Health & Medicine

A WINTER'S S

Hibernation's secrets may help treat a host of human afflictions

By Katherine Hobson

Hibernation seems simple enough: Animals fatten up in the summer, disappear into their dens during the winter, when food is scarce, then emerge in the spring alive and alert, if a lot thinner. But if you could peek inside a hibernating ground squirrel, you'd witness a physiological wonder. The animal's metabolism slows to almost nothing. Its body temperature plummets to a few degrees warmer than outside. Its heartbeat slows from 300 beats per minute to fewer than 10. And other, more mysterious changes protect the squirrel in a state that would kill many other animals.

It's that self-protection that intrigues medical researchers. Figuring out how mammals survive such extreme conditions offers clues to how humans might be protected against their own health threats. Fueling interest in the field is a recent paper published in *Science* showing that mice—which don't hibernate—were induced to do so by a calibrated whiff of a normally toxic gas. When the gas was removed, the mice emerged apparently unharmed from their sluggish state. While any human applications are years away, says the paper's lead author, Mark Roth, of the Fred Hutchinson Cancer Research Center in Seattle, a group of venture capitalists is hopeful enough to invest $10 million in a start-up company. Here is a sampling of medical problems that hibernation research is addressing:

Organ preservation. A big problem in organ transplantation is time. Lacking fresh blood, even cooled organs quickly become unusable. So scientists are looking at what protects the organs of hibernating animals even during periods of very low blood flow. Tsung-Ping Su, at the National Institute on Drug Abuse, heard from a colleague about a protein from a hibernating woodchuck that seemed to have the same pain-fighting ability as opioids like morphine. He found that a synthetic version could in-

Does this hibernating arctic land squirrel carry clues that could someday help emergency medical workers?

LEEP


LESA HOLLEN AND LEONE THIERMAN

duce a ground squirrel to go into hibernation off schedule. Su, working with a cardiac surgeon, discovered that a dog's lung preserved with the substance survives longer than one bathed in a control solution, raising the possibility for use in human organs.

Stroke. Most strokes are caused by a blocked blood vessel to the brain, which starves brain cells. But the brains of hibernating animals somehow survive restricted blood flow. "Metabolism slows so much that cells think they're in hypoxia and turn on a response that helps tissues survive," says Kenneth Storey, a molecular physiologist at Carleton University in Ottawa. They also survive the "reboot" during arousal periods, when their metabolism revs up for short stints during hibernation. Kai Frerichs, director of interventional neuroradiology at Brigham & Women's Hospital in Boston, has studied how squirrels protect themselves during restricted blood flow. He's examined still-living brain slices from hibernating and nonhibernating squirrels and shown that the hibernating ones were less sensitive to removing nutrients like glucose, even at normal temperatures.

If a substance were isolated, it might buy stroke victims some time. "If you could turn off metabolism right away—if the EMT had something to inject—you could turn off the demand for blood flow," says Kelly Drew of the Institute of Arctic Biology at the University of Alaska–Fairbanks.

Trauma. Soldiers in combat and gunshot victims often bleed to death from their wounds. Instead of focusing on increasing blood supply through transfusions, Patrick Kochanek is looking at rapidly reducing the body's demand, potentially giving medics time to evacuate or treat the victim. With collaborators, Kochanek, director of the Safar Center for Resuscitation Research at the University of Pittsburgh, replaced the blood of wounded dogs with a near-freezing saline solution that cooled their brains to as little as 7 degrees Celsius. The dogs stopped breathing, and their hearts stopped. But two hours later, when they were reinfused with blood and had recovered, they were fine. Kochanek is now working with a trauma surgeon, to design potential human trials.

Osteoporosis. When our bones don't bear weight for a long time, they become brittle. That's what happens to astronauts and to the bedridden. But hibernating bears loll around for months, and yet in the spring their bones are as strong as ever. Researchers think bears recycle the calcium lost from inactivity by recapturing it in the blood and using it to rebuild bone. Seth Donahue, a biomedical engineer at Michigan Technological University, is part of a group analyzing changes in blood hormone levels of hibernating black bears to identify what is regulating this process. They're also interested in how bears might actually supercharge their bone building right after hibernation. The long-term goal is to treat all human osteoporosis, not just that caused by disuse.

CHARLIE ARCHAMBAULT FOR *USN&WR*

"If you could turn off metabolism right away...you could turn off the demand for blood flow."

Kelly Drew, University of Alaska–Fairbanks

Direct human use of hibernators' secrets is years off, and it's unlikely that we'll ever regularly spend months in a state of extreme torpor. But our basic similarity to these animals is close enough to make their protective tricks theoretically applicable. "Thus far, there don't seem to be any special gene products that are unique to the mammals that hibernate," says Hannah Carey, a physiologist at the School of Veterinary Medicine at the University of Wisconsin–Madison. Last year, scientists reported hibernation behavior in one species of lemur—a primate, like humans. It all adds to the promise that the outwardly simple process of hibernation will yield answers to some of medicine's most complex problems. ●