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Hattage*

By Peter J. Stern, MD

President Light, colleagues, and distinguished international guests:

It is a great and humbling honor to address you and to serve as President of the American Orthopaedic Association (AOA). Jim Beaty, President of The American Academy of Orthopaedic Surgeons, used an aphorism in his recent address to the membership that I would like to share with you: "If you see a turtle on a fence post, it didn't get there by itself." I stand here because of the support and encouragement of my orthopaedic colleagues, partners, and family as well as the countless medical personnel and administrative staff who help me on a daily basis.

This Association held its first meeting in 1887 in New York City with thirty-five charter members in attendance. The original constitution and bylaws, which can be found in the first volume of the *Transactions of the American Orthopedic Association,* stated: "The purpose of this Association shall be the advancement of Orthopedic science and art"; this is still a part of the Association's mission[1]. This volume, now in my library, was originally owned by Albert H. Freiberg of Cincinnati, the Association's president in 1911. His son, Joseph A., also of Cincinnati, was president in 1962, and his grandson Richard A. is a colleague of mine in Cincinnati and is chief of the Veterans Administration Hospital. Finally, his great-grandson Andrew, a recently elected member of the AOA, is an orthopaedic surgeon who practices at Massachusetts General Hospital in Boston. What a testimony to our specialty!

Hattage is a nonword. I first heard it used by my chief, Dr. Henry Mankin, when I was an orthopaedic resident. Every morning, Dr. Mankin's house officers gathered for breakfast at 6:30 AM, and a designated resident presented a case to him. One morning, I presented the case of a patient with a four-month history of radicular back pain and a positive myelogram. I recommended operative treatment. He suggested hattage. I looked at him quizzically and asked what he meant. He explained that

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hattage was performed by placing the patient supine on the examining table and waving a hat over the patient in a back and forth fashion. I have not forgotten hattage or its meaning and figuratively use this treatment on a near daily basis.

Hattage, from my perspective, is placebo treatment. A PubMed search for *placebo* revealed over 116,000 citations, and Google, more than twenty-nine million.

Placebo is difficult to define. *The American Heritage Dictionary of the English Language* defines it as "a substance containing no medication and prescribed or given to reinforce a patient's expectation to get well."[2] If you think about it, the history of medicine is a history of the placebo response. Until recent times, there were no scientifically proven treatments for most illnesses. Healers maintained a supply of inert pills to be used when an authentic cure was unavailable or unnecessary. Today, in stark contrast, knowingly prescribing placebo medication is deceptive, a violation of the trust that our patients place in us.

Symptomatic improvement when a placebo is taken is known as the *placebo effect*. On the other hand, if the patient experiences a worsening of symptoms, this is termed the *nocebo effect*. Such individuals tend to be pessimistic, and their expectations are realized in terms of worsening of symptoms or an illness.

For example, in the Framingham Heart Study, women who believed they were prone to heart disease were more likely to die compared with women with similar risk factors who did not hold such fatalistic views. This so-called cardiac neurosis had nothing to do with known risk factors, such as elevated cholesterol levels, hypertension, smoking, and obesity; rather, it correlated with the self-fulfilling prophesy that if you think you are sick you will be sick[3]. While the placebo effect refers to health benefits produced by a treatment that should have no effect, patients experiencing the nocebo effect experience the opposite. They presume the worst in regard to health, and that is just what they get.

Placebos work in several ways:

1. If a placebo is given for a self-limited disorder that waxes and wanes, such as the common cold, there will be resolution with or without treatment.

2. Some diseases, such as inflammatory arthropathies, are cyclical. A remission during treatment may be a coincidence, but it can also be attributed to the effect of medication.

3. When taking a placebo, patients often have altered perception of their symptoms. They psychologically expect a beneficial effect from a remedy with no scientific basis. For example, as a jogger, I have taken glucosamine for knee pain and seem to run faster and with less pain despite strong level-I evidence to the contrary[4].

4. Placebos reduce anxiety. We all see patients with an absence of objective findings who benefit from reassurance[5].

5. Finally, the caregiver can figuratively be a therapeutic agent. A physician's attitude toward an illness or disease plays an important role in a patient's recovery. Norman Cousins, a political journalist and a professor of medical humanities, strongly advocated for the power of positive thinking. He said: "Patients want to be looked after, not just looked over."[6]

Along similar lines, two decades ago, a fascinating study was published in the *British Medical Journal*[7]. Two hundred patients presented to a general practice with symptoms but no abnormal physical signs. They were randomly assigned to one of four groups. Groups 1 and 2 received a consultation conducted in a positive fashion, with or without treatment, and groups 3 and 4 received a consultation conducted in a negative fashion, with or without treatment.

Two weeks later, there was a significant difference in patient satisfaction between the positive and negative groups ($p = 0.001$) but not between the treated and untreated groups. More importantly, 64% of those receiving a positive consultation got better compared with recovery in only 39% of those receiving a negative consultation. Finally, 53% of those treated had improvement, and 50% of those untreated had improvement. Today, to knowingly deceive a patient is paternalistic and unethical. On the other hand, an alternative treatment such as a copper bracelet for arthritis is permissible because both the healer and the patient are aware that such treatment has no scientific basis.

Randomized, double-blinded, placebo-controlled trials are considered the so-called gold standard when evaluating medical treatment alternatives because they offer the most effective way to control for the placebo effect. A correctly performed trial allows the investigator to establish a scientific basis for treatment: the basis for so-called evidence-based medicine. There are three basic elements of a randomized clinical trial[8]:

1. All entered subjects must have a similar illness and are equally likely to fall into either the control (placebo group) or the treatment group.

2. The end point to success or failure is decided on in advance.

3. Both the subjects and the investigators are blinded as to which treatment is being received, to eliminate bias.

Figure 1 depicts a theoretical randomized clinical trial comparing an analgesic with a placebo for the treatment of chronic pain. Both a placebo and an analgesic were administered over a twelve-week period and were then discontinued. Note that patients who received the placebo experienced 35% to 40% relief of pain (the placebo effect); however, the patients receiving the analgesic medication did 10% to 15% better. The difference between the two lines is termed the therapeutic effect, and in this trial the therapeutic effect was substantial. At twelve weeks, both the placebo and the medication were discontinued such that, by sixteen weeks, pain relief in both groups decreased, but not to zero. The black circle (at sixteen weeks) represents the loss of both therapeutic and placebo effects,

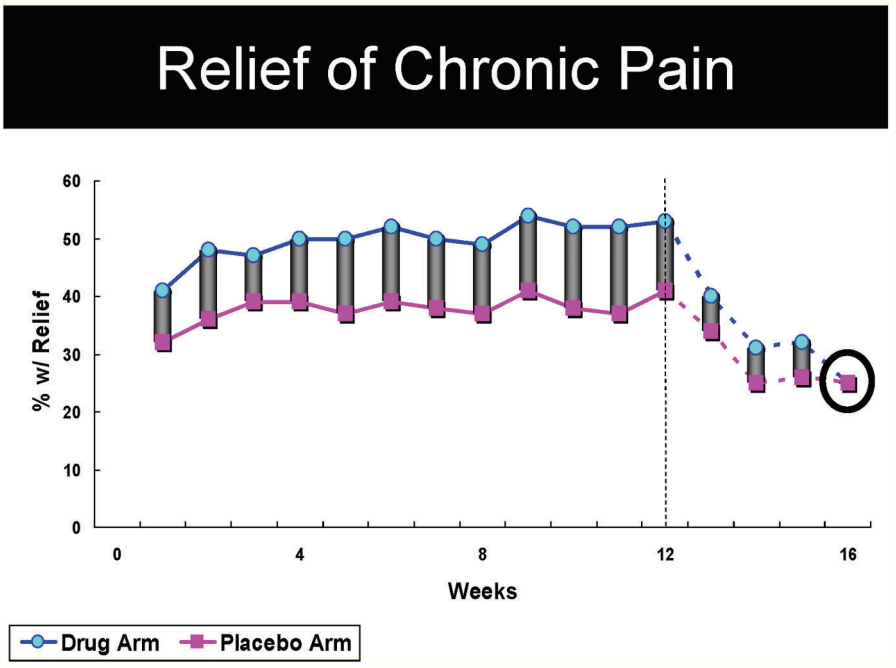

Fig. 1

A hypothetical randomized, placebo-controlled trial comparing pain relief from an analgesic medication (the therapeutic arm, indicated by circles) with placebo medication (the placebo arm, indicated by squares). Both medications were discontinued at twelve weeks. The difference between the arms is the therapeutic effect. After twelve weeks, pain relief in both groups decreases considerably but not to zero. At sixteen weeks, the two lines converge, and this suggests that the natural history of any painful condition tends to be cyclical. (Modified, with permission of the author and publisher, from: Thompson WG. The placebo effect and health: combining science and compassionate care. Amherst, NY: Prometheus Books; 2005. p 24.)

but, more importantly, it represents the natural history of painful conditions, which by their very nature are cyclical. In any therapeutic intervention, three factors must be considered: natural history, placebo effect, and therapeutic effect.

Sham surgery in randomized clinical trials, especially in orthopaedic surgery, is a rare event[9]. On the other hand, controlled, randomized medical trials are commonplace. In medical studies (such as an evaluation of the efficacy of a drug), the treatment group is exposed to the risks of a new therapy, but participants may potentially reap the benefits of the drug being tested. The placebo group does not benefit from the new treatment but generally does not incur risk.

The requirements for placebo surgical trials include the following[10]: (1) There must be potential value enhancements for health or knowledge. (2) The scientific methodology must be valid and rigorous. (3) Subject selection must be fair and nonbiased. (4) There must be a favorable risk-benefit ratio. That is, risks must be minimized, and the potential benefits to individuals and the knowledge gained for society must outweigh the risks. (5) An independent review to approve, amend, or terminate the research must be performed by individuals who have no conflict of interest. (6) Participants must provide voluntary informed consent. (7) Subjects should have their privacy protected, they should have the opportunity to withdraw, and their well-being should be monitored.

The seminal article on placebo surgery was written by Henry K. Beecher more than five decades ago[11]. In a review of fifteen studies involving >1000 patients, he found that placebo therapy produced satisfactory pain relief in approximately 35% of the patients. Subsequent reports in the literature have noted relief among 30% to 40% of the patients who had been managed with a placebo for a variety of conditions ranging from myocardial infarction to asthma.

Five years later, Beecher published an article in *The Journal of the American Medical Association* that produced a paradigm shift in the management of coronary artery disease[12]. It was a commentary on ligation of the internal mammary arteries for the relief of intractable angina pectoris. The procedure was first described in Italy, and at least two American studies had subsequently endorsed it[13,14]. In the 1950s, this procedure was popular and >90% of patients reported that it helped.

Beecher's article cited two studies that clearly refuted the efficacy of the procedure[15,16]. One was conducted by a young Seattle cardiologist named Leonard Cobb[15] and, although probably of insufficient power, it was particularly well designed. Seventeen patients volunteered. They were not informed of the double-blind nature of the study but were merely told that they were participating in a study to evaluate internal mammary artery ligation. The patients were blindly randomized to one of two groups. Both procedures were done with the patient under local anesthesia: one operation involved a skin incision only and the other, ligation of the internal mammary arteries. It was evident that both procedures provided symptomatic benefit; however, more importantly, the ligation procedure produced no greater benefit than the sham procedure. Beecher noted the powerful action of the placebo in surgery and stated: "It is, therefore, essential for the surgeon to be on his guard, lest he deceive himself, and others, in perpetrating costly, dangerous, even fatal operations whose effectiveness is only that of a placebo."[12]

Following the publication of Beecher's study, internal mammary artery ligation was abandoned. Over the ensuing decades, however, the whole idea of placebo surgical trials fell out of favor. Vocal medical ethicists and patient advocates stated that if placebo surgery did not violate the Hippocratic Oath "First, do no harm," what did?

I now "fast forward" some forty-five years and discuss osteoarthritis of the knee. The prevalence of symptomatic knee osteoarthritis in the United States in individuals older than sixty years has been estimated to be 12%[17]. Arthroscopic lavage and débridement has been commonly used to relieve pain and mechanical symptoms, improve function, and delay the need for total knee arthroplasty. Generally, studies that support this treatment have been retrospective, small in size, and have not used validated outcome measures. In preparing this manuscript, I found several randomized studies that shed doubt on the efficacy of arthroscopic lavage and/or débridement of the knee[18-20]. The study that was most frequently quoted was by Moseley et al. and was published in the *New England Journal of Medicine* in 2002[21]. It made a compelling argument for changing the indications for arthroscopic treatment of osteoarthritis of the knee. Although many of you are far more familiar than I am with this study and its repercussions, I would like to briefly review the design, findings, and conclusions. One hundred and eighty patients with osteoarthritis of the knee were enrolled and were randomly assigned to one of three groups. The surgery was performed by a single, well-qualified surgeon, and both the patients and the subsequent evaluators were blinded as to treatment group.

The three groups included (1) treatment with a placebo, which consisted of a surgical incision and simulated débridement without insertion of an arthroscope; (2) arthroscopic lavage in which the joint was irrigated with at least 10 L of irrigation fluid; and (3) arthroscopic débridement, which consisted of lavage and débridement.

The patients were followed serially over twenty-four months, and outcomes were assessed with use of five self-reported scales (three for pain and two for function). Less than 10% of the patients were lost to follow-up. The authors found that at no point over the two years did either of the intervention groups report less pain or better function than the placebo group.

Moseley et al. concluded: "If the efficacy of arthroscopic lavage or débridement in patients with osteoarthritis of the knee is no greater than that of placebo surgery, the billions of dollars spent on such procedures annually might be put to better use."[21]

In June 2004, the Centers for Medicare and Medicaid Services issued a National Coverage Determination, which essentially stated that arthroscopic lavage or débridement for osteoarthritis of the knee would not be compensated through Medicare[22].

Many bioethicists argue that placebo surgery falls short and is patently unethical. A patient undergoing sham surgery has no chance of benefit, may not have received adequate informed consent, and is exposed to the very real risks of a surgical procedure. On the other hand, by definition, randomized, controlled studies are the best research tool to determine proper therapeutic decisions, and they form the basis of evidence-based medicine. A moral dilemma, however, arises: how can clinical investigators use the best possible research methodology and simultaneously maintain the highest level of ethics? Macklin, who is staunchly opposed to sham surgery, put it this way: "The placebo-controlled trial may well be the gold standard of research design, but unlike pure gold, it can be tarnished by unethical applications."[23] She believes that physicians have a moral obligation to advocate categorically for the primacy of the patient, thereby following the Hippocratic principle of exclusive commitment to patient welfare.

Perhaps, in the pursuit of improving patient care through scientifically sound placebo-controlled surgical trials, there is a middle ground. Miller, from the National Institutes of Health, made three suggestions in favor of placebo-controlled surgical trials[24], reasoning that such trials could pass the ethical smell test.

First, make every effort to minimize risk. This is well exemplified in the study by Moseley et al., in which the placebo group received sedation and an opioid rather than a formal general anesthetic when the small skin incisions were made. The ethical question, of course, is how much risk should the placebo group be subjected to? This is unclear and must be sorted out collaboratively by bioethicists and surgeons.

Next, ensure that the study participants understand that they may be randomly assigned to the sham group. Again, the knee study by Moseley et al. is exemplary. Patients not only signed an informed consent statement but they wrote in their chart, "On entering this study, I realize that I may receive only placebo surgery. I further realize that this means that I will not have surgery

on my knee joint. This placebo surgery will not benefit my knee arthritis."[21] Interestingly, 44% of the 324 patients who were asked to participate declined.

Finally, consider the consequences of not performing sham-controlled surgical studies. Again, with use of the data in the study by Moseley et al., it is clear that knee arthroscopy with lavage and/or débridement for degenerative arthritis is no better than sham surgery. Consider the future cost savings and benefits to future patients who are potentially exposed to non-beneficial surgery.

At the risk of stirring the pot, I would like to make some observations and comments related to arthroscopy. In 2006, William Garrett and the Directors of the American Board of Orthopaedic Surgery had an article published in *The Journal of Bone and Joint Surgery* regarding the case mix of candidates taking Part II, or the oral certification examination[25]. Each candidate is required to submit a six-month operative case list, which served as the basis for their article.

They found that four of the top ten procedures were arthroscopic codes. Furthermore, shoulder arthroscopy and/or subacromial decompression moved up seven places in performance frequency in the five years from 1999 to 2003. In 2003, it was the second most common procedure an orthopaedic surgeon two years into practice was performing. I wonder why there has been an incremental increase in shoulder arthroscopy; are we doing too much shoulder arthroscopy? Would it be worthwhile to design randomized, controlled placebo trials to define more accurately the placebo and therapeutic effects of shoulder arthroscopy? I believe this would be a worthwhile endeavor.

Most of the procedures that we as orthopaedic surgeons perform are remarkably beneficial. Outcomes can be measured objectively. Hip and knee arthroplasty, fracture fixation, and even drainage of an abscess rapidly restore function and relieve pain. On the other hand, when surgery is done primarily for pain relief, the placebo effect is very real. Surgical garb, cap and mask, loupes, bright operating-room lights, monitors, and beeping sounds create a surrealistic atmosphere. This environment, coupled with a surgeon's optimistic attitude, cannot help but predispose patients to the placebo effect. I believe that we could better serve our patients if we designed more level-I studies evaluating procedures with subjective outcomes.

Another aspect of placebo therapy is complementary and alternative medicine. When patients have ailments that cannot be effectively treated by their physician, they often turn to complementary and alternative medicine. In contradistinction to evidence-based medicine, complementary and alternative medicine is defined as a group of diverse medical and health-care systems, practices, and products that are not presently considered to be part of conventional medicine[26].

In recent years, the use of complementary and alternative medicine has grown considerably. Probable explanations include market forces, availability of information on the Internet, and the desire of patients to be actively involved with medical decision making; they want to be empowered to find cures. Astin reported that the majority of alternative medicine users were not so much dissatisfied with conventional medicine, but rather they see conventional medicine as being unable to adequately treat many chronic conditions such as debilitating pain[27]. Today's physicians are intently focused on disease and technology; most of us steer clear of poorly understood complex medical conditions such as fibromyalgia and musculoskeletal pain syndromes. Almost by default, this opens the door for complementary and alternative medicine.

Although there are potential dangers to the use of complementary and alternative medicine, it has definite merits. It is more hands on, and usually more time is devoted to the patient. The approach is personalized, and patients are evaluated as a whole rather than as a focused problem. Emphasis is placed on healing rather than curing and on wellness rather than illness. Most important, the patient shares in decision making with an empathetic health-care provider.

Barnes et al. reported data from the National Center for Health Statistics regarding complementary and alternative practices in the United States for the year 2002[28]. Sixty-two percent of all adults, or more than seventy million people, had used some form of complementary and alternative medicine within the previous twelve months. When prayer therapy specifically for health reasons was excluded, 36% of adults had used some form of complementary and alternative medicine therapy during the past twelve months. In a lifetime, this number was estimated to increase to 50%. When all forms of prayer therapy were eliminated, natural products, including herbal medicine, functional foods (garlic), and animal-based (glucosamine) supplements were used by 19% of adults. Nearly one-third of all conditions for which complementary and alternative medicine was used involved disorders of the musculoskeletal system or chronic pain.

Public expenditure on complementary and alternative medicine is staggering. In the United States, it is estimated that $47 billion is spent annually[29]. A decade ago, Eisenberg et al. reported that, for 1997, the total out-of-pocket expenditures relating to alternative therapies were conservatively estimated at $27 billion, which was comparable with the projected out-of-pocket expenditures in 1997 for all physician services in the United States[30].

In 1991, the United States Congress passed legislation that provided $2 million to establish the Office of Alternative Medicine within the National Institutes of Health. The purpose was to investigate and evaluate promising unconventional medical practices. In 1998, the name was changed to The National Center for Complementary and Alternative Medicine. Today, it is one of twenty-seven centers that make up the National Institutes of Health and, in fiscal year 2007, it had a $121

million budget. It states that its mission is to "explore complementary and alternative healing practices in the context of rigorous science, train complementary and alternative medicine researchers, [and] disseminate authoritative information to the public and professionals."[26]

There are several advantages to complementary and alternative medicine. First, it empowers patients to consult alternative providers. When patients become disenchanted with conventional therapies and medication, they often seek a change in direction. I believe the majority of our patients trust us and see physicians as the first line of defense. However, when answers are lacking, when patients perceive they are not being taken seriously, or when their condition does not improve, they go elsewhere. Freedom of choice empowers patients to make such a move.

Next, in Western countries, as medicine has become more scientific, the cost of medical care has skyrocketed. When patients with diagnoses such as nonspecific low-back pain or tendinitis can find successful treatment with complementary and alternative medicine, the strain on the health-care budget potentially can be diminished. In truth, many conditions that orthopaedic surgeons treat are self-limited. If, with complementary and alternative medicine therapies, patients are reassured and hopeful, costs potentially can go down. On the flip side, we have all seen serious medical conditions in which such therapies have produced disastrous outcomes.

Finally, alternative medicine in some circumstances may be substituted for conventional medical treatment. Today, more physicians find it acceptable to suggest alternative treatments when conventional medical treatment has failed. In a sense, these caregivers view themselves as a healer first and a physician second.

One of the primary objections to alternative medicine is that it lacks scientific validity. Critics contend that observational bias and poor design invalidate most studies. Proponents, on the other hand, reject such criticism as being founded in prejudice, financial self-interest, and ignorance. Phil Fontanarosa, Executive Deputy Editor of *The Journal of the American Medical Association,* and George Lundberg, former editor of that journal, declared: "There is no alternative medicine. There is only scientifically proven, evidence-based medicine supported by solid data."[31]

There are many objections to complementary and alternative medicine. First, it is the antithesis of evidence-based medicine. The cornerstone to its success is patient testimonials[32]. Just turn on your television early on a Saturday morning and listen to the testimonials. You will learn how to lose twenty pounds in six weeks, money back guaranteed. Next, alternative medicine may have serious or even lethal side effects. The National Center for Complementary and Alternative Medicine points out that just because an herbal supplement is labeled "natural" does not mean it is safe or without any harmful effects. Finally, the use of alternative therapies can delay conventional treatment. I recently was referred a sixty-year-old man with a diagnosis of refractory tennis elbow. He had been treated with chiropractic adjustments but was experiencing increasing pain, especially at night. Radiographs showed a lucency in the neck of the radius and subsequent biopsy demonstrated lymphoma of bone.

Unfortunately, much of alternative medicine is quackery, which exploits patient fears and gullibility. The laetrile story is emblematic[33]. Laetrile, or vitamin B17, has been used to treat cancer since the 1950s. It contains amygdalin, found in the pits of many fruits, nuts, and plants. The active anticancer ingredient is believed to be cyanide. Despite legal and political controversy, it was widely used for more than three decades.

In 1980, the movie star and one of my early heroes, Steve McQueen, attracted considerable attention when he went to Mexico to receive laetrile for the treatment of a mesothelioma. The medication was administered by a dentist who had lost his license in Texas. I can still remember hearing McQueen's upbeat reports of this treatment. Sadly, he died shortly thereafter.

In 1982, a National Cancer Institute-sponsored study at the Mayo Clinic evaluated 178 patients with advanced cancer who were treated with laetrile[34]. Prior to treatment, the patients were in good general condition; however, there were no other treatments available. The study findings were clear: "No substantive benefit was observed in terms of cure, improvement or stabilization of cancer, improvement of symptoms related to cancer, or extension of life span." Several patients had symptoms of cyanide toxicity or blood levels approaching the lethal range. Arnold Relman, then editor of *The New England Journal of Medicine*, in an accompanying editorial concluded: "Laetrile has had its day in court. The evidence, beyond reasonable doubt, is that it doesn't benefit patients with advanced cancer . . . The time has come to close the books."[35]

Despite several studies showing no anticancer effects, a potential for cyanide poisoning, lack of Food and Drug Administration approval, and a United States Supreme Court decision against laetrile, it is still marketed on the Internet today. Miracle cures do not come along very often. The combination of a life-threatening illness and no answers from mainstream medicine leads to desperation. In such a situation, we are all vulnerable.

In closing, hattage has many meanings. Dr. Mankin saw it as hands-off treatment, particularly in vague clinical situations. I see it as the placebo effect, which from ancient times has played an important role in medical care. Placebo trials are the basis for evidence-based medicine. In your next patient encounter, consider the placebo effect. Listen carefully to the history and carry out a thorough physical examination. Consider a nonsurgical option, particularly when dealing with a condition in which there is a large component of unexplained pain.

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