

A 60-Year-Old Woman Considering Acupuncture for Knee Pain

Brian Berman, MD, Discussant

DR DELBANCO: Mrs A is a 60-year-old woman who is considering acupuncture for her chronic knee pain. She is married, has children, lives in the suburbs, and works in a health profession. She has private commercial insurance. Mrs A has a family history of lung and breast cancer. She drinks wine with dinner, no more than 2 glasses, and gets lots of exercise.

Mrs A is basically healthy. She has mild hypertension that her doctor is trying to manage with salt restriction; she is an avid user of salt. She was quite ill years ago after a lumbar puncture, when she was told she has a myofascial pain syndrome, primarily manifested by headaches. At that time, a trial of acupuncture did not help these symptoms. They have not recurred in the past 10 years.

Mrs A has had surgery for varicose veins, and on occasion she experiences low back pain. At this time, she has some numbness on the lateral aspects of her feet. This is under evaluation, possibly as a manifestation of a radiculopathy.

Her knee pain started about 15 years ago when she skied aggressively and developed a torn meniscus. Arthroscopic surgery left her with little deficit. She now wears an unloading knee brace when she plays tennis or skis.

Eight years ago she experienced the onset of diffuse joint pain, primarily affecting both knees. The knee pain has been slowly progressive. She has treated it intermittently with nonsteroidal anti-inflammatory drugs (NSAIDs), in part because she does not like to take medicines. She has tried chondroitin sulfate and glucosamine on occasion, but never with much regularity. She currently has a swollen left knee from recent skiing.

She takes calcium supplements daily. She weighs 158 lb (71 kg) and is 68 inches tall. On physical examination by her primary care physician before she went skiing, she had a small amount of crepitus in both knees. She did not have localized tenderness or findings suggestive of joint encroachment.

Her laboratory work is unremarkable. In her knee film taken this week (FIGURE 1), the left knee, where she had the surgery, demonstrated mild joint space narrowing of the medial compartment and osteophytes along the joint surfaces. The joint surfaces appear well preserved.

See also Patient Page.

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Mrs A, an active 60-year-old woman, has a history of degenerative osteoarthritis of her knee with pain that has progressed over the past 8 years. She has undergone arthroscopic surgery for a meniscal tear and has taken nonsteroidal anti-inflammatory drugs (NSAIDs), glucosamine, and chondroitin sulfate occasionally, but generally does not like taking medications. She is open to other therapeutic approaches and wants to know if acupuncture can help the pain, improve function, and stop her condition from progressing. The evidence for the effectiveness of acupuncture for knee pain and other common treatments, including exercise, NSAIDs, glucosamine and chondroitin, and intra-articular knee injections are compared, and costs and methods of acupuncture and selecting an acupuncturist are discussed.

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MRS A: HER VIEW

I've had a knee problem for about 15 years. Ten years ago I was out west skiing, and I was in a racing program. I overdid it, had a really terrible pain in my left knee, and I had to stop skiing for the rest of that vacation. I came back, went through a lot of evaluations with a lot of different doctors, and then they finally figured out that I had a torn meniscus. I had arthroscopic surgery, and that was actually very successful. I'm still able to ski and play tennis, but I have to wear an unloading brace on my knee.

I have arthritis on top of everything. That's my major issue right now. It's not my meniscus and my unloading brace, it's the knee pain that I have all the time.

My knee pain keeps me from being as active as I really want to be. I'm a very, very active person. I'm 60 years old,

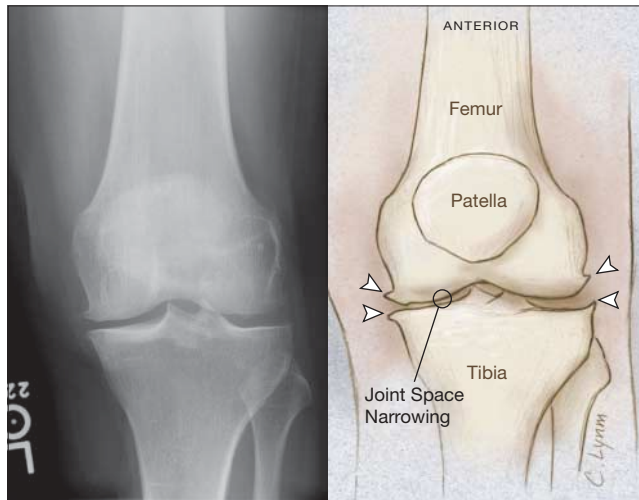
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Figure 1. Radiograph of Mrs A's Knee

White arrowheads indicate location of osteophytes.

and I work full time. I have 3 kids, take care of a house and a yard, and I have a summer house. And I'm always having trouble at the end of the day. I'm in a lot of pain. A lot of times it'll keep me from doing something the next day. And every morning, when I walk down the stairs in the morning, I have to hold onto the side of the walls to kind of hold my weight, because I can't put all my weight on my knees.

I take glucosamine and chondroitin occasionally. I have a couple friends that take it and swear by it. I heard a talk at our hospital by an orthopedic surgeon who said that glucosamine and chondroitin will help 50% of people, and specifically those people with knee problems. So I started taking it, and it actually helps, I think. And then I forget about it, because my knees feel a bit better. And then I'm back in pain again. I'm not a good pill taker. I probably would do better if I would take it regularly. And then I take [ibuprofen] if I'm in a lot of pain, before I'm going to do a lot of work outside, like yard work, and then afterwards.

I think if my pains in my knees were such that I didn't have any other way to control it, I would seek pain management with relaxation techniques. I think the mind can be involved a lot in maintaining or helping with pain.

About 20 years ago, I had a very serious headache problem as a result of an epidural. I had a 10-year headache, and it was very unusual and very difficult. My neurologist, after about 5 years of treating me, said the only thing he could think of is acupuncture. So I went and had to commit to it, twice a week for 10 weeks. It didn't do one single thing.

I never thought about acupuncture for my knees. I'd like to have somebody explain to me my knee pain, and if I had acupuncture, what would happen? How would that be translated into chemical changes? I think I would like to experience that.

The only problem about acupuncture is that, while I personally can afford it, it's expensive. Our health insurance is not picking it up. And if you're going to commit to it, you need to commit to it for a period of time. But \$75 twice a week for an hour is a lot of money. I'm not sure I would spend, at this point, hundreds and hundreds of dollars to feel a little bit better for a short period of time. If I had a session, say 10 sessions right now, would this be just short-term? Or would this have some effect, lasting effect, on my physical condition?

I think there is a placebo effect, and I think it's curious. But that doesn't bother me. That doesn't mean it doesn't work. I think the process of our brains is so interesting, and I don't get it all. But I'm okay with that. If somebody told me it was just a "placebo effect"—fine.

AT THE CROSSROADS: QUESTIONS FOR DR BERMAN

What is the prevalence of knee pain in persons around Mrs A's age, and how often is acupuncture used in the United States and worldwide for this type of pain? What is the current understanding of the mechanism of action of acupuncture for such patients? What mechanisms are in place to educate and certify clinicians in the use of acupuncture and how can one find a reputable acupuncturist? Is acupuncture appropriate primarily for short-term pain relief? What are the data concerning longer-term relief? What are the risks, such as viral or bacterial infection? What are the comparative data for other forms of therapy? What is the impact of health insurance on the various forms of therapy? What would you recommend for Mrs A? What does the future hold for acupuncture therapy in the United States?

DR BERMAN: Mrs A is an active 60-year-old woman with a history of knee pain that has progressed over the past 8 years. She has a past history of arthroscopic surgery for a torn meniscus. Mrs A's primary care physician told her that she has osteoarthritis, which is confirmed by physical examination and her knee films (Figure 1). The arthritis is affecting her quality of life, causing increased pain at the end of the day and difficulties performing routine daily activities, such as walking, bending, and climbing. She has taken NSAIDs, glucosamine, and chondroitin sulfate occasionally, but generally does not like taking medications. She seems open to other therapeutic approaches and wants to know what she can do to help the pain, improve function, and stop her condition from progressing over the next 5 to 10 years. I will not address the evaluation and differential diagnosis of the painful knee, but will focus on the role of acupuncture relative to other treatments for pain from osteoarthritis of the knee.

Knee pain is a common symptom, affecting up to 30% of adults older than 45 years.¹ Some of the most common causes of knee pain in adults older than 50 years are osteoarthritis, inflammatory arthropathies, bursitis, and tendinitis.² The most likely cause of knee pain in Mrs A's case is osteoar-

thritis. This is confirmed by a history of pain on most days for 1 month, findings on examination of bony tenderness, bony enlargement, and crepitus, and radiographs showing osteophytes.

The Spectrum of Osteoarthritis

Osteoarthritis is the most common joint disorder in the world and a major cause of physical disability in the United States, affecting approximately 21 million Americans.³ It is especially prevalent among women and those who are older than 50 years.³⁻⁵ By the year 2020, more than 59% of Americans are projected to have pain from arthritis, including its most widespread form, osteoarthritis.^{3,6} The number of people affected will only grow as life expectancy increases and the baby boomer generation ages.^{1,3,6} Osteoarthritis manifests most often in weight-bearing joints, such as the hip and the knee, thereby affecting mobility and contributing to time lost at work, early retirement, increased health care utilization, and joint replacement surgery.⁷ Recent estimates suggest that the total costs of arthritis may be close to 2.5% of the gross domestic product.⁷

Osteoarthritis, rather than being a single entity, is believed to be the final pathway of a variety of conditions.⁸ Numerous factors, such as genetics, nutrition, inflammation, and local biomechanics, lead to its pathological manifestation of cartilage loss and the clinical symptom of joint pain with movement.⁹ Past treatment of torn meniscus and surgical repair can also be contributing factors.^{9,10} It is not always realized that in addition to bony joint changes, soft tissue structures around the joint are often affected, including weak muscles (especially quadriceps), lax ligaments, and inflammation of the synovium.⁹ Recent data suggest that inflammation plays an important role in the pathophysiology of osteoarthritis, with respect to both production of pain and stiffness and structural progression.¹¹

Current Management of Knee Osteoarthritis

No therapies have been definitively demonstrated to cure osteoarthritis.¹² Current recommendations for its management, including guidelines published by the American College of Rheumatology (ACR) and the European League of Association of Rheumatology, focus on the relief of pain and stiffness and maintenance or improvement in physical function.¹³⁻¹⁵ The ACR recommendations outline nonpharmacological therapies as the foundation of a multidisciplinary therapeutic approach to osteoarthritis that also includes the use of pharmacological therapies. In the comparisons below, standardized mean differences (SMDs) are used to express the size of the treatment effect observed in a randomized controlled trial (RCT) relative to the variability in that RCT. They are useful for comparing treatment effects across studies that assess the same outcome but measure it in various ways. In general, an SMD of

about 0.2 is considered small, 0.5 is moderate, and 0.8 is large.¹⁶

Nonpharmacological therapies range from patient education, social support, physical and occupational therapy, aerobic and resistive exercises, to weight loss. Physical therapy may include range-of-motion exercises, quadriceps strengthening exercises, or aerobic exercises. A systematic review of the literature of land-based (as opposed to water-based) exercise for knee and hip osteoarthritis evaluated 17 RCTs including 2562 participants.¹⁷ The results demonstrated that compared with nonexercise control groups, a wide range of muscle strengthening and aerobic exercises reduce pain (SMD, 0.39; 95% confidence interval [CI], 0.30-0.47) and improve physical function (SMD, 0.31; 95% CI, 0.23-0.39) for people with knee osteoarthritis. There were insufficient data to determine optimal exercise type or frequency. Single studies suggest that aquatic exercise programs¹⁸ and use of a knee brace¹⁹ may improve pain and function. A systematic review of 7 studies, totaling 294 patients, found transcutaneous electrical nerve stimulation to be effective over placebo for pain control in patients with knee osteoarthritis (SMD, -0.45; 95% CI, -0.70 to -0.19).²⁰ However, the studies were somewhat heterogeneous and more well-designed trials are needed.

Commonly used pharmacological interventions for osteoarthritis include NSAIDs, acetaminophen, intra-articular therapy, opioids, glucosamine, and chondroitin sulfate.²¹ TABLE I summarizes the most current meta-analyses to present the level of evidence for pain relief and improved function with these therapies.

Use of Complementary and Alternative Medicine

The limited ability of many commonly used interventions to reduce pain and improve function, combined with significant adverse effects of some pharmaceuticals,³⁵⁻⁴⁰ has led many patients and physicians to try therapies outside the mainstream of medicine.⁴¹⁻⁴⁴ According to the 2002 National Health Interview Survey (N=30 785), which included a section on complementary and alternative medicine (CAM), 41% of those who reported having arthritis had used some form of CAM.⁴⁵ Of these, 24% used biologically based therapies, 21% used mind/body therapies, and 1.2% used acupuncture. Other community surveys have shown similarly high use of CAM for rheumatologic disorders.^{46,47} While high-quality evidence evaluating CAM has been sparse, evidence is increasing as more randomized trials are conducted.

Acupuncture

Mrs A expressed interest in a number of the available approaches for knee pain and wants to know specifically if and how acupuncture might be effective for knee osteoarthritis. Acupuncture typically involves stimulating defined points on the skin by inserting fine stainless steel needles

Table 1. Commonly Used Therapies for Osteoarthritis of the Knee: Level of Evidence and Meta-analytic Effect Size Estimates Relative to Placebo

| Therapy | Time Point* | Pain | | | Function | | | Comments | |
|---|----------------|-------------|-----------------|------------------|----------------------|--------------------|------------------------------------|---|--|
| | | No. of RCTs | No. of Patients | SMD (95% CI)† | No. of RCTs | No. of Patients | SMD (95% CI)† | | |
| NSAIDs oral ²² | 2-13 | 23 | 10 845 | 0.32 (0.24-0.39) | 11 | 7433 | 0.29 (0.18-0.40) | Overall pooled results heterogeneous, but after restricting to RCTs that did not exclude NSAID nonresponders, results were homogeneous, and SMDs decreased to 0.23 (95% CI, 0.16-0.31; 10 RCTs; N = 4565) for pain and 0.20 (95% CI, .09-.30; 3 RCTs; N = 2928) for function | |
| NSAIDs topical ²³ | 2 | 6 | 893 | 0.40 (0.15-0.65) | 4 | 540 | 0.35 (0.19-0.53) | Topical NSAIDs superior to placebo only during first 2 wk after treatment; reviewers suggested these benefits may have been overestimates because of evidence of publication bias; no benefit over placebo at weeks 3 and 4 | |
| Acetaminophen ²⁴ | 6 | 5 | 1835 | 0.13 (0.04-0.22) | 2 | 829 | 0.04 (-0.10 to 0.18) | Function SMDs from an analysis that pooled only RCTs reporting outcomes on the WOMAC function scale | |
| Intra-articular hyaluronic acid ^{25‡} | 8-12§ | 22 | 2927 | 0.32 (0.17-0.47) | 6 ²⁶ | 1023 ²⁶ | 0.11 (-0.09 to 0.31) ²⁶ | Overall pooled results heterogeneous, but excluding the 3 RCTs evaluating the highest-molecular-weight hyaluronic acid reduced both heterogeneity and SMDs to 0.19 (95% CI, 0.10-0.27); evidence of publication bias led authors ²⁵ to conclude that reported SMDs may be overestimates (other meta-analyses found smaller ²⁶ and larger ²⁷ effects than Lo et al ²⁵ ; results of the meta-analyses may depend on methods used) | |
| Intra-articular corticosteroids ²⁸ | 2 | 5 | 283 | 0.55 (0.31-0.79) | NR | NR | NR | Significant improvement also seen at 16-24 wk, according to results pooled from 2 RCTs (N = 124) (this was only reported as dichotomous global improvement measure [relative risk, 2.09; 95% CI, 1.2-3.65]) | |
| Opioids ²⁹ | 5 | 28 | 3741 | 0.60 (0.50-0.69) | 20 | 3221 | 0.31 (0.22-0.41) | SMDs provided are from meta-analyses that pooled data for patients with all noncancer pain types, not osteoarthritis specifically, and for all opiate classes | |
| Glucosamine ³⁰ | | | | | | | | Mixed results in favor of glucosamine, with positive results for only the Rottapharm preparation; treatment effect not significant in pooled analysis of only RCTs with adequate allocation concealment; lack of treatment effect also found in a large, recent RCT ³¹ not included in this meta-analysis | |
| | Rottapharm¶ | ~ 24 | 7 | 730 | 1.31 (0.64-1.99) | 4# | 741 | 0.51 (0.05-0.96) | |
| | Non-Rottapharm | ~ 9 | 8 | 751 | 0.15 (-0.05 to 0.35) | 4 | 336 | 0.03 (-0.18 to 0.25) | |
| Chondroitin sulfate | | | | | | | | Early meta-analyses ^{32,33} suggested significant effects of chondroitin; however, results from 2 recent, large RCTs ^{31,34} found no significant effect; current meta-analytic estimates are unavailable | |

Abbreviations: CI, confidence interval; NR, not reported; NSAID, nonsteroidal anti-inflammatory drug; RCT, randomized controlled trial; SMD, standardized mean difference; WOMAC, Western Ontario and MacMaster.

*Time point: follow-up time points are duration from baseline, in weeks.

†Results are presented as SMDs, the difference between the active treatment and placebo groups, divided by the pooled SD of this difference. In meta-analyses, SMDs from the individual included RCTs may be calculated as either (1) differences in improvements from baseline between the 2 randomized groups divided by SDs of pooled improvements, or as (2) differences in posttreatment scores between the 2 groups divided by SDs of pooled posttreatment scores. Two meta-analyses used the differences in improvements method,^{22,23} 4 used the differences in posttreatment scores method,^{24,29-30} and one²⁵ used either differences in improvements (as preference) or differences in posttreatment scores, depending on which was available for the included RCTs at the time of interest. Standardized mean difference reported for pain and function were extracted from the meta-analysis referenced in the first column unless otherwise noted. A negative SMD indicates that the comparison favors the placebo and 95% CIs that cross zero indicate no significant effect.

‡For reviews of intra-articular therapies, the placebo was an intra-articular placebo injection (eg, saline injection).

§An 8- to 12-week time point used, if available; if not, data extracted on pain at 1 to 4 months after the first hyaluronic acid injection.

||SMDs were calculated using the posttreatment means and SDs of the included RCTs, as reported in Figure 4 of Arroll and Goodyear-Smith.²⁸

¶Rottapharm SpA, Monza Milan, Italy.

#Function SMDs provided are from an analysis that pooled only the 4 Rottapharm RCTs reporting results on the Lequesne scale; 2 other Rottapharm RCTs reported results on the WOMAC scale instead and found smaller SMDs, which were not statistically significant when pooled.

(TABLE 2 and FIGURE 2). Frequently, stimulation of the needles is augmented by electrical current, moxibustion (burning the herb *Artemisia vulgaris* close to the acupuncture point or needle), heat, laser, or pressure. Acupuncture is an essential component of traditional Chinese medicine (TCM), and its use dates back over 3000 years in China and Korea.⁵⁴ Over time it spread from Asia to the Western hemisphere, and distinct approaches and styles evolved. A 2002 survey estimated that 8 million Americans have used acupuncture, predominantly for pain-related problems.⁴⁴ The perception of acupuncture as a legitimate medical intervention expanded when the National Institutes of Health (NIH) and the Food and Drug Administration (FDA) held consensus development and technology assessment conferences^{55,56} that resulted in recommendations on the potential use of acupuncture, in particular for pain-related conditions as well as post-

operative and chemotherapy-induced nausea and vomiting, and when the FDA reclassified acupuncture needles from investigational devices to medical devices.⁵⁷ In a national survey of rheumatologists and an international survey of pain specialists, 56% and 84%, respectively, considered acupuncture a legitimate medical practice.^{41,58}

How Does Acupuncture Work?

Traditional practice of acupuncture is based on TCM concepts that are not readily understood from a Western medical viewpoint. Health and sickness are seen in terms of balance (*Yin-Yang*) both within oneself and with external factors, and the free flow of energy or vital force (*Qi*) and blood through the body. The *Qi* is believed to travel through 14 meridians in the body, and acupuncture needles are inserted at points along the meridians to unblock energy that is stuck and causing imbalance in the body.⁵⁹

Table 2. Acupuncture for Osteoarthritis of the Knee: Randomized Controlled Trial Effect Size Estimates Relative to Sham Acupuncture*

| Source | Patient Population | No. of Patients Receiving Acupuncture/Sham | Acupuncture Intervention | Time Points, wk† | Difference in Pain, WOMAC Scale 0-20 (95% CI) ⁴⁸ | Pain SMD (95% CI)‡ | Difference in Function, WOMAC Scale 0-68 (95% CI) ⁴⁸ | Function SMD (95% CI)‡ |
|-----------------------------------|--|--|--|------------------|---|--|---|--|
| Berman et al, ⁴⁹ 2004§ | Volunteers recruited through advertisements | 190/191 | 23 sessions over 26 wk, with electrical stimulation at 2 knee points | 14 26 | 1.0 (0.1-1.8) 0.9 (0.0-1.7) | 0.24 (0.01-0.46) 0.23 (0.00-0.47) | 2.8 (0.2-5.4) 2.5 (-0.03 to 5.4) | 0.23 (0.01-0.45) 0.21 (-0.03 to 0.44) |
| Vas et al, ⁵⁰ 2004 | Recruited from patients of 3 primary care practices | 48/49 | 12 sessions over 12 wk, with electrical stimulation at all knee points; diclofenac received by both groups | 12 | 5.0 (2.9-7.1) | 1.01 (0.56-1.45) | 16.6 (9.5-23.7) | 0.99 (0.55-1.43) |
| Witt et al, ⁵¹ 2005 | Volunteers recruited through advertisements | 150/76 | 12 sessions over 8 wk | 8 52 | 1.4 (0.3-2.6) 0.3 (-1.1 to 1.7) | 0.35 (0.06-0.63) 0.07 (-0.21 to 0.35) | 5.0 (1.3-8.8) 3.1 (-1.2 to 7.3) | 0.36 (0.08-0.65) 0.19 (-0.09 to 0.48) |
| Scharf et al, ⁵² 2006 | Recruited from patients of 315 primary care clinical practices | 330/367 | 10 sessions over 6 wk (with option for 5 additional sessions if initial treatment graded partially successful); 6 physiotherapy sessions and as-needed anti-inflammatory medication received by all groups | 12 26 | 0.6 (-0.1 to 1.3) 0.4 (-0.3 to 1.3) | 0.14 (-0.02 to 0.29) 0.09 (-0.06 to 0.24) | 1.4 (-0.9 to 3.6) 1.4 (-1.0 to 3.7) | 0.09 (-0.06 to 0.24) 0.09 (-0.06 to 0.24) |

Abbreviations: CI, confidence interval; SMD, standardized mean difference; WOMAC, Western Ontario and MacMaster.

*For all sham-controlled RCTs, the sham acupuncture procedure was given on the same schedule as that used for the true acupuncture group. The types of sham acupuncture control groups differed among RCTs: Vas et al⁵⁰ used nonpenetrating needles placed at acupuncture points; Scharf et al⁵² and Witt et al⁵¹ used needles inserted superficially at nonacupuncture points; and Berman et al⁴⁹ used a combination of inserted needles and noninserted sham devices.

†The table includes 2 measurement time points: a short-term end point defined as up to 25 weeks from randomization and taking the data point closest to 12 weeks, and a long-term end point defined as the last reported measurement between 26 and 52 weeks.⁴⁸ With this time point selection, the only results not presented are the 26-week postbaseline data from the Witt et al trial,⁵¹ at which time the SMDs were similar to but slightly larger than the SMDs at 52 weeks; the 8-week postbaseline data from the Berman et al trial,⁴⁹ at which time the SMDs for function were slightly larger and pain slightly smaller, compared with the SMDs at 14 weeks; and the 4-week postbaseline data for the Berman et al trial, at which time the SMDs were not statistically significant.

‡Standardized mean differences were calculated using differences in improvements between groups divided by SDs of improvements.^{48,53}

§For this study, there are slight discrepancies between the CIs reported in this table and the *P* values reported in the publication⁴⁹; the *P* values reported in the publication,⁴⁹ clearly statistically significant for both outcomes at both the 14- and 26-week time points, were calculated using a mixed-effects model that controlled for baseline values of the outcome variable, within-participant correlation, and clinical site; the CIs reported in this table were calculated using only the raw values of the mean changes and SDs of the changes.

From a Western viewpoint, however, research is elucidating how acupuncture may work from the perspective of 2 widely accepted theories of pain relief: (1) activation of a gate control system and (2) stimulation of the release of neurochemicals in the central nervous system.^{60,61,60,61} Animal studies suggest that acupuncture stimulates peripheral nerves in muscles that send impulses to 3 levels of the nervous system: the spinal cord, midbrain (periaqueductal gray matter and the raphe nucleus), and hypothalamus-pituitary system. This leads to the release of neurotransmitters and hormones (endorphins, monoamines, and cortisol), causing analgesia.⁶²⁻⁶⁴ Furthermore, acupuncture appears to activate descending pain-inhibiting pathways and to deactivate limbic structures that are the mechanisms involved in the sensory and affective components of pain.^{62,65} Acupuncture also appears to work locally, inducing peripheral vasodilation, increasing blood flow through the release of neuropeptides,^{66,67} and stimulating anti-inflammatory responses by inhibiting the release of histamine and prostaglandins.⁶⁸

More recently, research focused on persistent inflammatory pain models has found that electroacupuncture attenuates thermal hyperalgesia and reduces inflammatory paw edema in rats.^{69,70} These antihyperalgesic and anti-inflammatory effects of acupuncture appear to correlate with the change of a biomarker (Fos protein) expression in the spinal level.⁶⁸

The Evidence for Acupuncture for Osteoarthritis of the Knee

A recent systematic review of the literature of acupuncture for knee osteoarthritis included 13 RCTs.⁴⁸ The 8 RCTs that used an adequate acupuncture protocol and provided Western Ontario and MacMaster (WOMAC) pain and function outcomes were combined in meta-analyses. For the meta-analyses comparing acupuncture with sham acupuncture, a short-term end point ranged from 7 to 13 weeks after randomization and the data point closest to 12 weeks was taken. A long-term end point was defined as the last reported measurement between 26^{49,52} and 52⁵¹ weeks.⁴⁸ The meta-analyses found that acupuncture was statistically superior to sham acupuncture for pain (weighted mean difference in WOMAC pain subscale score, 1.54; 95% CI, 0.49-2.60) and function (weighted mean difference, 4.32; 95% CI, 0.60-8.05) at the short-term. The results were still statistically significant at the longer-term follow-up for pain (weighted mean difference, 0.54; 95% CI, 0.05-1.04) and function (weighted mean difference, 2.01; 95% CI, 0.36-3.66). However, there was heterogeneity in some results and the authors suggest that further research is required to confirm these findings and provide more information on long-term effects.

Four large RCTs⁴⁹⁻⁵² that comprise most of the evidence in the meta-analysis are described in Table 2. All 4 RCTs used the WOMAC index pain and function subscales for measuring outcomes. (The SMDs in Table 2 were provided by

Figure 2. Common Acupuncture Points for Treatment of Knee Pain



The acupuncture points in this figure represent some of the primary points used in traditional Chinese medicine to treat the main subcategories of “Bi” syndrome—the closest traditional Chinese medicine diagnosis for arthritis. These points were used in standardized treatment protocols in 2 of the large randomized controlled trials in Table 2.^{49,50} The other randomized controlled trials^{51,52} listed in Table 2 used a variety of standardized and individualized treatment protocols that included a minimum of 8 points, including some of those indicated. BL indicates bladder meridian; GB, gallbladder meridian; KI, kidney meridian; SP, spleen meridian; ST, stomach meridian. For additional information on acupuncture points, see Cheng X, ed. *Chinese Acupuncture and Moxibustion*. Beijing, China: Foreign Languages Press; 1987.

Adrian White, MD, BM, BCh, Peninsula Medical School, Plymouth, England, via e-mail, January 22, 2007.)

In these RCTs, the SMDs for acupuncture were moderate to large compared with both waiting list and usual care controls.^{49,51,52} Compared with the sham acupuncture control (Table 2), acupuncture showed significant, but small effects at the short-term follow-up time point⁴⁸ for 2 of the RCTs^{49,51}; one RCT showed large effects⁵⁰ and the other showed no effect.⁵² One large trial that administered monthly maintenance treatments had statistically significant results for pain and function at 26 weeks.⁴⁹ Two of the studies^{51,52} showed no significant long-term effect, although both showed a trend in favor of acupuncture for both outcomes at both time points. The investigators for the RCT that showed no significant short-term effect suggested that the lack of effect may reflect either the placebo effect or a physiological effect of needling. The sham acupuncture control in that study involved minimal depth needling at 10 sites not defined by traditional Chinese acupuncture as acupuncture points, in contrast to other studies^{49,71} that have attempted to minimize the physiological effects of sham needling by mostly using nonpenetrating needle placement. The definition of an appropriate sham acupuncture control is still not resolved and is a point of serious consideration when interpreting the results of sham-controlled acupuncture trials.⁷²

How do the effects of acupuncture compare with other knee osteoarthritis treatments? Based on the SMDs alone (Table 1), the effects of some of the other knee osteoarthritis treatments (relative to placebo) are larger than the effects of acupuncture (relative to sham acupuncture). However, direct comparisons are difficult because the various SMDs presented in Table 1 are associated with varying levels of evidence and lengths of follow-up. For example, while the SMDs for the pain outcome for intra-articular corticosteroids would be considered of a moderate size, these SMDs are from a meta-analysis that included 5 RCTs with a total of only 283 participants, and most of the evidence was from the time period 2 weeks after injection.²⁸ Two studies did have longer-term follow-up, however, and those results were also significant.

Safety Considerations in the Use of Acupuncture

In a systematic review of the English literature of adverse effects of acupuncture from 22 countries between 1965 and 1999, Lao found a total of 202 case reports, half of which were from the United States.⁷³ The most common complications were infections and internal organ and tissue injuries. Eighty percent of the infections reported (94 cases) were hepatitis. However, since 1988, there were no new cases of hepatitis, and only 8 cases of infections of any type associated with acupuncture. This may reflect the introduction of US certification requirements for clean needle techniques and the use of disposable needles, which are required by law in most states. Even less frequent were inter-

nal organ and tissue injuries—60 cases over the 35 years. More common adverse effects were local bruising, pain at the needle site, light-headedness, and minor bleeding. The 4 acupuncture trials in Table 2 reported no adverse events except bruising. It appears that the risks from acupuncture are minimal when acupuncturists are licensed, use disposable needles, and practice clean needle techniques. However, patients should inform their acupuncturist if they are taking anticoagulant medication or have a cardiac pacemaker.^{74,75}

Adverse effects of pharmacological treatments for knee osteoarthritis include gastrointestinal and cardiac toxicity in the case of NSAIDs⁷⁶ and acute liver failure from acetaminophen.⁷⁷ Acetaminophen can elevate liver enzyme levels in healthy adults, even when taken in recommended doses over a short period of time.⁷⁸

Diagnosis and Treatment of Osteoarthritis With Acupuncture

The wide variety of schools of acupuncture range from those teaching traditional forms of practice that stem from TCM, to Western styles, such as trigger point therapy, to approaches that are a hybrid of Western and traditional practices. As a result, there are many distinct styles of practice. Acupuncturists trained in more Westernized schools of thought, for example, are likely to treat patients based on tender “trigger” points on the body. On the other hand, TCM practitioners will base their treatment on TCM tongue and pulse diagnosis, as well as history taking that includes discussion of the nature of the symptoms and the patient’s likes, dislikes, and lifestyle.

On the whole, in all schools of acupuncture, treatment is individualized to each patient. In TCM, while certain points may be typically used to treat arthritis-type symptoms, disease classifications do not exist in the same sense as in Western medicine. Each patient is usually evaluated at every session to treat the underlying “root” cause of the problem, as well as its “branch” aspects, or presenting symptoms.⁵⁹ This may result in some needling in the vicinity of the painful area and some distal needling, with points chosen varying from treatment to treatment, depending on the diagnosis at the start of each patient visit.

Parameters of needling may also vary among practitioners and acupuncture schools. Variations include depth of needle penetration, number of needles used, diameter (0.12–0.34 mm) and length (0.5–3 inches) of the needles, and the length of time that needles are left in place. Different types of needle stimulation (eg, manual, heat, electrical) may be used. In general, acupuncturists consider stimulation important to elicit the sensation of *de Qi* or “arrival of Qi” (a localized, dull, heavy, tingling feeling, sometimes described as the “grab” of the needle by the muscle).⁷⁹

No strict rules can be applied to treatment duration. However, 1 “dose” will usually not be sufficient and, in general, a course of treatment should run over a number of weeks. In all recent trials of acupuncture for knee osteoarthritis,

acupuncture was administered 1 to 2 times a week for a minimum of 8 weeks, with some protocols continuing treatment sessions on a tapering basis over longer periods.⁴⁹⁻⁵¹ Treatment usually involved at least 8 needles left in place for approximately 30 minutes.

Choosing a Practitioner

How would Mrs A find an acupuncturist, and how are they regulated? Most acupuncturists in the United States are non-physicians; many have trained at the 47 accredited acupuncture schools in this country (the Accreditation Commission for Acupuncture and Oriental Medicine [<http://www.ACAOM.org>]). Regulation of acupuncture practitioners is on a state-by-state basis; 44 states currently have legislation in place (AOMAlliance [www.aomalliance.org]). Some have their own licensing examinations, while many accept those of the National Commission for the Certification of Acupuncture and Oriental Medicine (a list of their diplomates can be found at <http://www.nccaom.org>). Acupuncture is also practiced by some physicians, although training for such providers is not required in most states. However, training programs specifically for physicians have been developed. Physician acupuncturists who are members of the American Academy of Medical Acupuncture (<http://www.medicalacupuncture.org>) have had 220 hours of formal training and 2 years of clinical experience.

Communication between the patient's physician and acupuncturist is important, as acupuncture should be part of a multidisciplinary approach to osteoarthritis. In addition, if TCM practitioners and acupuncturists use other modalities, such as herbs, adverse effects and potential for interactions with prescription or over-the-counter drugs should be assessed.

Costs

Typical costs for acupuncture will vary depending on the region of the country and can range anywhere from \$65 to \$125 per session. Currently, there is no national standard for third-party insurance coverage regarding acupuncture, but coverage is increasing. In 2002, 33% of employers offered acupuncture as a covered health benefit, and by 2004 this had increased to 47%.^{75,80} Medicare and Medicaid do not reimburse for acupuncture.

The Future of Acupuncture in the United States

A recent report on CAM by the Institute of Medicine recommends "integrative" models of care as safety and efficacy is established.⁸¹ Most clinicians, in line with ACR and other recommendations, already use multidisciplinary approaches in the management of osteoarthritis, recognizing that most available treatments have small effects and that different treatments used concurrently may provide incremental improvements.⁸² Adding acupuncture as one option in a multimodal approach may increase costs. While 1 long-term study found that cost may be off-set by postponement of surgery, further research is needed.⁸³

With continued advances in modern technology and genetic research, it may become possible to determine why some individuals respond to acupuncture and others do not. Some characteristics under study include brain cholecystokinin levels⁸⁴⁻⁸⁶ and the effects of genotype on sensitivity to acupuncture analgesia.⁸⁷

RECOMMENDATIONS FOR MRS A

Mrs A has recently returned from skiing with pain and swelling in the her knee, so she likely should see her orthopedist to determine whether she has a new injury. To deal with the pain, Mrs A emphasized that she felt it important for physicians to take a holistic approach, with emphasis on the mind-body interconnection. I agree with her and recommend the Arthritis Foundation's self-help program⁸⁸ as a way to learn more about arthritis and how to help herself. Mind/body techniques, such as mindfulness-based stress reduction, can also help with chronic pain.^{89,90} She is interested in nonpharmacological approaches to pain management, and I would also recommend she try a course of acupuncture treatments, but first she may want to check if her insurance company now provides coverage under her plan. I expect acupuncture will provide relief in the short run, but I don't have good answers for the long-term impact. Although a very active person, Mrs A is not on an exercise regimen designed to address her knee problems. I strongly recommend physical therapy, in particular an exercise program designed to strengthen her quadriceps.⁹¹ Particularly during the early stages of physical therapy when her pain may increase, Mrs A may want to consider taking a course of acetaminophen or NSAIDs, as long as she has no contraindications. She should be advised that as long as she is tolerating them well, taking NSAIDs regularly over this time, rather than sporadically, should improve her pain control. Mrs A mentioned that glucosamine and chondroitin seemed to have helped her, but that she had not taken it consistently. In light of this, although evidence to support its effectiveness is weak,^{30,31} she could consider taking glucosamine and chondroitin sulfate on a continuous basis. Finally, I would also recommend she continue to wear a knee brace for tennis and skiing, as these activities could exacerbate pain and accelerate the worsening of her osteoarthritis.

QUESTIONS AND DISCUSSION

DR DELBANCO: The experimental psychology literature demonstrates that patient expectations make a big difference in clinical trials. When we randomize patients for clinical trials, we rarely control for their expectations. Should we?

DR BERMAN: Clinical improvement in a patient's condition with respect to pain treatments can be due to many factors, including (1) natural history and regression to the mean, (2) specific effects of treatment, and (3) nonspecific effects of treatment, including patient and physician expectations, beliefs, and interaction. These nonspecific or so-called placebo effects can play a role in all interactions between patient and

provider and are found with drugs, surgery, psychotherapy, medical devices, diagnostic tests, and acupuncture.⁹²

In our study,⁴⁹ we did not look specifically at the relationship between patients' expectations and their response to treatment, but we attempted to control for these effects by randomly assigning participants, using adequate allocation concealment, either education or true or sham acupuncture arms.

This issue of an adequate control for acupuncture RCTs is complex and has received a great deal of attention.^{93,94} Some researchers believe that the incidental (placebo) factors in nonpharmaceutical therapies are intertwined with the characteristic (specific effects), and that the use of sham or placebo-controlled designs for complex interventions may lead to false-negative results.⁹⁵ In addition, nonspecific factors, such as a patient expectations and beliefs regarding a potentially beneficial treatment, may modulate activity in the midbrain.⁹⁶

DR DELBANCO: So whenever we send someone to a pain specialist, we know they're going to get better before they arrive at the door?

DR BERMAN: Pain is a multifaceted problem, and the mind and brain play a role in how we perceive it. At the extreme end, we're all familiar with accounts of phantom limb pain and, conversely, accounts of soldiers who are wounded and experience no pain while in the midst of the battle. Whether we send someone to a pain specialist or enter them in a study, the attention they experience or anticipate will probably affect them.

MRS A: I just want to say to physicians here how important it is to experiment and look at alternative sources for patients with chronic problems. I work with a lot of doctors who have blinders on. I get in lots of trouble talking about alternative therapies, because I think they threaten doctors. I will absolutely follow through with what Dr Berman is recommending.

QUESTION: Can you explain the difference or the rationale for using electrical acupuncture vs nonelectrical acupuncture, vs acupuncture with moxibustion? And maybe tell us a little bit about the differences between Chinese and Japanese acupuncture?

DR BERMAN: Japanese acupuncture and Chinese acupuncture are very different. Japanese acupuncture often involves relatively superficial needling and is less invasive, with less needle manipulation. Chinese acupuncture tends to involve deeper penetration of the needles, active needle manipulation, and often electrical stimulation.

Use of electrical stimulation is largely a factor of the style of acupuncture used and the acupuncturist's training. A lot of acupuncturists in China and in the US combine needles with electrical stimulation. Particularly in the case of chronic conditions, like osteoarthritis, it seems to be more effective. Han's work in Beijing⁶² has shown that different electrical frequencies stimulate different neurochemicals: low frequencies up to 10 Hz stimulate endorphins, higher frequencies around 100 Hz stimulate serotoninlike substances. Additionally, low frequencies tend to have a longer duration of effect.

Moxibustion is used in TCM practice when, in the case of arthritis, there is a diagnosis of "cold-related Bi Syn-

drome."⁹⁷ The aim is to counteract the cold by introducing heat into the treatment. However, due to its strong aroma, moxibustion isn't often used in hospitals in the US.

QUESTION: You studied a very specific protocol of acupuncture and showed some benefit. If, as referring physicians, we send somebody to an acupuncturist, how likely is it that he or she would get that protocol, and is that something that should be important to us?

DR BERMAN: There are many styles of acupuncture, and in clinical practice the treatment is usually individualized to the particular person. So, it's not likely the acupuncturist would use our specific protocol. In our study we used a protocol that covered the main TCM syndromes for osteoarthritis and did not individualize the treatment. Most acupuncturists would probably use many of the same points eventually. There haven't been studies to let us know if an individualized approach works better than formula acupuncture.

QUESTION: I have a lot of colleagues that graduated from China and now practice acupuncture in America. They tell me that acupuncture works well for Western patients, but not that well for the Oriental patients. What's your opinion?

DR BERMAN: I am not aware that Westerners do better with acupuncture than Asians. However, I think cultural factors, which include expectation and beliefs, are all extremely important influences on the outcomes of many treatments, acupuncture included. Through our NIH-funded collaborative research center with the Chinese University of Hong Kong, we are now studying the efficacy of TCM in its native setting, with the collaboration and cooperation of indigenous people and practitioners. We hope to improve our understanding of the effects of cultural predispositions, both indigenous and Western, and observe cultural factors that may modify the impact of treatment.

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