The Placebo Effect

Colds, asthma, high blood pressure and heart disease are among the many conditions that can respond to treatment with a placebo.

Should doctors be prescribing sugar pills?

by Walter A. Brown

After a day of cross-country skiing in subfreezing weather a couple of years ago, I developed severe lower back pain. Even tying my shoes was agony. Despite my suffering, I knew there was no serious underlying disease, so I was certain I would be back to normal in no time.

But the days wore on with no change. A heating pad and suggestions from a friend with a chronic back problem (lie down, tuck your chin when you bend over) didn't help. After a week, I became desperate. I called my cousin Gary, who is a physical therapist. When I have consulted him in the past about sprains and tendonitis, his advice has always been on target. I was confident I was in the hands of an expert.

As usual, Gary was upbeat and authoritative. After taking my history and putting me through some maneuvers, he identified the muscles involved. He told me to ice the area, prescribed a set of exercises to stretch the constricted muscles and suggested that I take ibuprofen. When the consultation was over, I still had the back pain, but I had a technique for relieving it and the conviction that it would improve. Although my back was not yet better, I was.

I avoided the ibuprofen (it upsets my stomach), but I applied ice and exercised faithfully. Every time I did these things I felt a real sense of satisfaction. I was finally taking charge. Within two days the back pain had been reduced to a twinge; in a week it was gone.

I don't know whether the ice and exercise actually healed my inflamed, constricted muscles or whether they would have healed on their own in the same time. I do know that just seeking and receiving treatment made me feel better—less disabled, less distressed, more hopeful—and this in turn may have speeded my recovery. These benefits are called, often derisively, the placebo effect.

Powerful Healing

Medicine has become vastly more scientific in the past century—gone are the potions, brews and bloodlettings of antiquity. Nevertheless, doctors and their patients continue to ascribe healing powers to pills and procedures that have no intrinsic therapeutic value for the condition being treated (think of the widespread—and medically pointless—use of antibiotics to fight colds and flus caused by viruses). Some studies, including one by the U.S. Office of Technology Assessment, suggest that only about 20 percent of modern medical remedies in common use have been scientifically proved to be effective; the rest have not been subjected to empirical trials of whether or not they work and, if so, how. It is not that these treatments do not offer benefits: most of them do. But in some cases, the benefit may come from the placebo effect, in which the very act of undergoing treatment—seeing a medical expert, for instance, or taking a pill—helps the patient to recover.

Since the early 1980s, I have been investigating the placebo effect. In the course of my research, I have learned something about how placebos work, why they are disparaged by both patients and physicians, and who is most likely to benefit from them. My information on these matters is far from complete. But based on what is known, I believe that the placebo effect is a powerful part of healing and that more effort should be made to harness and enhance it.

My interest in the placebo effect began when my colleagues and I found something unexpected while investigating the biochemistry of depression. In 1984 we were testing patients for the hormone cortisol, which is produced by the adrenal gland. In previous work, we and others had found that about half the patients with severe clinical depression produced excessive amounts of the hormone. We thought this group of patients might do better taking antidepressants than depressed patients with normal levels of cortisol would. (We speculated that patients with a biochemical imbalance might respond better to a biochemical treatment.)

To test this idea, we recorded levels of cortisol in patients who were about to enter a study of a new antidepressant medication. Mihály Arató, a young Hungarian psychiatrist working in my

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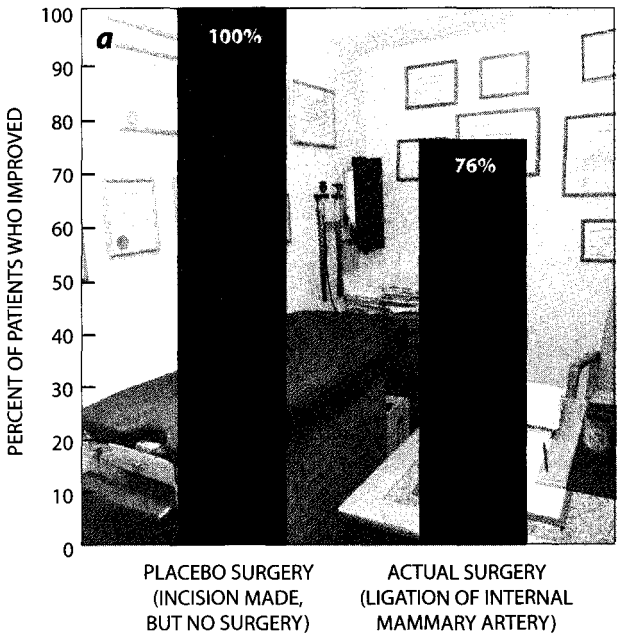
laboratory at the time, took on the job of analyzing the results. At first glance, the conclusions were disappointing. Contrary to our hypothesis, depressed patients responded equally well to the drug, regardless of how much hormone was present in their system. And yet they did show one fascinating difference.

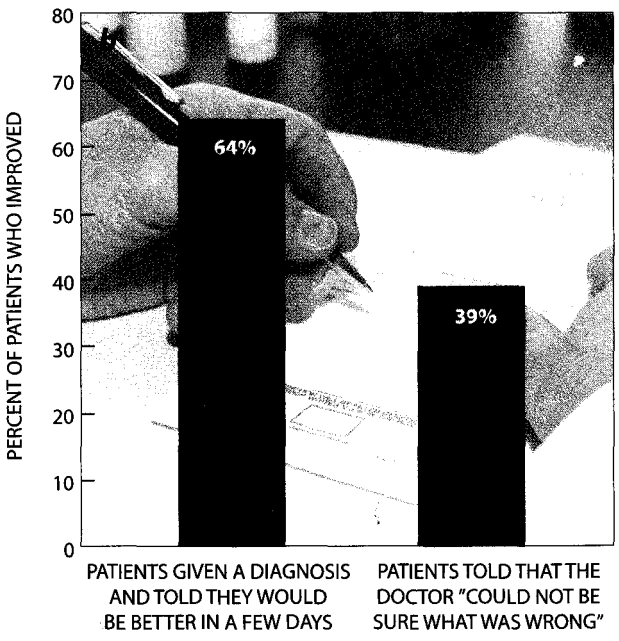
This research was part of a so-called double-blind study: some patients were treated with a placebo, and neither the doctors nor the patients knew who received the placebo and who received the antidepressant. When Arató examined the results from the placebo group, the outcome was striking. Typically 30 to 40 percent of depressed patients benefit from taking a placebo. In this case, close to half the 22 patients with normal levels of cortisol felt better after taking a placebo, but among the nine patients with elevated levels, none improved.

These findings, which have been confirmed in our lab and by other researchers, indicate that depressed patients who respond to placebos differ biochemically from those who do not. I wondered if they differed in other ways as well. As it turns out, they do. People suffering from short-term depression, lasting less than three months, for instance, are more likely to benefit from a placebo. But longer-term depression, lasting more

ANGINA PECTORIS: BENEFITS OF PLACEBO VS. SURGERY



GENERIC SYMPTOMS: BENEFITS OF DIAGNOSIS ALONE



than a year or so, often does not improve after placebo treatment.

Relieving Stress

The placebo effect is not unique to depression or psychiatric illness. A landmark study in the early 1950s by Henry K. Beecher of Harvard University suggested that for a wide range of afflictions, including pain, high blood pressure, asthma and cough, roughly 30 to 40 percent of patients experience relief after taking a placebo. In some cases, the response can be even more pronounced: researchers led by Edmunds G. Dimond of the University of Kansas Medical Center in the late 1950s investigated the effectiveness of the then routine arterial ligation surgery to treat angina pectoris (chest pain caused by insufficient blood supply to the heart). The doctors performed the surgical procedure in one set of 13 patients; with a second group of five patients, they made only a chest incision but did no further surgery. Among the patients who received the actual surgery, 76 percent improved. Notably, 100 percent of the placebo group got better. (Arterial ligation surgery is no longer performed.)

So what exactly is this placebo treatment that compares so favorably with conventional methods? Placebos are usually defined not in terms of what they are but what they are not. They are often described as inactive, but placebo agents are clearly active: they exert influence and can be quite effective in eliciting beneficial responses. Placebos are also described as nonspecific, presumably because they relieve multiple conditions and because exactly how they work is not fully understood. Yet by either of these standards, placebos are no less specific than many valid and accepted remedies, such as aspirin or certain tranquilizers. Most narrowly, a placebo is a pharmacologically inert capsule or injection, yet even this definition does not capture the full range of procedures that can have a placebo effect.

Today the most common situation in which people use substances known to be placebos is during double-blind clinical trials. Patients who take a placebo in the course of such trials receive much more than a pharmacologically inert substance: like the patients receiving a "real" drug, they benefit from a thorough medical evaluation, a chance to discuss their condition, a diagnosis and a plausible treatment plan. Patients also

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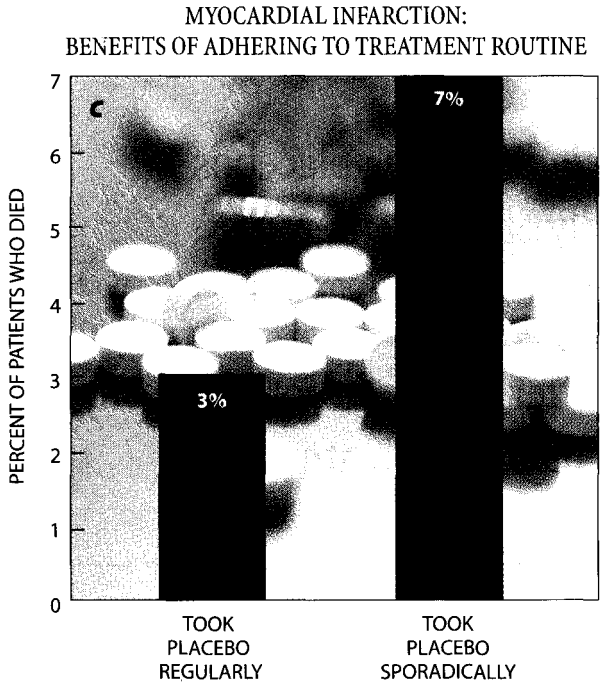

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PLACEBOS ARE EFFECTIVE for a variety of conditions. Patients with angina pectoris (insufficient blood flow to the heart) responded to placebo surgery in which doctors made only an incision in the chest but did nothing further (*a*). In a study of patients with generic symptoms but no organic ailment, researchers found that reassuring words from a doctor helped patients to feel better (*b*). And in a study of the drug propranolol, which is used after heart attacks to prevent further damage, investigators noticed that patients who took placebo pills regularly had a lower death rate than patients who took placebos sporadically (*c*).

typically enjoy the enthusiasm, effort, commitment and respect of their doctors and nurses. These factors, which many people view as incidental to the healing process, provide an important clue as to why placebos work.

The healing environment is a powerful antidote for illness. The decision to seek medical assistance restores some sense of control. The symbols and rituals of healing—the doctor's office, the stethoscope, the physical examination—offer reassurance. An explanation for the illness and a prognosis, when favorable, reduce fear; even when the report is unfavorable, it allays the anxiety of uncertainty. And merely the act of taking a pill can have a therapeutic effect. For example, the drug propranolol is often prescribed after a heart attack to regulate the heartbeat and prevent further damage. In a recent study of more than 2,000 patients, the death rate was cut in half among patients who took propranolol regularly compared with those who took the medication less regularly. But in the same study, patients who took placebos regularly also had half the death rate of those who took them less regularly—even though the two groups of placebo users were similar medically and psychologically.

Notably, placebos seem to be most reliably effective for afflictions in which stress directly affects the symptoms: in certain forms of depression and anxiety, for example, distress *is* the illness. And conditions such as pain, asthma and moderate high blood pressure can become worse when the patient is upset. Indeed, placebos may work in part by lessening the apprehension associated with disease. Studies of both animals and humans have shown that the functioning of the immune system falters under stressful conditions. For instance, stress increases the secretion of hormones such as cortisol, which in turn lowers resistance to disease. It is not inconceivable that by reducing anxiety, placebos could influence countless diseases, including some that we do not usually think of as subject to psychological influence.

Great Expectations

A patient's expectation of improvement is also crucial. Researchers know that across a wide range of illnesses, patients who think they will feel better are more likely to do so. Expectation operates more specifically as well. For example, when participants in a study were told that their pharmacologically inert drink contained alcohol, they often felt and acted intoxicated and even showed some of the physiological signs of intoxication. A 1968 study led by Thomas J. Luparello of the State University of New York Downstate Medical Center in Brooklyn showed that patients with asthma who were given an inhaler containing only nebulized saltwater but were told they would be inhaling an irritant or allergen displayed more problems with airway obstruction. When the same group was told that the inhaler had a medicine to help asthma, their airways opened up.

Given their demonstrated effectiveness, why do placebos have such a dubious reputation? The word "placebo" itself comes with unfortunate baggage. Latin for "I shall please," it is the first word of the vespers for the dead, and in the 12th century these vespers were commonly referred to as placebos. By the 1300s, the term had become secular and pejorative, suggesting a flatterer or sycophant, a meaning probably derived from the depreciation of professional mourners, those paid to sing placebos. When the word entered medical terminology, the negative connotation stuck. It was defined as a medicine given to please patients rather than to benefit them. In the modern era, the lack of pharmacological activity became part of the definition as well.

As a result, the name brings with it connotations of deception and inauthenticity. A modern myth about placebos reflects this stigma: if a condition improves with placebos, the condition is supposedly "all in the head." But the many examples of physical ailments—high blood pressure, angina pectoris and asthma, to name a few—that respond to placebos demonstrate that this notion is far from the case.

The very effectiveness of a placebo is troublesome to us doctors and to other medical experts. It impugns the value of

ABRAHAM MENASHE (*photographs*); JENNIFER C. CHRISTIANSEN (*graphs*); SOURCES: (*a*) E. G. DIMOND ET AL., 1960; (*b*) K. B. THOMAS, 1987; (*c*) R. I. HORWITZ, 1990

our most cherished remedies, it hampers the development of new therapeutics, and it threatens our livelihood. Nevertheless, given the astounding advances in medical technology over the past two decades, including the development of indisputably efficacious drugs and procedures, we in the medical community may now be ready—secure that medicine is scientific—to accept and put to good use this component of healing that we do not fully understand.

Decades of research offer guidance as to how physicians can incorporate aspects of the placebo effect, in ways that are both medically and ethically sound, to make accepted medicines more effective. Yet many of these ideas have not been tried by doctors. Some of the suggestions are not surprising. For instance, patients should be made to feel confident and secure that they are in the hands of a recognized healer; diplomas, board certifications and medical instruments in sight generally provide these signals. Patients should also be reassured by items associated with the relief of symptoms—a white coat, a physical examination, a written prescription when necessary. A careful analysis of a patient's complaint is far more comforting than an immediate diagnosis, no matter how accurate.

Administering a thorough evaluation, however, does not mean that a patient should be subjected to unnecessary diagnostic procedures. Rather the doctor should listen carefully, ask suitable questions and perform a complete examination. The fact that someone has bronchitis may be obvious to a doctor within seconds; an additional five minutes of evaluation that includes a stethoscope on the chest may not add to the accuracy of the diagnosis, but it does add to the patient's confidence. Physicians and nurses of yesterday seemed to understand intuitively the importance of a good bedside manner. Many of today's medical experts still appreciate the healing power of a compassionate consultation, but under pressure to provide "cost-effective" care, they (and particularly insurance companies) may be losing sight of this crucial component of effective care.

The initial evaluation should include specific questions regarding the patient's previous experiences with a variety of remedies, including treatments (such as alternative therapies) most physicians consider to be placebos. What has worked and what has not for this person? In particular, the doctor or nurse should elicit the patient's ideas about what might or might not be helpful for the present complaint.

If physicians can see placebos as broadly effective therapies, whose mechanisms of action are not completely understood and which tend to be more effective for some conditions than others, they can then offer placebos both honestly and as plausible treatment.

Determining a Diagnosis

The physician should provide a diagnosis and a prognosis whenever possible. In a recent study of 200 patients with physical complaints but no identifiable disease, doctors at the University of Southampton in England told some that no serious disease had been found and that they would soon be well; others heard that the cause of their ailment was unclear. Two weeks later 64 percent of the first group had recovered, but only 39 percent of the second group had recuperated.

If a specific drug or medical procedure is called for, it should be offered with realistic optimism and information about its specific desirable effects—something along the lines of "This medicine will help you breathe" for an asthma medication. The doctor should also provide information about side effects and about the most likely course of symptoms. This information adds to the patient's confidence and to the sense that the condition is known and controllable.

If a number of treatment options are equally appropriate, the patient should be given the chance to make a choice. But doctors should offer a limited number of options (no more than three or four) and should provide sound information to help the patient in making the decision. Allowing patients—no matter how well informed they may be—to choose whatever course of therapy they would like deprives them of a major benefit of seeking medical advice. If people want to treat themselves, and many do, they do not go to experts.

When managing conditions such as the common cold that typically run their course without treatment or when handling diseases such as certain cancers that have no effective treatment, doctors often prescribe palliative medication to relieve symptoms such as congestion or pain. For these therapies to be most useful, however, it is important that doctors offer them with the same thoughtfulness and authority as when they recommend other, more definitive remedies.

In practice, though, this is not always the case. Doctors often tell patients with colds or the flu that they will probably feel better in a few days and that they can take cold medicine if they want to. Such patients, feeling miserable and bereft of treatment, often request and receive antibiotics—pharmacologically active but inappropriate drugs that they are unwittingly using as placebos. These same patients would very likely feel quite differently if, after a medical examination complete with diagnostic instruments, their doctors wrote the name of a cold medicine on a prescription form (even if the drug did not require a prescription) and handed it to them with

instructions on how and over what interval this medicine will be helpful.

Some of these suggestions may seem like hocus-pocus. Yet I see them as an approach to medicine informed by an understanding of all the processes involved in healing. In the case of the common cold, such an approach could go a long way toward reducing the unnecessary use of antibiotics and the attendant expense and dangers of the practice.

Prescribing Placebos

What about the deliberate use of placebos? Should physicians, in order to take advantage of the placebo effect, prescribe drugs or procedures that they know to be of no intrinsic value?

For many medical experts, this situation presents what has seemed an insolvable dilemma. Doctors have felt that if they tell patients they are prescribing a sugar pill, the placebo response, which depends in part on patients' expectations of receiving a plausible remedy, will be lost. On the other hand, if doctors tell patients that the placebo is a pharmacologically active medicine, they are engaging in a type of deception that is neither ethical nor, in the long run, therapeutic. I think much of this dilemma arises from the pejorative connotations associated with placebos and a general uncertainty about their value.

If physicians can see placebos—like many conventional drugs—as broadly effective therapies, whose mechanisms of action are not completely understood and which tend to be more effective for some conditions than others, they can then offer placebos both honestly and as plausible treatment. The decision to prescribe a placebo should be based, as with any drug, on the risks and benefits. The specific placebo chosen should be free of toxicity and should be in keeping with the patient's beliefs and expectations. In this regard, it is worth noting that, according to a study published in 1993 in the *New England Journal of Medicine,* at least 30 percent of adult Americans use alternative medicine—such as massage, homeopathy, spiritual healing and megavitamins—and that the total number of visits to alternative therapy providers each year exceeds the number of visits to primary care physicians. Although alternative medicine healers and their patients believe fervently in the effectiveness of megavitamins and herbal mixtures, many of these popular remedies probably derive their benefit from the placebo effect.

So how can a doctor ethically prescribe a placebo? Consider a specific example—the treatment of mild to moderately high blood pressure. Clinical trials, such as the study conducted in the early 1990s by Barry J. Materson of the Veterans Affairs Medical Center in Miami, have shown that at least 20 percent of people with this condition achieve normal blood pressure after several weeks of taking placebos. Because blood pressure medication is expensive and has troublesome side effects, some patients might want to consider taking a placebo as a course of treatment.

A doctor could explain the situation to a patient in the following manner: "You have several options. One is to take a diuretic. It will probably bring your blood pressure down, but it does have some side effects. There are also other treatments that are less expensive and less likely to cause side effects and that help many people with your condition. Some find that herbal tea twice a day is helpful; others find that taking these pills twice a day is helpful. These pills do not contain any drug. We do not know how the herbal tea or these pills work. They may trigger or stimulate your body's own healing processes. We do know that about 20 percent of the people with your type of high blood pressure get their blood pressure into the normal range using this approach. If you decide to try one of these treatments, I will check your progress every two weeks. If after six weeks your blood pressure is still high, we should consider the diuretic."

Disease is typically defined as an abnormal state of the body—high blood glucose, a fractured forearm, a lung infection. But illness is something else: it is the suffering that accompanies disease. In our culture, pills and other symbols of the physician's healing arts have great power to ease that suffering. As physicians, we should respect the benefits of placebos—their safety, effectiveness and low cost—and bring the full advantage of these benefits into our everyday practices. SA

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Further Reading

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