Eat Less, Live hunger?

Restricting calories extends animal life, so doctors want to know if going hungry would help us too.

■ Bryan Walsh

1.John Apollos is losing weight the old-fashioned way -- by eating less, A whole lot less. As a volunteer in the two-year Comprehensive Assessment of Long-Term Effects of Reducing Intake of Energy (CALERIE) study at Tufts University in Boston, Apollos has lowered his daily caloric intake 25% over the past eight months. The fat, not surprisingly, has melted away; the 52-year-old physical trainer has lost more than 25 lb. (11kg) since the study began and is down to his high school weight.

2.But that's not the real reason. Apollos and the other participants in the program are eating only three-quarters of what they to. The researchers running the multicenter CALERIE study are trying to determine whether restricting food intake can slow the aging process and extend out life span. "I feel better and healthier," says Apollo。 "But if it could help you live longer, that would be pretty amazing."

3. The idea is counterintuitive: If we eat to live, how can starving ourselves add years to our lives? Yet decades of calorie-restriction study involving organisms ranging from microscopic yeast to rats have shown just that, extending the life

spans of the semi-starved as much as 50%. Last July a long-term study led by researchers at the University of Wisconsin nudged the implications of this a bit closer to our species, finding that calorie restriction seemed to extend the lives of humanlike rhesus monkeys as well. The hungry primates fell victim to diabetes, heart and brain disease and cancer much less frequently than their well-fed counterparties did.

4. But there may be more than just the absence of disease operating here. Anytime you go on a diet, after all, you stand a good chance lowering your blood pressure, cholesterol level and risk of diabetes and other health woes. Al that can translate into extra years. With calories restriction -- usually defined as a diet with 25% to 30% fewer calories than normal but still containing essential nutrients – something else appears to be at work to extend longevity.

5.Finding out what that something is-- and determining if it works in people – is what CALERIE is all about. By putting people on a carefully reduced diet for two years, investigators hope to home in on the biological mechanism that links eating less to living longer. They will also explore whether such a strict diet is even feasible in the overweight U.S. “We want to see if the same metabolic adaptations occurring in calorie-restricted rats and monkeys occur in humans,” says Dr. Luigi Fontana, a researcher at Washington University in St. Louis, Mo., who is helping lead the CALERIE study. “But we also want to know if people will really stick with

this."

6.Scientists have suspected that calorie restriction could extend the life span of animals since at least 1935, when researchers at Cornell University noticed that severely food-restricted lab rats lived twice as long as normal ones and were healthier. Other investigators began exploring the idea and learned that the secret is not merely a matter of body weight: lab mice that ate normally but became skinny by exercising a lot showed no longevity improvements. Only the ones that didn't get many calories to begin with benefited.

7.One theory is that a state of slight hunger acts as a mild but constant stressor that makes an organism stronger and more resistant to the ills of aging. (The effect could be an evolutionary adaptation, increasing the odds that animals would survive periods of scarcity) Taking in fewer calories also slows metabolism, and some data indicate that humans with a slower metabolism live longer. But even if these theories are correct, simply defining the mechanism is not the same as identifying the molecular pathways behind it. If researchers could determine those pathways, they might be able to pharmacologically mimic of the CARLERIE study.

"Calorie restriction is pretty much the only thing out there that we know will not just prevent disease but also extend maximal life span," says Dr. Marc Hellerstein, a nutritionist at the University of California, Berkeley, who studies the biological effects of fasting.

8.Volunteers for the CALERIE study – all of whom must start at a reasonably healthy body weight – first determine their resting metabolic rate, or the number of calories they tend to burn in a day. That figure is then reduced 25%. (In animal studies, the sharper the calorie cut, the greater the impact on aging, but 25% was chosen as a level that could be effective but still realistically achievable in humans.) For the first month, and nutrients they need and no more. After that, they design their own menu, though they receive frequent checkups.

9.The meals that the participants eat aren't unusual. Apollos, whose new daily limit is 2,408 calories – as an active trainer, his limit is unusually high – had room for a couple of pieces of fudge to go with his grilled-chicken salad at a recent lunch. Instead of reducing the portion size, people tend to switch to low-calorie, high-satiety diets – lots of fruits, vegetables and fiber – that help quell hunger. "it's a lot of normal food," says Rachel Murray, another CALERIE volunteer. "You just have to plan what you're eating."

10.The dieters lose weight almost immediately, usually reducing their body mass about 15% in the first year before plateauing. And they reap the expected health benefits: cholesterol and blood pressure drop precipitously. What intrigues CALERIE researchers, though, is the protein IGF-1 (which helps regulate aging) similar to that found in studies of calories-restricted animals. "We'll be able to see whether

calorie-restricted humans undergo the same adaption," says Dr. John Helloszy, a professor of medicine at Washington University and a lead researcher on the CALERIE study.

11.Even if it turns out that calorie restriction can slow the human aging process, there's ample reason to doubt that service dieting will ever be a realistic option for most people, In contemporary America, where calories are cheap and plentiful, cutting back 25% means almost constantly saying no, Alcohol is largely out, and dining with friends who aren't denying themselves would become a chore. There are some side effects as well: it's harder to maintain a very active lifestyle on a restricted diet, and libido often ebbs. Given the risk of eating disorders, especially among teenage girls, responsible doctors would be wary of recommending so obsessive a regimen. Even members of the Calorie Restriction Society, a group formed in the mid-1990s by people interested in the benefits of semistarvation, doubt their diet will work for many people. "A lot of people think this is crazy." Says Brian Delaney, the society's co-founder, who believes that calorie restriction is probably unsuitable for the broader population. "I wouldn't want to advocate it."

12.Still, studying calorie restriction should shed valuable light on the biology of aging, and anything we understand better we have at least shot at controlling better. As for Apollos, who has 16 months to go on the CALERIE study, he has grown fond of abstention and says he wants to continue the diet even after the

experiment is over. His improved health is, by itself, a form of renewed youth. But getting some extra years would be an even better one.

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