

The Placebo Effect Reconsidered

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Usage of the terms *placebo* and *placebo effect* has changed dramatically within medical history. Although placebos are still useful within research, the placebo effect has become a large and ill-defined concept threatening to obscure rather than to clarify whatever phenomenon is being described. Placebos and placebo effects should be fundamentally reconsidered if they are to be of continued use in medical practice.

There was a time when the placebo was a handy, common, and accepted component of medical practice. In recent years physicians have found it necessary to distinguish between placebos and the placebo effect, and to move the consideration of both to the frontiers of medical science.

This paper will briefly trace the history of the placebo in medicine, exploring in some detail the recent revival of interest in placebos and in the development of the placebo effect. Some of the current problems in applying this renewed interest will then be outlined, and recommendations will be made for dealing with placebos and the placebo effect in current practice.

The Historical Placebo

The literal translation of the Latin verb *placebo* is "I shall please" or "I shall serve." Its independent use as a noun in English dates to the 14th century, when the word was used colloquially to denote a vesper sung for the dead in the Roman Catholic Church ("Placebo Domino in regione vivorum"). Such masses were sung after payment of a substantial fee; thus a negative connotation appeared early. In 1386 Chaucer used *placebo* to mean a sycophant or flatterer. Although explicit recognition of the power of positive expectation in medical practice was frequent in literature throughout the 17th and 18th centuries, the word *placebo* first entered the medical vocabulary late in the 18th century, defined as "a commonplace method or medicine" in both Motherby's *New Medical Dictionary* and Quincy's *Lexicon*.¹

Beginning in the early 1800s many writers commented upon the use of placebos:

One of the most successful physicians I have ever known, has assured me that he used more of bread pills,

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drops of colored water, and powders of hickory ashes, than of all other medicines put together.

Thomas Jefferson²

. . . nothing serious intended—a mere placebo—just a divertissement to cheer the spirits.

Sir Walter Scott¹

. . . an epithet given to any medication adopted more to please than benefit the patient

Hooper's *Medical Dictionary*³

It is a mere placebo—but there is every reason to please as well as cure our patients.

Principles of Medicine, Fogge and Rye-Smith¹

The concept of the placebo was limited to that of an inert medicine given with deception to placate or please the patient. There was no apparent perplexity on the part of physicians regarding why placebos worked, no questioning of the extent to which other specific medicines or treatments were actually placebos, no suspicion that a placebo effect existed for any circumstance other than in the giving of a known placebo. Even Richard Cabot's often-cited discussions of ethics and placebos in the first decade of the 1900s gave no hint of an understanding of placebos in some larger context; his remarks were limited entirely to the use of placebos as inert medicines, given knowingly by physicians to unsuspecting patients.⁴

Modern Placebo and Placebo Effect

The 1940s and early 1950s saw the development of a new use for placebos as well as the emergence of a new concept, the placebo effect, both within the context of clinical research. In the controlled trial, for the first time patients were given placebo, not for their own potential benefit, but for the benefit of someone else, the physician researcher. Surprising observations on the clinical consequences of administering placebos in the research setting entailed a new term, the *placebo effect*. Thus, although placebos were still defined as inert medicines or treatments, both inert and active therapies were observed to produce effects beyond their predicted physiologic properties. This

collection of unexplained consequences of administering placebos and active treatments became loosely known as the placebo effect.

Thoughtful physicians soon recognized that principles found in the use of placebos for research generalized to all of medical therapeutics. This recognition was presaged in a short review article by Pepper in 1945,⁵ and was well developed in work of Lasagna and colleagues (1954),⁶ Beecher (1955),⁷ and especially Modell,⁸ who in 1955 defined the "placebo reaction" quite simply as "the only single action which all drugs have in common."

Since the 1950s placebo effects have been found lurking in all sorts of specific therapies. A positive placebo effect may be elicited by an appropriate demeanor on the part of the physician, by the proper color, shape, or taste of medication, by the encouragement of positive expectation on the part of patients, by attention to the healing context of the medical visit (eg, diplomas displayed, physician wearing a white coat), all in addition to the (presumably) specific positive effect of the prescribed treatment. Brody and Waters⁹ have suggested that the act of diagnosis itself has important placebo effects. Thus the placebo effect may now be observed not only when using pure placebos, but in both the diagnosis and the treatment of all medical problems.

Research on placebo effects has been limited. Aside from a number of reviews and descriptive studies,¹⁰⁻¹² remarkably little has been written. Some researchers have attempted, without success, to identify "placebo reactors" with the objective of eliminating individuals so identified from the conduct of experimental trials, obviating the need for controls. With the exception of the demonstration of the role of endorphins in placebo-induced analgesia,¹³ mechanisms of placebo effects have been addressed only theoretically and philosophically. Brody, in his recent monograph on the subject of placebos,¹⁰ proposes the "meaning model" as a potential framework for understanding placebo effects. This model, in the tradition of medical anthropology established by Adler and Hammett¹⁴ and by Kleinman et al,¹⁵ suggests that patients and physicians work within a culturally determined healing context rich with symbolic implications for the outcome of care. This framework points the direction for future research, but does not suggest underlying mechanisms by which placebo effects are mediated.

Ethical issues in the use of placebos have received a good deal of attention. It is generally recognized that the use of placebos in the historical sense requires deception on the part of the physician.^{16,17} Yet even for modern specific therapies Brody proposed elicitation of the placebo effect by making the illness experience more understandable, by instilling a sense of caring and social support, and by increasing a feeling of mastery over the illness.¹⁸

Finally, the original definition of the placebo itself has been subtly altered in modern practice. Formerly, deception was a necessary concomitant of placebo administration, yet there are recent reports of giving placebos with full disclosure to patients, not only as part of randomized trials, but in actual therapeutic practice.¹⁹ Whether an inert substance given without deception to a patient constitutes effective therapy is something that perhaps only the patient may determine, but it certainly represents a change in the historical use of the word *placebo*.

The modern views of placebos and of placebo effects are thus very broad indeed. Placebos may be inert substances given with or without deception, and placebo effects, an enormous new category of explanation defined as any change in a patient's condition not attributable to some known mechanism, may be observed in any specific or nonspecific therapy.

The Problem

The gulf between the historical and modern views of placebos is vast. To the physician of 1850, a placebo was a prescribed inert substance that made the patient better, perhaps barely distinguishable from other common therapies in that the mechanism of action was not understood or even cared about. From the vantage point of the late 20th century it is easy to claim (as many have) that most nonplacebo therapy at the time owed its success to the placebo effect, since few then-popular remedies have withstood scientific scrutiny. Although placebo prescriptions are rarely given now, placebo effects are said to be observable any time patient meets physician. Thus today

placebos and placebo effects cover an immense number of observations not yet scientifically understood, leading to the unfortunate result that reference to the placebo effect neither clarifies nor explains, but only threatens to add another wastebasket of problems to a profession already possessing its share.

Several recent cases will add focus to the current problems in use of placebos and placebo effects:

Case 1. An experienced resident was video-monitored as he reassured an anxious young mother whose infant was having feeding problems. At the end of the visit, the mother was clearly relieved and reassured. When asked later to analyze his effectiveness, the resident seemed surprised by the question, answering, "I am a pretty good placebo."

Case 2. After being started on antidepressants a week earlier, a patient returned for follow-up. She was more relaxed and sleeping better, and was pleased with the effectiveness of the treatment. The physician explained that it was a placebo effect, since antidepressants are not effective until after three weeks of treatment. The patient was disappointed.

Case 3. A retired university professor returned a month after injection of a bursitis with a local anesthetic-steroid combination. He had experienced relief that lasted only two weeks and informed the physician that his early improvement must have been a placebo effect.

Case 4. Chronic pain patients are often prescribed "pain cocktails"—mixtures of analgesics and potentiators in a flavored base. The patients are usually not informed of the composition of the cocktail. Several patients have had their active medication reduced and finally eliminated from the cocktail, so that they take only the inactive vehicle. One or two have been informed that they are no longer on active drugs, but they insist on taking the cocktail anyway.

Case 5. A young man with depression gradually improved over four counseling visits with a resident whose approach was empathetic and supportive. The resident attributed her success in managing this patient to a placebo effect.

Case 6. In the course of a continuing medical education presentation to primary care physicians, an otolaryngologist referred several times to tonsillectomy as a good example of placebo surgery.

Case 7. A drug company changed the appearance of a popular drug used to treat arthritis. A patient on the "new" drug for a month complained that it did not work as well as the old and asked the physician if she might have been given a placebo by mistake.

There is little in common among these seven usages of placebos and the placebo effect. If anything, the placebo effect seems to be a handy, ambiguous term covering a variety of poorly understood happenstances in the course of medical events. In some of the cases, placebo effects are used as a synonym for psychological effects. Of more concern is that the placebo effect is in other cases used as an explanation itself, as if labeling something as such settles the issue.

Comment

The placebo effect needs to be seriously reconsidered. The concept now covers too many circumstances and is too often used imprecisely as a cover-up for muddled thinking. There is no evidence that what currently passes for placebo effects could not be further described in terms of psychology, medical anthropology, behavioral sciences, or even physiology and biochemistry. Invoking the placebo effect evades the issue.

Other than in research, placebos given with deception probably have no place in modern medical practice, and the placebo effect as a category of explanation may be an illusion owing its existence to a desire to leave a little romance and mystery to the art of medicine. As popularly used, the placebo effect is a comfortable old shoe, ready to be donned when rigorous analysis would require more thoughtful inquiry.

This discussion is not meant to suggest that what passes for placebo effects these days is not of interest. In fact, each of the usages presented in the cases above represents a fascinating vignette worthy of careful study. Further research, however, should pursue each issue separately, rather than assume that some common conceptual thread binds them together. There is certainly enough theoretical and empirical work available to justify specific study of placebo effects within the context of psychology, anthropology, and other sciences.

There may be a class of phenomena not covered by current sciences that is subsumed under modern usage of the placebo effect. It is honorable to refer to such events as "poorly understood," rather than to use the explanation of a placebo effect.

Finally, there can be no argument with suggestions made by recent writers to produce "placebo effects" without the use of placebos. Such strategies as encouraging positive expectation with specific therapy, explaining medical diagnosis and treatment within the patient's cultural experience, and bolstering social supports are sound medical interventions; but they may be practiced and studied without reference to the placebo effect.

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