

Why do we need all these clever tricks, these special research paradigms? The answer is easy: the world is much more complicated than simple stories about pills making people get better. We are human, we are irrational, we have foibles, and the power of the mind over the body is greater than anything you have previously imagined.



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## THE PLACEBO EFFECT

For all the dangers of complementary and alternative medicine, to me the greatest disappointment is the way it distorts our understanding of our bodies. Just as the big bang theory is far more interesting than the creation story in Genesis, so the story that science can tell us about the natural world is far more interesting than any fable about magic pills concocted by an alternative therapist. To redress that balance, I'm offering you a whirlwind tour of one of the most bizarre and enlightening areas of medical research: the relationship between our bodies and our minds, the role of meaning in healing, and in particular the placebo effect.

Much like quackery, placebos became unfashionable in medicine once the biomedical model started to produce tangible results. An editorial in 1890 sounded its death knell, describing the case of a doctor who had injected his patient with water instead of morphine; she recovered perfectly well, but then discovered the deception, disputed the bill in court, and won. The editorial was a lament, because doctors have known that reassurance and a good bedside manner can be very effective for as long as medicine has existed. "Shall [the placebo] never again have an opportunity of

exerting its wonderful psychological effects as faithfully as one of its more toxic conveners?" asked the *Medical Press* at the time.

Luckily, its use survived. Throughout history, the placebo effect has been particularly well documented in the field of pain, and some of the stories are striking. Henry Beecher, an American anesthetist, wrote about operating on a soldier with horrific injuries in a World War II field hospital, using salt water because the morphine was all gone, and to his astonishment the patient was fine. Peter Parker, an American missionary, described performing surgery without anesthesia on a Chinese patient in the mid-nineteenth century; after the operation, she "jumped upon the floor," bowed, and walked out of the room as if nothing had happened.

Theodor Kocher performed sixteen hundred thyroidectomies without anesthesia in Switzerland in the 1890s, and I take my hat off to a man who can do complicated neck operations on conscious patients. Mitchel in the early twentieth century was performing full amputations and mastectomies, entirely without anesthesia; and surgeons from before the invention of anesthesia often described how some patients could tolerate knife cutting through muscle, and saw cutting through bone, perfectly awake and without even clenching their teeth. You might be tougher than you think.

These are just stories, and the plural of "anecdote" is not data. Everyone knows about the power of the mind—whether it's stories of mothers enduring biblical pain to avoid dropping a boiling kettle on their babies or people lifting cars off their girlfriends like the Incredible Hulk—but devising an experiment that teases the psychological and cultural benefits of a treatment away from the biomedical effects is trickier than you might think. After all, what do you compare a placebo against? Another placebo? Or no treatment at all?

## THE PLACEBO ON TRIAL

In most studies we don't have a "no treatment" group to compare both the placebo and the drug with, and for a very good ethical reason: if your patients are ill, you shouldn't be leaving them untreated simply because of your own mawkish interest in the placebo effect. In fact, in most cases today it is considered wrong even to use a placebo in a trial; whenever possible you should compare your new treatment with the best preexisting, current treatment.

This is not just for ethical reasons (although it is enshrined in the Declaration of Helsinki, the international ethics bible). Placebo-controlled trials are also frowned upon by the evidence-based medicine community, because it knows it's an easy way to cook the books and get easy positive trial data to support your company's big new investment. In the real world of clinical practice, patients and doctors aren't so interested in whether a new drug works better than *nothing*; they're interested in whether it works *better than the best treatment they already have*.

There have been occasions in medical history when researchers were more cavalier. The Tuskegee Syphilis Study, for example, is one of America's most shaming hours: 399 poor, rural African-American men were recruited by the U.S. Public Health Service in 1932 for an observational study to see what happened if syphilis was left, very simply, untreated. Astonishingly, the study ran right through to 1972. In 1949 penicillin was introduced as an effective treatment for syphilis. These men did not receive that drug, nor did they receive Salvarsan, nor indeed did they receive an apology until 1997, from Bill Clinton.

If we don't want to do unethical scientific experiments with "no treatment" groups on sick people, how else can we determine the size of the placebo effect on modern illnesses? First, and rather ingeniously, we can compare one placebo with another.

The first experiment in this field was a meta-analysis by Daniel Moerman, an anthropologist who has specialized in the placebo effect. He took the trial data from placebo-controlled trials of gastric ulcer medication, which was his first cunning move, because gastric ulcers are an excellent thing to study: their presence or absence is determined very objectively, with a gastroscopy camera passed down into the stomach, to avoid any doubt.

Moerman took only the placebo data from these trials, and then, in his second ingenious move, from all these studies, of all the different drugs, with their different dosing regimes, he took the ulcer-healing rate from the placebo arm of trials in which the placebo treatment was two sugar pills a day, and compared that with the ulcer-healing rate in the placebo arm of trials in which the placebo was four sugar pills a day. He found, spectacularly, that four sugar pills are better than two (these findings have also been replicated in a different data set, for those who are switched on enough to worry about the replicability of important clinical findings).

### WHAT THE TREATMENT LOOKS LIKE

So four pills are better than two, but how can this be? Does a placebo sugar pill simply exert an effect like any other pill? Is there a dose response curve, as pharmacologists would find for any other drug? The answer is that the placebo effect is about far more than just the pill; it is about the cultural meaning of the treatment. Pills don't simply manifest themselves in your stomach; they are given in particular ways, they take varying forms, and they are swallowed with expectations, all of which have an impact on a person's beliefs about his own health and, in turn, on outcome. Homeopathy is, for example, a perfect example of the value in ceremony.

I understand this might well seem improbable to you, so I've corralled some of the best data on the placebo effect into one place,

and the challenge is this: see if you can come up with a better explanation for what is, I guarantee, a seriously strange set of experimental results.

First up, Blackwell (1972) did a set of experiments on fifty-seven college students to determine the effect of color—as well as the number of tablets—on the effects elicited. The subjects were sitting through a boring hourlong lecture and were given either one or two pills, which were either pink or blue. They were told that they could expect to receive either a stimulant or a sedative. Since these were psychologists, and this was back when you could do whatever you wanted to your subjects—even lie to them—the treatment that *all* the students received consisted simply of sugar pills, but of different colors.

Afterward, when they measured alertness—as well as any subjective effects—the researchers found that two pills were more effective than one, as we might have expected (and two pills were better at eliciting side effects too). They also found that color had an effect on outcome: the pink sugar tablets were better at maintaining concentration than the blue ones. Since colors in themselves have no intrinsic pharmacological properties, the difference in effect could only be due to the cultural meanings of pink and blue: pink is alerting; blue is cool. Another study suggested that oxazepam, a drug similar to Valium (which was once unsuccessfully prescribed by our doctor for me as a hyperactive child) was more effective at treating anxiety in a green tablet and more effective for depression when yellow.

Drug companies, more than most, know the benefits of good branding; they spend more on PR, after all, than they do on research and development. As you'd expect from men of action with large houses in the country, they put these theoretical ideas into practice, so Prozac, for example, is white and blue, and in case you think I'm cherry-picking here, a survey of the color of pills currently on the market found that stimulant medication tends to

come in red, orange, or yellow tablets, while antidepressants and tranquilizers are generally blue, green, or purple.

Issues of form go much deeper than color. In 1970 a sedative—chloridiazepoxide—was found to be more effective in capsule form than pill form, even for the very same drug, in the very same dose; capsules at the time felt newer, somehow, and more sciencey. Maybe you've caught yourself splashing out and paying extra for ibuprofen capsules in the pharmacy.

Route of administration has an effect as well: saltwater injections have been shown in three separate experiments to be more effective than sugar pills for blood pressure, for headaches, and for postoperative pain, not because of any physical benefit of saltwater injection over sugar pills—there isn't one—but because, as everyone knows, an injection is a much more dramatic intervention than just taking a pill.

Closer to home for the alternative therapists, the *British Medical Journal* recently published an article comparing two different placebo treatments for arm pain, one of which was a sugar pill, and one of which was a ritual, a treatment modeled on acupuncture. The trial found that the more elaborate placebo ritual had a greater benefit.

But the ultimate testament to the social construction of the placebo effect must be the bizarre story of packaging. Pain is an area where you might suspect that expectation would have a particularly significant effect. Most people have found that they can take their minds off pain—to at least some extent—with distraction, or have had a toothache that got worse with stress.

Branthwaite and Cooper did a truly extraordinary study in 1981, looking at 835 women with headaches. It was a four-armed study, in which the subjects were given either aspirin or placebo pills, and these pills in turn were packaged either in blank, bland, neutral boxes or in full, flashy, brand-name packaging. They found—as you'd expect—that aspirin had more of an effect on headaches

than sugar pills, but more than that, they found that the packaging itself had a beneficial effect, enhancing the benefit of both the placebo and the aspirin.

People I know still insist on buying brand-name painkillers. As you can imagine, I've spent half my life trying to explain to them why this is a waste of money, but in fact, the paradox of Branthwaite and Cooper's experimental data is that they were right all along. Whatever pharmacology theory tells you, that brand-named version is better, and there's just no getting away from it. Part of that might be the cost; a recent study looking at pain caused by electric shocks showed that a pain relief treatment was stronger when subjects were told it cost \$2.50 than when they were told it cost 10 cents. (And a paper currently in press shows that people are more likely to take advice when they have paid for it.)

It gets better—or worse, depending on how you feel about your worldview slipping sideways. Montgomery and Kirsch (1996) told college students they were taking part in a study on a new local anesthetic called trivaricaine. Trivaricaine is brown, you paint it on your skin, it smells like a medicine, and it's so potent you have to wear gloves when you handle it: or that's what they implied to the students. In fact, it's made of water, iodine, and thyme oil (for the smell), and the experimenters (who also wore white coats) were using rubber gloves only for a sense of theater. None of these ingredients will affect pain.

The trivaricaine was painted onto one or other of the subjects' index fingers, and the experimenters then applied painful pressure with a vise. One after another, in varying orders, pain was applied, trivaricaine was applied, and as you would expect by now, the subjects reported less pain, and less unpleasantness, for the fingers that were pretreated with the amazing trivaricaine. This is a placebo effect, but the pills have gone now.

It gets stranger. Sham ultrasound is beneficial for dental pain, placebo operations have been shown to be beneficial in knee pain

(the surgeon just makes fake keyhole surgery holes in the side and mucks about for a bit as if she were doing something useful), and placebo operations have even been shown to improve angina.

That's a pretty big deal. Angina is the pain you get when there's not enough oxygen getting to your heart muscle for the work it's doing. That's why it gets worse with exercise: because you're demanding more work from the heart muscle. You might get a similar pain in your thighs after bounding up ten flights of stairs, depending on how fit you are.

Treatments that help angina usually work by dilating the blood vessels to the heart, and a group of chemicals called nitrates are used for this purpose very frequently. They relax the smooth muscle in the body, dilating the arteries so more blood can get through (they also relax other bits of smooth muscle in the body, including your anal sphincter, which is why a variant is sold as "liquid gold" in sex shops).

In the 1950s there was an idea that you could get blood vessels in the heart to grow back, and thicker, if you tied off an artery on the front of the chest wall that wasn't very important, but that branched off the main heart arteries. The idea was that this would send messages back to the main branch of the artery, telling it that more artery growth was needed, so the body would be tricked.

Unfortunately this idea turned out to be nonsense, but only after a fashion. In 1959 a placebo-controlled trial of the operation was performed: in some operations they did the whole thing properly, but in the "placebo" operations they went through the motions but didn't tie off any arteries. It was found that the placebo operation was just as good as the real one—people seemed to get a bit better in both cases, and there was little difference between the groups—but the strangest thing about the whole affair was that nobody made a fuss at the time. The real operation wasn't any better than a sham operation, sure, but how could we explain the

fact that people had been sensing an improvement from the operation for a very long time? Nobody thought of the power of placebo. The operation was simply binned.

That's not the only time a placebo benefit has been found at the more dramatic end of the medical spectrum. A Swedish study in the late 1990s showed that patients who had pacemakers installed but not switched on did better than they had been doing before (although they didn't do as well as people with working pacemakers inside them, to be clear). Even more recently, one study of a very hi-tech "angioplasty" treatment, involving a large and sciencey-looking laser catheter, showed that sham treatment was almost as effective as the full procedure.

"Electrical machines have great appeal to patients," wrote Dr. Alan Johnson in *The Lancet* in 1994 about this trial, "and recently anything to do with the word LASER attached to it has caught the imagination." He's not wrong. I went to visit an alternative therapist once, and she did gem therapy on me, with a big shiny science machine that shone different-colored beams of light onto my chest. It's hard not to see the appeal of things like gem therapy in the context of the laser catheter experiment. In fact, the way the evidence is stacking up, it's hard not to see all the claims of alternative therapists, for all their wild, wonderful, authoritative, and empathic interventions, in the context of this chapter.

In fact, even the lifestyle gurus get a look in, in the form of an elegant study that examined the effect of simply being told that you are doing something healthy. Eighty-four female room attendants working in various hotels were divided into two groups. One group was told that cleaning hotel rooms is "good exercise" and "satisfies the Surgeon General's recommendations for an active lifestyle," along with elaborate explanations of how and why; the "control" group did not receive this cheering information and just carried on cleaning hotel rooms. Four weeks later, the "informed" group perceived themselves to be getting significantly

more exercise than before and showed a significant decrease in weight, body fat, waist-to-hip ratio, and body mass index, but amazingly, both groups were still reporting the same amount of activity.\*

### WHAT THE DOCTOR SAYS

If you can believe fervently in your treatment, even though controlled tests show that it is quite useless, then your results are much better, your patients are much better, and your income is much better too. I believe this accounts for the remarkable success of some of the less gifted, but more credulous members of our profession, and also for the violent dislike of statistics and controlled tests which fashionable and successful doctors are accustomed to display.

—Richard Asher, *Talking Sense*, Pitman Medical, 1972

As you will now be realizing, in the study of expectation and belief, we can move away from pills and devices entirely. It turns out, for example, that both what the doctor says and what the doctor believes have an effect on healing. If that sounds obvious, I should say they have an effect that has been measured, elegantly, in carefully designed trials.

Gryll and Katahn (1978) gave patients a sugar pill before a dental injection, but the doctors who were handing out the pill gave it in one of two different ways: either with an outrageous oversell (“This is a recently developed pill that’s been shown to be very effective . . . effective almost immediately . . .”) or downplayed, with an undersell (“This is a recently developed pill . . . personally I’ve

\*I agree: this is a bizarre and outrageous experimental finding, and if you have a good explanation for how it might have come about, the world would like to hear from you. Follow the reference, read the full paper online, and start a blog, or write a letter to the journal that published it.

not found it to be very effective . . .”). The pills that were handed out with the positive message were associated with less fear, less anxiety, and less pain.

Even if he says nothing, what the doctor knows can affect treatment outcomes; the information leaks out, in mannerisms, affect, eyebrows, and nervous smiles, as Gracely (1985) demonstrated with a truly ingenious experiment, although understanding it requires a tiny bit of concentration.

He took patients having their wisdom teeth removed, and split them randomly into three treatment groups: they would have salt water (a placebo that does “nothing,” at least not physiologically) or fentanyl (an excellent opiate painkiller, with a black-market retail value to prove it), or naloxone (an opiate receptor blocker that would actually increase the pain).

In all cases the doctors were blinded to which of the three treatments they were giving to each patient, but Gracely was *really* studying the effect of his doctors’ beliefs, so the groups were further divided in half again. In the first group, the doctors giving the treatment were told, truthfully, that they could be administering placebo, or naloxone, or the pain-relieving fentanyl; this group of doctors knew there was a chance that they were giving something that would reduce pain.

In the second group, the doctors were lied to; they were told they were giving either placebo or naloxone, two things that could only do nothing or actively make the pain worse. But in fact, without the doctors’ knowledge, some of their patients were actually getting the pain-relieving fentanyl. As you would expect by now, just through manipulation of what the *doctors believed* about the injections they were giving, even though they were forbidden from vocalizing their beliefs to the patients, there was a difference in outcome between the two groups. The first group experienced significantly less pain. This difference had nothing to do with what actual medicine was being given or even with

what information the patients knew; it was entirely down to what the doctors knew. Perhaps they winced when they gave the injection. I think you might have.

## PLACEBO EXPLANATIONS

Even if they do nothing, doctors, by their manner alone, can reassure. And even reassurance can in some senses be broken down into informative constituent parts. In 1987, Thomas showed that simply giving a diagnosis—even a fake “placebo” diagnosis—improved patient outcomes. Two hundred patients with abnormal symptoms, but no signs of any concrete medical diagnoses, were divided randomly into two groups. The patients in one group were told, “I cannot be certain of what the matter is with you,” and two weeks later only 39 percent were better; the other group was given a firm diagnosis, with no messing about, and confidently told they would be better within a few days. Sixty-four percent of that group got better in two weeks.

This raises the specter of something way beyond the placebo effect, and cuts even further into the work of alternative therapists, because we should remember that alternative therapists don't just give placebo treatments; they also give what we might call placebo explanations or placebo diagnoses: ungrounded, unevidenced, often fantastical assertions about the nature of the patient's disease, involving magical properties, or energy, or supposed vitamin deficiencies, or “imbalances,” which the therapist claims uniquely to understand.

And here it seems that this placebo explanation—even if grounded in sheer fantasy—can be beneficial to a patient, although interestingly, perhaps not without collateral damage, and it must be done delicately; assertively and authoritatively giving someone access to the sick role can also reinforce destructive illness beliefs

and behaviors, unnecessarily medicalize symptoms like aching muscles (which for many people are everyday occurrences), and militate against people's getting on with life and getting better. It's a very tricky area.

I could go on. In fact, there has been a huge amount of research into the value of a good therapeutic relationship, and the general finding is that doctors who adopt a warm, friendly, and reassuring manner are more effective than those who keep consultations formal and do not offer reassurance. In the real world, there are structural cultural changes that make it harder and harder for a medical doctor to maximize the therapeutic benefit of a consultation. First, there is the pressure on time; a doctor can't do much in a six-minute appointment.

But more than these practical restrictions, there have also been structural changes in the ethical presumptions made by the medical profession, which make reassurance an increasingly *outré* business. A modern medic would struggle to find a form of words that would permit her to hand out a placebo, for example, and this is because of the difficulty in resolving two very different ethical principles: one is our obligation to heal our patients as effectively as we can; the other is our obligation not to tell them lies. In many cases the prohibition on reassurance and smoothing over worrying facts has been formalized, as the doctor and philosopher Raymond Tallis recently wrote, beyond what might be considered proportionate: “The drive to keep patients fully informed has led to exponential increases in the formal requirements for consent that only serve to confuse and frighten patients while delaying their access to needed medical attention.”

I don't want to suggest for one moment that historically this was the wrong call. Surveys show that patients want their doctors to tell them the truth about diagnoses and treatments.

What is odd, perhaps, is how the primacy of patient autonomy and informed consent over efficacy, which is what we're talking

about here, was presumed but not actively discussed within the medical profession. Although the authoritative and paternalistic reassurance of the Victorian doctor who "blinds with science" is a thing of the past in medicine, the success of the alternative therapy movement—practitioners mislead, mystify, and blind their patients with sciencey-sounding "authoritative" explanations, like the most patronizing Victorian doctor imaginable—suggests that there may still be a market for that kind of approach.

About a hundred years ago, these ethical issues were carefully documented by a thoughtful native Canadian Indian called Quesalid. Quesalid was a skeptic. He thought shamanism was bunk, that it worked only through belief, and he went undercover to investigate this idea. He found a shaman who was willing to take him on, and he learned all the tricks of the trade, including the classic performance piece in which the healer hides a tuft of down in the corner of his mouth and then, sucking and heaving, right at the peak of his healing ritual, brings it up, covered in blood from where he has discreetly bitten his lip, and solemnly presents it to the onlookers as a pathological specimen, extracted from the body of the afflicted patient.

Quesalid had proof of the fakery, he knew the trick as an insider and was all set to expose those who carried it out; but as part of his training he had to do a bit of clinical work, and he was summoned by a family "who had dreamed of him as their saviour" to see a patient in distress. He did the trick with the tuft and was appalled, humbled, and amazed to find that his patient got better.

Although he continued to maintain a healthy skepticism about most of his colleagues, Quesalid, to his own surprise, perhaps, went on to have a long and productive career as a healer and shaman. The anthropologist Claude Lévi-Strauss, in his paper "The Sorcerer and His Magic," doesn't quite know what to make of it, "but it is evident that Quesalid carries on his craft conscientiously, takes pride in his achievements, and warmly defends the tech-

nique of the bloody down against all rival schools. He seems to have completely lost sight of the fallaciousness of the technique that he had so disparaged at the beginning."

Of course, it may not even be necessary to deceive your patient in order to maximize the placebo effect; a classic study from 1965—albeit small and without a control group—gives a small hint of what might be possible here. The researchers gave a pink placebo sugar pill three times a day to "neurotic" patients, with good effect, and the explanation given to the patients was startlingly clear about what was going on:

A script was prepared and carefully enacted as follows: "Mr. Doe . . . we have a week between now and your next appointment, and we would like to do something to give you some relief from your symptoms. Many different kinds of tranquilizers and similar pills have been used for conditions such as yours, and many of them have helped. Many people with your kind of condition have also been helped by what are sometimes called 'sugar pills,' and we feel that a so-called sugar pill may help you, too. Do you know what a sugar pill is? A sugar pill is a pill with no medicine in it at all. I think this pill will help you as it has helped so many others. Are you willing to try this pill?"

The patient was then given a supply of placebo in the form of pink capsules contained in a small bottle with a label showing the name of the Johns Hopkins Hospital. He was instructed to take the capsules quite regularly, one capsule three times a day at each meal time.

The patients improved considerably. I could go on, but this all sounds a bit wishy-washy. We all know that pain has a strong psychological component. What about the more robust stuff, something more counterintuitive, something more . . . sciencey?



Dr. Stewart Wolf took the placebo effect to the limit. He took two women who were suffering with nausea and vomiting, one of them pregnant, and told them he had a treatment that would improve their symptoms. In fact, he passed a tube down into their stomachs (so that they wouldn't taste the revolting bitterness) and administered ipecac, a drug that should actually *induce* nausea and vomiting.

Not only did the patients' symptoms improve, but their gastric contractions, which ipecac should worsen, were *reduced*. His results suggest—albeit it in a very small sample—that a drug could be made to have the opposite effect from what you would predict from the pharmacology, simply by manipulating people's expectations. In this case, the placebo effect outgunned even the pharmacological influences.

### MORE THAN MOLECULES?

So is there any research from the basic science of the laboratory bench to explain what's happening when we take a placebo? Well, here and there, yes, although they're not easy experiments to do. It's been shown, for example, that the effects of a real drug in the body can sometimes be induced by the placebo "version," not only in humans but also in animals. Most drugs for Parkinson's disease work by increasing dopamine release; patients receiving a placebo treatment for Parkinson's disease, for example, showed extra dopamine release in the brain.

Zubieta (2005) showed that subjects who are subjected to pain and then given a placebo release more endorphins than people who got nothing. (I feel duty bound to mention that I'm a bit dubious about this study, because the people on placebo also endured more painful stimuli, another reason why they might have had higher endorphins; consider this a small window into the wonderful world of interpreting uncertain data.)

If we delve further into theoretical work from the animal kingdom, we find that animals' immune systems can be conditioned to respond to placebos, in exactly the same way that Pavlov's dog began to salivate in response to the sound of a bell. Researchers have measured immune system changes in dogs using just flavored sugar water, once that flavored water has been associated with immunosuppression, by administering it repeatedly alongside cyclophosphamide, a drug that suppresses the immune system.

A similar effect has been demonstrated in humans when the researchers gave healthy subjects a distinctively flavored drink at the same time as cyclosporine A (a drug that measurably reduces your immune function). Once the association was set up with sufficient repetition, they found that the flavored drink on its own could induce modest immune suppression. Researchers have even managed to elicit an association between sherbet and natural killer cell activity.

What does this all mean for you and me?

People have tended to think, rather pejoratively, that if your pain responds to a placebo, that means it's "all in the mind." From survey data, even doctors and nurses buy into this canard. An article from *The Lancet* in 1954—another planet in terms of how doctors spoke about patients—states that "for some unintelligent or inadequate patients, life is made easier by a bottle of medicine to comfort the ego."

This is wrong. It's no good trying to exempt yourself, and pretend that this is about other people, because we all respond to the placebo. Researchers have tried hard in experiments and surveys to characterize placebo responders, but the results overall come out like a horoscope that could apply to everybody: placebo responders have been found to be more extroverted but more neurotic, more well adjusted but more antagonistic, more socially skilled, more belligerent but more acquiescent, and so on. The placebo responder is everyman. You are a placebo responder. Your body plays tricks on your mind. You cannot be trusted.

How do we draw all this together? Moerman reframes the placebo effect as the meaning response—"the psychological and physiological effects of meaning in the treatment of illness"—and it's a compelling model. He has also performed one of the most impressive quantitative analyses of the placebo effect and how it changes with context, again on stomach ulcers. As we've said before, this is an excellent disease to study, because ulcers are prevalent and treatable, but most important because treatment success can be unambiguously recorded by having a look down there with a gastroscope.

Moerman examined 117 studies of ulcer drugs from between 1975 and 1994 and found, astonishingly, that they interact in a way you would never have expected: culturally, rather than pharmacodynamically. Cimetidine was one of the first ulcer drugs on the market, and it is still in use today; in 1975, when it was new, it eradicated 80 percent of ulcers, on average, in the various different trials. As time passed, however, the success rate of cimetidine deteriorated to just 50 percent. Most interestingly, this deterioration seems to have occurred particularly after the introduction of ranitidine, a competing and supposedly superior drug, onto the market five years later. So the selfsame drug became less effective with time, as new drugs were brought in.

There are a lot of possible interpretations of this. It's possible, of course, that it was a function of changing research protocols. But a highly compelling possibility is that the older drugs became less effective after new ones were brought in because of deteriorating medical belief in them. Another study from 2002 looked at seventy-five trials of antidepressants over the previous twenty years and found that the response to placebo had increased significantly in recent years (as had the response to medication), perhaps as our expectations of those drugs increased.

Findings like these have important ramifications for our view of the placebo effect, and for all medicine, since it may be a potent

universal force. We must remember, specifically, that the placebo effect—or the meaning effect—is *culturally specific*. Brand-name painkillers might be better than blank-box painkillers over here, but if you went and found someone with toothache in 6000 B.C., or up the Amazon in 1880, or dropped in on Soviet Russia during the 1970s, where nobody had seen the TV advert with the attractive woman wincing from a pulsing red orb of pain in her forehead, who swallows the painkiller, and then the smooth, reassuring blue suffuses her body . . . In a world without those cultural preconditions to set up the dominoes, you would expect aspirin to do the same job no matter what box it came out of.

This also has interesting implications for the transferability of alternative therapies. The British novelist Jeanette Winterson, for example, has written in *The Times* (London) trying to raise money for a project to treat AIDS sufferers in Botswana—where a quarter of the population is HIV positive—with homeopathy. We must put aside the irony here of taking homeopathy to a country that has been engaged in a water war with neighboring Namibia, and we must also let lie the tragedy of Botswana's devastation by AIDS, which is so phenomenal—I'll say it again: *a quarter of the population is HIV positive*—that if it is not addressed rapidly and robustly, the entire economically active portion of the population could simply cease to exist, leaving what would be effectively a noncountry.

All this tragedy left aside, what's interesting for our purposes is the idea that you could take your Western, individualistic, patient-empowering, antimicrobial establishment, and very culturally specific placebo to a country with so little health care infrastructure and expect it to work all the same. The greatest irony of all is that if homeopathy has any benefits at all for AIDS sufferers in Botswana, it may be through its implicit association with the white-coat Western medicine that so many African countries desperately need.

So, if you go off now and chat to an alternative therapist about the contents of this chapter—as I very much hope you will—what will you hear? Will he smile, nod, and agree that his rituals have been carefully and elaborately constructed over many centuries of trial and error to elicit the best placebo response possible? That there are more fascinating mysteries in the true story of the relationship between body and mind than any fanciful notion of quantum energy patterns in a sugar pill?

To me, this is yet another example of a fascinating paradox in the philosophy of alternative therapists: when they claim that their treatments are having a specific and measurable effect on the body, through specific technical mechanisms rather than ritual, they are championing a very old-fashioned and naive form of biological reductionism, in which the mechanics of their interventions, rather than the relationship and the ceremony, have the positive effect on healing. Once again, it's not just that they have no evidence for their claims about how their treatments work: it's that their claims are mechanistic, intellectually disappointing, and simply less interesting than the reality.

### AN ETHICAL PLACEBO?

But more than anything, the placebo effect throws up fascinating ethical quandaries and conflicts around our feelings on pseudoscience. Let's take our most concrete example so far: Are the sugar pills of homeopathy exploitative if they work only as a placebo? A pragmatic clinician could only consider the value of a treatment by considering it in context.

Here is a clear example of the benefits of placebo. During the nineteenth-century cholera epidemic in London, deaths were occurring in the London Homeopathic Hospital at just one-third of the rate as in the Middlesex Hospital, but a placebo effect is unlikely to be all that beneficial in this condition. The reason for ho-

meopathy's success in this case is more interesting: at the time, nobody could treat cholera. So while hideous medical practices such as bloodletting were actively harmful, the homeopaths' treatments at least did nothing either way.

Today, similarly, there are often situations where people want treatment, but medicine has little to offer—lots of back pain, stress at work, medically unexplained fatigue, and most common colds, to give just a few examples. Going through a theater of medical treatment, and trying every medication in the book, will give you only side effects. A sugar pill in these circumstances seems a very sensible option, as long as it can be administered cautiously, and ideally with a minimum of deceit.

But just as homeopathy has unexpected benefits, so it can have unexpected side effects. Believing in things that have no evidence carries its own corrosive intellectual side effects, just as prescribing a pill in itself carries risks: it medicalizes problems, as we shall see, it can reinforce destructive beliefs about illness, and it can promote the idea that a pill is an appropriate response to a social problem, or a modest viral illness.

There are also more concrete harms, specific to the culture in which the placebo is given, rather than the sugar pill itself. For example, it's routine marketing practice for homeopaths to denigrate mainstream medicine. There's a simple commercial reason for this: survey data shows that a disappointing experience with mainstream medicine is almost the only factor that regularly correlates with choosing alternative therapies. This is not just talking medicine down; one study found that more than half of all the homeopaths in the U.K. approached advised patients against the MMR vaccine for their children, acting irresponsibly on what will quite probably come to be known as the media's MMR hoax. How did the alternative therapy world deal with this concerning finding, that so many among them were quietly undermining the vaccination schedule? Prince Charles's office tried to have the lead researcher into the matter sacked.

A BBC *Newsnight* investigation found that almost all the homeopaths approached recommended ineffective homeopathic pills to protect against malaria, and advised against medical malaria prophylactics, while not even giving basic advice on mosquito bite prevention. This may strike you as neither holistic nor “complementary.” How did the self-proclaimed “regulatory bodies” in homeopathy deal with this? None took any action against the homeopaths concerned.

And at the extreme, when they’re not undermining public health campaigns and leaving their patients exposed to fatal diseases, homeopaths who are not medically qualified can miss fatal diagnoses or actively disregard them, telling their patients grandly to stop using their inhalers and to throw away their heart pills. There are plenty of examples, but I have too much style to document them here. Suffice to say that while there may be a role for an ethical placebo, homeopaths, at least, have ably demonstrated that they have neither the maturity nor the professionalism to provide it. Fashionable doctors, meanwhile, stunned by the commercial appeal of sugar pills, sometimes wonder—rather unimaginatively—whether they should simply get in on the act and sell some themselves. A smarter idea by far, surely, is to exploit the research we have seen, but only to enhance treatments that really *do* perform better than placebo and improve health care without misleading our patients.



6

## THE NONSENSE DU JOUR

Now we need to raise our game. Food has become an international obsession. The newspapers sometimes seem to be engaged in a bizarre ongoing ontological project, diligently sifting through all the inanimate objects of the universe in order to categorize them as a cause of—or cure for—cancer. At the core of this whole project are a small number of repeated canards, basic misunderstandings of evidence that recur with phenomenal frequency. These intellectual crimes are ferried to you by journalists, celebrities, and, of course, “nutritionists,” members of a newly invented profession who must create a commercial space to justify their own existence. In order to do this, they must mystify and overcomplicate diet and foster your dependence upon them. Their profession is based on a set of very simple mistakes in how we interpret scientific literature: they extrapolate wildly from “laboratory bench data” to make claims about humans; they extrapolate from “observational data” to make “intervention claims”; they “cherry-pick”; and last, they quote published scientific research evidence that seems, as far as one can tell, not to exist.

It’s worth going through these misrepresentations of evidence, mainly because they are fascinating illustrations of how people can