

The Placebo Effect in Alternative Medicine: Can the Performance of a Healing Ritual Have Clinical Significance?

Ted J. Kaptchuk, OMD

In alternative medicine, the main question regarding placebo has been whether a given therapy has more than a placebo effect. Just as mainstream medicine ignores the clinical significance of its own placebo effect, the placebo effect of unconventional medicine is disregarded except for polemics. This essay looks at the placebo effect of alternative medicine as a distinct entity. This is done by reviewing current knowledge about the placebo effect and how it may pertain to alternative medicine. The term *placebo effect* is taken to mean not only the narrow effect of a dummy intervention but also the broad array of nonspecific effects in the patient–physician relationship, including attention; compassionate care; and the modulation of expectations, anxiety, and self-awareness. Five components of the placebo effect—patient, practitioner, patient–practitioner interaction, nature of the illness, and treatment and setting—are examined.

Therapeutic patterns that heighten placebo effects are especially prominent in unconventional healing, and it seems possible that the unique drama of this realm may have “enhanced” placebo effects in particular conditions. Ultimately, only prospective trials directly comparing the placebo effects of unconventional and mainstream medicine can provide reliable evidence to support such claims. Nonetheless, the possibility of enhanced placebo effects raises complex conundrums. Can an alternative ritual with only nonspecific psychosocial effects have more positive health outcomes than a proven, specific conventional treatment? What makes therapy legitimate, positive clinical outcomes or culturally acceptable methods of attainment? Who decides?

Ann Intern Med. 2002;136:817–825.

www.annals.org

For the author affiliation and current address, see end of text.

Efficacious therapy, in one biomedical definition, is therapy that has positive effects greater than those of an indistinguishable dummy treatment in a randomized, controlled trial (RCT) (1–3). Such specific efficacy is actually a comparative measure: intervention contrasted with placebo. This relative effectiveness, which is estimated by statistical testing, is taken to indicate “authenticity.” The clinical significance, that is, the outcome measured by using the patient’s original condition as a baseline, is usually a secondary consideration for determining “legitimate” medical interventions. Any clinical impact due to the placebo, which is deemed to lack “truthfulness,” is even less notable and is valued only as a comparison baseline for “genuine” effects (3). Specific effects are by definition superior to nonspecific effects. The clinical repercussions of the placebo are tolerated as necessary nuisance noise but are otherwise considered inconsequential or treated with contempt (4).

Given the privileged status of specific effects, it is not surprising that the clinical impact of alternative medicine’s placebo effects are routinely ignored (5). The only serious question has been whether alternative medicine has more than a placebo effect. Discarding all placebo effects in a single trash basket of “untruthfulness,” however, diminishes our knowledge of important dimensions of health care. This essay examines the neglected clinical significance of the placebo effect in alter-

native medicine and raises the possibility that some types of unconventional medicine may produce placebo outcomes that are dramatic and, from the patient’s perspective, especially compelling. The term *placebo effect* is taken to mean not only the narrow effect of an imitation intervention but also the broad amalgam of nonspecific effects present in any patient–practitioner relationship, including attention; communication of concern; intense monitoring; diagnostic procedures; labeling of complaint; and alterations produced in a patient’s expectancy, anxiety, and relationship to the illness. This essay asks whether alternative medicine can have an “enhanced” placebo effect. In some conditions, can any of alternative medicine’s particular rituals have a greater impact than the rituals of conventional medicine or than a proven physiologically active treatment? After all, as many of the examples in this essay will demonstrate, “two interventions may have different effects on patient outcome even though both [are] equivalent to placebo in clinical trials” (6). Dismissing a treatment as “just a placebo” may not be enough.

Alternative medicine may be an especially successful placebo-generating health care system. Rather than specific biological consequences, which epidemiologists designate as “fastidious efficacy” (7), alternative medicine may administer an especially large dose of what anthropologists call “performative efficacy” (8). Performative

efficacy relies on the power of belief, imagination, symbols, meaning, expectation, persuasion, and self-relationship. This essay takes five components of the placebo drama—patient, practitioner, patient–practitioner interaction, nature of the illness, and treatment and setting—and examines their “placebogenic” potentials in unconventional healing practices. Much of the evidence is derived from conventional research and is speculatively applied to alternative medicine. Also, it should be noted that most of the placebo research discussed in this essay does not represent an “artificial” placebo effect explainable by natural history or regression to the mean. Rather, it usually involves comparative experiments with two different types of placebo or the same placebo delivered under different cognitive or emotional circumstances where two distinct placebo outcomes would not support the idea of placebo effect as only natural history. Finally, this essay argues mostly in generalities. Obviously, the placebo effect is likely to be at least as heterogeneous in alternative medicine as in conventional medicine, but it is hoped that raising these questions will encourage further discussion and research.

PATIENT CHARACTERISTICS

Although the patient is the protagonist in the placebo drama, research has failed to find consistent placebo responders or to identify personality traits or other qualities of persons who frequently react to placebo (9–11). However, evidence shows that patient expectations influence outcomes of both placebo and active treatment. Asthmatic patients who believe that an inert substance is a bronchodilator or a bronchoconstrictor respond accordingly (12–14). In a small but classic crossover experiment, healthy volunteers received a placebo pill in which a magnet was embedded. In random order, at different times, they were told that they were receiving a relaxant, a stimulant, or a placebo. Subsequent gastric motility was significantly consistent with patients’ expectations (15). Patient expectancies also significantly change or even reverse the actions of many potent pharmaceutical agents (16–19).

Adherence to placebo may also be a surrogate marker for a patient’s own contribution to the activation of the placebo response (20, 21). In RCTs, such “placebo adherence effects”—the post hoc differences observed in the placebo arm between those who comply

with taking placebo and those who do not—are associated not only with symptom relief but also with concrete end points, including survival (22–24). Indeed, differences in adherence are associated with differences in outcomes that exceed the effects of many pharmaceutical agents (25). Patient preferences for one type of intervention, especially in participative interventions (for example, exercise or diet programs), may contribute significantly to outcomes, including increased placebo responses (26–28).

In contrast to conventional medicine, with its measured objectivity, alternative medicine offers a charged constellation of expectations. Alternative medicine’s romantic vision is inhabited by benevolent and intentional forces (for example, the innate intelligence of chiropractic or the *qi* of acupuncture) that are unrestrained by the laws of normative physics (29). An exaggerated notion of the possible readily elicits patients’ magical anticipation. These unconventional concepts do not require absolute belief “in the sense that their truth value is certified by logic or argument” but rather requires moderate openness “in the sense that they are taken into the imagination and lived with, if only for a time” (30).

Alternative medicine emphasizes personal responsibility, which can facilitate adherence. Indeed, the act of switching to another medical system and exhibiting preference by action demonstrates an openness to active participation and adherence and possibly enhances it. Paying out-of-pocket and other signs of commitment, such as following daily lifestyle regimens, undoubtedly marshal adherence effects. The reasons that patients choose alternative medicine may also potentiate a placebo response. Patients with chronic diseases often turn to unconventional healing after long-term negative conditioning with mainstream medicine (31). In this situation, patients’ hope (based on no previous experience with alternative medicine) may provide an opportunity for “deconditioning” from previous unsuccessful medical experiences.

PRACTITIONER CHARACTERISTICS

The practitioner-healer must expertly play the role of heroic rescuer to facilitate a placebo effect (32). Numerous RCTs have compared optimistic or enthusiastic physician attitudes toward drug or placebo with neutral or doubtful physician attitudes. Practitioners have had

significant impact on such clinical conditions as pain (33–36), psychiatric illness (37–41), hypertension (42, 43), obesity (44), and perimenopause symptoms (45). Although some studies have shown no effect of physicians' expectations on clinical end points (46–48), a systematic review of 85 studies found that although more research is needed, provider-induced "expectancies are a mechanism for placebo effects, [which have] received support across a range of clinical areas in a variety of studies" (49). A second review, which used more stringent entry criteria, found 25 RCTs that examined the impact of randomly assigning patients with physical illnesses to different levels of expectancy and emotional support. Although researchers found inconsistent effects and determined that further research was needed, they also found that "enhancing patients' expectations through positive information about the treatment or illness, while providing support or reassurance, [seemed to] significantly influence health outcomes" (50).

Even in blinded RCTs, practitioner certitude seems to influence the magnitude of the placebo effect. In one RCT that simultaneously compared two double-blind RCTs, dental patients in one trial received placebo, narcotic analgesics, or narcotic antagonists and those in the other trial received only a placebo or a narcotic antagonist. Dentists knew the possible interventions in both trials but remained blinded to administration of medication. Pain in placebo recipients was significantly worse in the second trial, in which narcotic drugs were not an option, than in the first trial (51). An earlier RCT of the effect of physician expectations on hypertension drugs also found that practitioner belief can transform outcomes (52).

Practitioners of unconventional medicine are less restrained by scientific objectivity than practitioners of conventional medicine. The sensibilities of alternative practitioners are therefore often more optimistic and positive than those of their mainstream counterparts (53). The characteristics thought to enhance the placebo effect (and any active intervention) seem to be fully operational in the offices of alternative medicine.

PATIENT–PRACTITIONER INTERACTION

The placebo drama is probably more successful if the patient and practitioner find each other's beliefs and actions mutually credible or at least intriguing. Recipro-

cal expectations need to be negotiated and joined in the patient–physician duet. Many studies indicate that the patient–practitioner encounter is a potent factor in health outcomes (54–56) and that for many non-life-threatening illnesses, clear diagnosis, assurance of recovery, opportunity for dialogue, and physician–patient agreement about the nature of the problem hasten recovery or relief (57, 58). One study examined 200 patients who presented to general practitioners with symptoms but no abnormal physical signs and in whom no definite diagnosis could be made. Patients were randomly assigned in a 2×2 design to treatment or no treatment and to a positive consultation, in which they received "a firm diagnosis and [were] told confidently that [they] would be better in a few days," or a negative consultation, in which they were told that their condition was uncertain. Although provision of treatment made no difference, positive interaction produced significantly faster recovery (59). A similar experiment in 100 patients with acute tonsillitis had analogous results (60).

Consultation in unconventional medicine is more likely than its mainstream counterpart to produce a precise diagnosis that matches patients' perceptions. In unconventional medicine, patient experience is never devalued or brushed aside as unreliable (61). Inevitably, since the alternative world is not as constrained by the dichotomy of objectivity and subjectivity, the chiropractor will find the subluxation, the acupuncturist will detect the yin–yang disharmony, and the health food advocate will identify the transgression that makes sense of the patient's life-world. In addition, if a patient is new to alternative medicine, an opportunity for exchange is invariably offered, providing the patient with "theoretical explanations designed to take the mystery out of process and problems" (62). When it is considered that 40% to 60% of patients may never receive a firm diagnosis in conventional medicine (63, 64), an alternative diagnosis may be a potent form of nonspecific healing that changes the circumstances under which the patient exists (65–67), including reducing the "dysphoria of uncertainty" (68).

Besides diagnosis, the healing encounter also establishes therapeutic goals. Paradoxically, while the alternative diagnosis tends to be precise, treatment aims can be diverse. Because of such notions as "holistic medicine" and "body, mind, spirit," alternative medicine can have extremely broad, indeterminate therapeutic targets and

therefore, at least from a cultural view, “in some sense cannot fail” (69). Such amorphous goals can provide additional maneuvering room for positive progress, or at least incremental change (70). If the patient’s symptoms do not directly improve, it is likely that something positive will happen and be attributed to the intervention (even if the change pertains only to alternative constructs, such as the homeopathic spiritual force or the acupuncture *qi*). Taken together, the alternative diagnosis, prognosis, and treatment aims serve “to regulate symptom intensity and distress” and “create enough certainty to diminish the threat of the inchoate while preserving enough ambiguity to allow for fresh improvisation” (71).

THE NATURE OF THE ILLNESS

The placebo effect may benefit from the types of illnesses that alternative medicine commonly treats. Data indicate that the overwhelming majority of medical conditions treated by unconventional medicine fall into the following categories: highly subjective symptoms lacking identifiable physiologic correlates, chronic conditions with a fluctuating course often influenced by selective attention, and affective disorders (2, 72). Not surprisingly, these conditions are precisely those that researchers believe are especially susceptible to inordinately strong placebo responses: back and chronic pain (73–75), fatigue (76, 77), arthritis (78, 79) headache (80, 81), allergies (82, 83), hypertension (in some situations) (84, 85), insomnia (86, 87), asthma (13, 88), chronic digestive disorders (89, 90) depression (91, 92), and anxiety (93). Even researchers who question the existence or significance of a placebo effect—at least in the narrow sense of the outcome produced by a dummy intervention—concede its impact when outcomes are continuous and subjective (94). Also, persons with self-limiting diseases, such as the common cold and sprains and strains, also frequently use alternative medicine. In these cases, the natural course of the disease undoubtedly creates the appearance of treatment response and enhances the perception of unconventional medicine’s effectiveness.

TREATMENT AND SETTING

Treatment paraphernalia and setting affect the impact of a placebo performance. For placebo pills, a regimen of four times per day seems more effective than a regimen of twice per day (95). A “brand-name” therapy that includes

either active or inert ingredients may often yield better results than an identical treatment that is not as well known (96), and devices or elaborate procedures can have greater placebo effects than pills (97, 98). Active placebos (placebos containing medications, such as atropine, that are ineffective for the condition being studied but produce recognizable drug-related side effects) seem to provide genuine treatment recognition that leads to heightened placebo effects (99, 100). With good showmanship, a well-designed, totally inert stage prop can offer this kind of “feedback loop” and can produce exaggerated placebo effects.

Two RCTs—one of transcutaneous electrical nerve stimulation and one of “placebo electronic machines”—demonstrated that, with good staging, blank machines can provide feedback sensations. In the first study, all patients reported an electrical sensation after adjustment of the dummy apparatus, which was equipped with visual and sound feedback (101). In the second trial (which used only dummy machines under two different sets of expectations), a significant number of participants “felt” the nonexistent current, and some even volunteered that the sensation was “just amazing” (102).

Biomedicine and alternative medicine each have a special allure of mystery and exotic power; it would be hard to argue that one backdrop consistently provides a superior placebo effect. However, alternative medicine has the advantage of always having an intervention scenario. Therapeutic passivity is rarely an option, and practitioners can, at a minimum, offer something that is likely to have a placebo effect. In some situations, and at least for continuous subjective outcomes, an intervention presumably has a greater effect than no treatment (94, 103). Also, to demonstrate “active” intervention, alternative medicine treatments have unique feedback loops that are likely to facilitate, if not heighten, substantial placebo responses. For example, chiropractic adjustment often triggers an audible “pop” so that the patient can hear the subluxation being fixed (104), acupuncturists propagate a sensation of vital energy coursing through invisible meridians (105), and psychic healers summon tingling vibrations (106).

DOES ALTERNATIVE MEDICINE HAVE ENHANCED PLACEBO EFFECTS?

Despite the arguments and speculations already presented, there is scant empirical evidence that any partic-

ular type of alternative medicine used for any particular condition has an augmented placebo effect. Even concerning the placebo effect in general, the evidence cited earlier is often methodologically weak and limited by small numbers and short follow-up periods. Some social scientists argue that “for the believer in science, medical care that appears to be scientific would provide a superior placebo; for the believer . . . of whatever other cultural system of meaning and values,” alternative medicine may “provide a superior placebo” (107). Perhaps biomedicine’s effort to eliminate ritual or placebo interventions itself produces an improved placebo effect.

Two examples from RCTs may help readers concretely envision an enhanced placebo effect. In a four-arm crossover RCT involving 44 patients with chronic cervical osteoarthritis of more than 6 months’ duration, acupuncture, sham acupuncture, and diazepam were all equivalent and were superior to a placebo pill (108). In this study, the outcome of the ritual of acupuncture (real and sham acupuncture were not different) equaled the outcome of an effective drug. In a second RCT, which studied spinal manipulation, 256 patients with nonspecific back and neck disorders were randomly assigned to receive manual therapy (the Dutch equivalent of chiropractic), physical therapy, placebo-device therapy with a “detuned” ultrasonography machine and “detuned” short-wave diathermy that emitted sounds and lights, or treatment from a general practitioner (109). Six weeks of manual therapy and physical therapy were equally and significantly better than the sham machine, which significantly outperformed the general practitioner. It cannot be determined whether the manual and physical therapies had specific treatment effects or simply yielded better placebo effects than the inanimate gadget. Nonetheless, in this experiment, treatment with a sham machine surpassed treatment from a competent physician for relief of low back pain.

To more rigorously test these possible relative nonspecific effects, my colleagues and I are performing a National Institutes of Health–funded RCT that randomly assigns patients with chronic pain to one of two parallel run-in phases. Before entering two subsequent RCTs, one run-in group receives a conventional-appearing placebo pill and the other receives an alternative medicine sham procedure; the main goal of the run-in phases is to detect differing placebo effects (97). Any confident assertion about a placebo effect enhanced by

alternative medicine would probably require many such experiments.

Some may dismiss these types of investigation as useless. After all, a placebo is just a placebo. Others would argue that such avoidance impoverishes and narrows the understanding of what patients receive from alternative medicine (and, by extension, conventional medicine). Even those who doubt the existence or significance of a “narrow” placebo effect seem open to the possibility of “broad” placebo effects embedded in the psychosocial context of the patient–practitioner relationship (110, 111).

WHAT IS LEGITIMATE HEALING?

Besides clinical and scientific value, the question of enhanced placebo effects raises complex ethical questions concerning what is “legitimate” healing. What should determine appropriate healing, a patient’s improvement from his or her own baseline (clinical significance) or relative improvement compared with a placebo (fastidious efficacy)? As one philosopher of medicine has asked, are results less important than method (3)? Both performative and fastidious efficacy can be measured. Which measurement represents universal science? Which measurement embodies cultural judgment on what is “correct” healing? Are the concerns of the physician identical to those of the patient? Is denying patients with nonspecific back pain treatment with a sham machine an ethical judgment or a scientific judgment? Should a patient with chronic neck pain who cannot take diazepam because of unacceptable side effects be denied acupuncture that may have an “enhanced placebo effect” because such an effect is “bogus”? Who should decide?

Patients’ attitudes toward placebo interventions (especially enhanced interventions) probably differ from physicians’ attitudes (112). This distinction is probably most evident in surgery, another field in which a heightened placebo effect is possible (97, 113), as illustrated by two RCTs that tested implantation of fetal dopaminergic cells for Parkinson disease. Patients with Parkinson disease seem to have a robust placebo response (114, 115); the biochemical substrate of this response in relation to the release of dopamine in the striatum has recently been shown on positron emission tomography (116). At the conclusion of one of the two RCTs,

patients were unblinded, and half were told they had received sham surgery that had performed the same as real surgery. In the early reports from this study, both groups experienced significant clinical improvement. (The subsequent full report, which included long-term data, reported a less durable placebo effect [117].) When patients who had received the sham surgery were told that they could not receive the real but now “discredited” surgery, as they had been promised in the informed consent form, 70% were disappointed or “outraged” because of the dramatic benefits they had already received from sham surgery (118–120). They wanted the “real” procedure even if it was equivalent to the sham. Of interest, the second RCT, which also found no difference between active and imitation surgery, demonstrated a stable and significant placebo effect after 18 months (121). For many patients, performative efficacy may be more critical than fastidious efficacy. Obviously, this illustration is not meant to advocate ritualistic surgery. Rather, it is meant to highlight the complex relationship among clinical, scientific, and ethical judgments.

CONCLUSION

Alternative medicine may be composed of healing rituals that have especially potent performative efficacy. Therapeutic characteristics that may enhance placebo effects seem especially prominent in unconventional healing. Although more research into this question is necessary before any such assertion can be made with confidence, an enhanced placebo effect raises complex questions about what is legitimate therapy, and who decides.

From Harvard Medical School, Boston, Massachusetts.

Acknowledgment: The author thanks Robb Scholten, June Cobb, Pat Wilkinson, John C. Wilson, Maria Van Rompay, and Marcia Rich for editorial and research assistance.

Grant Support: In part by the National Institutes of Health (1R01AT00402-01, U24 AR43441, and 1R21AT00553), the John E. Fetzer Institute, the Waletzky Charitable Trust, the Friends of Beth Israel Deaconess Medical Center, and American Specialty Health Plan.

Requests for Single Reprints: Ted J. Kaptchuk, OMD, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston, MA 02215.

References

1. Temple RJ. When are clinical trials of a given agent vs. placebo no longer appropriate or feasible? *Control Clin Trials*. 1997;18:613-20. [PMID: 9408723]
2. Kaptchuk TJ, Edwards RA, Eisenberg DM. Complementary medicine: efficacy beyond the placebo effect. In: Ernst E, ed. *Complementary Medicine: An Objective Appraisal*. Oxford: Butterworth-Heinemann; 1996.
3. Sullivan MD. Placebo controls and epistemic control in orthodox medicine. *J Med Philos*. 1993;18:213-31. [PMID: 8315363]
4. van Weel C. Examination of context of medicine. *Lancet*. 2001;357:733-4. [PMID: 11253959]
5. Kaptchuk TJ. Powerful placebo: the dark side of the randomised controlled trial. *Lancet*. 1998;351:1722-5. [PMID: 9734904]
6. Vickers AJ, de Craen AJ. Why use placebos in clinical trials? A narrative review of the methodological literature. *J Clin Epidemiol*. 2000;53:157-61. [PMID: 10729687]
7. Feinstein AR. *Clinical Epidemiology*. Philadelphia: WB Saunders; 1985.
8. Tambiah SJ. *Magic, Science, Religion, and the Scope of Rationality*. Cambridge, United Kingdom: Cambridge Univ Pr; 1990.
9. Shapiro AK, Shapiro E. *The Powerful Placebo: From Ancient Priest to Modern Physician*. Baltimore: Johns Hopkins Univ Pr; 1997.
10. Wolf S, Doering CR, Clark ML, Hagans JA. Chance distribution and the placebo “reactor.” *J Lab Clin Med*. 1957;49:837-41.
11. Liberman RP. The elusive placebo reactor. *Neuropsychopharmacology*. 1967;5:557-66.
12. Luparello TJ, Leist N, Lourie CH, Sweet P. The interaction of psychologic stimuli and pharmacologic agents on airway reactivity in asthmatic subjects. *Psychosom Med*. 1970;32:509-13. [PMID: 4097491]
13. Butler C, Steptoe A. Placebo responses: an experimental study of psychophysiological processes in asthmatic volunteers. *Br J Clin Psychol*. 1986;25(Pt 3):173-83. [PMID: 3768575]
14. Sodergren SC, Hyland ME. Expectancy and asthma. In: Kirsch I, ed. *How Expectancies Shape Experience*. Washington, DC: American Psychological Assoc; 1999.
15. Sternbach RA. The effects of instructional sets on autonomic responsivity. *Psychophysiology*. 1964;62:67-72.
16. Kaptchuk TJ. The double-blind, randomized, placebo-controlled trial. Gold standard or golden calf? *J Clin Epidemiol*. 2001;54:541-9. [PMID: 11377113]
17. Mitchell SH, Laurent CL, de Wit H. Interaction of expectancy and the pharmacological effects of d-amphetamine: subjective effects and self-administration. *Psychopharmacology (Berl)*. 1996;125:371-8. [PMID: 8826542]
18. Flaten MG, Simonsen T, Olsen H. Drug-related information generates placebo and nocebo responses that modify the drug response. *Psychosom Med*. 1999;61:250-5. [PMID: 10204979]
19. Dworkin SF, Chen AC, Schubert MM, Clark DW. Cognitive modification of pain: information with N₂O. *Pain*. 1984;19:339-51. [PMID: 6483450]
20. Horwitz RI, Horwitz SM. Adherence to treatment and health outcomes. *Arch Intern Med*. 1993;153:1863-8. [PMID: 8250647]
21. Czajkowski SM, Chesney MA. Adherence and the placebo effect. In: Shumaker SA, Schron EB, Ockene JK, eds. *The Handbook of Health Behavior Change*. New York: Springer; 1990.
22. Influence of adherence to treatment and response of cholesterol on mortality in the coronary drug project. *N Engl J Med*. 1980;303:1038-41. [PMID: 6999345]
23. Horwitz RI, Viscoli CM, Berkman L, Donaldson RM, Horwitz SM, Murray CJ, et al. Treatment adherence and risk of death after a myocardial infarction. *Lancet*. 1990;336:542-5. [PMID: 1975045]
24. Gallagher EJ, Viscoli CM, Horwitz RI. The relationship of treatment

- adherence to the risk of death after myocardial infarction in women. *JAMA*. 1993;270:742-4. [PMID: 8336377]
25. **Mattocks KM, Horwitz RI.** Placebos, active control groups, and the unpredictability paradox. *Biol Psychiatry*. 2000;47:693-8. [PMID: 10773175]
 26. **Wennberg JE.** What is outcomes research? In: Gelijns AC, ed. *Modern Methods of Clinical Investigation*. Washington, DC: National Academy Press; 1990.
 27. **McPherson K, Britton AR, Wennberg JE.** Are randomized controlled trials controlled? Patient preferences and unblind trials. *J R Soc Med*. 1997;90:652-6. [PMID: 9496288]
 28. **Brewin CR, Bradley C.** Patient preferences and randomised clinical trials. *BMJ*. 1989;299:313-5. [PMID: 2504416]
 29. **Kaptchuk TJ.** History of vitalism. In: Micozzi MS, ed. *Fundamentals of Complementary and Alternative Medicine*. New York: Churchill Livingstone; 2001.
 30. **Kirmayer LJ.** Healing and the invention of metaphor: the effectiveness of symbols revisited. *Cult Med Psychiatry*. 1993;17:161-95. [PMID: 7693395]
 31. **Zollman C, Vickers A.** ABC of complementary medicine. Complementary medicine and the patient. *BMJ*. 1999;319:1486-9. [PMID: 10582937]
 32. **Shapiro AK.** Iatroplacebogenesis. *International Pharmacopsychiatry*. 1969;2: 215-48.
 33. **Gryll SL, Katahn M.** Situational factors contributing to the placebo effect. *Psychopharmacology (Berl)*. 1978;57:253-61. [PMID: 97705]
 34. **Hashish I, Hai HK, Harvey W, Feinmann C, Harris M.** Reduction of postoperative pain and swelling by ultrasound treatment: a placebo effect. *Pain*. 1988;33:303-11. [PMID: 3419838]
 35. **Ho KH, Hashish I, Salmon P, Freeman R, Harvey W.** Reduction of post-operative swelling by a placebo effect. *J Psychosom Res*. 1988;32:197-205. [PMID: 3404502]
 36. **Bergmann JF, Chassany O, Gandiol J, Deblois P, Kanis JA, Segrestaa JM, et al.** A randomised clinical trial of the effect of informed consent on the analgesic activity of placebo and naproxen in cancer pain. *Clin Trials Metaanal*. 1994;29: 41-7. [PMID: 10150184]
 37. **Uhlenhuth EH, Rickels K, Fisher S, Park LC, Lipman RS, Mock J.** Drug, doctor's verbal attitude and clinic setting in the symptomatic response to pharmacotherapy. *Psychopharmacologia*. 1966;9:392-418. [PMID: 4872909]
 38. **Fisher S, Cole JO, Rickels K, Uhlenhuth EH.** Drug-set interaction: the effect of expectations on drug response in outpatients. *Neuropsychopharmacology*. 1964;3:149-56.
 39. **Wheatley D.** Influence of doctors' and patients' attitudes in the treatment of neurotic illness. *Lancet*. 1967;2:1133-5. [PMID: 4168567]
 40. **Rabkin JG, McGrath PJ, Quitkin FM, Tricamo E, Stewart JW, Klein DF.** Effects of pill-giving on maintenance of placebo response in patients with chronic mild depression. *Am J Psychiatry*. 1990;147:1622-6. [PMID: 2244639]
 41. **Affleck DC, Eaton MT, Mansfield E.** The action of a medication and the physician's expectations. *Nebr State Med J*. 1966;51:331-4. [PMID: 4227004]
 42. **Agras WS, Horne M, Taylor CB.** Expectation and the blood-pressure-lowering effects of relaxation. *Psychosom Med*. 1982;44:389-95. [PMID: 6755527]
 43. **Amigo I, Cuesta V, Fernández A, González A.** The effect of verbal instructions on blood pressure measurement. *J Hypertens*. 1993;11:293-6. [PMID: 8387087]
 44. **Freund J, Krupp G, Goodenough D, Preston LW.** The doctor-patient relationship and drug effect. *Clin Pharmacol Ther*. 1972;13:172-80. [PMID: 4552819]
 45. **Wied GI.** Über die Bedeutung der Suggestion in der Therapie klimakterischer Ausfallerscheinungen. *Ärztliche Wochenschrift*. 1953;8:623-5.
 46. **de Craen AJM.** Impact of experimentally induced expectancy on the analgesic effect of tramadol in chronic pain patients: a 2 × 2 factorial, randomised, placebo-controlled, double-blind trial. In: *Placebos and Placebo Effects in Clinical Trials* [Dissertation]. Amsterdam: Univ of Amsterdam; 1998.
 47. **Cooper WD, Currie WJ, Vandenburg MJ.** The influence of physicians' instructions on the outcome of antihypertensive therapy. *Br J Clin Pract*. 1983; 37:99-103. [PMID: 6882631]
 48. **Kincheloe JE, Mealiea WL Jr, Mattison GD, Seib K.** Psychophysical measurement on pain perception after administration of a topical anesthetic. *Quintessence Int*. 1991;22:311-5. [PMID: 1891606]
 49. **Crow R, Gage H, Hampson S, Hart J, Kimber A, Thomas H.** The role of expectancies in the placebo effect and their use in the delivery of health care: a systematic review. *Health Technol Assess*. 1999;3:1-96. [PMID: 10448203]
 50. **Di Blasi Z, Harkness E, Ernst E, Georgiou A, Kleijnen J.** Influence of context effects on health outcomes: a systematic review. *Lancet*. 2001;357:757-62. [PMID: 11253970]
 51. **Gracely RH, Dubner R, Deeter WR, Wolskee PJ.** Clinicians' expectations influence placebo analgesia [Letter]. *Lancet*. 1985;1:43. [PMID: 2856960]
 52. **Shapiro AP, Myer T, Reiser MF, Ferris EB.** Comparison of blood pressure response to Veriloid and to the doctor. *Psychosom Med*. 1954;16:478-88.
 53. **Kaptchuk TJ, Eisenberg DM.** The persuasive appeal of alternative medicine. *Ann Intern Med*. 1998;129:1061-5. [PMID: 9867762]
 54. **Stewart MA.** Effective physician-patient communication and health outcomes: a review. *CMAJ*. 1995;152:1423-33. [PMID: 7728691]
 55. **Ong LM, de Haes JC, Hoos AM, Lammes FB.** Doctor-patient communication: a review of the literature. *Soc Sci Med*. 1995;40:903-18. [PMID: 7792630]
 56. **Kaplan SH, Greenfield S, Ware JE Jr.** Assessing the effects of physician-patient interactions on the outcomes of chronic disease. *Med Care*. 1989;27: S110-27. [PMID: 2646486]
 57. **Finkler K, Correa M.** Factors influencing patient perceived recovery in Mexico. *Soc Sci Med*. 1996;42:199-207. [PMID: 8928029]
 58. **Bass MJ, Buck C, Turner L, Dickie G, Pratt G, Robinson HC.** The physician's actions and the outcome of illness in family practice. *J Fam Pract*. 1986;23:43-7. [PMID: 3723083]
 59. **Thomas KB.** General practice consultations: is there any point in being positive? *Br Med J (Clin Res Ed)*. 1987;294:1200-2. [PMID: 3109581]
 60. **Olsson B, Olsson B, Tibblin G.** Effect of patients' expectations on recovery from acute tonsillitis. *Fam Pract*. 1989;6:188-92. [PMID: 2792618]
 61. **Hahn RA.** "Treat the patient, not the lab:" internal medicine and the concept of "person". *Cult Med Psychiatry*. 1982;6:219-36. [PMID: 7172711]
 62. **Oths K.** Communication in a chiropractic clinic: how a D.C. treats his patients. *Cult Med Psychiatry*. 1994;18:83-113. [PMID: 8082319]
 63. **Thomas KB.** The placebo in general practice. *Lancet*. 1994;344:1066-7. [PMID: 7934451]
 64. **Adler HM, Hammett VB.** The doctor-patient relationship revisited. An analysis of the placebo effect. *Ann Intern Med*. 1973;78:595-8. [PMID: 4694043]
 65. **Sox HC Jr, Margulies I, Sox CH.** Psychologically mediated effects of diagnostic tests. *Ann Intern Med*. 1981;95:680-5. [PMID: 7305144]
 66. **Adler HM.** The history of the present illness as treatment: who's listening, and why does it matter? *J Am Board Fam Pract*. 1997;10:28-35. [PMID: 9018660]
 67. **Brody H, Waters DB.** Diagnosis is treatment. *J Fam Pract*. 1980;10:445-9. [PMID: 7354290]
 68. **Novack DH.** Therapeutic aspects of the clinical encounter. *J Gen Intern Med*. 1987;2:346-55. [PMID: 3309210]
 69. **Csordas TJ.** The rhetoric of transformation in ritual healing. *Cult Med*

- Psychiatry. 1983;7:333-75. [PMID: 6661923]
70. Csordas TJ. Elements of charismatic persuasion and healing. *Med Anthropol Q*. 1988;2:121-42.
71. Kirmayer LJ. Improvisation and authority in illness meaning. *Cult Med Psychiatry*. 1994;18:183-214. [PMID: 7924400]
72. Eisenberg DM, Davis RB, Ettner SL, Appel S, Wilkey S, Van Rompay M, et al. Trends in alternative medicine use in the United States, 1990-1997: results of a follow-up national survey. *JAMA*. 1998;280:1569-75. [PMID: 9820257]
73. Turner JA, Deyo RA, Loeser JD, Von Korff M, Fordyce WE. The importance of placebo effects in pain treatment and research. *JAMA*. 1994;271:1609-14. [PMID: 7880221]
74. Wall PD. Pain and the placebo response. In: Bock G, Marsh J, eds. *Experimental and Theoretical Studies of Consciousness*. Ciba Foundation Symposium 174. New York: J Wiley; 1993.
75. McQuay H, Carroll D, Moore A. Variation in the placebo effect in randomised controlled trials of analgesics: all is as blind as it seems. *Pain*. 1996;64:331-5. [PMID: 8740611]
76. Lasagna L, Laties VG, Dohan JL. Further studies on the "pharmacology" of placebo administration. *J Clin Invest*. 1958;37:533-7.
77. Brodeur DW. The effects of stimulant and tranquilizer placebos on healthy subjects in a real-life situation. *Psychopharmacologia*. 1965;7:444-52. [PMID: 4378577]
78. Morison RA, Woodmansey A, Young AJ. Placebo responses in an arthritis trial. *Ann Rheum Dis*. 1961;20:178-85.
79. Pillemer SR, Fowler SE, Tilley BC, Alarcón GS, Heyse SP, Trentham DE, et al. Meaningful improvement criteria sets in a rheumatoid arthritis clinical trial. MIRA Trial Group. Minocycline in Rheumatoid Arthritis. *Arthritis Rheum*. 1997;40:419-25. [PMID: 9082927]
80. Couch JR Jr. Placebo effect and clinical trials in migraine therapy. *Neuroepidemiology*. 1987;6:178-85. [PMID: 3317098]
81. Diener HC, Dowson AJ, Ferrari M, Nappi G, Tfelt-Hansen P. Unbalanced randomization influences placebo response: scientific versus ethical issues around the use of placebo in migraine trials. *Cephalalgia*. 1999;19:699-700. [PMID: 10570722]
82. Kagan G, Dabrowicki E, Huddleston L, Kapur TR, Wolstencroft P. A double blind trial of terfenadine and placebo in hay fever using a substitution technique for non-responders. *J Int Med Res*. 1980;8:404-7. [PMID: 6108264]
83. D'Souza MF, Emanuel MB, Gregg J, Charlton J, Goldschmidt J. A method for evaluating therapy for hay fever. A comparison of four treatments. *Clin Allergy*. 1983;13:329-35. [PMID: 6411382]
84. Preston RA, Materson BJ, Reda DJ, Williams DW. Placebo-associated blood pressure response and adverse effects in the treatment of hypertension: observations from a Department of Veterans Affairs Cooperative Study. *Arch Intern Med*. 2000;160:1449-54. [PMID: 10826457]
85. Suchman AL, Ader R. Classic conditioning and placebo effects in crossover studies. *Clin Pharmacol Ther*. 1992;52:372-7. [PMID: 1424409]
86. Storms MD, Nisbett RE. Insomnia and the attribution process. *J Pers Soc Psychol*. 1970;16:319-28. [PMID: 5479134]
87. Bootzin RR, Herman CP, Nicassio P. The power of suggestion: another examination of misattribution and insomnia. *J Pers Soc Psychol*. 1976;34:673-9. [PMID: 993978]
88. Godfrey S, Silverman M. Demonstration by placebo response in asthma by means of exercise testing. *J Psychosom Res*. 1973;17:293-7. [PMID: 4206466]
89. Moerman DE. Cultural variations in the placebo effect: ulcers, anxiety, and blood pressure. *Med Anthropol Q*. 2000;14:51-72. [PMID: 10812563]
90. Ilnyckij A, Shanahan F, Anton PA, Cheang M, Bernstein CN. Quantification of the placebo response in ulcerative colitis. *Gastroenterology*. 1997;112:1854-8. [PMID: 9178676]
91. Brown WA, Johnson MF, Chen MG. Clinical features of depressed patients who do and do not improve with placebo. *Psychiatry Res*. 1992;41:203-14. [PMID: 1594707]
92. Kirsch I, Sapirstein G. Listening to Prozac but hearing placebo: a meta-analysis of antidepressant medications. In: Kirsch I, ed. *How Expectancies Shape Experience*. Washington, DC: American Psychological Assoc; 1999.
93. Rosenberg NK, Møllergård M, Rosenberg R, Beck P, Ottosson JO. Characteristics of panic disorder patients responding to placebo. *Acta Psychiatr Scand Suppl*. 1991;365:33-8. [PMID: 1862732]
94. Hróbjartsson A, Gøtzsche PC. Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment. *N Engl J Med*. 2001;344:1594-602. [PMID: 11372012]
95. de Craen AJ, Moerman DE, Heisterkamp SH, Tytgat GN, Tijssen JG, Kleijnen J. Placebo effect in the treatment of duodenal ulcer. *Br J Clin Pharmacol*. 1999;48:853-60. [PMID: 10594490]
96. Branthwaite A, Cooper P. Analgesic effects of branding in treatment of headaches. *Br Med J (Clin Res Ed)*. 1981;282:1576-8. [PMID: 6786566]
97. Kaptchuk TJ, Goldman P, Stone DA, Stason WB. Do medical devices have enhanced placebo effects? *J Clin Epidemiol*. 2000;53:786-92. [PMID: 10942860]
98. de Craen AJ, Tijssen JG, de Gans J, Kleijnen J. Placebo effect in the acute treatment of migraine: subcutaneous placebos are better than oral placebos. *J Neurol*. 2000;247:183-8. [PMID: 10787112]
99. Moncrieff J, Wessely S, Hardy R. Meta-analysis of trials comparing antidepressants with active placebos. *Br J Psychiatry*. 1998;172:227-31. [PMID: 9614471]
100. Fisher S, Greenberg RP. How sound is the double-blind design for evaluating psychotropic drugs? *J Nerv Ment Dis*. 1993;181:345-50. [PMID: 8501455]
101. Marchand S, Charest J, Li J, Chenard JR, Lavignolle B, Laurencelle L. Is TENS purely a placebo effect? A controlled study on chronic low back pain. *Pain*. 1993;54:99-106. [PMID: 8378107]
102. Schwitzgebel RK, Traugott M. Initial note on the placebo effect of machines. *Behav Sci*. 1968;13:267-73. [PMID: 5663895]
103. Ernst E, Resch KL. Concept of true and perceived placebo effects. *BMJ*. 1995;311:551-3. [PMID: 7663213]
104. Kaptchuk TJ, Eisenberg DM. Chiropractic: origins, controversies, and contributions. *Arch Intern Med*. 1998;158:2215-24. [PMID: 9818801]
105. Kaptchuk TJ. *The Web That Has No Weaver: Understanding Chinese Medicine*. Chicago: Contemporary; 2000.
106. McGuire MB. *Ritual Healing in Suburban America*. New Brunswick, NJ: Rutgers Univ Pr; 1988.
107. Riley JN. Western medicine's attempt to become more scientific: examples from the United States and Thailand [1]. *Soc Sci Med*. 1977;11:549-60. [PMID: 339357]
108. Thomas M, Eriksson SV, Lundeberg T. A comparative study of diazepam and acupuncture in patients with osteoarthritis pain: a placebo controlled study. *Am J Chin Med*. 1991;19:95-100. [PMID: 1816730]
109. Koes BW, Bouter LM, van Mameren H, Essers AH, Verstegen GM, Hofhuizen DM, et al. The effectiveness of manual therapy, physiotherapy, and treatment by the general practitioner for nonspecific back and neck complaints. A randomized clinical trial. *Spine*. 1992;17:28-35. [PMID: 1531552]
110. Hróbjartsson A, Gøtzsche PC. Is the placebo powerless? [Letter] *N Engl J Med*. 2001;345:1278-9.

111. Hróbjartsson A, Gøtzsche PC. Core belief in powerful effects of placebo interventions is in conflict with no evidence of important effects in a large systematic review. *Advances in Mind-Body Medicine*. 2001;17:312-8.
112. Lynøe N, Mattsson B, Sandlund M. The attitudes of patients and physicians towards placebo treatment—a comparative study. *Soc Sci Med*. 1993;36:767-74. [PMID: 8480221]
113. Johnson AG. Surgery as a placebo. *Lancet*. 1994;344:1140-2. [PMID: 7934500]
114. Shetty N, Friedman JH, Kieburtz K, Marshall FJ, Oakes D. The placebo response in Parkinson's disease. Parkinson Study Group. *Clin Neuropharmacol*. 1999;22:207-12. [PMID: 10442249]
115. Goetz CG, Leurgans S, Raman R, Stebbins GT. Objective changes in motor function during placebo treatment in PD. *Neurology*. 2000;54:710-4. [PMID: 10680808]
116. de la Fuente-Fernández R, Ruth TJ, Sossi V, Schulzer M, Calne DB, Stoessl AJ. Expectation and dopamine release: mechanism of the placebo effect in Parkinson's disease. *Science*. 2001;293:1164-6. [PMID: 11498597]
117. Freed CR, Greene PE, Breeze RE, Tsai WY, DuMouchel W, Kao R, et al. Transplantation of embryonic dopamine neurons for severe Parkinson's disease. *N Engl J Med*. 2001;344:710-9. [PMID: 11236774]
118. Husten L. Fetal-cell-implantation trial yields mixed results. *Lancet*. 1999;353:1501.
119. Macklin R. The ethical problems with sham surgery in clinical research. *N Engl J Med*. 1999;341:992-6. [PMID: 10498498]
120. Johannes L. Sham surgery is used to test effectiveness of novel operations. *Wall Street Journal*. 1998;11 December:A1, A8.
121. Watts RL, Freeman RA, Hauser RA, Bakay SA, Ellias AJ, Stoessl AJ, et al. A double-blind, randomized, controlled, multicenter clinical trial of the safety and efficacy of stereotaxic intrastriatal implantation of fetal porcine ventral mesencephalic tissue (NeurocellTM-PD) vs. imitation surgery in patients with Parkinson's disease (PD) [Abstract]. *Parkinsonism and Related Disorders*. 2001;7 (Suppl):S87.

Sometimes we no longer know what is true for us, in which direction our own integrity lies . . . Reclaiming ourselves usually means coming to recognize and accept that we have in us both sides of everything. We are capable of fear and courage, generosity and selfishness, vulnerability and strength. These things do not cancel each other out but offer us a full range of power and response to life. Life is as complex as we are.

One of the blessings of growing older is the discovery that many of the things I once believed to be my shortcomings have turned out in the long run to be my strengths, and other things of which I was unduly proud have revealed themselves in the end to be among my shortcomings . . . What a blessing it is to outlive your self-judgments and harvest your failures.

Rachel Naomi Remen, MD
Kitchen Table Wisdom: Stories That Heal
New York: Riverhead Books; 1996:35-8

Submitted by:
George Ho Jr., MD
East Carolina University School of Medicine
Greenville, NC 27858

Submissions from readers are welcomed. If the quotation is published, the sender's name will be acknowledged. Please include a complete citation (along with page number on which the quotation was found), as done for any reference.—*The Editor*