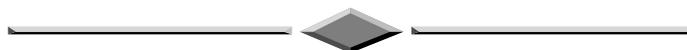
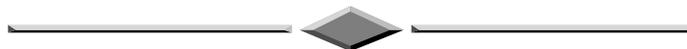


NIH Consensus Development Conference on Acupuncture



**November 3-5, 1997
William H. Natcher Conference Center
National Institutes of Health
Bethesda, Maryland**



Sponsored by:

Office of Alternative Medicine • Office of Medical Applications of Research

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National Institutes of Health

Continuing Medical Education

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Introduction

Acupuncture is a family of procedures involving penetration of specific superficial anatomic locations on the skin called acupuncture points by thin, solid, generally metallic needles. Closely related to and often practiced with acupuncture is moxibustion, the local and focused application of heat to acupuncture points using a compressed, powdered combustible substance (moxa), which is burned at or near the points to be stimulated. Acupuncture and moxibustion are the two best-known aspects of traditional Chinese medicine (TCM) in the United States and are used by many Americans.

There are a variety of approaches to functional diagnosis and treatment in American acupuncture that incorporate medical traditions from China, Japan, Korea, France, and other countries. Because an acupuncture treatment is a procedure like a psychotherapy session or surgery (rather than a drug), it has been difficult to study using the gold standard of randomized double-blind trials. Nevertheless, acupuncture is used by millions of American patients and performed by thousands of physicians, dentists, master's degree-level acupuncturists, and other practitioners for relief or prevention of pain and for a variety of health problems. The Food and Drug Administration, after years of deliberation, recently removed acupuncture needles from the category of "experimental medical devices" and now regulates them just as it does other devices, such as surgical scalpels and hypodermic syringes, under good manufacturing practices and single-use standards of sterility.

Over the years, the National Institutes of Health (NIH) has funded a variety of research on acupuncture, including studies on the mechanisms by which acupuncture may have its effects as well as clinical trials and other studies. There is also a considerable body of international literature on the risks and benefits of acupuncture, and the World Health Organization lists a variety of medical conditions that may benefit from the use of acupuncture and/or moxibustion. Such applications may include prevention and treatment of nausea and vomiting; treatment of pain and addictions to alcohol, tobacco, and other drugs; prevention of pulmonary problems such as asthma and bronchitis; and rehabilitation from neurological damage such as that caused by stroke.

To address the most important issues regarding the American use of acupuncture, NIH has organized this 2¹/₂-day conference to evaluate the scientific and medical data on the uses, risks, and benefits of acupuncture procedures for a variety of conditions. The conference will bring together national and international experts in the fields of acupuncture, pain, psychology, psychiatry, physical medicine and rehabilitation, drug abuse, family practice, internal medicine, health policy, epidemiology, statistics, physiology, and biophysics, as well as representatives from the public.

After 1¹/₂ days of presentations and audience discussion, an independent, non-Federal consensus panel chaired by Dr. David J. Ramsay, president of the University of Maryland

Medical Center, will weigh the scientific evidence and write a draft statement that will be presented to the audience on the third day. The consensus statement will address the following key questions:

- What is the efficacy of acupuncture, compared with placebo or sham acupuncture, in the conditions for which sufficient data are available to evaluate?
- What is the place of acupuncture in the treatment of various conditions for which sufficient data are available, in comparison or in combination with other interventions (including no intervention)?
- What is known about the biological effects of acupuncture that helps us understand how it works?
- What issues need to be addressed so that acupuncture can be appropriately incorporated into today's health care system?
- What are the directions for future research?

On the final day of the meeting, the conference chairperson, Dr. David J. Ramsay, will read the draft statement to the conference audience and invite comments and questions. A press conference will follow to allow the panel and chairperson to respond to questions from media representatives.

General Information

Conference sessions will be held in the Natcher Conference Center, National Institutes of Health, Bethesda, Maryland. Sessions will run from 8:30 a.m. to 5:00 p.m. on Monday, from 8:00 a.m. to 12:45 p.m. on Tuesday, and from 9:00 a.m. to 11:00 a.m. on Wednesday. The telephone number for the message center is (301) 496-9966. The fax number is (301) 480-5982.

Cafeteria

The cafeteria in the Natcher Conference Center is located one floor above the auditorium on the main floor of the building. It is open from 7:00 a.m. to 2:00 p.m., serving breakfast and lunch.

Continuing Education Credit

American Medical Association

The NIH/FAES is accredited by the Accreditation Council for Continuing Medical Education to sponsor continuing medical education for physicians.

The NIH/FAES designates this continuing medical education activity for a maximum of 14 credit hours in Category I of the Physician's Recognition Award of the American Medical Association. Each physician should claim only those hours of credit that he/she actually spent in the educational activity.

American Academy of Family Physicians

An application has been filed with the American Academy of Family Physicians for continuing education credits for this conference.

Sponsors

The primary sponsors of this conference are the NIH Office of Alternative Medicine and the NIH Office of Medical Applications of Research. The conference is cosponsored by the National Cancer Institute; the National Heart, Lung, and Blood Institute; the National Institute of Allergy and Infectious Diseases; the National Institute of Arthritis and Musculoskeletal and Skin Diseases; the National Institute of Dental Research; the National Institute on Drug Abuse; and the Office of Research on Women's Health of the National Institutes of Health.

Agenda

Monday, November 3, 1997

- 8:30 a.m. Welcome
Wayne B. Jonas, M.D., Director, Office of Alternative Medicine
- Charge to the Panel
John H. Ferguson, M.D., Director, Office of the Medical Applications of Research
- Panel Chair Remarks
David J. Ramsay, D.M., D.Phil., President, University of Maryland Medical Center

I. Introduction: History and Status of Acupuncture Treatment

- 9:00 a.m. What Is Acupuncture?
Lorenz K.Y. Ng, M.D., National Rehabilitation Hospital
- 9:20 a.m. Acupuncture: History, Context, and Long-Term Perspectives
Ted J. Kaptchuk, O.M.D., Beth Israel Deaconess Medical Center
- 9:40 a.m. Acupuncture Around the World in Modern Medical Practice
Joseph M. Helms, M.D., American Academy of Medical Acupuncture
- 10:00 a.m. Acupuncture Licensure, Training, and Certification in the United States
Kevin V. Ergil, M.A., M.S., L.Ac., Pacific Institute of Oriental Medicine
- 10:20 a.m. Current Utilization of Acupuncture by United States Patients
Patricia D. Culliton, M.A., Dipl.Ac., L.Ac., Hennepin County Medical Center
- 10:40 a.m. Discussion

II. Issues Affecting Incorporation of Acupuncture Into Today's Health Care System

- 11:15 a.m. Methodological and Ethical Issues in Acupuncture Research
Richard Hammerschlag, Ph.D., Yo San University of Traditional Chinese Medicine

Monday, November 3, 1997 (continued)

11:40 a.m. Safety and Regulation of Acupuncture Needles and Other Devices
C. David Lytle, Ph.D., U.S. Food and Drug Administration

11:55 a.m. Discussion

12:30 p.m. Lunch

III. Efficacy of Acupuncture in Treating Various Conditions

1:30 p.m. Acupuncture Activates Endogenous Systems of Analgesia
Ji-Sheng Han, M.D., Beijing Medical University

1:50 p.m. Overview of Clinical Trials on Acupuncture for Pain
Brian M. Berman, M.D., University of Maryland School of Medicine

2:10 p.m. Efficacy of Acupuncture in Treating Low Back Pain: A Systematic Review
of the Literature
Daniel C. Cherkin, Ph.D., Group Health Center for Health Studies

2:30 p.m. Overview of the Efficacy of Acupuncture in the Treatment of Headache
and Face and Neck Pain
Stephen Birch, L.Ac., Ph.D., Anglo-Dutch Institute for Oriental
Medicine

2:45 p.m. Efficacy of Acupuncture in the Treatment of Osteoarthritis and
Musculoskeletal Pain
Gary Kaplan, D.O., Medical Acupuncture Research Foundation

3:00 p.m. Discussion

3:30 p.m. Dental and Postoperative Pain
Lixing Lao, Ph.D., L.Ac., University of Maryland School of Medicine

3:45 p.m. Neuropathic Pain
Judith C. Shlay, M.D., Denver Public Health

4:00 p.m. The Role of Physiologic Imaging in the Investigation of the Effects of Pain
and Acupuncture on Regional Cerebral Function
Abass Alavi, M.D., Hospital of the University of Pennsylvania

4:15 p.m. Summary of Acupuncture and Pain
Bruce Pomeranz, M.D., Ph.D., University of Toronto

4:35 p.m. Discussion

5:00 p.m. Adjournment Until Tuesday

Tuesday, November 4, 1997

8:00 a.m. Nausea and Vomiting
Andrew Parfitt, Ph.D., National Institute of Child Health and Human Development

8:20 a.m. Neurological Rehabilitation: Acupuncture and Laser Acupuncture To Treat Paralysis in Stroke and Other Paralytic Conditions and Pain in Carpal Tunnel Syndrome
Margaret A. Naeser, Ph.D., Lic.Ac., Dipl.Ac., Boston University School of Medicine

8:40 a.m. Acupuncture and Addictions
Janet Konefal, Ph.D., Ed.D., M.P.H., C.A., University of Miami School of Medicine

9:00 a.m. Discussion

9:30 a.m. Respiratory Indications
Kim A. Jobst, D.M., M.R.C.P., Gardiner Institute

9:50 a.m. Gastrointestinal Indications
David L. Diehl, M.D., University of California, Los Angeles

10:10 a.m. Induction of Ovulation With Acupuncture
Jin Yu, M.D., Shanghai Medical University

10:35 a.m. Discussion

IV. New Horizons for Acupuncture

11:05 a.m. Protective Effect of Acupuncture on Immunosuppression
Xiao-Ding Cao, M.D., Ph.D., Shanghai Medical University

- 11:30 a.m. Late-Breaking Data and Other News from the Clinical Research Symposium (CRS) on Acupuncture at NIH
Hannah V. Bradford, M.Ac., Society for Acupuncture Research
- 11:50 a.m. American Acupuncture: Primary Care, Public Health, and Policy
Alan I. Trachtenberg, M.D., M.P.H., National Institute on Drug Abuse
- 12:10 p.m. Discussion
- 12:45 p.m. Adjournment Until Wednesday

Wednesday, November 5, 1997

- 9:00 a.m. Presentation of the Consensus Statement
- 9:30 a.m. Public Discussion
- 11:00 a.m. Panel Meets in Executive Session
- 1:00 p.m. Press Conference
- 2:00 p.m. Adjournment

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Abstracts

The following are abstracts of presentations to the NIH Consensus Development Conference on Acupuncture. They are designed for the use of panelists and participants in the conference and as a reference document for anyone interested in the conference deliberations. We are grateful to the authors, who have summarized their materials and made them available in a timely fashion. Abstracts for the following presentations do not appear:

Acupuncture Around the World in Modern Medical Practice—Joseph M. Helms, M.D.

Respiratory Indications—Kim A. Jobst, D.M., M.R.C.P.

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What Is Acupuncture?

Lorenz K.Y. Ng, M.D.

Introduction

Taken at face value, the question “what is acupuncture?” is deceptively simple. The word *acupuncture* is derived from two Latin roots, *acus*, meaning “needle,” and *punctura*, meaning “puncturing.” Acupuncture, therefore, refers to the insertion of needles through the skin into underlying tissues at different depths and at strategic points on the body to produce a desired therapeutic effect. However, although the definition of acupuncture requires that the needle be a necessary condition, it is not a sufficient condition, just as a scalpel does not give us an adequate definition of what surgery is. The act of puncturing with a needle to accomplish a desirable therapeutic effect cannot be separated from the context in which the needle is being used: how the needle is being used, where in the body it is inserted, when and why. What we will try to accomplish here in the next 2 days is to find out what is known about the biological effects of acupuncture, whether it is more effective compared with placebo in certain conditions, how it can be used either by itself or adjunctively, in combination with other treatment modalities, and how it can be appropriately incorporated into today’s health care armamentarium. Finally, what are the gaps in our knowledge and the directions for future research?

Traditional Chinese Medicine and Western Scientific Medicine

Acupuncture is part of Traditional Chinese Medicine (TCM), a system of healing that is empirically derived over several millennia. Philosophically based from observations of nature, TCM views the human organism as a microcosm of the larger cosmos. As such, it is holistic and spiritualistic. The theoretical structure of TCM derives from its medieval origin and is both complex and metaphorical. It is pattern oriented, and its approach qualitative and analog. Western scientific medicine, on the other hand, is mechanistic and reductionistic in its orientation and quantitative and digital in its approach (see Table 1). Historically, this paradigm shift may be traced to the 17th century French philosopher Descartes, who split the human being into mind and body. This mind-body dualism permitted the study of the body without bothering with the mind. The mind was believed to have more to do with the soul, and hence remained the domain of the Church. This separation of body from mind enabled doctors and scientists in the Western world to study the body without worrying about the soul. It was largely responsible for the establishment of the anatomical and structural bases upon which the biomedical model of Western scientific medicine has evolved. This scientific biomedical model, embracing the prevailing strategy of reductionism, has been applied to the study of diseases with remarkable results. The success of this biomedical model in the area of infectious diseases has given us germ

theory and the concept of pathogenesis. Now, molecular biology can provide us with the answer to our quest for etiology. These are dazzling, irresistible concepts and accomplishments resulting from our systematic feats of reductionism and digitization.

Within this framework, how are we to view Traditional Chinese Medicine, and specifically acupuncture, since they were developed before the advent of scientific methodology. This predicament was poignantly presented by Lu and Needham:

“The theoretical structure of Traditional Chinese Medicine is indeed medieval, but at the same time subtle and sophisticated; it never lost sight of the psycho-physical organism as a whole, Explanations of the effects of acupuncture today tend to be in terms of neurophysiology, neurobiochemistry, endocrinology and immunology, sciences of which the old Chinese physicians necessarily knew nothing. We are consequently faced with the profoundly difficult problem of translating the medieval theories into terms of modern science, a process that may prove impossible, yet traditional physicians used them for some 2.5 millennia for organizing their vast clinical experience. There is a paradox here not yet resolved.”

The challenge, I would submit, is not whether we can literally translate medieval metaphors of healing into terms of modern science. Rather, the task could be posed differently: Can the phenomena and practices observed in Traditional Chinese Medicine offer us some insight from which we can draw parallels for systematic studies? Just to mention some of these parallel concepts and constructs that have emerged: The concept of yin and yang balance finds its modern equivalence in Claude Bernard's *milieu interieur* and Walter Cannon's doctrine of homeostasis. The TCM concept of flow of qi and blood through the body in rhythmic fashion has its material counterpart in William Harvey's discovery of blood circulation and the concept of chronobiology elaborated by Franz Halberg. Similarly, certain acupuncture points may have their equivalence in motor points and myofascial trigger points, leading Melzack et al. to comment that this close correlation suggests that trigger points and acupuncture points for pain, though derived independently and labeled differently, represent the same phenomenon and can be explained in terms of the underlying neural mechanism.

Indeed, to frame the question in a modern context, can the TCM analog model of healing and therapeutics be digitized without losing its essence and efficacy? Can the emperor be stripped of his clothing and yet retain his potency?

Toward the Development of an Acupuncture Treatment Paradigm

It has been claimed that the therapeutic efficacy of acupuncture is what has kept it in existence through so many centuries of use. Our task today is to examine the evidence in support of this hypothesis within the current scientific framework at both the basic and clinical levels. Are the observed effects and effectiveness the result of specific and quantifiable components of the acupuncture procedure, or do they derive from placebo (i.e., nonspecific) factors? What are the key basic elements that may be responsible for therapeutic efficacy? Is the needle insertion a critical component or is the stimulation itself the important component? Is the combination of

needle with manual or electrical stimulation more effective than use of either stimulation alone without needles or needles alone? How specific are these so called acupuncture points? Is specific localization of these points vital, or is the neural modulation produced by stimulation of particular sensory or motor areas the critical variables? Obviously, these questions will require much intensive research conducted through properly controlled studies before they can be adequately answered. These next 2 days will provide the beginnings of our search for answers to these questions.

A generic multifactorial/multicompartment interactive scheme is presented as a way to stratify and analyze the effects of the acupuncture intervention (see Figure 1). Looking at the input end (Box I stimulus), the needle in the acupuncture paradigm may be a necessary condition if we define acupuncture as “puncturing with a needle.” However, it is not in and of itself a sufficient condition for successful therapeutic effects. The *deqi* (needling sensations) may be a crucial factor in the relief of local myofascial pain. However, to achieve a regional, extrasegmental or distant effect, one may need to tap into neural mechanisms in the spinal cord and/or brain stem or above. To achieve this, different stimulus parameters may be needed. Besides intensity of the stimulus, modulation by frequency and perhaps even by wave form may be required. This may be compared with the various manual techniques of needle manipulation described in Traditional Chinese Medicine. In scientific terms, the critical factors, of course, would be the types of receptors and fibers that need to be activated at particular bodily sites under controlled conditions.

Although increasing laboratory evidence suggests that manual or electrical stimulation may activate certain somatosensory pathways, including central neurohumoral mechanisms involving endorphin, dynorphin, or cholecystokinin, at the clinical level, it needs to be determined which of the various components embodied in the acupuncture paradigm may be causally responsible for successful therapeutic outcome. Because of the complexities of the therapeutic process, we need also to focus attention on the nature of interactions that can produce sufficient conditions for effective outcomes and not confine ourselves just to the search for single causal effects. It is clear that the input can interact with many possible intervening variables to result in particular observed effects. These intervening variables include the psychobiological program of the patient (Box II, which includes genetic, learning, and environmental factors), the motivation and expectation of the patient (Box III, interacting variables), and the interoceptive factors (Box IV, internal biological events). All of these may interact with each other and with the stimulus input to produce a particular end-effect (Box V, Identifiable Response). The end-effects can vary depending on the set and setting under which the modality is administered. Similarly, different individuals may respond to the same agent or modality differently on the basis of genetic predisposition or because of different learning, conditioning, motivational, or cultural factors.

This interactive process model is presented as a framework that can be used to analyze and understand the multifactorial nature embodied in the acupuncture paradigm. If it is the sensory stimulation that should prove to be the critical variable in producing a desired effect, then the needle in the acupuncture paradigm would merely be a vehicle for sensory modulation using manual or electrical stimulation. Further research will be needed to give us greater specificity as

to what physical stimulus parameters may be optimal for particular disease conditions. However, as clinicians, we should not lose sight of the patient and the doctor-patient relationship, which is critical in the therapeutic process. In this regard, the practice of acupuncture should be viewed only as a means to an end, where the end is the health and well-being of the patient.

Finally, the situation cannot be better described than by Rudyard Kipling in *The Ballad of East and West* [1889] (23).

“Oh, East is East, and West is West, and never the twain shall meet
Till Earth and Sky stand presently at God’s great judgment seat;
But there is neither East nor West, border, nor breed, nor birth
When two strong men stand face to face, though they come from the ends of the earth!”

Table 1.

Western Medicine	Traditional Chinese Medicine
Reductionistic	Holistic
Mechanistic/logical	Empirical/practical
Interventional (“Fix-it”)	Restorative (Lifestyle Change)
Quantitative	Qualitative
Disease-oriented	Prevention-oriented
“Digital”	“Analogue”

Example: Duodenal Ulcer

Patient	Identify Causative Agent	Treatment	Patient	Identify Patient	Treatment
A	x	T	A	a	1
B	x	T	B	b	2
C	x	T	C	c	3

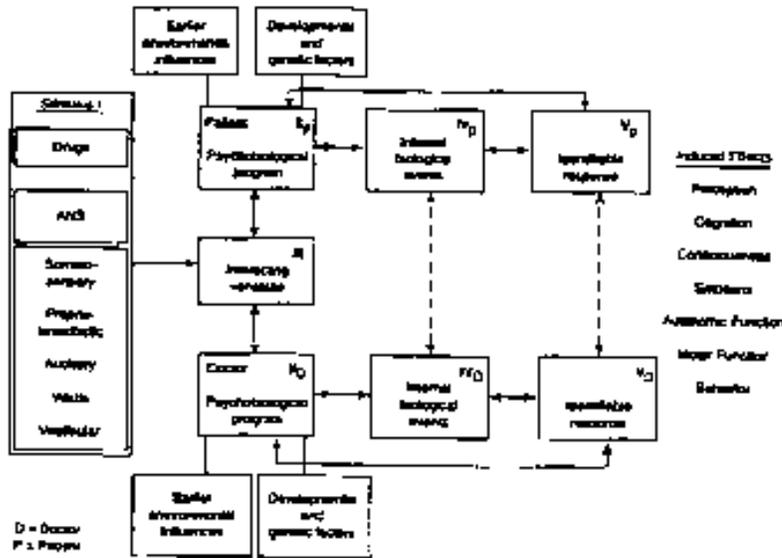


Figure 1.

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Acupuncture: History, Context, and Long-Term Perspectives

Ted J. Kaptchuk, O.M.D.

Acupuncture has been a component of the health care system of China and other East Asian countries for at least 2,500 years. This therapy has been utilized in different contexts that have had different assumptions, preconceptions, and premises. In its earliest, preliterate phase, acupuncture was part of a supernatural system of healing. In its classic, current, and most important phase, acupuncture has been part of a rational, human-centered, qualitative (humoral) system of health care. In its encounter with the modern West, it is faced with the question of whether it can survive the new premises that underlie the randomized clinical trial (RCT).

Many medical practices have not been able to adjust to these broad shifts in historical consciousness. For example, bloodletting was common in supernatural and rational-humoral systems but has been discarded with the advent of modern science. Other practices have made the shift. *Herba ephedra* is an example from the Chinese *materia medica*. Although its origin was in a context of expelling the supernatural agents thought to inflict asthma, it later became an important herb for use in balancing the qualitative disturbances that are the underlying cause of asthma. In this century, this herb has become the basis for critical medications. Will acupuncture go the route of bloodletting or *herba ephedra*?

Acupuncture's Origins and Earliest Shamanic Context

Two credible theories on acupuncture's origins have been proposed by historians. One has to do with bleeding and the other with massage. Epler (1980) proposed a notion that acupuncture was developed from early bloodletting therapies. This theory is supported by frequent references to bloodletting in the earliest Chinese texts and the universal utilization of bloodletting in archaic cultures. (In fact, bloodletting was common in Western medicine until World War I.) The other theory of acupuncture's origins has to do with massage. This theory is supported by the findings unearthed from the Ma Wang Dui Tomb Three in Hunan province in 1973. The burial itself is dated precisely to 168 B.C., and the material appears to have been composed before the end of the third century B.C. These manuscripts referred to burning moxa (*artemisa vulgaris*) along 11 pathways on the body (Harper, 1990). These pathways were also utilized for massage and significantly resembled the classic acupuncture meridians.

Whether either of these two theories is correct, acupuncture's origins took place in the context of placating ancestors and removing demons. The earliest practitioners of healing in East Asian culture (called *wu* in China) probably used needling as a shamanic weapon to placate or expel demons. Acupuncture was situated in a context of symbols, beliefs, suggestion, expectation, and persuasion. This approach has more to do with religion and misfortune than modern notions of science and disease.

Acupuncture in China's Classical Period

The context of acupuncture shifted by the time of Confucius (551-479 B.C.) whose famous writings clearly distinguished shamans from physicians. The earliest acupuncture and medical text still in use by the East Asian medical tradition is the *Yellow Emperor's Classic of Internal Medicine* (Huang di Nei-jing), which clearly demonstrated this transformation. Acupuncture was set in the context of a naturalist schema. The discussion of acupuncture was in terms of directly perceived sensory information. The world of qualities—sounds, colors, forms, and even pleasure, pain, and passion—the world encountered with the unaided senses—was the basis of knowledge.

Information was gathered and synthesized into a metaphorical image based on meteorological conditions or humoral elements. Is a person hot or cold? Is a person damp or dry? Is a person flaccid or brittle? What are the sensations a patient can report? What do the tongue, pulse, and manners of the person's behaviors imply about the quality of internal health (or meteorological condition)? Could a gestalt of *Yin* and *Yang* qualities be used to describe and communicate a replicable treatment? Were positive outcomes perceived? Did people return to the physician? Did people feel better? Did the physician see improvement? Illness and health were activities negotiated within the context of being understandable in a human context.

Acupuncture in the West Before the Randomized Controlled Trial

With the scientific revolution, Western medicine adopted the authority of science but for a long time retained the importance of human experience, especially under the rubric of "art." The clinical arena continued to emphasize the importance of human experience. Medical science, until after World War II, more often than not meant investigation in the laboratory outside the clinical arena. Patient care depended on visible symptoms and the subjective reports of patients well into the 20th century. Clinical medicine primarily relied on the critical judgment of physicians with acknowledged clinical acumen, moral integrity, and scientific knowledge to evaluate clinical outcomes and the purported value of newly introduced therapeutics. In this context, acupuncture actually found many influential advocates because of its purported results. Important examples include William Osler (Osler, 1931); Franklin Bache, great-grandson of Benjamin Franklin (Cassedy, 1974); Sydney Ringer (Veith, 1975); Berlioz (the father of the composer) (Berlioz, 1833); the surgeon John M. Churchill (Churchill, 1822); and John Elliotson, who introduced the stethoscope to England (Fuller, 1982). The acceptance of acupuncture does not seem to have been confined to major urban elite areas. For example, in 1836, a Dr. William Markely Lee of Indian Town, South Carolina, reported that he had found acupuncture useful in the treatment of rheumatism (Greenwood, 1976), and there is a report of widespread use in Scotland in 1830 (Renton, Penicuik, 1830). Academic dissertations also were published (Carrubba, Bowers, 1974).

The Era of the Randomized Controlled Trial

After World War II, Western medicine underwent a dramatic shift in premises (Marks, 1997; Kaptchuk, in press). Medicine developed critical new tools to separate perceptions of effectiveness from a scientific determination of "genuine" efficacy. The introduction of the RCT significantly realigned the power relationships between "art" and "science" in clinical medicine. Clinical epidemiology developed new tools that it hoped would establish scientific certainty in health care. In a short time, the ability to produce perceived therapeutic outcomes was no longer the basis of the value of a therapy. Now the method (i.e., that it was more than a placebo) justified the results (Sullivan, 1993). A treatment was legitimate if it met the fastidious standards of a quantitative model that separated "human perception" (resulting from possible genuine outcomes and such "noise" as bias, placebo effects, variability, and chance) and genuine efficacy. The main tools to disentangle the "more-than-placebo" value of a therapy were blind assessment, randomization, and inferential statistics. Therapeutic effects were to be isolated from placebo and other "nonspecific" effects.

These new premises and methodologies have only recently been applied to acupuncture. Many RCTs appear in the literature. Although few RCTs are perfect, the acupuncture RCTs fall short of the ideal clinical experiment, perhaps more than many conventional RCTs. Money for large-scale trials in acupuncture has been especially scarce; so inadequate sample sizes make statistically significant results more difficult to obtain and the likelihood of a beta error extremely great. Was the acupuncture "dose" sufficient in these trials? Was the acupuncturist well trained? Was blinding adequate? Was the sham legitimate? (Vincent, Lewith, 1995). Did the outcome measures make sense? Was patient suitability assessed in these trials? Do these trials have external validity?

Yet one has to ponder and try to make judgments even with imperfect information. Will acupuncture survive and be accepted in the new era of the RCT? Is there enough information? What more needs to be examined? The answer to these questions will significantly determine whether acupuncture goes the route of bloodletting or becomes the source of significant scientific therapeutic intervention.

Addendum: Important Landmarks in Acupuncture History in East Asia

Han Dynasty (206 B.C.-A.D. 221): *Yellow Emperor's Classic of Internal Medicine* stated that there are 365 points but mentioned only 160 points by name. The theory of systematic correspondence and a rational synthesis of sensory information are well described.

Jin Dynasty (265-420): *Classic of the Pulse* (Mai Jing) systematically develops pulse diagnosis. *Systematic Classic of Acupuncture* (Zhen-jui Jia-yi Jing c.A.D. 282) fully described 349 points and their indication.

Southern and Northern Dynasties (420-581): In 562, *Systematic Classic of Acupuncture* was brought to Japan.

Tang Dynasty (618-907): *Thousand Ducat Prescriptions* (Qian-jin Yao-fang, 652) described point locations accurately and provides many treatment protocols.

Song Dynasty (960-1280): *Illustrated Classic of Acupuncture Points as Found on the Bronze Model* (Tong-ren Shuy-xue Zhen-jui Tu Jing, 1026) described the points in anatomical order on the meridians. *Classic of Nourishing Life With Acupuncture* (Zhen-jiu Zi-sheng Jing, A.D. 220) further developed point indications and treatment protocols.

Yuan Dynasty (1280-1368): *Elaboration of Fourteen Meridians* (Shi-si Jing Fa-hui, 1341) described extra meridians and special points.

Ming Dynasty (1368-1644): *Gathering From Eminent Acupuncturists* (Zhen-jiu Ju-ying, 1529) described many common treatment formulas. *Great Compendium of Acupuncture* (Great Compendium of Acupuncture, 1601) presented the last classic synthesis.

Republic of China (1911-1949): Influenced by Western ideas in 1914 and 1929, the Republic of China considered the practice of Chinese medicine and acupuncture illegal.

People's Republic of China (1949-): September 1951, a research institute of acupuncture was established by the Ministry of Health. One hundred forty-four traditional medical hospitals were established in 1955. Seventy-seven were added in 1956. By 1958, 13 government-sponsored colleges of traditional medicine were established. First research institute of acupuncture was established by the Ministry of Health in Beijing in 1951.

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Acupuncture Licensure, Training, and Certification in the United States

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Although acupuncture has been practiced in the United States since the 19th century, it was not until the early 1970s, when diplomatic relations with the People's Republic of China were restored, that acupuncture burst onto the American scene.

The Development of Licensure

One of the most remarkable aspects of the interest in acupuncture in the United States was the rapidity with which some States adopted legislation to permit its practice by individuals who were not medical doctors. The acceptance of professional acupuncture in the 1970s by a number of States led to its establishment as a viable medical alternative in the United States. In late 1972, California passed a law permitting nonphysician acupuncturists to practice with physician supervision for the purpose of research. This was the first of a series of laws that would eventually lead to California's establishing an exceptionally high educational standard and scope of practice for acupuncturists by 1985. In 1973, Nevada was the first State to adopt a system of licensure. Oregon followed shortly thereafter, conducting the first formal examinations of acupuncture candidates in 1974. New York adopted standards for licensure in 1975. Over time, other States followed suit. Today 34 States and the District of Columbia license or otherwise regulate the practice of acupuncture by nonphysicians, that is, the professional practice of acupuncture.

Acupuncture laws vary from State to State because each State is allowed by the Constitution to set its own standards for medical practice. Laws typically define the meaning of "acupuncture" and the scope of an acupuncturist's practice, educational standards, and standards of professional conduct. New York State's description of the practice of acupuncture is particularly apt.

"Profession of acupuncture is the treating, by means of mechanical, thermal or electrical stimulation effected by the insertion of needles or by the application of heat, pressure or electrical stimulation at a point or combination of points on the surface of the body predetermined on the basis of the theory of the physiological interrelationship of body organs with an associated point or combination of points for diseases, disorders and dysfunctions of the body for the purpose of achieving a therapeutic or prophylactic effect." [Article 160 8211.(1)(a)]

In the 25 years that have elapsed since the first efforts to describe and regulate the practice of acupuncture, a great deal has occurred, especially in the field of education. We will examine some of these trends and return to aspects of the regulatory process.

Education in Acupuncture and Oriental Medicine

By the mid-1970s, formal instructional programs had been created. By the early 1980s, the number of schools was sufficient to warrant the creation of an organization called the National Council of Acupuncture Schools and Colleges (NCASC), known today as the Council of Colleges of Acupuncture and Oriental Medicine. The organization was formed in June 1982 with a membership of 10 founding programs. Later in the year, NCASC went on to establish an independent accreditation commission, the National Accreditation Commission for Schools and Colleges of Acupuncture and Oriental Medicine (NACSCAOM), which was to establish and support standards for programs in the field. By 1990, NACSCAOM had established acupuncture education as a legitimate field of study in the United States, winning recognition for its accreditation process from the U.S. Department of Education. Today there are 32 programs in NACSCAOM's process. Twenty-four are accredited, and eight are in candidacy. In addition to these, a number of other programs in the United States do not yet subscribe to NACSCAOM standards.

Educational Standards

The course of training offered by most schools in the United States responds to and typically exceeds the minimum standards required by NACSCAOM. These include, for programs providing training in acupuncture and oriental medicine, a minimum of 123 semester credits (2,175 hours) of training. This training consists of 47 semester credits (705 hours) in oriental medical theory, diagnosis, and treatment techniques in acupuncture and related studies, 30 semester credits (450 hours) in studies related to oriental herbal medicine, 24 semester credits (360 hours) in studies of biomedical clinical sciences, and 22 semester credits of clinical observation and practice (660 hours).

On average, accredited programs provide more than 30 semester credits (450 hours) of training above and beyond this standard, and the leading programs in the field provide considerably more. Programs typically accept students with a minimum of 2 years of college course work and award a master's degree or master's-level diploma on completion of the program.

Distinct titles, such as Master of Acupuncture, Master of Science in Traditional Chinese Medicine, Master of Traditional Oriental Medicine, Diploma of Acupuncture, and others, are awarded by these programs. However, on a State-by-State basis, the resulting license that graduates of these programs may receive is the same.

Training programs in China typically award a medical baccalaureate or M.B./B.S., which indicates that the graduate has completed from 4 to 5 years of education after leaving high school. China uses a system of medical education similar to Great Britain's and does not award the title M.D. but considers graduates of these programs as "doctors." Advanced training in the field in China can lead to either an M.S. or a Ph.D. with an emphasis on research.

The title O.M.D. has gained some currency in the United States but has never been awarded by a State licensing agency or authorized training programs in China, nor is the title currently offered by any legally operating and accredited program in the United States. For a brief period this title was legally offered by programs operating in California. Very often, the use of this title indicates a less comprehensively trained practitioner than does the use of one of the titles associated with the master's degree programs.

Qualification for Licensure

Many States make use of the examinations provided by the National Certification Commission for Acupuncture and Oriental Medicine (NCCA). These examinations test for entry-level competency in acupuncture, oriental medical theory, and oriental herbal medicine but do not assess knowledge in biomedical sciences. Most States require that the candidate for licensure has met a minimum educational standard, usually the standard provided by NACSCAOM. Some States, such as California, require a higher standard than that used by NACSCAOM and develop testing independently of NCCA.

The State has complete discretion over the title that may be used by the holder of the license. Examples of licensure titles include Licensed Acupuncturist (New York, California, Massachusetts), Certified Acupuncturist (California), Registered Acupuncturist (Pennsylvania, Vermont), Doctor of Acupuncture (Rhode Island), Doctor of Oriental Medicine (New Mexico), and Acupuncture Physician (Florida). Interestingly, States that offer the most prestigious licensure titles do not always require the highest educational standards.

The variation in license titles used by States, as well as the variation in educational requirements, can lead to interesting situations. For example, although most acupuncture and oriental medicine programs in California grant some kind of master's degree, this degree is not required for licensure in California; what is required is that the program attended by the candidate for licensure be approved by the California Acupuncture Committee. In Rhode Island, any individual who obtains a license to practice acupuncture automatically receives the title of Doctor of Acupuncture, without regard to his or her educational background. In New Jersey, however, an acupuncturist's educational background is so important that the State requires that the applicant have a bachelor's degree and graduate from an accredited training program, even though New Jersey requires a prior diagnosis by a physician for treatment and simply uses the title of Licensed Acupuncturist.

Other Health Care Professions and Acupuncture

Most States permit a licensed physician to practice acupuncture as part of his or her medical practice. Approaches to this vary extensively from State to State. In New York, physicians and dentists may practice acupuncture in relation to the scope of their clinical practice

Table 1. Table of States licensing or otherwise regulating the professional practice of acupuncture based on Mitchell (1997) and other sources.

State	Professional Acupuncture by Law	Year	Supervision or Referral Required	#s	Who May Practice	MD	DO	DDS	DPM	DC	RN	PA	PT	Th	Notes
Alabama			N/A		LAc	MD	DO			DC*					*DC needs 100 hours of training
Alaska	Law	1990	No	28	LAc	MD		DDS							*50 Hrs Legislation Anticipated
Arizona	Law	1997	No		LAc	MD	DO			DC*					*100 *Supervision Req'd & Optometrists
Arkansas	Law	1976	No	3692	LAc	MD		DDS	DPM						*100
California	Law	1989	No	202	LAc	MD	DO		?	DC*					*Supervision Req'd & Optometrists
Colorado	Law	1995	No	8	LAc	MD	DO	DDS	DPM	DC	RN*	PA*	PT	Th	*250 hrs
Connecticut															
Delaware						MD				?					
District of Columbia	Law	1989	Required	42	LAc	MD	DO		DPM	DC*					*100 hrs
Florida	Law	1981	No	537	LAc	MD	DO			DC*					*100 hrs
Georgia			N/A			MD	DO								
Hawaii	Law	1974	No	338	LAc	MD	DO			DC*					*Must be licensed as an acupuncturist unregulated
Idaho															
Illinois	Law	1987	Required		LAc	MD	DO			?					Legislation introduced
Indiana			N/A			MD	DO			DC					
Iowa	Law	1993	Required	3	LAc	MD	DO	DDS	DPM	DC					
Kansas	Act		Required		LAc	MD	DO	DDS		DC		PA			
Kentucky															
Kentucky	Law	1975	Required	2	LAc	MD	DO								*six months
Louisiana															
Maine	Law	1987	No	53	LAc	MD				DC		PA			MD may practice with NCCA *200 hrs
Maryland	Law	1973	No	433	LAc	MD		DDS							*specialized exemption
Massachusetts	Law	1986	Required	589	LAc	MD	DO						PT*		
Michigan	Act		Required		Ac	MD	DO								
Minnesota	Law	1995	No	13	LAc	MD	DO			DC*					*100 hrs
Mississippi			N/A			MD		DDS							
Missouri	Act		Required		Ac	MD	DO			DC*					*100 hrs
Montana	Law	1974	No	92	CA	MD	DO	DDS*	DPM	DC*					*must meet requirements for licensed acupuncturist

Table 1. Table of States licensing or otherwise regulating the professional practice of acupuncture based on Mitchell (1997) and other sources (continued).

State	Professional Acupuncture by Law	Year	Supervision or Referral Required	#s	Who May Practice	MD	DO	DDS	DPM	DC	RN	PA	PT	Tel	Notes	
Nebraska			N/A			MD	DO									
Nevada	Law	1973	No	30	DOM	MD	DO									
New Hampshire			N/A			MD	DO									
New Jersey	Law	1983	Required	62	CA	MD	DO	DDS								Legislation Introduced *300 hrs
New Mexico	Law	1978	No	390	DOM	MD				DC						
New York	Law	1975	No	700	LAc	MD	DO	DDS*								
North Carolina	Law	1993	No	67	LAc	MD	DO			DC						*160 hrs
North Dakota			N/A			MD				DC*						
Ohio			N/A			MD	DO									
Oklahoma			N/A			MD	DO			DC*						*with training
Oregon	Law	1973	No	236	LAc	MD	DO									
Pennsylvania	Law	1986	Required	282	LAc	MD	DO									*200 hrs
Rhode Island	Law	1978	No	60	DAC	MD	DO									
South Carolina	Law	1974	Required	?	Ac	MD	DO	DDS								
South Dakota			N/A			?	?			DC*						*200 hrs
Tennessee			N/A			MD	DO									
Texas	Law	1993	Required	500	LAc	MD				DC*						*with training
Utah	Law	1983	No	27	LAc	MD										
Vermont	Law	1985	No	34	CA	?	?					?				
Virginia	Law	1993	Required	14	LAc	MD										
Washington	Law	1985	Required	299	LAc	MD	DO									
West Virginia	Law	1995	No	4	LAc	MD	DO		DPM							*with training
Wisconsin	Law	1989	No	172	LAc	MD	DO		DPM			PA				unregulated
Wyoming			N/A			?										
States Permitting Professional Acupuncture				35	Total L.Ac.											
States Permitting Autonomous Practice				20	8729											

Prepared on the Basis of Mitchell 1997 and other materials

once they have completed 300 hours of training. Completion of this training and registration with the State allows them to use the title of Certified Acupuncturist. In California, a physician, dentist, or podiatrist may practice acupuncture without additional training; Montana requires that medical doctors pass the NCCA examination; and Hawaii requires them to be licensed as acupuncturists. Some States have not yet determined whether acupuncture is within a physician's scope of practice.

A national organization for physicians who include acupuncture in their medical practices, the American Academy of Medical Acupuncture (AAMA) supports a 200-hour training program for physicians who plan to incorporate acupuncture into their practices. The AAMA is also now offering physician acupuncturists an AMA Category I Continuing Medical Education (CME) introductory as well as intermediate and advanced CME courses in medical acupuncture.

Several States provide for the practice of acupuncture by chiropractors on the basis of an additional 100 to 200 hours of training. Doctors of naturopathy, podiatrists, physical therapists, physician's assistants, and nurses are permitted to practice acupuncture in some States with widely varying training requirements.

Looking Toward the Future

At present it seems likely that all 50 States will license or otherwise provide for the practice of professional acupuncture within their jurisdiction. The continued increase in educational standards, the recognition by the U.S. Food and Drug Administration of the acupuncture needle as a medical device, widespread popular acceptance, use by health maintenance organizations, and the availability of standardized testing provided by the NCCA makes it fairly likely that the 16 States that do not currently provide for the practice of professional acupuncture will do so within the next decade.

Resources for Learning More About Acupuncture

National Organizations:

National Acupuncture and Oriental Medicine Alliance
14637 Starr Road S.E.
Olalla, WA 98359
(253) 851-6896

American Association of Oriental Medicine (AAOM)
433 Front Street
Catasauqua, PA 18032
433-2448

American Academy of Medical Acupuncture (AAMA)
5820 Wilshire Boulevard, Suite 500
Los Angeles, CA 90036
937-5514

For information about research and scholarly initiatives in the fields of acupuncture and oriental medicine:

National Academy of Acupuncture and Oriental Medicine (NAAOM)
Box 62
Tarrytown, NY 10591
(914) 332-4576
e-mail: 75776.1734@compuserve.com

Medical Acupuncture Research Foundation
5820 Wilshire Boulevard, Suite 500
Los Angeles, CA 90036
937-5514

Society for Acupuncture Research
6900 Wisconsin Avenue, Suite 700
Bethesda, MD 20815
Fax: (301) 961-5340
e-mail: hannahb@erols.com

For information about educational programs and training in the field:

Council of Colleges of Acupuncture and Oriental Medicine (CCAOM)
Suite 1270
1010 Wayne Avenue
Silver Spring, MD 20910
(301) 608-9175

National Accreditation Commission for Schools and Colleges of Acupuncture and Oriental Medicine (NACSCAOM)
Suite 1270
1010 Wayne Avenue
Silver Spring, MD 20910
(301) 608-9680

For information about certification:

National Certification Commission for Acupuncture and Oriental Medicine (NCCA)
P.O. Box 97075
Washington, DC 20090-7075
(202) 232-1404

Further Reading:

If you are interested in reading more, the following materials may be helpful:

The Web That Has No Weaver
by Ted Kaptchuk
New York: Congdon & Weed; 1983.

This is still the best overview of the clinical world view of Chinese medicine. It has little to say about specific therapies but explains a great deal about how Chinese medicine looks at the world.

Fundamentals of Complementary and Alternative Medicine
Marc Micozzi, Editor
New York: Churchill Livingstone; 1996.

This book contains chapters on most major forms of alternative medicine including a substantial chapter on Chinese medicine: China's Traditional Medicine, by Kevin Ergil.

Medicine in China: A History of Ideas
by Paul Unschuld
Berkeley: University of California Press; 1985.

This is the best book on the history of the practice of Chinese medicine. Well written and interesting, this book makes it impossible to have a simple view of Chinese medicine.

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Current Utilization of Acupuncture by United States Patients

Patricia D. Culliton, M.A., Dipl.Ac., L.Ac.

Introduction

Acupuncture has been available on a limited basis in the United States since the 1800s. Asian communities are purported to have provided this treatment since they began emigrating to the United States, but utilization by non-Asians was infrequent. The medical community was informed by Sir William Osler that acupuncture was a treatment for lumbago in the *Principles and Practice of Medicine* (Osler, 1892). However, acupuncture was generally not a part of the knowledge base of consumers or providers until the 1970s, when President Nixon opened the doors to the People's Republic of China with "Ping Pong Diplomacy."

New York Times journalist James Reston reported that acupuncture successfully alleviated his postoperative pain following an emergency appendectomy in Beijing. This report created a flurry of activity that included National Institutes of Health (NIH)-funded studies and a range of hopes from discovering a new form of surgical analgesia to solving the problem of intractable pain. In a few years, the excitement within the medical community subsided for numerous reasons, although consumers remained interested (Wolpe, 1985). Training programs for nonphysicians began to emerge, primarily in California, New York, and other areas with large Asian communities, and acupuncture clinics began to emerge.

Availability—Practitioners

The American Academy of Medical Acupuncture estimates that there are currently more than 3,000 physicians practicing acupuncture in the United States (Diehl, Kaplan, Coulter, et al., 1997). The National Commission for the Certification of Acupuncturists reports that it has certified 10,000 individuals, 4,600 of whom hold active certification status. The National Acupuncture Detoxification Association (NADA) has trained more than 4,000 substance abuse professionals in an ear acupuncture protocol specific to the field of addictions, and it is estimated that at least 3,000 chiropractors also practice acupuncture. Although it is difficult to ascertain an exact number of acupuncture practitioners because of the likelihood of cross-certification, there are currently at least 10,000 individuals actively providing acupuncture in the United States.

At present, there are at least 70 schools of acupuncture with curriculums developed for the education of nonphysician providers, 34 of which are accredited (National Accreditation Commission of Schools and Colleges of Acupuncture and Oriental Medicine. Personal communication, 1997). There are also programs that teach physicians and chiropractors. With more than 5,000 students enrolled at accredited institutions, an estimated 5,000 more attending

nonaccredited schools, and the continued training of both chiropractors and physicians, the acupuncture provider community could potentially double by the year 2000.

Utilization

A. Estimates of overall use of acupuncture

Precise data are unavailable regarding the number of patients in the United States who use acupuncture; however, according to the American Association of Oriental Medicine, an acupuncturist membership organization, some 15 million Americans have tried acupuncture (Molony, 1996). Industry figures supplied by needle distributors report that up to 150 million needles per year are sold in the United States (Lee, personal communication, 1997). Assuming that 10 to 15 needles are used per treatment, sales of needles indicate that more than 12 million acupuncture treatments may be provided annually in this country.

B. Patient Profile

Eisenberg (1993) reported that of 1,539 patients who received complementary and alternative medicine (CAM) interventions, most were persons ages 25 to 49, significantly more likely to be Caucasian than any other racial group, and significantly more likely to have college educations and greater than \$35,000 per annum. Norms of acupuncture patients in studies by Bullock (1997) on 760 patients in a Minneapolis clinic and Cassidy (1995) on 575 patients in six different cities appear to be consistent with CAM patients in general.

	<u>Bullock (N = 760)</u>	<u>Cassidy (N = 575)</u>
Gender		
Female	69.5%	75%
Age		
Average age	48	NA*
Race		
White	87.6%	89%
Black	3.7%	2%
Education		
BA or above	47.2%	73%

* Largest group of patients between the ages of 41 and 50.

The addictions treatment field may actually be the largest subset of acupuncture consumers. NADA now has more than 4,000 members and claims to provide acupuncture at 700 to 1,000 treatment facilities in the United States (Smith, 1997). The profile of this patient population is almost the opposite of clinical populations: it tends to be male, black, urban, undereducated, underemployed, and younger.

C. Presenting Complaints

Other than for addictions, most Americans use acupuncture for the treatment of pain. Bullock (1997) reports that 65.3 percent of 760 patients presented with musculoskeletal complaints and 13.8 percent with headaches. Diehl (1997) reports that the top 11 conditions treated by medical acupuncturists are pain related, the most frequent being low-back pain at 93.2 percent of respondents.

After pain, the most frequently reported presenting complaints appear to fall within a functional or nonspecific category of symptoms such as anxiety, fatigue, depression, insomnia, and the like. Again, it is of note that the most common presenting complaints for acupuncture appear to mirror quite closely the 10 most reported principal medical conditions identified by Eisenberg and colleagues (1990).

Summary

Acupuncture providers and consumers are steadily increasing in prevalence. Providers of acupuncture may double their ranks in the next few years, and based on needle sales, consumers are increasing their use of this service annually. The majority of individuals who access acupuncture in the United States are well educated, employed, white, middle-aged, and female, but there is also a large subset of addictions patients who have almost opposite demographics. Pain is by far the most frequently listed primary symptom of consumers, although treatment is sought for a vast array of symptoms.

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Methodological and Ethical Issues in Acupuncture Research

Richard Hammerschlag, Ph.D.

The design and performance of clinical trials of acupuncture are faced with a major challenge: To adhere to the generally accepted guidelines for biomedical clinical trials while preserving the unique aspects of the medical traditions within which acupuncture is practiced. At present, relatively few of the considerable number of acupuncture trials with positive outcome (Birch, Hammerschlag, 1996) have adequately satisfied *both* aspects of this challenge.

Difficulties with the first aspect—satisfying the biomedical model—are exemplified by the problem of designing appropriate controls for a treatment that is neither a drug nor a surgical intervention. Problems inherent in the second aspect—maintaining the oriental medical model—are illustrated by the need for the acupuncture treatment plan to be individualized and based on oriental medical diagnoses.

With these caveats in mind, we can examine how acupuncture efficacy has been assessed in clinical trials. Research designs can be grouped into four categories:

1. Acupuncture compared with no treatment (wait-list controls).
2. Acupuncture compared with control treatment, either placebo (noninvasive needling or inactive transcutaneous electrical nerve stimulation [TENS]) or sham (invasive needling).
3. Acupuncture compared with biomedical standard care (medication, medical device, or physiotherapy).
4. Acupuncture plus standard care compared with standard care alone.

Examination of these trials will help the Consensus Development Panel answer several broad questions: Is there sufficient evidence that acupuncture outperforms control treatment? Does acupuncture perform at least as well as biomedical care? Is acupuncture an effective adjunct to standard care?

Acupuncture Versus No Treatment

This infrequently used design, in which a delayed-treatment group is used to assess the rate of spontaneous remission, is applicable for relatively stable, chronic conditions. The design is ethical in that all patients receive active treatment, but it does not control for placebo effects. As an example, patients with severe osteoarthritis of the knee who received immediate acupuncture treatment outperformed the wait-list group in objective motion tests. After all

patients received treatment, 80 percent experienced significant decreases in pain and in use of nonsteroidal anti-inflammatory drugs (NSAIDs) (Christensen, Iuhl, Vilbek, et al., 1992).

Acupuncture Versus Control Needling

Because the placebo control was developed for clinical testing of pharmaceuticals whereas the sham control was created for assessing surgical procedures, it can be argued that neither is formally applicable to clinical trials of acupuncture. As a result, acupuncture trials are notable for their variety of control treatments. For the present discussion, a useful distinction is to consider as placebo those control procedures that are noninvasive and as sham those procedures that are invasive. Placebo controls used in acupuncture trials include tapping needleless guide tubes, pressing the blunt end of the needle, or applying inactive TENS electrodes, each directed at the same acupoints used for the acupuncture treatment group. Sham controls have included acupuncture-like needling at non-points in the immediate vicinity of treatment points, superficial needling at treatment points, and, what is considered the most appropriate procedure, superficial needling at non-points.

A confounding problem, unique to the use of sham controls, is that invasive needling—irrespective of site—induces nonspecific physiological effects including both local and neurally mediated responses (LeBars, Villaneuva, Willer, et al., 1991). As a result, sham needling often produces treatment outcomes that are intermediate between those of true acupuncture and no treatment, making statistical significance of results more difficult to achieve (Vincent, Lewith, 1995). Sham designs, however, have the advantage of controlling for both placebo and nonspecific effects.

An additional problem is that true double-blind procedures cannot readily be applied to acupuncture trials because acupuncturists must know whether to place needles at correct or incorrect sites. This difficulty is best surmounted by a modified double-blind design in which neither patients nor outcome assessors are aware of treatment group assignments. The best designed acupuncture trials have also included validity testing, wherein patients are asked, posttrial, to guess their group assignment (Vincent, 1990).

Two examples of well-designed placebo controlled trials of acupuncture are those of Lao and colleagues (1995), for managing postoperative oral surgery pain, and Macdonald and colleagues (1983), for relief of chronic low-back pain. In the dental study, as the anesthetic wore off, the acupuncture group (needling through guide-tubes) reported a longer duration of pain-free time (181 minutes) relative to the placebo group (tapping of empty guide-tubes; 71 minutes). In the back pain study, patients who received acupuncture showed significant reductions in visual analog scale (VAS)-assessed pain, activity pain score, and clinical signs relative to those “treated” at the same acupoints with a disconnected TENS unit. Examples of positive-outcome studies utilizing superficial needling at non-acupoints as sham controls are those of Vincent (1989) for migraine and Deluze and colleagues (1992) for fibromyalgia.

It should be noted that controlled trials of acupuncture, as with all controlled clinical

trials, are meeting increasing disfavor from institutional review boards because they violate the “intent to treat” maxim for half the patients.

Acupuncture Versus Biomedical Standard Care

In this research design, a control group for acupuncture is not essential. Instead, acupuncture is challenged to perform at least as well as a drug, a medical device, or physiotherapy that has previously been shown to outperform a placebo for the condition being studied. The design is ethically favored because there is an “intent to treat” all patients. It is also especially useful for comparing the two medicines with regard to time of onset, duration, side effects, and cost-effectiveness.

An example of such comparative outcomes studies is that of Lee and colleagues (1992) for treatment of renal colic. Among patients treated with acupuncture, 19 of 22 reported a pain-free condition within 2 hours, compared with 11 of 16 patients given an intramuscular injection of analgesic medication. The acupuncture group became pain-free within 1 to 10 minutes and reported no side effects, whereas the medication group reported a pain-free state by 10 to 30 minutes with 43 percent (7) developing side effects of skin rash, tachycardia, drowsiness, or facial flush.

Trials of acupuncture vs. standard care were recently evaluated on the basis of 25 criteria of good study design and reporting (Hammerschlag, Morris, 1997). On a rating system of “adequate,” “partial,” or “not done/not reported,” only nine studies received “adequate” scores on more than half the criteria. Among the highest scoring criteria were randomization of patients and use of multiple end points. Low-scoring criteria included use of a blinded treatment assessor, monitoring of side effects, and statement of acupuncturist’s training. The findings emphasize that inadequacies in research design and reporting can call into question positive as well as negative outcomes of clinical trials.

Acupuncture Plus Standard Care Versus Standard Care Alone

This is considered as a highly ethical research design because all patients receive standard care. Using this study design, acupuncture given as adjunctive treatment to physiotherapy was more effective than physiotherapy alone in promoting recovery from low-back pain (Gunn, Milbrandt, Little, et al., 1980) and stroke (Sallstrom, Kjendahl, Osten, et al., 1996). In a three-arm variation of this design—in which all patients received antiemetic medication to suppress chemotherapy-induced nausea and vomiting—preliminary findings indicate that electroacupuncture outperformed sham electroacupuncture, which, in turn, was more effective than medication alone (Shen, 1997).

A Final Consideration

In conclusion, we should reemphasize the methodological challenge highlighted at the outset of this talk: to test acupuncture within the framework of its own medical tradition. However, in a considerable proportion of acupuncture trials, as will be apparent from subsequent talks, patients in the acupuncture group received a fixed-protocol treatment (same acupoints, same number and duration of sessions) that was based on biomedical diagnostic criteria. In contrast, the clinical practice of acupuncture involves individualized acupoint selection, based on patient-specific systemic imbalances informed by oriental medical diagnostic procedures. Serious consideration should thus be given to the argument that most clinical trials of acupuncture have undervalued its efficacy.

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Safety and Regulation of Acupuncture Needles and Other Devices

C.D. Lytle, Ph.D.

Before 1996, the U.S. Food and Drug Administration (FDA) treated acupuncture devices as instruments of unproved effectiveness in a therapeutic modality for “the many and varied uses for which such devices [were] being promoted.” It recognized the needle as the primary tool and devices for electroacupuncture and point location as less frequently used ancillary tools (Lytle, 1996; Parisian, Lytle, Sheehan, et al., 1996). Following recommendations of an advisory committee, the FDA labeled all acupuncture devices investigational in 1972, based primarily on the lack of information on effectiveness. There was also recognition of the need for use by knowledgeable practitioners. Subsequently, the FDA allowed the sale of acupuncture needles provided they were labeled “investigational.” Compliance actions have been focused primarily on labeling issues, specifically to prevent claims of effectiveness for any disease or condition. Low risk was formally recognized in the 1980 Compliance Policy Guide, where it was stated that acupuncture devices do not have a history of “significant risk.”

What are the most important issues to the FDA regarding acupuncture needles and safety? The first is who actually uses the needles and their qualifications for doing so safely. The second is how many needles are used. The third is what types of problems occur and how often.

Mechanisms for recognition and certification or licensure of acupuncturists have evolved over the past two decades (Lytle, 1993). There are several professional acupuncture organizations, and most States specifically regulate the practice of acupuncture by defining who is a qualified practitioner (National Acupuncture Foundation, 1994). Acupuncture practitioners can be grouped into two basic categories: physicians and nonphysicians. The physicians are typically trained and credentialed in Western medicine and then add acupuncture training later. About 2,000 physicians have training in acupuncture. The nonphysician practitioners obtain training through a domestic or foreign acupuncture school and are credentialed through either the National Commission for the Certification of Acupuncturists (NCCA) or programs provided by individual States. There are approximately 10,000 such acupuncturists, with perhaps half that number in California (Lytle, 1993).

For an earlier overview of acupuncture (Lytle, 1993), the author interviewed numerous acupuncturists and estimated that there were 9 to 12 million acupuncture treatments annually in the United States. About 70 percent of those treatments were for pain control, with 6 to 20 needles typically used per treatment. From these values, it is estimated that 100 million needles are used each year.

Although piercing with acupuncture needles always has potential risk, injuries from

acupuncture are infrequent (Lao, 1996; Ernst, 1995; Abbot, White, Ernst, 1996; Norheim, Fønnebø, 1996). Four primary types of problems associated with acupuncture have been documented, usually as case reports. They are essentially what would be expected with the use of needles, and some may be life-threatening.

1. Infectious diseases have been transmitted from one patient to another, the most commonly reported example being hepatitis B. Local infections have also been reported.
2. Improper needling, especially by inadequately trained individuals, may result in tissue damage. Nerve damage and pneumothorax are most commonly reported, along with other organ punctures, including a fatal cardiac tamponade.
3. Needles have broken, leaving remnants to migrate to critical locations. Needle tips have been found to have migrated to the spinal cord and to the heart. This is rare in the United States.
4. Numerous less serious, transient effects may occur, including dermatitis, hematoma, fainting, dizziness, and nausea. Because these types of adverse effects are not normally seen as significant, they are not often reported.

The frequency with which these problems occur is difficult to estimate and depends greatly on the ability and understanding of the practitioner (Lao, 1996; Ernst, 1995; Abbot, White, Ernst, 1996; Norheim, Fønnebø, 1996). A literature search of adverse events (English language only) over the last 10 years suggests that the total number of incidents was no more than a few hundred (approximately one-half of which occurred in the United States). This estimate, of course, suffers from some degree of underreporting of actual events. Surveys in England (Abbot, White, Ernst, 1996) and Norway (Norheim, Fønnebø, 1996) on adverse events, while methodologically imperfect (Margolin, Avants, Birch, 1997), indicated which events occurred most often and that control over acupuncture practice can reduce such events. The Norway survey found that transient effects were most common: a number of skin infections were reported, broken needles were not reported, and pneumothorax was the most common serious problem. With an estimate that an acupuncturist might see (cause?) less than one serious event per 100 years of full-time practice, the overall conclusion was that acupuncture was “a relatively safe therapeutic measure” (Norheim, Fønnebø, 1996). This is consistent with an American Medical Association (AMA) assessment in 1981 that “there are . . . remarkably few serious complications” in acupuncture (American Medical Association, 1981).

Taking safety and other considerations into account, the FDA reclassified acupuncture needles in March 1996 (Federal Register, 1996), thereby removing the investigational label. All other acupuncture devices remain investigational. The purpose of the needle was recognized to be that of piercing the skin in the practice of acupuncture. This general purpose is comparable to that of the scalpel or hypodermic needle, where the therapeutic value relies on use by the practitioner. No claim of effectiveness for any specific disease is permitted on the label. The

present Class 2 category requires special controls so that the needles can be used safely. They include requiring that the needles be sterile, nontoxic, and labeled for single-use and that sales be restricted to qualified practitioners as determined by the States (Federal Register, 1996). In addition, the needles will have to meet future standards for strength, sharpness, smoothness, and so on. It is expected that the sterility and single-use requirements will help to reduce infections and disease transmission; the restricted sales will help prevent injury by unqualified users; and the future standard will ensure the availability of high-quality needles.

In summary, the safety of acupuncture needles, as with all medical devices, is of concern to the FDA. The present level of information on the low level of risks of acupuncture and the requirements of the Class 2 regulations should provide reasonable assurance of safety during use of acupuncture needles.

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Acupuncture Activates Endogenous Systems of Analgesia

Ji-Sheng Han, M.D.

Introduction

Although acupuncture has been used in China for more than 2,000 years, the study of its mechanisms of action is a recent issue. To rule out the immediate concern that hypnotic-type suggestibility may play a key role in the therapeutic effect of acupuncture, animal experimentation is indispensable. In the long history of evolution, the brain has developed complex systems for modulating (diminishing or augmenting) pain perception. Notably, the opioid (morphine-like) system and nonopioid analgesic system (e.g., the monoamine neurotransmitters) suppress pain perception, whereas the antiopioid system (e.g., cholecystinin [CCK]) works against opioid analgesia. By activating the endogenous systems of analgesia, acupuncture is able to lessen the pain to a degree that is clinically significant and applicable.

Animal Models for Acupuncture-Induced Analgesia

Animals. Although monkeys and cats are closer to humans, rabbits and rats are the most frequently used animals in most studies published so far. Comparative anatomy is used to determine the site for the insertion of a needle corresponding to the point for acupuncture (“acupoint”) of humans.

Pain modalities. Pain can be classified as acute (caused by wound, surgical trauma, etc.) or chronic (caused by inflammation, nerve injury, etc.). In animal experiments, what is measured is not subjective feeling; rather, it is the objective reactions to “painful” (noxious) stimuli, manifested as escape behavior or vocalization. Nociceptive responses can be induced by heat and mechanical, chemical, electrical, and other stimuli that mimic acute pain. Chronic pain can be induced by nonbacterial inflammation or nerve injury (partial ligation or complete severance). A lowering of the pain threshold or an exaggerated pain behavior (hypersensitization) indicates the existence of chronic “pain.” Compared with acute pain models, chronic pain models are obviously closer and more relevant to most clinical situations.

Method of acupuncture. Manual twisting of the needle, the classical means of acupuncture, has often been replaced by electroacupuncture (EA), whereby electrical pulses are administered via stainless steel needles inserted through the skin into the deep tissues. The intensity (1 to 3 mA), pulse-width (0.2 to 1.0 ms), and frequency (1 to 100 Hz) can thus be precisely determined. A further modification is to use skin electrodes applied on the acupoints to replace the needles, which is called “acupoint nerve stimulation” (ANS), or “acupuncture without a needle,” which is technically close to “transcutaneous electrical nerve stimulation”

(TENS), although the principle and rationale of the two therapeutic methods are essentially different.

Acupuncture Activation of Endogenous Opioid Systems

Twenty years after the publication of the first biochemical evidence for the existence of opioid receptors by Pert and Snyder in 1973, the delta opioid receptor was cloned independently in 1992 by Evans and colleagues in the United States and Kieffer and colleagues in France, followed by the cloning of mu and kappa opioid receptors in 1993. On the other hand, five different kinds of opioid peptides have been characterized in the recent two decades (1975 to 1997). The possible relation of opioid peptides and opioid receptors with acupuncture-induced analgesia (AA) is listed in the following table.

Opioid peptide	Aminoacid residues	Year discovered	Opioid receptor matching	Optimal frequency	Site of Action	
					Brain	Cord
Enkephalin	5	1975	delta > mu	2 Hz	++	++
(-Endorphin	31	1976	delta = mu	2 Hz	+++	+
Dynorphin	17	1979	kappa	100 Hz	+	+++
Orphanin FQ	17	1995	ORL ₁	100 Hz	(---)	+ (antioioid)
Endomorphin	4	1997	mu	?	++	+++

The involvement of opioid peptides and opioid receptors in AA has been studied from different approaches, for example, (1) blockade of the effect of AA by opioid receptor antagonists, including the universal opioid antagonist naloxone (Pomeranz, Chiu, 1976; Mayer, Price, Rafii, 1977) and selective mu, delta, or kappa receptor antagonists (Chen, Han, 1992; Han, Wang, 1992); (2) blockade of AA by microinjection of an antibody against enkephalin, (-endorphin, or dynorphin into the central nervous system (CNS) (Han, Xie, Zou, et al., 1982); (3) measurement of the release of opioid peptides in brain and spinal cord during and following EA stimulation (Han, Chen, Sun, et al., 1991), and the like.

An important finding was that the ability of EA to accelerate the release of endogenous opioids in CNS depends, among other things, on the frequency being used. The 2-Hz EA increased the release of (-endorphin in the brain and enkephalin in the whole CNS, whereas 100-Hz EA increased the release of dynorphin in the spinal cord. This finding, originally discovered in rats (Fei, Xie, Han, 1987) has been verified in humans (Han, Chen, Sun, et al., 1991). In a recent study, the neural pathways for 2-Hz and 100-Hz EA stimulation have been worked out (Guo, Fang, Wang, 1996a, 1996b). Thus, by turning the dial of the stimulator, one could differentially control the release of three kinds of opioid peptides. To accelerate the release of all three kinds of opioid peptides, one could use the “dense-and-disperse” wave, that is, 2 Hz for 3 seconds followed by 100 Hz for 3 seconds, shifting back and forth automatically (Chen,

Guo, Chang, Han, 1994). This wave form results in the simultaneous release of all three kinds of opioid peptides. The synergistic interaction between the opioid peptides (Huang, Ren, Lu, Han, 1987) can produce a most potent analgesic effect.

Orphanin FQ was a newly cloned (1995) opioid peptide that seemed to play an antagonistic role against opioid analgesia (Tian, Xu, Fang, et al., 1997a; Tian, Xu, Zhang, et al., 1977b). A novel opioid peptide, endomorphin, reported by Zadina and colleagues in 1997, is a small peptide with high selectivity for the mu receptor. Its possible role in AA has yet to be determined.

The Role of Monoamines: Serotonin, Dopamine, and Noradrenaline

Most of the serotonin (5-HT) existing in the CNS stems from neurons aggregated along the midline of the brain. Blocking the biosynthesis of 5-HT by pCPA, destruction of the 5-HT neurons by 5,6-DHT, or blockade of 5-HT receptors by cinnanserine led to a marked reduction of AA, suggesting the importance of 5-HT in the mediation of AA, both in the brain and the spinal cord (Han, Chou, Lu, et al., 1979). The receptors involved were 5-HT_{1A} and 5-HT_{1C/2} (Xu, Qiu, Han, 1994). In contrast to 5-HT, catecholamines (dopamine [DA] and noradrenaline [NA]) play different roles in different parts of the CNS; that is, they antagonize AA in the brain and potentiate AA in the spinal cord (Xie, Tang, Han, 1981).

Antioioid Peptides: Cholecystokinin and Orphanin FQ

One of the basic principles of Chinese traditional medicine (TCM) is that everything can be divided into two, and overactivation of one part inevitably leads to a corresponding change on the counterpart of the system. A delicate balance between the two parts is symbolized as yin and yang. In the study of AA, it was found that prolonged acupuncture or EA stimulation for several hours produces a gradual decrease of the analgesic effect, which was titled "acupuncture tolerance." It simulates the development of morphine tolerance after its repeated injection (Han, Lin, Tang, 1981). Detailed studies revealed that prolonged EA stimulation accelerated the production and release of the peptide CCK that works against opioid effect (Zhou, Sun, Han, 1993). The cellular and molecular mechanisms of the antioioid effect of CCK have been elucidated (Han, 1995). In the rat experiment, acupuncture tolerance can be prevented or reversed by intracerebroventricular (icv) injection of CCK antiserum that prevents CCK from binding to its receptor (Han, Ding, Fan, 1986). The results suggest that (1) the use of EA for a single treatment should not exceed 1 hour and that (2) CCK antagonist may be useful in preventing the development of acupuncture tolerance.

Another interesting phenomenon is the individual variation in the effect of AA. About two-thirds of the animals are high responders (increase of pain threshold more than 60 percent), and one-third are low responders (pain threshold changes less than 60 percent). The mechanisms of being a low responder are at least twofold: (1) a low level of opioid peptides is released in the CNS (Fei, Xie, Han, 1987) and (2) a high level of CCK is released in response to EA stimulation

(Liu, S.X. et al., unpublished). Recent studies have revealed that a low-responder rat can be changed into a high responder if the CCK gene expression is suppressed by the antisense technology (Tang, Dong, Wang, et al., 1997). The CCK-B antagonist L-365260, a product of Merck Sharp Dohme, now available only for experimental use, could be taken as an adjunct for acupuncture treatment once it is clinically available, so that even a low responder can benefit from acupuncture treatment.

It is interesting to note that the newly cloned peptide orphanin FQ (OFQ) may perhaps be categorized into the antiopioid family because icv injection of OFQ dose dependently attenuated both morphine analgesia (Tian, Xu, Wang, et al., 1997a) and AA (Tian, Xu, Zhang, et al., 1997b) and icv injection of antisense RNA complementary to OFQ receptor, which reduces the number of OFQ receptors, produced a marked potentiation of EA analgesia (Tian, Xu, Zhang, et al., 1997b).

Conclusions

Acupuncture is a kind of medical technique whereby a moderate degree of peripheral stimulation can cause a maximal activation of the endogenous systems of analgesia that form the physiological and neurochemical mechanisms of AA. Because this is a kind of physiological modulation, the effect of acupuncture can only reduce rather than abolish pain. Although properly managed acupuncture produces little aversive side effects, it should not be used too often to avoid the development of tolerance. The efficacy of AA may be further improved by modulating the delicate balance between opposing neurochemical factors.

Future research

Study on chronic pain. Most of the knowledge about AA in animal experiments today was obtained in acute pain models. It was only recently that the effect of acupuncture on chronic pain was observed. Preliminary results have shown that the optimal parameters of EA (intensity, frequency, spacing of multiple treatments, etc.) for the treatment of chronic pain are different from those for acute pain, which requires further investigation.

A combination of acupuncture with drugs. By combining acupuncture with certain analgesic or anesthetic drugs, it is possible to achieve a state of complete analgesia, with the amount of drug reduced to as little as 50 percent of normal dosage, thereby reducing the unwanted side effects of the analgesics or anesthetics (Han, 1996).

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Acknowledgment: This work is supported by NIDA grant DA 03983 and a grant from the National Natural Science Foundation of China.

Overview of Clinical Trials on Acupuncture for Pain

Brian M. Berman, M.D.

Clinical trial data on acupuncture for the treatment of pain do indeed exist. Approximately 101 clinical trials in acupuncture for pain control use can be identified when searching electronically between the years of 1976 and 1995 depending on the specific search strategy (Singh, 1996). More than half these articles indicate that more members of the acupuncture groups improved than members of the control groups, regardless of the type of control used in the study. However, these articles are of mixed quality. They often do not have sufficient sample size to test for simple differences between groups, validation of the effectiveness of the randomization procedure used, or demonstration of the success of alternate methods to produce group equivalence. Reliance on nonstandardized measures for the area of pain occurs frequently, and the issues around the relative effectiveness of the placebo or sham control are not addressed (Anderson, Jamieson, Man, 1974; Emery, Lythgode, 1986; Moret, Forster, et al., 1991). In addition, safety issues often are not addressed (Lao, 1996a, 1996b).

More than half the clinical trials and 19 of 30 outcome studies, derived from an electronic search of acupuncture and pain studies from 1976 through 1995, indicate that acupuncture can be an effective therapy in the reduction of pain. However, these studies are not methodologically rigorous and are often not the best evidence of the efficacy of acupuncture. Until there is sufficient clinical trial literature that is free from concerns over the internal and external validity of the results presented, more research in this area will be required (Singh, Berman, 1997).

Future studies in the area of pain and acupuncture must pay particular attention to the use of sufficient sample sizes for the trial as proposed, use standardized outcome measures when available, address questions concerning appropriate length of followup treatment to determine treatment decay patterns, and determine optimum maintenance regimes for various diagnoses. Description of the evaluation or validation of the adequacy of the treatment protocol should be reported in the literature, along with detailed descriptions of the acupuncture treatment protocol, to allow for subsequent replication of studies reported. As the basic questions around efficacy and safety are addressed, so too should questions around the relative influence that (1) cultural perspective, (2) gender, (3) age, (4) life style, or (5) other individual difference parameters might have on patient outcome. Last, the patient's perspective of the clinical experience beyond the collection of standardized scores must be collected, and the relationship of this clinical perspective on outcome must be assessed.

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Efficacy of Acupuncture in Treating Low Back Pain:A Systematic Review of the Literature

Daniel C. Cherkin, Ph.D.

Background

Low back pain is a major cause of dysfunction, medical expenses, absenteeism, and disability in industrialized countries (Deyo, Cherkin, Conrad, et al., 1991; van Tulder, Koes, Bouter, 1995). Although low back pain is usually a self-limiting and benign illness that improves without treatment (Waddell, 1987), numerous therapeutic interventions are available (Spitzer, leBland, Dupuis, 1987). The effectiveness of most of these interventions, however, has never been adequately evaluated.

Objectives

The objective of this study is to systematically review the literature to determine whether acupuncture is more effective than a placebo, sham acupuncture, or reference treatments (e.g., exercise or medication) for nonspecific low back pain with regard to pain intensity, overall improvement, functional status, and return to work.

Study Team

This project is being undertaken by an international team of investigators: Maurits van Tulder, Ph.D. (principal investigator), and Bart Koes, Ph.D., of the Institute for Research in Extramural Medicine at the Free University in Amsterdam; Dan Cherkin, Ph.D., of the Group Health Center for Health Studies and the University of Washington in Seattle; and Brian Berman, M.D., and Lixing Lao, Ph.D., L.Ac., of the Division of Complementary Medicine in the Department of Family Medicine at the University of Maryland in Baltimore.

This review is being undertaken under the auspices of the Cochrane Collaboration. The Cochrane Collaboration is an international network of researchers whose objective is to prepare, maintain, and disseminate high-quality systematic reviews of randomized controlled trials and other sources of evidence of health care interventions (Bero, Rennie, 1995). Within the Cochrane Collaboration, systematic reviews in specific areas are coordinated by Collaborative Review Groups. This review of the effectiveness of acupuncture for low back pain is being conducted under the auspices of the Back Review Group for Spinal Disorders (Bombardier, Esmail, Nachemson, 1997) in cooperation with the Cochrane Complementary Medicine Field.

Materials and Methods

Inclusion criteria. Only randomized controlled trials (RCTs) evaluating the use of needle acupuncture for subjects with nonspecific low back pain are included. Thus, RCTs involving either traditional acupuncture (in which the needles are inserted in classical points situated on meridians) or contemporary acupuncture (in which the needles are inserted closer to the dermatome of the injury) are included, regardless of whether electrical stimulation was used.

Outcome measures. Outcomes of primary importance are pain intensity, global improvement (e.g., subjective improvement of symptoms), functional status, or work loss. Measures of physical outcomes (e.g., range of motion), generic health status (e.g., SF-36), and outcomes such as medication use and acupuncture side effects are considered secondary.

Search strategy. RCTs meeting the inclusion criteria for this review will be identified by:

- A computer-aided search of the MEDLINE (1966-96), EMBASE (1988-96), PsycLIT (1984-96), and complementary-medicine databases.
- Screening of references given in relevant reviews and identified RCTs.
- Screening of the Cochrane Library, 1997, issue 1.
- Communication with the Cochrane Center in Baltimore, MD (K. Dickersin), to identify additional RCTs from the manual searching currently being undertaken by the Cochrane Collaboration.
- Communication with the Cochrane Complementary Medicine Field to identify additional RCTs from this field's trials register.
- Citation tracking of the RCTs identified by using the Science Citation Index.

Selection of studies. Two reviewers will independently complete the search strategy to identify RCTs that might meet the criteria for inclusion in the review. The same two reviewers will then be given copies of these studies and will independently determine whether they meet the inclusion criteria. A consensus method will be used to resolve disagreements, and a third reviewer will be consulted if disagreements persist.

Methodological quality assessment. Methodological quality of the RCTs will be independently assessed by two reviewers blinded to authors' names, institutions, and journals. The following aspects of internal validity of the RCTs will be used to assess methodological quality: (1) concealment of treatment allocation, (2) similarity of baseline characteristics, (3) blinding of patients, (4) blinding of outcome assessment, (5) blinding of care provider, (6) co-interventions, (7) adherence to interventions, (8) withdrawal/dropout rates, and (9) identical timing of outcome assessment. These criteria are based on those used in previous systematic reviews (Koes, Assendelft, van der Heijden, et al., 1991; Koes, Bouter, Beckerman, et al., 1991; Koes, van den Hoogen, 1994; Koes, van Tulder, van der Windt, et al., 1994; Koes, Scholten, Mens, et al., 1995; Assendelft, Koes, van der Heijden, et al., 1992; van der Heijden, Beurskens,

Koes, et al., 1995). The items will be weighted equally and will be scored as positive, negative, or unclear. Authors will be contacted for additional information when necessary. A consensus method will be used to resolve disagreements, and a third reviewer will be consulted if disagreements persist.

Data extraction. Two blinded reviewers will independently extract the data on the relevant outcomes: (1) pain intensity, expressed on a visual analog or similar scale; (2) global measure of improvement, expressed as the proportion of patients recovered or improved according to a (forced) dichotomized overall assessment of the clinical state by the patient or an assessor; (3) functional status, expressed on a back pain-specific scale or a more generic scale; (4) return to work, expressed as the number of days of sick leave or the proportion of patients returned to work; (5) physical outcomes (e.g., range of motion); and (6) other symptoms (e.g., medication use, side effects). If data are not reported in a form enabling quantitative pooling, the authors will be contacted for additional information. If the information is no longer available, the trial will not be included in the pooling for that specific outcome.

Meta-analysis. For each outcome for which there are adequate data, the results of each RCT will be plotted as point estimates with corresponding 95-percent confidence intervals. If there is inconsistency in the results of the RCTs, the relationship between certain characteristics of the RCT and the observed outcome will be investigated. For example, the RCTs might be characterized along the following dimensions: (1) type of comparison group (e.g., placebo, sham acupuncture, other types of conservative treatment); (2) type of acupuncture (e.g., traditional vs. nontraditional acupuncture, with vs. without “teh chi”); (3) experience of acupuncturist; (4) methodological quality of study; (5) duration of back pain (e.g., <12 weeks vs. >12 weeks); or (6) duration of followup (e.g., <6 months vs. >6 months). Meta-analysis will be performed separately for each outcome measure. “RevMan” software will be used to perform the meta-analyses.

Results

The results will be available by November.

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Overview of the Efficacy of Acupuncture in the Treatment of Headache and Face and Neck Pain

Stephen Birch, L.Ac., Ph.D.

Pain is a major problem for the U.S. health care delivery system. Estimates are that as many as 10 percent of all Americans have pain conditions that are present for over 100 days a year (Hanson, Gerber, 1990), and up to 14 percent of all males and 28 percent of all females in the United States complain of relatively frequent headaches (Blanchard, Andrasik, 1985). The overall health care costs for chronic pain are very high. Treatments that are less expensive and relatively effective for these chronic pain problems should acquire a growing place in the United States health care system.

Many studies have been conducted to investigate the efficacy of acupuncture for chronic pain. The majority of these studies have been inadequately designed from the clinical trial standpoint (Birch, Hammerschlag, 1996; Ter Riet, Kleijnen, Knipschild, 1990; Vincent, 1993; Vincent, Lewith, 1995) and can have, for example, insufficient sample size, and/or outcome measures, and/or problems with control groups. Many studies have also been unsatisfactory from the standpoint of the practice of acupuncture. Examples included administering clearly inadequate treatment, not using a qualified acupuncturist to administer the treatments, and administering inappropriate needling procedures, which were often confused with placebo (Birch, 1995, 1997a). The complexities of designing studies to test acupuncture have yielded many different study designs (Birch, 1997b; Vincent, 1993), but there has been little effort to replicate the results of these studies (Lytle, 1993). Taken together, these issues complicate the process of drawing conclusions about the efficacy of acupuncture, principally because of difficulties in interpreting the findings. While previous reviews have reached different conclusions (Birch, Hammerschlag, 1996; Lytle, 1993; Patel, Gutzwiller, Paccaud, et al., 1989; Ter Riet, Kleijnen, Knipschild, et al., 1990; Vincent, 1993), the weight of positive evidence of the efficacy of acupuncture has continued to increase, warranting further studies and reviews.

The medical literature contains at least 26 controlled clinical trials in which acupuncture is used to treat headache (16), face pain (4), or neck pain (6). Headache trials primarily included patients with tension headache, migraine, or a combination of these two. Face pain trials included pain of muscular origin, with some focus on the problem of trigeminal neuralgia. Neck pain trials covered a range of medical problems including osteoarthritis, myofascial pain, cervical spondylosis, cervical osteophytes, and nerve root problems leading to radiculopathy. Generally speaking, up to 23 of these 26 studies found that acupuncture was relatively effective.

The studies will be examined according to their design. These clinical trials fall into two general design categories:

- Acupuncture versus a “placebo” treatment (sham TENS or noninvasive placebo needling), or a control invasive needling procedure (commonly called “sham” or “minimal” acupuncture).
- Acupuncture versus a standard biomedical treatment for that condition (e.g., medication or physiotherapy) or a no-treatment control (e.g., a wait-list control group).

Some studies with more complex designs will also be included (Hesse, Mogelvang, Simonsen, et al., 1994; Lenhard, Waite, 1983; Thomas, Eriksson, Lundeberg, 1991). Related studies that did not include sufficient detail (Yue, 1978) or were abstracts (Teng, Liu, Chang, 1973), and studies that tested nonacupuncture techniques, such as lasers (Ceccherelli, Altafini, LoCastro, et al., 1989), will not be included in the discussion.

The following table shows the number of studies in categories one, two, and the more complex designs category:

Category	One	Two	Complex Designs
Headache	9	5	2
Face Pain	1	3	--
Neck Pain	3	2	1

Of the nine headache studies in category one, six used a control needling treatment (Baust, Strutzbecher, 1978; Hansen, Hansen, 1985; Henry, Baille, Dartigues, et al., 1985; Tavola, Gala, Conte, et al., 1992; Vincent, 1990, 1989), and three used some form of placebo treatment (Dowson, Lewith, Machin, 1985; Jensen, Melsen, Jensen, 1979; White, Eddleston, Hardie, et al., 1996). In eight of the nine studies, the acupuncture treatment was more effective than the control needling or placebo, reaching significance in three studies (Hansen, Hansen, 1985; Henry, Baille, Dartigues, et al., 1985; Vincent, 1989). Of the five headache studies in category two, acupuncture was roughly equivalent in efficacy to the standard therapies in all five studies (Ahonen, Hakumaki, Mahlamaki, et al., 1983; Carlsson, Fahlcrantz, Augustinsson, 1990; Carlsson, Rosenhall, 1990; Doerr-Proske, Wittchen, 1985; Loh, Nathan, Schott, et al., 1984). Of the two headache studies in the last category, the study by Hesse and colleagues (1994) found acupuncture to be superior to placebo needling, at least as effective as the standard therapy, and with less side effects than the standard therapy. The study by Lenhard and Waite (1983) found the acupuncture treatment to be effective and apparently not endorphin mediated. In toto, the weight of evidence for

acupuncture in the treatment of tension and migraine headaches is positive, with a clear need for larger, well-designed studies to attempt replication of previous results.

The face pain study in category one found acupuncture to be significantly more effective than the control needling (Hansen, Hansen, 1983). All three face pain studies in category two found acupuncture to be as effective as standard treatment (Johansson, Wenneberg, Wagersten, et al., 1991; List, Helkimo, Andersson, et al., 1992; List, Helkimo, 1992; Raustia, Pohjola, Virtanen, 1985). While the small numbers of studies of acupuncture for face pain may make it difficult to reach clear conclusions, the evidence so far is all positive but again indicates a clear need for larger, well-designed replications of this work.

Of the three neck pain studies in category one, one used control needling treatment (Matsumoto, Levy, Ambruso, 1974), and two a placebo treatment (Petrie, Hazleman, 1986; Petrie, Langley, 1983). Acupuncture was found to be more effective than control needling. It was found to be more effective than sham TENS in the pilot study (Petrie, Langley, 1983), but not in the followup study (Petrie, Hazleman, 1986). Of the two neck pain studies in category two, acupuncture was quite effective and slightly more so than standard therapy (Loy, 1983) and was significantly more effective than a wait list (no treatment) control (Coan, Wong, Coan, 1982). The final neck pain study (Thomas, Eriksson, Lundeberg, 1991) found acupuncture to be significantly more effective than a placebo medication, and, while more effective than the medication and sham acupuncture, it did not achieve significance against these treatments. The interpretation of these studies is difficult. Since there have been significant problems with some of these studies (Birch, 1995), it is important to conduct better designed studies to clarify the question of efficacy of acupuncture for neck pain.

In all three pain categories, evidence that acupuncture was more effective than placebo or sham acupuncture was found, with that evidence strongest in the treatment of tension and migraine headache. In all three pain categories, evidence that acupuncture was performing as well as, and sometimes better than, standard therapy for the same problem was found. In one study, additional evidence showed that acupuncture had less side effects than the standard therapy.

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Efficacy of Acupuncture in the Treatment of Osteoarthritis and Musculoskeletal Pain

Gary Kaplan, D.O.

Introduction

Acupuncture is most frequently used in this country for the treatment of a wide variety of painful medical conditions. Two of the most common pain conditions for which individuals seek acupuncture treatment are myofascial pain syndromes and the pain and disability associated with osteoarthritis. One survey of physician acupuncturists found that myofascial pain syndrome was the second most common medical condition treated with acupuncture. Of the physicians surveyed, 96 percent rated acupuncture as effective for the treatment of this condition. Complaints of pain related to osteoarthritis were treated by more than 80 percent of the physicians polled. Effectiveness for the treatment of osteoarthritis was rated at between 80 and 85 percent, depending on the joint treated. Numerous case reports in the literature further substantiate the widespread use of acupuncture for these conditions. The goals of this presentation are twofold: (1) It will summarize the English-language literature of controlled trials of the use of acupuncture for the treatment of myofascial pain syndromes and the pain associated with osteoarthritis. (This presentation will exclude all of the literature on low-back pain, as these data will be presented elsewhere.) (2) It will discuss briefly some of the important deficiencies in our knowledge that will require further research in this area.

Conclusions

There is good although limited evidence for the efficacy of acupuncture in the treatment of myofascial pain syndromes. For the pain and disability of osteoarthritis, the studies are limited but consistently demonstrate evidence for the efficacy of acupuncture. The study of acupuncture has been hampered by the difficulties in designing good controls, improper application of acupuncture in some studies due to incomplete understanding of acupuncture diagnoses and therapeutics by some researchers, lack of standardization of outcome measurements, and lack of funding. These problems are being addressed in numerous studies presently under way. On the basis of the work presented as well as the author's clinical experience, there is strong evidence that acupuncture should be made available for the treatment of patients suffering with myofascial pain syndromes and osteoarthritis.

Myofascial Pain Syndrome. The controlled studies on acupuncture's efficacy for the treatment of myofascial pain syndrome focused primarily on regional pain complaints involving the neck or lateral epicondyle area. All the patients in these studies suffered with chronic pain complaints. Most of the studies involved patients who had received standard medical interventions that had failed to resolve their medical problems. The majority of the participants in all the studies

reported improvement in both subjective and objective measurements of pain. Not all the studies recorded both subjective and objective outcome measurements. At least one study failed to show any statistical difference between real acupuncture and sham acupuncture control groups. Most of these studies have methodological problems. Nevertheless, there is a clear and consistent demonstration of acupuncture's efficacy in the treatment of these conditions.

Osteoarthritis. The controlled studies for osteoarthritis focus primarily on osteoarthritis of the cervical spine and knees. Similar studies also showed acupuncture to be potentially useful for osteoarthritis affecting the hips and hands. This group of studies includes evaluations of the efficacy of acupuncture compared with drug therapies. Subjects in these studies reported pain relief as not only good if not better than that provided by the medication but also without the side effects. The ability of acupuncture to provide pain relief in one study was so impressive that several of the patients in the study awaiting surgery were able to avoid surgery. Gaw and colleagues (1975) were successful in obtaining pain relief in the majority of their patients, although they failed to demonstrate a statistically significant difference between sham and real acupuncture groups. (Again, many of these studies have methodological problems.) The more recent studies have successfully addressed these issues. In all the studies, the majority of the patients treated reported significant relief of their pain and disability.

The Future

The majority of the studies reviewed, although demonstrating consistent efficacy of acupuncture for the treatment of myofascial pain and pain associated with arthritis, suffer from methodological problems. Most of these problems are not unique to the study of acupuncture. They are consistent with those found in the literature attempting to evaluate medical procedure interventions. From this perspective, the acupuncture studies reviewed may in fact be adequate to prove that acupuncture is as efficacious as the majority of medical procedures. One problem unique to the study of acupuncture has been the inappropriate performance of acupuncture by researchers not adequately trained in acupuncture diagnostics and therapeutics. This problem has been addressed with the availability of a large and growing body of well-trained physician acupuncturists and licensed acupuncturists. From these studies, we have learned much not only about the efficacy of acupuncture but also about how to design proper controls and utilize proper outcome measurements. One major obstacle that is beginning to be overcome is the need for research funding. Lack of funding in the past has hampered the design of large-scale studies with proper statistical and data collection support. Future studies need to evaluate acupuncture's efficacy as sole and adjunctive therapies for these conditions. Cost-benefit analysis will also need to be done in the future. These studies indicate that acupuncture has much potential for the treatment of the pain associated with myofascial pain syndrome and osteoarthritis. Present studies in conjunction with the numerous case reports in the literature demonstrate that acupuncture is a viable treatment option that should be made available for patients with these pain problems.

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Dental and Postoperative Pain

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Introduction

Acupuncture, used for the treatment of pain for thousands of years in China, is well documented in ancient Chinese literature. In recent decades, the Chinese have reported successfully using acupuncture as anesthesia during operations. In 1971, a New York Times journalist working in China reported his experience of acupuncture treatment for postoperative abdominal pain. Since then, studies have been conducted to evaluate the effectiveness of acupuncture on postoperative pain relief. Although case reports from China and within the West are numerous, well-controlled studies on the effective use of acupuncture for dental and postoperative pain are limited. The articles used for this review were identified by searching the key words acupuncture, postoperative pain, and dental pain throughout various databases. Foreign articles, containing only English abstracts, were not included in this review.

Conclusion

Overall, the research shows positive trends suggesting that acupuncture is a promising method of providing relief from dental and postoperative pain. However, methodological design insufficiencies need to be addressed. Well-designed studies of acupuncture analgesia on postoperative pain are warranted.

Acupuncture and Postoperative Pain

Randomized controlled studies. Four randomized studies on the effects of acupuncture on postoperative pain after general surgery have been identified. In 1981, Facco and colleagues compared the effects of acupuncture and pentazocine for the treatment of 34 patients with postoperative hysterectomy pain. The results indicated that the analgesic effect of acupuncture is equivalent to the analgesic medication used in the study. In addition, acupuncture significantly increased the net vital capacity of patients who received treatment. Martelele and Fiori (1985) investigated the effect of acupuncture in 72 patients undergoing various types of surgeries involving the upper or lower abdominal, rectal, or lumbar area. The results indicated that acupuncture is superior to both pain medication and transcutaneous nerve stimulation (TNS) in terms of pain intensity and duration. In a study of gynecological postoperative surgical pain (Christensen, Noreng, Andersen, et al., 1989), 20 women were randomized into either electroacupuncture (EA) treatment or no acupuncture treatment. The treatment was conducted before the patient recovered from general anesthesia; therefore, the patient was blind to the treatment type. The results indicated that the patients who received EA consumed significantly

less (50 percent) of the postoperative pain medication compared with the group that received no acupuncture. Grabow (1994) reported contrasting findings, suggesting that the analgesic effect of acupuncture is no better than the effect of a placebo medication.

Three randomized studies of acupuncture on postoperative dental pain were reviewed. Sung and colleagues (1977) reported a study of the effect of acupuncture on postoperative pain compared with codeine and placebos. Forty patients who underwent dental surgery, mainly wisdom tooth extraction, were randomly assigned to treatment or control groups immediately after they reported postoperative pain. The study indicated that acupuncture in combination with pain medication may be more effective than acupuncture, medication, or a placebo. In addition, acupuncture was shown to be better than sham acupuncture. However, the results reported by Lapeer and colleagues (1987) indicated no difference in postoperative pain between the acupuncture treatment group and the conventional medication treatment group, although significant reduction in pain and medication consumption was observed over the 10-day followup period.

Lao and colleagues (1995) reported a randomized, patient-blinded study on the effect of acupuncture on postoperative oral surgical pain. Nineteen patients were randomly assigned to either an acupuncture treatment group or a placebo acupuncture control group (in which no acupuncture needles were inserted into the skin). The results indicated that patients treated with acupuncture received a significantly longer pain-free time and experienced less pain intensity than those who received placebo acupuncture.

Clinical observation studies. A number of nonrandomized clinical studies of acupuncture on postoperative pain have been reported. Zhou and colleagues (1981) treated 102 patients with postoperative anal pain using an embedded acupuncture needle. Sixty-nine percent of the patients achieved instant relief, and 27.5 percent of the patients reported gradual pain relief. Mastroianni (1985) reported 50 percent fewer doses of analgesic medication consumption in the acupuncture group compared with the control group in 100 patients after abdominal surgery. Kho and colleagues (1990) observed the effect of acupuncture in combination with small doses of pethidine in 20 patients undergoing surgery for the removal of thyroid adenoma. The patients who underwent acupuncture treatment had rapid and uncomplicated recoveries. In addition, the majority of patients reported either no pain or mild pain on the first postoperative day.

Acupuncture and Dental Pain

A few studies have reported on the effects of acupuncture for dental pain relief. An uncontrolled study by Selden (1978) reported both immediate and lasting acupuncture analgesia in 92 percent of patients ($n = 55$) with oral-facial pain, especially for pain of dental origin. A similar clinical observation study (Silva, 1989) found that 86 percent of patients ($n = 94$) receiving acupuncture after normal tooth extraction had no pain, 10 percent experienced slight pain, and only 3 percent had no pain relief following treatment. Wong (1989) reported clinical

observation findings supporting the effect of acupuncture in general dental practice.

Laboratory experiments indicate that acupuncture increases dental pain threshold in normal subjects. Chapman and colleagues (1982) tested the effect of EA on dental pain threshold in 40 healthy subjects. The results revealed that EA was effective in increasing the pain threshold. In addition, the findings indicated that the effectiveness of acupuncture was not influenced by cultural differences. Yukizaki and colleagues (1986) tested the pain threshold in 10 healthy humans. Of 10 subjects tested, 6 showed an elevated tooth pain threshold after receiving EA. Ernst and Lee (1987) reported that EA applied to a single point (*Hegu*) increased pain threshold after 30 minutes of experimentally induced dental pain. These increases were partially blocked by intravenous naloxone. The results from animal studies have confirmed the findings from human subjects. Two studies (Ha, Wu, Contreras, et al., 1978; Ha, Tan, 1982) tested the pain threshold measurements of tooth pulp in monkeys. Both studies found that acupuncture significantly increased the pain threshold in monkeys treated with acupuncture compared with the control group.

Research Design Issues

In spite of positive results obtained from published literature, the methodological deficiencies remain and need to be addressed. A major problem with acupuncture research has been the lack of development of appropriate control groups.

Placebo considerations. In evaluating analgesic effect, the placebo component is real and must be taken into account (Fields, 1981). The patient motivation and expectation should also be taken into consideration (Lapeer, Biedermann, Hernsted, 1987; Taub, Mitchell, Stuber, 1979). A few studies (Lao, Bergman, Langenberg, et al., 1995; Christensen, Noreng, Andersen, et al., 1989) make an effort to test the influence of the placebo effect or to validate patient blindness.

Lao and colleagues are conducting a randomized placebo-controlled trial to evaluate the use of Chinese acupuncture on postoperative oral surgical pain. The placebo control procedure in this study is identical to that used in the treatment group, but there is no needle insertion into the skin. The validity of the placebo model, patient expectation, patient motivation, and psychological impact are being evaluated through use of a questionnaire. Preliminary results show that acupuncture is significantly more effective than the placebo in treating postoperative pain. The preliminary study concluded that the positive effects of acupuncture are not associated with patient motivation or expectation.

Future Considerations

To confirm the previous findings of the effect of acupuncture on postoperative pain, randomized, well-controlled studies with sufficient sample size, definitive criteria, standardized outcome measurements, and appropriate acupuncture treatments are desirable.

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Neuropathic Pain

Judith C. Shlay, M.D.

Peripheral neuropathy is defined as deranged function and structure of peripheral motor, sensory, and autonomic neurons, involving either the entire neuron or selected levels. The disorders can appear clinically in diverse ways, depending on the severity of the process, the rate of progression, the anatomic structures affected, the population of neurons affected, the level within the neurons affected, and the subcellular pathologic process involved (Dyck, 1982).

From a symptom standpoint, the first noticeable features tend to be sensory and consist of tingling, prickling, burning, or bandlike dysesthesia in the balls of the feet or tips of the toes, or in a general distribution over the soles. Symmetry of symptoms and findings in a distal graded fashion is typical. As worsening occurs, sensory loss moves centripetally in a graded “stocking” fashion, and the patient may complain of severe numbness in his/her feet leading to difficulty with ambulation (Simpson, Wolfe, 1991).

Peripheral neuropathy is commonly associated with numerous metabolic or neoplastic conditions. Conditions causing peripheral neuropathy include hypothyroidism, B vitamin malnutrition, diabetes, uremia, liver disease, carcinoma, HIV disease, and numerous drugs and environmental toxins, as well as an inherited neuropathy (Ashbury, 1994).

Treatment of peripheral neuropathy due to a treatable cause is usually amenable to therapy. But for patients with HIV or diabetes, the therapy has been mainly symptomatic and treated with antidepressants, anticonvulsants, and nonnarcotic and narcotic analgesics (Portenoy, 1993). The problem with many of these medications is the numerous side effects and the difficulty in tolerating the treatment.

The role of acupuncture in the relief of pain has been studied (Murray, 1995; Birch, Hammerschlag, Berman, 1996). There is good evidence for the short-term effectiveness of acupuncture when used for the relief of pain. The extent of the relief varied, but the proportion of patients who benefited ranged from 50 percent to 80 percent. This is significantly larger than the 30 percent or 35 percent of patients who would benefit if the effects of acupuncture were mediated entirely by placebo-related factors (Vincent, Richardson, 1986).

A pilot study of acupuncture for symptomatic treatment of HIV-associated peripheral neuropathy evaluated both objective and subjective sensory motor nerve function testing and the quality-of-life measurements. The patients received twice weekly acupuncture treatment for 6 months in a non-randomized observational study. Of 39 enrollees, 26 patients completed followup. A significant improvement was seen in the quantitative sensory testing of vibration of the toe, with a baseline mean = 44.4 microns versus followup = 35.0 microns; $p = .05$. Data from the neurologic examination showed qualitative improvement in 7, unchanged in 16, and worsened

in 3. Tests of motor function were improved in 5 and unchanged in 21 patients. Using group means, five of the seven quality of life indicators showed an improvement, although none were statistically significant. The study suggested that there may be a role for acupuncture as a treatment for peripheral neuropathy, but further controlled studies were needed (Tosches, Cohen, Day, 1992).

Because of the need for more studies on HIV-related peripheral neuropathy and because of a large interest by the community in studying complementary medicine, the Community Programs for Clinical Research on AIDS (CPCRA) of the National Institute of Allergy and Infectious Diseases (NIAID) conducted a study entitled "The efficacy of a standardized acupuncture regimen and amitriptyline compared with placebo as a treatment for pain caused by peripheral neuropathy" (Shlay et al., 1994). The goal of the study was to evaluate the separate and combined efficacy of a standardized acupuncture regimen and amitriptyline on the relief of pain due to HIV-related peripheral neuropathy. Results of the study will be presented.

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The Role of Physiologic Imaging in the Investigation of the Effects of Pain and Acupuncture on Regional Cerebral Function

**A. Alavi, M.D., R. LaRiccia, C. Lattanand,
D. Mozley, and A. Newberg**

Single photon emission computed tomography (SPECT) was originally introduced in the early 1960s to demonstrate breakdowns in the blood-brain barrier as a consequence of central nervous system (CNS) disorders. The introduction of 18F-Fluorodeoxyglucose (FDG) technique along with positron emission tomography (PET) in 1976 opened a new era for the measurement of regional cerebral function under various physiologic and pathologic conditions. Over the past two decades, this technique has been widely utilized to examine brain function in a variety of neuropsychiatric disorders. By now, it is quite clear that functional imaging is far more sensitive than anatomic studies in detecting CNS abnormalities due to psychiatric and neurological disorders. PET imaging has been used in a limited number of sites because of its complexity and the high costs involved in establishing such sites. The success of PET has resulted in the resurgence of SPECT as an alternate modality for determining regional brain function. The introduction of 123-iodine and 99m technetium (99m-Tc) labeled tracers for determining regional cerebral blood flow as well as modern SPECT instruments has enhanced the role of this technique as a sound research and clinical tool. The latter modality particularly lends itself well to research studies related to acupuncture and meditation.

We have examined five normal volunteers without pain before and following the insertion of acupuncture needles to determine the effects of this therapeutic intervention under normal physiologic conditions. In addition, five patients who had previously benefited from acupuncture were studied before and after treatment. SPECT imaging was performed by use of a dedicated three-headed instrument (Picker Prism 3000) and 99m Tc-labeled hexamethylpropyleneamine oxime (HMPAO) as a tracer to map regional cerebral function. Every subject was examined in a resting baseline state following the administration of 7 mCi of the radiotracer. Acupuncture was administered immediately following the baseline scan in both the controls and patients with pain. In control subjects 15 to 20 minutes following the insertion of the needles and in patients at the height of pain relief, another dose (25 mCi) of 99m Tc HMPAO was administered, and the subjects were scanned with SPECT later. Images were examined by assigning regions of interest around the caudate nuclei, putamen, thalami, brain stem, and the entire brain. Region to whole brain count ratios were generated from the assigned regions.

In four of five normal volunteers, an average increase of approximately 20 percent in count ratios was noted in the thalamus. In patients, the pattern of resting regional cerebral blood flow was different from that of normal subjects. The uptake of the tracer in the thalamus was asymmetric in four of five subjects who were suffering from pain at the time of injection. This pattern changed significantly following the administration of acupuncture with the disappearance of the asymmetry noted in baseline scans. In three patients, there was substantially increased

uptake in the brain stem following the introduction of acupuncture. All patients reported improvement in pain following acupuncture.

These preliminary data demonstrate that SPECT Tc HMPAO imaging is a sensitive and reliable technique for revealing the effects of pain and acupuncture in patients and in normal subjects. Further investigation is needed to determine the potential role of this and similar techniques in elucidating the mechanism of action of acupuncture in various clinical settings.

Summary of Acupuncture and Pain

Bruce Pomeranz, M.D., Ph.D.

Introduction

In March 1996, the U.S. Food and Drug Administration (FDA) reclassified acupuncture from Class III (investigational) to Class II (safe and effective but requiring restrictions). The process began with a workshop in April 1994, organized by the Office of Alternative Medicine (OAM), at which 13 acupuncture researchers from around the world presented papers to 22 FDA officials who were free to comment and critique the presentations (Eskinazi, 1996). Speakers presented evidence from clinical trials in five main areas: pain, drug-dependence, stroke, asthma, and antiemesis. This author presented the basic science on the biological effects of acupuncture. On the whole, the FDA officials were impressed by the large body of basic and clinical research data for pain but were concerned about the heterogeneity of the clinical papers. There were no multicentered clinical trials, such as the ones used by the FDA to classify a new drug. More important, the clinical studies on pain were extremely heterogeneous in design, making meta-analysis difficult. Moreover, sham needling (the placebo control) was itself effective in producing some analgesia, raising doubts about many of the controls (Eskinazi, 1996).

In contrast, the research on antiemesis allowed for meta-analysis because more than a dozen studies treated pericardium 6 (a point over the median nerve in the forearm) and found that it worked significantly better than a nearby sham point (which had no effect). After this workshop, the acupuncture lobby submitted a petition more than 3,000 pages long requesting reclassification of acupuncture for five indications: pain, stroke, antiemesis, drug-dependence, and asthma. On March 29, 1996, the FDA reclassified the needle from Class III to Class II but did not make reference to effectiveness for any particular condition (even antiemesis), perhaps to avoid the political consequences of endorsing certain indications for medical insurance purposes. The message was clear: much work remains to be done to determine acupuncture's efficacy for clinical pain despite a large body of heterogeneous data and good biological evidence. As a possible solution to the sham acupuncture dilemma, some FDA officials recommended that future clinical studies should compare acupuncture with conventional therapies (for example, nonsteroidal anti-inflammatory drugs [NSAIDs]) in a head-to-head randomized trial, forgetting about placebo controls. The FDA merely wanted to determine "efficacy and safety" and not a mechanism of action (for example, placebo need not be factored out). If acupuncture performed as well as NSAIDs, with fewer side effects, that would satisfy the FDA. In the meanwhile, it legitimized the needles and left the specific disease indications for a future determination.

Conclusions

Many of the biological effects of acupuncture for chronic pain are well documented. Based on extensive literature with 15 lines of evidence from 99 papers, it is generally accepted that acupuncture blocks pain by releasing brain endorphins (Stux, Pomeranz, 1995).

Unfortunately, the clinical efficacy question is not as clear cut. The literature is confounded by sham controls that produce analgesia and by heterogeneity of designs using diverse stimulation parameters (many of which are now known not to work) (Eskinazi, 1996). An informal nonsystematic review by this author concluded that acupuncture is effective (Stux, Pomeranz, 1995). Nevertheless, multicentered studies are needed with homogeneous parameters of stimulation that avoid sham controls; perhaps a head-to-head comparison of acupuncture versus NSAIDs in a randomized clinical trial (RCT) is the best approach for this multicentered study.

Efficacy of Acupuncture for Chronic Pain

For chronic pain, there have been seven reviews of acupuncture RCTs (Birch, Hammerschlag, Berman, 1996; Hsu, 1996; Lewith, Machin, 1983; Reed, 1996; Richardson, Vincent, 1986; Stux, Pomeranz, 1995; Vincent, Richardson, 1986) and two meta-analytic reviews of acupuncture (Patel, Gutzwiller, et al., 1989; Ter Riet, Kleijnen, Knipschild, 1990). In addition, there have been several articles summarizing the problems caused by performing sham acupuncture (as placebo controls) (Leewith, Vincent, 1996; Vincent, Lewith, 1995). Unfortunately, needling at sham locations can have analgesic effects almost as large as at “true” locations. As a result of this problem, effects of true and sham become too close, requiring large subject numbers to show a significant difference (for example, statistical power is too low to detect small differences). Generally, acupuncture studies do not have a large number of subjects. Unfortunately, meta-analyses, which sought to enhance the power of the data and solve this dilemma, are not reliable because of the heterogeneity of designs and hence variations in the databases. Parameters of acupuncture treatment vary among studies: depth of needle, rate of stimulation, type of stimulation (manual or electrical), location (classical points, nonclassical points, trigger points), and site of stimulation (same spinal segment or distant points). Perhaps the most serious confounding variable is the intensity of stimulation used (weak stimulation that activates types I and II afferents or strong that activates type III to produce de qi). Failing to make these parameters homogeneous is like doing a meta-analysis on a drug that was given at vastly varying doses (often outside the dose response curve range). Not to produce de qi, for example, is less likely to secrete endorphins (see below).

Even meta-analyses that do quality assessments usually focus on statistical issues (for example, randomness, dropouts) and are ignorant of clinically relevant issues such as parameters of stimulation.

Several studies have avoided the sham needling dilemma by using other placebos (for

example, transcutaneous electrical nerve stimulation [TENS], or minimal needling with extremely weak intensities).

Finally, there are studies that ignored placebo entirely, by comparing acupuncture to a conventional treatment (for example, NSAIDs, physiotherapy), as recommended by the FDA (see introduction). When I did a “nonsystematic” review of the chronic pain literature, taking into account these issues (Stux, Pomeranz, 1995), I concluded that acupuncture often worked better than placebo controls and in the head-to-head studies as well as the conventional treatments, but with fewer side effects. I am now in the process of doing a proper meta-analysis of the pain literature that for the first time includes all the issues summarized above. Of two published meta-analyses to date, one concluded that acupuncture was better than controls (Patel, Gutzwiller, et al., 1989), and the other that acupuncture was no better (Ter Riet, Kleijnen, Knipschild, 1990). As pointed out by Feinstein (1995), meta-analyses are only as good as the underlying data. In other words, “garbage in, garbage out.” These authors did not take into account many of the issues raised above.

Biological Effects of Acupuncture for Chronic Pain

In my recent review of this topic, I summarized convergent lines of evidence that strongly support the following acupuncture endorphin hypothesis (Stux, Pomeranz, 1995): acupuncture activates type II muscle afferents (that cause de qi sensations) that send signals to sites in the brain to release endorphins: met-enkephalin, beta endorphin, and dynorphin. These then suppress pain signals in the dorsal horn of the spinal cord. Also, emotional aspects of pain are suppressed by endorphins acting in the limbic system.

The 15 lines of evidence are backed up by 99 papers, all published in rigorously reviewed mainstream journals in the United States, Canada, United Kingdom, and Sweden (Stux, Pomeranz, 1995).

When the FDA saw the endorphin evidence, it was convinced. In addition, there are other mechanisms implicated in acupuncture: brain serotonin, diffuse noxious inhibitory convergence, or the gate theory of pain, but the evidence is less extensive for them.

Incorporation Into Health Care

Evidence-based medicine with risk/benefit ratios are needed. Also, cost-effectiveness studies are desirable. These have not been achieved for most of conventional medicine, let alone for acupuncture.

Directions for Future Research

Drugs have patent protection, and there are monetary incentives to do multimillion dollar multicentered studies to determine efficacy for the FDA. Needles are not patentable. Hence, we

must find inexpensive ways to do multicentered studies. The FDA proposed head-to-head studies comparing acupuncture with conventional therapies in which everyone gets “real” therapy so patients can pay for the treatment, lowering the costs. In these multicentered studies, parameters of treatment in the studies should be harmonized. Sham acupuncture should be discouraged, since placebo controls are not necessary at this time.

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Nausea and Vomiting

Andrew Parfitt, Ph.D.

The most convincing evidence for the efficacy of acupuncture in the treatment of nausea comes from studies of its use in the treatment of perioperative emesis and the emetic side effects of cancer chemotherapeutic agents.

The majority of the studies of perioperative emesis were done by J.W. Dundee of the Department of Anesthesiology of Queens University, Belfast. They took place over 5 years and involved some 500 women. Stimulation of the acupoint Pericardium 6 constituted the active treatment, and stimulation of a non-point on the elbow served as control. Timing of acupuncture treatment relative to the administration of preoperative medication was critical. Under optimum conditions, Pericardium 6 stimulation always produced a highly significant reduction of perioperative emetic sequelae.

The efficacy of acupuncture as an antiemetic in patients receiving a variety of cancer chemotherapeutic drugs was also evaluated by J.W. Dundee, in this case using Pericardium 6 stimulation as an adjunct to standard chemical antiemetics. Of 170 patients treated over several years, 93 percent experienced good to very good results, and 7 percent poor to nil. In all, 65 percent experienced a complete abolition of sickness.

Neurological Rehabilitation: Acupuncture and Laser Acupuncture To Treat Paralysis in Stroke and Other Paralytic Conditions and Pain in Carpal Tunnel Syndrome

Margaret A. Naeser, Ph.D., Lic.Ac., Dipl.Ac.

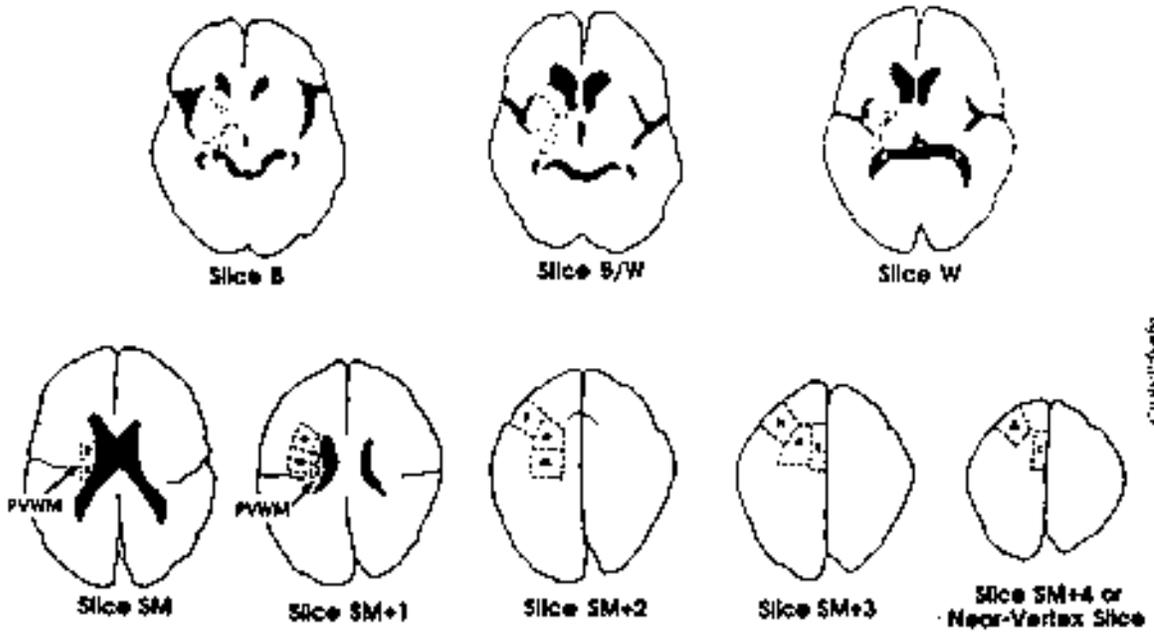
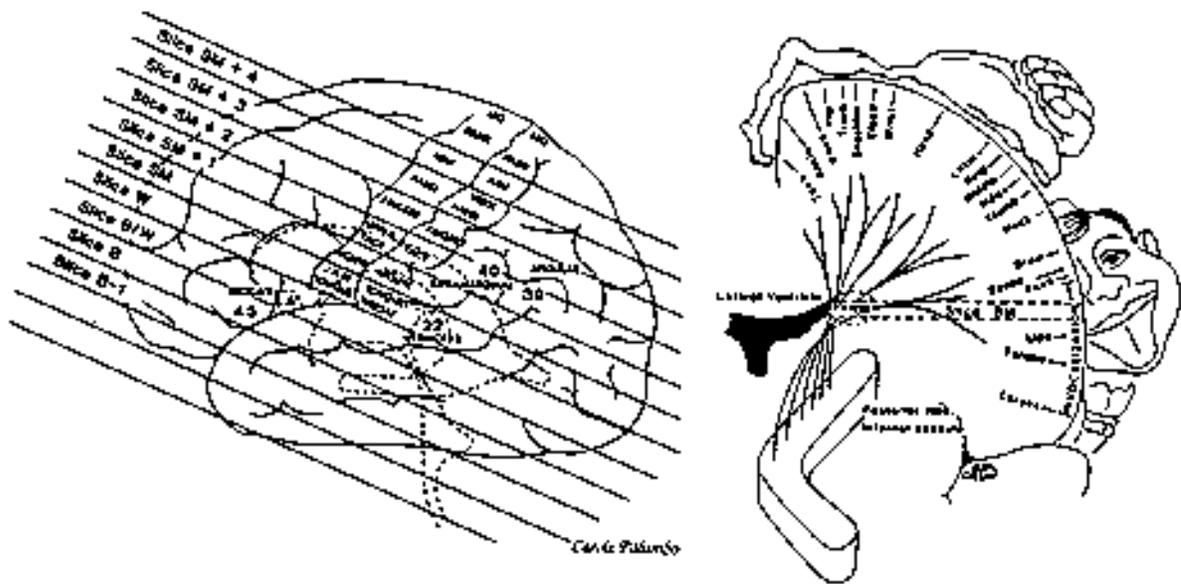
This report reviews acupuncture and laser acupuncture to treat paralysis in stroke, cerebral palsy, spinal cord injury, and peripheral facial paralysis (Bell's palsy), and pain in carpal tunnel syndrome.

Acupuncture or Laser Acupuncture To Treat Paralysis in Stroke

Stroke is the major cause of disability among adults in the United States (Weinfeld, 1981). Every day, more than 1,200 Americans suffer a stroke, and 400 of these patients are permanently disabled. Today, more than 2 million Americans suffer long-term disabilities from stroke, and stroke costs more than \$25 billion each year (NIH Report, NINDS, 1992).

Recently, there have been 10 studies in which acupuncture was used to treat paralysis in stroke patients. Sham acupuncture (insertion of needles into nonacupuncture points on the limbs) was performed in only one study (Naeser, Alexander, Stiassny-Eder, et al., 1992). This study observed significantly more acute stroke patients with arm or leg paralysis to have good response following real acupuncture than following sham acupuncture if the computed tomography (CT)–scan lesion site was a variable ($p < .013$). When there was lesion in less than one-half of the motor pathway areas on a CT scan (especially the PVWM area, as shown in figure 1), acupuncture was effective in increasing limb range of motion (ROM) in these patients with mild to moderate paralysis. Good response postacupuncture was defined as an increase of at least 10 percent in isolated active ROM, on at least two arm or leg tests (shoulder abduction, knee flexion, or knee extension, etc.). No patients who received sham acupuncture had good response, whatever the lesion. All patients in this study were treated with acupuncture beginning at 1 to 3 months poststroke.

Acute and chronic stroke cases with arm or leg paralysis of mild to moderate severity who had lesion in less than one-half of the motor pathway areas on a CT scan were observed to have a significant increase in shoulder abduction, knee flexion, and knee extension ($p < .04$ and beyond) following 20 to 40 acupuncture treatments over a 2- to 3-month period (Naeser, Alexander, Stiassny-Eder, et al., 1994a). Cases with some isolated finger movement have the best prognosis for improvement in upper extremity ROM following acupuncture treatments. Severe hemiplegia patients with lesion in more than one-half of the motor pathway areas on CT scan had little or no increase in limb ROM following acupuncture treatments; however, they did have a beneficial effect where a decrease in spasticity was observed (arm, leg, or hand spasticity) (Naeser, Alexander, Stiassny-Eder, et al., 1994a).



Lateral, coronal and cross-sectional diagrams showing location of neuroanatomical areas visually assessed for extent of lesion (amount of infarction) on CT scan, comprising, in part, descending pyramidal tract pathways. The deep, subcortical periventricular white matter area (PVWM) is outlined in the upper right coronal diagram and shown on CT scan slices SM and SM+1 (arrows). The total extent of lesion in the 2nd and 3rd quarters of the PVWM area was related to Good Response, versus Poor Response, following Real acupuncture treatments. Key to abbreviations: L = leg cortex area; A = arm cortex area; 2 = 2nd quarter PVWM; 3 = 3rd quarter PVWM; PL = posterior limb, internal capsule (continues on slices B and B/W). (CT scan angle is 20 degrees to the cantho-mental line.)

Maier MA, Alexander MP, Siasmy-Eder D, Gallet V, Hobbs J, Bushman D: Real versus Sham Acupuncture in the Treatment of Paralysis in Acute Stroke Patients - A CT Scan Lesion Site Study. *Journal of Neurological Rehabilitation*. 1992;6:163-173.

Figure 1. CT scan lesion site anatomy and acupuncture research in the treatment of arm/leg and hand paralysis in stroke patients.

All acute and chronic stroke cases who had no major arm or leg paralysis but only a milder hand paresis (all with lesion in less than one-half the motor pathway areas on CT scan) had significant improvement in finger/hand strength and dexterity tests ($p < .04$ and beyond), even if acupuncture was initiated as late as 6 to 8 years poststroke (Naeser, Alexander, Stiassny-Eder, et al., 1994b). Across these three studies performed by Naeser and colleagues, all cases ($n = 18$) who had lesion in less than one-half of the motor pathway areas had good response, and overall 19 of 31 cases (61 percent) had good response. On followup testing in 11 stroke patients at 2 months after the last acupuncture treatment, 72 percent to 83 percent of the improved hand, arm, or leg tests were stable or better (Naeser, Alexander, Stiassny-Eder, et al., 1994a, 1994b).

In a recent study in Sweden, when 20 acupuncture treatments were initiated at 4 to 10 days postonset in acute stroke cases, there was significantly better outcome (walking, balance, activities of daily living, quality of life) at 1, 3, and 12 months poststroke in cases receiving acupuncture plus physical therapy compared with cases receiving physical therapy alone ($p < .01$ and beyond) (Johansson, Lindgren, Widner, et al., 1993; Johansson, 1993). There was an estimated savings of \$26,000 per stroke patient treated with acupuncture resulting from fewer days in nursing homes and rehabilitation facilities. Followup on these cases 2 years later showed significantly better postural control for the acupuncture group ($p < .01$) (Magnusson, Johansson, Johansson, 1994).

In Japan, a special form of scalp needle acupuncture, Yamamoto New Scalp Acupuncture (YNSA), is used with stroke patients (Yamamoto, Maric-Oehler, 1991). Small, one-half-inch acupuncture needles are inserted into specific areas on the scalp immediately before a physical therapy (PT) or occupational therapy (OT) session. Often patients are able to gain better ROM and greater benefit from PT or OT with this technique; the needles are left in place for the rest of the day.

In studies in Norway, Taiwan, and China, acupuncture plus PT versus PT alone reported that with acute, subacute, or chronic stroke cases, those patients who received acupuncture early postonset (within 36 hours of stroke onset) had significantly better outcome (Sallstrom, Kjendahl, Osten, et al., 1995; Hu, Chung, Liu, et al., 1993; Zhang, Li, Chen, et al., 1987). Early complementary treatment with acupuncture poststroke (< 36 hours) was especially important in patients with severe paralysis in the very acute stage (Hu, Chung, Liu, et al., 1993). A study by Li and colleagues (1989) observed that acupuncture could be initiated within 24 hours postonset, even in acute cerebral hemorrhage cases, after the bleeding was controlled. Acupuncture's effect to increase cortisol (Cheng, McKibbin, Roy, et al., 1980; Shi, Bu, Lin, 1992) may contribute to less brain swelling, hence less brain damage, in acute stroke cases treated in the very early stage poststroke. This is an area for more research.

Naeser and colleagues (1995) used painless, noninvasive low-level laser light (780 nm, 20 mW) instead of needles to stimulate acupuncture points as a treatment for paralysis in stroke patients. The results were similar to those observed with needle acupuncture in stroke cases with similar CT scan lesion sites. Laser acupuncture is desirable especially for hand paresis cases because the patients can be trained to perform additional home treatment with a 5-mW red-beam

diode laser pointer, under the supervision of a licensed acupuncturist trained in laser acupuncture (Naeser, Wei, 1994). Laser acupuncture is considered investigational by the Food and Drug Administration, and informed consent is required.

In summary, comparisons were available between a control group and an acupuncture group in 8 of the 10 stroke studies reviewed here. The acupuncture groups had significantly better outcome levels ($p < .05$ and beyond). Overall, 128 of 193 cases, or 66.6 percent, had an outcome level of good response or markedly effective, following 20 to 40 acupuncture treatments over a 2- or 3-month period. The patients who received acupuncture very early postonset (within 24 to 36 hours poststroke or 4 to 10 days) had the best outcome levels at 1 and 3 months and again at 1 and 2 years later, with one study showing a savings of \$26,000 per patient who began acupuncture at 4 to 10 days poststroke because of fewer days in hospitals and rehabilitation facilities. No adverse reactions were reported. Moreover, acupuncture may improve cerebral circulation (see below).

Possible Mechanisms for Acupuncture's Effectiveness in Stroke

The mechanism through which acupuncture may produce improvement in motor function or reduce spasticity in stroke patients with paralysis is not understood at this time. It is hypothesized that it may increase cerebral blood flow or promote vasodilation (Alavi, LaRiccia, Sadek, et al., 1996, 1997; Chen, Erdmann, 1977; Omura, 1975). A blood-flow brain single photon emission computed tomography (SPECT) scan study is currently in progress in the author's neuroimaging section at the Boston Department of Veterans Affairs (VA) Medical Center and the West Roxbury VA Medical Center, where blood flow is measured before and immediately after one acupuncture treatment (needles with electroacupuncture and laser acupuncture) on the same day. Three of four chronic stroke cases examined thus far showed an increase in blood flow to the thalamus and hand primary motor cortex area, especially ipsilateral to the paralysis (contralateral to the lesion) following the acupuncture treatment, ranging from 3 percent and 4 percent to 24 percent. The latter increase of 24 percent was observed in a patient (case WM) who had already had 3 years of acupuncture treatments, whereas this was the first acupuncture treatment for the other two cases (see figure 2). The studies by Alavi and colleagues (1996, 1997) had observed an increase of approximately 23 percent in blood flow postacupuncture in the brainstem and thalamus areas in four of five chronic pain patients who had previously had several weeks of acupuncture treatments. Thus, the greater increase of 24 percent in the patient who had received 3 years of acupuncture treatments versus the smaller increases in the patients for whom this was the first treatment deserves further research. This increase may indicate that acupuncture promotes a maximal alteration in blood flow patterns following a series of treatments over time.

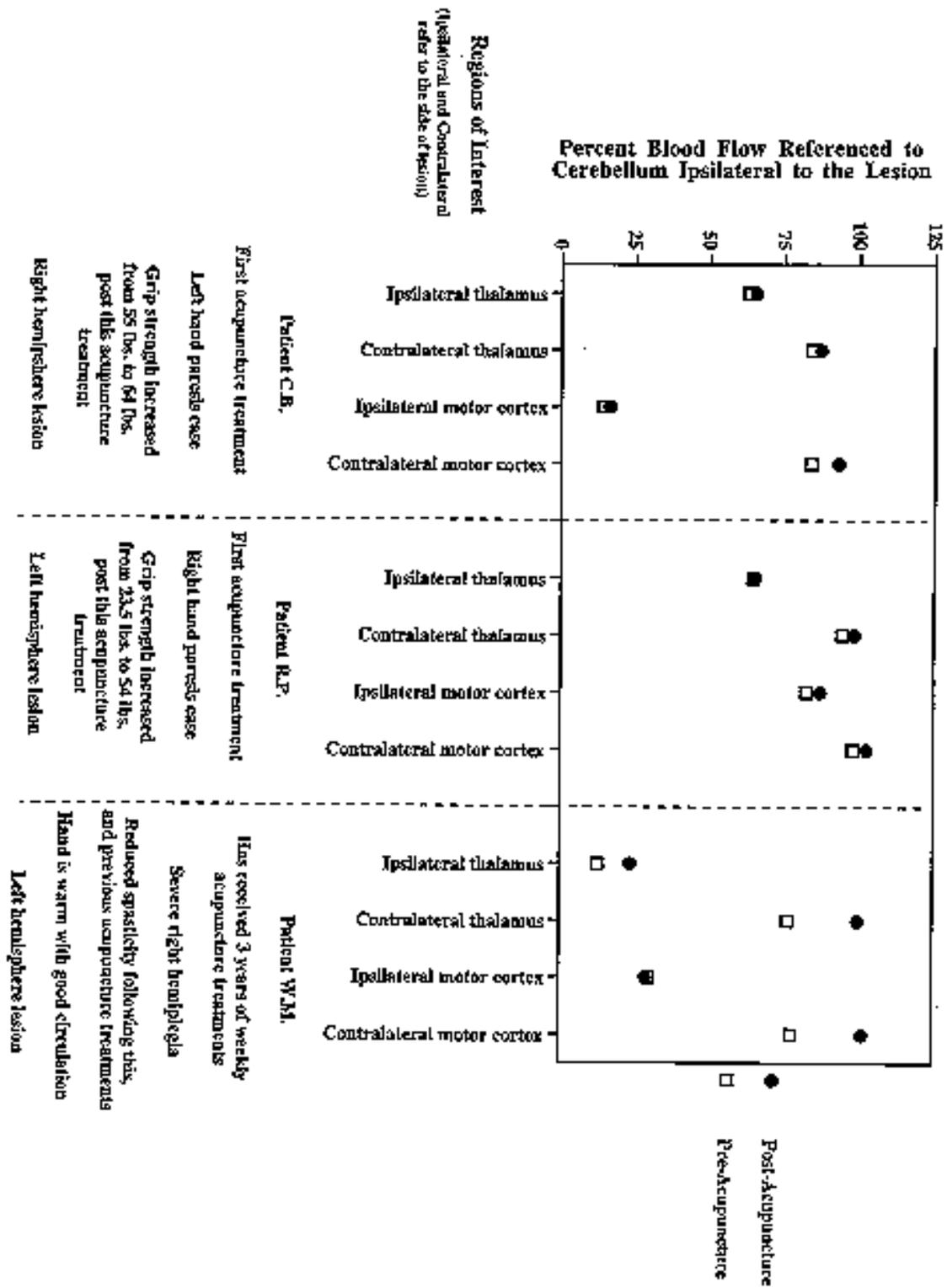


Figure 2. Percent blood flow on brain SPECT scans, pre- and post-acupuncture treatment in stroke patients.

An increase in regional cerebral glucose metabolism on positron emission tomography (PET) scans has been observed in the thalamus and primary motor cortex areas (sometimes bilateral) in stroke patients who have had good spontaneous recovery from paralysis within a few months poststroke (nonacupuncture studies) (Frakowiak, Weiller, Chollet, et al., 1991; Weiller, Chollet, Friston, et al., 1992; Weder, Knorr, Herzog, et al., 1994; Binkofski, Seitz, Arnold, et al., 1996; Bookheimer, Cohen, Dobkin, et al., 1995). After a series of acupuncture treatments over several weeks, if acupuncture does significantly increase blood flow or regional glucose metabolism in the thalamus and primary motor cortex area (and possibly other areas) in stroke patients with paralysis, this acupuncture-induced alteration may promote more rapid and improved brain reorganization for motor control poststroke. Additional brain imaging studies are recommended.

Acupuncture or Laser Acupuncture To Treat Cerebral Palsy in Babies and Children

Cerebral palsy (CP) may be defined as a chronic disability originating in the central nervous system and characterized by aberrant control of movement or posture, appearing early in life and not the result of a progressive disease. It is estimated to occur in 0.1 percent of births (approximately 250,000 cases in the United States). It is more frequently observed in babies born with a low birthweight (less than 2,500 grams) (Cummins, Nelson, Grether, et al., 1993).

Several studies have recently been conducted to study the effects of acupuncture on cerebral palsy. Two studies compared acupuncture with a control treatment—limb massage only in one study (Xiao, Meng, 1995) or vitamins and Chinese herbs only in the other (Ma, Zhang, 1995); each study observed better outcome in the acupuncture group ($p < .01$). Laser acupuncture was included in two other studies (Filipowicz, 1994; Likicka, Hegyi, 1991); both studies observed stimulation of acupuncture points with low-level, red-beam laser to help reduce spasticity and improve motor function for sitting, crawling, and walking. Laser acupuncture may be performed in the home by the mother with a 5-mW red-beam diode laser pointer, under supervision from a licensed acupuncturist trained in laser acupuncture. Home laser acupuncture treatment has been observed to reduce the number of seizures, thus allowing a CP child to require less medication (Agatha Colbert, M.D., personal communication). This condition requires lifelong treatment; adjunctive home treatment with laser acupuncture could reduce some of these costs. Studies recommend initiating acupuncture very early (preferably 2 weeks postbirth or less than 1 year of age) (Lidicka & Hegyi, 1994; Lao, 1992).

In summary, the results across these seven studies indicate an outcome level of good response or markedly effective in 190 of 279 cases (68 percent) of the babies and children treated with acupuncture or laser acupuncture. These treatments are especially helpful in reducing spasticity. Plasma cortisol levels were reported to be significantly increased in 77 percent of the children treated with acupuncture for cerebral palsy (Shi, Bu, Lin, 1992).

Acupuncture To Treat Paralysis in Spinal Cord Injury

In America, approximately 200,000 persons are now permanently confined to

wheelchairs because of spinal cord injury. Each year, approximately 10,000 more people are injured, suffering paralysis and loss of sensation. Most of these people (two-thirds) are younger than 30 years of age. The specialized care that is required for these people costs approximately \$5 billion each year in the United States (NIH Report, NINDS, 1992).

Result of three acupuncture studies are summarized here. None had a control group. Overall, 340 of 360 cases, or 94.4 percent, had an outcome level of beneficial progress, including reduction in muscle spasms, some increased level of sensation, and improved bladder and bowel function. Patients were treated for longer periods, from 5 months to 2 to 3 years. The acupuncture treatments were also helpful in the treatment of bedsores with these patients. Red-beam laser acupuncture may be used on the hands or feet to help reduce muscle spasms (Naeser, personal observation; Naeser, Wei, 1994). These authors recommend beginning acupuncture as soon as possible after spinal cord injury, even during acute stage of spinal cord shock, to help reduce development of spasms.

Acupuncture or Laser Acupuncture To Treat Peripheral Facial Paralysis (Bell's Palsy)

Bell's palsy is the most common disease of the facial nerve. It is presumably due to an inflammatory reaction in or around the facial nerve near the stylomastoid foramen. Adams and Victor state, "Fully 80 percent of patients recover within a few weeks or in a month or two" (1977).

Results of five acupuncture studies are summarized below. None had a control group. Overall, 983 of 1,009 cases (97.4 percent) had an outcome level of cured or markedly effective. Cases were treated ranging from 1 day to several years postonset. When acupuncture was initiated within 3 days postonset in 684 cases, 100 percent of the patients were cured or there was a marked effect (Liu, 1995). Even 80 percent of cases who were treated starting at more than 2 months postonset and 83 percent of severe cases were cured or had excellent effect (Gao, Chen, 1991). Red-beam laser acupuncture was also effective in mild to moderate cases; it was combined with needle acupuncture in severe cases (Wu, 1990). Most patients were treated for 2 to 4 weeks (up to 8 weeks).

Laser Acupuncture or Acupuncture To Treat Pain in Carpal Tunnel Syndrome

Carpal tunnel syndrome (CTS) is an entrapment neuropathy of the median nerve at the wrist (Rosenbaum, Ochoa, 1993). Patients have pain in the wrist that radiates into the hand and sometimes into the forearm, with numbness and tingling in the thumb and index and middle fingers and weakness in the hand. The exact etiology is unknown; however, CTS occurs more commonly in workers whose tasks involve repetitive hand movements, such as operating machinery, working on assembly lines, and typing on computer keyboards. CTS is a particularly severe example of repetitive strain injury (RSI).

In 1995, the Bureau of Labor Statistics, U.S. Department of Labor, reported that half of

all workers afflicted with CTS missed 30 days or more of work. In 1996, the incidence of CTS was 2 million cases (N.Y. Times, Feb. 28, 1996). Conservative treatments are first used (adjusting work environment, using wrist splints, and nonsteroidal anti-inflammatories) (Mackinnon, Novak, 1994). If steroid injection is later necessary, between 65 percent and 90 percent of patients have recurrence of symptoms, usually after 2 to 4 months (Slater, Bynum, 1993). Approximately 40 percent of cases have surgical release across the transverse carpal ligament, with variable success. Workers' compensation figures suggest a cost of \$6,000 to \$10,000 per case for medical management (Dimmitt, 1995). One firm estimates that it costs a company \$37,000 in lost work time, medical treatments, and rehabilitation for each worker who develops CTS (Respondex Systems, Dixon, IL, personal communication). There is a need for a less expensive, painless, noninvasive, nonsurgical treatment for CTS.

Results of four studies where laser acupuncture and microamps TENS or needle acupuncture were used to treat CTS are presented below. It is possible to conduct controlled acupuncture research with use of low-level laser and microamps TENS to stimulate acupuncture points because each device produces no feeling—no heat, no cold, no pain. The patient's hand is treated behind a curtain, and the patient is not aware whether either device is turned on or off. In a randomized, double-blind, placebo-controlled, cross-over study, a 15-mW, red-beam, HeNe laser (1 to 7 joules) and a microamps TENS device (< 900 microamps) were used to stimulate acupuncture points on the hand and arm areas in nine patients with CTS. A significant reduction in pain was observed following 9 to 12 real treatments ($p < .01$), but not following 9 to 12 sham treatments (Naeser, Hahn, Lieberman, 1996, 1997). Patients were able to resume prior work (keyboard, handyman) with less or no pain. Three other cases were treated in an open protocol with home treatment using a 5-mW red-beam diode laser pointer and microamps TENS; all cases resumed work (secretarial) without pain after 4 to 6 weeks. The advantage of the red-beam diode laser pointer and microamps TENS device is home treatment under the supervision of a licensed acupuncturist trained in laser acupuncture for less than \$1,100 per case (diode laser pointer, \$142; microamps TENS, \$895; treatment training, \$60).

Red-beam laser and microamps TENS may increase ATP levels on the cellular level (Passarella, Casamassima, Molinari, et al., 1984; Cheng, Van Hoof, Bockx, et al., 1982), and red-beam laser may have an anti-inflammatory effect (Mester, Toth, Mester, 1982) and promote an increase in serotonin levels (Walker, 1983). Use of an 830-nm infrared laser to stimulate (9 joules) at five points (not specified as acupuncture points) along the median nerve has been observed in an uncontrolled study to normalize latencies in 10 of 14 nerves and to reduce pain in 9 of 11 cases of CTS treated in an open protocol for 6 to 15 visits (Weintraub, 1996).

Branco (in preparation) has used the laser acupuncture protocol (5 mW, red-beam, 670 nm diode laser pointer) and microamps TENS protocol of the Naeser, Hahn, and Lieberman study (1996), to successfully treat CTS pain in 21 of 23 cases (91.3 percent) in an open protocol for 12 to 15 treatments. Eight cases had previously failed to obtain pain relief following surgical release of the transverse carpal ligament; two cases had failed surgery twice. All cases who had previously failed surgery were successfully treated with laser acupuncture and microamps TENS in the Branco study. Needle acupuncture or 904-nm infrared laser acupuncture was also used on the shoulder and neck areas in cases where cervical compression was present. All cases who

were not retired returned to their work (photographer, nurse's aide, auto mechanic, retail manager, artist/painter, computer operator, nail technician, secretary, lobsterman).

Two studies that used needle acupuncture, electroacupuncture, moxibustion, and Chinese herbs are also reviewed (Chen, 1990; Wolfe, 1995). These studies reported success rates of 97.2 percent and 87.5 percent, respectively. The Chen study reported followup in 29 cases at 2.5 years to 8.5 years postacupuncture, where 24 of 29 cases (82.5 percent) were still pain-free at a mean of 5.1 years postacupuncture treatment.

In summary, 77 of 84 CTS cases (91.6 percent) were successfully treated with laser acupuncture, microamps TENS, or needle acupuncture. The treatments with laser, microamps TENS, and needle acupuncture are often performed in the acupuncture office; however, the laser acupuncture and microamps TENS treatments may be performed by the patient in a home treatment program with a red-beam diode laser pointer and microamps TENS device under the supervision of a licensed acupuncturist trained in laser acupuncture (Naeser, Hahn, Lieberman, 1997; Naeser, Wei, 1994). The cost for a home treatment program is approximately \$1,100. The current estimated workers' compensation average cost for medical management including surgery is \$8,000 per case. Home treatment with laser acupuncture would represent a savings of \$6,900 per CTS case. If half the current 2 million cases of CTS in the United States were successfully treated using laser acupuncture and microamps TENS with home treatment, this would represent a savings of \$6.9 billion dollars per year in the treatment of carpal tunnel syndrome. The savings are about the same if the laser acupuncture treatments or needle acupuncture treatments are provided in the acupuncture office (15 visits at \$60 per visit = \$900) or if the laser acupuncture treatments are performed by the patient at home, where the equipment is purchased by the patient (\$1,100); this is compared with \$8,000 for current medical treatments.

Overall Summary and Recommendations for Future Areas of Research

Stroke. Acupuncture or laser acupuncture was effective to reduce severity of paralysis in 66.3 percent of the 193 cases reviewed. The best results were observed when acupuncture treatments were initiated within 24 to 36 hours poststroke onset in ischemic infarct cases and after bleeding was controlled in hemorrhagic cases. Acupuncture's effect to increase cortisol levels (Cheng, McKibbin, Roy, 1980; Shi, Bu, Lin, 1992) may contribute to less brain edema in acute stroke, hence less brain damage. Acute patients are treated at least 3 times per week, and chronic patients 2 times per week for 20 to 40 treatments over a 2- or 3-month period. The Swedish study observed that when acupuncture was initiated 4 to 10 days poststroke, there was a savings of \$26,000 per stroke patient as a result of fewer days in hospital and rehabilitation facilities (Johansson, Lindgren, Widner, et al., 1993; Johansson, 1993). These patients also had better motor function, activities of daily living, and quality of life measures at 1 and 3 months and 1 year poststroke as well as better postural control at 2 years poststroke compared with those cases treated only with PT beginning at 4 to 10 days poststroke ($p < .01$ and beyond).

Acupuncture is beneficial for chronic as well as acute stroke cases. It is an excellent complementary treatment for stroke patients with paralysis, and it is recommended that it be used as an adjunctive treatment with current therapies. Often patients are able to gain better

ROM and greater benefit from PT and OT when acupuncture is administered immediately before a therapy session. In Japan, with the Yamamoto New Scalp Acupuncture method, short acupuncture needles are left in place on specific points on the scalp of the stroke patient for the duration of the day, including during PT or OT sessions (Yamamoto, Maric-Oehler, 1991).

Severity of paralysis in stroke patients is quite variable. In general, for patients with mild to moderate paralysis, improvement in knee flexion and extension and shoulder abduction is expected, and in mild cases where some isolated finger movement is present (acute or chronic mild hand paresis), improvement in finger/hand strength and dexterity is expected. Injection of Bo-Tox into the wrist area may prevent a positive acupuncture response for the hand, perhaps in part caused by the destruction of the nerve endings following Bo-Tox injection (Naeser, personal observation). For patients with severe paralysis and spasticity, a reduction in spasticity is expected following acupuncture, but little change in limb ROM. For these severe cases, improved circulation to the limbs and hand may be maintained with acupuncture, preventing contractures and keeping the extremities warm (see Case WM, figure 2). A reduction in spasticity is expected in almost all cases—acute or chronic, mild to moderate, or severe. These reductions in spasticity are above and beyond what current medications and therapies are able to provide.

Adjunctive home treatment programs using a 5-mW red-beam diode laser pointer to stimulate acupuncture points can further help to reduce spasticity and increase finger and hand strength and dexterity. These home treatment programs should be performed under the supervision of a licensed acupuncturist trained in laser acupuncture and are not intended to replace standard acupuncture treatments where scalp needle acupuncture and other methods of treatment with needle acupuncture (electroacupuncture and moxibustion) should be performed weekly or monthly, as necessary.

CT scan lesion site information and benefit from acupuncture treatment. With acute stroke patients, the results from studies reviewed in this report suggest acupuncture treatments should be initiated as soon as possible poststroke (within 24-36 hours), when medically possible. CT scans performed within this time period are important for medical management (presence or absence of hemorrhage, etc.), but the final borders of the area of brain damage will not yet be visible on these acute CT scans (Palumbo, Naeser, Samaraweera, et al., in preparation). Acute CT scans or MRI scans will not show whether lesion is present in less than half or more than half the motor pathway areas; therefore, these acute scans are not helpful for understanding the specific benefits a given stroke patient is likely to gain from acupuncture (e.g., increased limb ROM, improved finger or hand strength and dexterity, or only reduced spasticity).

With chronic stroke patients, however, a CT scan obtained after 3 months poststroke will show the final borders of the area of infarction or brain damage. Thus, a noncontrast CT scan obtained after 3 months poststroke would be helpful for understanding the expected level of benefit from a series of acupuncture treatments. For example, if severe hemiplegia is present with no isolated finger movement after 3 months poststroke and lesion on CT scan is present in more than one-half the motor pathway areas (especially the PVWM area shown in figure 1), then little or no increase in limb ROM will be expected; however, a reduction in spasticity and

improved limb circulation will be expected. If a mild-to-moderate paralysis is present with some isolated finger movement after 3 months poststroke and lesion is present in less than one-half of the motor pathway areas on a CT scan (figure 1), then a significant increase in limb ROM and a reduction in spasticity will be expected. In patients with no arm or leg paralysis who have only a mild hand paresis, a significant increase in finger and hand strength and dexterity is expected. All these mild hand paresis cases have lesion in less than one-half of the motor pathway areas on a CT scan.

To summarize, an acute CT scan is not helpful for understanding the specific type of improvement expected with acupuncture treatments; however, studies cited in this report uniformly recommend the initiation of acupuncture treatment as soon as possible poststroke (within 24 to 36 hours). These early acupuncture treatments appear to have an effect on better long-term outcome at 1 and 2 years later. A chronic CT scan obtained after 3 months poststroke onset would be helpful, however, for understanding the specific type of improvement expected following a series of acupuncture treatments initiated at that time. Stroke patients receiving acupuncture often benefit in other areas besides paralysis such as better sleeping or better control of hypertension (Naeser, personal observation), and acupuncture should not be withheld based on CT scan lesion site information. The lesion site information is helpful for providing realistic expected benefits, but it is not necessary to have a CT scan performed prior to acupuncture treatment in chronic stroke cases.

Possible mechanisms for acupuncture's effectiveness(neuroimaging studies. It is possible that acupuncture and laser acupuncture alter or increase blood flow to specific areas of the brain, including the thalamus and primary motor cortex areas in stroke patients with paralysis. Research with acupuncture and neuroimaging studies where cerebral blood flow or regional glucose metabolism are monitored following a series of acupuncture treatments is recommended. This information will help provide a better understanding of the physiological mechanisms that may underlie the benefits gained from acupuncture to treat paralysis in stroke patients. It is also recommended that neuroimaging research be conducted with acute stroke patients given acupuncture treatment in the very early phase of stroke onset (24 to 36 hours poststroke) to better understand why this early intervention appears to be so important regarding later outcome. One hypothesis is that acupuncture improves or attempts to normalize blood flow in the brain and reduces brain swelling. However, sophisticated neuroimaging techniques, such as PET or functional MRI that can best measure these early changes, are expensive imaging techniques at this time.

Results from neuroimaging studies may also help to explain why acupuncture appears to be helpful in the treatment of other paralytic conditions reviewed in this report, including cerebral palsy, spinal cord injury, and peripheral facial paralysis (Bell's Palsy), and paralytic conditions not reviewed in this report but reviewed in a previous report for the National Institutes of Health's Office of Alternative Medicine, for example, head injury, multiple sclerosis, pseudobulbar palsy, and reversal of coma (Naeser, 1996). In all areas reviewed, acupuncture was helpful in the majority of cases, and it was recommended that acupuncture (or laser acupuncture) treatments should be initiated as soon as possible after onset.

Cerebral palsy. Acupuncture or laser acupuncture was effective to reduce spasms and improve motor function in 68 percent of the 279 cases reviewed. Treatments were especially effective when initiated within a few weeks or 1 year postbirth. Initially, treatments are administered daily or three times per week. Later, the frequency may be reduced. Cerebral palsy is a lifelong condition, and acupuncture treatments should be continued over several years, as necessary. Laser acupuncture with a red-beam diode laser pointer should be considered for adjunctive home treatment programs under the supervision of a licensed acupuncturist trained in laser acupuncture; this may help reduce overall treatment cost.

Future recommended research would include performing red-beam laser or needle acupuncture beginning at 2 weeks postbirth (or within the first year of life) on babies who were hypoxic at birth and who are at high risk for developing cerebral palsy.

Spinal cord injury. Acupuncture was effective in reducing muscle spasms, increase the level of sensation, and improve bladder and bowel function in 94.4 percent of the 360 cases reviewed. It was recommended that acupuncture be initiated as soon as possible after spinal cord injury and that treatments continue for 2 to 3 years, or even 5 years. Electroacupuncture along the bladder meridian (paravertebral) area is especially recommended. Laser acupuncture can also be applied in a home treatment program to help reduce muscle spasms in the hands and feet. Research with both needle electroacupuncture and laser acupuncture are recommended in this field, especially when the treatments can be initiated as soon as possible after the spinal cord injury.

Peripheral facial paralysis (Bell's palsy). Acupuncture or laser acupuncture was effective to cure or markedly improve peripheral facial paralysis in 97.4 percent of the 1009 cases reviewed. It was 100 percent effective (cured or marked effect) when initiated within 3 days following onset of the facial paralysis. It was also helpful in 80 percent of cases who were greater than 2 months postonset and in 83 percent of severe cases. Thus, the overall success rate with needle acupuncture or laser acupuncture is very high, especially when the acupuncture treatments are initiated at less than 3 days postonset. The current recovery rate without acupuncture is 80 percent within 2 months of onset. The rate of success with acupuncture initiated at 2 months postonset, however, is an additional 80 percent. Therefore, it would seem that early intervention with acupuncture or laser acupuncture is clinically indicated in cases of Bell's palsy.

Carpal tunnel syndrome. Laser acupuncture, microamps TENS, or needle acupuncture produced outcome levels of good-to-excellent pain relief in 91.6 percent of the 84 cases reviewed. There is a laser acupuncture and microamps TENS home treatment program that can be used over a 4- to 6-week period for a cost of approximately \$1,100, including equipment and training in home treatment under the supervision of a licensed acupuncturist trained in laser acupuncture. Use of this treatment program with half of the current 2 million cases of CTS in the United States could represent a savings of \$6.9 billion dollars per year for treatment of CTS. The savings are about the same whether laser acupuncture or needle acupuncture treatments are provided in the acupuncture office (15 visits at \$60 per visit = \$900) or the laser acupuncture treatments are performed by the patient at home, where the equipment must be purchased by the patient

(\$1,100), compared with \$8,000 for current medical treatments.

Future research with laser acupuncture or needle acupuncture to treat CTS should focus on large-scale clinical trials of this form of treatment. The high success rate reported in the studies reviewed for this report indicate that laser acupuncture or needle acupuncture is a successful and cost-effective treatment for CTS. Additional research would better define exactly when to intervene with this form of treatment (e.g., during conservative management and prior to surgery) and in which specific level of severity (e.g., prior to development of severe muscle atrophy). This research has great potential for significantly decreasing the cost of current medical management of carpal tunnel syndrome and repetitive strain injury in the United States

Acknowledgments

The author thanks Errol Baker, Ph.D., for statistical consultation; the Radiology Service at the Boston Department of Veterans Affairs Medical Center (Ranji Samaraweera, M.D., and M. Elon Gale, M.D.) and the Nuclear Medicine Department at the West Roxbury Department of Veterans Affairs Medical Center (Donald Tow, M.D.; Steven Moore, Ph.D.; Chanh Samone Syrvanh, R.T., CNMT; and Robert English, R.T., CNMT); Susan Norton and James E. Kelsey, K.T., for assistance in obtaining copies of the articles; the Library at the New England School of Acupuncture, Watertown, Massachusetts; and Carole Palumbo, Steven Hodge, M.A., and Marjorie Nicholas, M.S., for additional assistance.

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Acupuncture and Addictions

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Acupuncture has been part of substance abuse treatment programs in the United States since the mid-1970s, when Dr. Michael Smith, director of the Lincoln Hospital Substance Abuse Program, in the South Bronx, NY, incorporated acupuncture as a therapy modality based on the work of Dr. H.L. Wen. Presently more than 300 government-supported and private clinics use acupuncture as an adjuvant treatment for persons dependent on opiates, cocaine, alcohol, tobacco, and other substances. At least 40 percent of the drug courts in America include acupuncture among their treatment services (Guidepoints, 1997). Although this started as a clinical, nonexperimental phenomenon, the subsequent research has generally supported the conclusion that acupuncture is useful as an adjuvant therapy in the treatment of substance abuse and drug dependency.

Research on the application of acupuncture to addiction treatment is complicated by the enormity of the problem of substance abuse, the economics and politics of the treatment industry, the great variety of both formal and informal interventions, and the emotionality that permeates the problems and players (Culliton, Kiresuk, 1996). Historically, acupuncture research design has been flawed in numerous ways. Basic guidelines have been recommended in order to produce results that are better substantiated (World Health Organization, 1995). Reviews of the research literature on acupuncture and substance abuse treatment, while not in agreement, tend to support acupuncture as an effective adjuvant therapy (Reit, Kleijnen, Knipschild, 1990; Dale, 1993; Brewington, Smith, Lipton, 1994).

History

In 1972, Drs. Wen, Patterson, and Cheung, a group of surgeons in China, used electrical acupuncture to prepare their patients for surgery. Several of their patients who were addicted to various drugs, including opium and heroin, reported that after receiving acupuncture treatments, their cravings had diminished (Patterson, 1975). This discovery led to clinical observations of addicts receiving acupuncture as an adjuvant treatment to surgery, and then to a research study. In 1973, 40 subjects addicted to either heroin or morphine were given acupuncture with electrical stimulation, and a greater than 90 percent success rate for the duration of the 2-week treatment period was reported (Wen, Cheung, 1973). In subsequent studies using a combined treatment regimen of naloxone and electrical acupuncture, it was found that 51 percent of the subjects in the treatment group were drug-free at the 1-year followup (Wen, Teo, 1975; Wen, 1979).

Mechanism

In animal addiction research, successful replication of Wen's work regarding the decrease in withdrawal symptoms was reported, but the biological mechanism was not clear (Pomeranz, 1989). Some investigators suggest that individuals experience well-being when the naturally occurring endogenous opioids occupy specific receptor sites in the brain. Interference with this mechanism by alcohol, drugs, or even stress may cause cravings and other signs of distress (Blum, Briggs, Trachtenberg, et al., 1987; Blum, Trachtenberg, 1986; Trachtenberg, Blum, 1987). Acupuncture has been demonstrated to affect the levels of various neurotransmitters and hormones (Steiner, 1983). Investigators now postulate that the biomechanisms of acupuncture can be understood in terms of neuroscience (Han, 1987; Pomeranz, 1989; Ulett, 1992; Han, Terenius, 1982; Sytinsky, Galebskaya, 1979). The mechanisms of acupuncture are certain to be highly complex, and continued interest and research in this field is promising (Physiology of Acupuncture, 1996).

Standardization of Treatment

The standard of treatment used by most of the treatment centers throughout the United States and in clinical trials funded by the National Institutes of Health is based on the five-point auricular NADA (National Addiction Detoxification Association) protocol developed by Smith in the late 1970s. The protocol shifted from electrical acupuncture to a more simple approach of needling five distinct locations on the ear (Smith, 1979; Shukar, Smith, 1979; Smith, Khan, 1988; Smith, Squires, Aponte, et al., 1982).

Research

The landmark research for acupuncture and substance abuse treatment was done using a placebo or sham acupuncture treatment for a control comparing it with a modified NADA protocol for severely addicted, recidivist, alcoholic subjects in a single-blind design with independent assessment (Bullock, Umen, Culliton, et al., 1987; Bullock, Culliton, Olander, 1989). In both of these studies, significantly more patients completed treatment in the acupuncture group than in the control group. The acupuncture group recorded significantly less need for alcohol, fewer drinking episodes, and a smaller number of detoxification admissions. In the second study, 21 of the 40 subjects in the acupuncture group, and only 1 of the 40 controls, completed the full study. In addition, a 6-month followup period clearly showed that the acupuncture group did better on the outcome measures.

Another clinical trial (Worner, Zeller, Schwarz, et al., 1992) examining acupuncture and alcoholics did not get results as distinct as Bullock's studies, but the six outcome measures all favored the acupuncture treatment group. Differences as to sample size, point location, frequency, and duration of treatment make it difficult to compare these studies.

In a well-designed pilot study comparing acupuncture with medication or placebo for cocaine-dependent, methadone-maintained subjects, the acupuncture treatment arm was lower in treatment compliance but significantly better for the abstinence rate. The acupuncture arm was 8

weeks in duration, with up to five treatments a week on a daily basis, and it used the standard five-point auricular protocol. One-half of the subjects completed the 8-week program, with 88 percent of these abstinent for at least the last 2 weeks of treatment (Margolin, Avants, Chang, et al., 1993).

Numerous other research studies reporting favorable results from using acupuncture for drug and alcohol abuse have had serious problems with study design, including a limited number of subjects, poor retention, lack of any biophysical evidence, and lack of blinding to treatment (Washburn, Fullilove, Fullilove, et al., 1993; Lipton, Brewington, Smith, 1994; Newmeyer, Johnson, Klot, 1984; Kroening, Oleson, 1985).

A large clinical trial looking at a population of mostly cocaine and crack users was completed in two phases. In Phase I of the study, using acupuncture in an ongoing outpatient substance abuse treatment center in a large metropolitan area, those receiving acupuncture showed a significant increase in the number of negative urines during the initial 8 weeks of treatment (Konefal, Duncan, Clemence, 1994). In Phase II of the above study (in the same clinical setting), a comparison treatment design of three different acupuncture treatments was used. The findings indicated that the most stabilizing acupuncture treatment protocol was the standard five-point auricular treatment with additional body points for symptom control. Also in this study, the use of one point in the ear (*shen men*) was found to be effective in decreasing the number of dirty urines during the initial 2 weeks of the study, but the decrease was not maintained (Konefal, Duncan, Clemence, 1995).

Implementation and Design

Implementation difficulties in an ongoing clinic setting are noteworthy because they offer some insight into additional problems with acupuncture and substance abuse treatment research. The necessity of offering different treatments within a substance abuse treatment center in order to meet the criteria for good experimental design may in fact be detrimental to the overall effect of the treatment program (Konefal, Duncan, Clemence, 1994). Traditional acupuncture treatments are not standardized according to the disease but rather are determined according to the various clinical manifestations of the presenting patient. In a clinical report concerning acupuncture procedure for treating drug addiction, auricular points were used for all patients, but auxiliary points as well as frequency and duration of treatments were determined extemporaneously according to the presenting symptoms (Kao, Lu, 1974). This aspect of the experimental design may in fact be crucial for successful results and is supported by the findings in other studies and by the tradition of acupuncture (Konefal, Duncan, Clemence, 1995).

In addition to research studies, reports from nonexperimental clinics using acupuncture as part of their treatment program indicate acupuncture to be beneficial as an adjuvant therapy. The key to their success is making the acupuncture treatment, including the manner in which it is administered, an integral aspect of the total treatment approach (Brumbaugh, 1993). These include outpatient, inpatient, private and public, as well as correctional and court-ordered

programs (Lane, 1988; Brumbaugh, 1993; Smith, Squires, Aponte, et al., 1982; Lowe, 1994; Miami Drug Court Report, 1992).

Cigarette Smoking

The research on cigarette smoking cessation is more complicated to interpret because, in addition to many design flaws, the literature is often characterized by the emotional tone and prior beliefs of the authors (Steiner, May, Davis, 1982; Fuller, 1982; Lamontagne, Annable, Gagnon, 1980; MacHovec, Man, 1978; Martin, Waite, 1981; Olms, 1981; Olms, 1984; Yongren, 1981). In addition, it is not possible to compare the studies because the acupuncture protocols varied in needle location, number of needles, type of needles, electrical stimulation, and laser stimulation, as well as the frequency and duration of treatments.

A randomized comparison study measuring exhaled carbon monoxide looked at acupuncture, nicotine gum, and a control group. This study found that both treatment groups were significantly more improved than the control group (Clavel, Benhamou, Company-Huertas, et al., 1985). A review of 84 French language publications on the use of acupuncture concluded that psychotherapy with acupuncture provided greater success than psychotherapy and drug therapy (Leibeau, 1986).

Other Studies

Clinical acupuncture includes treatments for psychological disorders including stress, depression, anxiety, and neurotic symptoms (Bensoussan, 1990; Hammer, 1990; Kaptchuk, 1983). These psychological states have been recognized as factors in substance abuse for many individuals (Brecher, 1972). Addressing these issues of mood modification is a key to successful drug treatment (McPeake, Kennedy, Gordon, 1991). There is research indicating that acupuncture is helpful for mood modification (Tao, 1993; Han, 1986; Shuaib, Haq, 1977; Lewis, Litt, 1987). A recent study explored the effects of constitutional acupuncture (according to traditional Chinese medicine), symptomatic acupuncture, and a wait-listed control group. Although the sample size was small, the results indicated that those in the first group fared markedly better than those treated just for presenting symptoms. Both treatments compared favorably with the current pharmacological and psychotherapeutic treatments and had marked improvement over the control group (Schnyer, in press 1997). Combining acupuncture with appropriate mental imagings and thought patterns may be the next step in developing effective healing processes (Ulett, 1996).

The future of acupuncture research in addictions may need to include new approaches to experimental design which feature treatment more directly in accord with the individual. Examining the effect of treating some of the underlying factors involved in addictions, whether psychological, as in depression, or biological, as in increasing the production of neurotransmitters, may add greatly to effective applications of acupuncture to substance abuse treatment programs.

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Gastrointestinal Indications

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Introduction

Few areas of clinical application of acupuncture practice are as widely praised, but incompletely researched, as indications for gastrointestinal disease. With the exception of clinical trials of acupuncture antiemesis (discussed elsewhere in this report), the medical literature regarding clinical gastrointestinal disease consists mainly of case reports. Indeed, some of these reports involve large numbers of patients and represent decades of expert clinical experience. Other papers report randomization of subjects into different treatment groups, but usually there are insufficient data included to be able to judge whether the studies were properly controlled or blinded or had sufficient clinical followup. Reports in the literature suggest acupuncture treatment is effective for treatment of peptic ulcer disease (PUD), dyspepsia, abdominal pain, biliary tract disease, diarrhea, ulcerative colitis, irritable bowel disease, and acute appendicitis and may be useful as analgesia for gastrointestinal endoscopy.

Despite the paucity of well-done prospective, randomized, controlled trials, there is a plethora of information regarding the physiological basis of acupuncture effects on the digestive system. Extensive research in animal models, as well as human subjects, have shed light on how acupoint stimulation leads to changes in gastric acid secretion, gastrointestinal motility, and hormone and neuropeptide metabolism. These studies support a real physiologic basis for the positive clinical results that are claimed by practitioners and mentioned in the case report literature.

In clinical practice, acupuncture point selection may follow standard “point prescriptions” or may be based on the “pattern of illness” according to traditional Chinese medicine (TCM) (Dill, 1992). In addition, TCM practitioners commonly combine acupuncture with herbal medicine when treating gastrointestinal illness.

Conclusions

1. There is a clear physiologic basis for acupuncture effects on the digestive system that has been shown in human and animal studies. Alterations in acid secretion, gastrointestinal motility, and hormone and neuropeptide release have been demonstrated.

2. There is a paucity of prospective, randomized, controlled trials of acupuncture for any clinical digestive conditions although there is a long history of use of acupuncture for digestive disorders.
3. Acupuncture has been found to be effective for analgesia for gastrointestinal endoscopic procedures, both gastroscopy and colonoscopy.
4. Acupuncture use for functional bowel diseases (FBDs) (including irritable bowel disease and non-ulcer dyspepsia [NUD]) is a potentially rich area for clinical research.

Gastrointestinal Motility

Controlled animal and human studies have demonstrated an effect of acupuncture on gastric motility. Effects on motility have also been noted (variably in animals and humans) in the esophagus, lower esophageal sphincter (Guelrud, Rossiter, Souney, Sulbaran, 1991), intestine, and colon (Li, Tougas, Chiverton, Hunt, 1992). Some studies have demonstrated a somatovisceral reflex that is partially responsible for mediating the motility effect (Chang, Chey, Ouyang, 1996), and the influence of vagal nerve efferent stimulation has also been shown. An intriguing possible clinical application is the use of acupuncture in cases of postoperative ileus or gastric atony after vagotomy (Matsumoto and Hayes, 1973). In case reports in humans and animals, positive effect was noted.

Gastric Acid Secretion

The effect of acupuncture on acid secretion has been examined in animal models as well as in humans. In one prospective randomized study on human volunteers (Lux, Hagel, Backer, et al., 1994), electroacupuncture (although not sham acupuncture, nonelectrical acupuncture, or “laser acupuncture”) reduced vagally stimulated acid secretion. Another randomized, placebo-controlled study (Tougas, Li, Rademaker, Chiverton, Hunt, 1992) showed that this effect was through a naloxone-sensitive opioid mechanism. In the canine model, electroacupuncture inhibits acid secretion (mediated by endorphin and somatostatin [Jin, Zhou, Lee, Chang, Chey, 1996]) and increases gastric bicarbonate secretion (involving a somatic afferent-visceral reflex and cholinergic effect [Zhou and Chey, 1984]). Despite the physiologic basis of acupuncture effect on acid secretion, no prospective, controlled study has been done on the treatment of peptic ulcer disease with acupuncture.

Management of Cholelithiasis

There have been several reports of success in treating cholelithiasis and choledocholithiasis with acupuncture. In one large case report type series (Zhang, Zhang, Yang, Zhang, Zhu, 1991), 1,291 cases of cholelithiasis were treated with electrical stimulation of auricular acupoints, with stone expulsion monitored by examination of stool for calculi. Stone

expulsion was high, but complete expulsion of stones could not be proven. In addition, the theoretic risk of inducing gallstone pancreatitis was not mentioned in this report, so the safety or advisability of this treatment cannot be commented on. Research has shown that acupuncture can cause gallbladder contraction, stimulate bile secretion, and lower the sphincter of Oddi basal pressure. These effects may theoretically allow stone clearance from the biliary tree.

Use for Analgesia in Gastrointestinal Endoscopy

In the United States, “conscious sedation” with pharmaceutical agents is the norm for gastrointestinal endoscopic procedures. In other countries, unsedated endoscopy is often more common. One prospective, randomized, controlled (sham acupuncture) trial was done in 90 patients undergoing gastroscopy (Cahn, Carayon, Hill, Flamant, 1978). It was found that endoscopy was much easier and better tolerated after real acupuncture analgesia. A prospective, randomized study comparing electroacupuncture analgesia versus meperidine for colonoscopy (Wang, Chang, Liu, Ho, 1997) demonstrated comparable levels of pain tolerance in patients, increased serum levels of endorphin, and significantly less dizziness with the electroacupuncture.

Future Directions

The clinical area in gastroenterology of greatest potential application of acupuncture is for the FBDs, for example, irritable bowel syndrome (IBS) and NUD (Diehl and Mayer, 1994). There is evidence that symptoms in IBS correlate with specific autonomic nervous system abnormalities (Aggarwal, Cutts, Abell, et al., 1994). Because acupuncture is known to influence autonomic function, it is reasonable to hypothesize that it may be useful in selected cases of FBD. Prospective, randomized, and properly performed studies are clearly needed in this area. Unfortunately, FBDs are among the most difficult to study because of the lack of objective end points, high rate of placebo response, and variable clinical course of the disease. As research methodology improves, especially in the area of quality of life measures and outcomes research, these techniques can be applied to the study of acupuncture treatment of FBD.

Clinical research on the possible application of acupuncture treatment for inflammatory bowel disease is also worthy of study because of the known effects of acupuncture on immune function. Well-designed studies investigating acupuncture treatment of peptic ulcer disease have not been done and are probably of diminishing relevance in light of current understanding of the pathophysiology of PUD and the availability of effective treatment.

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Induction of Ovulation With Acupuncture

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Introduction

In traditional Chinese medical (TCM) literature, acupuncture has long been indicated for menstrual disorder and infertility. The possibility of inducing ovulation with acupuncture has been observed for more than three decades; however, different results led to difficulty in commenting on the efficacy. Multiple factors involved in the etiology of chronic anovulation and various acupuncture points or therapeutic methods used in the different studies are the main problems. In this study, a uniform group of acupuncture points with similar stimulation intensity and timing were studied in clinical and animal experiments.

General and particular success rates were observed for induction of ovulation with these acupuncture points for various kinds of chronic anovulatory diseases.

Clinical and laboratory data were studied to explain the neuroendocrine mechanism contributing to the success rates. Based on these results, anovulatory patients were selected and treated.

Conclusion

- The success rate of induction of ovulation with acupuncture in pubertal dysfunctional uterine bleeding is 86.7 percent; in pubertal oligomenorrhea, 60 percent; and in polycystic ovarian syndrome (PCOS), 36.87 percent.
- Clinical candidates for induction of ovulation with acupuncture include:
 - Suppression of the sympathetic nervous system after acupuncture.
 - Adequate estrogen levels before acupuncture.
 - Low pulsatile frequency of follicle-stimulating hormone (FSH) secretion with normal ovarian reaction before acupuncture.
- Peripheral estrogen levels may contribute to synthesis of hypothalamic β -endorphin, and acupuncture induces release and depletion of hypothalamic β -endorphin leading to luteinizing hormone releasing hormone/luteinizing hormone (LH-RH/LH) surge and consequent ovulation.

General Observation

According to TCM literature, meridians associated with kidney, liver, and spleen, as well as ren,^{1*} and du^{2*} are considered to be closely related to reproduction. Acupuncture points Ren 3, Ren 4, Spleen 6, and extra 16 have been used in the treatment of patients with chronic anovulation since 1960. Chronic anovulation is diagnosed in different types by menstrual disorder history, consecutive monophasic basal body temperature (BBT) for 3 months, serum hormone, and pelvic ultrasonography data. Acupuncture treatment starts on the 14th day from the first day of last uterine bleeding episode for 3 consecutive days. Not only regular menstruation, but biphasic BBT, pregnancy, and ovulatory signs on ultrasonography or serum progesterone levels are taken as criteria for success on ovulation. As a whole, the success rate is around 50 percent; in pubertal dysfunctional uterine bleeding, 87.7 percent; in pubertal oligomenorrhea, 60 percent; and in PCOS, 36.8 percent.

Clinical Factors Related to Efficacy of Induction of Ovulation With Acupuncture

Sympathetic nerve activity. The acupuncture test on hand temperature was measured on the 13th day (1 day before the acupuncture treatment) in 31 anovulatory cases with 79 cycles. After acupuncture treatment, 22 of the 39 cycles with elevation of hand temperature and 10 of the 40 cycles with decrease in hand temperature in the acupuncture test showed ovulation ($P < .05$). This result was repeatable in another study on 13 cases, in which blood β -endorphin-like immunoreactive substance (β -EPIS) levels within the acupuncture test were measured by RIA. Blood β -EPIS levels were about normal values (90.74 (89.56 fmol/mL) in six cases (134.65 (185.81 fmol/mL, $P > .05$), showing ovulation, while significantly high in seven cases (279.64 (203.15 fmol/mL, $P < .05$) and failing to show biphasic BBT after acupuncture. Changes of hand temperature and blood β -EPIS were negatively correlated ($r = -0.677$; $P < .01$). This correlation suggests patients with sympathetic activity suppressed by acupuncture (a sign of fluent flow of Qi and blood in TCM) are likely to ovulate after acupuncture.

Peripheral Estrogen Levels

The eosin index (EI) of vaginal exfoliating cell smears before and after acupuncture was examined every other day in 30 anovulatory cases with 60 cycles. In the EI less than 30 percent group, 10 of 19 cycles with elevation of EI after acupuncture showed biphasic BBT, whereas none of the remaining 13 cycles with no change of EI showed ovulation ($P < .05$). In the EI between 31 and 70 percent group and EI of more than 70 percent group, 8 of the 18 cases showed biphasic BBT after acupuncture.

^{1*} Anterior and posterior midlines, also known as conception vessel (anteriorly) and governing vessel (posteriorly).

Serum estradiol (E_2) levels on the 12th day from the first uterine bleeding day were measured by RIA in 19 cases with PCOS. Induction of ovulation with acupuncture was successful in 7 cases with serum E_2 levels at 541.40 (439.83 pmol/L) and unsuccessful in 12 cases with serum E_2 levels at 283.24 (178.22 pmol/L ($P < .05$)). These data suggest that adequate estrogen levels representing a good ovarian reaction are necessary in induction of ovulation with acupuncture.

Pulsatile secretion of FSH and LH. Serum FSH and LH were observed every 15 minutes in 4 hours before and at the time of acupuncture in 10 cases. Seven cases were diagnosed as PCOS; two cases as dysfunctional uterine bleeding; one case as hypogonadotropic amenorrhea; and eight cases as infertility. After acupuncture, five cases showed ovulation (ovulatory group) and significant increase in FSH pulsatile frequency (from 2.10 (0.24 to 3.70 (1.64/4 h, $P < .05$)), whereas the remaining five cases (nonovulatory group) did not (FSH frequency from 3.50 (1.00 to 3.30 (0.67/4 h, $P > .05$)). Serum LH and FSH levels increased in four of the five ovulatory cases ($P < .05 \sim .01$) and three of the four cases became pregnant during the acupuncture cycles, whereas serum LH and FSH levels increased in two of the five nonovulatory cases, but neither normal follicular growth nor pregnancy occurred. These results suggest that ovulation may be induced by acupuncture via a regulation on hypothalamic-pituitary function, but acupuncture could not help in cases with relatively normal central neuroendocrine function with poor ovarian response. This result suggests that central β -endorphin may be involved in this process.

After the previous observations, 27 anovulatory cases with adequate estrogen levels and low serum FSH and LH levels and suppression of sympathetic activities after acupuncture test were treated with acupuncture. Of these, 22 cases (81.5 percent) showed ovulation and 6 cases became pregnant during the acupuncture cycle.

Serum Estradiol and Central Endogenous Opioid Levels in the Process of Preovulatory LH Surge

Push-pull perfusion in the MBH, MPOA of the hypothalamus, autoradiography of the β -receptor, immunohistochemistry, in situ hybridization, image procession, and RIA were used to observe dynamic changes in the synthesis and release of β -endorphin, density of μ -receptor, estrogen receptor (ER) and gonadotropin-releasing hormone (Gn-RH) secretion in the hypothalamus and E_2 , and LH levels in the blood during the process of LH surge were monitored in rats and rabbits.

Changes of POMC mRNA, ER in the arcuate nucleus during GnRH surge in the proestrus rat. In the proestrus rat, before the LH surge in the blood and the GnRH surge in the ME, a serum E_2 peak appeared, accompanied by a negative regulation on the ER in the arcuate nucleus ($P < .05$). Paralleled by a decrease in ER, POMC mRNA in the arcuate nucleus was significantly reduced, negatively correlated to serum E_2 levels ($r = -0.6623$; $P < .01$) and GnRH levels in the ME ($r = -0.4926$; $P < .05$) and positively correlated to ER in the arcuate nucleus ($r = 0.5730$; $P < .01$). These results suggest that before ovulation, the estradiol peak down-regulates

ER, which may cause a decrease in POMC mRNA expression of the β -endorphin neurons in the arcuate nucleus resulting in a cascade of GnRH release.

Dynamic release of β -endorphin and μ -receptor density in the POA and MBH during GnRH surge induced by cupric acetate in rabbits. Rabbits were primed with estradiol benzoate; however, none of them ovulated. The classic method, cupric acetate (CuAC) injection, was used for inducing ovulation in the rabbits. β -endorphin levels in the MPO and density of β -receptor in the MPO and MBH of the hypothalamus increased in 1 hour (from 43.16 (5.99 to 82.37 (22.2 ng/L; $P < .05$) and immediately decreased, reaching its nadir (21.19 (10.48 ng/L) 3.5 hours after the CuAC injection ($P < .05$). Release of GnRH in the MBH increased and rose to a peak (from 2.24 (0.15 to 11.45 (3.26 pg/mL; $P < .05$) 3.5 hours after CuAC injection, when a concomitant serum LH peak was observed.

Effect of electroacupuncture on hypothalamic GnRH release and density of μ -receptor in MPO and MBH. In rabbits, corpora lutea in the ovaries and GnRH surge in MPO and MBH were produced after electroacupuncture (EA) on specific points (similar to positions of acupoints in human beings) but not in the estrogen group or EA on nonspecific points group. The density of μ -receptor in MPO and MBH increased immediately after EA, just as it occurred in the CuAC injection experiment.

Prediction of Central β -Endorphin Level With Peripheral Estradiol Level.

In animal experiments, data showed that peripheral estradiol levels are correlated to central β -endorphin levels, which directly affects the release of hypothalamic GnRH, and acupuncture changes the values of central β -endorphin and μ -receptor in the process of an LH surge. In a clinical study, adequate estrogen level is essential to inducing ovulation with acupuncture. For patients' and doctors' convenience, another study was conducted to determine whether central β -endorphin levels could be predicted by serum estradiol levels.

A naloxone (NAL) test was conducted on the 12th day from the first uterine bleeding day, which was 2 days before acupuncture treatment in 19 cases of PCOS and 5 normally menstruating women. Serum LH levels were measured every 15 minutes for 3 hours before, 4 hours during, and 2 hours after the NAL test. Serum LH levels were elevated during the NAL test in control (group a), 9 cases succeeded in ovulation (group b), and 12 cases failed to ovulate (group c) in various amplitudes, although on average they did not make any difference. After the NAL test, serum LH levels were significantly higher than those before NAL test in group a (9.36 (6.79 vs. 5.06 (3.88 IU/L; $P < .01$) and group b (8.51 (3.74 vs. 6.15 (3.04 IU/L; $P < .01$), but not in group c (7.12 (2.66 vs. 6.92 (2.61 IU/L; $P > .05$). Serum estradiol levels on the 12th day were significantly higher in group a than those in the 19 PCOS cases (1108.300 (454.93 vs. 378.38 (274.62 pmol/L; $P < .01$), but estradiol levels in group b were much higher than those in group c (541.40 (439.83 vs. 283.29 (185.22 pmol/L; $P = .05$). These data suggest that serum estradiol levels may predict central β -endorphin activities; just as in a normal menstrual cycle, the NAL test shows little LH secretion in the early follicular phase with the lowest estrogen level and

shows highest LH release in the preovulatory phase with an estrogen peak.

Indication for Induction of Ovulation With Acupuncture

An adequate estrogen level is essential to the efficacy of induction of ovulation with acupuncture, but chronic anovulation may be complicated by disorders from the adrenal, thyroid, pancreas and liver and neurotransmitters other than β -endorphin.

Puberty is indicated by maturity of the ovarian axis in adolescents with a positive LH reaction in NAL test. Pubertal dysfunctional uterine bleeding refers to irregular endometrial shedding caused by unopposed estrogen fluctuation, a sign of a functioning ovary without normal central neuroendocrine function.

Thirty patients with pubertal menstrual disorder were divided into two groups: 15 cases with dysfunctional uterine bleeding (DUB) and 15 cases with oligomenorrhea or amenorrhea (OLA); estrogen levels were higher in the DUB group than in the OLA group. After acupuncture, 13 of the 15 DUB cases (87.7 percent) and 9 of the 15 OLA cases (60 percent) showed ovulatory signs on biphasic BBT and regular menstruation ($P < .05$). These results reconfirm that peripheral estrogen may predict the central β -endorphin level, which is important for acupuncture to stimulate in a large pulsatile release of central β -endorphin. The depletion of central β -endorphin withdraws the suppression on GnRH, which results in ovulation. The manifestation of DUB meets all indications for induction of ovulation with acupuncture.

Future Directions

1. To increase estrogen levels in cases of chronic anovulation to extend the success rate with acupuncture.
2. To examine the specificity of acupuncture points for induction of ovulation.
3. To observe the effect of induction of ovulation with acupuncture on the central neurotransmitter, for example, NPY, GABA, NE, and so forth to treat anorexia nervosa, obesity in menstrual disorder, and postmenopausal syndrome with acupuncture.
4. During the acupuncture test for hand temperature, to determine whether ER is involved on the vascular wall.
5. To study a model of acupuncture in obstetrics and gynecology: clinical trials before and after acupuncture (mechanism (promotion of efficacy in induction of ovulation, induction of labor, premenopausal syndrome, and the like. To conduct controlled studies on breech presentation, dysmenorrhea, urinary retention, migraine, and other dysfunctions.

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Protective Effect of Acupuncture on Immunosuppression

X.D. Cao, M.D., Ph.D.

Introduction

Acupuncture has been clinically useful in treating inflammatory, hypersensitive, or autoimmune diseases (Yang, Chen, Zhao, et al., 1995; Liao, 1995). Substantial studies have demonstrated that this given effect of acupuncture results from its diphasic modulation on immune function. Yet, only in recent years has attention been paid to the effect of acupuncture on the interaction of neuroimmune systems. Immune function may be suppressed by surgical trauma or morphine via the central nervous system. Limited research has shown that acupuncture has a profound effect on alleviating this kind of suppression. However, little is known about the mechanisms of acupuncture in this regard.

Conclusions

Surgical trauma stress and/or epidural injection of morphine depress the immune function. Acupuncture can improve the immunosuppression induced by surgical trauma and/or epidural morphine. The central opioid system is involved in the effect of acupuncture on immune function.

Effect of Electroacupuncture (EA) on Immunosuppression Induced by Surgical Trauma

In our laboratory, we found that the ConA-induced lymphocyte proliferation and the IL-2 production of rats' splenocytes were significantly decreased within a week after surgical trauma. EA treatment induced an obvious increase in the proliferative response and the induction of IL-2 production of the traumatized rats' spleen lymphocytes (Cheng, Wu, He, et al., 1997). These results indicated that EA prevented the decrease of the lymphocyte proliferation and the activity of IL-2 and improved the immunosuppression induced by surgical trauma.

It was noted that when the spleen lymphocytes of normal mice were incubated with the serum from rats with surgical trauma, the proliferation of lymphocytes was also significantly inhibited. The suppression of lymphocyte proliferation of the traumatized rat and inhibition of the rat serum were positively correlated. These results suggested that an immunosuppressive factor might be produced in the serum after trauma stress (Cheng, Wu, Jiang, et al., 1997). We further analyzed the extract from the traumatized rat spleen and found that the fraction 11 possessed a significant immunosuppressive effect and had a molecular weight of 5,000 to 7,000. When a traumatized rat was pretreated with EA, the serum had no inhibition on proliferation of

lymphocyte.

Activation of tyrosine protein kinase (TPK) is the earliest biochemical event in transmembrane signal transduction of activation and proliferation of T lymphocytes (Klausner, Samelson, 1991). It was found that the activity of TPK in the membrane and cytosol of T cells from normal rats was increased on the 5th sec and peaked on the 45th sec after Con A stimulation, then decreased gradually. The activity of TPK in subcellular fractions of activated T cells from rats with trauma stress was markedly decreased, especially in membrane. EA treatment enhanced the activity of TPK in subcellular fractions of activated T cells from traumatized rats (Cheng, Wu, He, et al., in press). It is possible that the immunosuppression induced by trauma stress is caused by the inhibition of TPK activity in subcellular fractions of activated T cells. The enhancement of TPK activity might be one of the molecular mechanisms of EA's protective effect on immunosuppression induced by trauma stress.

Clinical Investigation and Laboratory Research on the Effect of EA on Morphine-Induced Immunosuppression

Postoperative and cancer pain can be relieved efficiently by epidural or intrathecal (ith) injection of morphine, but there is a series of adverse reactions (Du, Jiang, Du, et al., 1994). In the laboratory, it was found that morphine (40 g, ith) suppressed the lymphocyte proliferation, Con A-induced IL-2 production of splenocytes and NK cell activity in rats postoperatively. EA treatment combined with morphine obviously improved the above-mentioned morphine-induced immunosuppression. Clinically, in patients who received cholecystectomy, it was observed that epidural injection of morphine (1 mg) after operation induced a marked depression of lymphocyte proliferation, decrease in IL-2 production, and inhibition of NK cell activity. Simultaneous EA treatment after operation significantly reversed the above immunosuppression and normalized the decreased IL-2 production earlier (Zhang, Du, Wu, et al., 1996; Zhang, Du, Cao, 1996). These results suggest that EA combined with epidural morphine treatment is a better way of relieving clinical postoperative pain.

Participation of the Opioid System in EA's Action on Immune Function

The role of the opioid system in immune function has been demonstrated (Carr, Blalock, 1991; Heijnen, Kavelaars, Ballieux, 1991). Our recent works have shown that EA induced significant changes in the central opioid system, including the increase of release and gene expression of endogenous opioid peptides and the function of opioid receptors in the central nervous system (CNS) (Yu, Gao, He, 1994; Zhu, Jin, Xu, 1995; Zhu, Li, Zhu, et al., 1995; Zhu, Li, Zhu, et al., 1997). In normal rats, we found that EA treatment significantly increased the lymphocyte proliferation of splenocytes and the induction of IL-2 production, indicating the enhancement of immune function by EA (Du, Jiang, Cao, 1996). These results suggest that EA-induced enhancement of immune function was related to the activation of the opioid system in the normal state.

However, it is more complicated in the pathological state. For example, surgical trauma can induce immunosuppression, such as inhibition of NK cell activity, lymphocyte proliferation, and IL-2 production, with increased level (higher than normal) of opioid peptides and corticosterone in plasma (Cs). EA could improve immunosuppression as well as reduce the plasma beta-endorphin and Cs (Du, Jiang, Wu, et al., 1996). Icv injection of naloxone (20 (g) or EA treatment obviously antagonized the trauma-induced inhibition of NK cell activity (Du, Jiang, Wu, et al., 1997), suggesting that the central opioid system participated in trauma-induced immunosuppression and might be involved in the action of EA.

The orphanin FQ (OFQ) is a newly discovered opioid peptide structurally resembling other opioid peptides, but it possesses distinct characteristics in pharmacological and physiological profiles. In recent studies, we have found that icv injection of OFQ also antagonized the inhibition of immune function induced by surgical trauma (Du, Jiang, Wu, et al., in press), further suggesting the involvement of the central opioid system in immunosuppression.

Morphine has extensive immunosuppression, which can be reversed by EA treatment. There is evidence that morphine acts on the immune system via CNS pathways (Hernandez, Flores, Bayer, 1993): N-methylmorphine, which does not penetrate the blood-brain barrier, was not observed as having an immunosuppressive effect when injected peripherally, but an inhibition of blood lymphocyte proliferation happened when it was microinjected into the third ventricle or anterior hypothalamus, similar to the effect of systematically administered morphine. Our investigation showed that microinjection of naloxone (1 (g), an antagonist of opioid receptors, into periaqueductal gray (PAG) partially antagonized the inhibition of NK cell activity but not IL-2 production induced by ith injection of morphine; EA significantly elevated both the inhibited NK cell activity and the IL-2 production. When EA was combined with PAG-injection of naloxone, a better effect in alleviating the morphine-induced immunosuppression appeared than by using either naloxone or EA alone (Zhang, Du, Wu, et al., 1996). These results suggest that opioid receptors in PAG mediated, at least in part, the morphine-induced inhibition of immune function; the enhancement of EA on immune function inhibited by morphine might involve the regulation of the central opioid system.

It has been demonstrated that the hypothalamus-pituitary-adrenal axis constitutes the most powerful circuit in regulating the immune system. In this powerful axis, endogenous opioid peptides and many other substances, such as ACTH, Cs, and so forth, play an important role (Blalock, 1994). Acupuncture most probably acts on the immune system by regulating this axis. In this regard, there is much to be studied.

Taken together, it may be inferred that central opioid systems participate in the regulation of immune function, and they may play a different role in normal and in pathological states. The action of EA on the immune system might be related to the modulation of the opioid system as well as other systems.

Future Directions

Laboratory and clinical studies have demonstrated that acupuncture has no obvious effect on normal functions, but it can modulate or normalize the abnormal ones. Although acupuncture has been proven to be beneficial to the immune functions, much is waiting to be investigated on the modulation of acupuncture on the immune system and the relevant mechanisms. The following are some recommendations for research questions.

- What are the best parameters and the acupoints for acupuncture or EA in modulating the immune functions?
- What are the central mechanisms of improvement of EA on immunosuppression, including the immunomodulatory effect on the central nervous system, and interactions between opioid peptides and immunomodulation?
- What are the modulatory pathways of the acupuncture-mediated immunomodulation?
- What are the cellular and molecular mechanisms involved in the modulation of EA on immune functions?

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Late-Breaking Data and Other News From the Clinical Research Symposium (CRS) on Acupuncture at NIH

Hannah V. Bradford, M.Ac.

During the Clinical Research Symposium on November 2, 1997, the following presentations will be made:

- Review of research tools applicable to acupuncture investigations.
- Reports from Office of Alternative Medicine (OAM/NIH) centers conducting acupuncture research.
- Presentations on outcomes research project initiatives and preliminary data.
- Reports on developing studies in the areas of depression, emesis, and other clinical research projects conducted outside the OAM centers.
- Discussion and development of a statement on future research directions.

The Clinical Research Symposium (CRS), sponsored by the Society for Acupuncture Research, continues the Society's central mission of creating a forum for researchers and clinicians with an interest in acupuncture and related East Asian healing practices to share information. Starting in 1993, the Society has sponsored three symposia to support this mission. The CRS is its fourth symposium and has been designed to meet the needs of the Society's mission as well as to provide an expanded perspective on research issues in acupuncture and a summary of recently completed studies to the NIH Consensus Development Conference on Acupuncture.

American Acupuncture: Primary Care, Public Health, and Policy

Alan I. Trachtenberg, M.D., M.P.H.

In terms of American primary care, I would like to consider how it is that we decide, as individual clinicians or professional groups, which treatments to perform or recommend to our patients.

Certainly, the whole modern movement of evidence-based medicine tells us that the best recommendations are those based on replicated randomized and blinded trials (RBTs). However, the fact that we have needed a movement for evidence-based medicine reinforces the observation that current medical practice is not necessarily based on this high standard. The sad fact remains that a majority of interventions recommended to Americans by their physicians are based not on RBTs but on the clinical experience of American physicians and their teachers. They are interventions that have “stood the test of time” in American medicine. However, the history of medicine reveals many such interventions that later, when finally subjected to quantitative comparisons, did not hold up to those tests. It is most important, however, to subject the intervention to the proper test, for the proper indication and under the proper circumstances. Pierre Charles Alexandre Louis firmly documented that bleeding was not helping the majority of patients being bled in the clinics and hospitals of the Paris Medical Academy. Bleeding was, however, a very useful procedure accompanying foxglove when treating a patient with dropsy (congestive heart failure), and, for the “MOST DAMP”* of our pulmonary edema patients today we still use phlebotomy. On the other hand, physicians doing this procedure when it was not indicated was the cause of George Washington's iatrogenic death.

While we may not be able to fully account for or explain the allegorical descriptions of traditional Chinese medicine (TCM) diagnosis in our own terms, it may be that the best test of acupuncture will be had only when taking these into account. Future studies may do this by stratifying, for instance, migraine patients into their different TCM typologies or by excluding all but a single type from a given study. Or, a reproducible clinical protocol may be enunciated according to a complex flow sheet or computer program that would serve as an "expert system" for treatment of any of the common TCM descriptions for a given diagnosis. This could then be

* “MOST DAMP” is a mnemonic taught to medical students to facilitate rapid treatment of pulmonary edema:

- Mercurials (diuretics)
- Oxygen
- Sitting (position helps them breathe better)
- Tourniquets (rotating, to slow venous return)
- Digoxin
- Aminophylline
- Morphine
- Phlebotomy (to lessen the overload in blood volume)

tested in a clinical trial. Parameters for nonrelevant points could also be added, and such a program could even perform the randomization, leaving the actual needling to operators who are well-trained in anatomy but who are blinded to the treatment protocols being utilized. This would facilitate an experimental model more closely approaching the gold standard of a double-blind trial and give acupuncture a test more true to the way that it is typically practiced, in accordance with TCM.

Some acupuncturists will voice the criticism that it is unethical to puncture control subjects without a therapeutic goal, asking whether we would allow surgery to be done in such a double-blind fashion. But it must be admitted that the risks of adverse effects from sham acupuncture are far less than the comparable risks for sham surgery. In fact, the lack of data from controlled trials for surgical procedures is one of the greatest challenges facing evidence-based medicine today. Furthermore, the history of the few randomized trials of surgical procedures that have been conducted shows that there must be adequate diffusion of a given technique and an adequate number of skilled operators available (already doing the procedure) to make it both relevant to subject the procedure to such a trial as well as to define the clinical protocol that consensus will dictate to be adequate in answering the relevant clinical questions in a definitive way.

For acupuncture, as well as for many standard interventions, these definitive tests are mostly still in the future. How, then, are patients to be advised about acupuncture today? I would submit that the fairest test of the data supporting the use of acupuncture is to weigh it against the data supporting standard medical interventions being used now for the same problems. If the data for acupuncture are as good as or better than those for current standard interventions, then any absolute medical preference for the standard intervention over acupuncture must be based merely on availability, cost, or prejudice. “But what,” you may ask, “about the years of clinical experience that American physicians have with these standard interventions that they learned from their distinguished professors in medical school? What about the prior probability that we attach to acupuncture's effectiveness? Isn't this an important factor?” I think it is clear from the centuries of Chinese experience with acupuncture, and the decades of experience by distinguished European professors as well as a few trailblazing Americans, that acupuncture deserves just as high a Bayesian prior probability for effectiveness as any typical American intervention and that any advantage of one over the other should be based primarily on the data rather than on any cultural bias.

In this presentation, data from the literature will be presented to examine some of the common clinical problems seen by American physicians and the regular interventions for these problems and to examine the weight of the data for those interventions compared with that for acupuncture treatment for the same clinical problems.