The results of those three studies were not analyzed separately but instead were included in the combined analysis of noncardiac studies. Therefore, no conclusions about aprotinin use in orthopaedic surgery could be drawn from that Cochrane review.

Five of the twenty studies that we initially found were excluded because of their design (retrospective or partially retrospective) or because of irrelevant end points. We categorized the fifteen remaining studies on the basis of the type of surgery and assigned every study a level of evidence as described in the Materials and Methods section. We identified four Level-I, two Level-II, and one Level-III, two Level-II, and two Level-II spine studies, and one Level-III and three Level-II or III, orthopaedic surgery studies that included different types of orthopaedic operations (Table I). Level-I studies from every category are discussed below, and the results of those studies are summarized in Table III.

Four hip studies were graded as Level I. In the randomized, double-blind, clinical trial by Janssens et al., forty patients scheduled to have primary elective hip replacement were randomly allocated to receive either aprotinin (twenty patients), given as a bolus injection of two million kallikrein inhibitory units (KIU) over thirty minutes followed by an infusion of 0.5 million KIU/hr until the end of the surgery, or the same volume of normal saline solution according to the same protocol (twenty patients). The surgeon and the anesthesiologist did not know whether the patients were receiving aprotinin or the placebo. The methods of randomization and allocation concealment were not specified. Intraoperative blood loss was estimated by measuring the volume in the suction bottles and counting sponges. Postoperative blood loss was measured from the surgical drains. Intravenous infusion of lactated Ringer solution was started on induction of anesthesia, and gelatin solution was given intraoperatively and postoperatively to maintain normovolemia. Packed red blood cells were transfused to maintain a hematocrit of 30%. The two groups of patients were comparable with respect to age, weight, height, sex, operative time, and hemorrhagic risk. The average operative time was 169 ± 27 and 176 ± 32 minutes in the aprotinin and placebo groups, respectively. All patients who entered the study were included in the final analysis. The
study showed that the average total blood loss (perioperative and postoperative) was reduced by 26% in the aprotinin group (p < 0.05). Blood transfusion requirements were also reduced, from 3.4 ± 1.3 units/patient in the placebo group to 1.8 ± 1.2 units/patient in the aprotinin group (an average difference of 1.6 units, p < 0.001). Deep venous thrombosis developed in four patients in the placebo group and in none in the aprotinin group (difference not significant). No other adverse effects were reported.

Murkin et al. performed a study of fifty-three patients who underwent revision total hip arthroplasty (fifty patients) or bilateral total hip arthroplasty (three patients). Patients were randomly assigned (with a computer-generated random code) to receive either aprotinin (twenty-nine patients) or a placebo (twenty-four patients). In the aprotinin group, patients who weighed between 60 and 80 kg were given a loading dose of 2 million KIU over fifteen minutes followed by an infusion of 0.5 million KIU for the duration of the surgery and for one hour postoperatively. Patients who weighed <60 kg or >80 kg received a loading dose of 2.8 mL/kg and an infusion of 0.7 mL/kg/hr. Patients in the placebo group received an equivalent volume of 0.9% saline solution. The study was double-blind, with the aprotinin or saline solution administered from uniformly blinded bottles. Intraoperative blood loss was estimated from the volume in the suction bottles and the weight of the sponges by a blinded observer, and postoperative blood loss was determined from volumetric wound drains. Lactated Ringer solution was administered intravenously for intraoperative volume replacement. Transfusion of packed red blood cells was permitted to achieve an intraoperative blood volume exceeding 15% of the preoperative blood volume or a postoperative hemoglobin level of <8 g/dL ( <80 g/L). The two groups were similar regarding age, gender, and duration of the operation (average duration, 180 ± 7.5 minutes in the aprotinin group and 194 ± 11.0 minutes in the placebo group), and all patients were included in the final analysis of the results. The study demonstrated that the average total blood loss was decreased to 1498 ± 110 mL in the aprotinin group compared with 2096 ± 223 mL in the placebo group (p < 0.022). Transfusion requirements were reduced as well, with the patients in the aprotinin group receiving an average of 2.0 ± 0.2 units and those in the placebo group receiving an average of 2.9 ± 0.4 units (average difference, 0.9 unit; 95% confidence interval = −1.69 to −0.07). Deep venous thrombosis developed in three of the placebo-treated patients and in none of the aprotinin-treated patients. No other complications were observed.

In their second clinical trial, Murkin et al. took the study a step further and compared different concentrations of aprotinin. In this multicenter, randomized, double-blind trial, patients were assigned to four groups. Seventy-six patients received a low dose of aprotinin (a 0.5-million-KIU bolus), seventy-five patients received a medium dose of aprotinin (a 1-million-KIU bolus followed by an infusion of 0.25 million KIU/hr), seventy-seven patients received a high dose of aprotinin (a 2-million-KIU bolus followed by an infusion of 0.5 million KIU/hr), and seventy-three patients received normal saline solution. Intraoperative blood loss was monitored by the anesthesiologist. Postoperative blood loss was estimated from the surgical drains. Patients were given a blood transfusion when the hematocrit was ≤18% (or if “clinically necessary”). The patients were comparable with respect to race, age, height, weight, and operative approach. Despite randomization, the high-dose-aprotinin group had more men (p = 0.08) and the medium-dose-aprotinin group had a lower mean baseline hemoglobin level (p = 0.005) than the placebo group.

### TABLE II Randomized Clinical Trials of Aprotinin Effects on Blood Loss and Transfusion Requirements in Orthopaedic Surgery

<table>
<thead>
<tr>
<th>Year</th>
<th>Study</th>
<th>Type of Surgery</th>
<th>Level of Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>2003</td>
<td>Amar et al.</td>
<td>Orthopaedic</td>
<td>I-1b</td>
</tr>
<tr>
<td>2003</td>
<td>Cole et al.</td>
<td>Spine</td>
<td>I-1a</td>
</tr>
<tr>
<td>2003</td>
<td>Khoshhal et al.</td>
<td>Spine</td>
<td>II-2</td>
</tr>
<tr>
<td>2003</td>
<td>Jeserschek et al.</td>
<td>Orthopaedic</td>
<td>II-2</td>
</tr>
<tr>
<td>2002</td>
<td>Samama et al.</td>
<td>Orthopaedic</td>
<td>II-2</td>
</tr>
<tr>
<td>2000</td>
<td>Langdown et al.</td>
<td>Hip</td>
<td>I-1b</td>
</tr>
<tr>
<td>2000</td>
<td>Murkin et al.</td>
<td>Hip</td>
<td>I-1a</td>
</tr>
<tr>
<td>2001</td>
<td>Engel et al.</td>
<td>Knee</td>
<td>II-2</td>
</tr>
<tr>
<td>2001</td>
<td>Urban et al.</td>
<td>Spine</td>
<td>II-2</td>
</tr>
<tr>
<td>1999</td>
<td>Lentschener et al.</td>
<td>Spine</td>
<td>I-1a</td>
</tr>
<tr>
<td>1998</td>
<td>Capdevila et al.</td>
<td>Orthopaedic</td>
<td>II-2</td>
</tr>
<tr>
<td>1996</td>
<td>Hayes et al.</td>
<td>Hip</td>
<td>II-2</td>
</tr>
<tr>
<td>1995</td>
<td>Murkin et al.</td>
<td>Hip</td>
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</tr>
<tr>
<td>1994</td>
<td>Thorpe et al.</td>
<td>Knee</td>
<td>II-2</td>
</tr>
<tr>
<td>1994</td>
<td>Janssens et al.</td>
<td>Hip</td>
<td>I-1a</td>
</tr>
</tbody>
</table>
The mean operating time was 1.7 hours in the low-dose group, 1.7 hours in the medium-dose group, 1.8 hours in the high-dose group, and 1.9 hours in the placebo group. Transfusion requirements, which were expressed as the percentage of patients in each group who received blood, were reduced from 47% in the placebo group to 28% in the low-dose-aprotinin group (p = 0.02) and 27% in the high-dose-aprotinin group (p = 0.08). Forty percent of the patients who received the median dose of aprotinin received a transfusion; however, the 7% difference between this group and the placebo group did not reach significance. Blood loss was reduced from 698 mL in the placebo group to 558 mL (p = 0.02), 573 mL (p = 0.04), and 603 mL (p = 0.1) in the low, medium, and high-dose-aprotinin groups, respectively. Deep venous thrombosis developed in a few patients, but there was no significant difference among the groups.

Langdown et al. investigated the effects of low-dose aprotinin on blood loss in sixty patients with primary osteoarthritis requiring total hip arthroplasty. The patients were randomly assigned to receive either a 1.5-million-KIU bolus of aprotinin (thirty patients) or an equal volume of normal saline solution (thirty patients). In this study, the patients did not receive a maintenance dose of aprotinin. The study was double-blind, with the patient, anesthesiologist, and surgeon unaware of which solution was given. Intraoperative blood loss was estimated by weighing the swabs and measuring suction losses, and postoperative blood loss was estimated from the drains. There was no significant difference between the two groups with regard to total blood loss, which averaged 414 ± 213 mL in the placebo group and 417 ± 203 mL in the aprotinin group. The transfusion requirements were not quantified, and the transfusion threshold was not specified. However, the authors did include a comment that postoperative hemoglobin and transfusion requirements were similar between the two groups. The average operative time was 100 minutes in both groups. There was no report of any side effects associated with aprotinin use.

In these studies, a high-dose aprotinin regimen decreased blood loss by 14% to 29% and transfusion requirements by 0.9 to 1.6 units. As these were all high-quality studies with no major methodological flaws, we make a grade-A recommendation for the use of high-dose aprotinin in hip surgery. Another equally important conclusion that can be derived from the above studies, is that there is conflicting evidence for the benefit of the low-dose aprotinin regimen in hip surgery; thus, we cannot recommend its use in hip surgery (grade-I recommendation).

We found no Level-I knee studies. Both of the Level-I spine studies demonstrated a clinically relevant effect of aprotinin on blood loss and transfusion requirements. Lentschener et al. randomly assigned seventy-two patients scheduled to undergo elective posterior lumbar fusion for degenerative spine disease to receive high-dose aprotinin therapy or a placebo. The assignments were made in a double-blind fashion with use of a computer-generated random code. Patients in the aprotinin group received an initial dose of 2 million KIU over twenty minutes followed by a continuous infusion of 0.5 million KIU/hr until skin closure. An additional bolus of 0.5 million KIU of aprotinin was infused for every three transfusions of packed red blood cells. Patients in the placebo group received an equivalent volume of 0.9% saline solution. Intraoperative blood loss was measured by adding the volume of the blood in suction bottles to the weight of sponges and deducting the volume of fluids added to the surgical field. Blood harvested up to six hours after surgery was systematically reinfused. Drainage that occurred after six hours postoperatively was quantified and included in the final assessment of blood loss. The target hematocrit was 26%. The average duration of surgery was 195 ± 53 minutes in the aprotinin group and 175 ± 44 minutes in the placebo group. The study demonstrated that aprotinin reduced blood loss from 2839 ± 993 mL in the placebo group to 1935 ± 873 mL in the experimental group (a 32% difference, p < 0.007). The drug also reduced the total amount of transfused blood from

### TABLE III Results of Level-I Studies of Aprotinin in Orthopaedic Surgery

<table>
<thead>
<tr>
<th>Study</th>
<th>Type of Surgery</th>
<th>Av. Duration of Surgery in Placebo Group (min)</th>
<th>Av. Blood Loss in Placebo Group (mL)</th>
<th>Patient Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amar et al.</td>
<td>Orthopaedic</td>
<td>284 ± 148</td>
<td>1300</td>
<td>Cancer</td>
</tr>
<tr>
<td>Cole et al.</td>
<td>Spine</td>
<td>340 ± 94.7</td>
<td>930 ± 772</td>
<td>Pediatric</td>
</tr>
<tr>
<td>Langdown et al.</td>
<td>Hip</td>
<td>100</td>
<td>414 ± 213</td>
<td>Elderly</td>
</tr>
<tr>
<td>Murkin et al.</td>
<td>Hip</td>
<td>114</td>
<td>698</td>
<td>Adult</td>
</tr>
<tr>
<td>Lentschener et al.</td>
<td>Spine</td>
<td>175 ± 44</td>
<td>2839 ± 993</td>
<td>Adult</td>
</tr>
<tr>
<td>Murkin et al.</td>
<td>Hip</td>
<td>194 ± 11</td>
<td>2096 ± 223</td>
<td>Adult</td>
</tr>
<tr>
<td>Janssens et al.</td>
<td>Hip</td>
<td>176 ± 32</td>
<td>1943 ± 700</td>
<td>Adult</td>
</tr>
</tbody>
</table>

*NS = not significant. †High = a bolus of 2 million KIU followed by a maintenance dose of 0.5 million KIU/hr. Low = a bolus of 1.5 million KIU, with no maintenance dose. ‡The transfusion requirements were expressed in terms of the percentage of patients who received transfusion, which was 47% in the placebo group and 27% in the high-dose-aprotinin group.
95 units in the placebo group to 42 units in the aprotinin group (p < 0.001). No adverse drug effects were detected.

Cole et al. studied the effects of aprotinin administration during long-segment spinal fusions in children. Forty-four children were randomized to either a placebo or an aprotinin group by drawing an odd or even number from an envelope. Aprotinin was administered as a 240-mg/m² load over thirty minutes followed by a continuous infusion of 56 mg/m²/hr until four hours after surgery (equivalent to the high-dose aprotinin regimen). Neither the surgeon nor the anesthesiologist knew whether the patient had received the drug or the placebo. Blood loss was estimated by weighing surgical sponges, measuring blood collected in drainage and suction canisters, and subtracting the volume of all irrigation fluids added to the surgical field. Transfusion was performed to maintain a hematocrit of >27%. The average duration of the surgery was 371 ± 128 and 340 ± 94.7 minutes in the aprotinin and placebo groups, respectively. The estimated blood loss in the aprotinin group (545 ± 312 mL) was significantly less than that in the placebo group (930 ± 772 mL) (p < 0.039), and this reduction in blood loss translated into decreased transfusion requirements: from 2.2 units/patient in the placebo group to 1.1 units/patient in the aprotinin group (p < 0.001). The investigators reported a 13% prevalence of deep venous thrombosis in the control group and no evidence of deep venous thrombosis in the aprotinin group (difference not significant).

On the basis of the results of these two high-quality studies, we make a grade-A recommendation for use of aprotinin in spine surgery.

We identified one Level-I study of aprotinin use in “major orthopaedic surgery.” In this double-blind study by Amar et al., sixty-nine patients with a malignant tumor who were scheduled to have pelvic, extremity, or spine surgery were randomized to three groups by the staff of the biostatistics department and the pharmacy, who used sealed treatment-code envelopes. Twenty-three patients received aprotinin (a bolus of 2 million KIU followed by infusion of 0.5 million KIU/hr), twenty-two patients received epsilon-aminocaproic acid (a bolus of 150 mg/kg followed by a 15-mg/kg/hr infusion), and twenty-four patients received a placebo. All patients and clinical study personnel were blinded to the group assignments. Blood loss was estimated on the basis of suction losses and weighed sponges during surgery and wound drainage losses for forty-eight hours after the surgery. Packed red blood cells were transfused when the hematocrit was <24%. The operative time averaged 291 ± 160 minutes in the aprotinin group, 368 ± 203 minutes in the group treated with epsilon-aminocaproic acid, and 284 ± 148 minutes in the placebo group. Bronchospasm attributed to the aprotinin developed in one patient, so administration of the drug was discontinued for that patient. All other patients completed the study and were included in the analysis of the final results. Other complications included deep venous thrombosis (in three patients treated with epsilon-aminocaproic acid and in three in the placebo group) and pulmonary embolism (in two patients in the aprotinin group and in one in the placebo group). The prevalence of complications did not differ significantly among the groups (p = 0.72), and the investigators also found no significant difference in blood loss or transfusion requirements among the groups. However, these results do not apply to all patients because this study dealt only with patients with cancer. For the same reason, the results do not contradict the findings of other studies presented in this review.

**Discussion**

It is well documented that aprotinin is effective as a blood-conserving agent in a variety of very different types of operative procedures. Consequently, it was postulated that aprotinin might reduce blood loss and transfusion requirements independently of the type of operative procedure being performed. Some authors proposed that the clinical benefit of aprotinin seems to be affected by variables such as the duration of surgery and amount of blood loss—that is, the longer the surgery and the greater the blood loss, the greater the effects of

**TABLE III (continued)**

<table>
<thead>
<tr>
<th>Benefit from Aprotinin</th>
<th>Reduction in Blood Loss in Aprotinin Group* (% )</th>
<th>Av. Reduction in Transfusion Requirements in Aprotinin Group* (unit/patient)</th>
<th>Aprotinin Dose†</th>
<th>Transfusion Trigger</th>
<th>Significant Increase in Complications in Aprotinin Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>NS</td>
<td>Not reported</td>
<td>High</td>
<td>Hematocrit &lt;24%</td>
<td>None</td>
</tr>
<tr>
<td>Yes</td>
<td>41</td>
<td>1.1</td>
<td>High</td>
<td>Hematocrit &lt;27%</td>
<td>?</td>
</tr>
<tr>
<td>No</td>
<td>NS</td>
<td>Not reported</td>
<td>Low</td>
<td>Not reported</td>
<td>?</td>
</tr>
<tr>
<td>Yes</td>
<td>14</td>
<td>†</td>
<td>High</td>
<td>Hematocrit ≤18%</td>
<td>None</td>
</tr>
<tr>
<td>Yes</td>
<td>32</td>
<td>1.4</td>
<td>High</td>
<td>Hematocrit &lt;26%</td>
<td>None</td>
</tr>
<tr>
<td>Yes</td>
<td>29</td>
<td>0.9</td>
<td>High</td>
<td>Hemoglobin &lt;80 g/L</td>
<td>None</td>
</tr>
<tr>
<td>Yes</td>
<td>26</td>
<td>1.6</td>
<td>High</td>
<td>Hematocrit &lt;30%</td>
<td>None</td>
</tr>
</tbody>
</table>
The use of aprotinin when orthopaedic surgery is performed in patients with cancer is a complex issue. The Level-I evidence, perhaps because knee procedures are too short for aprotinin to reach its therapeutic concentration. Possibly, the drug has to be administered hours prior to knee surgery to have the desired effect. Level-I studies on the use of aprotinin in knee surgery were administered. The answer probably depends on the pharmacokinetics of this drug that take aprotinin to reach its therapeutic concentration.

One of the most challenging aspects of determining the optimal therapeutic dose of aprotinin and its mechanism of action in blood conservation is the nonspecificity of the drug. In fact, many of aprotinin’s effects counteract one another (e.g., aprotinin inhibits plasmin, a substance that inhibits fibrinolysis, and it also inhibits thrombin and thus prevents thrombus formation). Beckmann et al.32 offered a solution to this problem. They described the synthesis of chemically mutated homologues of aprotinin and showed that substituting one amino acid residue of aprotinin with other amino acids modified the affinity of aprotinin for its substrates. The substitution of valine enhances inhibition of human leukocyte elastase. This mutant aprotinin shows no detectable affinity to pancreatic trypsin. This elegant idea could be used to enhance the specificity of aprotinin for the antifibrinolytic pathway and to diminish its anticoagulant (as well as other irrelevant) properties at the same time.

As noted above, we found no Level-I studies of aprotinin use in knee surgery. Level-II studies30,31 offered conflicting evidence, perhaps because knee procedures are too short for aprotinin effects to become apparent. Possibly, the drug has to be administered hours prior to knee surgery to have the desired effect. Level-I studies on the use of aprotinin in knee surgery would be helpful to prove or disprove this hypothesis.

The use of aprotinin when orthopaedic surgery is performed in patients with cancer is a complex issue. The Level-I study11 discussed in this review showed no reduction in blood loss or transfusion requirements by aprotinin in patients with malignant disease. On the other hand, several studies have shown that aprotinin decreases transfusion requirements in patients undergoing surgery for malignant tumors such as femoral osteosarcoma, metastatic adenocarcinoma, meningioma, and hepatic tumors.40-44 Malignant disease is associated with a coagulopathy. It is known that the degree of coagulation and activation of the fibrinolytic pathway depends on the tumor type. For example, some tumors generate thrombin, and others do not. Consequently, the effects of aprotinin on blood conservation in patients with malignant disease may also depend on the tumor type.

The use of aprotinin is associated with minimal risk. Anaphylactic reactions are very rare, can be avoided by giving a small test dose, and are a risk only in patients who have already been sensitized to aprotinin by a prior exposure or exposures to the drug. Given its antithrombotic properties, it is logical to ask if aprotinin use increases the prevalence of deep venous thromboses and pulmonary emboli. We found no evidence of such an association in the studies presented in this review. Furthermore, Haas38 found no association between the use of aprotinin and the prevalence of deep venous thrombosis.

Aprotinin should not be used in pregnant patients as it is a pregnancy class-B drug (i.e., it was found to be safe in animal studies, but there are no data from clinical trials in humans). Aprotinin is expensive. Even though there have been encouraging cost analysis studies35,36, it would be interesting to know how this antifibrinolytic drug compares with other, less extensively studied and less expensive drugs such as tranexamic acid and epsilon-aminocaproic acid.

How does the effect of aprotinin on patients undergoing orthopaedic surgery compare with that on patients undergoing cardiac surgery, a procedure for which the FDA has already approved the use of aprotinin? According to the Cochrane review, by Henry et al., of fifty-five trials of aprotinin use in cardiac surgery, aprotinin reduced the need for allogeneic blood transfusion by 31% (relative risk = 0.69; 95% confidence interval = 0.63 to 0.76). Thus, the effects of aprotinin in cardiac surgery are comparable with those in orthopaedic surgery.

Overall, we propose a grade-A recommendation for the use of high-dose aprotinin in long orthopaedic procedures that are associated with large blood losses, such as spine or hip surgery. The drug has been successfully used in both pediatric and adult populations. On the basis of current evidence and until proven otherwise, aprotinin should be first given as a bolus of 2 million KIU and then as a maintenance dose of 0.5 million KIU/hr throughout the surgery. The data on the use of low-dose aprotinin are inconsistent and therefore this regimen cannot be recommended (grade-I recommendation).

Our conclusions are also supported by Level-II studies that were not included in this review for methodological reasons. Three studies of orthopaedic surgery32,33,35 and two studies of spine surgery32,39 showed a benefit of aprotinin in terms of decreasing blood loss and transfusion requirements. One Level-II hip trial32 showed no benefit of aprotinin given as a single bolus without a maintenance dose.
More high-quality Level-I trials are needed to investigate the optimal dose and mode of administration of aprotinin. Basic-science studies expanding our knowledge of this drug are needed as well, as it is important that the clinical trials be designed with a better understanding of the molecular context of aprotinin’s mode of action.

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The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.D.02240


Hip arthroscopy allows thorough visualization of the acetabular labrum, femoral head, and acetabular chondral surfaces as well as of the fovea, ligamentum teres, and adjacent synovium. Microsurgical tools developed specifically for arthroscopic hip surgery can be used to provide the least intrusive means of diagnosis and treatment of conditions involving the above-mentioned structures (Table I). No radiographic study, including high-contrast gadolinium-enhanced arthrography-magnetic resonance imaging, is entirely sensitive or specific for the diagnosis of labral tears or chondral lesions. Thus, a high level of clinical suspicion based on the patient's symptoms and positive physical findings is paramount for the clinician to recognize subtle abnormalities in the hip joint.

Hip arthroscopy is technically demanding, with a steep learning curve, and requires special distraction tools and operating equipment. Access to the hip joint is difficult because of the resistance to distraction resulting from the large muscular envelope, the strength of the iliofemoral ligament, and the negative intra-articular pressure. This operation should not be done without specific education in its methods.

**Disorders Managed with Hip Arthroscopy**

**Labral Tears**

A patient with a torn acetabular labrum has hip pain and often presents with catching, locking, or a painful click in the hip joint. There is not necessarily a history of trauma. Often, tears are associated with congenital or structural hip anomalies such as acetabular dysplasia, slipped capital femoral epiphysis, and Legg-Calvé-Perthes disease.

Progression of minor injuries seems to be the rule. The region of the acetabular labrum that is most prone to injury is avascular. Slight injury to the labrum, when subjected to repetitive motion and stress, tends to progress. Chondral surface lesions of the acetabulum or femoral head eventually develop, and there is a relationship between the duration of symptoms and the severity of labral injury found at arthroscopy. Harris described an intra-articular labrum with degeneration in patients undergoing total hip arthroplasty for end-stage degenerative changes.

Fitzgerald reported that most (forty-five) of forty-nine labral injuries that he documented occurred at the anterior marginal attachment of the acetabulum. In our experience with 436 consecutive hip arthroscopy procedures, 96% of labral tears were found in the anterior quadrant (Fig. 1). However, in a study of an adolescent Asian population by Ikeda et al., the posterosuperior aspect of the labrum was most commonly injured. Labral tears are not seen on plain radiographs, but the secondary degenerative changes, specifically a subchondral cyst of the anterior aspect of the roof of the acetabulum, can be observed on such images. Gadolinium-enhanced magnetic resonance imaging is much more sensitive than traditional magnetic resonance imaging for detecting labral tears, but it has not become as accurate as was hoped.

**Loose Bodies**

The clinical presentation of locking or catching with activity can be associated with intra-articular loose bodies. A variety of conditions, including synovial chondromatosis, may lead to loose bodies that can become trapped in the acetabular fossa and cause pain. Arthroscopy is the least invasive method of removing loose or foreign bodies from the joint.

Loose bodies may not be visible on plain radiographs, but computed tomography with contrast medium is highly sensitive for visualizing these structures. One of us (J.C.McC.) and Busconi found that up to 67% of loose
bodies may not be evident on conventional radiographs. When the bodies produce locking or catching, arthroscopy becomes a means with which to establish the diagnosis and simultaneously provide treatment (Fig. 2).

**Chondral Lesions of the Acetabulum and the Femoral Head**

Chondral lesions are one of the most elusive sources of hip joint pain. Because of the more constrained anatomy of the hip, currently available radiographic imaging cannot be used to diagnose the presence or extent of these lesions reliably. Even gadolinium-enhanced arthrography-magnetic resonance imaging has limitations with regard to identifying chondral injuries. This lack of sensitivity may be explained in part by the static nature of the examination as well as by the lack of distraction during the study. Yet chondral lesions do occur with frequency. It is important to note that the outcome of treatment of hip cartilage lesions depends directly on the severity and extent of the chondral damage. In a review of the findings of 436 hip arthroscopic procedures, one of us (J.C. McC.) and colleagues found that 259 (54%) of 477 chondral injuries occurred in the anterior aspect of the acetabulum. These lesions were seen most frequently in association with a labral tear, and what was most disturbing was the frequency and extent of the full-thickness cartilage injuries. Seventy percent of the anterior chondral injuries were Outerbridge Grade III or IV (Fig. 3).

Chondral injuries may occur in association with a multitude of hip conditions, including labral tears, loose bodies, posterior dislocation, osteonecrosis, slipped capital femoral epiphysis, dysplasia, and idiopathic degenerative arthritis. The common initiating site for labral as well as chondral injuries has been termed the watershed zone (Fig. 4). The watershed lesion, which occurs at the labrochondral junction, may destabilize adjacent acetabular cartilage. It is postulated that, when the damaged labral cartilage is subjected to repetitive loading conditions, joint fluid is pumped beneath acetabular chondral cartilage, causing delamination of the articular cartilage. By this same mechanism, the fluid eventually burrows beneath subchondral bone to form a subchondral cyst. This cyst is the result, not the cause, of the symptoms. Outcomes of surgery are directly dependent on the stage or extent of the labral and chondral lesions, a point that emphasizes the importance of early detection. Although it is too early to draw definitive conclusions, it is believed that early treatment will prevent or delay the progress of the degenerative process. The difficulty in diagnosing these lesions as well as in determining their effect on outcome provides a substantial rationale for arthroscopic hip surgery.

**TABLE I Hip Conditions That May Benefit from Arthroscopy**

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Labral tears</td>
</tr>
<tr>
<td>Loose bodies</td>
</tr>
<tr>
<td>Acetabular and femoral head chondral flap lesions</td>
</tr>
<tr>
<td>Foreign body removal</td>
</tr>
<tr>
<td>Synovial chondromatosis</td>
</tr>
<tr>
<td>Collagen diseases with impinging synovitis</td>
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<tr>
<td>Crystalline hip arthropathies</td>
</tr>
<tr>
<td>Ruptured or impinging ligamentum teres</td>
</tr>
<tr>
<td>Capsular shrinkage (Ehlers-Danlos syndrome)</td>
</tr>
<tr>
<td>Post-traumatic conditions (e.g., Pipkin fracture)</td>
</tr>
<tr>
<td>After total hip arthroplasty</td>
</tr>
<tr>
<td>Osteonecrosis (early stages prior to collapse)</td>
</tr>
<tr>
<td>Extra-articular conditions</td>
</tr>
</tbody>
</table>

**Fig. 1**

Intraoperative photograph showing surgical probing of an anterior labral tear.

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Osteonecrosis
The role of hip arthroscopy in the diagnosis and management of osteonecrosis of the femoral head is controversial. The focus of most efforts to diagnose and treat osteonecrosis has been on preventing collapse of the subchondral bone. Revascularization, especially with free vascularized fibular grafting, is done in an attempt to alter the natural history of the disease. Arthroscopy can help the physician to stage the changes in the articular surface to determine if osteotomy or bone-grafting is indicated, and it can aid in the treatment of the chondral flap lesions that are often associated with the disease. Arthroscopy has no role in the management of the later stages of osteonecrosis—i.e., after the femoral head has collapsed. Arthroscopy should be reserved for patients with mechanical symptoms such as locking, buckling, or catching, suggesting the presence of a loose body, a labral injury, or a chondral flap lesion.

Ruptured or Impinging Ligamentum Teres
Gray and Villar described lesions of the ligamentum teres, either alone or in conjunction with other articular lesions, as a source of hip pain. This lesion, although infrequent, may occur as a result of trauma such as a posterior dislocation or a Pipkin fracture. In addition, it may occur in association with dysplasia or degenerative arthritis.

Synovial Abnormalities
An open synovectomy requires dislocation of the femoral head from the acetabulum, which is traumatic to the joint. An arthroscopic synovectomy is less traumatic. Janssens et al. described arthroscopic synovectomy as an adjunct to the diagnosis and treatment of pigmented villonodular synovitis. Crystalline diseases such as gout or pseudogout can be treated with an arthroscopic examination and copious lavage, mechanical removal of crystals, and synovial biopsy and/or synovectomy if necessary. There are a variety of synovial disorders for which a synovectomy is the definitive treatment or plays a role in the treatment.

Collagen diseases such as juvenile rheumatoid arthritis, rheumatoid arthritis, systemic lupus erythematosus, and Ehlers-Danlos syndrome involve the hip, which may be the initial symptomatic joint. An arthroscopic examination permits a synovial biopsy and/or synovectomy as well as evaluation and treatment of accompanying damage to...
the articular cartilage and lavage.

Synovial chondromatosis is a metaplastic synovial condition that results in the production of numerous loose bodies. When the loose bodies are nonossified, diagnosis of this disease can be extremely difficult. In the authors’ experience with thirty cases to date, arthroscopic treatment consisted of clarification of the diagnosis, removal of between five and 300 loose bodies (especially those clustered within the fovea) from each patient, treatment of articular damage, and synovectomy (Fig. 6). Although recurrence has been reported in about 10% of cases despite intervention, arthroscopy can be repeated and should be beneficial in the absence of severe damage to the chondral surfaces.

**Miscellaneous Indications**

The senior one of us (J.C.McC.) has performed arthroscopy in ten hips after total hip arthroplasty. An infection had been suspected in two patients, but repeated joint aspirations had been negative. In both cases, low-virulent organisms were identified by fluid analysis as well as synovial biopsy. The senior author also removed a broken trochanteric wire (16 gauge, 1.75 in [44.45 mm] long) from the joint (Fig. 7). A screw that had shown progressive backing out from the acetabular component on serial radiographs was also removed.

**Trauma**

The senior author treated a patient who had had persistent excruciating hip pain for five days after a reduction of a dislocated hip. A computed tomography scan revealed a loose body. At the time of surgery, a large hematoma was evacuated, two chondral loose bodies were removed, and a posterior labral tear was repaired. The patient was able to start walking the next morning. The senior author also performed successful arthroscopic examination and treatment of patients with displaced bone and cartilage after a Pipkin fracture. In addition, he removed bullet fragments that had migrated into the joint, embedding itself into the superolateral aspect of the acetabulum.

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**Fig. 4**
The surgical probe is directed at a watershed lesion found in the anterior quadrant of the joint, at the labrochondral junction.

**Fig. 5**
Intraoperative photograph showing a chondral flap lesion of the femoral head (arrow) in a patient with osteonecrosis.
**Osteoarthritis**

Asymmetric, focal degenerative changes in the cartilage, particularly in the anterosuperior aspect of the femoral head or acetabulum, may not be visible on anteroposterior pelvic radiographs. When a patient is seen to have thinned articular cartilage, subchondral cyst(s), and osteophytes on radiographs, arthroscopy is not indicated. Arthroscopic lavage can relieve pain in patients with relatively advanced osteoarthritic changes, but this relief is often temporary. Débridement and chondral microfracture may have a role in the management of osteoarthritis that is not advanced enough to justify more aggressive surgical options such as joint replacement. This may be particularly applicable in young patients when the surgeon wishes to avoid or delay total joint arthroplasty.

**Intractable Hip Pain**

Arthroscopic evaluation may be considered when joint symptoms are unremitting, and no diagnosis has been made. The symptoms should have been present for more than six months. Villar reported that arthroscopy facilitated a diagnosis in 40% of patients in this situation.

A patient with protracted mechanical symptoms (buckling, catching, and locking) and positive physical findings (McCarthy hip extension sign; painful impingement with hip flexion, adduction, and external rotation; and inguinal pain on resisted straight-leg raising) is an acceptable candidate for surgery. The McCarthy hip extension sign occurs when, with both hips flexed, the patient’s pain is reproduced by extending the affected hip, first in external rotation and then in internal rotation. An intra-articular injection with a local anesthetic, done under fluoroscopic control, may help to clarify whether the source of pain is intracapsular.

**Technique**

Arthroscopy can be done with the patient in either the supine or the lateral position. We prefer to use a lateral approach (a modification of the approach described by Glick et al.), with the patient in the lateral decubitus position. A modified fracture table or a specially modified distraction device fitted to a regular fluoroscopic table is necessary. The patient must be carefully padded to protect against neurapraxia and pressure. Adequate visualization requires the femoral head to be distracted from the acetabulum to achieve 7 to 10 mm between their articular surfaces. Without sufficient distraction, the femoral head prevents maneuvering of instruments into the recesses of the acetabulum. The femur is placed in slight flexion (approximately 10° to 20°) with the foot maintained in neutral to slight external rotation. A well-padded lateral perineal post is positioned perpendicular to the long axis of the thigh, 10 to 15 cm distal to the ischial tuberosity. This acts as a fulcrum to aid in distraction. The lower-extremity muscles must be completely relaxed to minimize the amount of force required to distract the femoral head from the acetabulum. The depth of the hip joint requires specially designed extra-long arthroscopic instruments passed through a cannula that is long enough to protect the soft tissues surrounding the hip.

Portal placement requires palpation, identification, and marking of the anatomic landmarks, especially the femoral neurovascular bundle. The procedure commonly involves five portals: direct anterior, anterior paratrochanteric or anterolateral, proximal trochanteric, superior paratrochanteric or posterolateral, and direct posterior. The nomenclature and definitions of these portals and approaches are not consistent in the literature. We prefer the anterior and superior paratrochanteric portals, as they allow visualization of the entire articular portion of the joint in 95% of cases.

Once the location of the portals has been determined, a specially designed guidewire is passed through the center of a spinal needle. After the guidewire has been positioned in the joint, a blunt cannulated trocar is inserted for controlled penetration of the hip capsule. Once the portals have been established, the hip is distended with saline solution to overcome the native intra-articular negative pressure, and an arthroscopic pump is used thereafter to maintain constant pressure. Most of the joint can be seen with a standard 30° arthroscope. However, a 70° arthroscope is sometimes needed for complete visu-
alization, particularly when the patient has a tight hip joint. Extra-long, curved shaver blades allow operative arthroscopy around the femoral head. Long suction punches and long graspers are needed to resect and aspirate tissue and loose bodies. Thermal devices are useful for débriding the torn labral and chondral flaps or inflamed synovial tissue folds. High-frequency thermal energy or lasers can be used for cutting and coagulation as well as for ablation.

Outcomes

We previously analyzed the results of 170 arthroscopic procedures performed in patients with radiographic evidence of acetabular dysplasia (a center-edge angle of between 19° and 26°)²¹. All patients presented with pain and mechanical hip symptoms consisting of locking, catching, or buckling. Seventy-two had a labral tear, and sixty-six of the tears were in the anterior or anterosuperior aspect of the labrum. All tears were located at the articular free margin of the labrum; none were at the capsular attachment. Fifty-four patients had damage of the acetabular cartilage immediately adjacent to the labral tear. Twenty-seven patients had erosive cartilaginous damage on the femoral head directly subjacent to the acetabular lesion. After two years of follow-up, 85% of the patients reported a decrease or absence of pain. Seventeen patients eventually required a total hip arthroplasty. Of those seventeen patients, thirteen had moderate hip dysplasia and all were found to have Outerbridge¹¹ Grade-III or IV chondral changes at arthroscopy.

In another study, of sixty-one patients, we found that the outcomes of surgery were related to the severity of the labral and chondral lesions²². Nine of ten patients with a Stage-1 lesion (a discrete labral tear with an intact femoral head and intact acetabular chondral cartilage) had a good or excellent outcome. Nine of eleven patients with a Stage-2 lesion (a labral tear with focal articular damage to the subjacent femoral head but with intact acetabular cartilage) had a good or excellent outcome. Stage-3 lesions (labral tears with abnormalities of the adjacent acetabular cartilage) were associated with worse outcomes. Also, the extent of the lesion directly affected the outcome, which was rated as good for fifteen of twenty-one patients with a Stage-3A lesion (<1 cm of abnormal cartilage) but for only four of ten with a Stage-3B lesion (>1 cm of abnormal cartilage). Patients with a Stage-4 lesion, which involves diffuse chondral damage throughout the joint, had the worst outcomes, with seven of nine having recurrent pain. Regardless of the radiographic appearance, improvement was only transient if the articular cartilage involvement was diffuse on the femoral head and in the acetabulum. Three patients with a Stage-4 lesion had a total hip arthroplasty within two years after the arthroscopic surgery.

The above findings are similar to the results reported by Farjo et al.²⁴. Those authors reported that ten of fourteen patients without an articular lesion had a good result compared with only three of fourteen patients who had arthritis. Byrd and Jones found that patients with a labral tear or loose bodies but no articular disease had a 27-point improvement in the modified Harris hip score but those with degenerative arthritis had only a 14-point improvement²⁵. Specific long-term outcome data for arthroscopic hip surgery is needed to further define its role in orthopaedic practice. A validated, self-administered questionnaire designed to assess nonarthritic hip pain in patients with high activity demands and expectations can be used prior to intervention and after treatment²⁶ (see Appendix).

Complications

Complications occur in 0.5% to 5% of patients and are most often related to the required distraction of the joint. Transient neurapraxia is the most common injury²⁷⁻³⁰. Damage to the labrum on entry into the joint is a serious iatrogenic complication that can be avoided by using an image intensifier to confirm sufficient distraction. Scuffing of the femoral head can occur to various extents with or without distraction, and care should be taken to avoid this injury. We are aware of one reported death from fluid extravasation in a patient with an acetabular fracture²². A review of 530 arthroscopic procedures revealed that osteonecrosis of the femoral head developed postoperatively in one hip²⁷. The senior author has done more than 1500 hip arthroscopic procedures, with a 5% rate of complications, none of which were permanent or major.
There have been no infections or cases of pulmonary embolism. A deep vein thrombosis developed one month after the arthroscopy in one patient, who had Factor-V Leiden deficiency. No instruments broke within the joint. Magnetic resonance imaging performed after the arthroscopy in 5% of the patients revealed no cases of osteonecrosis. There has been no associated muscle or vessel damage and no permanent damage to the sciatic, peroneal, or pudendal nerve. Fewer than 2% of the patients experienced transient peroneal hyperesthesia, which have been associated with difficult distractions and long procedures. There were two neurapraxias to the lateral femoral cutaneous nerve, both of which resolved. Mild chondral scuffing occurred in 3% of the patients. Such scuffing has been associated with difficult distraction such as occurs with mild protrusio or associated degenerative joint disease.

**Prevention of Complications**

Proper patient positioning and adequate distraction are crucial to patient safety and successful arthroscopy. To minimize the risk to the patient, the traction boot and apparatus must be applied carefully and preferably by the surgeon. It is imperative that the distraction time be kept to a minimum. Use of adequate portals, saline fluid dynamics, and tapered telescoping cannulas helps to avoid the risk of instrument breakage or scuffing of articular surfaces. Electrothermal devices, long curved shavers, and long graspers are necessary to reach formerly inaccessible areas.

The ability to directly visualize the chondral articular surfaces has already greatly increased our understanding of early hip disease. Further improvements in hip-specific instrumentation, safer distractors, and surgical expertise will facilitate this procedure’s eventual role in enhancing our understanding of the pathophysiology of hip disease. Additional refinement of indications awaits prospective outcome studies. The importance of such studies cannot be overemphasized.

Avoiding complications involves judicious patient selection. Candidates for hip arthroscopy should include only patients with mechanical symptoms (catching, locking, or buckling) who have not responded to conservative therapy. Findings on physical examination can include any or all of the following: a positive McCarthy sign; inguinal pain with flexion, adduction, and internal rotation of the hip; and anterior inguinal pain with ipsilateral resisted straight-leg raising. Gadolinium-enhanced magnetic resonance imaging is much more sensitive than traditional magnetic resonance imaging for detecting labral tears. One of us (J.C. McC.,) and Busconi found that 78% of gadolinium-enhanced magnetic resonance images correctly predicted an anterior labral tear. However, the study is not as reliable for detecting chondral defects or nonossified loose bodies.

**Overview**

In summary, patient selection and diagnostic expertise are critical to successful outcomes. The technical challenge of hip arthroscopy involves a steep learning curve. Meticulous attention to positioning, minimizing distraction time, and portal placement are essential to prevent neurovascular complications. The reported complication rates of between 0.5% and 5% are most often related to distraction. Improvements in technique and instrumentation have made hip arthroscopy an effective way to diagnose and treat a variety of intra-articular problems.

The evolving understanding of intra-articular lesions in early hip disease has provided a convincing rationale for the early detection and treatment of labral and chondral lesions. It is now understood that acetabular labral tears do not have an adequate blood supply to heal and can contribute to or occur in association with lesions of the articular cartilage of the contiguous femoral head and eventually contribute to the progression of hip osteoarthritis. When a labral tear occurs in the watershed zone, it may destabilize the adjacent acetabular cartilage. When the damaged labral cartilage is subjected to reciprocating loading conditions, joint fluid is pumped under pressure beneath the delaminating acetabular cartilage and eventually burrows beneath subchondral bone to form a subchondral cyst. These lesions are most frequently anterior and often are associated with sudden twisting or pivoting motions. No radiographic study, including high-contrast gadolinium-enhanced arthrography-magnetic resonance imaging, is entirely sensitive or specific for diagnosing a labral tear. Thus, a high index of clinical suspicion based on positive physical findings is paramount for the clinician to properly determine treatment. The understanding of earlier stages of hip disease learned from arthroscopic investigation gives further credence to the importance of minimally invasive techniques to visualize and treat diseases of the hip.

**Appendix**

An example of a questionnaire designed to assess nonarthritic hip pain in active individuals is available with the electronic version of this article, on our website at jbjs.org (go to the article citation and click on “Supplementary Material”) and on our quarterly CD-ROM (call our subscription department, at 781-449-9780, to order the CD-ROM).

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The authors did not receive grants or outside funding in support of their research or preparation of this manuscript. J.C. McCarthy received payments or other benefits or a commitment or agreement to provide such benefits from commercial entities (consultant for Arthrex and Innomed). No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

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References


Introduction
Advancements in medical technology over the last several decades have occurred at an incredible pace. In our specialty of orthopaedics, there are numerous examples of rapid improvements in technology that have markedly improved the care of our patients with musculoskeletal disorders. Arthroscopic surgery is one such example. The field has made tremendous advancements from several decades ago, when visualization alone was a challenge in arthroscopic surgery, to today, when cruciate ligament surgery in the knee and rotator cuff repair in the shoulder are routinely performed through the arthroscope. In parallel with the explosion of new technology in orthopaedic surgery and medicine has been the acceleration of information transfer throughout the world. The Internet has become a tool that allows instantaneous distribution of new information. In the field of medicine in general and orthopaedics specifically, information received by the physician and potential patients may be uncensored.

It is only human nature for patients afflicted with musculoskeletal disorders or any other medical disorders to want the best care possible. It is also the challenge and requirement for industry to develop and sell new technology in order to build successful businesses. To many consumers, the best care equates with the care that involves the newest technology. Tried and true methodology is only a cliché. This is the atmosphere in which we practice orthopaedics, and it is the reason that direct-to-consumer marketing is so prevalent and effective today. This symposium explores the critical issue, “How should new technology be introduced into orthopaedic practice?” Various aspects of this question are explored. Insight into industry’s investment in new technologies and issues involved in recouping that investment are outlined. Regulatory statutes that govern the implementation of new technology are discussed. The direct-to-consumer marketing concerns are addressed. Finally, “the two sides of the coin” concerning when new technology should be introduced to the general orthopaedic community are debated. Should it be widely disseminated when it initially becomes...
available, or should there be a require-
ment for peer-reviewed acceptance be-
fore new technology is implemented in
our practices?

Investment of Industry
in New Technologies
By Roy D. Crowninshield, PhD

The orthopaedic industry has a history of
substantial growth of investment into
new technology for orthopaedic care. In
the last ten years, the annual level of
that investment has doubled. The cur-
cent investment trends of the industry are
in step with the most advanced sci-
centific thinking into future orthopaedic
treatments. This investment in ortho-
paedic treatment technologies is im-
portant not only for the future of the
industry but also for the future of the
orthopaedic profession and the ortho-
paedic patient.

Successful new technology pro-
vides a competitive advantage that can
differentiate a company in the market-
place. Having products and services
that are different and better than the
competitors’ can fuel business growth.
In many cases, new technology is pro-
tected from timely utilization by a com-
petitor because of restrictive patents,
long development times, the effort in
obtaining regulatory approval, and
large investment requirements. The
nature of technology investment in
orthopaedics is changing, with many
companies committing to more ex-
pensive, longer-term, and higher-risk
ventures.

Published estimates of market
history and growth rates have sup-
ported the projection that the world
market for orthopaedic products in
2005 will approach $20 billion in an-
ual sales. The research and develop-
ment spending in orthopaedics, across
a wide number of publicly reporting
companies, has been reported to vary
from about 4% to 6% of sales, and thus
is approaching $1 billion per year. It
can be estimated that the orthopaedic
industry has spent about $6 billion on
research and development over the past
decade.

Indeed, the industry is making
enormous investments in new tech-
nologies. The industry’s investment is
as diverse as the different companies
within the industry and as diverse as
the practice of orthopaedics. Histori-
cally, much of this money has been
spent on traditional orthopaedic de-
vices, such as total joint replacements,
fracture fixation devices, spinal fixation
devices, and arthroscopy. Investments
have been made in these areas because
that is where most of the current prac-
tice of orthopaedics is found.

Technology investment in ortho-
paedics is, however, changing as the
practice of orthopaedics changes. More
recently, investments have been made
in advanced surgical technologies, new
surgical techniques, advanced instru-
mentation, computer-assisted surgery,
and computerized operative planning.
These areas are representative of some
new surgical technologies that are be-
ing applied to current orthopaedic
surgical procedures. The industry is
also investing in less traditional ortho-
paedic devices, including spinal discs,
prosthetic cartilage, and resorbable fix-
ation. Finally, substantial investment
is being made in biologic and phar-
maceutical orthopaedic technologies.
These include tissue growth factors,
gene therapies, cell therapies, drug de-
vice combinations, and a variety of
untraditional orthopaedic products.

The research and development
investments of the industry include
product design engineering, licensing
of intellectual property, laboratory test-
ing, and other efforts in new product
development. Orthopaedic technology
also requires investment beyond tradi-
tional research and development. New
products sometimes require new pro-
duction technologies, manufacturing
plants, equipment, tooling, and quality
assurance. Additionally, investments in
product management, marketing, sales
training, surgical technique develop-
ment, instructional literature, and ad-
vertising may be required to support
the introduction of new technology.
An example of the scale of new
technology investment can be found in
traditional implant systems. Consider
for the moment a large implant distrib-
utor and a major new total knee im-
plant system. Because of their size and
scope, new total knee systems can have
enormous investment requirements.
Total knee systems come with many
options to include implants in many
sizes, rights and lefts, revision and pri-
mary implants, cemented and cement-
less components, and with complex
instrumentation. The cost of develop-
ing a comprehensive new knee system
is likely a $10 million to $20-million-
dollar investment. The regulatory pro-
cess for a class-II device, which does not
require a clinical trial, may cost several
hundred thousand dollars for market
clearance in the United States. The total
knee implant and instrumentation in-
ventory for a major manufacturer on a glo-
bal scale can be valued at $50 million to
$150 million. Finally, the time spent to
bring a major new total knee system to
market is probably two to four years.
If the design concept of a new
implant system causes it to be a class-
III device rather than a class-II device,
the development investment and the
return on that investment can be very
different (see the next section for a
definition of the classes). This change
in the United States regulatory ap-
proval process can add substantially to
the required investment. Perhaps more
important than the increase in finan-
cial investment is the time investment,
which is much higher for a class-III
device than for a class-II device. This
change in the device classification can
add five years to the process of obtain-
ing marketing approval in the United
States. The increased time requirement
before market clearance can substan-
tially change the return on a technol-
ogy investment.

The orthopaedic industry’s in-
vestment in orthobiologics is perhaps
the most interesting example of new
technology investment. These technolo-
gies include cell, protein, peptide, and
other biological technologies. These bi-
ologic elements may be combined with
an orthopaedic device. From a regulat-
ory point of view, these might be a
class-III device, a biologic product, a
A report on biomaterials sales in the United States, which includes bone graft substitutes, resorbable products, cartilage repair, and growth factors, has predicted a market growth over the next four years of $1.5 billion. The future growth in this market is largely dependent on the sales of bone growth factors. Bone growth factors provide a demonstration of the large investment requirement and the uncertain return on investment associated with orthopaedic technology development. Reported sales projections for growth factor products for all United States market participants indicate that, in five years, the market will be about $1.0 billion per year. If this large total sales market is realized, it does not ensure that the total industry investment to achieve those sales will be profitable. The return on investment for growth factor sales needs to account not only for the profit on current sales but also for the investment and timing of the investment that preceded the sale of the product. Industry efforts to develop orthopaedic bone growth-factor products have been ongoing for about fifteen years. Based on knowledge of the publicly reported and privately communicated expenditures by the industry in bone growth factors, the net present value of that investment is, by my estimate, about $1.5 billion. The present value of that investment will tend to grow in the future at some appropriate cost of capital. At the same time, that investment will be paid back by profit realized from sales of the product. As a result, industry net return on investment in growth factors may still be negative despite having achieved $1.0 billion in annual sales. There may be individual products and individual companies that are profitable within this market and valuable patient treatments realized, but it is possible that, from an overall industry perspective, the investment in bone growth factors will not prove to be a substantially profitable stand-alone endeavor for a considerable time.

The orthopaedic industry has experienced substantial growth in the global orthopaedic products market, and it is today approaching $20 billion in worldwide annual sales. This growth has come from favorable demographics, expanded access to health care, and new technology development. Technology investment is inherently risky. A technology may not succeed clinically, a clinically successful technology may not be commercially successful, future markets for a technology may not develop as predicted, and competitive technology may succeed and make other technologies obsolete. Despite these uncertainties, the industry continues to invest in technology to improve orthopaedic treatment. Successful orthopaedic technology investment is equally important for the health of the industry, the health of the profession, and the health of the orthopaedic patient.

Role of the Food and Drug Administration in the Employment of New Technology

By A. Seth Greenwald, DPhil(Oxon)

The role of the Food and Drug Administration in the regulation of orthopaedic devices is the reason most often cited to explain why these products are not made available to the American public in a timely fashion. The impact of these regulations focuses on three groups: orthopaedic surgeons, device manufacturers, and the Food and Drug Administration itself.

The evolution of this process began in 1976, with the amending of the Federal Food, Drug, and Cosmetic Act to include the regulation of medical devices in a similar way to the regulation of pharmaceutical products. This brought the orthopaedics industry under federal oversight, requiring that medical devices demonstrate both safety and effectiveness before becoming available to the American public. It dramatically increased oversight responsibility of the Food and Drug Administration with regard to medical product approval, compliance, and enforcement.

The Act defined a dual-track approach for bringing a product to market (Table I). Track I requires that the product to be marketed is, in fact, similar to one that had been in clinical use prior to 1976 or for which there is a post-Amendment predicate device. This enables a 510(k) application to be filed with the Food and Drug Administration, citing substantial equivalence with the predicate device. Some examples of product equivalence that have received 510(k) clearance include press-fit femoral stems, cemented hip systems, threaded acetabular components, hybrid porous-coated implants, and hydroxyapatite-coated implants. Track II, however, requires that a demonstration of safety and effectiveness first be made as there is no prior clinical experience with a similar device for which these as-

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**Footnotes:****

1. Spinal discs and biologic products represent current areas of high interest for technology investment. These two examples allow us to put a dimension on the market potential for new technology investments. They each have potentially large markets and large investment requirements. They are high-risk ventures.

2. Recent reports on the potential spinal disc market have projected, by one estimate, that within the next five years the global market will be about $1.4 billion. A second estimate projects that the world market will be $1.2 billion in the next three years. Whether either of these estimates will prove to be true is uncertain. However, the magnitude of this potential spinal disc market fuels the willingness of the industry to invest in related technology.

3. A report on biomaterials sales in the United States, which includes bone graft substitutes, resorbable products, cartilage repair, and growth factors, has predicted a market growth over the next four years of $1.5 billion. The future growth in this market is largely dependent on the sales of bone growth factors. Bone growth factors provide a demonstration of the large investment requirement and the uncertain return on investment associated with orthopaedic technology development. Reported sales projections for growth factor products for all United States market participants indicate that, in five years, the market will be about $1.0 billion per year. If this large total sales market is realized, it does not ensure that the total industry investment to achieve those sales will be profitable. The return on investment for growth factor sales needs to account not only for the profit on current sales but also for the investment and timing of the investment that preceded the sale of the product. Industry efforts to develop orthopaedic bone growth-factor products have been ongoing for about fifteen years. Based on knowledge of the publicly reported and privately communicated expenditures by the industry in bone growth factors, the net present value of that investment is, by my estimate, about $1.5 billion. The present value of that investment will tend to grow in the future at some appropriate cost of capital. At the same time, that investment will be paid back by profit realized from sales of the product. As a result, in about five years, the industry’s net return on investment in growth factors may still be negative despite having achieved $1.0 billion in annual sales. There may be individual products and individual companies that are profitable within this market and valuable patient treatments realized, but it is possible that, from an overall industry perspective, the investment in bone growth factors will not prove to be a substantially profitable stand-alone endeavor for a considerable time.

4. The orthopaedic industry has experienced substantial growth in the global orthopaedic products market, and it is today approaching $20 billion in worldwide annual sales. This growth has come from favorable demographics, expanded access to health care, and new technology development. Technology investment is inherently risky. A technology may not succeed clinically, a clinically successful technology may not be commercially successful, future markets for a technology may not develop as predicted, and competitive technology may succeed and make other technologies obsolete. Despite these uncertainties, the industry continues to invest in technology to improve orthopaedic treatment. Successful orthopaedic technology investment is equally important for the health of the industry, the health of the profession, and the health of the orthopaedic patient.
surprises exist. An Investigational Device Exemption application is submitted to the Food and Drug Administration, which seeks the conduct of a clinical trial. The trial itself is a rigorous, prolonged process, requiring a substantial number of patients with a minimum follow-up period of two years, and it generally takes four to five years to complete (Fig. 1). At study completion, the manufacturer then submits a Premarket Application, which undergoes scrutiny by the Food and Drug Administration as well as review by a peer advisory body of scientists and clinicians, resulting in a recommendation of approval, approval with conditions, or disapproval. When the manufacturer has addressed all of the concerns of the Food and Drug Administration, final clearance is granted and the device can go to market with appropriate labeling. Early examples of the Investigational Device Exemption-Premarket Application approval process include the porous-coated AML femoral stem (Anatomic Medullary Locking; DePuy, Warsaw, Indiana) and the LCS mobile-bearing knee system (Low-Contact Stress; DePuy). The conduct of a clinical trial, aside from the cost, length, and obtaining of patient consent, requires complete follow-up for a minimum of 85% of the patients at the end point of the study as well as participating surgeon-investigator compliance. This process has often been viewed by both small and large orthopaedic manufacturers as a bridge too far and has been criticized as inhibiting technological advance and contributing to corporate overseas flight. In this regard, it is interesting to watch the growth of the orthopaedic industrial complex, in which many companies are now multinational and products are manufactured and sold overseas before they are available to American patients because of the regulatory process. Contemporary examples of these include the majority of mobile-bearing knee designs, prophylactic use of prepackaged antibiotic-loaded bone cement, surface replacements, and the majority of spinal implants. This represents a elimination.

### Table I: Medical Device Approval Pathways Defined by the 1976 Amendments to the Federal Food, Drug, and Cosmetic Act

<table>
<thead>
<tr>
<th>Track</th>
<th>Description</th>
<th>Application Protocol*</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Requires demonstration of medical device equivalence with a product in clinical use prior to 1976</td>
<td>510(k)</td>
</tr>
<tr>
<td>II</td>
<td>Requires establishment of safety and effectiveness as no similar product was in clinical use prior to 1976</td>
<td>IDE with subsequent submission of a PMA at completion of a clinical trial</td>
</tr>
</tbody>
</table>

*IDE = Investigational Device Exemption, and PMA = Premarket Application.

Fig. 1
Flow diagram showing the Track-II medical device approval process. IDE = Investigational Device Exemption, PMA = Premarket Application, and FDA = Food and Drug Administration.
moving time scale, in which medical device products are used around the world, often years before they are available in the United States.

Orthopaedic products often have failed and been abandoned in the cauldron of clinical use despite Food and Drug Administration findings of substantial equivalence (510(k)) or the demonstration of safety and effectiveness through a clinical trial (Investigational Device Exemption-Premarket Application). Examples include first-generation surface replacements, threaded acetabular cups, synthetic ligaments, and metal-backed patellar components. Preclinical testing and the two to three-year data required in clinical investigations do not address in vivo issues of implant longevity and biological response. They suffice to provide an assurance of implant safety, but not effectiveness, which requires the tincture of time in vivo.

In 1990, Congress passed the Safe Medical Devices Act, which established the MedWatch surveillance program, as the Food and Drug Administration theorized that insight into early device failures could result in prompt product recalls to protect the American public. This resulting regulation required hospitals, manufacturers, and clinicians to submit incident reports on medical device failures. Unfortunately, the information received by the Food and Drug Administration was quantitatively inadequate and untimely. The rising tide of medical malpractice has also contributed substantially to the reluctance of clinicians to report. From this experience, however, came the realization that more could be gained if a nongovernmental agency facilitated the process.

The American Academy of Orthopaedic Surgeons (AAOS), in concert with governmental agencies, is currently working to establish an American hip and knee arthroplasty registry. This endeavor has been initiated by surgeons who recognize the value of successful implant registries, the most prominent of which are the Swedish, Norwegian, and emerging Australian national databases.

Another important facet of the Safe Medical Devices Act was to require the Food and Drug Administration to examine more closely the intended clinical use of orthopaedic devices. The first and perhaps best example is the reclassification of porous-coated hip prostheses in 1992, which allowed 510(k) applications for product introduction. This overcame the initial Food and Drug Administration approval dilemma, in which porous-coated devices were labeled and sold for cemented use only. Despite the fact that none of these devices were ever designed by manufacturers for cemented use, they were required to be labeled as such in order to go to market. Thus, an orthopaedic surgeon employing biological fixation did so through off-label use on the basis of both clinical judgment and common sense. In this regard, it is important to appreciate that the Food and Drug Administration does not regulate clinical practice or judgment, but neither does that inure the surgeon from the risk of exposure through the litigation process now rampant in the United States. It is important that sound judgment, common sense, and the standard of community and national care be appreciated. These represent the bulwarks that ensure that the best interest of the patient is served.

The last and perhaps most profound event on the regulatory timeline occurred in 1997. It is referred to as the Food and Drug Administration Modernization Act, and it established maximum response times for the submission of 510(k) applications (ninety days) and Premarket Applications (180 days). This often results, however, in additional questions as the deadlines approach. Of benefit to manufacturers, the Act also limits postmarket surveillance for products with Premarket Application approvals to thirty-six months unless it is mutually agreed that the experimental nature of a specific product requires a longer follow-up period. Additional clinical data from a product with an approved Premarket Application may now be used to support a subsequent product approval request. Perhaps most importantly, the Act clearly defined a classification scheme (Table II). Class III indicates a device that has not been established as safe and effective and requires an intervening clinical trial (an Investigational Device Exemption-Premarket Application). Class II refers to a device for which there is a similar, established premarket product, and the filing of a 510(k) application is required. Class-I products are 510(k) exempt, and examples include sutures, needles, and manual surgical instruments.

Under this revised classification scheme, several milestones have occurred.

In 1997, the first 510(k) approval was granted for enhanced cross-linked polyethylenes as part of an acetabular cup system, not as a material.

In 1998, spinal fixation devices, particularly pedicle screws, were reclassified from Class III to Class II.

<table>
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<td>510(k)</td>
</tr>
<tr>
<td>I</td>
<td>510(k) exempt</td>
<td>NA</td>
</tr>
</tbody>
</table>

*IDE = Investigational Device Exemption, PMA = Premarket Application, and NA = not applicable.
In 1999, 510(k) approvals were granted for a metal-on-metal hip articulation and a computer-assisted navigation system for hip and knee arthroplasty applications. Acrylic bone cement for use in total joint arthroplasty was reclassified from Class III to Class II after thirty years of clinical use. In 2003, porous-coated knee prostheses were reclassified from Class III to Class II, the first 510(k) clearance was granted for prepackaged antibiotic-loaded bone cement for use in revision arthroplasty, and the first Premarket Application approvals were granted for ceramic-ceramic hip articulations.

In 2004, 510(k) approval was granted for a bone cement to be used with kyphoplasty procedures. In June 2004, the Orthopaedic Advisory Panel met and recommended reclassification of mobile-bearing knees from Class III to Class II as well as approval of the first artificial disc as a Class-III device.

On October 26, 2004, the Charité artificial disc (DePuy Spine, a Johnson & Johnson Company, Raynham, Massachusetts) was cleared for marketing by the Food and Drug Administration, but extensive surgeon education and training in its use will be required.

On October 28, 2004, despite the approval recommendation of the Orthopaedic Advisory Panel to reclassify mobile-bearing knee systems, the Food and Drug Administration concluded that these systems still cannot be regulated as Class-II devices, given their kinematic displacement differences.

From the above extractions, it should be evident that the 1997 Food and Drug Administration Modernization Act has profoundly affected orthopaedic device availability despite a long road ahead.

In conclusion, the increasing role of the AAOS Device Forum is to continually assist the Food and Drug Administration as a voluntary think tank on issues including device reclassification, guidance documents, and education. At the end of the day, the availability of safe and effective products to the American public in a reasonable time frame remains the Congressional mandate to the Food and Drug Administration.

Direct-to-Consumer Advertising: Helpful or Harmful?
By Jay R. Lieberman, MD

Direct-to-consumer marketing has clearly emerged as an influential factor in the delivery of health care. Managed-care organizations, hospitals, doctors, drug companies, and implant manufacturers are all appealing directly to consumers to influence behavior. One cannot read a newspaper, watch television, or listen to the radio without being exposed to advertisements. In a recent study, 99% of respondents had seen at least one direct-to-consumer advertisement. The question is whether the increase in direct-to-consumer marketing is an advance because it enhances patient knowledge and empowers patients, or is it just an effective way to enhance sales?

Between 1996 and 2000, annual spending on direct-to-consumer prescription drugs skyrocketed from $600 million to approximately $2.5 billion. In the year 2000, Merck (Whitehouse Station, New Jersey) spent $161 million on direct-to-consumer marketing of Vioxx alone, and the drug has recently been pulled off the market. Figures are not yet available for such drugs as Via-gra (Pfizer, New York, NY) and Cialis (Lilly, Indianapolis, Indiana), but it seems that the advertising budgets for these products will be well beyond $200 million. Most direct-to-consumer promotion is concentrated on a few products. However, 80% of advertising dollars is still spent on promotion to health-care professionals, and the rest is spent on direct-to-consumer advertising. Other types of promotions, such as advertising in professional journals, have declined, and twice as much money currently is spent on print advertising to consumers than is spent on advertisements in professional journals.

The total spending on promotion for prescription drugs has increased 70% since 1996. However, relative to product sales, the total spending on promotion has stayed relatively constant at approximately 15%. It appears that this increase in spending on advertising is related to the appearance of new high-priced drugs in the marketplace.

Clearly, since 1996, there has been a major shift in the marketing strategy of a variety of companies that sell products in the health-care arena. A number of factors have contributed to this change in promotional tactics: first, the Food and Drug Administration developed new guidelines for consumer advertising, which allowed companies to advertise their products without stating the complications related to the product as long as they listed a toll-free number or Internet web site for the patient to obtain product information. The patient also had to be referred to a pharmacist or a physician for further explanation of the product. During the same period, there were other forces acting in this arena, including the availability of health-related information on the Internet and an increase in managed care. The Internet was a new source of information for patients that could be easily accessed. Finally, companies have realized that sales could be increased by altering the prescribing patterns of managed-care physicians and by trying to influence the products listed on managed-care formularies.

One way to induce these changes would
be to provide this information to patients so that they would pressure their physician to prescribe a specific product. Critics argue that direct-to-consumer advertising is that the underlying message of direct-to-consumer advertising is that the physician may not do what is best for the patient unless pushed by the patient. It alters the patient-physician relationship, particularly in a managed-care environment. Managed-care organizations monitor patient satisfaction. If patients are not satisfied because they did not receive a particular procedure or a drug that they requested, they may be dissatisfied with the physician. This dissatisfaction can affect a physician's income if salary bonuses are based on patient satisfaction. Critics also argue that the underlying message of direct-to-consumer advertising is that the physician may not do what is best for the patient unless pushed by the patient. In general, many physicians have been negative about these promotional campaigns because of the increased duration of office visits, the poor quality of the data presented to consumers, and pressure by patients to prescribe drugs that may not be appropriate for them. Recently, a mail survey of 523 Colorado physicians revealed that the majority of physicians had a negative attitude regarding direct-to-consumer advertising. The physicians believed that these advertisements did not provide sufficient information related to cost (98.7%), adverse side effects (54.8%), or alternative treatment options (94.9%). However, approximately 50% of the physicians believed that these advertisements could increase patient knowledge related to medical issues.

In this same study, 500 public respondents were interviewed on the telephone. Only 29% thought that direct-to-consumer advertising was a positive trend in health care, and only 28.6% believed that these promotions made them better informed regarding health-care issues. In addition, a minority of individuals (10.1%) agreed that these advertisements induced them to either seek care or request specific medications. Public respondents in lower socioeconomic classes were more likely to seek care as a result of exposure to direct-to-consumer promotion. An obvious weakness of this study is that a telephone survey may not truly reflect consumer behavior. Respondents may have been either reluctant to agree that these advertisements did influence their behavior or they may not have recognized the impact of these promotional campaigns on their behavior or the influence on their interactions with their physicians. In another survey of 1050 physicians, 56% of the respondents reported that, when a patient did discuss a direct-to-consumer advertisement at an office visit, the purpose was to request a test, a medication, or a referral to a specialist. The physicians considered 49% of these requests inappropriate, but 69% of these requests were filled anyway. Approximately one-third of these physicians thought that a discussion related to a specific advertisement improved the doctor-patient relationship, and 8% believed this type of interaction had a negative impact.

Clearly, there is evidence to suggest that these advertisements can have a negative impact on the doctor-patient relationship. The discussion of such advertisements can lengthen office visits and cause physician resentment if a great deal of time is required to discuss inappropriate requests. In addition, patients are often unhappy if their request is denied. Physicians must develop strategies to handle patient requests for drugs and procedures that may not be appropriate. The ethics related to direct-to-consumer advertising are confusing for the physician. For physicians and surgeons, “do no harm” is a critical tenet of treatment and the development of a strong doctor-patient relationship is an essential aspect of providing excellent patient care. Some patients may not be satisfied unless the physician gives them the treatment that they desire on the basis of their exposure to these advertisements even though it may be a waste of health-care resources. This creates a potential ethical conflict or resentment on the part of both parties. Medical ethics is different from business ethics. Ethical business practices focus on doing nothing unlawful or improper that might harm the organization. In addition, being good to the customer and being a loyal employee to the organization are important. Hence, from the business ethics perspective, these advertisements are ethical as long as they are accurate. However, there appears to be a gray line with respect to accuracy and this can lead to false expectations on the part of the patient, which damages the doctor-patient relationship. From the patient's standpoint, there may be confusion or difficulty in separating the general advertising, to which they are constantly exposed, from the medical advertising. Many consumers may be better prepared to evaluate household products than they are to evaluate medical products. A product may be inappropriate or potentially harmful to a specific patient. The patient becomes frustrated when told by the physician that the product or the procedure in the advertisement is not appropriate for him or her. In a managed-care environment, the patient may feel that the physician is just trying to save money. If a surgeon is not enthusiastic about a new procedure in question, the patient is concerned that the surgeon may be trying to reduce health-care costs or is not familiar with the new technique.

In summary, there is no evidence at this point that direct-to-consumer advertising improves patient outcome, cost-effectiveness of care, or physician prescribing patterns. It may encourage patients to seek preventive care, which is a great advance, but it also may increase health-care costs. It appears to be a successful strategy to promote sales of drugs and procedures, but it may damage the patient-physician relationship. Physicians must also recognize that they are now a growing part of the...
direct-to-consumer advertising frenzy. Web-site advertising, print advertising, and radio advertising by physicians are increasing at a rapid rate. The AAOS ethics manual guidelines should be reviewed and its recommendations implemented. Advertisements should be accurate. There should be no implied false claims or misleading information, no omissions of material facts, particularly with respect to risks and complications, and the claims must be substantiated. Terms like “cure,” “safe,” and “pain free” imply a certainty of result. Descriptions of clinics and offices as world-class, without any data, should be avoided.

Direct-to-consumer advertising is obviously not going to go away, because it works for companies. In addition, under certain circumstances, these advertisements could be beneficial to patients. Physicians must develop new strategies to deal effectively with the marketplace because patients are able to obtain alternative sources of information, which they trust, including the Internet, television, and magazine advertisements. What are some possible strategies? First, funding through the Food and Drug Administration can be increased to penalize violators of advertising guidelines. Unfortunately, at the present time, the Food and Drug Administration is completely overwhelmed. Even though the advertising revenues have increased, the number of violators identified have remained the same. Legislation could be passed to provide more resources for regulatory agencies to prescreen advertisements. Second, additional studies are needed to evaluate the effects of direct-to-consumer advertising on health care and health-care economics. Third, the AAOS and the American Orthopaedic Association could help to develop and teach strategies to orthopaedic surgeons for dealing with direct-to-consumer advertising in their practices. Fourth, these organizations could also implement programs to prescreen advertisements. Review committees could be developed to critique consumer advertisements and render an opinion as to their appropriateness. Since direct-to-consumer marketing is not going to disappear, orthopaedic leadership groups must take the initiative to ensure that these promotions do not harm our patients or our profession.

Why Should Surgeons Be Able to Use New Technologies as They Become Available?

By Aaron G. Rosenberg, MD

To answer the question “Should new technologies be used as soon as they become available?” one must define what one means by technology. What does one mean by adequate information? Who should be the one who decides? These are tough questions. They have been argued since the fifteenth century. To know where we are going, it helps to know where we have been. Our origins as surgeons are in the rapid and desperate assaults on the human body under the duress of severe suffering. But, with time, things have changed. Much of our surgical practice today consists of reconstructive and, for the most part, elective procedures, performed for the convenience of the patient and to lessen debility. Such procedures are no less important perhaps than the “cutting for stone” of antiquity, but they are done in a much more controlled environment subject to patient choice and the rational weighing of risk to benefit. The principles of evolution have allowed us to understand how change occurs. Daniel Dennett’s Darwin’s Dangerous Idea: Evolution and the Meanings of Life illustrates this phenomenon. There is a difference between nature, which works very slowly, and man, who by his nature changes very rapidly. The big difference is that the transmission, accumulation, and improvement of tool systems and concepts are not random. There is a cybernetic feedback loop that man uses, whereby he or she can model things, test them, and then collect information. Models can be modified, adding into the cycle of innovation both new ideas and information to improve upon them. It is this cybernetic feedback loop that allows mankind to change so rapidly. This was described by Buckminster Fuller as the process whereby humans evolve by creating variations, employing selection, and improving their productivity. He called this process ephemerization.

Consider the transmission of information and how it has changed. In the year 1800, a letter carried by horseback represented a reasonable standard of information transmission. It contained the equivalent of an average of 10,000 bytes of information that might take about a month to get where it was going, resulting in an information transmission speed of 0.03 byte per second. Just sixty years later, the telegraph had become a common means of information transmission, representing an improvement to two seconds per character or three bytes per second. Thus, over a sixty-year period, the transmission speed had increased by about 100 times. By the early 1960s, primitive computers were available and moved information at a rate of 300 bytes per second, a further increase of about 100-fold. But just thirty years later, fiber-optic cables were capable of moving information at a rate of one billion bytes per second, an improvement of three million fold. In a span of 200 years, the speed of information transmission increased by a factor of 33 billion. The result is dramatic. The improvement of information-processing abilities, which represents the development of high-speed computing devices, has radically transformed modern communications. The presence of Internet availability in much of the modern Western world has created an environment in which hugely increased amounts of information are readily available to the majority of the community in an almost instantaneous fashion. A single electronic toy today contains more computing power than was available in the whole world in 1960. Hans Christian von Baeyer, in Information: The New Language of Science, references the University of California at Los Angeles Institute of Technology and Assessment as predicting that humans and machines together will create...
more information in the next three years than has been created in the past 300,000 years. This is the world we and our patients are living in today. Innovations are coming. Innovations are a natural outcome of evolutionary forces. So, for example, as we witness the evolutionary growth of less invasive surgical procedures, we realize the extent to which these procedures will require innovation—in approaches, in instrumentation, and in visualization techniques. And most likely, they will come with increasing speed and without randomized controlled trials in lockstep with their promotion. Almost none of the innovations we now take for granted in orthopaedics were adopted on the basis of the rational evaluation of evidence accumulated in randomized controlled trials. And, while evidence-based medicine remains the current prescriptive approach, of greater importance is understanding the actual methods whereby innovations become adopted.

So the real question is “How do new technologies become adopted?” and the science of this is the science of how innovation is diffused in a society. The infusion of innovation has been described as a process by which an innovation is communicated through channels over time among members of a social system until it is either adopted or rejected. From many studies, we know that there is a degree of uncertainty that comes with all new adoptions. The innovation must have a benefit for potential adopters. The motivation for adoption is seldom certain at the outset. The barriers to the adoption of an innovation are the uncertainty of the benefit and the potential risks. There are several characteristics of any innovation that will influence how rapidly or how readily it is adopted. First, is there an obvious relative advantage? The advantage can be either economic, that is, improvement in productivity or profit, or it can be social, that is, improvement in prestige and associated factors as is commonly seen in fads and fashions. Compatibility is also an important factor. How well does the innovation correlate with prevalent beliefs, theories, and ideas? What are the current needs, and how does the innovation fit in with them from an economic standpoint, a technical standpoint, or from a strategic or tactical standpoint for an individual or an industry?

Increased complexity yields a less easily adaptable innovation. Complexity tends to favor specialists and subspecialists. Probability and observability are the characteristics of an innovation that are relatively easily understood. The more easily one can try something, and the more observable the benefit and the absence of risk, the more rapidly an innovation will be adopted. And reinventability is another characteristic that is important, especially for the technically minded. This is extremely important in the surgical community, where many of us are technically minded. If one can reinvent or modify an innovation, then they are more likely to adopt the innovation. Diffusion also occurs in a social system, either easily or with difficulty, depending upon the particular social system. There are many different types of systems, with social hierarchies that control the directional flow of information, and there are other aspects of communication systems that strongly influence how readily and rapidly innovations are adopted. These systems in general help to predict individual responses to adoption. System norms are important. They are established patterns of behavior or technology use, and they represent a range of tolerable behaviors in the community through which the innovation may be accepted. For example, resistance to adoption may relate to evidence levels or to influence from acceptable sources, which is actually the more common pattern in most of medicine. It may also relate to acceptable directions of information flow. In medicine, we are accustomed to having the information and relaying it to the patient. Now, we are experiencing information coming upward from the patient to us in some respects, and we are not very comfortable with that. This change will also certainly influence the rate of adoption. The mass media is becoming an increasingly popular source of information, but interpersonal relationships are usually a stronger method in support of adoption. In the world of physicians, this includes peers, drug company representatives, and our patients.

Resistance to change varies among individuals. If one draws a graph with the y-axis monitoring the number of people and the x-axis monitoring the resistance to change, with high resistance at one end and low resistance at the other, a bell-shaped curve results. Sociologists who have studied the diffusion of innovation have categorized individuals into five groups: innovators, early adopters, early majority, late adopters, and laggards. The innovators are venturesome and cosmopolitan, they come from the outside, they cope well with uncertainty, and they have a high tolerance for risk. The early adopters tend to be locally integrated opinion leaders or role models. They seek to maintain esteem in their community. They act as local missionaries for the innovation. They are more social and highly interconnected in their community. They are more in touch with mass media and interpersonal communication channels. They seek more information and know more about innovations. The early majority just beats the average adopter. They interact frequently with their peers but provide the common links to the practitioners in the community. The late adopters are the skeptical or cautious types, and they tend to be subject to peer, economic, or network pressures. For these individuals, the system norms must favor adoption. Then, finally, there are the laggards, who tend to have no opinion leadership. They are isolated, suspicious of innovations, measure things by comparison with the past, and tend not to be subject to peer or network pressures.

Now, whether it is right or wrong, some surgeons will use tech-
nologies when they are readily available. This is a fact with which we have to come to grips. If one tries to answer the question of who should decide, some would conclude that our system of free markets and consumer choice has served us well. There is little doubt that leaving decisions in the hands of any centralized authority, no matter how bright, has repeatedly demonstrated major inefficiencies and has often resulted in catastrophic errors. In The Wisdom of Crowds, James Surowiecki explains why, in general, markets work much more efficiently than individuals. Finally, everyone knows examples of innovators who, fortunately for their field, pushed their ideas forward despite resistance. Kurt Semm, MD, who died last year, was one such individual. He is, unfortunately, not well known in the orthopaedic community. Kurt Semm was an interesting pioneer and visionary. However, his reports of surgical techniques were shouted down at professional meetings, and his lectures were greeted with laughter, derision, and suspicion. He was forbidden to publish by his dean, and his first submitted papers were rejected because they were considered unethical. Indeed, the president of the German Surgical Society demanded that his license be revoked and that he be barred from practice. His associates at the University of Kiel asked him to have psychological testing, and then Chair of Orthopedics at the Mayo Clinic, noted one day on rounds that, in his then busy practice, he was performing only one operation that he had actually been trained to do during his residency (namely, triple arthrodesis). He said that all of the other procedures, and the many implants he used routinely at that time, he had learned about from others or, in many cases, he had taught himself to use, subsequent to his formal training. All of those in current practice or residency training will have to retrain themselves completely during their careers, and most will do so more than once.

The issue is not whether we will embrace new technology, new techniques, and novel methods of caring for our patients, but rather how these changes should be introduced. Progress must be managed so that the gains of the past are preserved without placing undue barriers before the improvements that may be possible as knowledge and technology advance. Examples of new methods that were developed or popularized over the past twenty-five years and survived an often haphazard and Darwinian selection process to become commonplace today are listed in Table III.

Looking to the not-so-distant future, we can anticipate major changes related to the development and widespread introduction of other technology (Table IV).

An explosion of new technology and supporting implants, methods, and surgical techniques will, in each of these instances, create a major dilemma for any early adopters. When is it appropriate to utilize a new method, material, or implant in our patients, if that use is not part of a study approved by the institutional review board and involving formal informed consent on the part of the patient?

Many of the challenges, controversies, and dilemmas that relate to the introduction of novel technology can be illustrated by specific examples from a project that is ongoing at our institution. At the 2004 Annual Meeting of the Orthopaedic Research Society in San Francisco, we reported on alterations of medial compartment loading in a cadaver model following implantation of subchondral periarticular permanent magnets. Placed with like poles in op-

### TABLE III Examples of New Methods Developed or Popularized Over the Past Twenty-Five Years That Have Become Commonplace Today

- Operative arthroscopy of the knee (and subsequently multiple other joints)
- Uncemented fixation for total joint arthroplasty
- Modular total joint implants to manage bone deficiency and correct deformity
- Distraction osteogenesis for limb-lengthening and deformity correction
- Microsurgical repair of neurovascular structures leading to reimplantation of amputated parts and vascularized tissue transfers for bone and soft-tissue reconstruction
- Bone allografting for massive bone defects
- Identification of bone morphogenetic proteins and other growth factors and their subsequent manufacture using recombinant DNA methods
- Limb salvage surgery for malignant neoplasms as an alternative to amputation
- Diagnostic imaging with use of magnetic resonance imaging, computerized tomography, fast computerized tomography, positron emission tomography, and other methods
position, magnets were inserted through a bone tunnel from a point proximal to the joint on the femoral side and from a point distal to the joint on the tibial side. The resulting opposing magnetic fields led to significant off-loading of the medial compartment and transfer of load to the lateral side of the joint (p < 0.05). Under simulated stance-phase loading to 90.8 kg, the implanted magnets decreased the peak medial compartment pressure by 71.2% and lowered the weight-bearing area by 60%. Concomitant lateral compartment peak loads increased to 172.2%, and the weight-bearing area increased to 142.8% of those values obtained prior to implanting the repelling periartricular magnets (p < 0.05). Despite the now demonstrated ability to significantly off-load such a joint, many barriers remain to the clinical application of such a concept. These include the prevention of corrosion, achievement of secure long-term anchorage of the magnet-bearing implants to bone, and ensuring accurate and controlled placement of the devices according to the estimated prerequisite mechanical joint-loading and calculation of the still-to-be-determined optimal goal for joint-loading following such a procedure.

Assuming that these problems can be solved, a very important dilemma is then created by the availability of such a device. If such implants can be validated, is it reasonable to pursue initial application in the treatment of knee osteoarthritis when there are highly successful, well-studied, and durable alternative options, such as unicompartmental and tricompartmental total knee arthroplasty? Conventional knee arthroplasty sets a very high bar for any alternative treatment to meet or exceed. Does the availability of a large potential market or the benefit to a treating surgeon’s practice volume justify subjecting patients to the substantial risks inherent in new technologies that are previously untested and without validation? While there are safeguards with regard to the introduction of new technology and implants through the regulatory process of the Food and Drug Administration, as has been detailed elsewhere in this symposium, these constraints really focus on establishing safety and fall well short of documenting long-term efficacy. This remains our responsibility as a profession. Performing procedures on patients with use of an implant that has not been shown to work, when there is a highly reliable and effective alternative, is not acceptable even if that new procedure can be demonstrated to be “safe” over the initial few months or years following implantation.

It is more reasonable and appropriate, when the benefit and well-being of the patient is used as the primary driver, to pursue the introduction of truly novel methods, materials, and treatments in areas for which no effective treatment exists or for which the results of conventional therapy are known to be unreliable or infrequently effective. In the case of a magnet-bearing implant, for example, an alternative application might be in the treatment of decubitus ulcers. The exact same concept behind periartricular implantable permanent magnets in the knee could be applied to implantation of an identical device in the ischial tuberosities of patients following spinal cord injury. As has been tragically demonstrated in many patients with a spinal cord injury, skin breakdown and decubitis ulcers are a lifelong plague and can contribute to a substantial decrease in life expectancy. These patients are frequently subjected to repeated surgical interventions with a variety of debridements, plastic surgical procedures, and muscle flaps aimed at eliminating areas of ulceration and providing, at least for a time, healthy soft-tissue coverage over weight-bearing insensate osseous prominences. Regardless of the quality of round-the-clock nursing efforts and the resources expended, periodic skin breakdown is all but inevitable for the majority of these patients. Either as part of treatment for this problem or preferably as a means of prevention, the implantation of a permanent magnet in the ischial tuberosities would allow decreased or even time-varying loading of the skin in the weight-bearing area of the ischial tuberosities of sitting patients without protective sensation or motor control. Typically, these patients are confined to motorized wheelchairs and the addition of an electromagnet system in the region of the seat would probably present very minimal practical problems. A strong argument can be made that it is more reasonable to pursue the validation of any substantially new technology for the treatment of clinical problems for which treatments frequently fail or do not exist than it is to pursue new technology for the treatment of problems that can be managed with reliable surgical treatments with a success rate of >90% at ten years postoperatively, as is the case with total knee arthroplasty for the treatment of osteoarthritis.

At the present time, the large potential markets for hip and knee arthroplasty and spinal implants virtually

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<th>TABLE IV Major Changes Related to the Development and Widespread Introduction of Technology That Can Be Anticipated in the Not-So-Distant Future</th>
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<td>- Computerized surgery and instrumentation</td>
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<td>- Novel therapies based on genetic determinants for multiple musculoskeletal diseases and conditions</td>
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<td>- Novel biomaterials such as highly porous metal foams for improved fixation and integration of bone, tendon, and ligament structures to implants</td>
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<td>- Cartilage replacement or regeneration</td>
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<td>- Bioimplants that modify their local environment by means of the controlled delivery of drugs, growth factors, or gene therapy to the host-implant interface</td>
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<td>- Tissue-engineering methods to allow replacement or regeneration of tissues or entire organs</td>
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guarantee that new platform technologies will be quickly adopted for these areas and may be in use for many years before they are made available for less profitable smaller-market applications in “orphan joints,” such as the wrist or elbow, regardless of the clinical need that exists.

It seems most reasonable that novel technology should be introduced for patients with conditions for which we have no good answer rather than for patients with conditions for which we already have effective treatments. We should be most willing to expose patients to risk in the areas where we do the poorest job, not those areas where we are most successful. Left to the influences of the free market, the use of new technology, and the risks of failure and complications that this exposes patients to, will most often occur where the greatest business opportunity exists. There is little downside for the community as a whole should a nonmedical traditional business venture fail. When a chain of grocery stores goes out of business, people in the community do not go hungry but may simply have to drive a little farther to find food. Medical care is different. Large scale failures subject large segments of our population, often the most vulnerable, to pain, suffering, repeat surgery, economic loss, and in some cases even death. Medical care must be viewed like other critical services in society, such as electricity or water, for which communities have moved toward a public utility model with appropriate controls and regulations to minimize the risk of problems such as blackouts or loss of water during a drought.

It is easy to argue that, as a society, we need rules in the “knife fight” of medicine to protect our patients and, ultimately, our profession. Our patients cannot and should not be made to bear the burden of judging between medical treatment options with regard to their efficacy and safety when most of us as physicians are unqualified to do so outside our own narrow areas of expertise. We must demand data on new ideas, technology, or procedures. We must do the work of carefully designed prospective studies guided by observational research and by our retrospective series, databases, and experience in order to appropriately validate new developments before widespread adoption. This is made all the more necessary by recent documentation of volume-related effects on surgical outcomes. Juxtaposed to the recent rapid changes in implant choice, instrumentation systems, and even surgical approach, a much reduced level of experience and reproducibility of results can be predicted for a large volume of our patients.

For those in the lead, for the innovators, for the proponents of pioneering new technology and methods, there is a responsibility to provide data from well-designed studies to validate the new approach before we encourage or even allow widespread use. Most of the rest of us should stay one fad behind and await the data needed to justify abandoning what we know works for that which may or may not be better.

Our common goal must be to remain true to our roots, and do no harm, as we strive to provide our patients with exactly the type of care we would want for ourselves and for our loved ones.

Overview

This symposium has attempted to address the critical issues related to the introduction of new technology to our orthopaedic practices. The development of new technology in medicine has occurred at an accelerated pace over every subsequent decade that all of us have been in orthopaedic practice. The information age, especially with the introduction of television and the Internet, has made any information concerning these technologies readily available. All would agree that some new technology and some pioneers involved with the development and implementation of these new technologies deserve great credit for advancing our field. Many of those who have been in orthopaedic practice for one or two decades realize that they are performing procedures much differently or are performing procedures that were not even available during their training. None of us would try to impede progress. However, we also know of devices and techniques in orthopaedics that were implemented, some possibly prematurely, and did not advance the field. In fact, some may have led to results that were inferior to the standard of the time. All ethical physicians would agree, “First do no harm.”

All would agree that the orthopaedic industries are a business and that good business practice involves the development of new products and bringing them to market, eventually creating a profit for that business. In orthopaedic surgery, this development has led to products that allow surgeons to take better care of their patients. In addition, the orthopaedic industry financially supports research and development at academic centers and the education of present and future orthopaedic surgeons (through such avenues as the Orthopaedic Research and Education Foundation and institutional educational and research grants). Today, this process is markedly improved through conflict-of-interest policies and ethical guidelines set by industry as well as our professional organizations.

Although there is consensus in the areas just described, a great debate has arisen with regard to when the new technologies should be implemented in general orthopaedic practice. How much scientific information should be available before the new technology is broadly used? Some reason that the current social and economic environment allows for free markets in orthopaedic surgery and all of medicine. They argue that the surgeon and the patient can decide when to implement these “hopeful” technological advances. They rationalize either that the technology has been “cleared” by regulatory agencies or that, in the many instances when regulatory clearance has not been necessary, the surgeon or physician is able to use the technology at his or her discretion. Also, in this free-market atmosphere in which we live, some surgeons believe they can advertise their use of this technology.
Others argue that medicine is becoming an expensive commodity. They argue that cost-effective medicine needs to be employed and that techniques and devices with scientifically validated outcomes should be the norm. They are concerned that the information age in which we live and the ethics of business rather than the ethics of medicine may create more confusion and deception than help for the patient. What direction can be taken to ensure that our patients get the best treatment with the best outcomes whether the technologies are new and novel or those accepted as tried and true? When new technologies are developed, they must not be promoted with false advertising concerning any proven efficacy when no peer-reviewed data are available. Watchdog groups may need to be established by the orthopaedic leadership groups to ensure this. The American Association of Hip and Knee Surgeons recently published an advisory statement to patients and surgeons concerning what is known and what is not known about any benefits of minimally invasive hip and knee surgery. Postmarketing surveillance must be used if scientific peer review of outcome studies has not been performed. Developing registries for procedures commonly performed, such as joint replacement surgeries, would go a long way toward establishing the risks and benefits of the new technology. Performing randomized clinical trials early to determine efficacy should be mandatory so that implementation can be aborted if early results are not comparable with those of established procedures, devices, or drug therapies. We must teach our students, residents, and colleagues to better understand the social pressures and ethical considerations related to this “innovation age” in which we live.

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In support of their research or preparation of this manuscript, one or more of the authors received grants or outside funding from Zimmer. In addition, one or more of the authors received payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity (Zimmer). Also, a commercial entity (Zimmer) paid or directed, or agreed to pay or direct, benefits to a research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

doi:10.2106/JBJS.E.00116

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The First Orthopaedic Researcher

by Zachary B. Friedenberg, MD

He was a surgeon whose credo was not to ponder, rationalize, or theorize about the solution of a surgical problem but to do the experiment. Nor was his inquiring mind limited to orthopaedic surgery or even to the entire field of surgery and medicine. It led him to conduct experiments on the temperature of fish and its effect on the clotting time of their blood, to investigate their organs of hearing, and to study the source of electricity in rays, the air sacs of birds, the behavioral instincts of birds and bees, the development of fossil bones, and the clockwise and counterclockwise rotation of vines.

He was the father of scientific surgery, transforming it from a craft to an experimental science. In addition to his experiments and observations on bone growth and development, he experimented with the healing of fractures and bone infections, the treatment of gunshot wounds, and the spontaneous separation of osteonecrotic bone from living bone. His revelations of the basic principles of bone physiology clearly entitle him to be recognized as the first orthopaedic researcher.

Henry T. Buckle (1821-1862), in his History of Civilization in England, wrote of John Hunter (Fig. 1), “I have only one more name to add to the splendid catalogue of Scotsmen of the eighteenth century. But it is the name of a man who for comprehension and original genius must be placed far above any philosopher whom Scotland has produced, whose only fault was an occasional obscurity, not merely in language but in thought.”

To understand the magnitude of his achievements, one must examine the state of surgery in the early years of the eighteenth century. The guild of barber surgeons controlled the field of surgery in the cities, regulating its members, training apprentices, and seeking to eliminate any competitors. This guild could not extend its control in the provinces where untrained bone setters, tooth pullers, and wound healers were free to roam and practice on the citizenry. Only in the universities of the Italian states at Bologna, Padua, Pisa, and others were surgeons formally trained in anatomy and some physiology.

Surgery in the eighteenth century was emerging from an almost barbarous state. At leading hospitals such as St. Bartholomew’s in London, cauteries were still in use to treat ulcers and tumors, and digestive and suppuratives were layered on clean wounds to encourage drainage, which was thought to be a stage in the normal healing of a wound. Thus, the treatments were impeding the healing that nature was striving to accomplish.

John Hunter (1728-1793), the tenth child of a Scottish farmer, had an older brother, William, who had attained fame in London giving courses in anatomy and invited John to join him as an assistant. John, in his own right, became an expert anatomist and pursued the study of investigational anatomy, which included the first description of the olfactory nerve. His anatomical investigations led to physiological and pathological studies.

As a surgical apprentice, he first assisted the prominent surgeon, William Cheselden, and later assisted Percivall Pott, who described the ankle fracture known as Pott’s fracture and the spinal deformity due to tuberculosis known as Pott’s disease. In 1767, Hunter received the diploma of the barber surgeons of London and was elected to the Royal Society.

His brusque, nonconciliatory manner and his inattention to his practice so he could spend more time on research deprived him of monetary success. He would travel great distances to recover an unusual specimen, neglecting his office hours to which he returned reluctantly. “Well, I must go and earn the damned guinea or I shall be sure to want it tomorrow.” When a highly respected staff member at St. George’s Hospital intruded into his laboratory one night and said, “‘My dear John Hunter,’ he looked up at him annoyed and said, ‘My dear Tom Fool.’” Not only was he brusque, but he was also intolerant of those doctors who did not measure up to his level of intellect.

Hunter’s Experiments on Bone

“I have often devised experiments by the fireside or in my carriage and have also conceived their results: but when I tried the experiment it could not be attended with all the circumstances that were expected. I think it may be set down as an axiom that experiments should not be repeated which merely tend to establish a principle already known or admitted, but that the next step should be application of that principle to useful circumstances.”

John Belchier, a young student in 1736, noted when dining that the bone of his pork roast was stained pink. On questioning his host, he was told that the pigs sometimes were fed bran soaked in the dye, madder. Belchier presented his finding at a meeting of the Royal Society, and, undoubtedly, Hunter was inspired by this talk to feed madder (alizarin) to experimental animals.

Hunter fed two pigs madder for two weeks, while a control pig was fed no madder. The first pig was killed at two weeks, and Hunter noted that the outer cortex of the long bones was stained red. The second pig was fed no madder for the next two weeks and was then killed. The outer cortex in that pig was of normal color, but the inner
cortex was stained pink. 

In a follow-up experiment, Hunter bored two holes exactly two inches apart in the tibial shaft of an immature pig and a fowl and embedded a bead of shot into each of the two holes. At maturity, the animals were examined and the measured difference between the two holes remained at two inches, but the length of the bone was much increased. Hunter concluded that bone grew in length at its ends, not interstitially as had been thought. Henri Louis Duhamel du Monceau also did a similar experiment in which he encircled the shaft of a long bone of a pigeon with a silver wire and, on reexamination at a later date, found the wire in the interior of the bone. He erroneously concluded that interstitial growth of bone had displaced the wire inward. Hunter viewed this phenomenon as the result of circumferential widening of the bone and the remodeling process.

From these experiments, Hunter showed that bone grew by two processes acting simultaneously. First, arteries brought nutrients that widened the exterior bone cortex, and absorbers (osteoclasts) at the same time narrowed the bone from the inner cortex, so that its shape remained unchanged, even after growth. Second, bone grew in length by the apposition of new bone at its ends.

Although surgeons for centuries had treated fractures, the healing of a fracture had never been carefully studied. A callus of tissue was thought to unite the bone ends. Hunter showed from his many experiments that the healing process began with a coagulum of extravasated blood between the fractured bone fragments, following which new blood vessels invaded the interval and a new tissue similar to the surrounding tissue united the bone ends. He further showed that this new tissue became cartilage and was then transformed into bone. In compound fractures, the blood between the fractured bones escaped to the exterior and was followed by suppuration and granulation tissue and slowed healing.

In other experiments, bone was necrosed by a cautery in several species and it was observed that the earthly (calcified) part of the living bone adjacent to the necrotic bone was absorbed, but the dead bone did not become decalcified. The intervening area between the living bone and the dead bone became mucilaginous and ultimately the dead part of the bone became detached and was extruded without having undergone any changes. "When a piece of bone becomes absolutely dead, it is then to the animal machine as any other extraneous body and adheres only by the attraction of cohesion to the machine. The first business of the machine, therefore, is to get rid of this cohesion and discharge it."

In Hunter’s first book, entitled *The Natural History of Human Teeth*, which was published in 1771, he described the composition of the jaw and teeth and reported that the tooth was divided into an organic vascular component and an enamel covering. Dye fed to young animals stained the teeth,
but this was not found to be true in mature animals; thus, he surmised that circulation to the enamel occurred only in growing animals.

In his chapter on gunshot wounds, Hunter commented, “It is curious to observe that firearms and spirits are the first of our refinements that are adopted in uncivilized countries.” He described four soldiers he had seen during his military service who had been wounded by musket balls and, although they had received no surgical treatment for several days, their wounds had begun to heal. On the basis of this and other similar experiences, he inveighed against the practice of enlarging wounds. The theory of wound enlargement, he believed, was the result of a surgical tradition based upon the efforts of surgeons to remove foreign bodies, which he believed was not always necessary. In this, he was in error. His contemporary, the surgeon Benjamin Gooch from Norwich, described the case of an eight-year-old boy who had been run over by a wagon and suffered a pin-hole wound in the skin at the fracture site, which was not enlarged. The condition of the child rapidly deteriorated, and the entire limb and abdomen were swollen. Gooch incised the swollen limb and described a hissing sound as the gas escaped. The boy died two days later, and Gooch inferred the swollen limb and described a hissing sound as the gas escaped. The boy died two days later, and Gooch described the use of the experimental approach to surgical questions. During his career, he trained 449 apprentices; some of his students crossed the Atlantic to establish the first medical schools in America. John Morgan was the founder of the first medical school in Philadelphia. William Shippen and Philip Syng Physick were professors of midwifery and of surgery, respectively, at this school, which later became the University of Pennsylvania. John Jones, another of Hunter’s students, was the first professor of surgery at the College of Physicians and Surgeons in New York. Hunter’s collection of preparations and experimental specimens, which numbered 13,682 and were kept in his home, can now be studied at the Hunterian Museum of the Royal College of Surgeons in London.

William Clift, his long-time laboratory assistant, said after his death, “From the very beginning I fancied without being able to account for it that nobody about Mr. Hunter seemed capable of appreciating him. He seemed to have lived before his time and to have died before he was sufficiently understood.”

John Hunter was buried in St. Martin-in-the-Fields. In 1859, his genius was accorded full recognition when his remains were interred in Westminster Abbey, where a plaque marks his grave and states, “The Royal College of Surgeons have placed this Tablet over the Grave of John Hunter to Record their Admiration of His Genius as a Gifted Interpreter of the Divine Power and Wisdom at Work in the Laws of Organic Life and their Grateful Veneration for his Services to mankind as the Founder of Scientific Surgery.” Sir James Mackenzie, the eminent cardiologist of the nineteenth century, said, “Hunter is the Shakespeare of medicine.”

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The author did not receive grants or outside funding in support of his research or preparation of this manuscript. He did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the author is affiliated or associated.

doi:10.2106/JBJS.E.00016

References
To The Editor: 
In the paper “Orientation of the Femoral Component in Surface Arthroplasty of the Hip. A Biomechanical and Clinical Analysis” (2004;86:2015-21), by Beaulé et al., information on the clinical outcome presented in the Results section had already been published in the Clinical Orthopaedics and Related Research article “Risk Factors Affecting Outcome of Metal-on-Metal Surface Arthroplasty of the Hip.”1 However, the CORR article was referenced only in the Materials and Methods section of the JBJS article. Our intent was to provide the reader with the clinical context and the relevant data that motivated us to create the biomechanical model for the analysis of the stresses within the femoral neck that was presented in the second manuscript. In retrospect, we realized that the appropriate way to accomplish this would have been to present a summary of the methods, results, and discussion sections of the CORR article in the introduction section of the JBJS paper rather than in the Materials and Methods and Results sections. Unfortunately, the way that we presented our information in the JBJS article gave the impression that this was the first time that the clinical study had been published. We offer our sincere apologies to the Editors of both journals for this oversight and would also like to extend our apologies to the readership of both journals. 

We would like to thank Dr. Heckman and Dr. Brand for bringing this to our attention, since maintaining the highest quality in peer-reviewed publications is something we all continue to strive for.

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This letter originally appeared on jbjs.org. It is still available on the web site in conjunction with the article to which it refers.

References

Below-the-Knee Compared with Above-the-Knee Amputation

To The Editor:
Recently my attention was directed to the article “Functional Outcomes Following Trauma-Related Lower-Extremity Amputation” (2004;86:1636-45, 2503), by MacKenzie et al. This multicenter study included a monumental mass of data and imparts valuable information about the psychological impact of traumatic amputations, but the authors also offered two major, unsupported conclusions.

First, the outcome of above-the-knee amputations was presented as superior to those of below-the-knee amputations, but this conclusion is contradicted by other data. The SIP (Sickness Impact Profile) scores showed that the outcomes of the above-the-knee amputations equaled or exceeded those of the below-the-knee amputations. This interpretation, however, is refuted by a statement in the text that “none of the differences . . . was significant at the p < 0.05 level.” Another contradiction is found in the statement: “the walking speed of the patients with a below-the-knee amputation was significantly faster than that of the patients with an above-the-knee amputation.” Sixty-two percent of the patients with a below-the-knee amputation had a walking speed equal to or faster than 4 ft/sec compared with 43.5% of those with an above-the-knee amputation, and 23.1% of those with an above-the-knee amputation were unable to walk independently over uneven ground compared with 11.3% of those with a below-the-knee amputation.

The statistical significance of the findings is challenged by the threefold difference between the number of subjects with an above-the-knee amputation (thirty-four) and the number with a below-the-knee amputation (109). Also, failure to identify the age distribution in each group introduces the high probability that nonmatched groups, particularly in reference to patients with an above-the-knee amputation, were being compared.

Another area of concern is the statement that “the technical sophistication of the prosthetic device did not appear to have an impact on outcome.” No data supporting this statement were presented in the body of the paper, although the readers who used The Journal’s web site found some data in the electronic appendix of the article. It is true that the assumption of no difference between prostheses is consistent with energy-cost studies of amputees walking performed at Rancho Los Amigos Medical Center and in other laboratories. Those studies also showed no significant differences among the SACH, Seattle Light, Flex-Foot, and other models. The Flex-Foot (high-tech), however, provides significantly greater dorsiflexion in terminal stance, which increases step length and gives a higher push-off power peak in pre-swing. I have been told that only amputees engaged in more vigorous activities (e.g., runners) can activate the flexible shafts of the high-tech prostheses. The difference in prosthetic mechanics between walking and running by amputees has not been reported.

LETTERS TO THE EDITOR MUST BE SUBMITTED ELECTRONICALLY; INSTRUCTIONS ARE AT WWW.JBJS.ORG/LETTERS
A final concern is the implications of relying on statistically non-significant data for much of the information discussed in the text. Among the thirty-nine data items listed in the three tables, only ten had significance at p < 0.05 and another fourteen reached significance at p < 0.2. Yet the thirty-nine data items were discussed with equal emphasis, even though the authors acknowledged p < 0.05 as the customary index of significance and used p < 0.2 for their modeling.

These inconsistencies are strong evidence that the overwhelming mass of data became “mind-boggling” and resulted in a product that was not adequately analyzed. The authors stated that a seven-year follow-up study was in progress. Hopefully, this will be used to correct or explain the inconsistencies.

I brought this to your attention because the prestige of JBJS imposes a status of validity that is not warranted by this paper.

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The author did not receive grants or outside funding in support of her research or preparation of this work. She did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the author is affiliated or associated.

E.J. MacKenzie, M.J. Bosse, and the LEAP Study Team reply:

Dr. Perry raises two concerns about the conclusions that we reached. The first focuses on our interpretation of the finding of no significant difference between the SIP outcomes of below-the-knee and above-the-knee amputations. As Dr. Perry correctly points out, the comparison of outcomes can be confounded by differences in patient populations. To adjust for these potential confounders (such as age), we performed multivariate regression analyses, and all of our conclusions are based on the results of those analyses. As we stated in the paper, the lack of a difference in SIP outcomes surprised us as well. The finding of no difference could be related to our choice of outcome. Although the SIP has been shown in previous studies to have good measurement properties, its responsiveness to small changes in daily function is less well documented.

It is important to emphasize that we did find significant differences in other outcomes; specifically, we observed that patients treated with a below-the-knee amputation had faster walking speeds and fewer problems with walking on uneven ground. These seemingly contradictory results suggest to us that, while a below-the-knee amputation may indeed be associated with better lower-limb function per se (as measured by walking speed), this difference may not always translate into improved function in daily activities (as perceived and reported by the patients on the SIP). This may be due to the fact that individuals experience similar frustrations and challenges following either below-the-knee or above-the-knee amputation and these difficulties can easily overwhelm the actual degree of lower-limb impairment. Indeed, some of the most powerful predictors of SIP outcome were education, race, and degree of self-efficacy. More research is needed to better understand how these patient characteristics influence the translation of impairment into disability so that appropriate post-acute-care interventions can be developed and targeted to those most in need. Our results suggest that if we can do a better job at addressing these needs, a below-the-knee amputation would indeed result in functional outcomes and a quality of life that are better than those following an above-the-knee amputation. We acknowledge, both here and in the paper, that our conclusions are based on a relatively small number of patients treated with above-the-knee amputation. We believe that our results, however, underscore the potential for poor outcomes, which is based less on the level of amputation than on the personal resources brought by the patients to the recovery process. We should believe that our study was limited in its ability to measure the quality of prosthetic fit and the extent to which the type of prosthesis actually matched the needs of the individual. However, we thought it important to make note of our results to underscore the urgent need for controlled trials to better delineate the relationship between device characteristics and outcomes. Dr. Perry raises some interesting hypotheses about the correlation of performance and the amputee’s baseline needs and expectations. We look forward to studies that can address these hypotheses.

We appreciate the opportunity to engage in further dialogue about the results of our paper. We hope the criticisms raised will serve to fuel further investigations in this important area of research.

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These letters originally appeared, in slightly different form, on jbjs.org. They are still available on the web site in conjunction with the article to which they refer.

References
Legg-Calvé-Perthes Disease: The Effect of Treatment on Outcome

To The Editor:
The paper “Legg-Calvé-Perthes Disease. Part II: Prospective Multicenter Study of the Effect of Treatment on Outcome” (2004;86:2121-34), by Herring et al., is a landmark in pediatric orthopaedics. Dr. Herring et al. and the Legg-Perthes Study Group are to be congratulated on accumulating so many data in a prospective long-term study.

The authors have performed an expansive analysis. Sample-size constraints led the authors to combine groups and to conclude that operative treatment was better than nonoperative treatment. However, if we compare bracing and surgical treatment (containment) with range-of-motion exercises and no treatment (noncontainment), the difference is highly significant in favor of containment (chi-square analysis; p < 0.01). When operative treatment is compared with bracing, no significant difference is observed, although the sample sizes are roughly equivalent (129 in the bracing group and 119 in the operative treatment group). The authors appear to have been selective in their comparisons. On the basis of logistic regression and Wald chi-square tests, the most important factors were classification and age, not treatment.

Another way to look at the effect of surgery is to examine the number needed to treat (NNT) in order to move a patient from one Stulberg class to another. If we compare bracing and surgery in percentage terms and accept the “best case” that surgery was superior, 7% of patients moved to class I or II results, two Stulberg class-I or II results, two Stulberg class-IV results whereas surgical treatment was associated with twenty-four Stulberg class-I or II results (73%), seven Stulberg class-III results (21%), and two Stulberg class-IV results (6%) (p = 0.079).

Third, among patients in the B/C border group who were over the age of eight years, bracing was associated with fifteen Stulberg class-I or II results (51%), fourteen Stulberg class-III results (42%), and four Stulberg class-IV results (12%) whereas surgical treatment was associated with twenty-four Stulberg class-I or II results (73%), seven Stulberg class-III results (21%), and two Stulberg class-IV results (6%) (p = 0.079).

Fourth, comparisons between the brace treatment group and the combined range-of-motion and no-treatment group among patients in lateral pillar groups B, B/C, and C who were over eight years old at the time of onset showed no notable differences (p = 0.84, 0.35, and 0.59, respectively). We conclude from this analysis that outcome in the brace-treatment group is not significantly different from that in the combined range-of-motion and no-treatment groups in older children.

Dr. Little’s “number needed to treat” analysis compared outcome between bracing and surgery for all hips and indicated that one of six patients would have an improved outcome in association with surgery. It is my hope that this study will begin to alter this sort of global thinking about treatment for patients with Legg-Calvé-Perthes disease. Our study clearly identifies groups of patients, based on the age at the time of onset and the severity classification, who are destined to have a good outcome without treatment. These patients should be analyzed separately from those who have a greater likelihood of a poor outcome. We noted significant advantages for the surgically treated hips of older patients with lateral pillar group-B and B/C border severity and no advantage for the hips with lateral pillar group-C border severity. The evidence that we have presented does not support universal bracing as being efficacious for Legg-Calvé-Perthes disease, nor does it support any specific treatment for 65% of the hips in this study. We present evidence that supports surgical treatment for a specific group of children.

Dr. Little’s final question regarding classification after treatment brings up a familiar dilemma. While the early surgical treatment was a planned part of the study, the finding of efficacy in specific groups was an outcome determined after completion of the study. Thus, we recommended a waiting period before advising surgery, which was not used in the study. This is fine, but what is the surgeon to do? Should one wait for classification or should the surgery be offered at the time of presentation to any child
who was more than eight years old at the time of onset? On the basis of the distribution of cases in this study, if the surgeon had operated on all children over the age of eight years, 84% would have benefitted and 16% would not have benefitted. While it is possible that some of the efficacy of surgery may be lost by waiting six or more months to determine the classification, we have no specific evidence to that effect. With our current state of knowledge, this issue becomes the surgeon’s and patient’s choice.

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These letters originally appeared, in slightly different form, on jbjs.org. They are still available on the web site in conjunction with the article to which they refer.

Stress Test for Predicting the Need for Surgical Fixation of Fibular Fractures

To The Editor:

We reviewed the article “Ankle Stress Test for Predicting the Need for Surgical Fixation of Isolated Fibular Fractures” (2004;86:2393-8), by E gol et al.

A number of conclusions made by the authors were not supported by the data presented in the paper. The authors stated that the study supported an algorithm that directs patients with a negative stress radiograph and no medial symptoms to be treated nonoperatively. However, the only data supporting this conclusion was that “all of the thirty-five patients... had clinical and radiographic evidence of healing.” No functional or follow-up radiographic data were provided. This group had a supination-external rotation stage-II pattern of injury, and nonoperative management is accepted as the standard of care. However, a more detailed analysis of this group to support the authors’ impression would be helpful.

The superficial summary of nonoperative treatment in older patients should at least have available to them current information presented by experts. This is especially sad because low back pain is the most common musculoskeletal disease and, if orthopaedists are expected to be the specialists who are knowledgeable in this area, they should at least have available to them current evidence-based treatment programs.

The authors did not receive grants or outside funding in support of their research or preparation of this work. They did not receive payments or other benefits or a commitment or agreement to provide such benefits from a commercial entity. No commercial entity paid or directed, or agreed to pay or direct, any benefits to any research fund, foundation, educational institution, or other charitable or nonprofit organization with which the authors are affiliated or associated.

N.C. Tejwani and K.A. Egol reply:

In our paper, we attempted to assess the outcomes of nonoperative treatment of fibular fractures despite a diagnosis of supination-external rotation stage-IV injury based on stress radiography. Like most surgeons, we do not routinely fix supination-external rotation stage-II fractures as we believe that these fractures will heal uneventfully. We did not evaluate the functional outcomes in this group as this was not the purpose or focus of our study. The patients who had a positive stress radiograph and clinical signs of medial injury were considered to have a supination-external rotation stage-IV injury, and they were treated surgically. It was the group that had a positive stress radiograph and no medial clinical signs that was of interest to us and that was followed both clinically and radiographically. As stated in the article, the functional outcomes of surgical and nonsurgical treatment were similar in this group of patients (AOFAS scores of 93 and 94 points). We stated that one of the limitations of our study was the small number of patients with positive stress radiographs and negative clinical findings on the medial side. The lack of randomization may have introduced a selection bias toward nonoperative treatment in older patients.

The use of magnetic resonance imaging may be beneficial for identifying medial ligamentous injury, as it has recently been found to be valuable for identifying interosseous membrane injury.

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These letters originally appeared, in slightly different form, on jbjs.org. They are still available on the web site in conjunction with the article to which they refer.

Reference


Nonoperative Management of Low Back Pain and Lumbar Disc Degeneration

To The Editor:

I am writing to express my disappointment in the recent Instructional Course Lecture, “Nonoperative Management of Low Back Pain and Lumbar Disc Degeneration” (2004;86:1810-8), by Brodkin and Ritter. It describes the issue of nonoperative back care at a medical student level, which is not at all appropriate for what an instructional course should provide—the most up-to-date information presented by experts. This is especially sad because low back pain is the most common musculoskeletal disease and, if orthopaedists are expected to be the specialists who are knowledgeable in this area, they should at least have available to them current evidence-based treatment programs.

The superficial summary of nonoperative care presented in this article further guarantees that the orthopaedist will continue his or her drift into the role of pure surgical technician, functioning at the behest of cli-
nicians more expert than they.

My specific problem is in the discussion of physical therapy. In this seven and one-half-page article, physical therapy merits half a page. Of all the areas of nonoperative care in which orthopaedic surgeons can have an opportunity for effective quality control, physical therapy is it. We are not expert in medications, injections, manipulation, or braces.

What is particularly disturbing is the authors’ apparent attitude that there is no rationale for physical therapy. The authors imply, in the half page on physical therapy, that one can do this or that and it doesn’t make any difference. Their references supporting specific exercises are very outdated. For instance, the two references discussing specifics are from 1983 and 1968. The latter, a study by Kendall and Jenkins, has long been discredited, and I doubt the authors ever read it—if they could even find it.

The authors disregard a substantial number of reports in the literature that identify myoelectric inhibition and atrophy of the lumbar extensors as corollaries to low back pain. This observation leads to a rationale for care quite parallel to the rationale for care of an injured knee—that is, progressive resistance exercises. A considerable number of recent reports in the literature have supported the efficacy of this approach, which was totally ignored by the authors.

The authors also ignored the literature supporting the efficacy of exercises based on the centralization of pain. Only one reference was made to McKenzie exercises, and that was to indicate that they had not been found to be different from resistive exercises with respect to the reduction of disability or pain in follow-up examinations; however, the authors failed to point out that both types of exercises provided considerable improvement in pain relief and disability when they were used to manage the patients in the referenced group. Furthermore, they included no recent references regarding injections, intradiscal electrothermal therapy, and chiropractic care.

My point is that, when such a superficial, nonexpert instructional course is presented, it gives the impression that orthopaedic surgeons do not have the capacity to mount a rational program in nonoperative care. Once we accept our lack of expertise as reflected by this instructional course, we will drift further into our emerging role as surgical technicians dependent upon the referrals of more expert clinicians. How sad!

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D.S. Brodke and S.M. Ritter reply:
We appreciate Dr. Mooney’s comments and agree with him that the depth of the coverage of nonoperative treatment of low back pain was superficial, but our goal was to introduce as broad coverage as possible to the practicing orthopaedic surgeon within the constraints of an Instructional Course Lecture. Those who are interested in more depth are referred to the bibliography and to the volumes of printed material available.

We agree with Dr. Mooney that physical therapy is of value in the management of low back pain. We did attempt to indicate this in the article. We also believed it was important to discuss other commonly used, though less well supported, treatment options. It is important for the readership to know that many of these commonly used treatments have little support. To leave them out of the discussion would be a disservice and, in our opinion, less complete.

While physical therapy is well supported in the article, there is not universal agreement that it is as valuable as Dr. Mooney asserts. As an example, Cherkin et al., in a prospective, randomized, controlled study, found physical therapy similar to chiropractic management and only mildly better than giving a booklet to the patient regarding the outcomes for patients with low back pain. In light of this, we find the treatment of low back pain to be an art as much as a science. The most successful practitioners use a combination of therapies tailored to the individual patient and do not stick to any single treatment option for all.

We would like to acknowledge the experience and expertise of Dr. Mooney, who has made a career in the study and understanding of nonoperative treatments of low back pain. The authors are pleased that Dr. Mooney took the time to write a letter regarding this important topic, and we hope this will stimulate others to learn more.

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These letters originally appeared, in slightly different form, on jbjs.org. They are still available on the website in conjunction with the article to which they refer.

Reference
Injured Limbs Recover Better with Early Mobilization and Functional Bracing Than with Cast Immobilization


Question: In patients with acute limb injuries, how does cast immobilization compare with early mobilization?

Data sources: Studies were identified by searching the Cochrane Central Register of Controlled Trials and Cochrane Database of Systematic Reviews, MEDLINE (1966 to 2002), EMBASE Excerpta Medica, and Web of Science, and the references of retrieved studies.

Study selection and assessment: Studies in any language were selected if they were randomized controlled trials comparing cast immobilization with early mobilization in patients with acute limb injuries, if the follow-up was ≥80%, and if the patient population was not predominantly young children. Study quality was assessed according to the criteria of the Cochrane Musculoskeletal Injuries Group (maximum score, 18).

Main outcome measures: Patient-centered outcomes (pain, swelling, and satisfaction), functional outcomes (range of motion and days lost from work), and complications.

Main results: 49 trials were included. Follow-up ranged from 1 to 60 months. 16 trials were considered high quality (score ≥11). Mobilization strategies included active exercise, orthoses, crutches, bandages, and minimal or no support (e.g., bandages, crutches, or tape). 10 trials were of lower-limb fractures; 21, of lower-limb injuries without fracture; 16, of upper-limb fractures; and 2, of upper-limb injuries without fracture. Early mobilization was associated with a reduction in pain and swelling in 14 trials. No study favored cast immobilization for this outcome. In 9 trials, patients were more satisfied with early mobilization than with cast immobilization. Among trials measuring global function with use of composite scores, early mobilization resulted in better scores after 6 months (6 trials) and 12 months (1 trial). Early mobilization prompted an earlier return to work (13 trials), particularly in patients with lower-limb nonfracture injuries (8 trials). 5 trials showed an earlier return to sport with early mobilization. Early mobilization was associated with improved range of movement in patients with upper and lower-limb fracture (14 trials). Early mobilization was associated with reduced deformity in Colles’ fractures (2 trials), metacarpal fractures (1 trial), and radial fractures (1 trial). 10 trials reported no change in deformity, no loss of fracture reduction, or any other complications with early mobilization.

Conclusion: In patients with acute limb injuries, early mobilization decreases pain and swelling and improves functional outcomes compared with cast immobilization.

Sources of funding: Centre for General Practice, University of Queensland and Primary Health Care Research, Evaluation and Development Strategy.

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doi:10.2106/JBJS.8705.ebo3

Commentary

This study represents a valid systematic review of the literature relating to the issue of immobilization compared with early mobilization following upper and lower-limb injuries. As is the case with most systematic reviews and meta-analyses in orthopaedic surgery, the study quality “was poor in most cases.”

The identified studies addressed ankle sprains and fractures, surgical treatment of Achilles tendon ruptures, and metacarpal and distal radial fractures, with only a few articles related to the elbow, knee, or flexor tendon injuries and one on gunshot wounds of joints. The generalizability of this information to other injuries is not known, and the authors did not specifically address weight-bearing in lower-extremity injuries. The application of early motion is consistently beneficial for all outcomes, including pain relief, range of motion, swelling, and earlier return to work. The only exception was in the management of Colles’ fractures, for which two studies reported greater dorsal angulation, increased radial tilt, and loss of radioulnar joint space.

There appears to be no downside to early mobilization and only deleterious effects with regard to casting. Whereas the application of mobilization has been widely applied in operative fracture management, it is not universally accepted for other injuries. Protection from re-injury may require bracing or even casting in certain unpredictable circumstances or in unreliable patients. For most patients, this is not necessary.

For practicing surgeons and other clinicians, the application of early mobilization in the treatment of stable fractures, ankle sprains, and surgically repaired tendons can be recommended without concern for any deleterious effects.

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**Review: Relocation and Anterior Release Tests Diagnose Shoulder Instability in Selected Patients**


**Question:** In patients presenting with shoulder pain, how accurate are history-taking and the use of clinical physical-examination tests in diagnosing shoulder instability and labral tears?

**Data sources:** Studies were identified through a search on MEDLINE (1966 to 2003), EMBASE Excerpta Medica (1980 to 2001), and CINAHL (1982 to 2001), using the terms “shoulder,” “glenohumeral,” “scapula,” “clavicula,” “acromion,” “rotator cuff,” “supraspinatus,” “infraspinatus,” “serratus anterior,” and “subscapularis” combined with diagnostic terms. The references of retrieved studies were also reviewed.

**Study selection and assessment:** Studies in English, Dutch, or German were selected if they compared clinical tests for instability or intra-articular pathology of the shoulder with surgical or arthroscopic findings. Studies of fibromyalgia or systemic disorders such as rheumatoid arthritis were excluded. The methodological quality of individual studies was assessed with use of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) checklist (14 items).

**Main outcome measures:** Sensitivity, specificity, and likelihood ratios of clinical tests for diagnosing shoulder instability and labral tears.

**Main results:** 17 studies were included, 5 of which enrolled patients when the clinician suspected shoulder instability and 12 of which enrolled patients when the clinician suspected labral tears or other intra-articular pathology. Surgery was used as the reference standard in 6 studies and arthroscopy in 11 studies. Shoulder instability was evaluated with provocation tests in 3 studies (including apprehension, relocation, clunk, and anterior release tests), and with laxity tests in 3 studies (including load and shift posterior, sulcus sign, and load and shift anterior tests, and examination under anesthesia). Labral tears were evaluated with anterior apprehension (1 study), active compression (4 studies), anterior slide (2 studies), biceps load I (1 study), biceps load II (1 study), compression rotation (1 study), cranck (3 studies), internal rotation resistance strength (1 study), the pain provocation test of Mimori (1 study), relocation (1 study), superior labrum anterior posterior (SLAP)-Prehension (1 study), tenderness of the bicipital groove (1 study), the Speed test (2 studies), and the Vergason test (1 study). No study evaluated the taking of patient history. The relocation test and anterior release test performed best for diagnosing shoulder instability (Table). The biceps load I and II tests, the pain provocation test of Mimori, and the internal rotation resistance strength test performed best for diagnosing labral tears (Table).

**Conclusions:** In patients who present with shoulder pain and who are on the waiting list for surgery or arthroscopy, physical examination with the relocation test and the anterior release test performs well for diagnosing shoulder instability, and the biceps load I and II tests, the pain provocation test of Mimori, and the internal rotation resistance strength test perform well for diagnosing labral tears. Evidence is lacking for the diagnostic performance of history-taking.

Source of funding: No external funding.

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doi:10.2106/JBJS.8705.ebo1

**Commentary**

This review adds value to our current clinical practice by demonstrating which findings on physical examination are useful in patients with instability or labral tears. The findings of the primary studies in this review have several limitations. First, it was not clear in the papers reviewed if the examiner was blinded to other clinical information. Second, because these tests were evaluated in selected patient populations by an orthopaedic surgeon-specialist, the accuracy of these tests may not be generalizable to a full spectrum of patients with shoulder pain evaluated by a less experienced physician. Third, in many patients with repetitive microtraumatic instability or single-event traumatic instability, there will be associated tears of the labrum (including superior labrum anterior posterior [SLAP] lesions). Thus, these two diagnostic categories often occur in the same patients, and the different physical-examination findings may be present in the same patient. Moreover, in the acutely painful or unstable shoulder, some of the tests for diagnosis of a labral tear cannot be performed due to patient guarding and apprehension, thereby decreasing the clinical applicability of those tests. In most circumstances, labral pathology or instability is a diagnosis that is made by a combination of a careful history-taking, the use of the clinical examination tests described in this review, and imaging studies. When surgical indications are present, the examination is performed with the patient under anesthesia, and arthroscopic findings are used to complete the diagnosis and create a definitive plan for surgical treatment that, in most cases, is performed at the time of that same surgical procedure.

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Evidence-Based Orthopaedics

An Internet-Delivered Cognitive-Behavioral Intervention with Telephone Support Improved Some Coping Skills in Patients with Chronic Low Back Pain


Question: In patients with chronic back pain, can an Internet-based cognitive-behavioral intervention with telephone support improve functioning?

Design: Randomized (allocation unconcealed), unblinded, controlled trial with 8-week follow-up.

Setting: Sweden.

Patients: 56 patients who were 18 to 65 years of age (mean age, 45 y; 63% women), had access to the Internet, were in contact with a physician, and had back pain (i.e., lumbar, thoracic, and/or cervical pain) of ≥3-month duration. Exclusion criteria were pain that resulted from activity, need for a wheelchair or assistive device, the presence of cancer, and heart or vascular disease. Duration of follow-up was 92%.

Intervention: Patients were allocated to treatment (n = 22) or a waiting list (n = 29) for 6 weeks. The treatment required that patients read material weekly and submit pain diaries by way of the Internet. The aim of the program was to teach patients to identify more active ways of coping with pain to improve functioning. The program included psychological (dealing with unhelpful thoughts and beliefs and changing focus) and physical (individualized, graded stretching and physical exercises) components. Patients could use a slideshow, audio files, or a compact disc to guide them through applied relaxation techniques. Weekly telephone conversations with a therapist allowed patients to review the previous week's homework, ask any questions, receive reminders, and maintain motivation.

Main outcome measures: The primary outcome measure was the Coping Strategies Questionnaire (CSQ). Secondary outcome measures were the Multidimensional Pain Inventory (MPI), the Pain Impairment Rating Scale (PAIRS), and the Hospital Anxiety and Depression Scale (HADS).

Main results: Greater improvement was seen in patients in the Internet group than in the control group with regard to the CSQ subscales of catastrophizing, control over pain, and ability to decrease pain (Table). Other outcomes did not differ significantly between groups.

Conclusions: In patients with chronic back pain, an Internet-based cognitive-behavioral intervention with telephone support improved the ability of patients to cope by reducing catastrophizing and increasing the feeling of control over pain and the ability to decrease pain.


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doi:10.2106/JBJS.8705.ebo2

Commentary

The authors of this study evaluated a new tool (the Internet) to deliver cognitive behavioral therapy with the intent of enhancing patient interaction and potentially lessening the burden on care providers. However, there was no control group of simple waiting and there was an appreciable amount of telephone contact with both groups, which in itself may help patients. Furthermore, because of the limited sample size, the study may not have detected differences in some of the outcomes. Finally, the authors did not include typical rating scales for back pain, such as the Short Form-36 (SF-36), the Roland-Morris Disability Questionnaire, or the Oswestry Disability Index.

Although the authors used a variety of chronic pain measures, the outcomes that achieved significance were decreased catastrophizing, control over pain, and ability to decrease pain. While the change was positive, before the alleviation of pain can be considered to be clinically significant, there needs to be an approximately a 30% reduction of the pain compared with the pre-intervention status. With use of visual analog pain-scale ratings, significant differences were not found between the groups with regard to the amount of change.

The take-home message is that while the patients who used the Internet did a better job of coping with pain (less catastrophizing), there was no substantial effect on the pain. The Internet appears to offer promise, but, given that there had to be frequent telephone contact as a part of this study, the value of a strictly Internet-based program was not conclusively proven. I see no harm in this undertaking; however, the hypothesis was not proven in such a way that I am prepared to alter my practice at the present time.

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The glossary below provides definitions for several terms found in the structured abstracts of the Evidence-Based Orthopaedics section, many of which may not be familiar to orthopaedic surgeons.

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td><strong>EER</strong></td>
<td>The experimental (new treatment) event rate.</td>
</tr>
<tr>
<td><strong>CER</strong></td>
<td>The control (old treatment or non-treatment) event rate.</td>
</tr>
<tr>
<td><strong>CI</strong></td>
<td>(Confidence interval) quantifies the uncertainty in measurement. CI is usually reported as a 95% CI, which is the range of values within which we can be 95% sure that the true value for the whole population lies.</td>
</tr>
<tr>
<td><strong>ARR</strong></td>
<td>(Absolute risk reduction) is the absolute arithmetic difference in bad event rates between the experimental and control groups, calculated as</td>
</tr>
<tr>
<td><strong>ABI</strong></td>
<td>(Absolute benefit increase) is the absolute arithmetic difference in good event rates between the experimental and control groups, calculated as</td>
</tr>
<tr>
<td><strong>RRI</strong></td>
<td>(Relative risk increase) is the proportional increase in bad event rates between the experimental and control groups, calculated as</td>
</tr>
<tr>
<td><strong>NNH</strong></td>
<td>(Number needed to harm) is the number of patients that, if they received the experimental treatment, would lead to 1 additional person being harmed compared with the number of patients who received the control treatment, calculated as 1/ARI, rounded up to the nearest whole number, and accompanied by a 95% CI.</td>
</tr>
<tr>
<td><strong>NNT</strong></td>
<td>(Number needed to treat) is the number of patients who need to be treated to achieve 1 additional favorable outcome, calculated as 1/ARR, rounded up to the nearest whole number, and accompanied by a 95% CI.</td>
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*Based on information from the American College of Physicians Journal Club.*
Specialty Update

What’s New in Pediatric Orthopaedics

BY MININDER S. KOCHER, MD, MPH, AND PETER O. NEWTON, MD

The purpose of this fifth Specialty Update is to serve as a primary source and review for the general orthopaedic surgeon who wishes to stay up-to-date in pediatric orthopaedics. The topics that have been selected have value for the practicing orthopaedist as well as for the pediatric orthopaedic specialist and are important in their own right for the advancement of knowledge and skills in the subspecialty. The material is not intended to represent the only, or necessarily best, method or procedure appropriate for the medical situations discussed.

Sources for this article were presentations at meetings of the Pediatric Orthopaedic Society of North America (POSNA) (St. Louis, Missouri, April 2004), the American Academy of Orthopaedic Surgeons (AAOS) (San Francisco, California, March 2004), the Scoliosis Research Society (SRS) (Buenos Aires, Argentina, September 2004), the American Academy of Pediatrics (AAP) (San Francisco, California, October 2004), and selected references. Orthopaedic surgeons, residents, and fellows are encouraged to attend educational programs on topics in pediatric orthopaedics presented at the AAOS conferences and courses, Specialty Day at the AAOS annual meeting, and the POSNA annual meeting. Upcoming educational events are listed at the end of this update.

Pediatric Orthopaedic Conditions and Management

Shoulder

Brachial Plexus Palsy

The management of children who have brachial plexus palsy continues to be an area of active research interest. The absence of biceps muscle function at the age of three months has been used as an indication for early brachial plexus microsurgery. Smith et al. evaluated the long-term outcome for twenty-eight patients who had absent biceps muscle function at the age of three months¹. The mean duration of follow-up was 11.1 years. Twenty-two patients did not have surgery on the brachial plexus, but nine of those patients had subsequent orthopaedic procedures. Patients who regained biceps muscle function between three and six months of age and patients with a C5-C6 lesion had better functional outcomes.

Moukoko et al. found that posterior shoulder dislocation can occur earlier and more rapidly in infants with neonatal brachial plexus palsy than has been appreciated previously². In that study, eleven (8%) of 134 consecutive infants had posterior shoulder dislocation. The mean age at the time of diagnosis was six months. There was no correlation between the occurrence of dislocation and the type of initial neurological deficit, and a rapid loss of passive external rotation between monthly examinations indicated dislocation.

Waters et al., in a study of twenty-five patients with a mean age of forty-two months who underwent latissimus dorsi and teres major transfers to the rotator cuff and extra-articular musculotendinous lengthening for the treatment of brachial plexus birth palsy, reported improved shoulder function but only modest changes in remodeling of glenoid retroversion.

Pearl et al. reported the minimum two-year results of twenty-six arthroscopic internal rotation contracture releases in children who were 0.8 to twelve years old. The mean increase in external rotation was 55° for younger children undergoing release alone and 86° for older children undergoing release with latissimus dorsi transfer. Improvements in elevation were only modest. James, in a study of the longer-term results of external rotation tendon transfer, found that longer-term improvement in external rotation may not be as good as the short-term results. At one year postoperatively, the average external rotation had improved from 19° to 61°. However, at the time of the latest follow-up, at a mean of 3.3 years postoperatively, the average external rotation had decreased to 48°.

Elbow

Wang et al. performed open radial head reduction, ulnar osteotomy, and annular ligament reconstruction in thirteen patients at an average of 5.9 months after radial head dislocation.
Most patients had excellent elbow and forearm motion, and there were no instances of redislocation.

**Forearm and Hand**
Many children with unilateral congenital below-elbow deficiency abandon the use of their prostheses. James et al., in a study of 152 such patients, evaluated the function associated with various prostheses with use of the Unilateral Below Elbow Test. Prosthetic wear did not improve function.

James et al. evaluated the relationship between congenital longitudinal deficiencies of the radius and thumb in a study of 227 affected upper extremities in 139 patients. They found that the severity of the thumb deficiency was directly proportional to the severity of the radial deficiency, supporting the concept that components of radial longitudinal deficiency represent a progressive spectrum of upper extremity abnormalities and a distal progression of severity, with distal structures likely to be more involved than proximal structures.

**Hip**

**Perthes Disease**
Both the etiology and the treatment of Perthes disease remain controversial. There is conflicting evidence regarding the relationship between Perthes disease and thrombophilia. Balasa et al., in a case-control study in which seventy-two patients with Perthes disease were compared with 197 healthy controls, found two thrombophilic risk factors: the factor-V Leiden mutation and anticardiolipin antibodies. Aksoy et al., in a case-control study involving twenty-six hips and reported six failures. Preexisting arthritis and evidence of arthritis on magnetic resonance imaging were associated with progression of arthritis after osteotomy.

Herring et al., in a large, multicenter, prospective study of 345 hips in patients with Perthes disease, more clearly defined the lateral pillar classification by adding a new intermediate group termed the B/C border group. The interobserver and intraobserver reliability of the lateral pillar classification were acceptable. Herring et al. then evaluated the effect of treatment and other risk factors on outcome in a study of 451 affected hips in 438 patients. They found that the lateral pillar classification and age at the time of onset of the disease were strongly correlated with outcome in patients with Perthes disease. Patients who were more than 8.0 years of age at the time of onset and who had a hip in the lateral pillar B or B/C border group at the time of treatment had a better outcome in association with surgical treatment than they did in association with nonoperative treatment. Children who were 8.0 years of age or less at the time of onset and who had group B hips at the time of treatment had very favorable outcomes regardless of the type of treatment, whereas children of all ages who had group C hips at the time of treatment frequently had poor outcomes regardless of the type of treatment.

**Developmental Dysplasia of the Hip**
Kim et al. utilized contrast-enhanced magnetic resonance imaging after closed reduction in infants with twenty-eight idiopathic hip dislocations. Decreased enhancement on magnetic resonance imaging was associated with the radiographic development of osteonecrosis, suggesting that magnetic resonance imaging may be useful for assessing both the adequacy of reduction and the risk of osteonecrosis after closed reduction of a dislocated hip in an infant.

Anderson et al. performed a limited open medial approach as an adjunct to closed reduction in a study of twenty-two children (average age, 15.6 months) with twenty-four reducible hips that remained relatively unstable, with a narrow safe zone. Patients who were less than twelve months old had stable hips with remodeling and a normal radiographic appearance. Patients who were more than twelve months of age had a predictable lack of remodeling, necessitating secondary procedures. Mosely et al. evaluated the value of the Salter pelvic osteotomy as an adjunct to open reduction in a study of sixty-two dislocated hips in patients who were more than 1.5 years old. Patients who had an adjunctive Salter osteotomy had improved femoral head roundness, improved acetabular coverage, and fewer subsequent procedures compared with patients who had open reduction alone, suggesting the value of a concurrent pelvic osteotomy at the time of open reduction.

The Bernese periacetabular osteotomy is being used increasingly for older adolescents and adults with acetabular dysplasia. Kim et al. prospectively studied a cohort of twenty-six hips and reported six failures. Preexisting arthritis and evidence of arthritis on magnetic resonance imaging were associated with progression of arthritis after osteotomy.

**Slipped Capital Femoral Epiphysis**
The treatment of the contralateral hip in patients with slipped capital femoral epiphysis is controversial, with some investigators advocating prophylactic pinning and others advocating watchful waiting. Kocher et al., in a study involving expected-value decision analysis in which the probabilities of a contralateral slip were determined from the literature and utility values were obtained from a questionnaire on patient preferences, concluded that watchful waiting was the preferred strategy if the risk of a contralateral slip was <27%.

Bhatia et al., in a study that was performed to identify patients with slipped capital femoral epiphysis who are at risk for contralateral involvement, found that a high body mass index (>35) was associated with an increased risk of a contralateral slip.

Armstrong et al. used finite-element analysis to study potential etiologic forces associated with slipped capital femoral epiphysis. The authors found increased femoral head coverage in patients with slipped capital femoral epiphysis, which increased forces on the proximal femoral physis.
What’s New in Pediatric Orthopaedics

Knee

Anterior Cruciate Ligament Injury
The treatment of anterior cruciate ligament injuries in skeletally immature patients is an area of much interest in the pediatric orthopaedic and sports-medicine communities. Ganley et al. performed survivorship analysis on 247 patients who were thirteen to eighteen years old and had undergone anterior cruciate ligament reconstruction with an Achilles tendon allograft. There was a 7.8% failure rate, with most failures occurring within three years after surgery. Kocher et al. reported on the prevalence of meniscal and chondral injuries associated with anterior cruciate ligament tears in a study of 102 skeletally immature patients. Meniscal tears were common (prevalence, 45%) and occurred more frequently in patients with chronic anterior cruciate ligament insufficiency.

Blount Disease
Abraham et al. found that the Taylor spatial frame was an effective and reliable fixator for the correction of adolescent tibia vara. In their study of twenty-seven limbs in twenty-five patients, the average measurements after correction were 7° valgus, 12° procurvatum, and 15° external rotation foot progression angle. Complications included delayed union (three limbs), overcorrection (two), undercorrection (two), transient peroneal nerve palsy (two), and pin-track infection (one).

Epiphyseodesis
Sanders et al., in a study of forty-four patients with limb-length discrepancy and/or angular deformity, investigated the efficacy of a technique for epiphyseodesis about the knee with use of cannulated 7.3-mm screws in lieu of physeal staples. There were two complications associated with screw malposition, and, in all three patients with desired temporary epiphyseodesis, growth resumed after screw removal.

Ehrlich et al. evaluated the efficacy of percutaneous radiofrequency epiphyseodesis in a rabbit model. Radiofrequency ablation was found to be effective for the reduction of growth in this experimental model.

Leg

Tibial Pseudarthrosis
The treatment of congenital pseudarthrosis of the tibia remains difficult and controversial. Dobbs et al., in a study of twenty-one consecutive patients, evaluated the long-term results of a technique consisting of excision of the pseudarthrosis, autologous bone-grafting, and insertion of a Williams intramedullary rod into the tibia. The mean duration of follow-up was 14.2 years. Initial consolidation occurred in eighteen of the twenty-one patients, refracture occurred in twelve, and amputation was eventually required in five. Overall, the authors concluded that this technique should be considered for the treatment of congenital pseudarthrosis of the tibia.

Fibular Hemimelia
Paley et al. reported their experience with seventy-eight patients (ninety-four limbs) who were managed with lengthening. Overall, there were forty-six excellent results, twenty-eight good results, and eighteen fair results; the remaining two limbs were lost to follow-up. There were twenty recurrent foot deformities. Functional results were not correlated with the number of rays in the foot. However, excellent long-term functional results have been reported following conventional treatment with amputation for more severe forms of fibular hemimelia.

Foot and Ankle

Clubfoot
Ponseti’s technique of manipulation and casting continues to be an area of great interest and inquiry. In a review of 374 idiopathic clubfeet that were treated with the Ponseti method, Morcuende reported successful correction in all but four feet. Percutaneous heel-cord tenotomy was performed in 81% of these clubfeet. There was a 10% rate of deformity relapse. However, only thirteen patients (5%) required surgery. Morcuende et al. also reported on the effective use of the Ponseti method for the treatment of thirty-two arthrogrypic clubfeet.

Dobbs et al., Scher et al., and Morcuende et al. all emphasized the importance of compliance with the prolonged use of the foot abduction orthosis after casting with use of the Ponseti method, with higher deformity recurrence rates being noted among noncompliant patients. Herzenberg described performing the percutaneous heel-cord tenotomy with the patient under general anesthesia instead of local anesthesia and reported no anesthetic complications and less stress for the family and surgeon.

Richards et al., in a nonrandomized trial of sixty-one feet, reported similar early results in association with the Ponseti method and the French physical therapy and taping method.

It is apparent that current trends in the treatment of clubfoot support nonoperative care with casting or manipulation. The results of the Ponseti and French methods are improved compared with those of older methods of nonoperative treatment.

In contrast, Dobbs et al. reported sobering long-term results following the use of extensive surgical release for the treatment of thirty-four idiopathic clubfeet. After a minimum of twenty-five years of follow-up, there were no excellent results and only one good result according to the Laaveg and Ponseti functional scale. In general, the patients had poor functional results as adults despite the fact that many of them had functioned well throughout childhood and adolescence.

The utility of radiographs for the evaluation and outcomes assessment of patients with clubfoot has been questioned. However, in a study of forty-five clubfeet in twenty-nine patients who were evaluated with radiographs, the Child Health Questionnaire, and a condition-specific outcome in-
What’s New in Pediatric Orthopaedics

Flatfoot
Calcaneal lengthening osteotomy has gained popularity for the treatment of painful idiopathic pes planovalgus in patients with tight heel cords. Puigdevall et al. reported the results of calcaneal lengthening osteotomy for the treatment of twenty-six feet in patients with planovalgus associated with cerebral palsy or myelomeningocele. A satisfactory clinical result was obtained in 83% of the feet.

Spine
Etiology of Adolescent Idiopathic Scoliosis
The etiology of adolescent idiopathic scoliosis remains a mystery, although several presentations this year continued to suggest a genetic link. Conflicting results regarding the role of melatonin in adolescent idiopathic scoliosis continue to be reported. Cheung et al. reported a lack of development of scoliosis in pinealectomized monkeys (as compared with previous reports describing the development of scoliosis in chickens), whereas Moreau et al. presented data suggesting a melatonin signaling dysfunction in osteoblasts of patients with adolescent idiopathic scoliosis. A study by Ogilvie et al. involving 100 families in Utah suggested that at least one gene is involved in the development of adolescent idiopathic scoliosis. Interestingly, two candidate genes, aggregan and type-I collagen alpha 2, were reported this year by Merola et al. and Cheng et al., respectively. Lowe et al. noted that patients with sustained high levels of serum platelet calmodulin are more likely to have progressive scoliosis.

Surgical Outcomes
Third-generation segmental posterior spinal instrumentation systems have led to increasing correction of scoliosis. Asher et al., in a study of 179 patients managed with Isola instrumentation, reported an average 63% correction in the thoracic Cobb angle two to twelve years after surgery. There were no instances of spinal cord injury or acute infection, and the prevalence of confirmed pseudarthrosis was low (2%). In a second study, the authors presented data supporting lasting transverse plane correction as well (average, 40%)..

Pulmonary Function
The effect of scoliosis on pulmonary function was clarified by Faro et al. in a presentation on 515 patients with adolescent idiopathic scoliosis. Thoracic scoliosis of >60° was associated with an increasing frequency of pulmonary dysfunction, as was thoracic hypokyphosis of <10° and thoracic hyperkyphosis of >60°. Gollogly et al. reported that three-dimensional chest-wall distortion as measured with computed tomographic scanning was a better predictor of diminished pulmonary function than Cobb angle measurements were.

Nonfusion Instrumentation Systems
The treatment of severe scoliosis in the young child who is less than eight years of age remains a substantial challenge. Several methods for addressing the spinal and chest deformities associated with severe scoliosis are under intense investigation. The vertical expandable prosthetic titanium rib received Food and Drug Administration approval with a humanitarian device exemption in 2004. The device was approved for use in the treatment of thoracic insufficiency syndrome, and Campbell et al. reported on the early outcomes associated with the use of this device for the treatment of severe conditions, including congenital scoliosis. In another study, Campbell et al. reported that application of the vertical expandable prosthetic titanium rib in combination with the performance of an opening-wedge thoracotomy at an early age (less than five years) may improve ultimate lung growth and aid in limiting the progression of scoliosis. Smith et al. confirmed an increase in lung volume as measured with computed tomography, but data regarding actual pulmonary function are as yet lacking.

Posterior spinal “growing rod” constructs were evaluated by Akbarnia and Thompson. Patients who were managed with a dual-rod system in whom lengthening was routinely performed every six months were compared with patients who were managed with a single-rod construct in whom lengthening of the rods was done only when curve progression was noted. In this relatively limited analysis of twenty-eight patients, the patients in the dual-rod group fared better, with greater overall gain in length (mean, 1.5 cm/yr) and fewer complications.

Experimental anterior solutions also are being investigated. Braun reported the ability to modify spinal growth with use of various anterior vertebral tethering methods in an experimental scoliosis model, as did Newton et al. in a non-scoliosis model. Mechanically limiting vertebral growth asymmetrically in patients with progressive scoliosis in order to effect a reduction in spinal curvature was the ultimate goal of these studies. Betz et al. presented limited clinical results following vertebral body stapling across disc spaces, suggesting a potential benefit, although a comparison with observation alone and bracing has not been completed.

Innovative Surgical Methods
Two relatively new methods for surgical correction of scoliosis, the use of thoracic pedicle screws and minimally invasive approaches, remain controversial, with studies supporting and criticizing both techniques. Parent et al. clarified the regional variation in the anatomic dimensions of thoracic pedicles, a necessity for safe screw insertion. Arlet et al. reported that the use of thoracic pedicle screws reduced the need for anterior release in patients with curves of between 70° and 90°, and Lenke et al. reported that the use of thoracic pedicle screws increased the percentage of thoracic curve correction (74% for screws compared with 52% for hooks). However,
Fractures in Children

**General**

Vitale et al. categorized pediatric orthopaedic injuries with use of the Healthcare Cost and Utilization Project Kids’ Inpatient Database. In 1997, more than 84,000 children were admitted for the treatment of orthopaedic trauma in the United States, accruing an estimated $932.8 million dollars in hospital charges. Femoral fracture was the most common injury in this inpatient population.

Loder reviewed 256 traumatic amputations in 235 children who had been managed at one center from 1980 to 2000\(^2\). Amputations were caused most frequently by lawn-mower injuries, farm machinery, and motor-vehicle accidents. Common patterns of traumatic amputations in children were elucidated on the basis of the mechanism of injury, the season, and the age of the child.

Flynn et al. emphasized the importance of early recognition and treatment of acute traumatic compartment syndrome of the leg in a series of twenty-nine children. Good end results without sequelae were observed in 93% of the patients. The two patients with sequelae both had had a late fasciotomy (more than eighty hours) after presentation.

Smith et al. advocated using mini C-arm fluoroscopy in the emergency room rather than radiographs for pediatric fracture reduction. In their study of 296 fracture reductions, use of the mini C-arm resulted in more efficient patient encounters, less radiation exposure, and fewer re-reductions.

**Supracondylar Humeral Fractures**

Skaggs et al. promoted the use of lateral entry pinning for the treatment of displaced supracondylar humeral fractures\(^3\). In their series of 124 consecutively treated type-2 and 3 supracondylar fractures, there were no instances of loss of reduction, malalignment, or loss of motion. The authors emphasized the technical aspects of lateral-entry pinning, including maximizing separation of the pins at the fracture site, engaging the medial and lateral columns proximal to the fracture, engaging sufficient bone in both the proximal segment and the distal fragment, and maintaining a low threshold for use of a third lateral-entry pin if there is concern about fracture stability or the location of the first two pins.

**Forearm Fractures**

Galpin et al. compared short-arm cast immobilization with long-arm cast immobilization in a randomized clinical trial of seventy-eight patients with displaced distal-third pediatric forearm fractures. There was no difference between the groups in terms of loss of fracture reductions; however, short-arm casts caused less interference with daily activities.

**Femoral Fractures**

Vitale et al. reviewed the treatment of pediatric femoral fractures in children six to ten years of age with use of the Kid’s Inpatient Database in 1997 and again in 2000. They found that children in this age-group were increasingly managed with internal fixation. In addition, care at a non-children’s hospital was associated with a higher rate of spica casting, higher charges, and longer length of stay.

Elastic nailing has become a widespread technique for the treatment of pediatric femoral fractures. In the study by Flynn et al., thirty-five children who were managed with traction and spica casting were compared with forty-eight children who were managed with titanium elastic nails\(^4\). Unsatisfactory results and complications were more common in...
association with traction and casting. Compared with the children who were managed with traction and casting, those who were managed with titanium elastic nails had a shorter period of hospitalization, walked with support sooner, walked independently sooner, and returned to school earlier. Frick et al. and Mehlman et al. evaluated complications associated with the use of elastic nailing for the treatment of pediatric femoral fractures, finding an increased risk of malunion in older children (more than eleven or twelve years old) and heavier children (>45 kg). Finally, submuscular plating has been advocated for the treatment of some pediatric femoral fractures. Sink et al. reported good results in a series of ten patients.

**Tibial Fractures**

Scher et al. compared the results of elastic nailing with those of external fixation in a study of thirty-one patients with high-energy tibial fractures who had a mean age of eleven years. Patients managed with elastic intramedullary nailing had a decreased time to union, reduced fracture complications, and improved outcome.

Mubarak et al. compared the results of operative and nonoperative treatment in a study of 147 Salter-Harris type-I and II distal tibial fractures. Premature physeal closure was noted in association with 32% of the fractures that were treated nonoperatively and 23.5% of those that were treated operatively. Older patients were more likely to have premature physeal closure.

**Other Musculoskeletal Conditions**

**Tumors**

Dormans et al. described a percutaneous technique for the treatment of nonossifying fibromas with use of percutaneous curettage, intramedullary decompression, and grafting with calcium sulfate pellets. Compared with traditional open treatment, the percutaneous technique was associated with faster resolution of pain, return to activities, and signs of healing.

Alman et al. found RNA markers of vascular progenitors in cyst-lining cells from six patients with simple bone cysts, suggesting a vascular etiology, and cited the potential for antiangiogenic treatment.

**Cerebral Palsy**

Botulinum toxin has become a common treatment for contractures in patients with cerebral palsy. Kay et al. performed a randomized trial in which serial casting only was compared with serial casting combined with botulinum toxin-A injection for the treatment of ankle equinus contractures in twenty-three children with cerebral palsy. Unexpectedly, the investigators found that the addition of botulinum toxin A to a serial casting regimen led to earlier recurrence of spasticity, contracture, and equinus during gait. Koman et al. performed a randomized clinical trial in which botulinum toxin-A injections were compared with placebo injections for the treatment of upper extremity spasticity in pediatric patients with cerebral palsy. The investigators found improved function in patients who received botulinum toxin.

Dietz et al. reported discouraging results in association with Achilles tendon lengthening for the treatment of spastic equinus of the ankle. In a series of seventy-nine patients with diplegia and quadriplegia, the authors found an unacceptably high prevalence of overweakening, with a crouched gait and the need for anterior floor-reaction braces.

Treatment of the dislocated hip in patients with cerebral palsy remains controversial. Noonan et al. studied seventy-seven adults with severe cerebral palsy who had hip subluxation or dislocation. Neither hip displacement nor osteoarthritis was found to be associated with hip pain or diminished function. Because the prevalence of hip pain was low and was not associated with hip displacement or osteoarthritis, they suggested that surgical treatment of the hip in severely affected patients should be based on the presence of pain or contractures and not on radiographic signs of hip displacement or osteoarthritis.

Johnson et al. evaluated the relationship between Pediatric Outcomes Data Collection Instrument scores and technical measures of gait in a study of fifty-three children with cerebral palsy who had bilateral lower extremity involvement and were able to walk. Technical measures of gait were found to correlate in expected directions with the Pediatric Outcomes Data Collection Instrument scores related to lower extremity function. Oxygen cost was most strongly correlated with Pediatric Outcomes Data Collection Instrument scores.

**Myelodysplasia**

Patients with myelodysplasia often experience wound dehiscence and ulcer formation. Yen et al. evaluated peripheral circulation with use of ankle brachial index and transcutaneous pO2 (TcO2) measurements in a study of forty-one patients with myelodysplasia and forty-one age-matched controls. Patients with myelodysplasia had lower ankle brachial indices but similar TcO2 values.

**Muscular Dystrophy**

Previous studies have shown that corticosteroid treatment slows the decline in muscle strength and stabilizes muscle strength in patients with Duchenne muscular dystrophy. Alman et al. studied fifty-four patients with Duchenne muscular dystrophy and found that steroid treatment appeared to slow the progression of scoliosis as well.

**Osteogenesis Imperfecta**

Treatment of osteogenesis imperfecta has been directed toward increasing bone density; however, the effect of bone density on function in these patients has not been established. Huang et al. evaluated the correlation between dual energy x-ray absorptiometry findings and Pediatric Outcomes Data Collection Instrument functional scores in a study of twenty-
four patients with osteogenesis imperfecta. Significant correlations between bone density and function were found.

**Fibrous Dysplasia**
Lesions of fibrous dysplasia involving the spine and causing scoliosis are thought to be uncommon entities in patients with polyostotic fibrous dysplasia and McCune-Albright syndrome. Leet et al. evaluated sixty-two patients who had polyostotic fibrous dysplasia with regard to the prevalence of lesions of the spine and scoliosis. Spinal lesions were observed in 63% of the patients and scoliosis was observed in 40%, indicating that both findings may be more common than previously thought in patients with polyostotic fibrous dysplasia.

**Limb-Length Discrepancy**
Muscle stiffness frequently occurs during limb-lengthening. Birch et al. evaluated muscle fiber and sarcomere length changes during tibial lengthening in a goat model and found insufficient sarcomere production in the posterior muscles, which may contribute to equinus deformity. Shilt et al. found that muscle function was diminished and normal neuromuscular junction morphology was lost following 30% diaphyseal lengthening in a rabbit model.

Hamdy et al., in a rabbit tibial lengthening model, found accelerated bone formation during distraction osteogenesis with use of bone morphogenetic protein. Kocaoglu et al. reported on complications encountered during lengthening over an intramedullary rod in a study of forty-two segments in thirty-five patients. The mean amount of lengthening was 6.3 cm. The complication rate was 38%. Complications were more likely to occur in association with lengthenings of >6 cm or 21.5% of the original bone length.

**Infection**
The timely and accurate diagnosis of septic arthritis of the hip is essential. Luhmann et al. tested Kocher’s clinical prediction rule for differentiating septic arthritis from transient synovitis of the hip in children and found decreased diagnostic performance. In their population, the best predictive model was based on a history of fever, a serum total white blood-cell count of >12,000/mm³, and a previous health-care visit. Kocher et al., however, found diminished, but still very good, performance of the prediction rule in a new patient population at the original institution.

**Health Policy**

**Surgical Referral Guidelines**
Guidelines for referral to pediatric surgical specialists were published in the journal *Pediatrics* in July 2002. The Surgical Advisory Panel of the American Academy of Pediatrics (AAP), in response to a recommendation from the AAP Subspecialty Work Group, created these referral guidelines intended to serve as “voluntary practice parameters to assist general pediatricians in determining when and where to refer their patients to pediatric surgical specialists,” including orthopaedic surgeons. The conditions recommended for treatment by pediatric surgical specialists include major congenital anomalies, malignant lesions, major trauma, and chronic illnesses in infants and children. The report stated that “the optimal management of the child with complex problems, chronic illness or disabilities requires coordination, communication and cooperation of the pediatric surgical specialist with the child’s primary care pediatrician or physician.” Many complex pediatric problems are more optimally treated by a medical-surgical team rather than by an individual surgical specialist. Centers dedicated to children may provide special expertise in areas such as imaging, pediatric medical subspecialty consultation, pediatric anesthesia, and pediatric intensive care. The guidelines may be viewed online at www.aap.org/policy/pprgtoc.cfm.

**Adolescents and Anabolic Steroids**
According to pediatric specialists, most pediatric athletes will find a way to meet their sports goals without using anabolic steroids. These athletes should be reminded that the health, fitness, and social benefits of sports participation can be met readily without use of performance-enhancing substances. According to the American Academy of Pediatrics, current clinical experience and scientific evidence support an approach to the anabolic steroid issue that minimizes preconceptions about the users, recognizes the potential benefits as well as risks of use, and maximizes informed, balanced, and open interaction with patients (www.aap.org/policy/pprgtoc.cfm).

**Atlantoaxial Instability in Patients with Down Syndrome**
According to the American Academy of Pediatrics, lateral plain radiographs of the cervical spine are of potential, but unproven, value for detecting which patients with Down syndrome are at risk for the development of spinal cord injury during sports participation. Radiographic evaluation is emphasized for patients with neurologic symptoms. Recognition of symptomatic patients requires frequent interval histories and physical examinations, including evaluations before participation in sports, preferably by physicians who have cared for these patients longitudinally. Parents must be taught the signs and symptoms of atlantoaxial instability that indicate the need to seek immediate medical care.

The Special Olympics does not plan at this time to remove its requirement for all athletes with Down syndrome to be evaluated with radiographs of the cervical spine. Pediatricians and orthopaedic specialists will continue to be called on to order these tests. Better research is needed in order to determine what symptoms, signs, and findings from imaging studies best identify which individuals with Down syndrome are at increased risk of a catastrophic spinal cord injury during sports participation (www.aap.org/policy/pprgtoc.cfm).
Managed Care and Children with Special Health-Care Needs
Dialogue opportunities exist for improving some aspects of care for children with chronic illness and disabilities in managed-care systems. The AAP has suggested several guidelines for discussion (www.aap.org/policy/pprgtoc.cfm) regarding the need to (1) create an understanding of major differences between adult and childhood disability and the resulting need for managed-care models to be sufficiently flexible to serve children with special needs and their families, (2) establish fair reimbursement to compensate for the increased time and complexity associated with providing and coordinating care for children and families of children with special health-care needs (which translates into risk adjustment for capitated systems), (3) ensure access to and appropriate use of pediatric subspecialists with defined roles and open lines of communication between secondary and tertiary care and the medical home, and (4) create viable systems of monitoring care capable of producing process and outcome data from which appropriate adjustments are made to refine care to benefit children and families.

Knee Brace Use in the Young Athlete
The AAP recommends that when prescribing the use of knee braces, physicians should establish an accurate diagnosis of the injury and understand the classifications, benefits, limitations, indications, and cost of any brace prescribed (www.aap.org/policy/pprgtoc.cfm).

Insufficient scientific evidence exists to recommend the use of prophylactic knee braces for the pediatric athlete. In fact, available studies do not support the prescription of most knee braces. The use of knee sleeves, functional braces, and postoperative braces has been accepted clinically on the basis of the physician’s assessment. When used, knee braces should complement, rather than replace, rehabilitative therapy and surgery.

Evidence-Based Orthopaedics
The editorial staff of The Journal reviewed a large number of recently published research studies related to the musculoskeletal system that received a Level of Evidence grade of I. Over 100 medical journals were reviewed to identify these articles, which all have high-quality study design. In addition to articles published previously in this journal or cited already in this Update, two level-I articles were identified that were relevant to pediatric orthopaedics. A list of those titles is appended to this review after the standard bibliography. We have provided a brief commentary about each of the articles to help to guide your further reading, in an evidence-based fashion, in this subspecialty area.

References

Upcoming Educational Events
POSNA Tutorials: Growing Rod Technique for Progressive Early Onset Scoliosis
July 22, 2005
San Diego, California

POSNA Tutorials: Cerebral Palsy Treatment: Current Concepts Update
November 9-11, 2005
Wilmington, Delaware

2nd International POSNA/AAOS Pediatric Orthopaedic Symposium
November 30–December 4, 2005
Orlando, Florida

POSNA Specialty Day
March 11, 2006
New Orleans, Louisiana

POSNA Annual Meeting
May 3-6, 2006
San Diego, California

Information regarding all events can be found at www.posna.org
What's New in Pediatric Orthopaedics


Evidence-Based Articles Related to Pediatric Orthopaedics


Seventy-four children with obstetric brachial plexus palsy who were registered with the British Paediatric Surveillance Unit were prospectively followed for a minimum of two years. Thirty-nine patients (52.7%) had spontaneous recovery to normal or nearly normal levels and another twenty-nine (39.2%) regained good function in the upper limb. The most important secondary deformity involved the glenohumeral joint, and twenty patients (27%) needed surgical correction. The brachial plexus was explored in nine patients (12.2%) and was repaired in seven. This study provides information regarding spontaneous neurologic recovery and glenohumeral deformity in patients with obstetric brachial plexus palsy.


This prospective, blinded, randomized, controlled study compared the effect of a perioperative infusion of aprotinin with the infusion of a placebo during long-segment spinal fusions (fusions involving seven or more segments) in forty-four children. There was a significant reduction in estimated blood loss (545 mL in the aprotinin group, compared with 930 mL in the placebo group) and transfusion requirements (1.1 U in the aprotinin group, compared with 2.2 U in the placebo group). The duration of intensive-care unit admission was similar in the two groups, as was the time until discharge. This study suggests that aprotinin can significantly decrease blood loss and transfusion requirements in pediatric and adolescent scoliosis patients undergoing spinal fusion.
Book Reviews

Low Back and Neck Pain. Comprehensive Diagnosis and Management. 3rd ed.

Comprehensive is right! This outstanding text provides an impressive collection of the knowledge relevant to the evaluation and management of low back pain and neck pain. Well written and offering clear and concise descriptions, the book is an excellent reference for anyone involved in the care of patients with back and neck pain.

The first section of the book provides an overview of the normal anatomy and biomechanics of the spine, the epidemiology of neck and low back pain, and the sources of spinal pain. These chapters review the basic sciences with excellent depth, highlight specific pertinent areas, and are well referenced for those who wish to delve deeper into specific areas. The chapter on sources of pain gives particular insight into the basic sciences of pain production, the clinical importance of the "fifth vital sign," and the distribution of radicular and referred pain.

In Section II, the authors provide an excellent discussion of the clinical evaluation of the symptoms of neck and low back pain. The chapter on history is extensive and includes a discussion of outcomes questionnaires and their relevant use. The succeeding chapters are of equally good quality and offer a review of physical examination, laboratory tests, and radiographic and miscellaneous evaluations. Section II concludes with a chapter on a standardized approach to the diagnosis and treatment of spinal pain and includes guidance on the evaluation of patients who have a specific diagnosis. The chapter offers information with regard to the specific symptoms associated with spinal pain and provides guidance on the sequence of evaluation of many common, specific pain patterns. Also included in this chapter are very practical treatment and evaluation algorithms for neck pain and back pain.

Section III provides a thorough review of the specific diseases associated with spinal pain and provides pertinent information on virtually all potential diagnostic entities directly or indirectly related to spinal pain syndromes. With excellent use of tables to amplify the text, each diagnosis-based chapter reviews the specific epidemiology, evaluation, treatment options, and prognosis related to the specific diseases. Each diagnostic entity also has a very helpful "capsule summary" at the beginning of the chapter, highlighting in brief the specific symptoms, tests, imaging findings, and treatment overview for the specific disorder.

The final section of the book provides an excellent overview of treatment options, including an excellent discussion of medical therapy and the rationale behind each therapeutic intervention. The book also includes a similar discussion of alternative medicine options and results, which is particularly helpful information when dealing with our current Internet-savvy patient population. Each of the chapters on medical management concludes with a summary of the author’s recommendations. Surgical therapy is discussed as an overview based on specific diagnoses and clear indications for surgical management, thus satisfying the need for a discussion of management options while avoiding an extensive discussion of comprehensive surgical details and techniques.

The book includes two comprehensive appendices on the differential diagnosis of low back pain (Appendix A) and neck pain (Appendix B), in which evaluation and management features are presented in a brief tabular form that is amplified in the text.

Low Back and Neck Pain represents a valuable resource for all healthcare professionals who are involved in the care of patients with low back pain or neck pain. It offers a great depth of knowledge with regard to the diagnosis and management of spinal disorders, and it also offers tabular information and capsule summaries that allow for a quick review between patients. It is particularly relevant for orthopaedic surgeons involved in spine care because it serves as both a review and an update of the diagnosis and management of back and neck pain.

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Orthopaedic Pathology. 4th ed.

The torn cover and tattered pages of my own copy of the first edition of this book attest to its enduring popularity, especially among students and residents in pathology and orthopaedic surgery. The first edition, marketed as an “atlas” with relatively little text, has now grown into a mature book, although emphasis on the visual reminds us of its origin.

While most orthopaedic pathology books tend to focus on tumors, Orthopaedic Pathology contains six major sections, only the last two of which deal with tumors and tumor-like lesions. The other sections illustrate normal bone morphology (including chapters that describe imaging techniques and methods of examining resection specimens), skeletal injury and repair, metabolic abnormalities, and arthritis.

Each chapter is very well illustrated with a variety of visual material, including diagrams, radiographic images, gross and microscopic photographs, and tables. The quality of the color photographs is excellent, and helpful correlations be-
between radiographic, gross, and microscopic images are seen throughout the book. Curiously absent from the text are citations to original literature. Instead, an appendix at the end of the book lists “Further Reading” sorted by subject. Indeed, some of the publications that have been loosely referred to in the text are not included in this modified bibliography, necessitating the use of other literature-searching tools to dig deeper into areas of interest.

Orthopaedic Pathology does not include a discussion of experimental studies, treatment, or areas of controversy. Although this omission may cause the experienced specialist to interpret the scope of this book as being too limited, such an authoritative approach allows the author to focus on a concise but beautifully illustrated presentation of pathology and differential diagnosis.

The relatively small number of orthopaedic oncologists and pathologists who devote most of their time to the treatment of bone and soft-tissue tumors will need to own other reference works, but Orthopaedic Pathology provides an overview of tumors that will be very useful to most practicing surgeons and pathologists. From the perspective of a medical student soon to start an orthopaedic surgery residency, Orthopaedic Pathology provides an excellent reference source that is useful for general background information and as an accompaniment to the review of microscope slides, images, and case studies. Indeed, for some orthopaedic surgery and pathology residency training programs, this text might be the best single source for orthopaedic pathology education.

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Textbook of Arthroscopy

Technical advances in the area of arthroscopic surgery are occurring with breathtaking speed. As stated in the introductory section of the book, “New techniques continue to be developed, humbling even the most technically adept arthroscopist who finds himself suddenly thrust to the bottom of the learning curve . . . Textbook of Arthroscopy was specifically written to fill this void.”

The editors state that the book provides a “state-of-the-art and comprehensive approach to arthroscopic surgical procedures.” The text itself is divided into eight parts. The introductory chapters in Part 1 discuss general issues, such as equipment, implants, anesthetic techniques, and arthroscopic knot-tying. The seven subsequent parts deal with specific anatomical areas: the shoulder, the elbow, the wrist and hand, the hip, the knee, the ankle, and the spine.

Each part includes a variety of procedures and techniques. In the editors’ own words, “Many chapters are authored by the original developers of specific arthroscopic techniques or by well-respected educators who provide the most accurate depiction of ‘how to’ perform virtually any arthroscopic procedure.” In each surgical technique chapter, a table clearly outlines the indications, postoperative management, results, complications, and other salient parameters surrounding the method described. The text is accompanied by numerous full-color, clear illustrations that complement the textual descriptions of surgical technique.

In this “how-to” manual, one would not expect to find detailed comparative information regarding the advantages or disadvantages of various similar techniques. Instead, results of each technique are reported independently and not contrasted directly. Also, there is no discussion of the alternative open techniques for the conditions being treated. Instead, the book focuses on arthroscopic technique with detailed procedural notations and on coverage of almost every imaginable arthroscopic operation. For instance, seven different types of arthroscopic shoulder stabilization are described—each with its own chapter.

Textbook of Arthroscopy will be of value to both the novice and the experienced arthroscopic surgeon. It will be a comprehensive reference for the surgeon-in-training and a useful library companion for the experienced arthroscopist who is interested in a new technique or wishes to brush up on a procedure that is performed infrequently.

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