

# New findings and old myths about the placebo effect

Dónal P. O'Mathúna, PhD

Attempts to understand the mysteries of placebos and the placebo effect have increased greatly in recent years. Some medical researchers view placebos as invaluable tools that allow them to learn about the efficacy of drugs and therapies, while others view placebos as means by which physicians manipulate patients with mysterious ailments. Placebos are necessary in clinical research to elucidate the effectiveness and safety of therapies and remedies. Groups must be compared to one another, and the placebo group is vital. This article defines the placebo effect, looks at the history of this phenomenon, clarifies myths surrounding the effect, and gives practical advice on using the effect to improve patient outcomes.

Key words: clinical trials, placebo, placebo effect, nocebo

Interest in placebos and understanding of the placebo effect have increased greatly in recent years. For many medical researchers, placebos are invaluable tools allowing much to be learned about drugs and therapies being investigated. But some view placebos less enthusiastically, seeing them as means by which frustrated physicians manipulate patients whose ailments they cannot, or will not, understand. Some patients are embarrassed to discover they responded to a placebo, fearing this will lead to them being perceived as gullible or stupid. Still others wonder that if they improved with a placebo, does that mean there was nothing “really” wrong with them in the first place? And then again, advocates of specific drugs or therapies recoil at the mention of the placebo effect, fearing it will lead to their favorite therapies being viewed as quackery or snake oil.

The connection between placebos and quackery is longstanding. So many physiologically inactive treatments have been used throughout the history of medicine that it has been claimed that “until very recently, the history of medical treatment was largely the history of the placebo effect.”<sup>1</sup> The recent interest in alternative medicine has contributed to renewed attention to the placebo effect. If a therapy brings improvement, and

there is no known physiological basis for that improvement, some would call that a placebo, by definition. Alternative medicine includes many therapies and remedies that are poorly understood, leading many to wonder if alternative therapists have somehow learned to make the most of the placebo effect.<sup>2</sup> Such interest led to the National Center for Complementary and

Alternative Medicine sponsoring a workshop on the placebo effect that received widespread recognition from many non-alternative authorities.<sup>3</sup>

Although placebos generally are well-respected in medical research, the value of the placebo effect in the clinic is only beginning to be acknowledged. Many of the reactions mentioned above are based on misconceptions and myths regarding placebos. These myths will be examined here, and evaluated based on the most recent research. Although much remains to be learned about the placebo effect, it has the potential to significantly impact healthcare outcomes, especially in such difficult-to-treat conditions such as pain and anxiety.

This recent research is producing a better understanding of what some call the mind-body connection: how one's thoughts and feelings impact one's physical health. In addition, more is being learned about how the interaction between patient and therapist impacts the patient. Through this, the “art of medicine” is being seen as not just something “nice” when the professional has some time to spare, but as an integral part of the healing dynamic of scientific medicine. “Placebo research and psychoneuroimmunology are beginning to clarify a role in which caring is no longer an act of compassion or indulgence but has everything to do with curing or, in the preferred modern term, ‘effectiveness.’”<sup>4</sup> The placebo effect is no longer

*Author Disclosure - According to ACCME and Research Practitioner policy, authors must disclose all associations with proprietary entities that may have a direct relationship to the subject matter of their presentation. Dónal P. O'Mathúna, PhD, has stated that he has no such associations.*

just an inconvenient set of subjective responses that interfere with the collection of good, hard research data. Rather, the placebo effect is being recognized as an important way by which healthcare professionals can promote caring and healing in their interactions with patients.

## Defining the placebo effect

Agreement over the definition of a placebo is much easier to find than agreement over a definition of the placebo effect. Placebos are tablets, injections, surgeries, or procedures that in-and-of themselves would not be expected to directly influence a patient's condition, symptoms, illness, or pain. And yet placebos do have these effects, which sometimes are viewed as placebo effects. For some, the causal connection is unimportant and all that matters is that the effects follow in time after administration of the placebo. However, the placebo effect is defined in at least 2 other ways.<sup>5</sup> The first of these is the effect of giving a placebo, or what is called the "treatment ritual." This is the idea that giving someone anything viewed as a remedy or therapy will lead to changes. Another definition is that the placebo effect is the sum of all those psychological processes that occur during an interaction between a healthcare professional and a patient. This is a very broad view of the placebo effect, raising the interesting implication that "a placebo effect does not require a placebo."<sup>6</sup>

Understanding the role of the placebo effect in any changes experienced after patients receive any therapy is complicated by several factors. People's symptoms and illnesses may improve due to a specific effect of the therapy on the illness. But improvements also may have more to do with the nature of the illness than the treatment.<sup>7</sup> Conditions such as pain, anxiety, multiple sclerosis, and many others normally fluctuate in their symptoms. Others, such as the cold or flu, improve spontaneously.

Another complicating factor is called "regression toward the mean." This phenomenon addresses the finding that intriguing results and fascinating conclusions from an initial study often are not found in later studies and underlies the importance of replicating measurements and studies. This statistical axiom represents the tendency of extreme values to move closer to the average upon repeated measurement. For example,

patients often come to doctors when their symptoms are worst. Thus, no matter what happens during the visit, the symptoms naturally will be somewhat better afterward. Similar things can happen in clinical trials, with the improvements ending up being ascribed to the placebo effect, when in fact they are more likely due to natural fluctuations. Some have even gone so far as to claim that "most improvements attributed to the placebo effect are actually instances of statistical regression."<sup>8</sup>

All of this means that efforts must be taken to ensure that the placebo effect is not defined so broadly that it includes all improvements after a therapy except those physiologically caused by the therapy.<sup>9</sup> This would define the placebo effect as more powerful than it actually is. As we will see, this has important implications for the design of research studies. The differences between a placebo group and the test treatment group may not necessarily be due only to the placebo effect. The true placebo effect is discovered by examining the differences between those who are in a placebo group and those who do not receive any treatment. This can be difficult to measure, and may add additional costs to a study. A common way to do this is by including a "waiting list control."

Patients randomly assigned to a "waiting list" group are told that they will be admitted to one of the study groups later. The pre-test clinical measurements are taken when they are placed on a waiting list at the beginning of the study, and then again when they are moved to one of the groups where they receive placebo or active treatment. These measurements allow changes due to natural variation and other factors to be measured, and allow the true placebo effect to be calculated.

Because of these complications and disagreements over definitions, a controversy is growing concerning whether or not the placebo effect is real. Some prefer to refer to the improvements experienced and observed by many as "non-specific effects."<sup>7</sup> (See *Table*.) Others continue to call them placebo effects, but limit them to those changes that occur due to the interpersonal interactions between healthcare professionals and the patients. In contrast with the physiological or pharmacological effects of a treatment, the placebo effects are those resulting from psychological and symbolic factors.<sup>6</sup> "These include physician attention, interest, and concern in a healing setting; patient

and physician expectations of treatment effects; the reputation, expense, and impressiveness of the treatment; and characteristics of the setting that influence patients to report improvement.”<sup>10</sup> As such, they constitute an important aspect of clinical practice, with the potential for significantly influencing people’s responses to any therapy.

### From humble humbug to powerful placebo, and back again?

The mid-1950s were important years in the history of the placebo. In 1954, the British medical journal, *Lancet*, published an editorial titled, “The Humble Humbug,” which described the dubious role of placebos in medicine. It concluded that a placebo was “a means of reinforcing a patient’s confidence in his recovery, when the diagnosis is undoubted and no more effective treatment is possible.”<sup>11</sup> The “humbug”

was that physicians could offer patients placebos when they believed none of their treatments would be truly effective. They would then know that by pretending to have effective treatments they could help their patients at least feel better. Thomas Jefferson (1743-1826) called this the “pious fraud,” noting that “one of the most successful physicians I have ever known has assured me that he used more bread pills, drops of coloured water, and powders of hickory ashes, than of all other medicines put together.”<sup>12</sup>

Such use of sugar pills and colored water underlies the meaning of the term. The word placebo in Latin means, “I shall please.” It was first used to refer to hired mourners at funerals because they would begin their wailing with Psalm 116:9, which in Latin states: *Placebo Domino in regione vivorum* (I shall please the Lord in the land of the living).<sup>6</sup> Just as mourners substituted for the grieving family, placebos would stand in for “real” medicines. By the early 1800s, the *Shorter Oxford Dictionary* defined a placebo as “a

medicine given more to please than to benefit the patient.”<sup>13</sup> Richard Cabot, a professor at Harvard Medical School, stated in 1903 that he was “brought up, as I suppose every physician is, to use placebo, bread pills, water subcutaneously, and other devices.... I doubt if there is a physician in this room who has not used them and used them pretty often.... I used to give them by the bushels.”<sup>14</sup>

This aspect of the placebo effect reflects the first way they have been used. It also brings with it much of the negative reaction people can have to the term. Few would find problems using placebos to truly please a patient, as in helping them feel better, especially when nothing else seems to work. But it seems too easy to move from this to frustrated practitioners condescendingly dishing out placebos to appease patients and get them out of their offices. Many prescriptions for antibiotics have been written for flu patients in this way, presumably with most benefits being ascribable to the placebo effect. With the current emphasis on informed consent, many raise ethical questions

**Table: Non-Specific Factors Complicating Reports on Placebo Effects**

Natural Course of Disease	Spontaneous remission
	Variation in symptoms
	Disease symptoms misinterpreted as due to placebo
	Regression to the mean
Treatment Effects	Other unreported treatments used
	Habituation to treatment
	Lingering effects of previous treatments
Research Effects	Improved investigator skill
	Poor methodology
	Subjective or objective outcomes
Patient Effects	Hawthorne effect
	Unreported lifestyle changes
Patient-Provider Interactions	Power of suggestion
	Expectations placed on subjects
	Non-verbal cues
	Unconscious conditioning

*Adapted from:* Kienle GS, Kiene H. The powerful placebo effect: fact or fiction. *J Clin Epidemiol.* 1997;50:1311-1318.  
Ernst E, Resch KL. Concept of true and perceived placebo effects. *BMJ.* 1995;311:551-553.

about giving patients placebos while apparently deceiving them into thinking these are active medications.

1955 saw the publication of another article that was to change the way placebos were viewed. Titled "The Powerful Placebo," and authored by the distinguished Harvard physician, Henry Beecher, it concluded "that placebos have a high degree of therapeutic effectiveness in treating subjective responses, decided improvement...being produced in  $35.2 \pm 2.2\%$  of cases."<sup>15</sup> Since that seminal article, the placebo effect has been regarded as a potent, yet mysterious force, "an entity with occult-like powers that could mimic potent drugs."<sup>14</sup> Placebos have become integral to the design of the gold standard in medical research: the randomized controlled trial.

However, re-analysis of placebo data, and Beecher's article in particular, has recently led some to wonder if the powerful placebo is actually "powerless."<sup>16</sup> This controversy will be examined below under the first of the myths regarding the placebo effect. The problem is that much remains poorly understood concerning the placebo effect. Such uncertainty leads to much speculation, some mistakes, and unfortunately the propagation of several myths concerning placebos. Some of these can be traced back to Beecher's original article. In spite of its importance and many insights, it contained a number of statements about the placebo effect that since have been revised or overturned. Clarification of these points based on more recent analyses and studies will help to correct past mistakes and lay a better foundation for the practical applications that will be proposed at the end of this paper.

## Myths about the placebo effect

### 1. One-third of patients respond well to placebos.

A common myth about the placebo effect is the claim that about one-third of patients will respond positively to any intervention because of the placebo effect. This claim can be traced back to Beecher's paper, which remains the most frequently cited article in discussions about the placebo effect.<sup>15</sup> Beecher randomly chose 15 studies involving a total of more than 1,000 patients and estimated the average percentage of subjects who were relieved satisfactorily by a placebo. This average was  $35.2 \pm 2.2\%$ . However, even within

Beecher's study, the effectiveness of the placebos ranged from 15% to 58%. An even wider range has been found in other studies. Roberts reviewed a number of treatments that once were believed to be effective, but subsequently were shown to work via the placebo effect.<sup>17</sup> These averaged an effectiveness of 70%, with some of the studies finding the placebo effective in 100% of people to whom it was given. Other studies reported no one benefiting from the placebo.

A recent re-analysis of Beecher's data has found serious problems. Two researchers obtained the original 15 studies used by Beecher and found that many of the improvements that Beecher classified as resulting from placebo effects actually were caused by other factors. For example, one of the studies Beecher used found that 35% of patients with the common cold reported improvements after 6 days of taking a placebo. Beecher classified these improvements as resulting from the placebo effect. However, these could have been due to the normal improvements experienced by people after 6 days with a cold. Even more problematic were mistakes in the presentation of data from the original studies. In a study of a cough medication, Beecher stated that 2 groups of 22 patients each were given lactose (the placebo), and that 36% of 1 group and 43% of the other group reported improvements due to the placebo effect. However, the original study reported no groups as large as 22 and no significant improvements with any placebo.<sup>7</sup> Mistakes were found in data Beecher took from 10 of the 15 studies.

The re-analysis reported that 14 of the 15 studies did not clearly demonstrate any placebo effect. The fifteenth study reported no information on its design so that Beecher's claims about it could not be assessed. The authors concluded: "Many factors and phenomena have been summed up under the terms 'placebo' and 'placebo effect,' without being placebos or effects of placebo administration.... Thus, 'The Powerful Placebo' turns out to be a fiction."<sup>7</sup>

Although this is an extreme reaction, other data do lend some support. A subsequent review examined the results of randomized controlled trials that had included both a placebo and a no-treatment group.<sup>16</sup> They found no significant effect from placebos as compared with no treatment. However, among sub-groups examined, there was a significant difference between



placebo and no-treatment with subjective outcomes and in the treatment of pain, but not with objective outcomes or treatment for any other condition. This review also found larger placebo effects in trials with smaller numbers of subjects. The aim of this review was to determine if placebos had a role in the clinic as a form of treatment, and they concluded against such use. They argued that reports of large placebo effects arise because of methodological problems that make it impossible to distinguish the effect of placebo from the natural course of the disease, regression to the mean, or patient-provider interactions.

Clearly, then, it is overly simplistic to claim that the placebo effect will lead to any treatment being effective for any particular proportion of its recipients. Some therapies for some conditions do appear to involve significant placebo effects. Much of the debate over whether the placebo is powerful or powerless can be traced to disagreements over terminology and the cause of resulting changes. Clinicians and patients have noted real changes after administration of inactive agents. Attributing the changes to the placebo itself commits the post hoc fallacy of assigning cause to the action most recently taken.<sup>2</sup> Several causes actually may have been involved and possibly interacted with one another.

Using placebos as clinical treatments, therefore, must grapple with the fact that “there is no evidence of a general and clinically important effect of placebo interventions.”<sup>5</sup> Yet even those who reviewed Beecher’s data and found no evidence of placebo effects did acknowledge the occurrence of “non-specific effects,” which they viewed as primarily “psychosomatic” arising out of interactions between patients and providers.<sup>7</sup> Promoting these effects may improve patient outcomes. But there is enough variation in results to conclude that claims that any therapy will bring improvements in one-third of patients are groundless. Different therapies vary in their placebo effects.

## **2. Certain types of patients respond well to placebos.**

Beecher believed some people were “reactors” to placebos and others were nonreactors. He hoped to use placebos most beneficially by identifying the personality characteristics of reactors. Earlier authors believed intelligence was one of those characteristics: “for some

unintelligent or inadequate patients life is made easier by a bottle of medicine to comfort their ego...that to decline to humour an elderly ‘chronic’ brought up on the bottle is hardly within the bounds of possibility.”<sup>11</sup> Beecher dismissed some of these ideas, showing that the placebo effect was not influenced by gender or intelligence. “There are, however, significant differences in attitudes, habits, educational background, and personality structure between consistent reactors and nonreactors.”<sup>15</sup>

Attempts to clarify what these personality traits might be have proved unfruitful. Beecher himself noted that 55% of his patients could not be classified consistently as either reactors or nonreactors. This since has been verified in numerous studies. If someone responds positively to a placebo, that should not be viewed as a negative evaluation of the patients’ intelligence or any other characteristic. Patients should be reminded of this if they fear being negatively labeled if they respond to a placebo. However, what has been demonstrated is that the extent of the placebo effect is influenced by certain factors in patients, such as their attitudes toward their health, their doctor, or their treatment, and how suggestible they are. All of these again point to the importance of the patient-therapist interaction.

## **3. Placebos are just sugar pills.**

Another common misconception is that placebos only come in the form of sugar pills or saline injections. Placebo effects have been observed with tablets, capsules, injections, ointments, medical instruments, surgery, and a host of other interventions. Some even would go so far as to suggest that inadvertent statements, or an unwary raising of the eyebrows, can cause a placebo effect—usually of the negative type in these situations. Basically, any medical intervention or interaction can involve placebo effects. Some evidence exists that more invasive procedures lead to larger placebo effects. For example, in studies of migraine medications, placebos given by subcutaneous injection had significantly greater effectiveness than placebos given orally.<sup>18</sup> These point to both the prevalence of these effects and the importance of understanding them more fully.

## **4. Placebos effects are short-lasting.**

Another myth is the idea that placebos have only

short-lasting effects. This often is tied into the idea that placebo effects arise from a positive environment surrounding the interaction between patient and professional. The myth is that once the patient leaves the office, the good feelings disappear as the placebo effect quickly wears off. However, this assumes that the placebo effect is a purely subjective psychological one. In fact, profound physiological changes can occur after a placebo. For example, ultrasound therapy after the extraction of molar teeth resulted in reduced pain, swelling, and face muscle spasms.<sup>19</sup> These objective changes were due to the placebo effect, broadly defined, since the results were the same whether the ultrasound instrument was turned on or off.

The long-term nature of the placebo effect was shown in studies of a surgical procedure called the internal mammary artery ligation. This was used during the 1950s to treat angina in the belief that the surgery increased blood flow to arteries supplying the heart. In a double-blind study, a small number of patients received this surgery while another group believed they were receiving the surgery, but only were given a skin incision.<sup>20</sup> Six months after the surgery, more than half the patients in each group reported significant improvements overall, and significant reduction in nitroglycerine use. A replication of this study monitored patients 1 year after their surgery.<sup>21</sup> Two-thirds of those in the group receiving the true surgery reported greater than 50% improvement in angina symptoms, while 100% of those who received the placebo surgery reported the same improvement. Clearly, placebo effects can be long-lasting.

### 5. Placebos cure imaginary illnesses.

One of the most painful myths about placebos is the claim that when people find relief through the placebo effect their illness must have been imagined. In other words, the illness or pain must have been "all in their heads." Subjective measurements, such as people's perception of pain, have been the focus of much placebo research. Pain is one of the conditions upon which placebos have a relatively large impact. It also has been noticed that conditions that are strongly influenced by stress are most amenable to the placebo effect. "Placebos seem to be most effective for highly anxious subjects, and placebo effects are often attributed to anxiety reduction and associated stress reduction."<sup>10</sup>

However, this is very different from claiming that placebos only relieve symptoms caused by stress. Even if an illness was caused by heightened stress or anxiety, this would not mean it was an imaginary illness. It could be as real as one caused by a microorganism or a trauma. However, placebos also have been shown to cause changes in numerous objective outcomes. Most recently, positron emission tomography (PET) has demonstrated increased dopamine release after placebo administration to people with Parkinson's disease.<sup>22</sup> PET scans also showed activation of the same area of the brain by both opioid analgesics and placebos, although the analgesic did provide greater pain relief.<sup>23</sup> Previous studies also have demonstrated that the opioid antagonist naloxone can abolish placebo effects.

Another study used an electromagnetic device alleged to bring pain relief.<sup>24</sup> The researcher rigged the instrument so that its lights and dials would give the appearance it was working, when in fact no magnetic field was being emitted. Of those who completed the study, 13% noted improvements in range of motion and existence of muscle spasm immediately after receiving the sham procedure. These outcomes were measured objectively by blinded physicians. Numerous other types of objective changes have been produced by placebos.

### 6. Placebos are the same as doing nothing.

With the increased attention given to placebos in clinical research, an unfortunate assumption has become prevalent amongst researchers. A search of Medline from 1987 to 1993 found 130 studies that referred to either a placebo control or an untreated control. In 52 of these (40%), the terms were used synonymously, which is incorrect. "These data show that many researchers are confused as to what constitutes a placebo response."<sup>25</sup> The problem is a view that a placebo is the same as no treatment. As noted earlier, changes after administration of a placebo could be caused by several non-specific factors other than the placebo effect.

During the 1950s, there was some debate over whether a placebo was the same as a "dummy" tablet. One authority distinguished a dummy tablet as "a form of treatment which is intended to have no effect.... A placebo is something which is intended to act through a psychological mechanism. It is an aid to

therapeutic suggestion, but the effect which it produces may be either psychological or physical.”<sup>13</sup> This distinction has been lost in the intervening years with the assumption that a placebo is the same as “doing nothing.” But there can often be a big difference.

For this reason, the best clinical trials will include a placebo group and a no-treatment group.<sup>9</sup> The placebo group captures the impact of the interactions between the researchers and subjects, and the effects of being involved in the research. Comparison with the test-treatment group will allow determination of the specific therapeutic benefit of the treatment above the placebo effect. Comparison between the no-treatment group and the placebo group will allow the natural course of the illness to be captured. This helps ensure that natural fluctuations in the course of the illness are not attributed to either the treatment or the placebo. Knowing that a placebo is not the same as doing nothing also can alleviate some of the anxiety felt about using placebos. In fact, some have wondered if the placebo effect occurs because placebos can stand as symbols for a physician saying, in effect, “I will take care of you.”<sup>15</sup>

## 7. Placebos can't do any harm.

Another serious misunderstanding about placebos is that they can't do any harm. This idea probably arose on the basis of the other myths that placebos only resolve imaginary problems and are the same as doing nothing. Negative effects that occur after administration of a placebo are called *nocebo* effects. A review of 109 research studies found that 19% of healthy volunteers given placebos in clinical studies had adverse *nocebo* reactions.<sup>26</sup> Beecher's seminar article included a section on toxic side effects of placebos. He himself had observed 35 different side effects, the most frequent of which were drowsiness, headache, fatigue, sensation of heaviness, and nausea.<sup>15</sup> In some of these studies, up to 50% of the placebo recipients had side effects. However, whether these effects are the direct result of the placebo administered, or indirect, non-specific effects, remains unclear.<sup>7</sup>

Studies continue to report *nocebo* effects, such as when research subjects were told a very mild electric current would be passed through their heads to determine whether it would cause mild headaches.<sup>27</sup> The subjects were told the focus of the research was to

examine natural means of relieving headaches. One group of subjects was told that the electric current had produced mild headaches in the past, and a second group was told the (non-existent) current might cause a mild headache. The researchers explained that the current would be too mild to feel, but they actually used no current at all. Regardless of which group the subjects were in, almost three-quarters of the subjects got headaches. This study demonstrates the role of suggestion in placebo effects.

Like placebo effects, *nocebo* effects can be severe and long-lasting. In a double-blind study, the impact of an electromagnetic device on pain was studied in 58 patients.<sup>24</sup> Each subject received 2 treatments with the magnet turned on, and 1 with it turned off (sham treatment). In all cases, the instrument was rigged to appear as if it was working, whether it actually did work or not. Overall, after receiving sham treatment, 17% of the patients had worsened pain, 10% had definitive improvement, and 73% had no change. Five subjects dropped out of the study after receiving only the sham therapy, reporting increased pain. Three of these people stated 6 months later that the treatment had made their pain permanently worse.

Much controversy has occurred recently regarding the ethics of placebo surgery. With this, patients undergo a surgical procedure except that the essential step in the surgery being evaluated is not performed in those receiving the placebo version. For example, transplantation of fetal brain cells into patients with Parkinson's disease was evaluated using a placebo where 4 small holes were bored into the subjects' skulls, but the fetal cells were not implanted. Surgical placebos clearly carry the same risks as those of any surgical procedure and also those of whatever anesthesia is used. The controversy led to the Council on Ethical and Judicial Affairs of the American Medical Association developing a position statement on the issue in 2002.<sup>28</sup> They concluded that placebo surgery could be justified when no other trial design will yield the needed information and when potential subjects are fully informed of all the risks. Using these type of criteria, some have deemed unethical the use of placebo surgery involving fetal tissue transplantation for Parkinson's disease,<sup>29</sup> and others have justified placebo surgery to investigate the effectiveness of arthroscopic surgery for osteoarthritis of the knee.<sup>30</sup>

The placebo can carry certain risks. Whatever the power of the placebo to do good, it also can do harm. The nocebo effect shows that suggestion can be the source of significant negative effects, and raises questions about how many side effects may occur because of nocebo effects.

## Practical application

After correcting for these myths, the placebo effect remains an important way in which patient outcomes can be improved. When placebos are believed to be merely inert tools for use in clinical research, important ways in which healthcare professionals can help their patients can be missed. Bedside manner and caring presence have been promoted as part of what traditionally is important in healthcare, or as part of providing healthcare ethically. Recent research on the placebo effect is revealing that these professional-patient interactions are also important factors in influencing patient outcomes.

An interesting study was conducted with 200 patients with a variety of relatively minor symptoms, but for whom a thorough examination led to no firm diagnosis.<sup>31</sup> The patients were randomly divided into 4 groups. Two of the groups received a "positive" interaction with the physician, with 1 of these groups getting a prescription for a placebo and the other receiving no treatment. The 2 other groups received a "negative" interaction, and then got either a placebo or no treatment. The "positive" interaction was one in which the patients were given a firm diagnosis and confidently told that they would be better in a few days. The "negative" interaction was one in which no firm assurance was given, including the statement, "I cannot be certain what is the matter with you." If these patients were to receive the placebo they also were told, "I am not sure that the treatment I am going to give you will have an effect."

Two weeks after this office visit, all patients were mailed a survey asking about their recovery. Of those who received the positive interaction, 64% said they had recovered. There was no difference between those who were treated and those who were not. Of those who received the negative interaction, 39% had recovered, again with no differences between those treated and not treated. However, given the natural

progression of the relatively minor illnesses that these patients had, 61% would have been expected to recover without medical help. Yet as a result of the negative interaction with the physician, many of these people remained ill. This study demonstrates very clearly the importance of being positive and generating hope in patients.

Yet the problem is that "a favorable therapeutic style requires the therapist's effort...the therapist must do the work of listening, perceiving, communicating, and giving of one's self in an appropriate manner."<sup>2</sup> The recent studies reveal that poorly understood non-specific effects do play a significant role in patient's health. Much of the controversy surrounds which of these effects should be called placebo effects. Regardless of how a placebo is defined, recent studies show that the interaction between patients and physicians or therapists can influence patient outcomes significantly. Therefore, time should be taken to maximize these interactions, not only because they are pragmatically useful, but also because they are central to the ethical practice of medicine.

## Conclusion

The placebo effect remains a mysterious phenomenon in human behavior. Some knowledge has been gained regarding its importance and usefulness. But much remains unknown about how it works or why. Its existence is a continued reminder of the intimate connection between mind and body, and the role of belief in healing. The beliefs and expectations of both patients and healthcare professionals, and the nature of their interactions, make a significant contribution to patient outcomes.

Placebos are central to high-quality clinical research to elucidate the effectiveness and safety of therapies and remedies. Groups must be compared to one another, and the placebo group is vital. However, changes in the placebo group are determined by more than just the placebo effect. To tease the placebo effect out from all these changes, a third group is needed in many studies: a no-treatment group. Comparing these 2 groups reveals more about the contribution of those non-specific, intangible factors also known by some as the placebo effect.



Practically speaking, healthcare professionals can increase the contribution of the placebo effect by promoting the art of medicine, in addition to the science of medicine. This also has been called the doctor's bedside manner or the nurse's caring presence. There are numerous practical ways in which this can be learned and promoted.<sup>4</sup> Availability to patients is important, and giving them the time they need. Being approachable, listening to patient's concerns, and empathizing with them are all important. This will serve to build trust, provide realistic hope, and bring reassurance that no matter what happens, someone they know will remain with them in their hour of need.

There also is a delicate art to using suggestion to influence patients' expectations and therefore the outcomes. This has to be done ethically so that unrealistic hopes are not built. In many ways, these are communication skills, which are of vital importance in healthcare. Obviously, these are complicated issues, and the task is daunting. This is probably at least part of the reason healthcare has drifted away from holistic care. But this is the essence of what medicine, nursing, and healthcare are all about. The following was stated regarding the role of physicians as healers, but it is equally applicable to nurses and other healthcare professionals. "The sheer difficulty of this role makes it all the more exciting, challenging, and important.... Not surprisingly, it has been said that 'some of the best brains should be in general practice because it is, of all the branches of medicine, the most difficult to do well.'"<sup>4</sup>

Learning to maximize the placebo effect would go a long way to promoting care of patients.

Dónal P. O'Mathúna, PhD

Professor of Bioethics and Chemistry

Mount Carmel College of Nursing, Columbus, OH

## References

- <sup>1</sup> Shapiro AK, Shapiro E. *The Powerful Placebo: From Ancient Priest to Modern Physician*. Baltimore and London: Johns Hopkins University Press; 1997.
- <sup>2</sup> Feinstein AR. Post-therapeutic response and therapeutic 'style': Re-formulating the 'placebo effect.' *J Clin Epidemiol*. 2002;55:427-429.
- <sup>3</sup> Russo E. The biological basis of the placebo effect. *Scientist*. 2002;16:30-31.
- <sup>4</sup> Dixon DM, Sweeney KG, Pereira Gray DJ. The physician healer: Ancient magic or modern science? *Br J Gen Pract*. 1999;49:309-312.
- <sup>5</sup> Hróbjartsson A. What are the main methodological problems in the estimation of placebo effects? *J Clin Epidemiol*. 2002;55:430-435.
- <sup>6</sup> de Craen AJM, Kaptchuk TJ, Tijssen JGP, Kleijnen J. Placebos and placebo effects in medicine: Historical overview. *J R Soc Med*. 1999;92:511-515.
- <sup>7</sup> Kienle GS, Kiene H. The powerful placebo effect: Fact or fiction. *J Clin Epidemiol*. 1997;50:1311-1318.
- <sup>8</sup> McDonald C, Mazzuca S, McCabe G. How much of the placebo 'effect' is really statistical regression? *Stat Med*. 1983;2:417-427.
- <sup>9</sup> Ernst E, Resch KL. Concept of true and perceived placebo effects. *BMJ*. 1995;311:551-553.
- <sup>10</sup> Turner JA, Deyo RA, Loeser JD, Von Korff M, Fordyce WE. The importance of placebo effects in pain treatment and research. *JAMA*. 1994;271:1609-1614.
- <sup>11</sup> Anonymous. The humble humbug. *Lancet*. 1954;ii:321.
- <sup>12</sup> Jefferson T. *The Writings of Thomas Jefferson*. Version 9, Ford PL, ed. New York: G. P. Putnam's, 1898; cited in Kaptchuk TJ. Powerful placebo: The dark side of the randomized controlled trial. *Lancet*. 1998;351:1722-1725.
- <sup>13</sup> Gaddum JH. Clinical pharmacology. *Proc R Soc Med*. 1954;47:195-204.
- <sup>14</sup> Kaptchuk TJ. Powerful placebo: The dark side of the randomized controlled trial. *Lancet*. 1998;351:1722-1725.
- <sup>15</sup> Beecher HK. The powerful placebo. *JAMA*. 1955;159:1602-1606.
- <sup>16</sup> Hróbjartsson A, Gøtzsche P. Is the placebo powerless? An analysis of clinical trials comparing placebo with no treatment. *N Engl J Med*. 2001;344:1594-1602.
- <sup>17</sup> Roberts AH, Kewman DG, Mercier L, Hovell M. The power of nonspecific effects in healing: Implications for psychosocial and biological treatments. *Clin Psychol Rev*. 1993;13:375-391.
- <sup>18</sup> de Craen AJM, Tijssen JGP, de Gans J, Kleijnen J. Placebo effect in the acute treatment of migraine: Subcutaneous placebos are better than oral placebos. *J Neurol*. 2000;247:183-188.
- <sup>19</sup> Hashish I, Feinman C, Harvey W. Reduction of postoperative pain and swelling by ultrasound: A placebo effect. *Pain*. 1988;83:303-311.
- <sup>20</sup> Cobb LA, Thomas GI, Dillard DH, Merendino KA, Bruce RA. An evaluation of internal-mammary-artery ligation by a double-blind technic. *N Engl J Med*. 1959;260:1115-1118.
- <sup>21</sup> Dimond EG, Kittle CF, Crockett JF. Comparison of internal mammary ligation and sham operation for angina pectoris. *Am J Cardiol*. 1960;5:483-486.

- 22 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;293:1164-1166.
- 23 Petrovic P, Kalso E, Petersson KM, Ingvar M. Placebo and opioid analgesia—imaging a shared neuronal network. *Science*. 2002;295:1737-1740.
- 24 Long DM, Uematsu S, Kouba RB. Placebo responses to medical device therapy for pain. *Stereotactic Functional Neurosurg*. 1989;53:149-156.
- 25 Ernst E, Resch KL. The importance of placebo effects [letter]. *JAMA*. 1995;273:283.
- 26 Rosenzweig P, Brohier S, Zipfel A. The placebo effect in healthy volunteers: Influence of experimental conditions on the adverse events profile during phase I studies. *Clin Pharmacol Ther*. 1993;54:578-583.
- 27 Schweiger A, Parducci A. Nocebo: The psychologic induction of pain. *Pavlovian J Biol Sci*. 1981;16:140-143.
- 28 Tenery R, Rakatansky H, Riddick F, Goldrich M, Morse L, O'Bannon J, Ray P, Smalley S, Weiss M, Kao A, Morin K, Maixner A, Seiden S. Surgical "placebo" controls. *Ann Surg*. 2002;235:303-307.
- 29 Clark P. Placebo surgery for Parkinson's disease: Do the benefits outweigh the risks? *J Law Med Ethics*. 2002;30:58-68.
- 30 Horng S, Miller FG. Is placebo surgery unethical? *N Engl J Med*. 2002;347:137-139.
- 31 Thomas KB. General practice consultations: Is there any point in being positive? *BMJ*. 1994;294:1200-1202.

**Submit an article to *Research Practitioner*  
Advertise in *Research Practitioner***

For more information,  
visit our Web site:  
[www.researchpractice.com](http://www.researchpractice.com)

## Subscribe to *Research Practitioner*

and earn 18 CE or CME credits a year

### Please enter my subscription to RP (6 issues annually):

- ☐ Individual subscription with nursing CE credit \$110\*
- ☐ Individual subscription with CME credit \$125\*
- ☐ Individual subscription without CE credit \$90\*
- ☐ Library rate \$165\*
- ☐ Group subscription (at least 10 subscribers)  
\$80\*/subscriber (call for details)

\*prices valid through Dec. 31, 2003

International subscriptions (add \$30)

### Payment (must be in U.S. funds):

- ☐ Check enclosed (payable to CCRP) ☐ P.O. # \_\_\_\_\_
- ☐ Credit: ☐ MC ☐ Visa ☐ AMEX ☐ Discover

Credit card number \_\_\_\_\_ Exp. date \_\_\_\_\_

Signature \_\_\_\_\_

### Mailing Address (please print):

Name \_\_\_\_\_

Company/Institution \_\_\_\_\_

Address \_\_\_\_\_

City/State/Postal code/Country \_\_\_\_\_

Phone \_\_\_\_\_

Fax \_\_\_\_\_

Email \_\_\_\_\_

### Subscribe:

Phone: 800.765.9647

Fax: 800.283.5967

Web: [www.ccrp.com](http://www.ccrp.com)

Mail: CCRP Subscriber Services  
PO Box 105109  
Atlanta, GA 30348-5109

**THOMSON**  
★  
CENTER FOR CLINICAL  
RESEARCH PRACTICE

RP/82160