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Lean Times

The Surprising Rise Of a Radical Diet: 'Calorie Restriction'

Most Would See It as Close
To Starvation, but Is
Longer Life a Result?

A Muffin Tips the Scales

By LAURA JOHANNES

If there were a magic elixir that extended life to 150 years, most people would drink it gladly.

But as scientists begin to uncover the secrets of longevity, they are finding a prescription for long life that few will want to take: a diet so low in calories that to most Americans, it would feel close to starvation.

The diet, dubbed "calorie restriction" in the clinical parlance of science, would be called severe deprivation in any other lexicon. Calorie restriction was first shown to create exceptionally long-lived rats in the 1930s. It later had the same effect in guppies, water fleas, yeast, spi-

ders and a microscopic water invertebrate called the rotifer. Last month, Labrador retrievers became the first large mammals to join the list.

Now, scientists appear on the verge of a finding that calorie restriction also extends the lifespan of monkeys, who share more than 90% of their genes with humans. At the National Institutes of Health, where researchers have been studying a colony of 120 rhesus monkeys for 15 years, evidence for calorie restriction is mounting. The control animals, fed a healthy lowfat diet, are dying at a normal rate, while animals fed 30% less appear to be living far longer—and avoiding age-linked maladies. One of the underfed monkeys is 38 years old, the human equivalent of 114 years.

"Calorie restriction has worked in every species in which it has ever been tested," says Massachusetts Institute of Technology biologist Leonard Guarente. "I'd be shocked if it doesn't work in humans."

Catalyzing Change

Calorie restriction appears to create biochemical changes in the body that have a more-profound effect on lifespan than simply avoiding diseases caused by excess fat. No one knows for sure how it works. It might lower the levels of free radicals, or potentially toxic particles created by the breakdown of food. Other scientists believe it triggers a state of emergency called "survival mode" in which the body eliminates all unnecessary functions to focus only on staying alive.

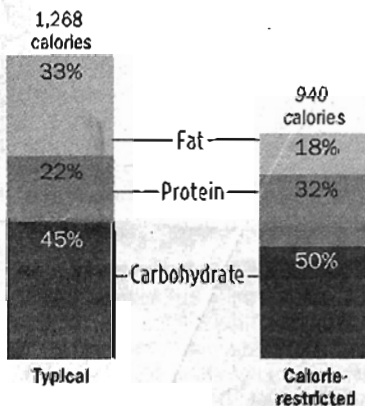
If scientists could figure out what the changes are and bottle them as a drug, "we'd have it made," says Roger McCarter, a scientist at the University of Texas Health Science Center in San Antonio.

Encouraged by the animal research, the NIH plans to spend \$20 million to test the effects of calorie restriction on hundreds of Americans. Some people have seen enough evidence already and have started self-depriving. Bob Cavanaugh, a 54-year-old landscaper from Morehead, N.C., has trimmed his intake to two meals a day, totalling 1,500 calories. Breakfast consists of one cup of quick oats, two tablespoons of toasted wheat

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Counting Calories

Source of calories in a typical and a calorie-restricted lunch or dinner



Source: Roy L. Walford, University of California

Lean Times: A Bare-Bones Diet Gains Followers

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germ, one cup of skim milk and blueberries. For dinner, he eats vegetables, fruit and a small portion of fish. "I'm hoping to see my great, great grandchildren," he says.

Mr. Cavanaugh's diet may sound extreme, particularly since at 5-feet 9-inches tall and 158 pounds, he isn't overweight. But over the next several years, if the monkey results hold up, they could represent a major shift in how we view food and nutrition. The U.S. Department of Agriculture says the average sedentary woman should eat 1,600 calories a day and the average man 2,200—benchmarks already significantly overshot by most Americans.

Minimal Intake

But those guidelines are based on ideal weight, and a calorie-restricted diet has nothing to do with weight. Rather, the NIH monkey experiments limit food intake to the minimum necessary to prevent negative effects on health—or at least 30% less than the current "healthy" diet. Translated into human terms, that would be 1,120 calories a day for the aver-

age woman, or 1,540 for a man.

For the average American, eating at that level would create deep hunger pangs. One meal at McDonald's—a Big Mac, supersize fries, and small Coke—weighs in at 1,450 calories. And if a woman on 30% calorie restriction had a cappuccino and a large muffin during her morning commute, she would already have consumed 75% of her allocation for the day, says Cathy Nonas, director of the Van Itallie Center for Nutrition and Weight Management at St. Luke's-Roosevelt Hospital in New York.

In the NIH tests, which will last as long as three years, volunteers will be asked to cut their current intake by 20% to 30%. Since many of those chosen will likely be overeaters, theirs will be a modest effort by comparison with the NIH monkeys. Still, to ensure compliance, the Pennington Biomedical Research Center in Baton Rouge, La., will initially require volunteers to eat only food provided by the scientists—and two of the three daily meals must be eaten in the laboratory cafeteria. Scientists will catalog the test subjects' metabolism and other biochemical markers, such as blood sugar, lipid

levels and body temperature.

The goal of the tests, says Evan Hadley, head of geriatrics at the National Institute on Aging, is to give scientists insight into how deprivation changes body chemistry. Residents of developing countries eat very low calorie diets. Their nutrition is so poor, though, that any positive effects are masked by medical problems caused by malnourishment, scientists say. But a study of the Japanese island of Okinawa—whose 1.3 million inhabitants have traditionally eaten a spartan, but nutrition-packed diet of 1,800 calories a day—provides some evidence for calorie restriction.

On Okinawa, where the diet consists of soy, vegetables and small amounts of fish, meat and rice, there are 34 centenarians for every 100,000 people—more than triple the U.S. rate, says Bradley Willcox, a gerontologist at Beth Israel Deaconess Medical Center in Boston. The oldest person in the world, 113-year-old Kamato Hongo, lives on a nearby island, he adds.

The Okinawa data fall short of a controlled experiment, because genetics or other factors could be at work. In rats, the effects of calorie restriction have been shown repeatedly, and they are dramatic. University of Wisconsin researcher Richard Weindruch says that broadly speaking, a 30% calorie restriction results in a 30% increase in maximum lifespan. Translated into human years, that would mean that the oldest members of the species would make it to about 150 on such a diet.

Even more striking is that the caloric intake of the rat, not its weight, matters most. Well-fed rats kept lean by regular exercise are less likely to die prematurely of disease than well-fed sedentary rats—but their maximum lifespan remains the same.

Primates, similar enough to humans that they have been used to study everything from congenital vision defects to Alzheimer's disease, remain the gold standard for proof when human experiments aren't practicable. But monkeys haven't been easy to study, because they live to be around 25, compared with three years for rodents.

At the NIH facility in Poolesville, Md., in a bucolic area about 40 miles from downtown Washington, scientists are growing increasingly excited about the results they are seeing. The experiment began in 1987, with monkeys of various ages. They were divided into two groups. One group was fed a normal low-fat diet, equivalent to the healthy diet recommended by nutritionists for humans. The other group received 30% less than that, or just barely enough to stave off starvation.

And that's the group that's thriving. Today, 14% of the calorie-restricted monkeys have died, compared with 22% of the monkeys on the normal healthy diet, says Mark Lane, a co-investigator on the study. Those figures exclude monkeys

whose deaths were deemed accidental, such as when a batch of overcooked food caused a fatal stomach ailment called gastric bloat.

"We're very excited," says Dr. Lane. "We think it's working."

Healthier Monkeys

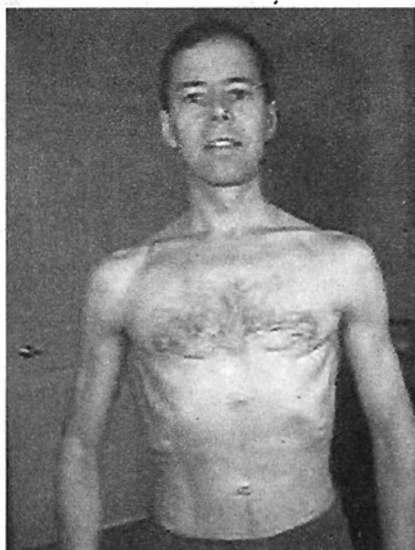
Not only do the calorie-restricted monkeys appear to be living longer, they also seem to be healthier. Only 14% of them have developed an age-related disease, such as cancer, cardiovascular disease, diabetes or failing kidneys, compared with 32% in the control group, Dr. Lane says.

Also, calorie restriction staved off the normal age-related decline in a multi-functioned hormone called dehydroepiandrosterone sulfate. DHEA, sold as a dietary supplement, has touched off a craze among Americans even though many scientists say there is no proof it will forestall aging.

It's too early to predict what the maximum lifespan will be in either group. But one of the calorie-restricted monkeys, a rhesus from Indian stock who goes only by the name given him by his breeders, C58, turned 38 in January.

That makes him one of the oldest rhesuses ever recorded. The University of Wisconsin, widely believed to have housed the oldest-ever rhesus, says the oldest monkey for which it had a firm date of birth lived to be 36. Another animal, still alive but without a well-documented birthdate, is believed to be about 39 years old. Neither of those monkeys were on calorie-restricted diets.

C58 looks thin but not gaunt. He weighs 17 pounds, compared with an average of 24 pounds for elderly control monkeys. Other than a touch of arthritis and a cataract, he appears in excellent health. Each day, he eats about 3.7 ounces of monkey chow—dried pellets



Dean Pomerleau, who practices a Calorie Restriction diet

Cronies, follow their own personalized diets, which share the common goal of minimal calories.

Many draw their inspiration from the Biosphere 2 project in the early 1990s. Volunteers attempting to live a self-contained existence in a glass-enclosed community were forced to reduce their calories sharply when food became unexpectedly restricted. One of the volunteers on Biosphere 2 was Dr. Roy Walford, a scientist at the University of California Los Angeles who is one of the pioneers of calorie restriction.

Michael Rae, a six-foot-tall 31-year-old from Calgary, Canada, weighs a gaunt 115 pounds after three years on a strict calorie-restricted diet. "I'd much rather weigh 50 more pounds, but I want to live longer and this is the only proven way to do it," says Mr. Rae. "Every calo-

bones commonly found in elderly women. One Cronie suddenly found himself severely anemic. He had to start taking iron supplements and eating more red meat.

Families sometimes resent the enormous amount of time it takes to maintain the Cronie lifestyle. For the most part, prepackaged food is out—because it would shoot the daily limit quickly, while providing inadequate nutrition.

Dean Pomerleau, a 37-year-old technology entrepreneur from Wexford, Pa., grows sprouts—bean, alfalfa, broccoli, arugula and a dozen other kinds—in his basement. "If you like arugula, you'd really like arugula sprouts," says Mr. Pomerleau, who is 5-foot-8 and weighs 127 pounds.

Terry, his wife, isn't enthusiastic. She told her husband the time-consuming preparation of his giant salads was dirtying the kitchen, he says. The solution: He spent \$1,000 to build a mini-kitchen for himself in the basement, adjacent to the sprout farm.

If scientists could discover what makes calorie restriction work, people might be able to enjoy the same effect without the hassle, and without the deprivation. One theory is that the lower body temperature caused by near-starvation somehow extends life. In case low temperature is in fact the secret, Mr. Rae avoids putting on a sweater even when he feels chilly.

There is mounting evidence for another favorite theory—that lower food intake results in fewer free radicals, or unstable particles created as a result of the breakdown of food. These particles can seriously damage genes and proteins, resulting in potentially fatal diseases. Advocates of this theory got a major boost when samples of thigh muscles from the calorie-restricted monkeys at the University of Wisconsin were shown to have suffered remarkably little free-radical damage, says Dr. Weindruch.

NIH scientists have also found preliminary evidence for the "survival mode" theory. The scientists found that human and rat cells grown in the blood of calorie-restricted monkeys are enormously resistant to heat and toxins—suggesting there is something in the blood that is fighting dangers aggressively.

Several groups of researchers are now racing to find which genes are "expressed," or turned on, during calorie restriction. In mice, the "gene-expression profile," or the list of genes whose functions are turned on and off, is strikingly similar in calorie-restricted animals to younger animals—indicating that calorie restriction may be directly reversing age-related biochemical changes.

In monkeys, so far, dozens of genes have been found turned on or off as a result of calorie restriction. But in preliminary data, the gene-expression profile of the restricted monkeys doesn't appear to mirror that of younger animals, says Stephen Spindler, a professor of biochemistry at the University of California at Riverside.

If scientists were able to figure out what makes calorie restriction work, people might be able to enjoy the same effect without the hassle—and without the deprivation.

compressed from wheat, corn, soybean, alfalfa, fish and brewer's yeast.

In his younger days, scientists say, C58 was an aggressive "alpha male," reaching out of his cage to grab passersby. But he's mellowed in his old age. On a recent day, he sat quietly, munching contentedly on a handful of chow and gazing out of his cage with mild curiosity.

A small group of humans are practicing C58-style calorie restriction in the hopes that it will provide a fountain of youth. These people, who communicate through an online chat group with 800 participants, call their philosophy "Calorie Restriction with Optimal Nutrition." Its practitioners, who dub themselves

rie you eat is a second off your life."

Cronies monitor their vital signs carefully. Like the Biospherians, their blood sugar, weight, blood pressure and cholesterol levels have dropped. They draw hope from the fact that they have few colds and flus, and that their bodies seem to be changing in ways similar to animal models. For example, just as the body temperature of rats and monkeys drops with calorie restriction, Mr. Rae's has fallen to 97 degrees, below the normal human temperature of 98.6 degrees.

But many Cronies become irritable and snappish. Testosterone drops, causing some of the men to lose interest in sex. Several men have developed early signs of osteoporosis—a disease of brittle