Hibernation: The Big Sleep

Scientists studying hibernation in mammals are finding promise for human medical applications

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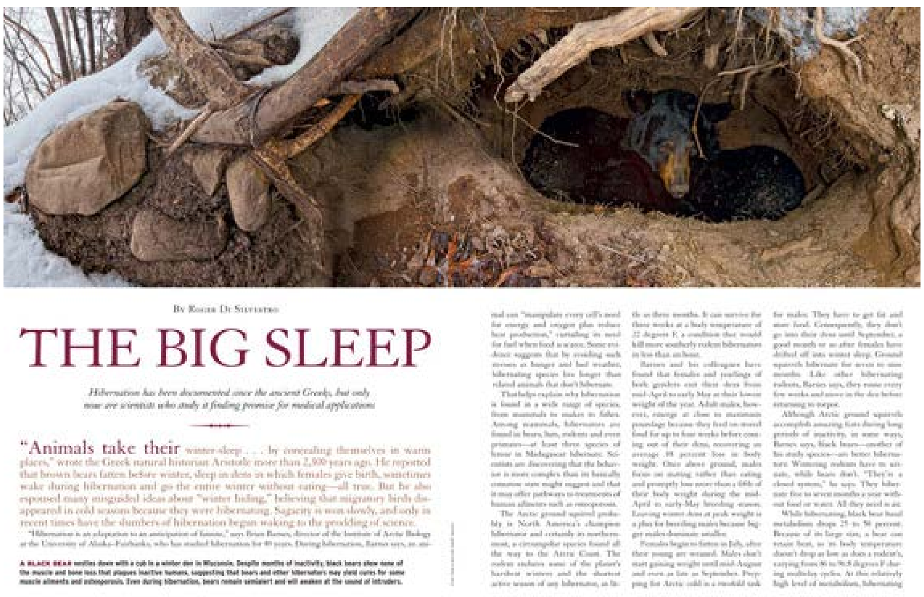

"ANIMALS TAKE THEIR WINTER-SLEEP . . . by concealing themselves in warm places," wrote the Greek natural historian Aristotle more than 2,300 years ago. He reported that brown bears fatten before winter, sleep in dens in which females give birth, sometimes wake during hibernation and go the entire winter without eating—all true. But he also espoused many misguided ideas about "winter hiding," believing that migratory birds disappeared in cold seasons because they were hibernating. Sagacity is won slowly, and only in recent times have the slumbers of hibernation begun waking to the prodding of science.

"Hibernation is an adaptation to an anticipation of famine," says Brian Barnes, director of the Institute of Arctic Biology at the University of Alaska–Fairbanks, who has studied hibernation for 40 years. During hibernation, Barnes says, an animal can "manipulate every cell's need for energy and oxygen plus reduce heat production," curtailing its need for fuel when food is scarce. Some evidence suggests that by avoiding such stresses as hunger and bad weather, hibernating species live longer than related animals that don't hibernate.

That helps explain why **hibernation is found in a wide range of species, from mammals to snakes to fishes.** Among mammals, hibernators are found in bears, bats, rodents and even primates—at least three species of lemur in Madagascar hibernate. Scientists are discovering that the behavior is more complex than its basically comatose state might suggest and that it may offer pathways to treatments of human ailments such as osteoporosis.

Who is the Better Hibernator, Ground Squirrels or Bears?

The Arctic ground squirrel (right) probably is North

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America's champion hibernator and certainly its northernmost, a circumpolar species found all the way to the Arctic Coast. The rodent endures some of the planet's harshest winters and the shortest active season of any hibernator, as little as three months. It can survive for three weeks at a body temperature of 22 degrees F, a condition that would kill more southerly rodent hibernators in less than an hour.

Barnes and his colleagues have found that females and yearlings of both genders exit their dens from mid-April to early May at their lowest weight of the year. Adult males, however, emerge at close to maximum poundage because they feed on stored food for up to four weeks before coming out of their dens, recovering an average 48 percent loss in body weight. Once above ground, males focus on mating rather than eating and promptly lose more than a fifth of their body weight during the mid-April to early-May breeding season. Leaving winter dens at peak weight is a plus for breeding males because bigger males dominate smaller.

Females begin to fatten in July, after their young are weaned. Males don't start gaining weight until mid-August and even as late as September. Prepping for Arctic cold is a twofold task for males: They have to get fat and store food. Consequently, they don't go into their dens until September, a good month or so after females have drifted off into winter sleep. **Ground squirrels hibernate for seven to nine months.** Like other hibernating rodents, Barnes says, they rouse every few weeks and move in the den before returning to torpor.

Although Arctic ground squirrels accomplish amazing feats during long periods of inactivity, in some ways, Barnes says, black bears—another of his study species—are better hibernators: **Wintering rodents have to urinate, while bears don't.** "They're a closed system," he says. They hibernate five to seven months a year without food or water. All they need is air.

While hibernating, black bear basal metabolism drops 25 to 50 percent. Because of its large size, a bear can retain heat, so its body temperature doesn't drop as low as does a rodent's, varying from 86 to 96.8 degrees F during multiday cycles. At this relatively high level of metabolism, hibernating bears change position from once every two days to twice a day and can wake to defend themselves from intruders.

In Alaska, where Barnes studies them, black bears leave their dens in April. By then the body temperature is normal at about 99 degrees F, but resting metabolism remains low for up to three weeks, hovering just above 50 percent of basal rate. Barnes suspects that the low metabolism may stem in part from changes in the digestive system. **"Bears probably shrink a number of organs during hibernation**—the gut, the liver," he suggests. "When they begin feeding, they need time to regrow the gut, which may be what we're seeing during the delay in metabolism. The bears that we have studied certainly are interested in food, though on day one or two they may not eat. Within a few more days they are ravenous—they're eating."

What Hibernators Could Teach Us

Both bears and squirrels, as well as other **hibernators, show physiological conditions of interest to researchers seeking medical applications**. For example, a nonhibernating mammal that remained inactive for 4 to 17 weeks would suffer bone loss of 9 to 29 percent due to decreases in bone formation as well as significant muscle loss. Although hibernating bears and ground squirrels are largely inactive, they show no loss of bone, little loss in muscle mass and strength, and maintain skeletal function and mobility during and after hibernation.

"**There's a lot to be learned from bears, especially for human medicine**," Barnes says. His studies show that in some black bear tissues more genes are turned on during hibernation than during summer months, which may result in physiological changes that prevent bone and muscle loss. For example, Barnes and his colleagues have found that 24 genes involved in the use of fats and in the construction of protein were turned on significantly more in both heart and liver during hibernation—changes that presumably help to reduce cardiac and other muscle atrophy. The researchers are trying to learn how the genetic mechanism works and if it can be replicated in humans.

Arctic ground squirrels may offer answers to another question on Barnes' mind: How are the rodents **protected from heart attacks** caused by blood clots while their hearts beat slowly? Researchers, he says, can stop a hibernating squirrel's heart for 45 minutes and start it again without causing any damage to the animal's brain, heart or body muscles.

Damage to tissues from heart attack is caused in part by inflammation. Squirrels "dial down the inflammatory response," Barnes says, and also undergo physiological changes—for example, the blood becomes more viscous—that decrease clotting. Apparently they survive by turning off all genes for sugar metabolism and switching to burning fat, which may offer **protection from strokes and heart attack**. The mechanism behind this change is unclear, but research in this area offers promise for cardiac treatments.

Across the continent, in the Department of Pediatrics and the Hospital for Sick Children at Canada's University of Toronto, Dr. Ronald Cohn is linking studies of a hibernating prairie rodent, the thirteen-lined ground squirrel, with potential treatments for muscular dystrophy, which in humans exposes muscle to injury and atrophy even if its victims remain active. "**Hibernating animals know something we don't know**," he says.

If he can locate **the mechanism that allows the ground squirrels to prevent muscular atrophy**, he may find applications to prevent wasting away in humans. Atrophy is caused by degradation of muscle-building protein. Cohn is focusing on SGK, a protein that in ground squirrels plays a role in protecting muscle from atrophy during inactivity. Cohen suspects that SGK prevents loss of muscle mass in squirrels by ensuring that proteins don't degrade. He is testing how the protein works in various animal models. Ideally, he wants to produce a pill that can be used to **treat atrophy caused by disease and even by aging**, allowing humans to mimic the benefits of hibernation without sleeping.

Similarly, **natural mechanisms used by hibernating turtles** to protect the heart and brain from oxygen deprivation may one day **improve treatments for heart attack or stroke**. Both conditions can lead to severe disability or death within minutes in patients deprived of oxygen. Richard K. Wilson, director of Washington University's Genome Institute, and his colleagues recently identified 19 genes in the western painted turtle's brain and 23 in the heart that are activated in low-oxygen conditions. These genes also occur in humans and may prove important for exploring treatments designed to reduce tissue damage from oxygen deprivation.

"**Turtles are nothing short of an enigma**," Wilson says "They resist growing old, can reproduce even at advanced ages, and their bodies can freeze solid, thaw and survive without damaging delicate organs and tissues. We could learn a lot from them."

Roger Di Silvestro is a senior editor for National Wildlife.

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