



The Truth to the Fountain of Youth

News on the Only Proven Anti-Aging Medicine

This year, a distinguished panel of 51 top aging researchers released a position paper bearing the innocuous title, “Is there an antiaging medicine?”¹ Some of the main authors of this paper then boiled down their conclusions in more accessible language for the June issue of *Scientific American*, under a much more in-your-face headline: “No Truth to the Fountain of Youth.”²

The position paper upset a lot of people in the life extension community. Reactions ranged from anger to futile depression. The reason: while the article acknowledges that serious research into the biology of the aging process might one day lead to revolutionary interventions into the human aging process, it *dismisses* the interventions on which many of us are resting our hopes of prolonged or restored youth, slower aging, and extended lifespans. From exercise and a healthy diet to hormone therapies, supplements, and drugs, none of the common “anti-aging” regimens escapes their scorn.

Depressing as those conclusions may be, if people passionate for the cause of radical life extension were to really look at the evidence, they’d be forced to admit that the position paper is fundamentally sound.

The reason: while we now know that, while improved diet and exercise, along with some supplements, can reduce a person’s risk of *specific* health problems and age-related diseases, none the less **no pill, potion, or conventional “healthy lifestyle” choice has been proven to slow biological aging**. That is, they may help reduce your risk of *specific, age-related diseases*, but they cannot interfere with the fundamental issue of *aging itself*: the progressive, systemic, intrinsic loss of function and ability to homeostatically adapt to challenges, occurring all the way from the cell up through tissues and organs to the whole body, which leads to an exponentially increasing risk of disease and death over time.

Make no mistake: better lifestyle practices can be expected to give you a few extra years of healthy life, especially if you’re obese or otherwise at higher risk of cancer or heart disease than the average person. And if you’re happy with that, then the issues at stake may be irrelevant to you. But if you love life enough to set your sights on a future extending well beyond a couple of extra trips around the sun, you’ll have to look elsewhere.

There is some preliminary evidence that some supplements may yet prove to slow down aging. Most notably, there seems to be great promise in **R(+)-lipoic acid**,³⁻⁶ **Carnosine**,⁷⁻¹⁰ and the few nutrients *clinically proven* to reduce the formation of **advanced glycation endproducts (AGEs)** – notably **Benfotiamin**¹¹⁻¹⁴ and **Pyridoxamine**¹⁵⁻¹⁷ (unlike supplements which – whatever their other merits – have only ever been shown to slow down AGE formation under test tube conditions, such as **thyme extracts**, **performed glutathione (GSH)**, **inositol**, **grapeseed extract**, or **diosmin**).

But despite their potential, even these are not yet *proven* anti-aging interventions in the fullest sense. And indeed, **some therapies currently promoted as “anti-aging” medicine may actually be pro-aging**. The most notable example of this is **hormone replacement therapy with human growth hormone (hGH) or sex hormones** such as testosterone or estrogen (including even natural estrogen, such as TriEst). These hormones actually appear to *accelerate* aging in animal models,¹⁸⁻²⁰ and are associated with an increased risk of cancer^{21,22} and total mortality²³⁻²⁵ in humans. And on the other hand, a lifetime of *low* exposure to growth hormone (or its mediator, **insulin-like growth factor-1 (IGF-1)**) along with prolactin and triiodothyronine extends longevity in several animal models¹⁸ and apparently in humans.²⁶ Ironically, in fact, it now appears that “topping up” declining levels of hGH or testosterone don’t even deliver the promised improvements in frailty or quality of life,²⁷⁻²⁹ let alone longevity.

Bottom line: until you intervene at the level of fundamental aging processes, real leaps in long-term health and longevity – a gain of more than a handful of healthy years – will elude you.



Conventionally-Fed Mouse at The Same Age. Images Courtesy of the Weindruch Lab, University of Wisconsin-Madison.

But there is one bright spot in this gloomy picture. Indeed, its fire shines light across the health landscape, banishing the darkness of “anti-aging” hype.

Real Anti-Aging Medicine

As we’ve discussed in past issues (see especially “The Road to Aging is Paved with Calories,” *The Holistic Lifestyle* 1(5)), there is one intervention which has been proven to slow down aging *itself*, and thereby push those practicing it beyond the maximum lifespan of the species. That intervention is **Caloric Restriction (CR** – sometimes called **Calorie Restriction with Optimal Nutrition (CRON)** to more clearly distinguish it from simple starvation or malnutrition). Again and again over the course of the last 65 years, scientists have proven that if a healthy, non-obese organism eats food which contains fewer Calories than its body “*thinks*” that it needs – but which ensures an adequate supply of protein, essential fats, vitamins, and minerals – then the intrinsic aging process in the organism will slow down dramatically.

As a result, mammals with calorically-restricted nutritional plans routinely live lives dramatically longer than their conventionally-fed cousins ... and, more excitingly, many exceed the species maximum lifespan as well (see **Figure 1**).³⁰⁻³² It’s not just that animals on CR plans live longer on average than their conventionally-fed siblings. Instead, **an organism eating the CR way can live longer than that life form is “supposed” to be able to live.**

Crucially, animals on a caloric restriction nutrition program don’t extend their lives by suffering through even more of the debilitating “old” years. Instead, **the added years are youthful, healthy ones.** In experiment after experiment, by criterion after criterion, CR-fed animals live longer, live healthier, and live *younger* than any other animals in the world. CR animals are smarter, faster, more energetic, and better-looking at ages where animals fed conventional

diets are entering the gloomy twilight of their lives.^{31,32}

The sweeping anti-aging effects of CR have been documented in such diverse species as yeasts, flatworms, fruitflies, rotifers, spiders, fish – and above all, in laboratory rodents. In the article published in *The Holistic Lifestyle* last year, we detailed the powerful evidence which has been accumulated from rodent studies. We also discussed the ongoing National Institute on Aging studies on the effects of CR in our closest relatives: nonhuman primates. The preliminary results of these studies have clearly shown that when monkeys are put on a CR program, they experience changes in metabolism which are consistent with what is seen in rodent experiments, including significant reductions in risk factors for major diseases.³⁴⁻³⁶ And in fact, while the results are not yet advanced enough to meet statistical rules of significance, **monkeys on the CR program are experiencing much lower rates of age-related disease and death** than those that are fed a conventional healthy diet.³⁵

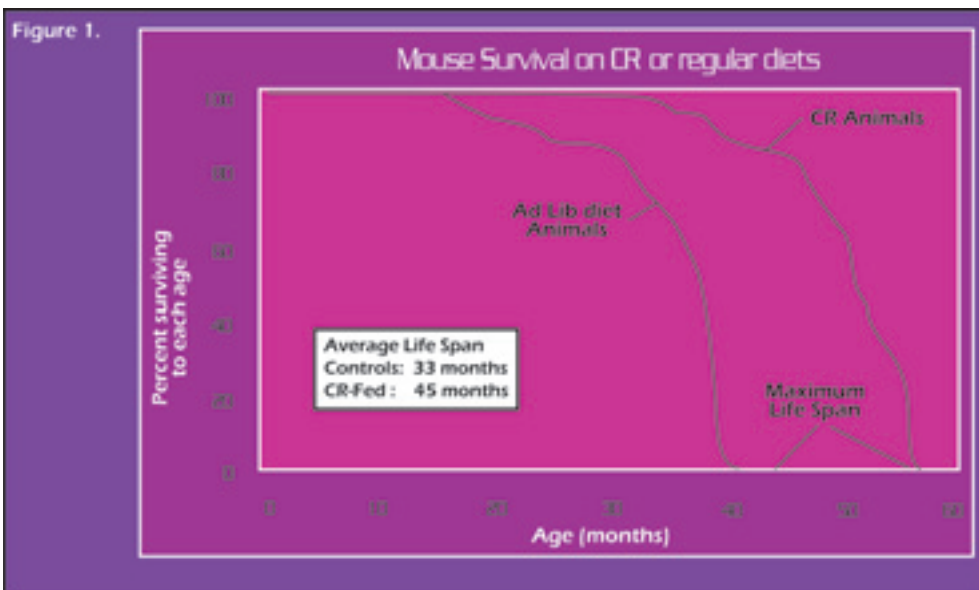
Some studies already exist which strongly suggest that CR works in humans. For instance, there is the case of Okinawa, Japan, where an unique series of cultural and geographical accidents created a population which appears to have lived much of its life on a limited CR program. The very low-Calorie, yet high-nutrition diet eaten by Okinawans is the only reasonable explanation for the

CR produces effects in humans which closely parallel those seen in CRed rodents and primates.

fact that the island boasts not only the highest overall life expectancy, but also the greatest incidence of centenarians, in the world – and that these centenarians tend to be in better health, by every available measure, than North Americans or even mainland Japanese who are decades their junior.³⁷⁻³⁹

There is also a small, three-year human study performed as far back as 1955,⁴⁰ in which sixty residents of a retirement home for elderly members of religious orders ate a standard 2300 Calorie diet, while another 60 consumed an average of 1500 Calories daily. Even in this short period, with a nutritionally suboptimal diet, **seniors on the CR plan only spent half as many days in the infirmary** as those eating a conventional diet (123 vs 219 days); and while the results were not strong enough to be considered meaningful

An organism eating the CR way can live longer than that life form is “supposed” to be able to live.



CR Dramatically Increases Lifespan. Redrawn from (33).

from a statistical point of view, **only half as many seniors living the CR lifestyle died** over the course of the study (6 vs. 13 deaths).

Since the publication of our last feature article on CR, studies have begun to tease out answers to the important question of *how* CR works its magic, including potential gene expression pathways redirected by CR⁴¹ and insights into the mechanism of CR's ability to reduce the generation of free radicals by **mitochondria** (the cellular "power plants" which are the main source of the body's free radical exposure).⁴² But the biggest news for most life extensionists has been the new studies performed in species much more longevous than rats, guinea pigs, and mice – evidence that strongly suggests that **CR will fundamentally intervene in the human aging process**, just as it does in rodents in the lab. In this followup article, we focus in on that new evidence.

Whispers in the Blood

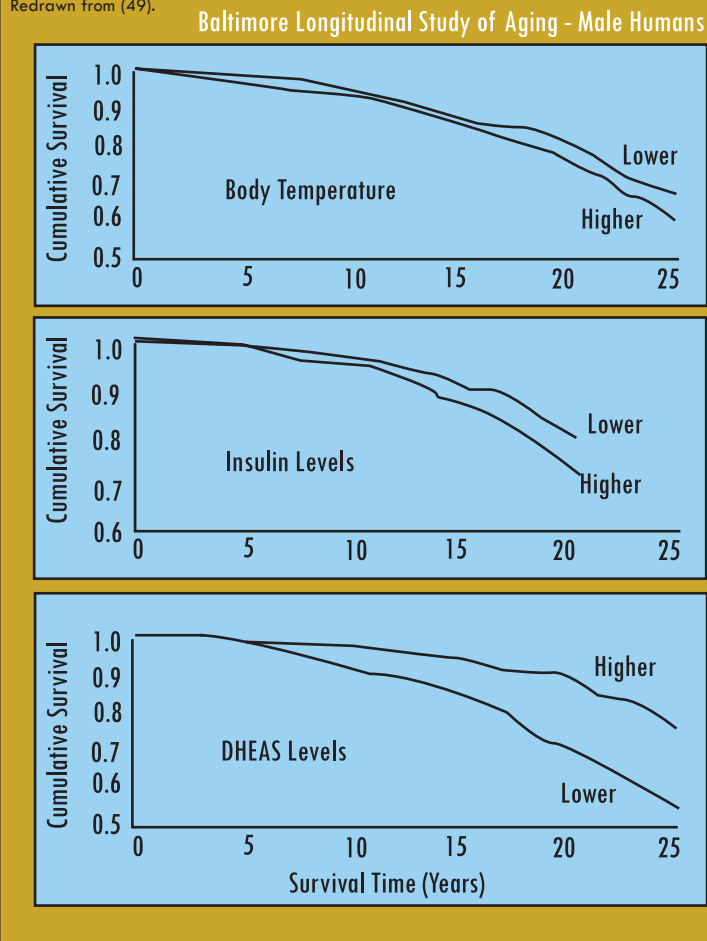
Much research has been performed to document the positive effects of Calorie-reduced diets on people who are overweight or who have diabetes. But these studies – and studies of people suffering with eating disorders or subjected to frank starvation – don't tell us much about how CR might work in otherwise healthy humans as an *anti-aging* therapy.

But beginning with the pioneering Biosphere 2 experiment performed by long-time CR researcher and UCLA Professor Emeritus of pathology Dr. Roy Walford, several small, short-term studies have been performed to see if the immediate biochemical effects of CR in rodents can be duplicated in healthy humans.⁴³⁻⁴⁸ These studies have documented changes in humans living a CR lifestyle which are strongly consistent with what has been seen in rodents during life-extending CR studies. And last year saw the publication of the most exhaustive collection of this data yet reported, using frozen blood samples drawn from the

Table 1: CR's Metabolic Effects in Humans, Rodents, and Nonhuman Primates. Data from (43).

| Variable | Humans | Rodents | Monkeys |
|-----------------------|--------|---------|---------|
| Blood Pressure | ↓ | ↓ | ↓ |
| Total WBC count | ↓ | ↓ | ↓ |
| Androstenedione | ↓ | ↓ | ↓ |
| Cortisol | ↑ | ↑ | ↑ |
| DHEA-S | ↑↑ | ↑ | ↑↑ |
| Insulin | ↓ | ↓ | ↓ |
| Triiodothyminine (T3) | ↓ | ↓ | ↓ |
| rT3 | ↑ | ↑ | ↑ |
| Cholesterol | ↓ | ↓ | ↓ |
| Triglycerides | ↓ | ↓ | ↓ |
| Blood Urea Nitrogen | ↓ | ↓ | ↓ |
| Creatinine | ↓ | ↓ | ↓ |
| Alkaline phosphatase | ↑ | ↑ | ↑ |
| ALT (SGPT) | ↑ | ↑ | ↑ |
| AST (SGOT) | ↑ | ↑ | ↑ |
| Glycated Hemoglobin | ↓ | ↓ | ↓ |
| Glucose | ↓ | ↓ | ↓ |
| Uric Acid | ↓ | ↓ | ↓ |

Figure 2: Humans Bearing the Signs of CR Show Greater Survivorship. Redrawn from (49).



"Biopsherans" a decade ago.⁴³ These results, combined with an additional decade of animal experiments, prove that **CR produces effects in humans which closely parallel those seen in CR red rodents and primates** on a wide variety of key biochemical, hormonal, and metabolic parameters (see **Table 1**).

Signs of CR, Signs of Life

But will these CR-induced metabolic shifts translate into slower aging in humans? Another report published this year⁴⁹ provides the first evidence that they will. This study examined the relationship between twenty-five year survivorship in human men and the known metabolic stigmata of CR in rodents and primates. The men were a group of 6000 participants in the massive **Baltimore Longitudinal Study of Aging**, the longest-running scientific study of the human aging process in the United States. The new study looked to see if healthy men who displayed three hallmarks of the CR state – lower body temperature and insulin levels, and a slower *decline* in levels of the hormone **dehydroepiandrosterone (DHEA)** – would also show signs of decelerated aging, in terms of better survival.

And indeed they did.

The results can be seen in **Figure 2**. Over the course of twenty-five years of followup, **men whose metabolic markers were naturally in line with the known effects of**

CR enjoyed significantly better survivorship.

Before You Reach For That Bottle...

It's important to note that the finding that men whose DHEA levels decline unusually slowly may also age at a reduced pace isn't necessarily a prescription for DHEA supplementation, as some supplement vendors have suggested. In fact, the monkey and human results show that, paradoxically, CR itself either has no effect upon, or even *decreases*, absolute DHEA levels (see **Table 1**). But once they get started on the program, the CR primates *hold onto* those levels, showing a slower age-related *decline* in their bodies' production of the hormone. Likewise, the men from the Baltimore aging study who were more likely to survive did not necessarily have *higher* levels of DHEA than their less fortunate cohorts – just levels that remained constant as they aged. This most likely means that, by intervening in the *underlying process of aging*, CR preserves the functioning of the body's DHEA-producing adrenal glands, and that this reduction in the aging rate preserves adrenal function as part of its preservation of the body as a whole. In other words, DHEA levels are a *result*, rather than a *cause*, of CR's anti-aging effect.

Lean, Mean, Thinkin' Machines

When going through the catalog of degenerative processes that accompany aging, the one entry that causes the greatest fear is the devastation of the mind. Even "normal" aging in basically healthy people causes a loss in the sharpness of the mind,⁶⁶ but this pales before the horrors of Alzheimer's disease and other neurological

CR protects rodents of animal studies conducted over the course of decades clearly documented the fact that **CR preserves brain structure and function**, keeping CR animals brighter and more active at all ages – including ages at which all of the conventionally-fed animals have died.^{67,68}

Most recently, Dr. Mark Mattson, who heads the Cellular and Molecular Neurosciences Section of the National Institute on Aging, has put out a series of studies documenting that **CR protects rodents against experimental Alzheimer's, Parkinson's, and Huntington's diseases, as well as from the neurological aftermath of a stroke.**⁶⁸ The impressive results of all of this research has convinced Dr. Mattson to initiate a much more ambitious and very *personal* experiment: he has cut about a third of the Calories out of his diet, and now stands at 175 centimeters (five feet nine inches) tall, yet a trim 50 kilograms (120 pounds).⁶⁹

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But while most people would acknowledge that reflexes, muscular strength, cancer, and kidney disease may be more or less the same diseases in mouse to (wo)man, most folks are a little more hesitant about making the jump when it comes to the workings of the brain. Mice may get cancer the same way that humans do, but there are no great rodent philosophers or scientists, and no great personal tragedies from dementia in pet hamsters. So when it comes to the effects of CR on brain aging, most of us want to see a little more proof.

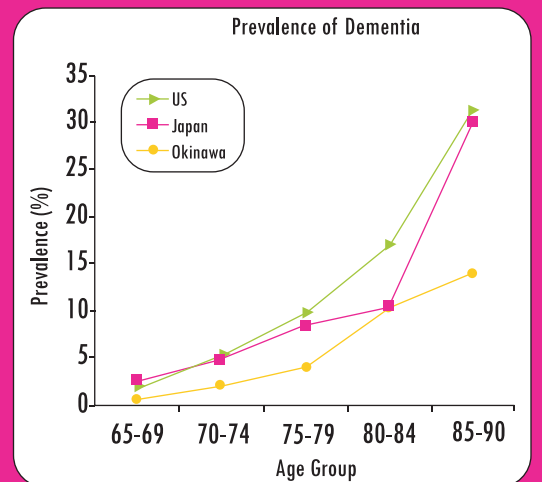
The CR lifestyle slashed the dogs' odds of developing age-related disease.

Fortunately, the last few years have seen the publication of a small flurry of new studies suggesting that **eating diets lighter in Calories preserves the human brain as well.**⁷⁰⁻⁷³ In the strongest of these studies,⁷⁰ 980 healthy, elderly Medicare recipients dementia or stroke were given neurological and neuropsychological assessments, and their diets were examined by interviews. Over the course of the next four years, a depressing 242 of these people fell prey to Alzheimer's disease.

But compared people whose Caloric intake was in the highest fourth of the study group, the **25% of the elderly people whose diets contained the fewest Calories were one-third less likely to develop Alzheimer's disease.** The trend was most powerfully demonstrated in people who carry a genetic susceptibility to the disease (**apolipoprotein-E variant eta-4 (ApoE ε4)**): in this subgroup, **people whose diets were lightest in Calories were 57% less likely to fall prey to Alzheimer's.**⁷⁰

While less powerful in their design, other recent studies have both added weight to the idea that lower Caloric intake is protective against Alzheimer's disease,⁷¹ and also

Figure 3: The CR-like Okinawan Lifestyle May Protect Against Dementia. Redrawn from (57).



suggested that **more CR-like diets will shield you from Parkinson's.**⁷² And among the elders of Okinawa – perhaps the closest thing to a population in which CR has

been practiced as a way of life for decades – the rate of dementia is just 6.7%⁷³ – a much lower rate than is seen in similar populations in the rest of Japan⁷⁴ or in the United States.⁷⁵ Perhaps most remarkably, the sudden jump in risk for dementia seen in other parts of the world is not clearly seen amongst people eating Okinawa’s traditionally light, nutritious diets (see **Figure 3**).

Longer, Healthier Life for Your Best Friend

Short of a lifelong study in humans, a successful conclusion to the nonhuman primate CR studies will be the best possible proof that CR will decelerate fundamental aging in humans. But waiting for results from even *these* studies will take too long for most of us. Last year saw the publication of a CR study performed in a species that bridges the longevity gap between short-lived rodents and long-lived monkeys: *dogs*.

In the late 1980s, just as the primate studies were getting underway, scientists at the Purina Pet Institute in St. Louis began a study on the effects of a Calorie-reduced diet on **canine hip dysplasia**, a common, painful, and debilitating genetic disease of the joints. The study quickly showed that a CR-style diet remarkably reduces the incidence and severity of the disease,⁵⁰ – and the overall effect on the dogs’ health was so impressive that the study was expanded into a small study of the long-term effects of CR in dogs.

Starting when the animals were a little over three years old, researchers monitored the Caloric intake of one group of Labrador Retrievers, weighing the animals weekly and controlling their diets by just enough to avoid obesity. The other group was given 25% fewer Calories than this obesity-controlled group, making these unusually lean dogs the first cases of true canine CR.⁵¹

Late in their lives, just *looking* at the big Labs would immediately have told you that something amazing was happening in the CR dogs (**Figure 4**). They weren’t just *leaner* than their more conventionally-fed fellows, but *younger-looking*. The CR-fed dogs showed fewer visible signs of aging, such as the graying of their muzzles. Their gaits were better, and they were more active than the animals whose diets had only been restricted enough to keep them from growing overweight. And, in fact, the CR dogs were “taller,” despite the fact that animals in the two groups had begun the study at roughly the same size: they had been protected from much of the shrinkage that accompanies “normal” aging.

Lab tests confirmed that **metabolic signs of the CR state are also seen in dogs**:⁵¹ such established markers of CR in rodents, primates, and humans as lower **triglycerides**,

triiodothyronine, insulin, and blood sugar (see **Table 1**) were also seen in the CR-fed dogs. Of more immediate concern, **the CR dogs stayed younger, and healthier, for longer** than their more conventionally-fed littermates.

By the end of their lives, at least *some* animals in both groups developed one of a host of age-related diseases, including **cancer, osteoarthritis, noncancerous tumors, skin diseases, liver disease, endometrial hyperplasia** (overgrowth of the cells of the uterus’ mucus membranes), **hypothyroidism, and seizures** – and *most* dogs had at least one of these health problems. But **the CR lifestyle slashed the dogs’ odds of developing any one of these age-related diseases** – and the diseases they *did* get, came on later and were less severe. Half of the dogs whose diets had only been controlled enough to keep them from growing fat needed treatment for one or more age-related health problems by the time they were 9.9 years old. By contrast, as late as 12 years of age, half of the CR-fed dogs were still free of the need for medical treatment.

Perhaps the most dramatic effect of canine CR on age-related dysfunction was its effect on **osteoarthritis**. Nineteen conventionally-fed dogs eventually developed this disease; indeed, 50% of them had it by age 10.3. Fewer of the CR dogs ever developed the disease (16 dogs), and in fact, *all of the conventionally-fed animals were dead* by the time that *half* of the dogs on the CR program developed osteoarthritis advanced enough to require medical treatment (age 13.3).

CR also seems to have protected the dogs from osteoporosis. Through much of their youth, the CR animals had a *lower* bone mass than the other dogs. This is what you’d expect: lower body weight means not just less fat, but also somewhat less muscle and bone tissue, too. Lower body weight is also associated with lower bone mass in humans,

People whose diets were lightest in Calories were 57% less likely to fall prey to Alzheimer’s.



Figure 4: Dogs on a CR Program (Left) or a Conventional Healthy Diet (Right). Photograph courtesy of Nestlé Purina PetCare Company. ©2002.



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and CR monkeys show a similar pattern in their youth.⁵² This has led some people to worry that CR might actually *cause* osteoporosis.

Instead, the dogs seem to be telling us that CR provides an anti-aging shield *against* the disease. The bone mineral density of the conventionally-fed animals began an inexorable downhill slide when they were eight years old. By contrast, the restricted dogs' bones remained at essentially the *same* level throughout their lives. As a result, the CR-fed dogs actually had *higher* bone masses from the age of 10.5 months onward, as they held onto healthy bone tissue while their littermates' bones deteriorated. In other words, **the CR dogs did not experience age-related, degenerative loss of bone.**⁵¹

The situation appears to be much the same for **sarcopenia**, the age-related muscular degeneration which leads to both a loss of muscle mass and the weakening of individual muscle fibers in older people. Predictably enough, dogs on the CR program initially had lower lean body mass than those who were only prevented from eating themselves into obesity. But as the conventionally-fed dogs aged, their lean mass began to fall around the age of nine years – while this decrease was delayed in the CR dogs for more than two additional years. Remarkably, beginning the at age of eleven years, **dogs living the CR lifestyle actually had more lean body mass than dogs fed a merely “healthy” diet**, despite being almost 22 pounds lighter!⁵¹

Extended Lifespan

And that leads us in to the ultimate test of a true anti-aging therapy. If an intervention is really getting at the basic mechanisms of aging itself, it will do more than protect you against the *specific, particular* diseases that cut short the average lifespan. If you have high cholesterol, then drugs or nutrients that bring your risky numbers down can prevent *premature* death by reducing your odds of an early heart attack. But neither **Mevacor**[®] nor **Pravachol**[®] (nor **Policosanol** nor **Pantethine!**) extends life *beyond* the normal bounds of the human lifespan; these drugs and supplements do not “slow down aging.”

The way to prove that you're slowing down the fundamental process of aging is to show that, not only does the *average* person (or rodent, or monkey) live longer by avoiding *specific* diseases, but that some of the animals undergoing your therapy live “unnaturally” long lives.

While the results were modest in this small, preliminary study, it looks like the CR dogs passed the test. It *appears* that **CR extends the maximum lifespan of dogs** (see **Figure 5**).

The median lifespan in the CR-fed dogs was thirteen years

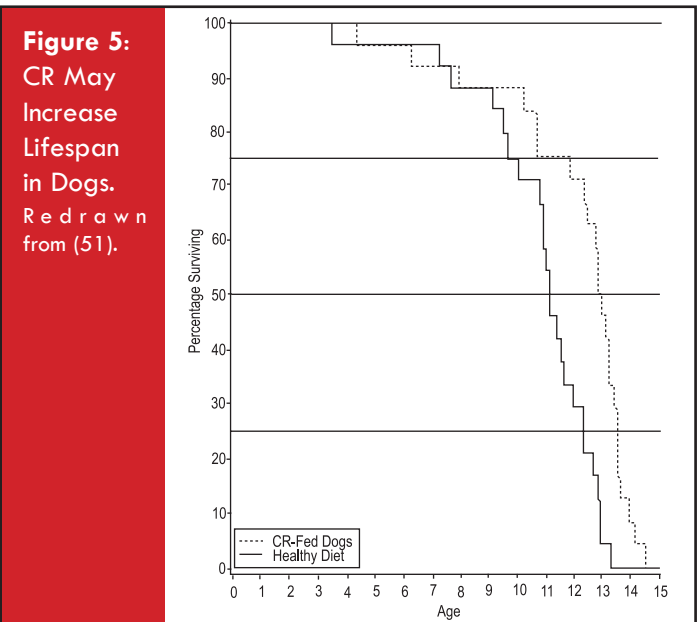
– about 91 “human years,” and nearly two dog years more than the 78 “human-year” median lifespan of the dogs who ate a diet controlled by just enough to avoid obesity. And the gap became more glaring as the study went on. While eleven of the original 24 CR-fed dogs were alive at the end of the twelfth year of the experiment, only one out of 24 control dogs survived that long. And 13.3 years into the study, the last conventionally-fed dog had died, while one in four of the CR-fed dogs were still alive and kicking. The last dog in the CR group pushed on to nearly fifteen years of age, becoming a canine “centenarian” nearly two years after the last of the conventionally-fed animals had died.

CR extends the maximum lifespan of dogs.

A Major New Study in Humans

Scientists at the National Institute on Aging takes the evidence for CR seriously. The effect is strong enough – and the implications urgent enough – that they have invested US\$20 million of their small budget into a seven-year human CR trial: the **Comprehensive Assessment of Long-term Effects of Reducing Intake of Energy (CALERIE)** study.⁵³

Research will be carried out on three University centers across the United States, with most of the funding earmarked for investigations to be performed at the Pennington Biomedical Research Center at Louisiana State



University. Each volunteer will practice a basic CR program for two years. Scientists will assess the impact of the regimen on a variety of risk factors for diabetes, hypertension, and heart disease, along with other parameters which may give clues as to whether the nutrition program will exert its anti-aging effects in humans.

Researchers will evaluate the volunteers' brachial artery function, energy usage, insulin sensitivity, and neuroendocrine function. They will look to see if CR reduces free radical damage to the volunteers' DNA, proteins, and lipids. Biopsies will even be taken to assess CR's effects on the expression of key genes in human muscle cells. By comparing these results with what we already know about CR in rodents, a clearer picture of CR's human potential will emerge.

“CR-Mimetics”

Seven decades of peer-reviewed scientific research powerfully suggest that CR will do for healthy humans what it does for so many other species: slow aging, preserve health, and dramatically extend life. Indeed, even the skeptical authors of the “No Truth to the Fountain of Youth” article seem prepared to admit that CR would work for us – if it weren't for the fact that most people are so weak-willed.

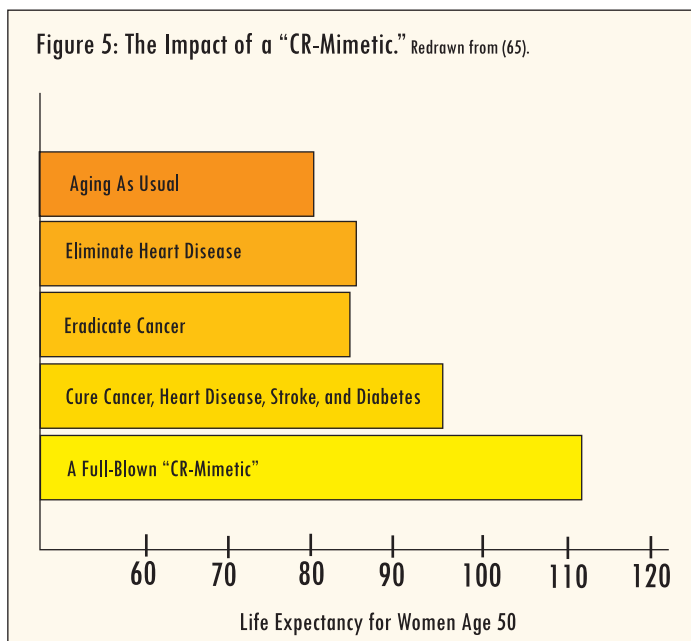
“Investigators have known for decades that caloric restriction extends life and the duration of good health in all species in which it has been studied,” they write. “These findings suggest that caloric restriction might have similar effects in humans.”²² But “few people would ever reduce their food intake enough to lengthen their lives,” they insist. So “biologists are now trying to discover the mechanism that underlies the benefits of caloric restriction and to find agents that might mimic those helpful effects in people without forcing them to go hungry.”²²

In other words, scientists are looking to produce drugs that would produce the “CR effect” without requiring us to change our lifestyles. Indeed, the very next issue of *Scientific American* boasts a feature article on the hunt for such “**caloric restriction mimetics**” under the bold title, “The serious search for an anti-aging pill.”⁵⁴

The impact on health and longevity of a drug that actually reproduced the effects of lifelong CR would be dramatic – far more powerful than a surefire cure for cancer or heart disease (see **Figure 6**). But no such pill has yet been discovered. In fact, the most promising candidate drug – a “tweaked,” unmetabolizable sugar called **2-deoxyglucose** – turned out to have long-term toxicity in rodents at doses which were so close to the minimum effective dose as to make its use in humans too risky,³⁶ sending researchers back to the drawing board after years of promising experiments. And even if a magic “CR potion” were shown to work in rodents tomorrow, it would still take decades of research to show that the drug is safe and effective enough to allow it onto pharmacy shelves. And as we know, the long-term side-effects of drugs often don't emerge until they've been on the market for five years or more.

Meanwhile, every day that we wait for more evidence from monkey and human studies, or for the advent of effective CR-mimetic drugs, our bodies are undergoing an irreversible process of molecular disordering: the ongoing “struggle between biology and chemistry” that underlies aging's toll on our bodies. The question each of us faces is, *how long are you willing to wait – how much aging are you prepared to suffer – before you'll start cutting your Caloric intake, even if you're not overweight?*

Figure 5: The Impact of a “CR-Mimetic.” Redrawn from (65).



You Are the Lab Rat!

A few resolute life-extensionists have already made their decision. As recently reported on the front page of *The Wall Street Journal*⁵⁵ and on feature reports on ABC and NBC evening news, more and more pioneering longevity radicals are adopting a human version of the classic CR diet, following principles laid out in *Beyond the 120 Year Diet* by Biosphere 2 Medical Officer Dr. Roy Walford,⁵⁶ who has spent decades researching the effects of CR in the laboratory and in humans, publishing his results in major scientific journals.⁴³⁻⁴⁶

Their numbers swelled this year when Oprah Winfrey invited Drs. Bradley and Craig Willcox (authors of *The Okinawa Program*⁵⁷ and scientific articles on the Okinawan

centenarians^{38,58,59}) to tell her viewers about the remarkable phenomenon of Okinawan health and longevity. The appearance rocketed their book to bestseller status, introducing thousands to the principles of CR.

Unfortunately, the Willcox brothers may have unintentionally “diluted” the elegant simplicity of the CR message. While acknowledging that the cornerstone of the

Scientific American on
**“The serious search for
 an anti-aging pill.”**

Okinawans' extended youth is their low intake of Calories, the authors fill the book with excessive scrutiny of the less important details of their lifestyle. Readers of the book may get the mistaken impression that the only way to enjoy the Okinawans' superlative health is to become a perfect mirror of the average Okinawan centenarian: changing their social networks, adopting new spiritual practices, making a variety of exotic Asian vegetables staples of their diets, and even replacing their dining room furniture.

The authors would have done their readers a much better service by skipping many of these minutiae in favor of a simpler, more focused message: an enormous body of research suggests that you can enjoy the Okinawans' "Everlasting Health" if you are prepared to eat a diet which – like theirs – is high in nutrition, but *much lower in Calories* than the one you're eating now.

How to Get Started

The remarkable thing about CR is its simplicity. The animal evidence clearly shows that, so long as you ensure that you're getting enough protein, vitamins, minerals, and essential fats, **any eating pattern that consistently reduces your Caloric intake by enough to lead to sustained weight loss will extend youth and prolong life.** You can eat the tofu, pork, Goya, and sweet potato diet of

Eat to Live ...

Instead of Living to Eat

Okinawa if it appeals to you, but you can also base your menus entirely on foods common to North American supermarkets. You can choose the kind of high-carbohydrate, low-fat, low-protein diet advocated by Dr. Walford and by much of the nutritional mainstream, but the higher-protein, higher-fat "Zone" nutrition plan promoted by Dr. Barry Sears^{60,61} will work just as well.

The first step toward creating your own CR program is to focus on removing high-Calorie, low-nutrition foods from your normal diet, in favor of foods which are Calorie-poor and nutrient-rich. This means, most obviously, removing added sugar, and reducing saturated fat by choosing low-fat meat and dairy. And you can go further, faster along this road by also reducing your *total* meat intake in favor of quality vegetarian protein.

But it also means sharply reducing your intake of carbohydrate-dense foods such as potatoes, rice, and grain-based foods such as pasta, bread, muffins, and bagels. Although there is much hype around the health benefits of whole grains, these foods are really just the lesser of two evils: they only shine in comparison to *refined-grain* versions of the same poor food choices. This

nutritional weakness may not make much difference on a diet in which you eat so much that the shortfalls are easily made up elsewhere in the diet, but it's much harder to get good total nutrition from a Calorie-reduced, grain-centered diet. Compare grains Calorie-for-Calorie to other carbohydrate sources, and you'll quickly see that **fruits and vegetables are dramatically more nutritious than any "starchy" food.**

Simply making these changes in your diet will often reduce your Caloric intake, as the Calorie-bloated refined sugars, saturated fats, and dense carbohydrates are crowded off of your dinner plate by the larger volume of nutrient-dense vegetables, fruits, and legumes. *Consistently* eating these foods instead of your old staples will likely lead to mild, spontaneous weight loss. It will also represent a major lifestyle shift, even for most *healthy* people, so give yourself plenty of time – weeks or months – to adjust to this first change before actively pursuing reduced Caloric intake.

You most likely won't feel hungry, and you probably will begin to feel a greater sense of well-being. You can confirm the positive impact on your health with tests that your doctor can order for you, such as your **cholesterol panel**, your **blood glucose and glycated hemoglobin**, and such paradoxical changes as *reduced white blood cell counts* and **thyroid hormones** and *increased cortisol*.

Once you've reoriented your food choices toward high-nutrition, low-Calorie eating, you can then use some of the **CR Resources** to refine your new lifestyle even further, moving fully into the CR eating pattern by actively cutting Calories and boosting nutrition. By now, you will have made the fundamental shift away from the conditioned, robotic eating habits you've picked up from your parents, agribusiness, and the McCulture, and into a lifestyle that recognizes food for what it is: a powerful drug, whose dose must be properly regulated to optimize results and minimize side effects.

You will no longer *live to eat*; you will have learned how to *eat to live*. And if a massive body of scientific evidence can be trusted, the harvest of good health, slower aging, and longer life will be yours to enjoy.

CR Resources

Internet

The Caloric Restriction Society Homepage. <http://www.calorierestriction.org>

An online community of CR practitioners. Resources, recipes, an online discussion forum, and the personal web pages of many people living in CR style. Feel free to sign up for the discussion group, but please bear in mind that the forum is **not** there to answer the questions typical of people just starting a CR voyage ("How many Calories should I eliminate?" "What about exercise?" etc), but for the kind of topics that come up once people already understand the basics. Before joining in on the discussion, get yourself up to speed on CR using such resources such as the FAQ, the searchable Archives of previous discussions, and above all Dr. Walford's books (below).

The CR Society Cohort Study. http://www.calorierestriction.org/our_studies/cr_study_intro.htm

A volunteer study organized by Dr. Walford and others, collecting blood test data and other information on human CR practitioners. Participants arrange for lab tests with their personal physicians and submit results to the Study for collection and ultimate publication. If you are considering starting a CR program, please consider contributing to human CR science by joining the Study.

Dr. Walford's Personal Website. <http://www.walford.com>

Mostly devoted to CR, although it includes some links on the Biosphere and Dr. Walford's multimedia explorations. Recipes, a food database search, and ways to order Dr. Walford's books and nutrition software.

Books

Walford RL. Beyond the 120 Year Diet. 2000; New York: Four Walls, Eight Windows.

The seminal 1986 book on the theory and practice of human CR, updated for the twenty-first century. Dr. Walford is an authority in biogerontology, with over 300 peer-reviewed scientific papers to his credit – many of them studies of the effects of CR in laboratory animals and humans. Dr. Walford took the bold step of recommending human CR at a time when the proposition was still heresy among his academic colleagues; subsequent decades have brought many of them around.

Sears B, Lawren B. Enter the Zone. 1995; New York: Harper Collins.

Sears B. A Week in the Zone. 2000; New York: Regan Books.

An alternative approach to CR preferred by some human practitioners. Sears' books often suffer from scientific misunderstandings and poor documentation, but his diet can be practiced as sound CR.

Willcox BJ, Suzuki M, Willcox DC The Okinawa Program. 2001; New York: Clarkson Potter Publishers.

A detailed look at the Okinawan longevity phenomenon. Extensive discussion of the lifestyle of the Okinawan centenarians.

Rolls B, Barnett R. The Volumetrics Weight-Control Plan: Feel Full on Fewer Calories. 2000; New York: Harper Collins.

Helps you choose foods, and prepare meals, with fewer Calories at the same total food volume. Too much emphasis on dense carbohydrates remains, but the overall approach is sound.

Nutrition Software

Doctor Walford's Interactive Diet Planner. Available from <http://www.walford.com/software.htm> Familiarly abbreviated to "DWIDP," this program empowers you to optimize your CR menus, ensuring maximum nutrition for minimal Calories. By plugging in the information on your meals, you can get insight into nutritional weaknesses you need to address. A specialized search allows you to choose foods based on high content of specific nutrients per Calorie.

NutriBase. Available from <http://www.dietsoftware.com/homepage.shtml>

Another nutrition software package favored by some hard-core CR enthusiasts for its more detailed nutritional analysis. Also somewhat more expensive than DWIDP.

CR Buddy. Available from <http://groups.yahoo.com/group/cr-buddy/files/> A free analysis program which uses the Excel spreadsheet software. Takes a little more effort to master, but the price is right and it has many unique features built into it because of the personal priorities of a long-time CR practitioner. Requires a free membership in Yahoo! to access.

Support Groups

Weight Watchers. <http://www.weightwatchers.com/> While the CR Society certainly can provide a lot of encouragement, many people find the direct human contact in support groups to provide invaluable motivation. These programs are oriented toward weight loss in the overweight, and not specifically to CR for the purposes of slowing aging, and weight loss is a **side effect**, rather than the **purpose**, of CR. But the Weight Watchers program can be very helpful way to provide structure and group support in reducing Caloric intake. Their "points" system is flexible enough to work a CR program into its structure, and the overall program seems to be the most successful system in terms of supporting weight loss and longer-term weight maintenance.⁶²⁻⁶⁴

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