

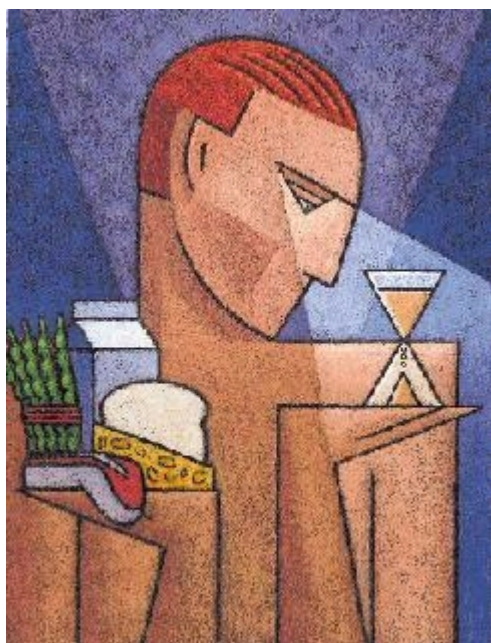
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## REPORT

Making the Choice  
Can Calorie Restriction  
Work in Humans?

Ben Best is betting that eating a low-calorie, nutrient-rich diet will slow his rate of aging and enable him to live longer. Here, he tells why and how he is conducting this experiment on himself.

By Ben Best



If you eat less, will you live longer? This is a question that scientists have been exploring in animal studies since the 1930s, when it was first observed that a very low-calorie diet can almost double the maximum life span of laboratory rats. Calorie restricted animals also have been shown to be more youthful in appearance, mentally quicker, and younger physiologically than normally fed animals. s But these experiments have been conducted in short-lived species, where results can be obtained within months or just a few years. The big question is whether calorie restriction can have the same benefits for humans or their close relatives. Scientists are now studying the effects of calorie restriction in monkeys. There has been evidence of the same age-retarding effects in these animals as in rats and mice, but it's too soon to know if the monkeys will live longer. An inadvertent calorie restriction experiment in Biosphere II showed that similar effects occur in humans. s Here, we present the experiences of author Ben Best, who is trying to slow aging and extend his own life span with calorie restriction. In future installments in this series, we will bring you updates on cutting edge studies with long-lived lab primates, whose experiments may portend similar results in mankind.

I have been practicing what is called "caloric restriction with adequate nutrition" (CRAN) for four years. Why? To live longer. Studies have shown that restricting calories by 30 to 60 percent (while maintaining adequate nutrition) extends the life span of rodents. This experiment has been repeated on hundreds of diverse

species of animals, including more than 200 mammalian species, with similar results.

A conclusive experiment on humans has not been feasible due to our long life spans, but it seems hard to believe that CRAN would not make us live longer.

The most thorough experiments on the life-extending effects of CRAN are documented in the book *The Retardation of Aging and Disease by Dietary Restriction*, by Roy L. Walford, M.D., and Richard Weindruch (who completed his Ph.D. under Dr. Walford). Walford has attempted to make his work accessible to lay people through other books, including *The 120-year Diet* and *The Anti-Aging Plan*. These books explain both theory and practice for adults desiring the health and life span benefits of CRAN. Weindruch has worked to popularize the benefits of CRAN among the scientific community.

Despite the extensive evidence of life span prolongation through CRAN among many short-lived species, it has been said their physiological adaptations would not be comparable to long-lived species like humans. To investigate this question, studies have been initiated on rhesus and squirrel monkeys at the National Institutes of Health, and on rhesus monkeys by Weindruch at the University of Wisconsin. Squirrel monkeys have a 20-year life span and rhesus monkeys have a 40-year life span. It is hoped that by studying biomarkers of aging (physiologic changes with age), much can be learned long before the experiments have ended.

Unfortunately, verified biomarkers of aging do not exist. In fact, one of the objectives of the experiments is to determine and validate biomarkers. One of the most promising candidates as a biomarker of aging is insulin resistance. With aging, there is increasing resistance to the effects of insulin, including facilitation of glucose transport into cells.

This may be due to glycation (protein cross-linking due to glucose) of insulin receptors. Since protein cross-linking may be an important mechanism of aging, insulin sensitivity and fasting blood glucose may be biomarkers of aging. Studies at NIH and the University of Wisconsin have found less insulin resistance in CRAN monkeys, when compared with control monkeys.

Inadvertent CRAN experimentation on humans occurred in the Biosphere 2-the experimental, self-contained environment in Oracle, Ariz., near Tucson, occupied by scientists from 1991 to 1994, and now part of Columbia University-in which the food available for the scientists was found to be less than anticipated, although nutritionally adequate. Because Walford was the physician for the eight-member Biosphere team, he monitored, documented and later summarized the results.

In the first six months, and on 1,800 calories per day, the Biospherians showed an average 15 percent weight loss, 18 percent lower blood glucose, 35 percent lower blood cholesterol, and 18 and 21 percent (systolic/diastolic) lower blood pressure. Although cholesterol and blood pressure are not biomarkers of maximum life span, they are biomarkers of average age of death.

I place a great emphasis on the fact that nutrition must be adequate to prevent deficiency disease in order for caloric restriction to work. The use of adequate nutrition might seem trivially obvious, but in 1971 the Annual Review of Biochemistry reported that 24 percent of the rat studies in the Journal of Nutrition contained inadequate amounts of vitamins and minerals. This undoubtedly accounted for a large portion of failures to extend life span with calorie restriction. Today, no serious gerontologist questions that CRAN can extend life span.

Six years ago I weighed 168 pounds. Now my weight is closer to 120 pounds. I am between 5 feet, 7 inches and 5 feet, 8 inches tall. My blood pressure has dropped from highs of 130/96 to about 100/70. In the first three years of my practicing CRAN, there was a 20 percent drop in my blood glucose, and a 47 percent drop in my blood uric acid. My LDL/HDL cholesterol ratio dropped from 2.0 to 0.86 and my blood triglycerides dropped to one-third of the previous value.

I do not use complicated computer programs to obtain adequate nutrition from foods. I rely on Life Extension Mix and other supplements to provide me with more than adequate nutrition. My breakfast consists of 100 grams of broccoli, 100 grams of strawberries, a spoonful of Life Extension Herbal Mix and a scoop of Natural Flavor Designer Protein powder blended together. This gives me about half of my daily requirement of protein, at less than 150 calories. My next meal is at 4 p.m., usually consisting of some fat-reduced tofu with sweet red pepper and berries (about 200 calories). Most of my calorie intake is in the evening.

The World Health Organization estimates that a 143-pound male requires 2,700 calories a day to maintain his weight, and that a 121-pound woman requires 2,100 calories. For six months, I kept below 1,600 calories a day, and below 1,400 calories a day for one of those months, although now it is probably more in the range of 1,800 to 2,000 calories a day. Vegetables are the staple of my diet, with skim milk cheese, defatted tofu, lentils and occasional fruit (usually strawberries). When people or laboratory animals eat a diet high in fiber, they consume fewer total calories.

Although much experimentation has been done on the effects of CRAN, there has been little or no experimentation to determine the combined effects of varying rates of weight loss at various ages on the life-extending benefits of CRAN. Walford had made some intuitive guesses about this, but his experience with Biospherians losing an average of 15 percent of their body weight in six months caused him to decide that weight loss could safely occur more rapidly than he previously thought.

A pound of fat corresponds to about 4,000 calories, whereas a pound of lean tissue (mostly protein) corresponds to less than half that many calories. A dieting fat person is more likely to lose fat than a dieting lean person, everything else being equal. Combining dieting with exercise results in less loss of lean tissue and more loss of fat. The greatest danger in excessively rapid loss of weight is potassium depletion and damage to and loss of heart muscle, leading to cardiac arrhythmias. Cardiac arrhythmias have been a major cause of death among anorexics and among dieters who used liquid protein diets.

Modern, very low-calorie diets use high quality protein (like egg albumen) along with carbohydrate to reduce electrolyte loss, as well as ketosis, a condition that occurs when fatty acids are incompletely metabolized as a result of (in this case) starvation-like conditions. Whey protein in the diet should be particularly good for weight loss because whey is high in branch-chain amino acids, a major component of muscle protein. The mortality rate for modern, very low-calorie diets is actually lower than that for obese controls. Adequate nutrition during weight loss will not be the same as adequate nutrition during steady-state caloric restriction.

Although exercise seems advisable to maintain lean tissue during weight loss and to reduce the risk of cardiovascular disease in the general population, it is debatable whether exercise is of benefit for people practicing CRAN. The most careful research on this subject has been the rat studies of John Holloszy at Washington University School of Medicine in St. Louis, Mo. His experiments seemed to indicate that aerobic exercise actually reduced the benefits of CRAN. But in his most recent experiment on the interaction of CRAN and exercise, Holloszy found no difference between the survival curves of exercising and non-exercising CRAN rats. He speculated that his previous results may have been due to a health problem in the rats under study.

If exercise is of neither benefit nor harm to the practice of CRAN, then why do it? One reason I exercise is to maintain physical strength and endurance. I also exercise to reduce my dependence on diet alone for calorie restriction. Yet another reason for my

exercising is to lift my spirits. Many of those practicing CRAN complain of weakness, lack of energy and depression. I think exercise has much to do with why I rarely experience those symptoms. However, I do sometimes feel sluggish and dispirited in the midafternoon, possibly due to low blood sugar. Instead of taking a lunch break, I take an exercise break. Afterwards, I usually feel terrific.

Psychologically, my practice of CRAN has been very beneficial for me. For years I had been afraid to diet because of the media claims that "diets don't work" and that yo-yo dieting is more harmful to health than maintenance of a steady weight. However, the claim about the health hazard of yo-yo dieting (for non-smokers at least) has been disproved.

Even if it were true that the extension of maximum life span seen in CRAN experimental animals is not applicable to human beings, there is much evidence that CRAN will extend the average life span of people.

Death by cardiovascular disease shortens human life by an average of 13 years. However, it has long been known that cardiovascular mortality is lowest among those who are leanest. For this reason, CRAN may actually be of more benefit to humans than to rodents, since rodents usually die of cancer rather than cardiovascular disease. Additionally, cardiovascular health will likely reduce the rate of vascular dementia, the second most common cause of dementia in the elderly (after Alzheimer's disease).

Fifteen percent of people over age 60 develop maturity-onset diabetes, usually due to excessive calorie intake. The likelihood of developing diabetes doubles with each decade of life, and also doubles with every 20 percent gain of body weight above average. Earlier cancer studies had shown that being 10 percent underweight is less of a risk factor for mortality than being 20 percent underweight. But more recent studies that carefully corrected for smoking and underlying disease have shown that the leanest people are the least likely to die.

One benefit is the fact that I seem to require less sleep, something other CRAN practitioners also have noticed. For a two-year period I had no sickness of any kind, not even my annual Christmas cold/flu. Nor do I feel that I lost the pleasures of food. In fact, I have never enjoyed food so much as since I have adopted the practice of CRAN. I eat less, but what I do eat I enjoy immensely. This has made it easier for me to learn to like foods such as low-fat tofu.

My practice of CRAN has had some difficult social consequences. Since so many social activities center around food, it can create problems. I don't want to insult people who prepare food for me and I don't want to cut myself off entirely from dinner parties. I keep the frequency of social dinners to fewer than one per week.

For nearly three years, I have been an active contributor to an Internet list server group of people who are practicing CRAN (more often called CR). Until last year, there were monthly postings that summarized data about the participants, including height, weight, estimated "set-point" and calories consumed per day. My practice of CRAN was among the more stringent (but by no means the most stringent) of the group. Comparisons are difficult, however, because bone thickness and muscular development may be different for two individuals of the same height and weight. Additionally, some people are naturally thin.

About a year ago, someone conducted a survey of 14 people on the Internet list in order to determine frequency of side effects, both positive and negative. About 50 percent reported low moods or depression, and about 30 percent reported muscular weakness. These symptoms were greater in the "higher-level" practitioners than in the "mild to moderate" practitioners. At my current level of "moderately rigorous" CRAN (120 pounds), I experience none of the above symptoms. Nor do I experience the drop in energy reported by 40 percent of the "high level" participants (most of the "mild to moderate" participants reported normal or increased energy). I believe this is because I exercise and take supplements.

"I have never enjoyed food so much as since I have adopted the practice of CRAN. I eat less, but what I do eat I enjoy immensely."

All participants reported greater sensitivity to cold weather. Eight respondents reported lower body temperature, averaging 97.0 F (36.1 C). Half reported a decreased sex drive and about 30 percent reported hemorrhoids.

On the positive side, most reported reduced sleep requirements as well as normal or increased alertness and clarity.

Aside from lack of exercise, I suspect that many CRAN practitioners suffer from weakness, depression and lack of energy as a consequence of vegetarianism. Most people attempting CRAN are vegetarians or near-vegetarians. In some cases there may be problems with vitamin B12 deficiency. But there may also be a problem due to carnitine, which is known to be significantly lower in the diet and bloodstream of vegetarians. Carnitine protects heart muscle from ischemic damage and has been used to treat chronic fatigue syndrome. The acetyl-L-carnitine form (I take 500 mg every morning) crosses the blood-brain barrier, is neuroprotective and has been used as an effective treatment to slow the progress of Alzheimer's disease. I think that supplements like DHEA may complement CRAN, and that antioxidants are of particular benefit for reducing free radicals produced from exercise and pollution. I have been taking deprenyl, coenzyme Q10, DHEA, tocopherols, melatonin, ginkgo and DMAE, acetyl-L-carnitine (especially good for vegetarians), and essential fatty acid and multi-mineral capsules, in addition to my Life Extension Mix. I take my supplements with my meals, at 8 a.m., 4 p.m. and midnight. In fact, my mealtimes are based on my attempt to take my supplements with food

and ensure even blood levels of my supplements (especially the DHEA and water-soluble vitamins).

I believe that most people can practice some degree of CRAN with few or none of the problems I have had if they are willing to learn from my experiences. I doubt that many are willing to go to the extremes that I have gone to. But I think that a mild to moderate practice of CRAN could be a way for most people to see present improvement in health and an extended life in the future.

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# REPORT

Continued from Can Calorie Restriction Work on Humans?

## Imposing Self-Restraint

People often speak of hunger as being a barrier to practicing CRAN, but people often eat for reasons other than hunger. People eat out of habit, often because it is "mealttime," a social ritual. Also, people regularly eat for enjoyment, to entertain themselves, as well as because of appetite, something very distinct from hunger. And people eat until they are "full." Eating to satiety is very difficult to avoid, although resisting the temptation to start eating is much easier than ceasing to eat once eating has begun, says author Best.

"I am not afraid to experience hunger," he notes. "If a person wants to seriously restrict calories, then will power and a willingness to experience feelings of hunger must eventually enter the picture. It is remarkable to me how absolutely unwilling people can be to allow themselves to feel even the slightest amount of hunger. Often, all that is needed is to wait a few minutes for the feeling to pass. But even if the feeling does not immediately pass, I think it is a discomfort that a person can learn to live with, like the necessity of getting up in the morning to go to work, or engaging in exertions required for exercise. Learning to accept various levels of hunger is like building a muscle. It takes practice."

Nonetheless, Best is still trying to find gimmicks he can use to reduce his calorie intake while minimizing his discomfort. "Changing eating habits involves training. Once skim milk tasted like water to me, and I avoided it. However, I trained myself to drink skim milk rather than 2-percent milk until I finally accepted skim. Now 2-percent milk tastes like overly rich cream to me. I have trained myself to eat low-calorie vegetables when my appetite might incline me to eat something else. And I have learned not to buy or keep high-calorie foods in my kitchen."

Best says a useful practice he has found is to refuse to eat any food that he has not first weighed and calculated the calorie content for. The book *Food Values* by Jean Pennington contains the calories per gram of all the foods he eats. These results are summarized in sheets of paper taped to his cupboard doors.

"Calculating the caloric content of all eaten foods does a great deal to increase awareness of calories, and the process is essential for anyone restricting themselves to an upper limit of calories per day. For six months I weighed all my food and calculated calories to ensure that I would not exceed 1,600 calories per day."

## Charting One Man's Physical Examinations

| Year | Weight (Pounds) | Blood Pressure | Glucose (MMOL/L) | Leucocytes (X10 <sup>9</sup> /L) | Uric Acid (UMOL/L) | Triglyceride (MMOL/L) | HDL (MMOL/L) | LDL (MMOL/L) |
|------|-----------------|----------------|------------------|----------------------------------|--------------------|-----------------------|--------------|--------------|
| 1989 | 158             | 130/96         | 4.8              | 9.0                              | 339                | 1.82                  | N/A          | N/A          |
| 1991 | 168             | 124/90         | 4.8              | 7.3                              | 358                | 2.10                  | 1.31         | 1.95         |
| 1992 | 157             | 130/94         | 5.1              | 6.3                              | 308                | 0.83                  | 1.12         | 1.76         |
| 1993 | 150             | 120/80         | 5.5              | 7.8                              | 349                | 1.94                  | 1.20         | 2.41         |
| 1994 | 130             | 110/80         | 4.7              | 5.1                              | 215                | 2.02                  | 1.45         | 1.03         |
| 1995 | 120             | 106/70         | 4.4              | 5.1                              | 233                | 1.00                  | 1.26         | 1.43         |
| 1997 | 112             | 100/80         | 4.4              | 5.1                              | 186                | 0.71                  | 1.52         | 1.31         |

Ben best in experimenting with calorie restriction over the past several years has recorded dramatically changing vital bodily measurements in that time

## Some CRAN Caveats

CRAN is not without its hazards, above and beyond the inability to indulge all the pleasures of the appetite. Nearly all CRAN practitioners experience an increased sensitivity to cold, particularly in the extremities. Author Ben Best reports that his feet are usually cold if he take no precautions. He wears at least two or three pairs of heavy socks, even when sleeping.

"Another hazard is hemorrhoids," Best says. "During various stages of my food restriction experiments I noticed that my stools would become small, dry and hard. Eventually I got hemorrhoids. I now know that adequate nutrition for CRAN must include adequate fiber. Eating many vegetables doesn't necessarily guarantee adequate fiber. The best fiber to prevent hemorrhoids is a mixture of psyllium and wheat bran. This mixture has the added benefit of having been shown to reduce the incidence of colon cancer in experimental animals to a quarter of that seen in controls. Colon cancer is second only to lung cancer as a cause of cancer death in humans.

The very worst hazards Best experienced in practicing CRAN were toward the end of his 6-month period on fewer than 1,600 calories per day. His weight had dropped below 115 pounds and he was experiencing lightheadedness, physical weakness, periodic cardiac acceleration and gastrointestinal pains. His lightheadedness was so extreme at one point that he fainted-not while driving, luckily. He experienced his first flu in more than two years, and had difficulty shaking it off. He was down to 112 pounds when it was time for his annual physical examination.

"My 15-hour fast in preparation for my examination caused me great discomfort, possibly including symptoms of hypoglycemia (low blood sugar). When my physician put me on an EKG he found bigeminal rhythm-extra systoles (heartbeat irregularities). He didn't rush me to the hospital, but he did warn me that I should gain some weight. Extra systoles are not usually life-threatening, but they can be. I immediately went on an eating binge. It took me a while to regain my stability and pursue a more 'moderately stringent' version of CRAN. Currently, my target weight is 120 pounds, and I rarely go above 123."

Laboratory animals are in protected environments. However, people who are living workaday lives may be subject to stresses and vulnerable to conditions that could make hypoglycemia or weight-loss due to a disease more dangerous. Best believes that keeping his weight between 119 and 123 pounds provides him with a certain buffer against such events. He also suspects that there may be an important difference between CRAN that is imposed upon laboratory animals and CRAN that is a voluntary practice-in short, voluntary CRAN can create psychological stress. Beyond a certain intensity this stress may be physically damaging because of secretion of excessive amounts of stress hormone (cortisol). In fact, hypercortisolism is seen in CRAN animals and in anorexics, he notes. One theory of aging makes a strong case for the idea that stress and glucocorticoids play a key role.

"Another thing I learned from my physical examination," Best says, "was that my testosterone levels were well below the normal range. I had noticed a dramatic drop in my libido and was well aware that CRAN animals typically show reduced levels of sex hormones. Female anorexics often stop menstruating. A silver lining to my low testosterone levels, however, is the reduced risk of prostate cancer. My prostate specific antigen (PSA) level was 1.5 nanograms per milliliter of blood serum, well below the normal limit of 4.

"Sex hormones are produced from DHEA, which in turn is produced from cholesterol. My blood DHEA had been equal to the level of an average 95-year-old-which is pretty low for a middle-aged man like me. After learning that my testosterone was also low, I began taking 15 mg of DHEA three times daily in the hope that my DHEA and testosterone levels could increase. As a result, my libido has increased somewhat, and a more recent Life Extension Foundation measurement of my DHEA has shown me to be at the level of an average 75-year-old."

DHEA is known to oppose the actions of cortisol, so this might be a way to oppose the "stress response" and boost his immune system, Best says. He plans to increase his DHEA and see what his blood levels of cortisol and testosterone are at his next physical examination.

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