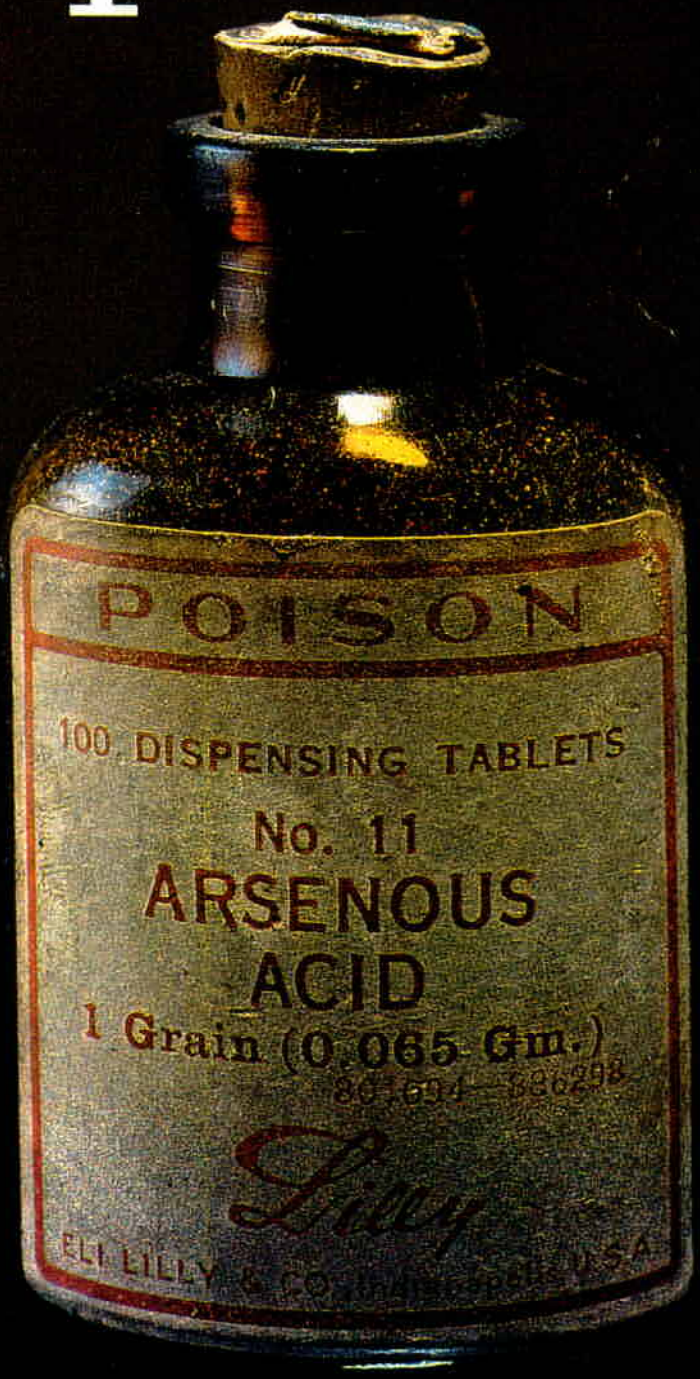
new remedies from old poisons



BY SUSAN FREINKEL • PHOTOGRAPH BY JAMES WORRELL

HEALERS HAVE KNOWN FOR CENTURIES THAT WHAT KILLS MAY cure and what cures may kill. As the Renaissance physician and apothecary Paracelsus observed: The poison is in the dose. That means there's a fatal dose of just about anything. For instance, you're likely to get sick if you don't drink plenty of fluids when you exercise hard enough to break a sweat. But a recent study of several marathoners who became deathly ill after races pointed to a surprising culprit: too much water, which diluted the salt content in the runners' blood and caused fluid to build up in the lungs and brain. On the other hand, the Paracelsus maxim implies that toxic substances can sometimes be transformed into healing potions. Indeed, drugmakers have recently extracted powerful remedies from some of the most deadly poisons known to humans.

ARSENIC: TARGETING LEUKEMIA

In centuries past, arsenic gained renown as the poison of choice for killing rats or an unwanted spouse. But now researchers have found that one common form, arsenic trioxide, safely works wonders against a lethal blood cancer, acute promyelocytic leukemia, giving hope to patients for whom other forms of treatment had failed. In recent studies involving 52 patients who were given a series of arsenic trioxide injections—about one-third the fatal dosage—87 percent went into complete remission, and nearly half were still alive two years later.

"That is a tremendous breakthrough," says Anthony Murgo, a senior investigator at the National Cancer Institute. Ironically, the arsenic treatments wreak less cellular havoc than standard chemotherapies, which essentially bludgeon cells to death. Like a teacher quieting an unruly class by ejecting the class clown, arsenic trioxide targets the wayward protein that prevents white blood cells from developing normally, thus triggering leukemia. The result is a godsend for patients like 26-year-old Derek Ross of Orange, California. "Everyone winces when I tell them what I took," says Ross, whose cancer has been in remission since September 2000. "But it turned my life back to normal."

BOTOX: TAMING UNRULY MUSCLES

The bacterium *Clostridium botulinum* produces a poison so deadly that a few hundredths of an ounce can kill a million people. Small wonder it's one of the most dreaded agents of biological warfare. Yet it is also one of the most widely used therapeutic drugs—at least in the domesticated form known as Botox. In this purified version the toxin is delivered in minute doses of a few trillionths of an ounce. It would take 70 times that amount to kill someone. Originally developed for the treatment of uncontrollable blinking, Botox is now used to help treat some 40 ailments, ranging from crippling diseases such as cerebral palsy and Parkinson's to less-than-life-threatening troubles like facial wrinkles and excessive sweating. It may even ease migraines for some people. "Besides aspirin and penicillin, there are very few drugs I can think of that have so many uses," says Eric First, a physician who has studied botulinum toxin for 12 years. "And Botox has fewer side effects." The drug helps regulate the release of a neurotransmitter called acetylcholine, which plays a key role in relaying messages from nerves to muscles, as well as in cognitive function and hormonal production. Too much acetylcholine can cause painful muscular contractions. In cervical dystonia, for instance, the neck is frozen at an excruciating angle (remember Ed Sullivan's famous leaning posture?). Injecting Botox into the affected muscles slows acetylcholine release, allowing them to relax.

NICOTINE: FOCUSING ATTENTION

Nicotine has potent effects on the brain, which is precisely why it is so addictive. It's known to focus attention and improve working memory; it can calm someone who is anxious and stimulate someone who is listless. The nervous system is studded with nicotinic receptors, neurons that help regulate the release of important neurotransmitters such as acetylcholine, serotonin, and dopamine. "Nicotine fine-tunes the system," says Paul Newhouse, a clinical neuroscientist at the University of Vermont College of Medicine. "It's the perfect psychotropic drug." As little as one ten-thousandth of an ounce of pure nicotine delivered in a single dose could kill you. But two times that amount delivered through nonaddicting time-release patches causes modest improvements in the memory and concentration of Alzheimer's patients, who are typically short on acetylcholine. Nicotine is an even bigger boon for children with Tourette's syndrome, whose illness is related to an excess of dopamine. When Paul Sanberg, a neuroscientist at the University of South Florida College of Medicine, gave young Touretters nicotine patches, he found that the children suffered fewer tics and were less aggressive and depressed. The same treatment seems to improve focus for children and adults with attention deficit hyperactivity disorder. Nicotine may even help keep schizophrenics anchored to reality and depressives from total despair. Nonetheless, the tendency of nicotine to elevate heart rate and blood pressure and cause nausea worries many physicians. So drugmakers are already working on copycat compounds with the same beneficial touch but none of nicotine's bite.

SNAIL VENOM: RELIEVING PAIN

A lowly cone snail buries itself in the sand, leaving only a brightly colored, wriggling wormlike appendage visible. When a curious fish moves in for a nibble, the snail harpoons it with this barbed appendage, injecting venom that causes paralysis in seconds. Around eight-hundredths of a fluid ounce of a compound extracted from the venom produces happier results when injected into the space surrounding the spinal cord of people with chronic pain, including those who are terminally ill. "It's 100 to 1,000 times more potent than morphine," says University of Utah psychiatrist and biologist Michael McIntosh, who isolated the compound for a drug, dubbed Ziconotide or Prialt, that is now awaiting FDA approval. Other researchers have isolated a promising analgesic from the snail venom, as well as a possible anticonvulsant. Still, one would be well advised to steer clear of live cone snails, which are found in reef environments throughout the world. The natural venom can cause weakness and loss of coordination. In extreme cases it can even result in respiratory muscle paralysis that can be fatal.

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