

# Bone Loss and the Three Bears

## A circulating secret of skeletal stability

By INGRID WICKELGREN

In late fall, black bears retreat to their dens, lie down and cease to move, eat, drink, urinate or defecate for about five months. They appear inactive but are fully alert, their cells burning up to 4,000 calories per day.

Humming along at 50 to 80 percent of its summer energy expenditure, the metabolic factory inside a denning bear apparently operates like that of no other mammal. The bear loses fat but actually increases its lean body mass while fasting, and female bears carry and nurse their young while in the den. Ralph Nelson, director of the department of medicine at the University of Illinois College of Medicine in Urbana, has spent nearly the last two decades pursuing the secrets hidden inside bears' metabolic "black box."

Instead of disposing of much of their metabolic waste, bears recycle it. In particular, Nelson finds that denning bears normally turn potentially toxic nitrogen compounds into protein. Bears that cannot do this die from uremia, a condition in which nitrogenous wastes, normally excreted by the kidneys, remain in blood.

Bears must clear another metabolic hurdle, this one involving their unbur-

dened bones. All other mammals that maintain non-weight-bearing positions for a long time suffer from osteoporosis, a thinning and weakening of bone. Their bones slough off tissue faster than it's made, dumping calcium into the bloodstream. These mammals must excrete their excess calcium, because more than a certain blood calcium concentration is lethal.

Human astronauts, as well as the el-

somehow have to prevent their blood calcium from rising to lethal levels.

The mystery went unsolved until it piqued the curiosity of a young orthopedic resident one night while he read a book about bears. Timothy Floyd of the San Francisco Orthopedic Residency Program "realized suddenly that this animal must have a mechanism to prevent osteoporosis," he says. If so, the key to preventing human osteoporosis

might lurk in chemical form inside the black bear, he reasoned.

Determined to learn whether denning bears do lose bone, Floyd telephoned Nelson and asked if he wanted to collaborate on a research project. Nelson agreed, offering Floyd access to the three black bears he keeps in a research facility just outside Urbana.

Nelson's bears are retired "nuisance" bears, recurrent haunters of garbage dumps and human homes that would other-

wise find themselves "looking down a gunbarrel," as Floyd puts it. Their abode, which rests on land donated by a farmer interested in wildlife research, is equipped with an outside exercise area and cement culverts that function as



Photos: Garshelis

*In an underground den, a fasting, nondrinking mother cuddles her cub.*

derly or bedridden, often suffer from osteoporosis because their bones support almost no weight — and so should black bears, which lie in dens too small for weight-bearing positions. But if denning bears did lose bone, they would

dens.

From July 1987 until June 1988, Floyd shuttled back and forth between San Francisco and the Urbana research facility to study the three bears. He drew monthly blood samples, from which he measured calcium levels. He also took biopsies of a pelvic bone in each bear, once in the summer, once after denning and once in the spring. From the biopsies, he measured bone volume and rates of bone formation and resorption.

The calcium measurements confirmed two earlier studies suggesting that the black bear's blood levels of calcium and phosphorus, both used to make bone, remain constant throughout the annual life cycle. But Floyd was the first to demonstrate that the denning bear's calcium and phosphorous levels are normal *because* the bear's bone metabolism operates like that of an active mammal, according to Nelson.

To measure bone formation, Floyd used two fluorescent substances, which he injected a week apart. Then he took small biopsies of bone and examined them under the microscope. Because each dye is taken up at the places where new bone is forming, "the distance between the two fluorescent lines is bone that's formed," Nelson explains.

Comparing winter and summer biopsies, Floyd found the three bears' bone volumes were the same at the end of the denning period as before denning. "To our surprise, the bear's calcium remains normal and he makes bone," Nelson says. "So [the bear] acts very normal in its bone physiology despite no food or water, no urination and no defecation in the non-weight-bearing position. It's really amazing."

"We think [the ability to conserve bone while immobile] is unique to the bear," he says. The hibernating ground squirrel, for example, controls its calcium levels by urinating during periodic awakenings, but this calcium loss results in osteoporosis.

"My feeling is that [black bears] probably produce a regulatory substance which is responsible for maintaining bone mass," Floyd says. "We think the factor may be circulating in the blood."

Floyd and Nelson believe that if they can purify the bear's bone-preserving factor(s), this may eventually enable physicians to prevent osteoporosis in humans, including postmenopausal women and astronauts in long-term weightless conditions. Last October, Floyd presented his findings in Washington, D.C., at the meeting of the American Society for Gravitational and Space Biology.

Floyd says he is "going to continue to look at both captive and wild bear bone metabolism and will try to work toward identifying and isolating a serum factor that may be the responsible factor." But Nelson and his co-workers may beat him to it. After two years of searching for

## Working with bears: Very, very carefully

Timothy Floyd remembers being bitten by a black bear cub at age 3, an event that created a lingering interest in the animals. Although he didn't begin studying bears until last year, "when that thing bit me, I became attracted to them," he says.

Researchers at the Illinois facility where Floyd conducts his bear research don't actually touch the bears while they are awake and mobile, but instead stick an anesthetic-filled needle through a small port in their cement



Researcher draws blood from an anesthetized wild bear.

culvert-cum-den. While the bear is anesthetized, the researchers take blood and bone samples, but they do so as quickly and infrequently as possible to minimize any harm to the bear.

To follow bears in the wild, researchers fit them with special collars that can be tracked by radio. To conduct studies, scientists anesthetize the animals before handling them briefly. Veteran bear researcher Ralph Nelson of the University of Illinois works in the wild with Dave Garshelis, bear project leader of the Minnesota Department of Natural Resources. "When [Garshelis] checks bears in the winter, we tail along

and collect blood samples," Nelson says. In future studies, says Floyd, "while [other researchers] are drawing blood, I'll just take a small piece of bone."

Nelson was bitten by the bear bug 19 years ago when he hit upon the idea that the healthy, non-urine-producing denning bear might provide a hint for treating people with kidney disease. He has since translated that research into a dietary management program to allow people with chronic renal failure to go for as long as 10 days without dialysis.

Asked why a medical researcher studies bears, he replies: "The bear has a secret — that's why." — I. Wickelgren

chemical compounds unique to black bears, the Illinois researchers have isolated a substance they hope will turn out to be important in maintaining bone.

"It's quite exciting work. We do know it's a unique substance but we don't know what it does [in the bear]," Nelson says. So far, the scientists have used every bit of the purified substance in experiments to determine its structure.

Whatever the circulating substance, bear bones remain metabolically active throughout denning and their recycling of bone seems to mirror their recycling of protein. Although their bone metabolism is most active in the spring, when the animals' activity increases, Floyd's preliminary measurements indicate that bone activity is actually greater during denning than during the summer/fall season.

Bone forms in different places in the winter than in the spring. In the spring, bear bones remodel, adding material to the "main pressure points where bones support the body," Nelson explains. "In winter, when the bear is lying in the den, bone formation occurs in nonstressful areas because there is no stress [on the bones]."

Floyd plans to repeat his experiment this year in captive bears to sample other types of bone. He also plans experiments using wild, "radio-tracked" bears living in Michigan and possibly Wisconsin, under an agreement with the states' departments of natural resources. Wild bear studies will give Floyd a larger sample size and a chance to prove his results are not an artifact of captivity.

Nelson says he is confident Floyd's findings will hold true in the wild. "We always reaffirm [our studies]," Nelson says, but he and others have already verified the data showing constant year-round levels of calcium and phosphorus in wild bears.

Nelson, who had just completed a study of the bear's calcium and phosphorus levels when Floyd contacted him, says he too had been thinking about the problem of what bears did with their bone. So when Floyd called, "it worked out just perfectly," Nelson says.

Maybe for Nelson. But Floyd, who must juggle this project with his residency, is himself something of a metabolic miracle, performing the bear research on weekends and vacations. "And I'm still married," he says. □