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REPORT

**Eat to Live,
Don't
Live to Eat**

Calorie restriction offers a multitude of health benefits

By Brian Manning Delaney

A breakfast business meeting. Sunday brunch with the kids. Lunch with a colleague. Dinner and dancing. A midnight snack. Eating has become a pastime and business facilitator, something to do for fun or discuss a deal over. It has become so ingrained in our lifestyles that our appointments and social gatherings are routinely scheduled around one such event. Eating now serves a social, even financial purpose. So much so that we have forgotten the reason why we engage in the activity to begin with: to live.

In an age where science is at the frontiers of revolutionary advances, it would seem unnecessary to take life extending measures that, on the surface, appear to lessen quality of life. Calorie restriction (CR) could be so classified, given the extent to which food and eating are an integral part of our contemporary lifestyle. But a closer look reveals the wisdom of eating to live, and the possible folly of living to eat.

Giving food consumption its original and sole responsibility back is partly what a calorically restricted diet does. Its purpose: life extension. In study after study conducted on a variety of laboratory animals, CR has been shown to dramatically extend life span. While it may prove challenging to break the social barriers that tie us to food, the promise of living longer may help us do just that.

Also known as “under nutrition without malnutrition” or the “high/low diet,” CR refers to a normal, healthy diet with one modification: the reduction in the diet’s caloric content, anywhere from 10% for a noticeable effect, to as much as 40% to 50% for a maximum effect. The latter definition applies to the use of CR for the purpose of slowing aging and, therefore, extending life.

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How CR alters aging is not yet clear, but there are some possible explanations. Aging is made up of various components, and there are theories to explain how CR affects each of these factors. CR, for instance, alters the way the body uses glucose; it enables the body to use glucose more efficiently. This “efficiency theory” also applies to other aging-related changes. For instance, it appears that, over time, insulin—essential to cells in order for them to use glucose properly—causes some of the changes seen in aging. CR causes a dramatic reduction in circulating insulin levels, probably because cells simply need less insulin: they are more efficient in their use of glucose, and in their sensitivity to insulin.

Many theories of aging focus on the deleterious effects of glucose itself. CR causes a reduction in average circulating glucose levels. Glucose molecules can cause chemical links to form between proteins, between parts of proteins or among other important biological molecules, links that can render the molecules useless. (See “Aging Revealed,” Life Extension magazine, November 1999, p. 52, for the results of some exciting CR research with wide-ranging implications.)

CR in humans

The gold standard of contemporary western medical research is the clinical trial. The essence of the clinical trial is to take two



groups of similar people, apply the drug or diet or exercise regimen being investigated to the members of one group but not to the other, then wait to see whether a difference between the two groups manifests itself. If all differences between the two groups other than the application of the regimen are minimal (“controlled”), an observed difference between the groups can be attributed with confidence to the regimen under examination. When the difference in question is, for example, the resolution of flu symptoms, the study can be completed in a matter of weeks. On the other hand, when the difference in question is the retardation of aging, the study requires decades, if not over a century, to complete.

The young and controversial field of anti-aging medicine is thus by its very nature beset by the difficulty of having to rely on indirect evidence in assessing its potential treatments. As it is, it may be necessary to piece together various factors. While indirect, the evidence is nonetheless compelling.

Evolutionary ubiquity

CR is a highly “trans-species” phenomenon. Indeed, it so far appears to be nearly “trans-animal kingdom.” That is to say, the longevity effect of the CR diet is elicited when the diet is applied to an extremely wide variety of creatures, creatures as distant as amphibians and mammals. If the CR effect has been preserved through numerous, widely divergent branches of evolution, why would homo sapiens have “lost” this effect?

Epidemiological data

While epidemiological data generally cannot provide the same strength of findings as large clinical trials, it does provide support for the thesis that CR works in humans. The ideal situation would be to find a culture or subculture that naturally ate a CR diet, then compare the mortality of this group to that of a group that is identical in as many ways as possible to the CR culture, but that doesn’t follow a CR diet. Finding such a “CR culture” is, however, quite difficult.

There are, of course, plenty of cultures where food is restricted, via famine, for example. But calorie restriction does not equate food restriction: calorie restriction for the purposes of slowing aging involves a healthy diet that is restricted in calories alone. The limitations do not extend to a restriction of vitamins and minerals. Such a longevity-enhancing diet would occur only in non-famine conditions, where ample, nutritious food is available. Yet where ample food of any kind is available, people tend to eat amply.

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One exception appears to be the residents of the Japanese island of Okinawa. On average, Okinawans appear to eat a mild version of the CR diet. Okinawans live much longer than genetically similar people on a more traditional Japanese diet. If the longest-lived of different Japanese sub-populations are compared, the difference is striking. According to a recent study, the overall proportion of centenarians in Japan was 21.6/100,000 people in 1990. By prefecture, the highest proportion of centenarians, by far, was in Okinawa. In Okinawa, the centenarian rate was found to be 133.8/100,000—a statistically significant difference. Note that this is the highest corroborated per capita centenarian rate in the world, among a large cohort.

Biomarkers

Biomarkers probably constitute the strongest evidence for CR’s efficacy in humans. It was noted earlier that anti-aging medicine requires decades-long studies in order to issue certain results. Nevertheless, strongly suggestive, if not quite certain results are possible with biomarker studies. A biomarker is simply a measurable parameter of some aspect of health. A biomarker of aging is a measurable parameter of aging. To see the potential power of biomarkers for anti-aging research, imagine that we discover a molecule that is absent at birth, but then consistently increases in the blood for normal, healthy people by one milligram per deciliter per year. For healthy people not on an anti-aging regimen, the molecule would be measured at 1 mg/dL on their first birthday, 10 mg/dL on their tenth birthday, 30 mg/dL at their thirtieth birthday, and so on. If we discovered a molecule like this, then we wouldn’t need a century to run anti-aging experiments, we’d only need a few years. For example, if we took our group of ten 50-year-olds and put them on a CR diet, then all we’d have to do is wait a few years to see how their age biomarker changed relative to similar people their age who aren’t following the CR diet. Three years down the road, if the non-CR group has levels of 53 mg/dL, as we’d expect for 53 year-olds, and the CR group had an average level of 52 mg/dL, then we’d have a good idea that CR works in people. With more subjects in the study, and a few more years, we’d be able to conclude quite solidly that CR works in humans.

Unfortunately, aging appears to have so many separate aspects that it may be difficult to find one simple, entirely reliable biomarker. However, there are a wide variety of biomarkers that provide strong, if imperfect, evidence that CR works in humans. Some of these are markers of one’s biological age, and some are markers of the rate at which one is aging. A few short-term human CR studies are beginning to suggest that these biomarkers change in a direction that is consistent with an anti-aging effect of CR. For example, circulating levels of glucose in the blood have been shown to be significantly lower in humans after just a few

months of CR, yet without concomitant symptoms of a pathological hypoglycemia. Likewise, insulin has been shown to be lower in humans on CR.

Although this and other evidence that has not been discussed here is compelling, it is not absolute. But anyone seeking absolutes when assessing anti-aging regimens, be it CR or any other regimen, will have to wait at least a few years, if not decades. In the meantime, it's reasonable to assume that CR will produce in humans similar changes to those seen in laboratory animals. The more difficult question is not about the efficacy of the diet, but rather about the day-to-day difficulties of the diet.

Should you begin CR?

The decision to go on the CR diet is one of trading off the hardships of the diet for a significantly increased likelihood of having a dramatically extended life span. Once the decision about the desirability of an increased life span has been made, the questions then become mostly personal: just how difficult is the diet for me? What kind of sacrifices are entailed, and how much will they interfere with my life? Will I be hungry all the time? Will the hunger bother me too much to enjoy life? Will people constantly tell me I'm "too skinny?"

According to over one hundred people on CR, perceptions of the diet's difficulties vary widely. The one constant, not surprisingly, is the presence of hunger. But even the degree of perceived hunger, or appetite, varies substantially.

Take two examples: John Hayes and Bob Davis.* John began CR four years ago, at the age of 41. When he started the diet he was unhappy with his physical appearance (Jon was obese), had dangerously high cholesterol levels (total cholesterol: 270 mg/dL) and moderately high fasting glucose levels (about 100 mg/dL). He now has a total cholesterol level of 140 mg/dL, a fasting glucose level of 72 mg/dL, and is satisfied with his body image. He enjoys the challenge of cooking with fruits, grains and vegetables, instead of eating fast food, as he used to. He "feels good in his body." He finds the hunger a nuisance but, relative to the gains of the diet, it's a small price to pay.

Now let's look at Bob. Bob started CR ten years ago, at the age of 28. When he first began he was healthy, trim and muscular. All of his biomarkers were excellent (though his fasting glucose was 90 mg/dL, perhaps a bit too high). He went on CR because he decided CR was by far the most effective way to extend life, and that any sacrifice would be worth the extra decades. He changed his mind less than one year later, and went off the diet. Although his biomarkers improved in a direction suggesting that his aging rate had been slowed significantly, and he felt healthy, he thought he looked less than attractive (and his friends frequently told him as much), found himself thinking about food "all the time" and simply "missed carefree eating."

Others likewise find the diet very difficult for the first six or so months. They think of food far more often than they want to. But soon enough they adjust psychologically even if physically the reduced calorie intake is evident, i.e. hunger strikes powerfully at certain times during the day.

Some, like Bob, would not want to live a life that involves this kind of denial, even if it may result in extra years of life. A life that is perceived as one of constant denial simply isn't worth it for many people. But others would not perceive it as a life of denial, and, even if they did, would prefer to have additional years instead of additional donuts.

In considering CR, it is important to weigh the discomforts of the diet today with the potential risks of disease tomorrow.

Then again, here's an issue with the rapid advancement of technology on the anti-aging front. A dramatically expanded life span may well just be around the corner. So it might beg the question, Why suffer this often difficult diet? Read on.

To do or not to do...

In this new century, those on CR (or those on any health regimen that involves sacrifice) often consider whether science will revolutionize the treatment of aging soon enough to make CR today an unnecessary choice. Why should someone in, say, their early 40s bother with CR today when dramatic pay-offs in anti-aging research may be just around the corner?

Other than being around and healthy when discoveries are made, there are still two reasons why CR is a good bet for anyone, even today. First, those on calorie restricted diets enjoy an immediate reduction in the risk of contracting and possibly dying from age-related illnesses such as cancer, heart disease and adult-onset diabetes. This might not matter so much for someone with great genes, but for others, CR could be a life-saver.

Secondly, the extraordinary pace of current medical research is due in large part to our current prosperity. Although some countries are now enduring difficult times, poverty and war, there is no world war or global economic crisis that is taking time and resources from the advancement of medicine. The strength of the U.S. and other countries should offer assurance of continued stability in the geo-political and economic realm. This scenario sets the stage for the allocation of large sums of money for



research. But human history is not a straight line upward. It is marked by wars, depressions, natural disasters and even lengthy dark ages, as well as by eruptions of scientific and artistic brilliance. While we appear to be moving in the right direction, there's no guarantee—the 21st century may very well endure a decades-long step backwards before there are two steps forward.

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*These names have been changed.

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