



Acupuncture for chronic pain

Peter T. Dorsher, MSc, MD

From the Department of Physical Medicine and Rehabilitation, Mayo Clinic, Jacksonville, Florida.

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Review

Acupuncture has been used to treat health conditions including pain for over 3000 years, yet it has only been in the last half a century that biochemistry and neural imaging advances have allowed scientific understanding of its physiological mechanisms. This treatise reviews the multiple lines of evidence that the endogenous opioid system is involved in acupuncture's pain-relieving mechanisms, and that the peripheral and central nervous systems are intimately involved in the transduction of acupuncture point stimulation via needling. Large, scientifically rigorous, controlled clinical trials of acupuncture for treating neck, lumbar, migraine, knee osteoarthritis, and other pain conditions have been performed in the last 2 decades that confirm acupuncture's clinical efficacy in treating chronic pain. Beyond its demonstrated efficacy in treating chronic pain, acupuncture's excellent safety record and cost-effectiveness compared to other interventions for chronic pain offer the potential that increased incorporation of acupuncture in managing patients with chronic pain could reduce the costs associated with their health care.

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Acupuncture is a part of the practice of traditional Chinese medicine (TCM), which is the most enduring healing tradition. Its tenets were formally described 200 BC in the *Nei Jing* text¹ that is believed to represent the culmination of at least 2000 years of clinical experience in treating human illness.² Acupuncture theory and practice have continued to evolve since then based on further clinical experience as well as the application of new materials and technologies (improved metallurgy in needle fabrication and use of electricity to stimulate acupuncture needles, as examples).

Although the Dutch–East Indian Trading Company and Jesuit missionaries brought the acupuncture tradition to Europe as early as the 1600s,³ it was not well known in North America until the “Ping-Pong” diplomacy of the Nixon administration in the 1970s, when journalist James Reston reported its remarkable pain-relieving effects in relieving

his postoperative pain after he underwent an emergent appendectomy while reporting in China.⁴ Acupuncture is probably best known for its use in treating pain conditions in the West, but only about 30% of acupuncture literature concerns its use for treating pain.³ The vast majority of the acupuncture literature reflects its use in other health disorders ranging from asthma to cancer to dermatitis to psychosis to xerostomia.³

Although the primary clinical indications of most of the 361 classical acupuncture points are for treating nonpainful medical conditions, all but 2 acupoints have at least 1 described pain indication.^{1,5}

Epidemiology

In North America, acupuncture is considered part of “complementary” medicine practices—a supplement to allopathic medicine rather than a substitute for it. Traditional medicine including herbal remedies, acupuncture, and massage represent 40% of the health care delivered in China⁶

Address reprint requests and correspondence: Peter T. Dorsher, MSc, MD, Department of Physical Medicine and Rehabilitation, Mayo Clinic, 4500 San Pablo Road, Jacksonville, FL 32224.

E-mail address: dorsher.peter@mayo.edu.

and was the first-line treatment for ~28% of respondents in one survey there.⁷

Although other complementary medicine measures such as chiropractic or osteopathic manipulation or massage are more frequently used than acupuncture by the US population, acupuncture's use has expanded in the last 3 decades, with 1% (~2.1 million) of surveyed individuals having reported receiving recent acupuncture treatment, translating to an economic impact of US\$5 billion in 2006.⁸ In 1998, the out-of-pocket economic impact of complementary health care expenditures was conservatively estimated at US\$27 billion—about the same as the out-of-pocket expenditures for US physician services that year.⁹

As the world's aging population's health care costs increasingly strain national budgets, acupuncture offers a cost-efficient, safe treatment that could potentially lead to reducing the cost of delivering health care.

What is acupuncture?

In the 1600s, Jesuit missionaries coined the term acupuncture from the Latin *Acus* (needle) and *punctura* (puncture) based on their observations of this healing tradition in use in China. The term acupuncture describes a group of procedures that stimulate precise anatomical locations by a variety of techniques to produce clinical effects. The style of acupuncture described in TCM will be considered in this treatise, but many other acupuncture styles have been described in the 20th century including Nogier auricular acupuncture,¹⁰ Koryo hand acupuncture,¹¹ Yamamoto scalp acupuncture,¹² and Po abdominal acupuncture.¹³ Acupuncture points can be stimulated by surface pressure (acupressure), insertion of needle without manipulation, insertion of needle with manipulation (twisting and/or thrusting of needle), heating of acupuncture needles through radiant heat or moxibustion, electrical stimulation of inserted needles, or laser stimulation of acupuncture points depending on practitioner preferences and/or desired treatment effects.

The Chinese characters for acupuncture points are 穴 (*xué* = hole, cave) and 位 (*wèi* = position, location). There are 361 classical acupoints, 95% of which were described by AD 200, that reflect the most frequently used and/or clinically important points described as of that time.¹ There have been many other clinically important acupuncture points described since that time (the so-called “miscellaneous” and “new” acupuncture points).¹

The acupoints are located in palpable depressions in the body surface between muscles, tendons, and/or bones. Acupuncture references 1 and 5 describe the approximate site of each acupuncture point using distances from major surface anatomic landmarks and also describe for each point the proper depth and direction of needle insertion there. To account for individual variations in body habitus, the *cun* system for measurement of acupoint locations was developed. Defined as the width of the interphalangeal joint of the

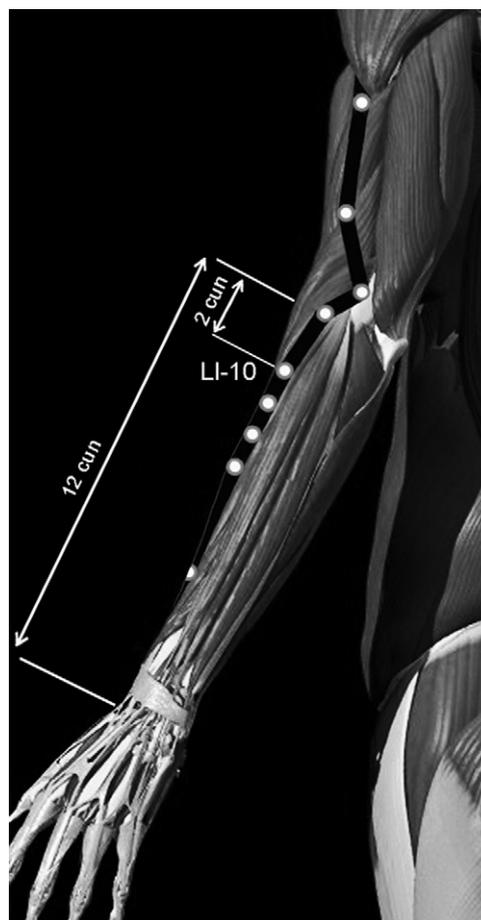


Figure 1 Cun system for localizing acupuncture point LI-10 two cun below the lateral elbow crease.

patient's thumb,^{1,5} the *cun* system for measuring distances on the patient's body surface serves to normalize size differences between individuals when localizing acupoints. For example, acupoint li-10 is described as being located in a depression 2 cun below the elbow crease on a line connecting li-11 (located in the depression at the lateral elbow crease) to li-5 (located at the lateral/radial wrist crease in the depression between extensor pollicis longus and brevis tendons) as demonstrated in Figure 1.⁵ In TCM practice, the acupuncture needle is inserted in the palpable depression at the described acupoint location until (optimally) the *deqi* sensation from needling is experienced by the patient. The *deqi* sensation may be described as numbness (A-beta fiber activation) or as an aching, dull, sore, heavy, and/or warm sensation (A-delta and C fiber activation).¹⁴⁻¹⁶

Classical acupuncture points with similar therapeutic properties are arranged on meridians, as shown in Figure 2A, B. There are 12 Principal meridians symmetrically arranged around 2 midline meridians (one on the anterior surface of the body and another on the dorsal aspect of the body). Beyond creating conceptual interconnections of acupoints with similar therapeutic properties, the meridians are postulated to have arisen from observing the phenomenon of the spread of *qi* (~energy) sensation from therapeutically

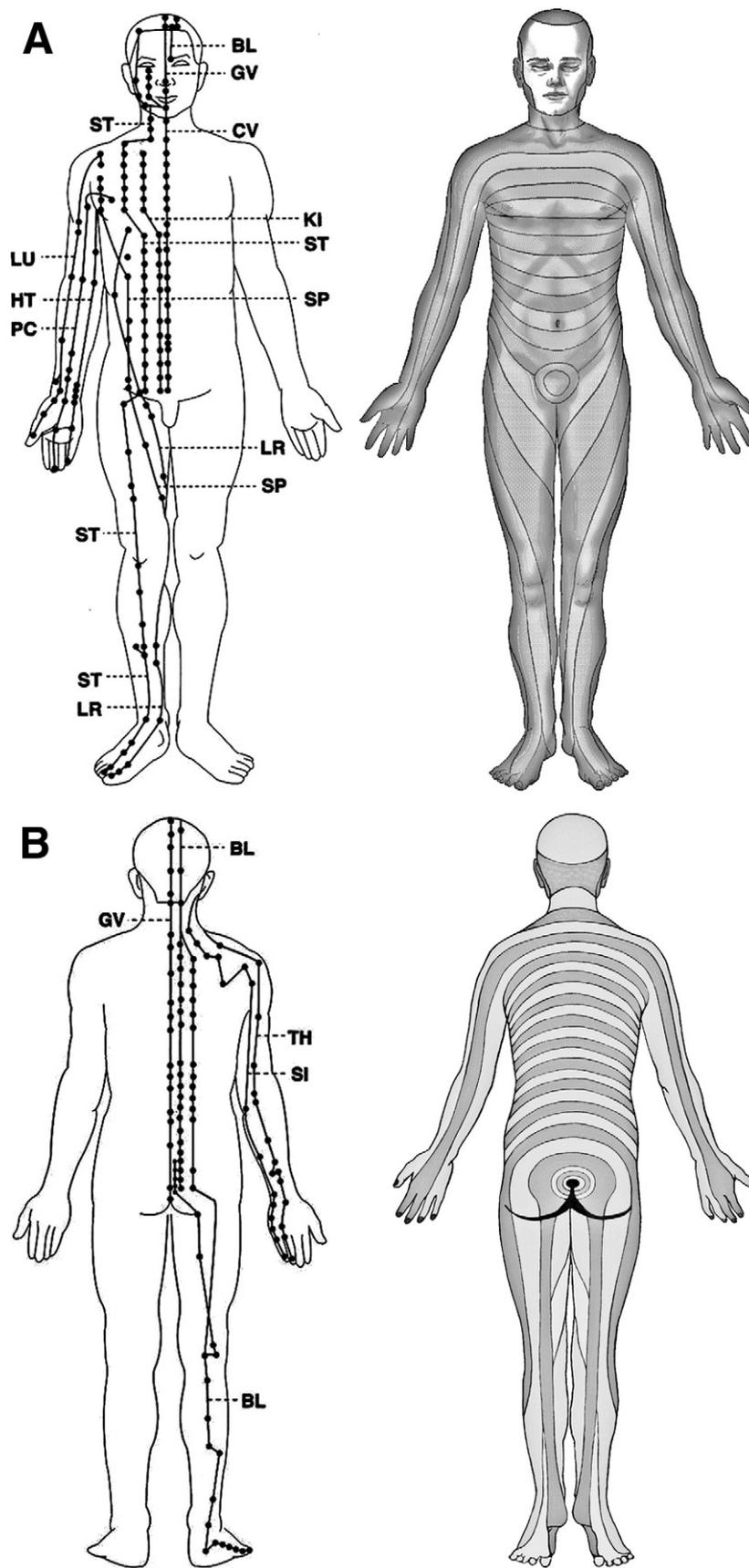


Figure 2 (A) Acupuncture meridians and dermatomes-anterior view. (B) Acupuncture meridians and dermatomes-posterior view.

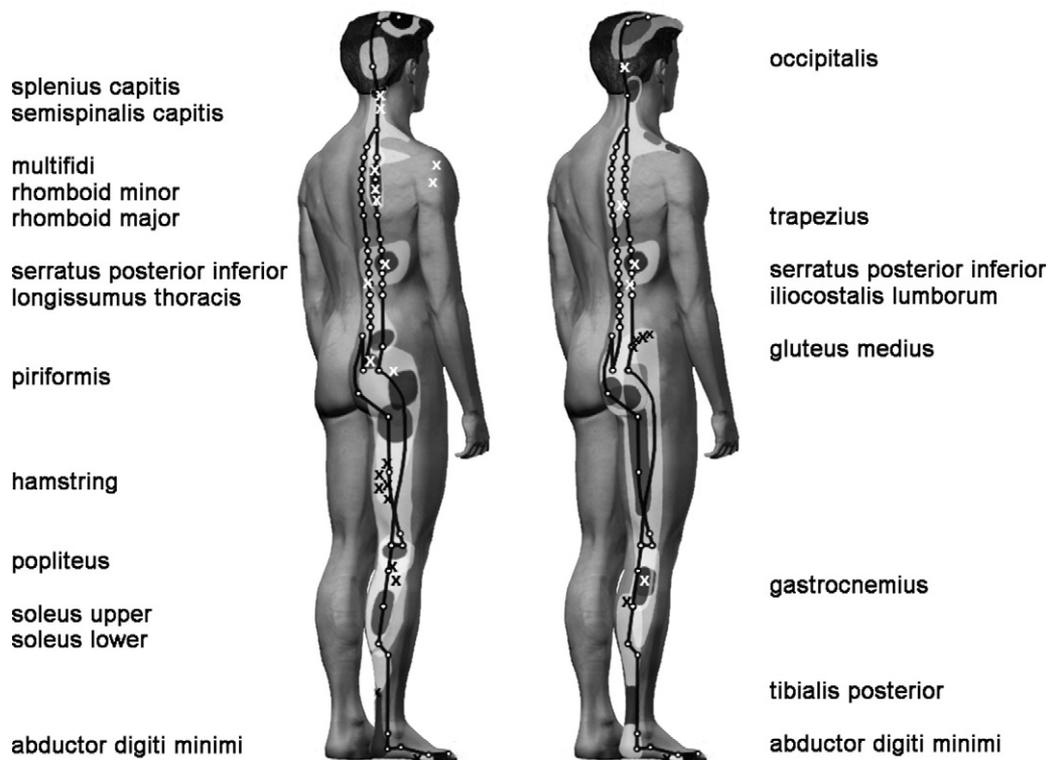


Figure 3 Myofascial referred-pain patterns sum to reproduce the course of the bladder meridian. Thin black line is the bladder meridian with classical acupoints shown, concentrated referred pain shaded gray within lesser referred pain shaded white.

related acupoints when stimulated.¹ The spread of *qi* from anatomically proximate acupoints with similar therapeutic properties coalesced (overlapped) to form linear structures termed meridians or channels. The clinical phenomenon of the spread of *qi* with acupoint stimulation is conceptually similar to that of inducing referred-pain with trigger point stimulation in the myofascial pain tradition,¹⁷ and the referred-pain data from Travell and Simons^{17,18} actually serves to confirm the physiological presence of the acupuncture meridians.¹⁹ This is demonstrated in Figure 3.

Each of the 12 Principal meridians is named for the organ it is associated with. Eleven of these meridians are named the Kidney, Heart, Bladder, Small Intestine, Spleen, Lung, Large Intestine, Stomach, Liver, Gallbladder, and Pericardium organs, while the other meridian is named the Triple Energizer organ, while the other meridian is named for the triple energizer organ, which has at least some overlap with the Western concept of the hypothalamic-pituitary-adrenal axis. Blood and *qi* are perceived to flow through these meridians. A discussion of TCM organ theory is beyond the scope of this article, but it is important to realize that certain points on a given meridian have clinical effects on the organ associated with that meridian—point Gallbladder 34 near the fibular head can be needled to treat symptoms of acute cholecystitis, for example. A future report will document how the effect of peripheral nerve stimulation on organ function may arise from the somatotopic mapping of the autonomic nervous system along the peripheral nervous system.

How does acupuncture influence pain?

In TCM, pain results when the normal cyclic flow of blood and/or *qi* in a meridian is interrupted (Figure 4). The pain may be felt locally or along the meridian as well. The acupuncturist needles not only the local site of pain where tenderness is present, but also distal points on the involved meridian (that crosses the local pain site) to attempt to restore normal circulation of blood and *qi* in the meridian. These distal acupuncture points used to treat pain are located at or below the elbow or knee joints. Discussion of the distal point selection is beyond the scope of this article. This stimulation of acupoints distant to the site of pain to ameliorate pain is perhaps the greatest difference between Eastern and Western approaches for treating pain.

The Trigger Point Manual,^{17,18} however, does give contemporary examples of distal myofascial trigger points that can be treated to reduce pain at distant anatomic sites. As examples, there is a trigger point in the soleus muscle that causes only distant referred pain in the lumbar region, and another in that muscle that is associated with ipsilateral cheek pain.¹⁸

Note that in the extremities the acupuncture meridians follow dermatomal/myotomal distributions (Figure 2). In the lower extremities, the Spleen meridian follows an L4 distribution, the Gallbladder an L5 distribution, the Bladder meridian an S1 distribution, and the Kidney meridian an S2 distribution. Since the urinary bladder has innervation from S2-S4 roots, it should not be surprising that 2000+-year-old

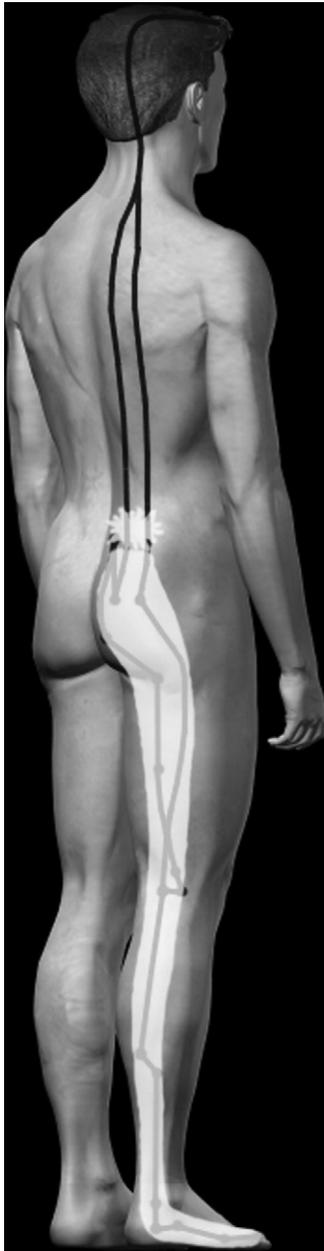


Figure 4 Right S1 radiculopathy shown in white shade obstructing the flow of energy and blood in the underlying Bladder meridian, which follows an S1 course.

acupuncture texts report that stimulation of the Kidney-3 point (located posterior to the medial malleolus on the tibial neurovascular bundle) can regulate bladder contractility.

Experimental evidence of acupuncture's efficacy

Pomeranz's work in the 1970s demonstrated the key role of endogenous opioids in acupuncture's pain-relieving effects.^{20,21} Electroacupuncture increased the latency of rat tail withdrawal to heat—this analgesic effect was eliminated

by simultaneous administration of naloxone but not saline.²⁰ Increasing doses of naloxone causes increasing blockade of acupuncture analgesia.²¹ Opiate antagonists will reliably prevent acupuncture analgesia from occurring, but may not fully reverse acupuncture analgesia that is already present (perhaps due to dynorphin activity accounting for some of acupuncture analgesia).^{22,23} Similar findings have been seen in pain studies in humans.²³ Other lines of evidence corroborate these findings including a lack of acupuncture analgesia in animals lacking opiate receptors²⁴ or deficient of endorphins.²⁵ Endorphin levels rise in blood and cerebrospinal fluid and fall in specific brain regions during acupuncture analgesia.²⁶⁻²⁸ Acupuncture analgesia can be transmitted to a second animal by transfer of cerebrospinal fluid or by cross circulation, and this effect is blocked by naloxone.²³

Contemporary neural imaging studies have confirmed the importance of the endogenous opioid system and the central nervous system in acupuncture analgesia. Positron-emission tomography scans demonstrate that acupuncture produces short- and long-term increases in limbic system *mu*-opioid-binding potential and reduction in clinical pain that was not seen in sham acupuncture.²⁹ Functional magnetic resonance imaging studies have demonstrated that acupuncture produces deactivation of limbic structures (including the amygdala, the hippocampus, and cingulate) to a painful stimulus via a mechanism that is distinct from pain and sham stimulation.³⁰⁻³² Thus, by reducing paleocortical activation (including limbic system structures) to painful stimuli without limiting neocortical activation, acupuncture can attenuate the affective/behavioral response to a painful stimulus without altering the ability to localize the site of that painful stimulus.

These biochemical and neuroradiologic studies demonstrate the fundamental importance of the peripheral and central nervous system in the transduction of acupuncture analgesia. Other lines of experimental evidence support this, as transaction¹⁴ or anesthetic block³³ of a peripheral nerve in the distribution of a given acupuncture point will eliminate (or nearly completely eliminate) that point's clinical effects.

Clinical evidence of acupuncture's efficacy

Although acupuncture has been in clinical use for millennia, application of rigorous scientific methodology (randomized, placebo-controlled protocols) to clinical trials studying acupuncture's clinical effects has been a recent phenomenon.

Neck pain

Witt et al³⁴ in 2006 published the results of the landmark German Acupuncture in Routine Care trials that studied 3600 subjects with chronic neck pain to compare the effects of acupuncture to a control intervention consisting of usual

care (medications and physical therapy). Subjects (56.5%) who received acupuncture demonstrated statistically significant ($P < 0.001$) improvements in their neck pain and disability scores compared to only 21.6% of the usual care (control) group. Those receiving acupuncture had nearly a 30% reduction in pain scores vs only 5% reduction in controls; and the physical and psychological function of those receiving acupuncture, as measured by SF-36 scores, likewise, were clinically and statistically ($P < 0.001$) significantly improved compared to the control subjects.³⁴

A 2007 Cochrane review of acupuncture in neck pain³⁵ concluded that for chronic mechanical neck disorders, the literature provides moderate evidence that acupuncture is more effective for pain relief than some types of sham controls when measured immediately posttreatment; that acupuncture is more effective than inactive, sham treatments measured immediately posttreatment and at short-term follow-up; and that there is limited evidence that acupuncture was more effective than massage at short-term follow-up. For chronic neck disorders with radicular symptoms, there is moderate evidence that acupuncture is more effective than a wait-list control at short-term follow-up; that acupuncture relieves pain better than some sham treatments, measured at the end of the treatment; that those receiving acupuncture report less pain at short-term follow-up than those on a waiting list; and that acupuncture is more effective than inactive treatments for relieving pain post-treatment, and this effect is maintained at short-term follow-up.³⁵

Lumbar pain

The GERAC (German Acupuncture Care) study of acupuncture for low back pain³⁶ was a randomized, multicenter, blinded, parallel-group trial that enrolled 1162 patients into 3 arms comparing true acupuncture, sham acupuncture, and conventional treatment (drugs, physical therapy, and exercise). Pain scales and back-specific and global functional scales were used to measure outcomes. Those subjects receiving acupuncture demonstrated clinically and statistically significant improvements in pain and back-related disability scores compared to those receiving conventional treatment (~55% responders in acupuncture groups vs only about 33% of conventional treatment group).³⁶

Cherkin et al³⁷ studied the effects of individualized, standardized, and simulated acupuncture to usual care in 638 individuals with chronic mechanical lumbar pain. The 3 acupuncture interventions consisted of 10 treatments over 7 weeks, while usual care subjects received medications and physical therapy. Outcomes as measured by Roland Morris Disability Questionnaire (RMDQ) and a 10-point visual analog scale back symptom bothersomeness score were measured at 8, 26 and 52 weeks. Those subjects receiving acupuncture interventions all had statistically significant improvements ($P < 0.003$ or less) in their RMDQ scores compared to those receiving usual care at all 3 follow-up intervals, with average improvement of RMDQ score for the

acupuncture groups being ~4.4 points at all follow-ups (compared to an average improvement of 2.6 points for the usual care patients).³⁷ Participants receiving real or simulated acupuncture were more likely than those receiving usual care to experience clinically meaningful improvements on the dysfunction scale (60% vs 39%; $P < 0.001$). Symptom bothersomeness decreased by 1.6-1.9 points in the treatment groups compared with 0.7 points in the usual care group at 8 weeks ($P < 0.001$) and was still significantly reduced ($P < 0.05$) 19 weeks after the last acupuncture treatment.³⁷ After 1 year, participants in the acupuncture treatment groups were more likely than those receiving usual care to experience clinically meaningful improvements in dysfunction (59% to 65% vs 50%, respectively; $P = 0.02$) but not in symptoms ($P > 0.05$).

A recent meta-analysis in 2005 of the acupuncture literature for treating low back pain³⁸ concluded that acupuncture is more effective than sham acupuncture [standardized mean difference, 0.54 (95% CI, 0.35-0.73); 7 trials] and no additional treatment [standardized mean difference, 0.69 (CI, 0.40-0.98); 8 trials] for providing short-term relief of chronic low back pain. This short-term relief seems to be sustained over the longer term, but its sustained effect is uncertain as longer term follow-up data are limited in quantity and quality.³⁸

Other pain studies

Large, placebo-controlled trials have demonstrated acupuncture's efficacy in treating knee osteoarthritis³⁹ and migraine headaches.⁴⁰ The NIH Consensus Conference in 1977 concluded that there was evidence of acupuncture's efficacy in postoperative dental pain and that it may be useful in headache, menstrual cramps, back pain, and fibromyalgia.⁴¹ The World Health Organization in 2003 concluded that there is evidence that acupuncture may be helpful in treating a variety of pain conditions, including dental pain, tennis elbow, sciatica, low back pain, rheumatoid arthritis, headache, migraine, trigeminal neuralgia, intercostal neuralgia, and peripheral neuropathy.⁴²

Acupuncture and placebo response

A major challenge for controlled acupuncture trials has been to find adequate placebo acupuncture interventions, since even minimal needling of skin over acupuncture and nonacupuncture point locations produces physiological responses. Indeed, a functional magnetic resonance imaging study demonstrated that superficial and deep needling at an acupuncture point elicited similar blood oxygen level-dependent responses in the brain.⁴³ A variety of sham acupuncture needles have been designed that do not pierce the skin (eg, the Park⁴⁴ or Streitberger⁴⁵ devices), but these devices are expensive and still stimulate cutaneous sensory fibers that could produce physiological effects (acupressure-like effect rather than acupuncture). Some of the earliest

described devices used in acupuncture practice were designed with blunt tips to stimulate acupoints without piercing the skin.^{1,2} Further, Lund and Lundeberg demonstrated that even touching the skin stimulates mechanoreceptors, which induce emotional and hormonal reactions that serve to alleviate the affective component of pain.⁴⁶ These issues may serve to explain why what has previously been thought to be “sham” acupuncture interventions often have produced clinical benefits similar to “true” verum acupuncture and that are superior clinically to no intervention or standard care.^{36,37,47,48} Infrared lasers for stimulating acupoints have been developed⁴⁹ that can penetrate light energy through the skin up to 4 cm deep. Since the infrared laser is nearly invisible to the naked eye when applied to the skin, this technology may permit true double-blinding (patients and operators) of acupuncture interventions in clinical trials.

Advantages of acupuncture

As outlined above, there is now evidence from large, well-designed, controlled clinical trials that demonstrate acupuncture's clinical efficacy in treating pain conditions including chronic neck and lumbar pain with results (pain, interference with activities, and functional status) superior to those seen with routine care.^{34-40,48} Data on the long-term clinical benefits of acupuncture are still accumulating, but certainly the GERAC and Cherkin et al controlled trials in chronic low back pain demonstrate long-term benefits of acupuncture treatment. The British National Health Service, in fact, now covers acupuncture treatments for low back pain based on their review of the available clinical research data.⁵⁰

Acupuncture is a safe intervention in properly trained hands. In a prospective observational study in Germany by Witt et al⁵¹ of 229,230 patients who received an average of 10 acupuncture treatments (over 2 million treatments total), 19,726 patients (8.6%) reported experiencing at least 1 adverse effect and 4963 (2.2%) reported 1 requiring treatment. The most common adverse effects noted were bruising/hematoma (6.1% of patients, 58% of all adverse effects), pain (1.7%), and vegetative symptoms (0.7%).⁵¹ Two patients experienced a pneumothorax (1 needed hospital treatment).⁵¹ This represents then 1 serious event per million acupuncture treatments, and overall a 0.2% rate for adverse events caused by acupuncture treatments. A British survey of acupuncture providers⁵² covering nearly 32,000 treatments found no serious adverse events and 671 minor adverse events per 10,000 acupuncture treatments. Bleeding was the most common adverse event at 310/10,000 treatments followed by pain from needling at 110/10,000 treatments and symptom aggravation in 96/10,000 treatments. Infections with acupuncture needles are rare particularly since the introduction of sterile, single-use acupuncture needles as part of routine acupuncture practice. Laser acupuncture is virtually risk-free with low-level lasers of 25-100

mW used to stimulate acupoints with no risk of infection or viscus perforation.⁴⁹

The morbidity of acupuncture treatment for pain thus is significantly less than that described for nonsteroidal anti-inflammatory agents (1-4% risk per year of serious gastrointestinal tract complications⁵³). Axial spine injections have a 1-2% risk of infection (although serious infections are less frequent, occurring in ~1/1000-1/10,000 procedures).⁵⁴ Complications from epidural injections include clinically significant epidural hematomas occurring in 1/4000-1/10,000 procedures and dural tears that can occur in up to 1/200 epidural procedures.⁵⁴ Radiofrequency denervation of lumbar facet joints is reported to have a 1% minor complication rate with local pain lasting over 2 weeks or neuritic pain lasting less than 2 weeks, each occurring in 0.5% of procedures (616 separate procedures studied).⁵⁵

Finally, acupuncture is a cost-efficient intervention. Sterile, disposable acupuncture needles (in quantity) cost between 3 and 10 cents each with typically 10 to 15 needles used in a given treatment session. Treatment sessions typically cost US\$60-\$100 each with acute pain issues often requiring 1-4 sessions to resolve, while more chronic pain issues may require 10-12 sessions to obtain maximal clinical benefit. Willich et al⁵⁶ studied direct and indirect costs of acupuncture treatment as well as incremental cost-effectiveness ratio in 3451 patients with chronic neck pain over a 3-month period. Although acupuncture added about €280 of extra cost over the 3-month period compared to routine care, the incremental cost-effectiveness ratio was nearly €12,500 per QALY (quality adjusted life year) gained and may have been higher if costs of over-the-counter medications had been included.⁵⁶ Health economists generally consider a health intervention cost-effective if it costs less than US\$50,000 per QALY. This cost-effectiveness of acupuncture has also been demonstrated in treatment of headache (£9180 per QALY gained)⁵⁷ and low back pain (£4241 per QALY gained).⁵⁸ These costs then compare favorably to use of long-term medication for low back pain (not cost-effective),⁵⁹ epidural spinal injections for sciatica (£44,701 per QALY),⁶⁰ or surgery (US\$77,600-\$115,600 per QALY gained)⁶¹ for treating chronic back pain from stenosis.

Conclusions

Although acupuncture has been in continuous and evolving clinical use for at least 3000 years, it has only been in the last half century that rigorous scientific methodology has been applied to study acupuncture's mechanisms and clinical effects.

Basic science research demonstrates the intrinsic importance of the endogenous opioid system and the peripheral and central nervous system in transducing acupuncture's clinical effects, including pain relief. In the last 20 years, large, scientifically rigorous controlled clinical trials of acupuncture have demonstrated its efficacy in treating chronic

neck and lumbar pain as well as migraine and knee osteoarthritis pain. Its efficacy for dental pain and nausea/vomiting has also been well established with controlled clinical trials. These effects are not placebo-related, and human and animal experiments have clearly demonstrated administration of mu-opioid antagonists will block acupuncture's pain relieving effects.

Acupuncture is also safe and cost-effective compared to medication, injection, and surgical therapies for chronic neck and back pain. In the setting of aging populations in countries with limited financial resources, the acupuncture tradition offers an efficacious, safe, cost-effective intervention to improve pain, function, and quality of life for a variety of chronic pain conditions.

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