

# **COMPLEMENTARY THERAPY ASSESSMENT ACUPUNCTURE FOR AGE-RELATED MACULAR DEGENERATION**

March, 2007

## **SUMMARY**

### **INTRODUCTION TO THE TOPIC**

Acupuncture refers broadly to a group of procedures that stimulate the skin. The most common technique uses thin, solid metallic needles, which are manipulated either manually or by electrical stimulation.

### **CONCLUSIONS**

Based on available evidence in the peer-reviewed scientific literature, the Academy believes that there is insufficient scientific evidence to demonstrate the safety or effectiveness of acupuncture for treatment of age-related macular degeneration (AMD).

### **EVIDENCE**

No reports of acupuncture treatment for age-related macular degeneration were identified in an English language search of the MEDLINE database. An Internet search identified reports published in a journal that is not indexed in MEDLINE. These reports were of two small case series, one including 10 patients seen at a single practice,<sup>1</sup> and one with 108 patients seen at a single practice.<sup>2</sup> There have been no randomized controlled double-masked study that have examined the use of acupuncture for AMD in the English language peer-reviewed scientific literature. Other available treatments for AMD (thermal laser photocoagulation, photodynamic therapy and anti-vascular endothelial growth factor (VEGF) agents) have all been validated through randomized controlled clinical trials (level I evidence).<sup>3</sup> Longer-term studies with larger samples of patients and adequate sham control groups to compare with needle acupuncture are needed to validate the results of these two small, uncontrolled studies.

### **RISKS**

Overall, the rate of general adverse effects from acupuncture has been reported to be low. Adverse effects may result from improper needling, organ puncture injuries, and the risk of infection related to use of unsterilized needles. The technique described in the two case series reviewed for this assessment was placing a needle as an electrode directly below the globe of the eye. A case report noted that acupuncture may cause an exacerbation of hemorrhage, and thus should not be used in a patient with retinal or subretinal hemorrhage.<sup>4</sup> A case series also noted that periorbital cellulitis was a concern.<sup>2</sup>

## **REPORT**

### **DESCRIPTION OF THE TECHNOLOGY**

Acupuncture has been a part of the health care system in China for several thousand years. It refers broadly to a group of procedures that stimulate the skin using a variety of techniques, and they are usually performed in an office setting. The most common technique involves inserting thin, solid metallic needles no more than three inches into the surface of the skin to the deep tissue. They are manipulated either manually or by electrical stimulation. This assessment focuses on the application of acupuncture for age-related macular degeneration.

### **MECHANISM OF ACTION**

The rationale behind acupuncture is that there is an energy flow (Qi) along specific channels throughout the body. According to this theory, disease occurs when there is too little or too much Qi or when the flow is blocked or interrupted. Stimulation of acupuncture points corrects the imbalance of energy flow. Studies in animals and humans have demonstrated that biological responses occur as a result of acupuncture.<sup>5,6</sup> These responses include the release of opioid peptides, which can account for the analgesic effects of acupuncture. There are also studies that have shown that acupuncture can alter immune functions, the secretion of neurotransmitters and neurohormones, and the regulation of blood flow. However, there is much that remains unknown about the anatomy and physiology of acupuncture points and the scientific basis for the theory of circulating energy flow.

### **DEFINITION OF THE PROBLEM**

#### **Age-Related Macular Degeneration**

Age-related macular degeneration is a leading cause of severe, irreversible vision impairment in developed countries. Approximately 1.75 million people in the United States have advanced AMD while 7 million may have intermediate AMD. Although an estimated 80% of AMD patients have the non-neovascular form, the neovascular form may be responsible for almost 90% of the severe visual loss (visual acuity 20/200 or worse) due to AMD. The prevalence, incidence, and progression of AMD and most associated features (e.g., large drusen) increase with age.

The cause of AMD remains unknown. The main risk factor for the development of advanced AMD is increasing age, as described in the previous section. Although a number of risk factors have been investigated, cigarette smoking is the only risk factor other than age and ethnicity that has been consistently identified in numerous studies.

The results of the Age-related Eye Disease Study (AREDS) support the use of antioxidant vitamins and minerals to reduce the rate of progression to advanced AMD in patients with intermediate AMD—those patients with extensive medium-sized drusen or one or more large drusen ( $\geq 125$  microns in diameter)—in one or

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both eyes, or advanced AMD in the fellow eye.<sup>6</sup> Prospective, randomized controlled clinical trials support the use of laser photocoagulation surgery,<sup>8,9</sup> photodynamic therapy,<sup>10,11</sup> and intravitreal injection of anti-VEGF agents<sup>12-14</sup> to treat choroidal neovascularization associated with advanced AMD.

### **FDA STATUS**

In 1996, the US Food and Drug Administration removed acupuncture needles from the category of Class 3 “experimental medical devices” and now regulates them as Class 2 devices, subjecting them to good manufacturing practices and single-use standards of sterility.

### **SUMMARY OF EVIDENCE**

#### **Statistical Issues and Study Design**

There are inherent difficulties and complexities in designing studies of acupuncture, mainly in using appropriate controls, such as placebos and sham acupuncture groups. This is complicated by the fact that many of the published studies involve issues of methodology, including insufficient sample size, questions about the effectiveness of randomization, lack of use of standardized outcome measures, short follow-up intervals, and inadequate placebo treatments for control groups.<sup>15</sup> The NIH Consensus Development Panel on Acupuncture concluded that “according to contemporary research standards, there is a paucity of high-quality research assessing efficacy of acupuncture compared with placebo or sham acupuncture. The vast majority of studies on acupuncture in the biomedical literature consist of case reports, case series, or intervention studies with designs inadequate to assess efficacy.”<sup>15</sup>

#### **Search Methods and Study Selection**

On March 22, 2007, the American Academy of Ophthalmology searched through MEDLINE in the English language for articles from January 1970 to March 2007 using the terms acupuncture; macular degeneration; and medicine, Chinese. A total of five articles were identified, but were found to be not relevant. An Internet search located two relevant articles published in a journal that is not indexed in MEDLINE; these articles were reviewed for study design and implementation.

#### **BENEFITS**

Of the two articles reviewed, neither were randomized controlled, double-masked studies. The articles were reports of case series at the same private practice. The first article summarized the experience with 10 persons with self-reported visual loss from macular degeneration.<sup>1</sup> The technique included treating electrically active ear points using A NET 2000 device (Auri-Stim Medical, Denver, CO) and directly stimulating the optic nerve by placing a needle as an electrode directly below the globe of the eye, inserting between 30 and 60 mm in depth either at the infraorbital notch directly caudal to the midline pupil or 1 cm laterally at another infraorbital notch. Electrical stimulation of 2 Hz was applied

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using the Pantheon Electric Stimulators (Pantheon Research, Venice, CA) for 25-35 minutes a session. Patients were treated until they dropped out or did not show additional gains in visual acuity. The outcome measure was visual acuity as measured on MNRead Eye Charts or Optec Vision Screen Machine, with a 6 month follow-up. An initial refraction for these patients was not reported. Eight out of the ten patients had improvement of 1 line (5 eyes) to 7 lines (1 eye). It is not stated if this is best-corrected visual acuity. Reported complications included an occasional ecchymosis.

The second article summarized the case series of 108 patients, who were treated in a technique similar to that described above, but with the addition of 3 needles placed in the other 3 quadrants of the orbital rim at notches medially and laterally on the superior orbital rim and on the inferior lateral rim.<sup>2</sup> The outcome measure was visual acuity as measured by Early Detection and Treatment of Diabetic Retinopathy Studies (ETDRS) visual acuity charts, without a standardized refraction protocol. The reported results of the study were an overall gain per treatment of 0.72 letters in distant vision and 0.70 letters in near vision (207 eyes). The study period was 21 months and 1264 total treatments were administered. The number of letters gained in total was 909 letters for distant vision and 889 letters for near vision. This study did not report standardized, validated outcome measurements such as best-corrected visual acuity using a refraction protocol.

Longer-term studies with larger samples of patients and adequate sham control groups compared with needle acupuncture are needed to expand upon the reported findings of these small uncontrolled studies.

### **RISKS**

The overall rate of general adverse effects from acupuncture has been reported to be low.<sup>16</sup> There have been rare events of potentially life-threatening events such as pneumothorax caused by improper needling or other organ puncture injuries. Fainting, local infection, and increased pain are more common adverse effects. It has been reported that 126 cases of hepatitis B have been linked to practitioners using unsterilized needles. Technical problems that can occur include bent or broken needles. One case report, titled "Macular Degenerative Disease and Acupuncture Safety Precautions", noted that acupuncture may cause an exacerbation of hemorrhage and could be implicated as a contributing factor in a medical legal issue.<sup>3</sup> The authors' opinion was that any ocular hemorrhage in a patient with macular degeneration is a contraindication to performing acupuncture. Also, an article raised the concern about the possibility of periorbital cellulitis as a complication of this treatment.<sup>2</sup> There may also be substantial financial costs to the patient for the series of treatment.

### **QUESTIONS FOR SCIENTIFIC INQUIRY**

If further scientific investigation is desired, the following questions are posed:

### **Ocular Conditions**

- What is the biological basis for acupuncture for treating AMD?
- Is acupuncture effective treatment for AMD using randomized controlled clinical trials in larger, well-designed studies with adequate statistical analyses?
- How effective is acupuncture compared to standard therapies for AMD, which have been validated through large, well-designed studies with adequate statistical analyses?

### **INFORMATION FOR PATIENTS**

Physicians can advise their patients who are contemplating acupuncture treatment to ask the following questions:

- Does the provider have state licensure and credentialing? (A majority of states provide licensure or registration.)
- What other treatment options for AMD are available, including use of anti-VEGF agents, PDT and thermal laser surgery?
- What are the expected prognosis and risks associated with the use of acupuncture?
- What safety protocols are in place to minimize the risks of acupuncture?
- Does the provider follow FDA regulations for acupuncture needles, including using sterile, single-use needles?

### **SUMMARY AND CONCLUSIONS**

Based on available evidence in the peer-reviewed scientific literature, the Academy believes that there is insufficient scientific evidence to demonstrate the safety or effectiveness of acupuncture to treat age-related macular degeneration.

In 2003, the Academy published a Complementary Therapy Assessment: Acupuncture for Ocular Conditions and Headaches. Based on available evidence in the peer-reviewed scientific literature, the Task Force on Complementary Therapies believes that sufficient scientific evidence has not been found to demonstrate the safety or effectiveness of acupuncture to treat various ocular conditions compared to standard therapies. These conditions included myopia, high myopia, paralytic strabismus, retinitis pigmentosa, optic atrophy, retrobulbar neuritis, maculopathy, iritis, conjunctivitis, cataracts, and dry eye.

### **DEVELOPMENT OF COMPLEMENTARY THERAPY ASSESSMENTS**

Complementary, or alternative therapies, are a growing part of health care in America. Americans spend an estimated \$14 billion a year on alternative treatments. Most U.S. medical schools offer courses in alternative therapies. The editors of the Journal of the American Medical Association announced that publishing research on alternative therapies will be one of its priorities. More

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scrutiny and scientific objectivity is being applied to determine whether evidence supporting the effectiveness of complementary and alternative therapies exists.<sup>17</sup> The National Institutes of Health National Center for Complementary and Alternative Medicine has broadly defined complementary and alternative medicine as those treatments and health care practices that are not taught widely in medical schools, not generally used in hospitals, and not usually reimbursed by medical insurance companies. The Cochrane Collaboration Complementary Medicine Field defines complementary medicine as including all such practices and ideas which are outside the domain of conventional medicine in several countries and defined by its users as preventing or treating illness, or promoting health and well being. These practices complement mainstream medicine by 1) contributing to a common whole; 2) satisfying a demand not met by conventional practices; and 3) diversifying the conceptual framework of medicine.<sup>19</sup>

In the fall of 1998, the Board of Trustees appointed a Task Force on Complementary Therapy to evaluate the peer-reviewed scientific literature on complementary therapies in eye care and develop an assessment on their safety and effectiveness in order to inform ophthalmologists and their patients. A scientifically grounded analysis of the data will help ophthalmologists and patients evaluate the research and thus make more rational decisions on appropriate treatment choices.

The Academy believes that complementary therapies should be evaluated similarly to traditional medicine: evidence of safety, efficacy, and effectiveness should be demonstrated.<sup>18</sup> Many therapies used in conventional medical practice also have not been as rigorously tested as they should be. Given the large numbers of patients affected and the health care expenditures involved, it is important that data and scientific information be used to base all treatment recommendations. In this way, we can encourage high-quality, rigorous research on complementary therapies.<sup>19</sup>

Ideally, a study of efficacy compares a treatment to a placebo or another treatment, using a double-masked controlled trial and well-defined protocol. Reports should describe enrollment procedures, eligibility criteria, clinical characteristics of the patients, methods for diagnosis, randomization method, definition of treatment, control conditions, and length of treatment. They should also use standardized outcomes and appropriate statistical analyses.

The goal of these assessments is to provide objective information about complementary therapies and to provide a scientific basis for physicians to advise their patients, when asked.

To accomplish these goals, the assessments, in general, are intended to do the following:

- Describe the scientific rationale or mechanism for action for the complementary therapy.

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- Describe the methods and basis for collecting evidence.
- Describe the relevant evidence.
- Summarize the benefits and risks of the complementary therapy.
- Pose questions for future research inquiry.
- Summarize the evidence on safety and effectiveness.

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