impact of the road system on wildlife. We have superimposed on our waving fields of grain and purple mountains a grid of interlocking roads that connect points for people but subdivide nature. We have built what Forman characterizes as a "megazoo." ~CHRISTOPHER REED

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VACUUM VIRUS

The Nocebo Effect

IF PEOPLE expect to feel better from a pill or medical treatment, they just might, even if the pill is made of sugar or the treatment is a sham. This kind of response is so well established that researchers regularly use placebos—inert or dummy drugs, classically described as "sugar pills"—in clinical trials to help gauge how much of an active medication's effectiveness comes from the drug itself.

But placebos have a flip side: some people claim to feel *worse* after taking the inert chemicals. They complain of headaches, fatigue, insomnia, stomachaches, nausea, dizziness, weakness, and other symptoms—side effects they claim weren't there, pre-placebo. These ailments are not only real, but can be disabling, and about a quarter of those taking placebos report them, says professor of psychiatry Arthur Barsky, who studies medically unexplained symptoms.

This puzzling phenomenon, the "nocebo" effect (in Latin, *placebo* means "I shall please," and *nocebo*, "I shall harm"), occurs in large part because people relabel existing ailments as side effects of their medication, according to Barsky. If the effect accompanies dummy drugs, then it generally does the same with active ones. Hence, nocebo effects can contaminate clinical trials, because doctors may attribute to a drug negative side effects that are actually nocebo effects.

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WIDENER
biography of a library

Wallace Stegner called its stacks "enchanted"; Barbara Tuchman called it "my Archimedes bathtub, my burning bush"; but to Thomas Wolfe it was a place of "wilderment and despair." Matthew Battles, Coordinating Editor of the *Harvard Library Bulletin* and author of *Library: an Unquiet History*, has written a book that will appeal to all those with memories of Widener, as well as bibliophiles and lovers of libraries everywhere. With copious illustrations and a wide-ranging narrative, *Widener: Biography of a Library* is the tale of the students, scholars, and staff who give a great library its life.

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The issue is "very important clinically," Barsky says, because nocebo effects can be distressing and costly. Patients who blame their symptoms on the pill they're taking may give up too soon on a potentially beneficial treatment. They can also waste time and money by returning to the doctor to have the medication changed, or to seek treatment for their nocebo symptoms.

Nonspecific side effects simply add to the burden of a patient's illness, and Barsky would like to see that change. But he admits it won't be easy. "It can be very complicated to decide if any given symptom is directly related to the drug," he says. In 2002, he and three colleagues published a literature review of nocebos in the *Journal of the American Medical Association (JAMA)*. The paper cites a study of a commonly prescribed drug in which researchers were able to link only 11 percent of adverse side effects reported by patients directly to the medication—leaving the other 89 percent, potentially at least, in the nocebo category.

Nocebo symptoms are often vague. Many of us walk around daily feeling mild aches and pains that we mostly ignore. But add to the mix an illness and a prescription medication, and it's easy to see how we might interpret our upset stomach or sleepiness as a side effect of the drug we're on.

The *JAMA* paper cites other factors. A patient who expects to suffer painful symptoms is more likely to. Depressed patients tend to feel bodily distress. Women, who report disturbing initial symptoms more often than men, are also more likely to report nocebo effects. Patients with a history of side effects can become conditioned to develop them again—and not only because of drugs. In one study, a third of chemotherapy patients felt extremely nauseous upon entering a room painted the same color as the one where they got their chemo treatments.

External factors come into play as well. A drug's reputation can make people wary. Many patients, for example, are aware of allergies to penicillin—up to 10 percent of those hospitalized report a penicillin allergy, according to Barsky's paper. But in a carefully supervised and monitored study of such patients, 97 percent of them actually had no reaction when they were administered oral penicillin. Even a pill's size, shape, and color can make a difference. Studies have shown that red, orange, and yellow pills are associated with stimulants; blue and green pills tend to make people sleepy.

Barsky's research shows that about three-quarters of both patients and healthcare workers are unacquainted with the nocebo effect. He offers this advice to doctors and nurses: take pains to identify any chronic symptoms that patients may suffer from *before* beginning a course of treatment, and discuss the nocebo phenomenon with them. Admittedly, "It's possible that some doctors will just switch the patient to another medication," says Barsky. But they then risk seeing the same pattern of side effects repeat itself. In the long run, he says, they'll save time by having these conversations. ~KATHARINE DUNN

FLY TARTARE

Leaves That Lunch

THE MOST FAMOUS CARNIVORE of the plant kingdom, the Venus flytrap, lures insects to its leafy green lips with a sweet-smelling scent, then snaps its mouth-like leaves shut in just 0.1 second to ensnare its prey. Scientists have long sought an explanation for how a plant, which has no muscles, can move fast enough to catch a fly. Lakshminarayanan Mahadevan, Gordon McKay professor of applied mathematics and mechanics, leading a cross-disciplinary team of mathematicians, engineers, and biologists, recently found the answer, which appears in the January 27 issue of *Nature*. The plant uses elastic energy stored in the curvature of its leaves, which buckle shut when an insect brushes a hair trigger on the inner leaf surface.

Illustration by Jean-François Martin