When modern medicine needs some help, surgeons call in mother nature's little helper—the leech

By Jack McClintock
Photography by Elinor Carucci

Hirudo medicinalis, **the four-inch-long leech that was once used for bloodletting, is finding new work in hospitals. Both ends of the leech are suckers. The smaller sucker houses the head and jaws.**

"I was scalped by a box-making machine," says Christine Lippincott. She was working in a factory in Greensboro, North Carolina, and her attention wandered. "It caught my hair from behind and ripped it right off in a second, from the back of my neck to my eyebrows." Gushing blood, Lippincott fainted. Coworkers carefully extricated her scalp from the box machine, packed it in ice, and rushed it and her to the local hospital. A helicopter took her to Duke University Medical Center in Durham, where plastic surgeon L. Scott Levin sewed her scalp back on, meticulously reconnecting its blood supply in a six-hour operation.

But the crisis wasn't over. Levin could see that blood was flowing through the reattached arteries into Lippincott's replanted scalp. But it wasn't flowing out very well through her veins, which are vulnerable to clots and increased pressure. So Levin did what many up-to-date surgeons would do: He applied leeches.

"I had them on my neck and the back of my head," says Lippincott, who is 25. "There was a bucket of them in the room with me. Blood was pouring out of my scalp 24 hours a day for a week."

But that was the point. Bloodsucking worms maintained her circulation and probably saved her scalp. "It's a time-honored method that works extremely well in the right patients, the right clinical situation, the right application. It's a living drug therapy," says Levin, chief of plastic surgery and professor of orthopedic and plastic surgery at Duke's medical center.

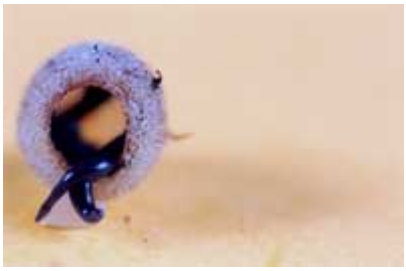
Leeches aren't a surgeon's first option, of course. Other methods are tried first—trying to connect as many small veins as possible, redoing the surgery and, when a finger or toe is involved, removing the nail, scoring

the nail bed with a scalpel, and putting the patient on heparin, an anticoagulant. But sometimes only a leech will do. That was the case with Lippincott. "If we hadn't done it," Levin says, "her replant might well have failed for lack of venous outflow."

The leech's peculiar talent is to create a wound that bleeds for hours. Substances in its saliva anesthetize the wound, prevent clotting, and dilate vessels to increase blood flow. Using them in surgery is simple: Poke the warm, blue, swollen, congested skin with a needle to start the flow of inviting, clot-dark blood. Apply a leech, and the voracious worm, having been stored unfed, will saw through the skin with the 300 teeth in its tripartite jaws. Its sucking mouth will draw out congested blood and maintain circulation until the patient's body creates new blood-flow channels. And when the leech has fed for 20 minutes to an hour, taken 15 to 30 milliliters of blood, and dropped off sated, its anticoagulant assures that the wound will ooze for 10 hours more. In Lippincott's case, Levin applied 30 to 40 leeches over six days.

Hirudo medicinalis, the European medicinal leech, is a four-inch-long carnivorous, hermaphroditic, segmented worm with a sucker on each end, five pairs of eyes, and 32 nerve bundles, or "brains," in the middle. It is one of 650 leech species and is found mostly in ponds and bogs. Some species are highly specialized—one, in fact, feeds only on earthworms. Another feeds on fish in freezing polar seas. One dwells in the nostrils of Saharan camels, another inside the rectum of the African hippopotamus. Another lives in New Guinea caves and sucks the blood of bats. Still another, the anaconda of leeches, inhabits the Amazon basin and grows up to 18 inches long.

For well over 2,000 years, humans have employed *Hirudo* for bloodletting, a practice thought to restore balance to the body's humors and heal everything from headaches to hemorrhoids. Leeches were so entwined with medicine that the words *leech* and *doctor* were synonymous in Anglo-Saxon English, and by the mid-19th century they had become the aspirin of their day—apply two leeches and call me in the morning. A French physician working in the early 19th century, François-Joseph-Victor Broussais, is said to have prescribed as many as 30 leeches at a time before he even saw his patients.



When leeches mate, they secrete a cocoon to house the fertilized eggs. Within two to four weeks, about 15 to 20 young leeches, just an inch long, squirm out in search of a blood meal. At Biopharm, a leech farm in Swansea, Wales, researchers rear leeches on pig blood. After about six months, the leeches are stored in a chamber cooled to 45 degrees Fahrenheit. They can remain there for a year, unfed and growth-inhibited,

until a hospital requests a batch of hungry ones.

As medical science advanced, leeching died out, but with the advent of microvascular surgery and tissue transfer, surgeons rediscovered the creature's value. Two Slovenian surgeons pioneered modern medical leeching in the 1960s, describing how the worms assisted them in a tissue-flap transplantation. Then, in 1985, Harvard plastic surgeon Joseph Upton was called to care for a 5-year-old boy whose ear had been bitten off by a dog. Ears, which have very small blood vessels, had never been successfully replanted. Upton had no trouble with the boy's arteries, but as he worked through the night reconnecting the veins, clots began to form.

Upton had used maggots to clean severe infections while serving in the Army, so the idea of a natural remedy came easily to him. He phoned Biopharm, a company in Swansea, Wales, owned by zoologist Roy T. Sawyer, who breeds *Hirudo* on the world's only leech farm. A box of leeches arrived overnight, and the boy's ear was saved. When Upton published his results in the journal *Plastic and Reconstructive Surgery,* leech sales soared. Nine years later, in a memorably bizarre case, leeches saved a life. During an operation for congenital facial abnormalities, an 8-year-old Dutch boy developed swelling so severe that his tongue filled with blood and protruded from his mouth, blocking his airway. Steroids and antibiotics didn't help. But six hours and 27 leeches later, the boy was out of danger, and leeches had been firmly reestablished as good medical science.

Nobody knows how many lives, limbs, and appendages they have saved, but medical literature describes leeches being used to relieve severe postsurgical venous congestion after finger, toe, ear, and scalp replantation and penile surgery, after skin-flap plastic surgery, and to relieve engorgement of the nipple following breast augmentation or reduction surgery. And the creatures have turned out to be miniature pharmaceutical factories—researchers have isolated a dozen compounds from leech saliva to prevent blood clots, treat inflammation, dilate blood vessels, kill bacteria, and relieve pain.

Carl Peters, the leech-growth technician at Biopharm, removes the muslin cover from a plastic bucket, and leeches crawl out. He pokes one. It creeps across a visitor's hand, humping along with the suckers at its head and foot and arching its back like a Halloween cat. The creature feels wet and cool, like a chilled strand of fettuccine. Every few seconds, it stands on its rear sucker and waves its head around ominously, as if searching for something, which is just what it's doing. It's out for blood.

"It's like a cross between a slimy slug and a Velcro barracuda," Peters says with a grin and a glance toward the movie poster on the wall for *The African Queen.* In the movie, Humphrey Bogart's character says: "If there's anything in the world I hate, it's leeches. Oh, the filthy little devils!" Peters has worked with them for nine years and has been bitten five times. He says it doesn't hurt, "but I don't think I'd like to be plastered

with leeches."

Blood doesn't flow easily in an injured and inflamed ear. Because leeches release enzymes that promote blood flow, they can help difficult wounds heal

In nature, the medicinal leech inhabits the wetter environments of western and southern Europe. Sensing the warmth, motion, or shadow of possible prey, the leech cozies up, attaches itself with its suckers, injects an anesthetic so that its presence is not detected, and goes to work. The three jaws of its head sucker stiffen, protrude, and slice into the prey's skin with a sawing motion. Immature leeches feed on the thin-skinned bodies of amphibians and young fish; mature leeches can move on to larger prey, such as cattle, horses, ducks, and humans. The leech's natural anticoagulant, hirudin, keeps blood flowing for the 20 to 40 minutes it takes to feed, during which time the leech's body weight may increase 10 times, reaching up to 60 grams (about two ounces). The secretions of one leech can prevent up to half a cup of blood from coagulating. Blood sucked into its crop can take 18 months to digest. During this time, the leech does little but lie around in a stupor, rousing itself only to reproduce. The hermaphroditic leech copulates on land, wrapping around its partner using a kind of mucus, and later secretes a cocoon, which it deposits in damp soil near the shoreline. Within two to four weeks, about 15 to 25 leeches hatch. Under the right conditions, a leech can produce up to 1,200 young in a five-year lifetime. At Biopharm, leeches feed on pig blood poured into an artificial membrane that simulates the skin of natural prey. After rearing the leeches for six months at 80 degrees Fahrenheit, Peters transfers them to a room chilled to a growth-slowing 45 degrees. They can live there for a year without food.

When leeches leave Biopharm—thousands a year—they are packed like Chinese takeout in little cardboard boxes. They go to such places as Carolina Biological Supply, in Burlington, North Carolina, where workers store them in buckets of icy spring water until a surgeon like Levin calls. "We maintain them so that when surgeons get one, it's a nice, clean, hungry leech," says Lawrence Wallace, the firm's director for live biological products. Hungry they are; sterile they are not. In the gut of every one, even those raised in sterile conditions, lives *Aeromonas hydrophila,* a bacterium that prevents putrefaction of the leech's blood meal and supplies enzymes crucial to its digestion. Studies have found that as many as 20 percent of leeched patients become infected by this bacterium, which increases the risk of serious wound infections. So preventive antibiotics are given to patients with weakened immune systems.

Aeromonas also kills other bacteria. Joerg Graf of the Institute for Infectious Diseases at the University of Bern, Switzerland, believes that a better understanding of *Aeromonas* could help researchers find a way to fight such bacteria as *Staphylococcus aureus,* which are becoming

resistant to antibiotics. For some reason, staph cannot grow inside a leech. This may be the result of inhospitable conditions within the leech, says Graf, but it's also possible that *Aeromonas* produces something that inhibits staph growth. Finding such a substance could lead to a way of controlling staph growth in humans.

But leeches themselves may prove a direct source of antibiotics. Michel Salzet of the University of Science and Technology in Lille, France, has found infection-fighting peptides in leeches akin to those that have already been discovered in insects and other invertebrates. In leeches, these peptides are produced within 15 minutes of a bacterial infection. "These antimicrobial peptides diffuse quicker and easier than antibodies," he says, suggesting that such speed and potency might add up to a defense that can outbreed and outrun pathogens. "Antibacterial peptides from leeches may cure human diseases," Salzet says.

That wouldn't surprise Roy T. Sawyer. Courtly and soft-spoken, the North Carolinian escorts a visitor through his leech museum. It's a tidy room, bright and cheerful despite its display of bowls and knives for bleeding, leech jars with perforated lids, and oil paintings of patients with leeches stuck on their necks. He speaks of a "veritable pharmacy" of leech products, referring to potentially useful compounds he and his researchers have turned up. There's the enzyme orgelase, a "spreading factor" that quickly distributes chemicals in leech saliva around the wound. Sawyer believes it could help carry local anesthetic deep into tissues before surgery. And there's calin, which neutralizes the effects of collagen, a natural blood clotter. He calls it a "collagen-coating paint" that could help prevent blood clots following vascular surgery. Sawyer and others have isolated a dozen more active substances from *Hirudo* and nine other leech species. Among these is a local anesthetic that renders a leech bite painless. How it works is still not understood, and Sawyer has been unable to isolate the analgesic. "Common sense is telling me something is there. This is a potentially rich area," he says. Salzet, who recently found a morphinelike compound in *Hirudo,* agrees.

The anticoagulant extracted from leech saliva highlights the difficulties of developing drugs from the animal. In the marketplace, hirudin competes against heparin, which is easily derived from vertebrate immune cells and works with certain cofactors to inhibit thrombin, a clot-producing enzyme. Hirudin works more simply than heparin, binding directly to thrombin alone, but its dosage must be carefully measured to prevent excessive bleeding. Long-term studies of hirudin in humans have not been carried out, but a series of small studies suggests it may boost short-term heart attack survival by as much as 30 percent over heparin. Other studies suggest it may be more effective than heparin in reducing deep-vein clotting after hip surgery.

Note the tripartite jaws in the sucker's center.

But to make enough hirudin from leeches for economical production, "you'd need a swimming pool of blood," says Maurice Moloney, professor of plant biotechnology at the University of Calgary in Alberta, Canada. So he tried another approach, altering Ethiopian brassica, a type of mustard, to contain the gene for hirudin. He planted five acres of the plant and produced 10 tons of seed, from which he extracted the drug.

Another candidate drug from leeches is hementin, derived from the 18-inch-long Amazon leech *Haementaria ghilianii,* which Sawyer brought back from French Guiana in 1977. He wondered if this leech, which lances large mammals with a six-inch-long proboscis, also produced anticoagulants to prolong its dinner. It did. But while hirudin prevents clot formation, hementin dissolves a particular kind of platelet-rich clot that can cause stroke and heart attack and against which clot busters like streptokinase and urokinase are ineffective. A German firm, says Sawyer, may decide to to clone the compound.

Other scientists are studying the leech's large, easily visible nerves. Figuring out how they work could help in promoting nerve regeneration in humans with spinal cord injuries. But the leech's future in science, like its past, will most likely stick close to its main interest: blood. "Secretions from bloodsucking animals could be to cardiovascular diseases what penicillin was to infectious disease in the past," Sawyer says. "Leeches are preadapted to human physiology. The secretions from their saliva cross the entire spectrum of physiology: blood clotting, digestion, connective tissue, disease, pain, inhibition of enzymes, anti-inflammation. You name it, the leech has it."

RELATED WEB SITES:

Find details about the life cycle, history, and medicinal uses of the leech at www.biopharm-leeches.com or see "A Sanguine Attachment: 2,000 Years of Leeches in Medicine," Roy T. Sawyer, *Medical & Health Annual,* Encyclopedia Britannica, 1998.

To learn about Michel Salzet's work, see the homepage of the University of Science and Technology at Lille Annelids Neuroimmune Laboratory at www.univ-lille1.fr/lea/Menu_du_Site/Menu_Laboratoire%20english.htm.

Gaze at leeches from various taxa at www.vims.edu/~mes/mes/leechfigs.html#other.

For general information about leeches, see the Australian Museum's leech page at www.amonline.net.au/factsheets/leeches.htm.