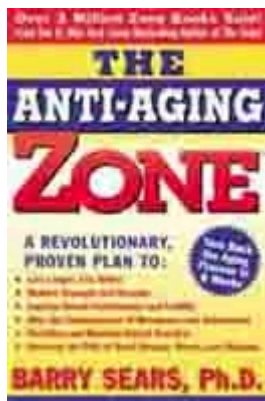


LE Magazine March 2000

REVIEW



Fish Oil and Carb Restriction on the Anti-Aging Front

A review of The Anti-Aging Zone, a new book by Barry Spears, Ph.D.

Book review by Ivy Greenwell

Anti-aging medicine is really a very ancient field, Dr. Barry Sears points out in his latest book, The Anti-Aging Zone. There exists an Egyptian papyrus, written 2,600 years ago, called "Book for Transforming an Old Man into a Youth of Twenty." Likewise, Taoist sages prescribed diet regimens, herb potions and special exercises in the hope of preserving vigor and attaining physical immortality. Stories of magical elixirs and immortality-giving, youth-preserving "food of the gods" are a common theme in mythology and literature, showing humanity's longing to conquer aging. Amazingly, for millennia humans believed that the right special food could preserve eternal youth; that there existed something the gods ate or drank

that prevented aging.

This aging-retarding food of the gods is right in our kitchen, Sears announces. But the secret is not so much in what we eat, as what we do not eat. If we eat less, we will live longer. Or, as Sears puts it, "The fewer calories you consume, the less energy is required to process the incoming food and the fewer free radicals you make. The fewer free radicals you make, the longer you live." And no, we do not have to go hungry. Sears promises that by using food wisely, we can slow down aging and still have plenty of energy and no feeling of deprivation at all.

Calorie restriction: the "Holy Grail" of anti-aging

The first rule of anti-aging seems a harsh one: we must eat less. "There is only one consensus in the world of anti-aging: the only proven way to reverse aging is to restrict calories," Sears explains. There is nothing new here, as attested by the old saying to the effect that most people dig their own graves with a fork. Yes, we readily agree that many people, perhaps most, in effect kill themselves by eating too much. There are no obese centenarians.

But what about the usual contention that Americans, the fattest people in the world and in the history of the world, are incapable of practicing calorie restriction? Sears finds that the main problem is ignorance about proper food choices. He asserts that it is indeed possible to feel perfectly sated and have a lot of energy if one eats the correct carbohydrate-restricted diet that includes sufficient protein and fat—the two macronutrients that will stabilize blood sugar in the longevity-promoting low-normal range and provide sustained energy. Then, instead of the government recommended 2000 calories/day for the average woman and 2500 calories/day for the average man, one can go down to 1200 calories for the average woman and 1500 calories for the average man. Health benefits should be enormous.

Why? Because, Sears explains, 90% of free radicals in our bodies are generated through the utilization of food. In spite of the outcry about pollution and radiation, these are relatively marginal sources of free radicals. The sad truth is that the more calories we eat, the more free radicals we generate. And if most of these calories come from high-glycemic carbohydrates (bread, cereal, pasta, pastry, most fruit juice, overcooked vegetables, etc.), then we also begin to suffer from hyperinsulinemia and hypercortisolism, with a corresponding drop in beneficial hormones such as DHEA and growth hormone. The result of both excess calories and the endocrine imbalance that follows is the creeping middle-age spread (as the saying goes, "middle age starts when you start growing in the middle"), and no end of degenerative disorders.

What is the secret of being able to reduce calories without going hungry? According to Sears, the crucial concept is the inversion of the USDA food pyramid, with its bizarre, pro-aging recommendation of up to eleven daily servings of starchy foods. Starches—cereal, bread, pasta and other refined carbohydrates—are placed at the very top of Sears' anti-aging pyramid, with the admonition: "Use sparingly." While the government urges us to eat mainly bread, cereal, pasta and the like refined carbohydrates, Sears says that these should be severely reduced, even eliminated. Instead of being the main staple, they should hardly be consumed at all. Humans evolved to thrive on the kind of food that was available before the relatively recent development of agriculture and food processing.

Sears is impressed with the diet of our remote ancestors. The Paleolithic hunter was a world-class athlete; the mostly vegetarian

agricultural people who followed later were stunted and disease-ridden by comparison. According to Sears, if all bread disappeared from the earth, we'd be better off. Bread, including the so-called whole-wheat bread, is very efficient at raising our blood sugar and insulin. If you ever see the insulin curve after a "meal containing bread," you would be quite motivated to eliminate all forms of bread except perhaps a bit of coarse rye. If we eliminated bread from our diet, most likely we'd live longer and remain practically free from heart disease and cancer. What would we eat in the place of bread and other cereals? Lots of vegetables, as long as they are not overcooked, and moderate servings of low-glycemic fruit.

When refined starches are used sparingly (if at all), and all meals including snacks contain adequate protein and fat, blood sugar and insulin stay in the optimal low-normal range. Calorie intake can thus be easily controlled, without insulin-induced hunger and the obesity that generally results from a low-fat, high-carbohydrate diet, especially when such diet is combined with the modern sedentary lifestyle rather than hard physical labor in the fields.

I think that in this volume Sears succeeds at last in clarifying the misunderstanding that followed his first book. He emphatically points out again and again that the Zone diet is not a weight-loss diet. It is a life-long calorie-restricted, carbohydrate-restricted diet aimed at controlling blood sugar and insulin. In other words, it is a special form of calorie restriction that should work to slow aging.

Sears thinks that anyone interested in extending life span should follow his plan-no ifs, ands or buts. The plan can be modified according to individual needs (athletes can use more fat, for instance; some people have genetically better metabolism and can do well on a higher carbohydrate protein ratio). But it is still the same idea: restrict high-glycemic carbohydrates. The typical American diet has become the very opposite of calorie restriction. With the emergence of breakfast cereals and fast food, it has also grown to be very unbalanced: cold cereal and fruit juice for breakfast, a white-bread sandwich for lunch, followed by a pasta dinner, with sugary junk food snacks in between. It is a high-carbohydrate prescription for obesity, disease and rapid aging.

Macronutrients

Sears calls his nutritional regimen a "protein-adequate diet," rather than a high-protein diet. Yet it is hard to deny that no macronutrient looks as good as protein in terms of the benefits it provides. For one thing, Sears attributes the dramatic increase in longevity (as well as the equally dramatic increase in the average height) during the twentieth century chiefly to greater consumption of protein. Adequate protein means an adequate immune system-and Sears convincingly documents that the decline in the rate of mortality from infectious diseases started even before the advent of antibiotics.

Protein plays a starring "good guy" role also because it stimulates the release of glucagon, the little-known but extremely important pancreatic hormone. Glucagon helps us sustain normal blood sugar levels. Unlike insulin, which is a storage hormone and thus keeps energy stored as fat, glucagon releases our energy stores. Protein-induced release of glucagon also makes it unnecessary for the body to rely on cortisol in an attempt to maintain an adequate supply of glucose. Cortisol can do the job, but at a big price.

In addition, certain amino acids play an important physiological role. Arginine, for instance, is necessary for the production of nitric oxide, which is of great importance for vasodilation, short-term memory and immune function. Sears recommends frequent consumption of turkey and soy protein as sources of arginine.

Healthy fats (Sears basically means fish oil and olive oil) also look extremely good: the benefits include lower and more stable blood sugar, lower insulin, higher metabolic rate and increased immune function, among others. Fat slows the rate of carbohydrate entry, thus helping keep blood glucose and insulin steady and normal, without harmful surges. In addition, fat signals the brain to produce the message: "Stop eating." Because fat is essential for controlling blood sugar, every meal, including snacks, should include fat, just as it should include protein.

It is, alas, carbohydrates, especially the grain-derived processed carbohydrates (bread, cereal, pasta) so beloved of many diet gurus, that lead to most trouble and can seriously accelerate aging.

There are essential amino acids and essential fatty acids, but insofar as we know, there are no essential carbohydrates. If we are to practice calorie restriction in order to live longer, this is the part of the diet that is most dispensable-and, according to Sears, the most pro-aging. Sears states, "The key to practical calorie restriction is to determine the minimum level of carbohydrates you need to function efficiently."

Still, it is unfair to accuse Sears of trashing all carbohydrates. He trashes only the high-glycemic, grain-derived starches and excess fruit and fruit juice. Otherwise, unlike Atkins and the high-protein school, he is emphatically in favor of including a certain minimum of low-glycemic carbohydrates in order to avoid ketosis.

The argument with Atkins is not successfully resolved. It has not yet been established whether mild ketosis is actually harmful-after all, mild ketosis is the state we wake up in every morning. Some experts claim that our Paleolithic ancestors were often in a state of mild ketosis, especially hunters out on a long hunt.

If the transition is slow rather than sudden, side effects such as a feeling of weakness (which in any case is transient) should not happen. What goes wrong in some cases is that a person on an 80% carbohydrate diet reads one of Atkins' books, and the next day it's nothing but cottage cheese for breakfast, and meat and salad for lunch and dinner. Then s/he goes for an evening run and discovers that s/he doesn't seem to have the energy to do it. With a slow transition to a ketogenic diet, the initial side effects are minimized, and a sense of well-being, alertness and high energy follows.

On the other hand, there is also something to Sears' argument that ketosis results in increased urination, and thus the risk of electrolyte loss. Since bananas are definitely the forbidden fruit when one is on a very carbohydrate-restricted, ketogenic diet, getting sufficient potassium may be difficult. But here again, the counterargument is that the kidneys do adapt, and the body learns how to preserve electrolytes.

Maybe the worst thing for those who rely on ketosis for weight loss is that fat cells also adapt to ketosis and are said to become "fat magnets," becoming more efficient in accumulating fat once more carbohydrates start coming in. This has indeed been observed: if a person returns to considerably higher carbohydrate consumption, the regain of lost fatty tissue is shockingly rapid. But this seems to happen after any low-calorie diet. The solution is basically to stay on the diet on a life-long basis-and here Sears' plan has an advantage, since his diet is not so extreme, and does include a satisfying amount of plant food.

And there is a truly compelling reason that Sears cites for our need to consume a certain minimum of low-glycemic carbohydrates: it is the only way to obtain many valuable phytochemicals, so important for the prevention of heart disease and cancer. And if we eat this plant food raw, we are also getting the benefits of natural, live, enzyme-rich food.

Type II diabetics: "Canaries in the coal mine of aging"

Sears points out that type II diabetics, with their high blood sugar and high (but ineffective) insulin, their greater rates of free radical formation, lipid peroxidation, glycation, and higher levels of inflammation are the very picture of accelerated aging. The higher the level of blood sugar, the more severe and frequent the problems typical of diabetes (and also of aging): impotence, depression, cataracts, glaucoma, atherosclerosis, kidney failure, dementia and more.

The main reason for this, according to Sears, is that insulin is our "passport to accelerated aging." Let us bear in mind that type II diabetics actually have elevated insulin levels; the problem is that they are insulin-resistant, so their pancreas keeps pumping out more and more insulin in the effort to lower blood sugar. Unlike diabetics and most of the elderly, individuals with low blood sugar and low insulin have been found to be healthiest and to live the longest. Diabetics, with high blood sugar and high insulin, age fast and die prematurely.

Insulin is a potent accelerator of aging for many reasons. By now many people know that it promotes obesity, with disastrous consequences for the cardiovascular system. But few know that insulin is a very powerful growth factor. It drives more frequent cell division, thus leading to faster telomere shortening. It makes tumors proliferate faster. Insulin also decreases the levels of cyclic AMP, the "second messenger" used by many hormones to communicate with the cells, thus decreasing endocrine regulation of body functions. The result is hormonal miscommunication and metabolic chaos. In addition to this, insulin also inhibits the release of glucagon, thus promoting the release of cortisol, another hormone whose levels tend to rise with aging. Excess cortisol has its own pro-aging consequences. That's why Sears calls elevated insulin "your worst aging nightmare."

It should be emphasized that this applies to elevated insulin-and aged people typically have higher insulin levels than young people. They also have higher blood sugar; the problem is insulin resistance. A certain level of insulin is essential for health. The same is true of "bad" prostaglandins. One of the virtues of Sears' book is that it stresses the notion of balance.

Calorie-restriction, Okinawan centenarians and Luigi Coronaro

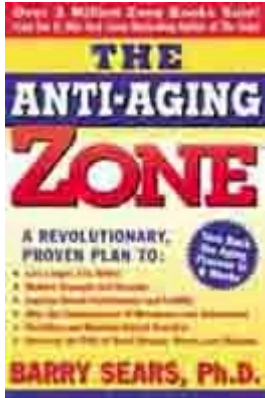
The island of Okinawa is famous for having four times as many centenarians per 100,000 people as the rest of Japan. Compared to other Japanese, Okinawans have 60% lower mortality due to heart disease, stroke and cancer. According to Sears, the secret of the superior health and longevity of the Okinawans is their Zone-like diet: less rice, more protein (fish and pork), and three times as many vegetables.

It is of special interest that Okinawans eat twice as much fish than the average Japanese. People for whom fish is the main source of protein seem to be the healthiest in the world, healthier by far than strict vegetarians. They have the lowest rates of heart disease and Alzheimer's disease. Part of the answer lies in the anti-inflammatory benefits of omega-3 fatty acids; we are becoming increasingly aware that inflammation plays an important part in most degenerative diseases of aging. At the same time, Sears points out, fish protein is the only animal protein that is a poor source of omega-6 fats; thus a fish-eater is not loading up on excess linoleic acid.

Sears quotes yet another example of calorie restriction: the longevity of Luigi Coronaro, a sixteenth-century Italian nobleman. Coronaro started his Spartan diet of coarse dark bread, red wine, meat broth and eggs only at the age of fifty, in a state of poor health, and still managed to live until 98-back then, an unheard-of great old age. It is a great pity that Coronaro began calorie restriction so late in life.

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Fish oil and eicosanoids

Sears says, "I believe that aging can be viewed as a growing eicosanoid imbalance over time," as well as "All roads to anti-aging lead to eicosanoids," and "Eicosanoid balance is the real key to anti-aging."

Another way of stating this is that Sears proposes something of an "inflammatory theory of aging." The levels of inflammatory chemicals (not only pro-inflammatory prostaglandins) go up quite dramatically with aging. Sears does not suggest that all of aging can be explained as a consequence of increasing inflammation, but he is a pioneer who emphasizes the pro-aging role of inflammation.

In order to understand his ideas more fully, we must first understand eicosanoids. If the newness of the term bothers you, you can substitute the term "prostaglandins." Prostaglandins are the best known and most studied member of the eicosanoid family. Synthesized from fatty acids, eicosanoids are powerful, short-range, short-lived cellular hormones that have a very direct role in controlling our physiological function. This is where the balance of omega-3 and omega-6 fatty acids becomes crucial, as well as hormones such as insulin, cortisol, glucagon and estrogens. Cortisol blocks the production of all prostaglandins, good and bad, radically decreasing inflammation. But this comes at a severe price if the action of cortisol continues unopposed. Insulin promotes the production of inflammatory eicosanoids through its activation of delta-5-desaturase, the enzyme that initiates the production of arachidonic acid, the substrate for inflammatory prostaglandins and other "bad" eicosanoids. Glucagon, the thyroid hormone triiodothyronine (T3), and estrogens decrease the activity of delta-5-desaturase, and thus lower the production of arachidonic acid and ultimately of inflammatory eicosanoids.

And then there is eicosapentaenoic acid (EPA), Sears' favorite fatty acid. It can be made by the body from alpha-linolenic acid (found in flax and Perilla oils, but can also be obtained pre-formed from the oil of cold-water fish such as salmon. Sears regards EPA as the most important modulator of eicosanoid production. In simpler words, EPA is a powerful anti-inflammatory.

But simply taking fish oil supplements is not as optimal as taking fish oil in addition to frequently eating fish. Why should you eat fish even if you already take fish oil? Because it is the only animal protein that happens to be poor in omega-6 fatty acids. Eating fish further helps to undo the ravages of our excess consumption of omega-6 fats.

The cardioprotective effects of fish oil are well-documented. Likewise, fish oil is one of the mainstays of alternative treatment of arthritis and other inflammatory disorders. Fewer people know that high consumption of fish is also associated with significantly lower risk of Alzheimer's disease.

Another great promise of Sears' anti-aging program is that the combination of insulin-lowering, calorie-restricted diet and fish oil will dramatically reduce the risk of cancer. Cancer is primarily a disease of aging, promoted by high insulin and pro-inflammatory prostaglandins. Calorie restriction and fish oil help reduce both.

The carbohydrate-restricted, anti-inflammatory Zone diet, Sears claims, also acts as an antidepressant. Interestingly, depressed individuals have been found to have higher levels of inflammatory prostaglandins. This may be one of the reasons why depression is such a strong risk factor for heart disease and cancer. It also implies that the anti-inflammatory omega-3 fats such as fish oil should ameliorate depression, which appears to be the case.

Can one get enough EPA by just eating fish? Probably, if you eat the way that inhabitants of traditional fishing villages do, enjoying freshly caught fish every day. The cardiovascular profile of such people has been found to be better than that of total vegetarians. The trouble is that most people do not really like fish all that much, and tend to think in terms of canned tuna rather than delicious freshly caught fish. That's why most of us could use fish oil supplements.

By the way, if you take fish oil, be sure you are also taking vitamin E. EPA and vitamin E synergize to produce benefits such as greater insulin sensitivity and increased cell-membrane fluidity.

Lower insulin resistance and maintenance of a low triglyceride/HDL ratio

One profound benefit of a carbohydrate-restricted diet, especially when combined with EPA supplements, is an improved triglyceride/HDL ratio, a marker for insulin resistance. A low (1 or less) ratio of triglycerides to HDL cholesterol, Sears states, may be the most important factor in predicting the kind of freedom from heart disease that centenarians seem to enjoy.

A high fasting triglyceride/HDL ratio indicates that the LDL particles are small and thus very prone to oxidation (only oxidized cholesterol is harmful). A high ratio also suggests a high degree of insulin resistance; it increases the risk of a heart attack 16 times (compared with only four times for smoking). Warning readers against the low-fat, high-carbohydrate diets, Sears quotes from a recent article by the American Heart Association Nutrition Committee:

Very low fat diets in the short term increase triglyceride levels and decrease HDL cholesterol levels without yielding additional decreases in LDL cholesterol levels.

The first step toward achieving lower triglyceride levels is a carbohydrate-restricted diet. After all, it's mostly excess carbohydrates that are turned into fat. It's bagels and pancakes and potato chips (even the low-fat variety) that people end up carrying as "saddlebags" around their waist. Fruit might also be a special culprit, since fructose is suspected of being easily turned into triglycerides. Taking EPA supplements is also an effective way to lower triglycerides. Higher EPA intake leads to increased mitochondrial fatty acid oxidation and improved glucose metabolism.

Ideally, the ratio of triglycerides to HDLs should be less than 1; studies show that very low triglycerides and very high HDLs give one virtual immunity to heart disease. A ratio of 1.5 is still pretty good; a ratio of 2 and above should be reason to take action. Even moderately high triglycerides, in the so-called "normal" range, contribute to atherosclerosis.

While EPA from fish oil is a crucial supplement, Sears failed to mention L-carnitine, lipoic acid, niacin, chromium and especially conjugated linoleic acid, or CLA. Likewise, polyphenols seem very promising. Green tea and bilberry extract have been shown to lower blood sugar and triglycerides. Dry red wine has also been found to lower blood glucose, fasting insulin, and triglycerides while raising HDLs, which may account for its effectiveness in preventing cardiovascular disease. (French women—who are known to consume dry red wine with meals—have the lowest cardiovascular mortality in the world, ahead even of Japanese women).

The better statin drugs also raise HDLs and lower triglycerides, though these drugs should be the last resort. And it is important to note that various hormones have an impact on both triglycerides and HDLs; in the right dose, DHEA and testosterone both lower triglycerides, as well as blood sugar and insulin.

Estrogens can also lower blood sugar and improve insulin sensitivity, but the effect is dose-dependent. Sears describes it as the bimodal effect: at low doses, estrogens decrease insulin resistance; at high doses, they increase it. The drop in estrogens at menopause is associated with increased serum glucose, insulin resistance, and higher insulin. For Sears, this explains why the rate of heart attacks skyrockets in women within the first ten years after menopause. We are now finding out that various phytoestrogens likewise affect blood sugar. Preliminary evidence also suggests that hormone replacement therapy reduces the risk of diabetes, although more studies are needed.

Sears points out that thyroid hormones (T3 and T4) also improve the serum lipid profile. It is shocking how few people (including physicians) know that thyroid hormones play an enormous role in preventing heart disease and preserving cardiovascular health. Hypothyroidism is associated with higher LDL cholesterol, lower HDL cholesterol, and higher triglycerides. Thus it is not surprising that a high degree of atherosclerosis is found in untreated hypothyroid patients. Sears also points out that excess insulin appears to cause a faster degradation of the more bioactive thyroid hormone, T3.

While some critics condemn Sears for being overly fixated on carbohydrates, blood sugar, insulin and eicosanoids, a careful reading of his latest book should clearly show that he is far from being simplistic, and does recognize complex interactions between various hormones. In fact, the chapter on the thyroid is one of the best in the book. Sears is one of the few voices of sanity insisting that the elderly need thyroid supplementation if they show symptoms of hypothyroidism—being cold all the time, lethargy, mental slowness, confusion—even if blood tests still pronounce their thyroid levels "within normal."

Sears is also to be commended for insisting that diet comes first: the public is still largely ignorant of the fact that high triglycerides are mainly due to excess consumption of refined carbohydrates ("glycemic gluttony," as Dr. Atkins calls it), combined with a sedentary lifestyle. But Sears' own enthusiasm for fish oil points to the fact that the right supplements can significantly enhance the benefits of diet, even if it is already carbohydrate-restricted. He does, however, make a very valid point about taking lots of supplements as one's sole anti-aging regimen: he warns that unless one follows the insulin and cortisol-reducing Zone diet, coupled with daily moderate exercise and meditation, supplements will be "relatively worthless" in the battle against aging.

Moderate exercise lowers blood sugar and insulin

Sears recommends daily moderate exercise as an essential part of his anti-aging program. For one thing, exercise lowers triglycerides and raises HDLs, and a low triglyceride/HDL ratio should be the grail of any life extensionist. But Sears stresses the

"moderate" injunction. He states point-blank, "The more intense the exercise, the fewer the benefits for longevity."

What about the philosophy that it's OK to eat lots of carbohydrates as long as you burn them off in hard daily exercise? Sears warns that this would be pro-aging. First, the consumption of a lot of calories results in the production of excess free radicals (90% of the free radicals in our bodies originate in the process of utilizing food). Second, intense exercise also increases the levels of free radicals. True, exercise also upregulates our own antioxidant defenses, but if the exercise becomes too strenuous and prolonged, these defenses are overwhelmed. Third, if the exercise is excessively prolonged, or if the diet lacks sufficient protein to stimulate the release of glucagon, cortisol will be needed to sustain blood glucose levels, and excess cortisol is a pro-aging disaster.

The current infatuation with excessive exercise such as marathon running is ironic in the light of historical knowledge. It has been known for millennia that a life of hard physical labor tends to be a short one. True, today's elite athletes tend to eat an excellent diet and take plenty of antioxidants; it's the beginning amateur athletes that Sears worries about, the kind who may think that more exercise is necessarily better, and not be aware of the need for extra antioxidants.

What about the high-carbohydrate sports drinks and bars? Absolutely not, Sears warns. They undo all the insulin-lowering benefits of exercise. And while he certainly recommends moderate exercise, Sears does not think that it is quite as important as the right diet. The Zone diet remains the primary anti-aging tool. According to Sears, "80% of your ability to lower insulin levels will come from the Zone diet. Only 20% will come from exercise." Still, combine the two, and you are farther ahead.

The basic exercise program that Sears recommends consists of a brisk 30-minute daily walk, and five to ten minutes of strength exercises such as push-ups. Once you are more fit, you can consider increasing the intensity of the workout. Sears warns, however, that one should do no more than 45 minutes of weight lifting every other day. The reason for the 45 minute limit is that beyond that point, the rise in cortisol overwhelms the beneficial effects.

Ideally, Sears says, our fasting insulin should be under 10, and our glycosylated hemoglobin (a marker of glycation) under 5%. These excellent youthful values indicate that a person is biologically aging more slowly than average. They can be achieved and maintained only through a combination of proper diet and exercise, with some assistance from the right metabolism-enhancing supplements such as fish oil.

Lowering cortisol

Even if we achieve an optimal diet, we still have another enemy that can greatly accelerate aging: stress. Life has become overwhelmingly complicated, family and social networks have weakened, commuting to and from work is nightmarish in large cities; no wonder we see more and more stress-related diseases. Working mothers have been found to have chronically elevated cortisol levels (cortisol is our main "stress hormone"). But practically everyone's cortisol levels go up with age.

Cortisol accelerates gluconeogenesis—the production of glucose from the breakdown of tissue protein (proteolysis). That protein is mostly derived from the breakdown of muscle tissue. Thus, chronically elevated cortisol leads to accelerated muscle atrophy. Furthermore, cortisol is a major culprit in bone loss. It is our primary catabolic hormone: it tears down tissue in order to raise serum glucose.

Cortisol also stops all eicosanoid production. This works for reducing inflammation, but unfortunately also shuts down the flow of chemicals that aid in the building of muscle and cartilage, for instance. Cortisol is also immuno-suppressive and toxic to the thymus. In addition, chronic high levels of cortisol damages neurons, leading to memory loss and poor brain function in general. The aging effects on the skin are obvious to anyone who has ever gone through a period of prolonged stress (in fact, the new theory of female adult acne places the blame on cortisol). In sharp contrast to antioxidant hormones such as DHEA, cortisol exhibits pro-oxidant properties. And more production of cortisol means less production of beneficial steroids such as DHEA, progesterone and testosterone, since the main precursor hormone, pregnenolone, is diverted into the production of glucocorticoids. Elevated cortisol also means lower production of the thyroid hormones, so important for the regulation of metabolism.

Cortisol is basically an "emergency hormone." It is meant to help us survive a fight-or-flight emergency, and then be quickly cleared out of the body.

How can we keep cortisol levels reasonably low? Obviously it's impossible to eliminate all stress, nor would it be necessarily desirable. Still, we can try to use the various stress-reduction techniques available. Sears is particularly enthusiastic about meditation as a cortisol-lowering, anti-aging tool. Sears believes that daily meditation is as important as daily exercise.

In addition, keeping your blood glucose levels as steady as possible should also keep cortisol within bounds. That's why it's important to eat frequent small meals (Sears recommends three main meals and two snacks; even the snacks should be fully balanced, containing protein and healthy fat as well as carbohydrates). If the interval between meals gets too long, cortisol is likely to be called into action in an attempt to elevate blood sugar. Lesson: keep your blood sugar steady by eating small, frequent meals and avoiding high-glycemic carbohydrates.

Finally, our body has a built-in defense against excess cortisol, and that is another adrenal hormone, DHEA. DHEA competitively binds to glucocorticoid receptors, helping to prevent harm that would be caused by high cortisol levels, such as muscle and bone wasting. "Most of the touted benefits of DHEA can be explained in terms of its role as an inhibitor of the biological actions of corticosteroids, especially cortisol," Sears believes. Researchers such as Dr. William Regelson, an ardent proponent of DHEA supplementation, would probably agree.

It is often said that DHEA is the most abundant steroid in the body, produced in the range of 25 to 30 mg per day. But as Sears points out, cortisol is the second most abundant steroid, produced in the range of 10 to 20 mg under "normal conditionic cyclic AMP, the "second messenger" needed for good hormonal communication and produced by the good eicosanoids. Another interesting inclusion is ginger, a good anti-inflammatory agent, capable, like cortisol, of inhibiting the synthesis of both prostaglandins and leukotrienes, but without producing the pro-aging side effects of cortisol.

Since every expert has different supplement recommendations, it is good to bear in mind that we need to read many books and make our own choices rather than blindly follow this or that person's advice. Sears is right about the importance of fish oil; other authors point to the importance of lipoic acid and the rest of the network antioxidants. It is up to the reader to integrate this complex information.

Objectively speaking. . .

How valid is Sears' approach? The main problem so far is the scarcity of research confirming some of the assumptions on which Sears bases his system. What he says about the destructive role of insulin and its crucial role in producing obesity is extremely plausible, but not definitely proven, according to many dissenting experts. They accuse him of demonizing insulin and of trashing cereals and other starches, traditionally regarded as a staple. Sears could reply that probably the most important way in which calorie restriction retards aging is by reducing insulin. Less insulin means less inflammation, less heart disease and cancer, and more production of health-promoting eicosanoids. As for starches, the consensus is that it's people who eat the most vegetables who are healthiest, not people who eat the most bread, corn flakes and pasta.

Another objection that one frequently hears is that the sanctified 4:3:3 macronutrient ratio surely can't be optimal for everyone. In this book, however, Sears readily admits that we should speak in terms of a range rather than an absolute ratio. People differ in their ability to handle carbohydrates. For some, 1:1:1 might work better. Others may tolerate as much as 60% carbohydrate diet without suffering pro-aging consequences. Furthermore, one could plausibly argue that the evening meal should contain more carbohydrates in order to promote relaxation rather than protein-induced rise in dopamine, generally desirable in daytime.

If Sears' recommendations are used flexibly rather than rigidly, the system becomes highly workable. Don't worry too much about hitting the precise ratio of macronutrients; just see how your body feels if you skip the pasta and have more salad instead. Also watch what happens to your energy and your aches and pains when you start taking fish oil and eating more seafood. And practically no one doubts the benefits of moderate exercise and meditation. Once it is understood that the system advocated by Sears is not an unbalanced high-protein diet, but a fairly conservative set of health guidelines, consisting of the vegetable-rich Zone diet plus fish oil plus exercise plus meditation, one is even tempted to say, "What else is new?"

Now if we could only have some controlled research to see if the combination of Zone diet, moderate exercise, meditation, and fish oil and other supplements is effective for slowing down aging, as indicated by various biomarkers. Intuitively speaking, it should work. Eating more vegetables rather than bread and pasta, consuming adequate as opposed to high amounts of protein and healthy fats, and emphasizing seafood and/or taking fish oil supplements should have multiple health and anti-aging benefits. Until more research is done, however, we will not know for sure about the specifics of Sears' recommendations. There is also some debate about which relationships are causal, and which only correlational. Much remains to be elucidated about the extremely complex interactions between the endocrine, immune, and other physiological systems, especially in relation to aging. In the meantime, however, this challenging book is a treasure house of anti-aging information, especially in relation to diet and hormones. It is Sears' best book.

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