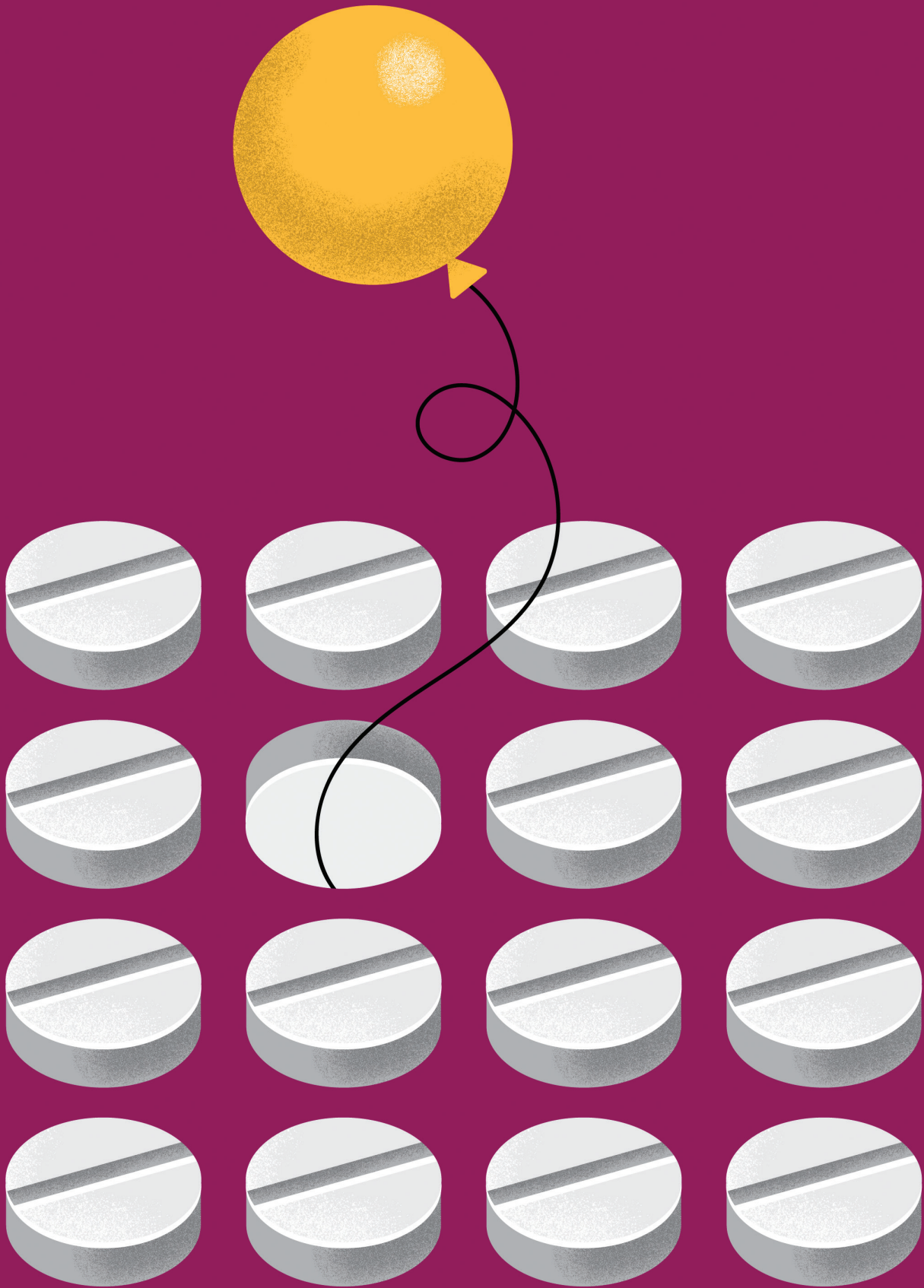
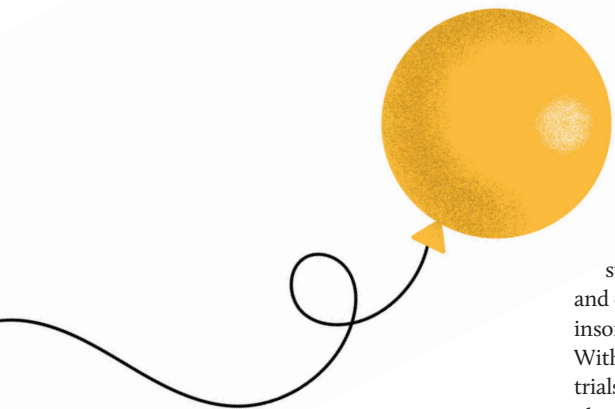


THE POWER OF placebo

The placebo effect remains one of medicine's greatest mysteries. Here's what we know about how it works and how we can use it to help our bodies heal.

BY STEPHANIE ANDERSON WITMER | ILLUSTRATIONS BY ROB WILSON





Rachel Carlton Abrams, MD, knows firsthand how wonky teenagers' sleep schedules can be. Three years ago, her then-17-year-old daughter couldn't fall asleep until well past midnight most nights, which resulted in unpleasant mornings on school days. Low light, sleep teas, and screen-free evenings weren't helping, so Abrams decided to add another element to the nighttime routine: a low dose of melatonin, a hormone supplement that may help regulate the sleep-wake cycle. Research shows it's been effective with sleep issues such as jet lag, but not with chronic insomnia.

But that melatonin worked like magic for her daughter, says Abrams, an integrative family medicine physician and author of the book *BodyWise*. "As a doctor and a parent, I know we are all suggestible: If the mind believes it will be sleepy, it will be sleepy."

Irina Todorov, MD, an integrative family medicine physician at Cleveland Clinic in Ohio, had a similar experience with one of her patients, who'd suffered from chronic knee pain for more than a year. Over-the-counter painkillers, physical therapy, and injections hadn't helped, and knee-replacement surgery was the likely next step. But Todorov wanted to try one more thing first. She recommended the patient start taking *Boswellia serrata*, also known as Indian frankincense. While research suggests the herbal supplement can reduce pain and inflammation from knee osteoarthritis, it usually takes several weeks. But Todorov's patient reported

that the morning after she took the first dose, her pain was completely gone, and it stayed that way.

Could either of these supplements have worked so quickly and completely all on their own to cure insomnia and chronic pain? Possibly. Without conducting controlled clinical trials, we can't know for certain, but both physicians credit their simple suggestion with the diminished symptoms—in other words, the placebo effect.

The basic premise of a placebo can be understood by looking to clinical trials: When a new drug is being tested to determine if it works, one group of participants in the study gets the actual drug, and another group gets a sugar pill or its equivalent (a placebo). It looks exactly like the real thing but is completely inert. If the drug doesn't perform significantly better than the placebo, it's considered a failure. Although most new drugs and treatments—90 percent, in fact—fail their clinical trials and don't receive Food and Drug Administration approval, even ones that do pass commonly demonstrate low assay sensitivity, which is the ability to differentiate between an effective treatment and a placebo.

Because placebos don't just *look* like the real thing; they routinely behave like it, too. There's no hard-and-fast number, and it varies by person and condition, but the placebo effect is estimated to be responsible for up to 50 percent of improvement in pain experiments. And according to a 2020 study published in the *New England Journal of Medicine*, as many as 25 percent of patients receiving placebos in clinical trials discontinue use because of reported "side effects." Furthermore, in a 2019 review of clinical trials of antidepressants, Irving Kirsch, PhD, associate director of Harvard Medical School's Program in Placebo Studies and Therapeutic Encounter (PiPS), took it as far as to conclude that "most (if not all) of the benefits of antidepressants in the treatment of depression and anxiety are due to the placebo response."

The placebo effect doesn't just happen with pills, either. Patients have also experienced the response from what's known as sham procedures—phony surgeries, ultrasounds, and acupuncture that look and feel like the real thing but deliver no actual treatment—conducted during research studies. For example, researchers found acupuncture provided female breast-cancer patients with relief from hot flashes and other menopausal symptoms. But the participants also reported feeling better after sham acupuncture that used retractable needles to prick the skin without penetrating it. In a famous 2002 study of arthroscopic knee surgery, patients in the placebo group—who received nothing more than a surgical knee incision—reported pain relief and improved knee function two years post-procedure with the same frequency as those who'd received the actual surgery.

Matthew Matava, MD, an orthopedic surgeon and chief of sports medicine at Washington University in St. Louis, has seen placebo responses in his own patients, sometimes before any treatment is even administered.

"I've had several people tell me they felt better after an MRI was done," he says. This is confounding: An MRI simply creates images but contains no mechanism for healing. Other patients of Matava's have reported feeling less pain in their joints after taking collagen supplements, even though the research that proves their efficacy is limited, and Matava isn't convinced they work.

But if his patients can feel better without surgery, which increases risk of infection and demands uncomfortable and sometimes lengthy recovery periods, Matava considers it a win—even if he's not sure how it happens. "I tell them, 'I don't have any physiologic or anatomic explanation for it. It may be a placebo effect. Quite frankly, though, I don't really care, as long as you're doing better,'" he says. He's not alone. Although placebos have traditionally been dismissed as bogus by Western

medicine, recently the medical community has been coming around to the phenomenon and is looking at it for what it is, all by itself—a powerful potential treatment.

Historically, placebos have held a negative stigma. They were foils to failed drugs, symbols of skulduggery. Charlatans peddled “snake oil” to cure a host of maladies. Physicians used a placebo (which means “I shall please” in Latin) to pacify sick patients when treatments were unknown or unavailable. Placebos were phonies masquerading as pharmaceuticals.

For a long time, doctors dismissed the fact that placebos often actually made their patients feel better, Abrams says. “There has been a misconception for many years that it’s not real healing if the healing happened ‘in your head,’ which

somehow suggests that what you think or feel is separate from the physiology of your body. That has been used derogatively in Western medicine to insult and discredit patients and self-healing mechanisms, when it’s actually really clear that feelings and thoughts impact the entire body, including chemical and physiologic measures of health.”

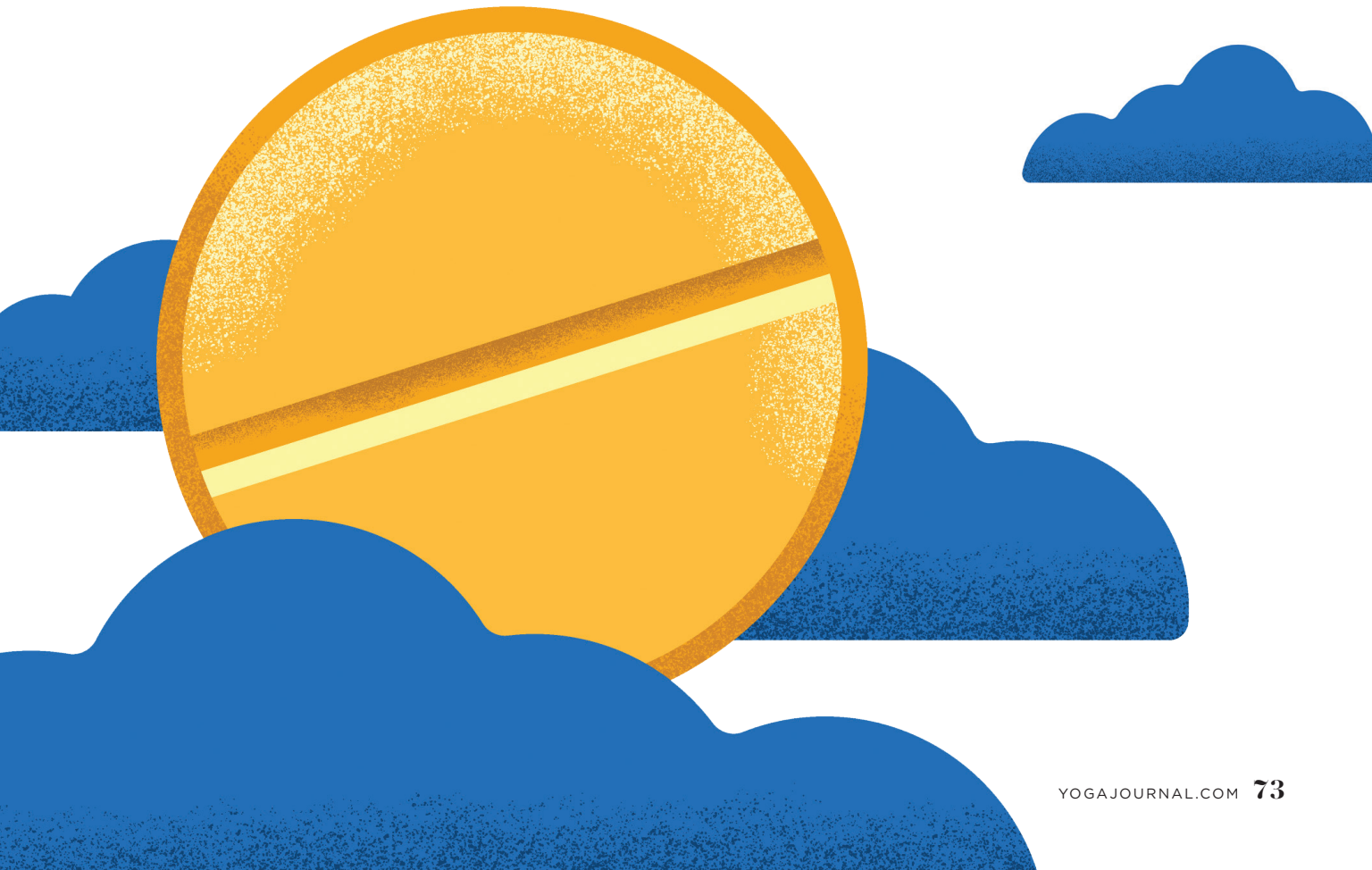
Ted Kaptchuk, a professor of medicine and director of PiPS at Harvard, is one of the world’s leading experts on the placebo phenomenon. Back in the mid-1990s, he was recruited by Harvard to study Chinese medicine and acupuncture to determine whether they worked better than a placebo.

“I asked my employers at Harvard, ‘What exactly is a placebo?’ and they told me, ‘It’s an effective inert substance,’” Kaptchuk recalls. “And I thought, *These are really smart people.*

How could they say something that’s an inert substance has an effect? That’s an oxymoron. I decided the more interesting question for me was, what is this placebo effect?” It was then that he decided to dedicate his life’s work to researching what it is and how it works.

When it comes to understanding how the placebo effect works, experts know one thing for sure: They don’t know, exactly. “Anyone who thinks they understand the placebo effect is slightly delusional,” Kaptchuk says. But there are a few theories.

Research has determined the placebo effect is strongest and occurs most consistently in subjective conditions, such as pain, anxiety, nausea, depression, fatigue, hot flashes, migraines, and irritable bowel syndrome. Kaptchuk says the easier an ailment is to identify with a blood



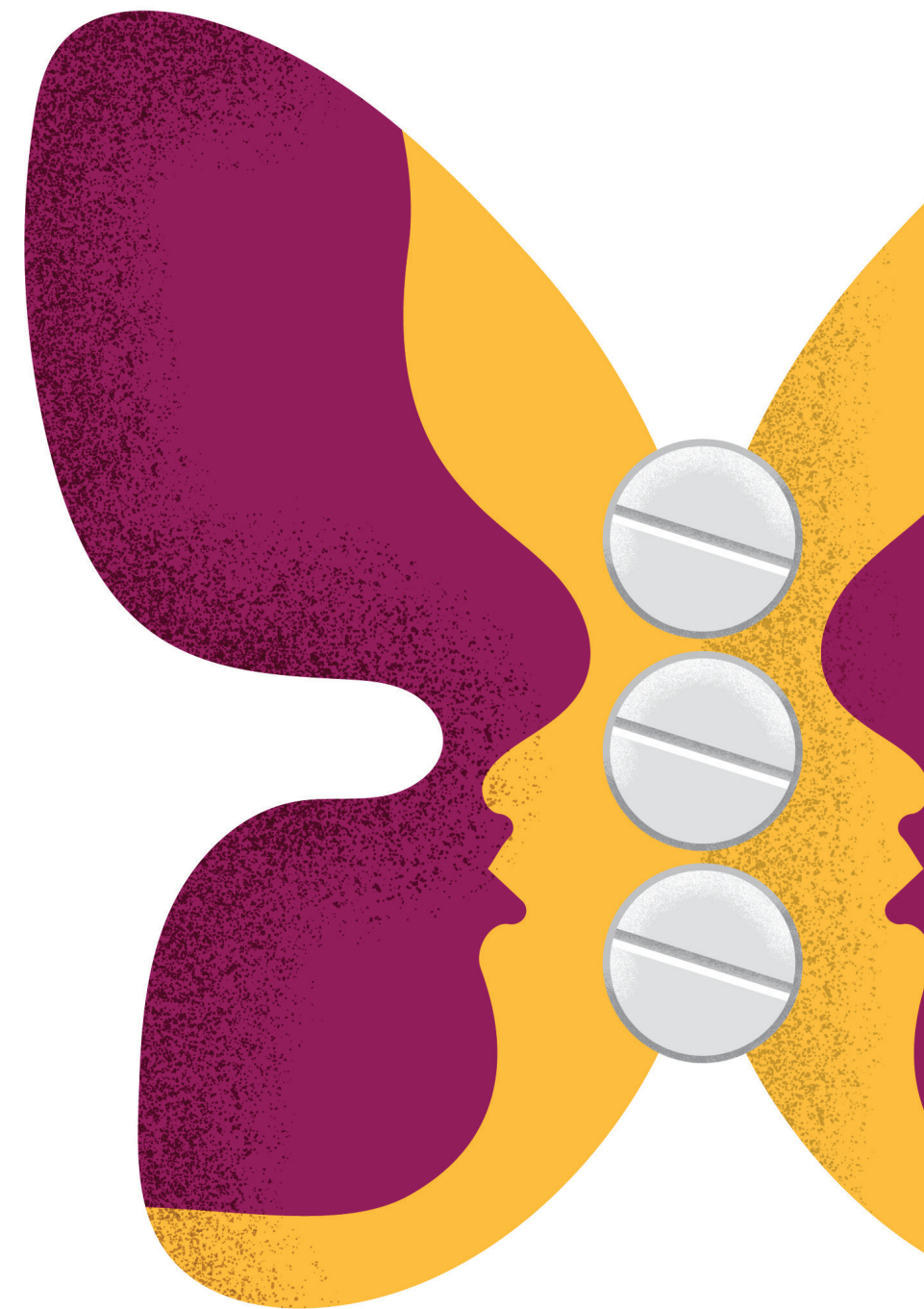
test or see on an X-ray, the less likely it is to respond to a placebo. “Malaria is not affected by a placebo pill,” he says. “Cancer tumors are not shrunk by placebos. You don’t lower cholesterol with placebos.”

Instead, a placebo alters our perception of a symptom that stems from another condition, like pain or nausea from migraines, cancer, or irritable bowel syndrome. But it’s not just how we think we’re experiencing the pain or nausea: Placebos have demonstrable, physiological effects on the brain. Neuroimaging technology shows placebos activate various regions that release neurotransmitters—endorphins, dopamine, cannabinoids—that communicate with the nervous system and regulate our sensations and perceptions of pain and other symptoms, Kaptchuk says.

Based on his clinical studies of placebo, Kaptchuk has pinpointed three intertwined, collaborative elements that he believes trigger a placebo response: what he calls “the symbols and rituals of treatment” and the relationship between the patient and the provider.

Imagine a visit to a physician’s office. Symbols of treatment are everywhere—the name of the practice on the door, the framed diplomas on the wall, latex gloves, white lab coats, stethoscopes, and prescription pads. We recognize these things and assign meaning to them. To us, they represent medical care.

These symbols are entangled with what Kaptchuk calls the rituals of treatment: the series of actions both patient and provider take to initiate healing. Consider how taking a class at a yoga studio is imbued with ritual, even before we move into the first pose. We don our yoga clothes, enter the space, remove our shoes, set up our mats and props, and immediately we may feel more relaxed and centered as we wait for class to start. The same principle applies to rituals in the health care setting. The interactions leading up to treatment tell the brain we have entered an environment conducive to healing—



the process of care has begun.

The final component that Kaptchuk believes initiates a placebo response is the relationship between the patient and provider. Research suggests patients are more likely to experience a placebo effect when working with a physician they’ve determined to be both likable and competent. According to Kaptchuk, the placebo effect is 50 percent stronger when there’s a positive interaction with a provider.

Consider healing practices such as yoga, meditation, acupuncture, and Reiki. These modalities work with the parasympathetic nervous system by lowering heart rate and inducing a state of calm and relaxation, says Chasse Bailey-Dorton, MD, chief of integrative oncology at Levine Cancer Institute in Charlotte, North Carolina. Some of these modalities haven’t been robustly researched, so the exact mechanisms by which they work aren’t precisely



known. But part of what's happening may be a placebo response initiated by the ritual of treatment and the patient-practitioner relationship, Bailey-Dorton says. That, combined with our own conditioning and openness to a treatment's potential efficacy, unleashes a cascade of events in the brain and body—and while that's as much as the experts know about what causes a placebo effect, it's enough information to put to work for our benefit.

One of the core tenets of integrative medicine is that it is both “heart-centered and patient-centered,” Abrams says. “Caring about your patients is actually essential to their healing. When you enter a practitioner’s care, do you feel safe? Do you feel listened to? These factors have a dramatic impact on your health outcomes.”

Experts agree there’s a connection between the mind and body. If you’ve ever had sweaty palms before a job interview or butterflies before giving a speech, you’ve experienced it, Bailey-Dorton says. Feelings that start in the brain—nervousness, anxiety, overwhelm—can cause physical sensations in the body. “If the mind-body connection is powerful enough to cause butterflies, what else is it powerful enough to generate to help our bodies heal?” she says.

And yet, experts don’t agree on the scope of the placebo effect or how it relates to the mind-body connection. Some, like Kaptchuk, confine the response to certain circumstances under clinical conditions. Others, like Abrams, say it’s evidence of the body’s ability to heal itself.

Even though the placebo effect is still shrouded in plenty of mystery and debate, there are ways we can tap into it on our own. Creating symbols and rituals of healing at home can be just as powerful as those we find in a physician’s office, says Lissa Rankin, MD, founder of the Whole Health Medicine Institute and author of *Mind Over Medicine*. “Create a home altar you associate with healing,” she says. “Imbue your herbs, supplements, and pharmaceuticals with your own rituals: Sage them, wave incense over them, pray to them.”

Paired with visits to caring practitioners, our own rituals of healing can encourage a placebo response and help chill us out, Rankin says. “Positive belief, meditation, prayer, and the loving presence of a true healer all relax the nervous system, taking us out of the chronic fight-or-flight that causes disease,

activating the body’s natural self-healing mechanisms,” she says.

To that end, visualization, with guided suggestions from a trusted health care provider, is a powerful tool associated with the placebo effect. “When my patients have procedures, even unpleasant ones such as injections or chemotherapy, I have them visualize that the substance entering their body is positive and is going to do its good work to help them,” Abrams says. “They might imagine the chemotherapy is pink and wrapping around the cancer and leaving the healthy tissue alone.” This technique has some scientific weight behind it. In a classic study from the 1990s by psychologist Henry Bennett, surgical patients who visualized blood moving away from the incision site during the surgery and moving back to the site afterward had measurably less blood loss during the operation.

Given this and the growing body of evidence of placebos’ power, Kaptchuk wants to see physicians embrace and prescribe open-label placebos. No randomized groups, no deception—just the placebo from a trusted provider. Placebos could mitigate the effects of nausea, anxiety, and pain that cancer patients often experience during treatment, particularly when combined with other healing practices such as yoga or meditation, or provide an alternative to pharmaceuticals with side effects that range from mildly unpleasant to downright devastating, as with opioid-based painkillers.

After all, Kaptchuk says, the lowly sugar pill has emerged as the most powerful, most reliable medical treatment we have, across countless studies of countless drugs and treatments for countless conditions: “The most common treatment in all the medical literature is the placebo control of randomized controlled trials,” he says. “In subjective symptoms, that placebo usually mimics, more or less, the effect of the drug. That’s unbelievable. We’re talking about hundreds of thousands of people. There’s no better evidence for anything.”