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## Efficacy of Acupuncture for Treating Depression

*By Yoon-Hang "John" Kim, MD, MPH, DABMA, and Jeanne Bowers*

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DEPRESSION IS A POTENTIALLY LIFE-THREATENING MOOD DISORDER. The World Health Organization identified major depression as the fourth leading cause of worldwide disease in 1990, causing more disability than either ischemic heart disease or cerebrovascular disease.<sup>1</sup> In the United States, the impaired functioning associated with depression is comparable to the impairment associated with heart disease and exceeds that of several other medical conditions, including hypertension, diabetes, and arthritis.<sup>2</sup>

In a given year, 9.5% of the population, or 20.9 million American adults, suffer from a depressive illness.<sup>3</sup> In addition to considerable pain and suffering that interfere with individual functioning, depression also affects those who care about the ill person, sometimes destroying family relationships and work dynamics. The annual economic cost of depressive illness is estimated to be \$30-44 billion in the United States alone.<sup>2</sup>

Depression is also associated with heightened concern about physical symptoms, such as pain and increased functional impairment.<sup>4</sup> Furthermore, post-myocardial infarction depression is an independent risk factor for increased mortality.<sup>5</sup>

A variety of medications are available to treat depression; the effectiveness of selective serotonin reuptake inhibitors and tricyclic antidepressants are well established. However, one potential side effect of these antidepressant therapies appears to be an increased risk of suicide in select populations.<sup>6</sup>

The popular use of complementary and alternative medicine (CAM) for depression has been well documented. In fact, research indicates that CAM therapies are used more than conventional therapies by people with self-defined anxiety attacks and people with severe depression.<sup>7</sup>

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The efficacy of CAM modalities, including acupuncture, for psychiatric purposes has been reviewed by a number of researchers,<sup>8,9</sup> and special attention has been given to describing the challenges associated with conducting research using acupuncture to treat depression.<sup>10</sup>

### Mechanism of Action

Acupuncture is probably the most thoroughly researched modality in complementary and alternative medicine,<sup>11</sup> and Paramore estimates that about one million people utilize acupuncture annually within the United States.<sup>12</sup> It is widely believed that acupuncture initiates stimulation of small diameter nerves in muscles, sending impulses to the spinal cord, midbrain, and pituitary, and results in the release of neurotransmitters such as monoamines and endorphins.<sup>11</sup>

Endorphins play a part in the mechanistic pathway for acupuncture. The discovery of naloxone, an endorphin antagonist, helped elucidate the role of endorphins in acupuncture. Naloxone was shown to block acupuncture analgesia in human volunteers in a randomized, double-blind study.<sup>13</sup> A subsequent study reproduced the same results, displaying a dose-response curve for naloxone and found that increasing doses produced increasing blockade.<sup>14</sup>

More importantly for the treatment of depression, in addition to endorphins, monoamines such as serotonin and norepinephrine have been shown to be involved in

acupuncture. Microinjection of serotonin antagonists blocked the effects of acupuncture,<sup>15</sup> and a similar study used microinjection of a norepinephrine antagonist to block acupuncture's effects.<sup>16</sup> The rise of serum serotonin during acupuncture treatments has been demonstrated by Sprott et al.<sup>17</sup> Another recent study characterized the serotonin receptor subtypes involved in modulation of electrical acupuncture.<sup>18</sup>

The monoamines' involvement in the acupuncture pathway provides possible mechanisms by which acupuncture is able to treat other monoamine-mediated conditions. A recent study documented that acupuncture treatments resulted in increased nocturnal melatonin secretion and reduced both insomnia and anxiety.<sup>19</sup>

In 1975, Riederer et al conducted a clinical trial demonstrating that needling of specific acupuncture points in subjects resulted in changes in norepinephrine levels measured in blood and urine.<sup>20</sup> In the 1980s, Han investigated the effects of electroacupuncture on serotonin and norepinephrine, two neurotransmitters commonly implicated in depression and anxiety.<sup>21</sup> The findings demonstrated that electroacupuncture accelerates the synthesis and release of serotonin and norepinephrine in the central nervous system. Furthermore, Fanqiang et al reported that plasma norepinephrine concentrations were significantly elevated in depressed patients who improved following a six-week course of electroacupuncture; whereas, the nonresponding patients did not show significant changes in serum norepinephrine levels.<sup>22</sup>

### Clinical Trials

In 1985, Luo et al conducted a clinical trial comparing the efficacy of acupuncture vs. amitriptyline, a tricyclic antidepressant medication, for treating depression.<sup>23</sup> The 47 patients were randomly assigned to two groups. One group received electric acupuncture at the Bai Hui and Yintang points for one hour per day, six days a week, for five weeks. The control group received amitriptyline. The results demonstrated that the electric acupuncture was as effective as amitriptyline for treating depression. In addition, electric acupuncture was found to be more effective for treating anxiety without the side effects often associated with drug treatment. In 1990, Luo et al reported the results from a repeat trial with 241 patients.<sup>24</sup> The results were similar to the earlier study: Acupuncture was as effective as amitriptyline for treating depression and more effective for treating anxiety.

Yang et al also compared the effect of acupuncture vs. amitriptyline and reported the results in 1994.<sup>25</sup> In contrast to the two previous studies conducted by Luo et al where only two acupuncture points were utilized, Yang

**Alternative Therapies in Women's Health**, ISSN 1522-3396, is published monthly by AHC Media LLC, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.  
**SENIOR VICE PRESIDENT/PUBLISHER:** Brenda L. Mooney.  
**ASSOCIATE PUBLISHER:** Lee Landenberger.  
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**EDITOR:** Leslie G. Coplin.  
**GST Registration Number:** R128870672.  
Periodicals postage paid at Atlanta, GA 30304.  
**POSTMASTER:** Send address changes to *Alternative Therapies in Women's Health*, P.O. Box 740059, Atlanta, GA 30374.  
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### Questions & Comments

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et al explored the use of traditional acupuncture taking account of the presenting traditional Chinese medicine syndromes. Again, the findings were similar: Acupuncture treatment was as effective as amitriptyline for the treatment of depression and more effective for treating anxiety.

In 1998, Allen et al published results of a pilot trial consisting of 33 female outpatients who met the criteria for major depression.<sup>26</sup> The patients were assigned to one of three groups: acupuncture treatment specific for depression; a nonspecific treatment using valid acupuncture points; and a no-treatment group consisting of wait-list. Sixty-four percent of patients who received acupuncture treatments specific for depression showed full remission, and improved significantly more than women in the nonspecific treatment group. However, no statistical differences were shown between the treatment group and the no-treatment group.

In a 1999 study, Roschke et al examined the effect of adding acupuncture to antidepressant medication. Seventy inpatients were divided into three groups: acupuncture plus antidepressant, sham acupuncture plus antidepressant, and antidepressant.<sup>27</sup> The addition of acupuncture produced improvements over antidepressants alone. However, there was no difference between the true acupuncture and sham acupuncture group.

Eich et al published results of a trial in 2000 comparing acupuncture to sham acupuncture for the treatment of depression.<sup>28</sup> They divided 43 patients into two groups: acupuncture and sham acupuncture. They concluded that acupuncture was significantly better than sham acupuncture after 10 treatments but not after five treatments.

In 2004, Manber et al reported findings of a randomized controlled trial comparing acupuncture vs. massage vs. sham acupuncture in pregnant patients with depression.<sup>29</sup> Sixty-one pregnant women with major depressive disorder were divided into three groups: acupuncture, sham acupuncture, and massage. The results demonstrated that symptoms among the acupuncture group improved more than in the massage group (69% vs. 32%, respectively). However, there was no statistical difference between the acupuncture group and sham acupuncture group.

Quah-Smith et al published results in 2005 of a randomized controlled trial comparing laser acupuncture and sham laser acupuncture for the treatment of depression.<sup>30</sup> Thirty patients were divided into two groups. Results showed that the laser acupuncture group improved significantly more than the sham laser acupuncture group ( $P = 0.007$ ).

In 2006, Allen et al published the results of larger ran-

domized controlled trial using same design as the earlier 1998 study.<sup>31</sup> The results failed to document effect of

## Depression in Women

**W**OMEN EXPERIENCE DEPRESSION ABOUT TWICE AS OFTEN as men.<sup>1</sup> Many hormonal factors may contribute to the increased rate of depression in women, particularly such factors as menstrual cycle changes, pregnancy, miscarriage, postpartum period, premenopause, and menopause. Many women also face additional stresses such as responsibilities both at work and home, single parenthood, and caring for children and for aging parents.

A recent National Institute of Mental Health study showed that in the case of severe premenstrual syndrome (PMS), women with a preexisting vulnerability to PMS experienced relief from mood and physical symptoms when their sex hormones were suppressed. Shortly after the hormones were re-introduced, they again developed symptoms of PMS. Women without a history of PMS reported no effects of the hormonal manipulation.<sup>2,3</sup>

Many women are also particularly vulnerable after the birth of a baby. The hormonal and physical changes, as well as the added responsibility of a new life, can be factors that lead to postpartum depression in some women. While transient “blues” are common in new mothers, a full-blown depressive episode is not a normal occurrence and requires active intervention. Treatment by a sympathetic physician and the family’s emotional support for the new mother are prime considerations in aiding her to recover her physical and mental well-being and her ability to care for and enjoy the infant.

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acupuncture for treating depression. Allen et al employed an individualized protocol rather than using the Yin Tang and Bai Hui protocol developed in China.

### Adverse Effects/Safety Trials

The safety of acupuncture is well documented. Ernst and White conducted a systematic review to determine the incidence of adverse events associated with acupuncture.<sup>32</sup> The most common adverse events were needle pain, tiredness, and bleeding. Feelings of faintness and syncope were uncommon. Pneumothorax was rare, occurring only twice in nearly a quarter of a million treatments. However, the use of nonsterile needles may cause infections. One overview identified 126 documented cases of hepatitis associated with acupuncture.<sup>33</sup>

### Conclusion

The chain of evidence, from the neurotransmitters research to clinical trials, supports the biological plausibility and efficacy of acupuncture for the treatment of depression.

### Recommendation

Depression is a prevalent medical problem with huge social, economical, and medical implications. Given the low risk of acupuncture, a trial of acupuncture should be considered a potentially useful option for patients with depression. ❖

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## The A TO Z Study: Examining the Efficacy of Weight Loss Alphabet Soup

By Dónal P. O'Mathúna, PhD

*Dr. O'Mathúna is a lecturer in Health Care Ethics, School of Nursing, Dublin City University, Ireland; he reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study.*

**Source:** Gardner CD, et al. Comparison of the Atkins, Zone, Ornish, and LEARN diets for change in weight and related risk factors among overweight premenopausal women: The A TO Z Weight Loss Study: A randomized trial. *JAMA* 2007;297:969-977.

**Context:** Popular diets, particularly those low in carbohydrates, have challenged current recommendations advising a low-fat, high-carbohydrate diet for weight loss. Potential benefits and risks have not been tested adequately.

**Objective:** To compare four weight-loss diets representing a spectrum of low- to high-carbohydrate intake for effects on weight loss and related metabolic variables.

**Design, Setting, and Participants:** Twelve-month randomized trial conducted in the United States from February 2003 to October 2005 among 311 free-living, overweight/obese (BMI 27-40 kg/m<sup>2</sup>) nondiabetic, premenopausal women.

**Intervention:** Participants were randomly assigned to follow the Atkins (n = 77), Zone (n = 79), LEARN (n = 79), or Ornish (n = 76) diets and received weekly instruction for two months, then an additional 10-month follow-up.

**Main Outcome Measures:** Weight loss at 12 months was the primary outcome measure. Secondary outcomes included lipid profile (low-density lipoprotein, high-density lipoprotein, and non-high-density lipoprotein cholesterol, and triglyceride levels), percentage of body fat, waist-hip ratio, fasting insulin and glucose levels, and blood pressure. Outcomes were assessed at months 0, 2, 6, and 12. The Tukey studentized range test was used to adjust for multiple testing.

**Results:** Weight loss was greater for women in the Atkins diet group compared with the other diet groups at 12 months, and mean 12-month weight loss was significantly different between the Atkins and Zone diets (P < 0.05). Mean 12-month weight loss was as follows: Atkins, -4.7 kg (95% confidence interval [CI], -6.3 to -3.1 kg); Zone, -1.6 kg (95% CI, -2.8 to -0.4 kg); LEARN, -2.6 kg (95% CI, -3.8 to -1.3 kg); and Ornish, -2.2 kg (95% CI, -3.6 to -0.8 kg). Weight loss was not statistically different among the Zone, LEARN, and Ornish groups. At 12 months, secondary outcomes for the Atkins group were comparable with or more favorable than the other diet groups.

**Conclusions:** In this study, premenopausal overweight and obese women assigned to follow the Atkins diet, which had the lowest carbohydrate intake, lost more weight and experienced more favorable overall metabolic effects at 12 months than women assigned to follow the Zone, Ornish, or LEARN diets. Although questions remain about long-term effects and mechanism of action, a low-carbohydrate, high-protein, high-fat diet may be considered a feasible alternative recommendation for weight loss.

### Comments

The search for effective ways to lose weight continues. The obesity problem persists in developed countries and is even starting to affect developing countries. A whole business enterprise has developed to promote the diets, books, programs, and supplements that offer

people ways to shed the extra pounds. Given the frustration experienced by many, controlled studies evaluating the various approaches are also multiplying. The A TO Z Weight Loss Study adds another trial to those available to help people decide which diet might work best for them.

A TO Z stands for the four diets studied in the trial: Atkins, Traditional, Ornish, and Zone. The Atkins diet is very low in carbohydrate; the Traditional diet is a lifestyle approach that is low in fat, high in carbohydrate, and based on national guidelines; the Ornish diet is very high in carbohydrate; and the Zone diet is low in carbohydrate. This choice reflects recent controversy centered on the carbohydrate content of diets: Are low-carbohydrate diets like Atkins superior to the traditional approach in national guidelines of replacing fat with carbohydrates (and reducing overall calorie intake)?

Controlled studies of different diets have not provided a definitive answer as to which strategy is superior. A meta-analysis published in 2006 reviewed trials that directly compared low-carbohydrate diets with low-fat diets in people with a BMI of at least 25 kg/m<sup>2</sup>.<sup>1</sup> Five studies were included, with between 53 and 132 participants. After six months, those on the low-carbohydrate diets had lost significantly more weight than those on the low-fat diets (on average, 7.3 lbs more). However, by 12 months there were no statistically significant differences in weight loss between the diets.

Significant differences were also found in the lipid profiles, although not consistently favoring one diet type. Total cholesterol and low-density lipoprotein (LDL) levels were lower for those on the low-fat diets (at six and 12 months). For those on the low-carbohydrate diets, total triglyceride was lower (at six and 12 months) and high-density lipoprotein (HDL) was significantly higher (at six months, but not at 12 months).

The A TO Z study was designed to compare larger numbers of participants than previous trials. The study enrolled 311 premenopausal women with a BMI of 27-40 kg/m<sup>2</sup>. At no point were there significant differences in weight loss between the Ornish, Traditional, or Zone diets. In keeping with previous studies, initial weight loss (at two and six months) was significantly greater on the Atkins diet compared to all the others. However, as usually happens, by 12 months, the differences were no longer significant—except between the Atkins and Zone diets. This change did not arise because of shifts among those on the Ornish or Traditional diets (their overall weight loss remained consistent). Instead, the average weight loss on the Atkins diet decreased between six and 12 months. In other words, people were regaining weight during this time.

The lipid profile changes in the A TO Z study were similar to those found in the meta-analysis, but with some findings more favorable for the low-carbohydrate diet. Total triglyceride was lower and HDL higher at all times for those on the low-carbohydrate diet. Total non-HDL cholesterol levels did not differ between diets at any time. The LDL levels were lower for those on the Ornish and Traditional diets at two months, but not at six or 12 months. These results further substantiate the view that the Atkins diet does not adversely impact cardiovascular health.

It is disappointing that while most studies and reviews of low-carbohydrate and low-fat diets comment that comparisons need to be extended past one year, the A TO Z study followed previous patterns and stopped at 12 months. The long-term effectiveness of low-carbohydrate diets has been an ongoing concern about low-carbohydrate diets. Long-term adherence to these diets is difficult because of the consistent consumption of high-protein foods. The long-term effects of maintaining these diets (or attempting to do so) need to be examined urgently given how many people are attempting to follow their guidelines. Although initial concerns about the impact of low-carbohydrate diets on markers of cardiovascular disease have been ameliorated by controlled studies, concerns about their long-term impact on kidney function remain.

The relatively small number of studies including long-term follow-up demonstrate that a combination of strategies is vital to successful weight loss.<sup>2</sup> Reduction in caloric intake is most important. While low-carbohydrate diets lead to more weight loss in the first six months, the goal is reduced caloric intake as part of a diet that people can adhere to for the rest of their lives. Also crucial is increased energy expenditure through some sort of exercise or physical activity. Again, the important factor is activity that becomes part of a person's ongoing lifestyle. Finally, various support programs that provide encouragement for those trying to lose weight and retain a more healthy weight are also important. The A TO Z study, unfortunately, did not add anything to our understanding of those features of weight loss. ❖

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### NIH Clinical Center Establishes Integrative Medicine Consult Service

The National Center for Complementary and Alternative Medicine (NCCAM) has established an Integrative Medicine Consult Service at the National Institutes of Health (NIH) Clinical Center. This service will provide physicians, nurses, and other members of the Clinical Center health care team the ability to discuss complementary and alternative medicine (CAM) therapies with knowledgeable medical staff from the consult service and learn how various CAM practices might complement or interact with a patient's care as a research participant at the Clinical Center.

The NIH Clinical Center already offers many CAM therapies. The Clinical Center's Pain and Palliative Care Service and the Rehabilitation Medicine Department offer acupuncture, reiki, hypnosis, guided imagery, massage therapy, acupuncture, tai chi, and qi gong training.

The Pharmacy Department consults on herbals and herb/drug interactions and has conducted research in these areas. The Integrative Medicine Consult Service will coordinate the resources of these services to meet the needs of the Clinical Center staff and its patients. In addition to offering clinical consultation regarding CAM therapies, the service will establish a research program embedded in NIH's clinical and translational research structure and provide CAM education for NIH staff, patients, and their families.

The director of the consult service will be Patrick J. Mansky, MD, a clinical oncologist and researcher at NCCAM. Mansky joined NCCAM in 2001 as a staff clinician and clinical investigator leading the oncology program in NCCAM's Division of Intramural Research. He conducts research on the application of CAM interventions in the care and treatment of cancer patients and survivors, including electroacupuncture for nausea from

### CME Objectives

After reading *Alternative Therapies in Women's Health*, the health care professional will be able to:

1. evaluate alternative medicine and complementary therapies for women's health concerns;
2. identify risks and interactions associated with alternative therapies;
3. discuss alternative medicine options with patients;
4. offer guidance to patients based on latest science and clinical studies regarding alternative and complementary therapies.

### CME Instructions

Physicians participate in this continuing medical education program by reading the article, using the provided references for further research, and studying the questions at the end of the article. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material. After completing this activity, you must complete the evaluation form provided and return it in the reply envelope provided at the end of the semester to receive a certificate of completion. Upon receipt of your evaluation, a certificate will be mailed.

### CME Questions

24. **The functional impairment of depression is comparable to which of the following conditions?**
  - a. Arthritis
  - b. Diabetes
  - c. Heart disease
  - d. Hypertension
25. **Which of the following are involved in the mechanism of action of acupuncture?**
  - a. Endorphins
  - b. Serotonin
  - c. Norepinephrine
  - d. All of the above
26. **Women experience depression about twice as often as do men.**
  - a. True
  - b. False
27. **The results of studies comparing low-carbohydrate and low-fat diets like the A TO Z Weight Loss Study have not allayed concern over:**
  - a. LDL levels.
  - b. HDL levels.
  - c. kidney function.
  - d. All of the above

Answers: 24. c, 25. d, 26. a, 27. c.

chemotherapy, use of mistletoe in combination with gemcitabine for treating advanced cancers, and effects of tai chi and exercise in cancer survivors.

### **Many Physicians Know Little about Dietary Supplement Regulation, Study Says**

Physicians could learn much more about dietary supplement regulation and adverse event reporting, according to a recent study.

Patients often rely on their physicians for education about herbs and other supplements since the passage of the Dietary Supplement Health and Education Act allowed supplements to be sold to the public without FDA approval or premarket evaluation, the researchers say. The researchers, however, wondered about the level of knowledge of the physicians in this area. To test this, they designed a study to evaluate physicians' level of understanding of dietary supplement regulation and the adverse event reporting process. The researchers also wanted to determine whether an interactive on-line curriculum could aid in improving knowledge.

After developing a multicenter on-line educational intervention, they administered it to physicians at 15 internal medicine residency programs throughout the United States between March 1, 2006, and June 30, 2006. The researchers used pretest performance to measure baseline knowledge, while posttest performance compared with pretest performance measured the effectiveness of the educational intervention.

A total of 335 physicians completed the module. Ninety percent of those completing the module were residents, while 10% were attending physicians. The researchers found that baseline knowledge of dietary supplement regulatory issues was poor, with a total average pretest score of only 59% (986/1,675). The average score rose to 91% (1,526/1,675) after completion of the curriculum. About one-third of physicians were unaware that dietary supplements did not require FDA approval or submission of safety and efficacy data before being marketed. Similar percentages believed that there are regulations in place to ensure supplement quality. Most physicians were unaware that serious adverse events due to the use of supplements should be reported through the FDA MedWatch system.

For more information about the study, see the May 14 issue of the *Archives of Internal Medicine*.

### **UK Physicians Recommend 'Unpacking' CAM Modalities**

An exploratory qualitative study of physicians in the United Kingdom found that most would prefer incorporating "effective" complementary and alternative medi-

cine (CAM) therapies into their practices in the National Health Service (NHS), rather than incorporating the wholesale practice of CAM.

The study was designed to look at the views of doctors, working primarily in general practice, about CAM. The results were published on May 30 on the BMC Complementary and Alternative Medicine web site (view the full text article at: [www.biomedcentral.com/content/pdf/1472-6882-7-17.pdf](http://www.biomedcentral.com/content/pdf/1472-6882-7-17.pdf)).

Researchers interviewed nine doctors for the study. Eight were general practitioners, and one was a homeopathic doctor working in a hospital setting and receiving homeopathic referrals from primary care. The data revealed three groups of doctors regarding their attitudes towards CAM: the enthusiasts, the skeptics, and the undecided. Five key themes identified within the data were: the role of doctors' personal experiences of conventional medicine and CAM in shaping their views of CAM; doctor-patient communication about CAM and patient disclosure; doctors' information and training needs regarding CAM; perceptions of the evidence base for CAM; and the role of CAM within the NHS.

The doctors identified the value of "unpacking" the term complementary and alternative medicine to distinguish those modalities that may be effective from others that are not, or those that may be acceptable to doctors (or patients) from those that are not. They viewed wholesale incorporation of CAM within the NHS as unlikely and maybe undesirable. Yet, the researchers say, there may be elements of some CAM approaches that could be applied more widely within mainstream NHS practice, to enhance patients' overall quality of care and even increase doctors' fulfillment in their practice. ❖

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