Low-Fat, Low-Salt, Whole-Food Vegan

Staying Lean and Healthy

into Ripe Old Age

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I. A Diet You Can Live With

Since my days as a medical student, I have been keenly interested in nutritional impacts on health. In particular, I have been studying for years in an effort to determine why many Third World societies, as long as they maintain their traditional diets and lifestyles, are relatively immune to so many of the disorders that take a devastating toll on the health and finances of elderly Americans. I have come to some provisional conclusions and recommendations that, while hardly original, are nonetheless quite controversial in some respects – at loggerheads not only with the health-destructive dietary practices of most Americans, but also with certain faddish views gaining popularity among many health scientists and the general public. It is precisely because my conclusions are controversial that they are worth setting down.

If I were asked to describe in one sentence the type of diet that, in my opinion, would minimize risk for the chief killing and crippling diseases of Western civilization – scourges that include coronary heart disease, stroke, diabetes, hypertension, the major cancers, autoimmune disorders such as rheumatoid arthritis, and Alzheimer’s disease – I would suggest the following:

Eat a very-low-fat, low-salt, whole-food vegan diet, very rich in potassium and relatively low in glycemic index.

This single sentence encapsulates six separate pieces of advice, which I will explain in more detail before summarizing the evidence that motivates this recommendation.

**Very-low-fat:** By this, I mean a diet in which fat constitutes not more than 15% of calories – the type of diet popularized by Nathan Pritikin and, more recently, Dr. Dean Ornish. This should not be confused with the so-called “low-fat” diet recommended by the American Heart Association, providing 25-30% of its calories as fat. Since the diet I endorse is vegan – thus excluding all fatty animal products – it is relatively easy to achieve the suggested fat target by simply moderating one’s intake of the few plant-derived foods that are high in fat: avocados, olives, nuts, seeds, and the oils and butters derived therefrom. Most grains, fruits, vegetables, and legumes – the core of a healthful vegan diet – are inherently low in fat. When buying processed foods, read the labels carefully and avoid foods that have significant amounts of added oils – saturated and partially hydrogenated fats are particularly bad for your vascular health. If your diet is quite low in fat in other respects, it may be appropriate to include not more than an ounce per day of unsalted nuts (or nut butter) in which monounsaturates predominate: almonds and hazelnuts are best in this regard. *Occasional* use of modest amounts of virgin olive oil or avocado – both monounsature-rich – is also acceptable.

**Low-salt:** Try to get your salt intake below 5 grams daily (which corresponds to 2 grams of sodium); the ideal target – not easy to achieve in modern society – is closer to 2.5 grams daily (1 gram sodium). Minimize or eliminate the use of table salt in your cooking – explore the wealth of alternative seasonings that are available. Fortunately, with the exception of dairy products (cows are fed salt to improve milk yields), natural
unprocessed foods are inherently low in salt. But most of us eat some of our meals in restaurants, or rely on certain processed foods that come pre-salted; it is estimated that at least 80% of the salt in our diet comes, not from our use of the salt shaker at the table or in our cooking, but from the salt pre-added to processed foods or restaurant meals. So when you purchase processed foods, examine the sodium content, and choose brands that go light on the sodium. If the milligrams of sodium in a serving is no higher than the number of calories (kcals) it provides, then it can be considered acceptably low in salt – particularly if you make a point of including a number of unsalted foods in your daily diet. You may need to shop in a health-food store to find a sufficient variety of unsalted or lightly salted processed foods. When dining in restaurants, don’t be afraid to ask the waiter to have your food prepared without salt – while this often won’t be feasible (they may rely on processed ingredients or on large pre-cooked batches of food they have already salted), it doesn’t hurt to ask.

Whole-food: By this, I refer to food that not only retains all or most of its original nutrient/phytochemical/fiber content, but that also, to the extent feasible, retains the intact structure of the food as it grew from the soil. For example, whole grain flour is certainly far more nutritious than refined flour – but whole kernel grains are even better for your health. Structurally intact grains are usually more slowly digested than are finely-ground flours (implying a lower glycemic index - see below), and the relatively high water and fiber content of whole foods often means that their calorie content is more dilute – you tend to get filled up before you have eaten an excessive number of calories in one sitting. When cooking vegetables, try to use cooking methods – such as steaming – that don’t leach out the protective micronutrients, phytochemicals, and potassium that they provide. By all means, avoid processed foods that contain a significant amount of added sugars or oils – these are “empty calories” that effectively rob your diet not only of essential nutrients, but also of fiber, phytochemicals, and potassium.

Vegan: This implies the absence of all animal products – flesh foods, dairy products, and eggs. While it is commonly accepted that the saturated fat and cholesterol found in most animal products (excluding non-fat dairy) are bad for vascular health, I subscribe to the much more avant garde view that animal protein is likely to be an important factor in our high rates of “Western” cancers, and may also contribute to high serum cholesterol and possibly even obesity. (This latter point will require some clarification, as I do not dispute the fact that diets high in animal protein can be useful for reducing appetite and achieving weight loss.) Contrary to much propaganda, a vegan diet featuring whole grains and legumes can provide more than enough protein to support buoyant health.

Since strictly vegan diets are virtually devoid of vitamins B12 and D, and may often be suboptimal sources of calcium and selenium, vegans are well advised to use comprehensive nutritional supplements (“nutritional insurance formulas”). Furthermore, the long-chain omega-3 fatty acids found in cold-water fish (EPA/DHA) can provide various health benefits that cannot be adequately reproduced by the shorter-chain omega-3s (α-linolenic acid) found in some plants; for this reason, I violate my veganism to the extent of taking an enriched fish oil supplement (a strategy endorsed by Dr. Ornish). Certain other non-essential nutrients found primarily in flesh foods – e.g. carnitine,
taurine, creatine – may be beneficial to health in certain circumstances, and can be provided in supplements; nonetheless, since the human body is capable of manufacturing these nutrients, vegans are rarely significantly deficient in them.

A vegan food which may have extraordinary potential for health promotion – as will be discussed below - is spirulina, a microalga (or, more properly, a cyanobacterium) that has remarkable antioxidant activity. I make a point of ingesting spirulina daily, in smoothies.

**High-Potassium:** Potassium appears to be Nature’s “antidote” to the harmful health consequences of salted diets. Our pre-agricultural ancestors ate unsalted diets exceptionally rich in potassium – whereas, thanks to the introduction of refined grains, sugars, and oils, our salted modern diets are substantially depleted of this crucial nutrient. To maximize your intake of naturally-occurring potassium, you will need to boost your intake of fruits, vegetables, and their juices, which typically are high in potassium on a per-calorie basis. Legumes and tubers (potatoes, yams) are also potassium-rich, and whole grains, while not potassium powerhouses, are about 3 times as rich in potassium as are refined grains. Thus, in pursuit of a high intake of potassium, you will get the concurrent benefits of the protective phytochemicals and fiber provided by fruits, vegetables, legumes, and other whole plant foods. A few processed foods and condiments are available that are potassium-enriched (e.g. Low-Sodium V-8 Juice™); these can profitably be included in your diet. However, make sure that the bulk of your dietary potassium comes from the naturally-occurring potassium in fruits and vegetables.

**Low-Glycemic-Index:** Starchy or sugary foods which are gradually digested and thus produce a modest but sustained rise in blood sugar, are preferable to rapidly digested carbohydrates that lead to an abrupt spike in blood sugar. Foods of the former type are said to have a “low glycemic index”. In non-diabetics, the harm from high-glycemic-index meals comes not from the rise in blood sugar per se, but from the large surge of insulin secretion which they evoke (as will be discussed below). Structurally intact grains are likely to have a lower glycemic index than flours do. However, many other factors play a role in determining the glycemic index of a food. For example, starch comes in two chief varieties, amylose and amylopectin. Amylose is an unbranched starch that, because of its compact chemical structure, is more gradually degraded by digestive enzymes than is the highly branched starch, amylopectin; thus, starchy foods in which amylose predominates tend to have a low glycemic index. A high content of soluble fiber likewise tends to lower glycemic index, and certain phytochemicals (such as some found in beans) can also slow the process of digestion.

Beans – especially home-cooked beans, as opposed to canned beans that usually have been pressure cooked – are particularly notable for a low glycemic index, owing to their high content of amylose, soluble fiber, and phytochemicals. Long-grain rice is usually higher in amylose – and thus lower in glycemic index – than the sticky short-grain rice preferred in Oriental cuisine; parboiling renders the rice kernel harder to digest, so long-grain parboiled rice is the best. High-amylose corn has been developed, but is not yet readily available in supermarkets. Fruits that are relatively low in glycemic index include
apples, pears and oranges, whereas ripe bananas and melons are relatively high in this regard. Surprisingly, juicing or pureeing fruit has little impact on its glycemic index, which is determined primarily by its fructose content - fructose has a very low glycemic index. As far as breakfast cereals go, old-fashioned (not instant) oatmeal and bran are good choices; most breakfast cereals are made from fine flours and are high in glycemic index (not to mention loaded with salt).

Sadly, the chief sources of starch in American diets – wheat flour products and potatoes – have a high glycemic index. The baked potato is particularly notorious in this regard (though it has the compensating merits of being rather calorically dilute and rich in potassium). Wheat flour (and this includes whole wheat flour) is not quite as high in glycemic index, but, possibly owing to its rather high protein content, provokes an insulin surge as dramatic as that produced by potatoes. A very fortunate exception is pasta – owing to the way in which the starch molecules are packed together, pasta has a much lower glycemic index than other wheat flour products. Unleavened bread – like pita bread – has a lower glycemic index than leavened products; the minute air pockets introduced by the leavening process gives the digestive enzymes ready access to the starch granules. Even lower in glycemic index are sprouted-grain breads, which contain structurally-intact kernels rather than fiber. For more information on the comparative glycemic indices of foods, you can consult tables such as that found in the book *The Glucose Revolution*; a comprehensive listing has also been published in the scientific literature.

Here’s a useful trick: as outlined in *The Glucose Revolution*, there is recent evidence that an ample intake of vinegar with meals (a little over a tablespoon) slows the absorption of carbohydrate and blunts the post-meal rise in glucose and insulin; the mechanism responsible for this effect is still obscure. So, instead of using oils on my salads, I smother them with my favorite balsamic vinegar. A wide range of flavorful vinegars is available – try them out. Perhaps the old folk myth about the health-promoting properties of vinegar is more than just a myth!

**In a Nutshell…**

In brief, what I am proposing is a diet comprised of virtually the entire range of fruits, vegetables, legumes (beans and soy products), and whole grains, complemented by a modest intake of monounsaturated-rich nuts or nut butters, and prepared with minimal added salt, oil, or added sugars, but seasoned liberally with all other spices as desired. Grains should be as structurally intact as feasible, though pasta is an excellent choice. Foods with a notably high glycemic index – wheat flour products (other than pasta) and baked potatoes, for example – should be avoided, as should all animal products (other than supplemental fish oil). For most people, moderate consumption of beer or wine is desirable (as will be discussed below), and including spirulina in one’s daily diet may also be wise.

Although these directives are consistent with a wide range of taste-tempting gastronomic possibilities, I will not pretend that they will be easy to follow within the context of the
typical meals that most Americans have been trained to prepare and consume. A friend of mine once showed me a list that the eminent Berkeley nutritionist Dr. Gladys Block had compiled of the 100 food items most consumed by Americans. On surveying the list, I was shocked to note that I could approve of only two of the first 25 items on the list! (One of these was spaghetti with marinara sauce – though even there, one could bet that the pasta would be made from white flour, and the marinara sauce was too high in salt. The other item was – alcoholic beverages!) Needless to say, most of the meals and convenience foods you will find in typical restaurants and supermarkets won’t make your task a lot easier. You will need to use your intelligence, resourcefulness, and self-discipline to follow through on the suggestions I offer.

Let’s face facts. Our current dietary habits have evolved in total ignorance of – and virtual indifference to – their consequences for long-term health. And there is no reason to expect that minor “practical” fixes of these habits will have much major impact healthwise. If your goal is to stay healthy, you need to rip those old habits out by the roots and start afresh, guided not by tradition or your old personal preferences, but by solid medical evidence. The good news is that, once your tastebuds have had a chance to adapt and you’ve made progress in finding the right recipes and the right restaurants, your healthful meals can be both delicious and satisfying.

But suffice it to say, I am not planning to win any popularity contests, and I’m not interested in telling people what they want to hear. If you are looking for confirmation that meat, grease, and salt are actually good for your waistline and your health, goodness knows there are plenty of faddishly popular books on the best-seller lists these days that will provide the self-delusive rationales you are seeking. But if you are looking for an honest perspective on the dietary and lifestyle habits that can give you the best chance of avoiding the whole range of major killing and crippling degenerative diseases of Western civilization, this little volume may have much to offer you.

I am reasonably confident that, sooner or later, (probably later than sooner!) the major medical organizations will endorse the recommendations which I offer, at least in large part. Actually, a reasonable proportion of medical experts might be willing to endorse them now in theory – but they won’t do so in practice because they presume that you, dear reader, are too lacking in self control to follow them; instead, they advise minimal “practical” modifications to the typical American diet that correspondingly will have minimal (if any) impact on subsequent disease risk. (Indeed, the subsequent discussion will provide examples of how ineffectual this approach has been.) As a result we are faced with a Catch 22: Until medical organizations have enough moxie to give people the straight scoop on what they should be eating, there will be little motivation for restaurants and suppliers of convenience foods to provide truly healthy alternatives for health-oriented consumers. But until such alternatives are more readily available, it is indeed rather hard for consumers to eat as well as they might like – thus confirming the views of the “experts” that truly optimal diets aren’t practical!

However, that’s not the whole story. There is in fact serious disagreement among medical experts regarding the type of diet that is best. In particular, there is considerable
support for diets high in monounsaturate-rich oils, or for “paleolithic” flesh-rich diets; and most medical people probably currently view a strictly vegan approach as unnecessarily extreme – if not harmful. Rather than dodging prominent points of view that run contrary to mine – or subjecting them to cartoonish misrepresentations – I intend to confront them head on and actually acknowledge the medical evidence that can be marshalled in their favor. It’s really only within this context that I can make a truly credible case that my recommendations offer the best overall health protection.

Don’t let these provisos discourage you. If you are truly dedicated to eating in a way that will best preserve your long-term health, you can find the means to do it. You won’t succeed (I know that I don’t) – in living up to your best intentions at every opportunity in every particular, but you can succeed often enough that your health and physique will be vastly the better for it. And, if you decide to “live to eat” instead (at least until your first heart attack or your first cancer surgery radically change your priorities) – well, that is your perfect privilege. All that I intend to do is spell out your options. If you are willing to do what you need to do to prevent, reverse, or at least greatly retard the progression of coronary disease, obesity, diabetes, stroke, many cancers, possibly even dementia – the tools are available to you now – you don’t need to wait for pie-in-the-sky gene transplants or mega-buck new wonder drugs. The fact of the matter is, the diseases that kill most Americans are virtually unnecessary, and indeed have been extremely rare in certain societies. To find out more, read on….
II. The Whys and Wherefores – Preventing Coronary Disease

Now that I have summarized the what and how of my recommendations, it’s time to get to the real “meat” of the issue – the why.

It is no secret that coronary heart disease – the type of heart disease that results from atherosclerotic inflammation of the arteries feeding the heart, the type that is involved in almost all heart attacks – is extremely rare if not non-existent in Third World societies whose traditional diets are low in fat and animal products. It was this observation that prompted Nathan Pritikin to organize clinics that treated heart patients with a very-low-fat near-vegan whole food diet and regular aerobic exercise. The published clinical experience of these clinics indicates that within three weeks, this regimen typically achieves substantial improvements in key risk factors, most notably marked reductions in LDL cholesterol. Exercise-induced heart pain – angina – also often improves promptly, and significant “spontaneous” weight loss is typical.2-5

More recently, Dr. Dean Ornish undertook the task of evaluating the long-term clinical results of a comparable regimen (in which he included stress reduction techniques).6-8 His one-year follow-up evaluation created a scientific sensation when he was able to report that his regimen achieved a modest but statistically significant regression in the narrowing (stenoses) of the coronary arteries – whereas, in a control group of patients following the standard guidelines of the American Heart Association, their arteries continued to narrow progressively. Ornish reported the same dramatic and rapid improvement in angina symptoms that the Pritikin Clinics had claimed, and after five years of treatment, he noted that the incidence of serious coronary events (heart attacks, or severe symptoms necessitating cardiac bypass surgery or angioplasty) had been about 60% lower in his treated patients than the control group. And Dr. Caldwell Esselstyn has had even more dramatic success with a low-fat vegan diet – but more on that in a moment. The findings of these clinical studies with heart patients are very consistent with the findings of other studies that have examined the blood fats of healthy vegans – they are found to be much lower than those of either omnivores or dairy/egg-consuming vegetarians. Similarly, total and LDL cholesterol levels have usually been found to be very low in the quasi-vegan cultures where coronary heart disease is rare or non-existent.

Reducing Cholesterol

Why do these regimens produce such rapid and substantial improvement in coronary disease? Substantial reductions in LDL cholesterol no doubt play an important part. The modest reductions in saturated fat and total fat intake recommended by the American Heart Association tend to reduce LDL cholesterol by just a few percentage points – not more than about 5%. In contrast, the Pritikin/Ornish regimens typically decrease this risk factor by about 20% or more. Very-low-fat vegan diets are extremely low in saturated fat – the type of fat which tends to raise serum cholesterol by inhibiting the liver’s capacity to manufacture receptors that remove LDL cholesterol from the bloodstream.9 Such diets also tend to be low in saturates relative to total fat intake – in other words, they have a high unsaturate-to-saturate ratio; this is important because the level of saturated fatty
acids in the liver will reflect not only the absolute dietary intake of these compounds, but also the proportion of total dietary fat which they represent.

In addition, the fact that vegan diets are essentially cholesterol-free (plants don’t manufacture cholesterol) contributes significantly to their cholesterol-lowering efficacy. In the population as a whole – most of whom are omnivores - each 100 mg increase in daily cholesterol intake translates into an increase of only about 2.2 (mg/dl) in serum cholesterol – barely more than a 1% increase in most people.\textsuperscript{10,11} However, this increase tends to be notably higher in people whose baseline dietary cholesterol intake is quite low – most notably vegans; as Dr. Paul Hopkins notes, “modest amounts of cholesterol added to a cholesterol-free diet would be expected to most efficiently elevate serum cholesterol”.\textsuperscript{10} Dietary cholesterol also raises serum cholesterol more efficiently in people who are lean\textsuperscript{12} – which most long-term vegans are. Furthermore, since vegans tend to have quite low serum cholesterols, a given absolute increase in serum cholesterol has a larger impact percentage-wise. So it is clear that the virtual absence of cholesterol in strict vegan diets contributes quite meaningfully to their favorably low LDL cholesterol values.

You should be aware that flesh foods somewhat lower in fat or in saturated fat than red meats – for example, poultry and fish – are just as high in cholesterol as red meat is. With respect to eggs – a rich source of cholesterol (about 250 mg per egg) that is rather low in saturated fat – some recent studies conclude that egg consumption in moderation does not increase the cardiovascular risk of non-diabetics.\textsuperscript{13} Vegans should be aware that these studies examined populations that contained few if any vegans, and that this result therefore cannot be presumed to apply to them – and almost certainly doesn’t.

The protein content of vegan diets also contributes to a reduction in serum cholesterol. For decades, it has been known that if you feed rabbits diets featuring any of a number of plant-derived proteins – in comparison to diets that are identical in every respect save that they feature animal protein – their serum cholesterol levels will be decisively lower on the plant protein diet.\textsuperscript{14} Though a number of these studies made use of soy protein – inasmuch as soy protein isolates are readily available – other types of plant protein were comparably efficacious in this regard. The mechanism responsible for this effect has never been clearly pinpointed, though the fact that plant proteins tend to be somewhat lower in certain essential amino acids – and thus are considered of “poorer quality” – is thought to be of key importance.\textsuperscript{14,15}

These rabbit studies were the inspiration for the original efforts by Dr. Cesare Sirtori and colleagues to lower elevated cholesterol in humans by feeding diets high in soy protein.\textsuperscript{16,17} These studies compared low-fat omnivore diets (featuring lean meats and reduced-fat dairy products) with virtually vegan diets high in texturized vegetable protein (a soy product). To insure that the studies tested the impact of protein per se, the diets were designed so that the quantity and type of dietary fat were nearly identical on the soy and omnivore diets; total protein intakes also remained nearly constant. The researcher found that, when the patients switched from the omnivore diet to the soy-based diet, total and LDL cholesterol dropped by about 20%! Although the low-fat omnivore diet contained a
small amount of cholesterol, theoretical considerations, as well as a study in which the soy diets were supplemented with cholesterol, indicated that absence of cholesterol was not primarily responsible for the dramatic fall in blood cholesterol during the soy diets.

Subsequent similar studies, often enrolling subjects whose initial cholesterol was less elevated, often did not see such dramatic results, and it became clear that soy-based diets had their greatest impact on patients with high cholesterol. A “meta-analysis” (a statistical analysis which lumps together the results of many comparable studies) of 38 controlled studies of soy protein diets concluded that, on average, both total and LDL cholesterol fell by about 20 points on the soy diet (corresponding to a reduction of about 13% in dangerous LDL cholesterol).18

It is important to note that these studies compared omnivore diets with vegan diets that happened to be high in soy products. They did not show that you could simply add some soy protein to your omnivore diet and achieve marvelous improvements in your blood fats – contrary to the expectations of many consumers who are now being hustled to buy soy products. Nor am I aware of any evidence that adding soy protein to a relatively low protein vegan diet has any important effect on serum cholesterol. Furthermore, the common assumption that the isoflavone content of soy protein concentrates was largely responsible for the cholesterol-lowering benefit appears to be dead wrong – Sirtori recently assayed the texturized vegetable protein used in his initial studies and found that it was essentially devoid of these phytoestrogens!19 The obsessive focus on soy and soy isoflavones ignores that fact that virtually all plant proteins are associated with low serum cholesterol in rabbit studies. Thus, while texturized soy protein products can come in handy if you want to eat a vegan diet while pretending to be an omnivore, there is no strong reason to expect that vegan diets in which other types of plant protein predominate will not have a comparably beneficial impact on LDL cholesterol. (As we shall see, regular consumption of soy isoflavones may indeed provide some valuable health benefits – albeit reduction of serum cholesterol is not one of them!)

One theory regarding the favorable effect of plant proteins on cholesterol levels is that plant proteins tend to provoke less insulin secretion (and greater secretion of a competing hormone known as glucagon) than animal proteins do.20,21 While this is unlikely to be the whole explanation – the quality of dietary protein can influence liver metabolism in more direct ways - it is clear that high insulin levels have effects on the liver that would tend to increase blood cholesterol and triglyceride levels, including an increase in the level and activity of the rate-limiting enzyme for cholesterol synthesis.20,22-24

Insulin secretion can also be moderated by choosing whole foods with a relatively low glycemic index. The Pritikin and Ornish clinics have always emphasized the importance of whole foods and have discouraged use of added sugars. When Dr. David Jenkins and colleagues – progenitors of the glycemic index concept – put healthy young men on two strictly controlled diets that differed only in glycemic index, serum cholesterol was about 15% lower during the low-glycemic-index diet.25
Thus, a number of interacting factors contribute to marked cholesterol reduction on an optimal vegan diet: a very low intake of saturated fat, the absence of dietary cholesterol, the characteristic impact of plant protein, and a low glycemic index. In the long run, a substantial reduction in body fat (we’ll discuss this later) often amplifies this benefit.

A classic study provides insight into the magnitude of the benefit achievable when such a diet is consumed in the long term. Back in the 1970s, Dr. Frank Sacks and colleagues from Harvard did a survey of macrobiotic vegan communes in the Boston area. The people in these communes work in a range of ordinary jobs in the outside community, but get together to share their meals communally. The macrobiotic diet which they practice is low-fat, whole-food vegan, but they don’t put any strictures on salt, and they try to keep fruit intake low, their calories coming chiefly from whole grains (especially brown rice), beans, and fresh vegetables. Some members eat fish once or more a week. Of particular note is the fact that they ban all wheat flour products, and don’t use added sugars – thus eliminating the chief sources of high-glycemic-index carbohydrate in the American diet. Thus, aside from the facts that they don’t discourage salt and they minimize fruit intake, their dietary practices are highly consistent with my recommendations.

You may be aware that a total cholesterol level over 200 is considered in the “danger zone”, whereas a cholesterol below 150 is thought to be extremely safe. Sacks found that the average total cholesterol in these Boston communes was 126! In contrast, a group of control subjects drawn from the Boston area, matched by age and sex to the commune subjects, had an average cholesterol of 184. The fact that most of the people in the commune were under 30 certainly contributed to their exceptionally low cholesterol readings – but the handful of commune residents over 40 had an average cholesterol of only 146. Also of note is the fact that the triglyceride levels of the commune members were also low, averaging 59 (mg/dl) as compared to 86 in the controls. (As we will see, this is an intriguing finding given the fact that the macrobiotic diet is extremely high in carbohydrates – and high-carbohydrate diets are said to raise triglycerides!) Some members of these communes use occasional eggs or dairy, and Sacks found that recent consumption of these foods did indeed correlate with higher cholesterol levels.

Sacks reported the case history of one commune member who evidently was genetically prone to high cholesterol. After 18 months at the commune, his cholesterol was 123. He then left the commune for 6 weeks, at the end of which time his cholesterol had shot up to 219. He returned to the commune, and after 3 weeks his cholesterol was back down to 116. Evidently, having “bad genes” does not mean that you have an inexorable date with the coronary care unit!

The effortless leanness of these vegans no doubt was an important factor in their low blood fat levels – their average skinfold thickness (a measure of subcutaneous fat) was only about one-third that of the control subjects. We’ll return to this important point soon.
Sacks is not the only investigator to have noted the highly favorable blood fat levels of free-living American or European vegans.\textsuperscript{27-29} One of these described a vegan diet as “a model for risk reduction”.\textsuperscript{29} Evidently, the exceptionally low cholesterol levels enjoyed by rural Asians – and their virtual freedom from coronary heart disease - are not just a function of semi-starvation, chronic infection, or good genes, as some might assume.

**Insulin Resistance – a Case of “Fat Poisoning”**

However, LDL cholesterol is not the only important determinant of heart disease risk. Insulin resistance – the failure of skeletal muscle and adipose tissue to respond efficiently to the key hormone insulin – is associated with a substantially increased risk for heart attack and coronary disease. People who are insulin resistant tend to have a syndrome (called “insulin resistance syndrome”, or “metabolic syndrome”) characterized by high fasting serum insulin levels, high triglycerides, relatively low HDL cholesterol (the “protective” cholesterol), an increased number of LDL particles which tend to be small and dense, and increased blood pressure. (LDL particle number is determined by measuring blood levels of apolipoprotein B, one molecule of which is present in each LDL particle.) To appreciate the impact of this syndrome on cardiovascular health, it is instructive to consider the results of an epidemiological study conducted in Quebec by Lamarche and co-workers.\textsuperscript{30} These scientists compared the subsequent heart attack risk of subjects whose fasting insulin and LDL particle number (i.e. apoprotein B) were above average and LDL particle size below average, with subjects whose fasting insulin and LDL particle number were below average and LDL particle size above average; the former group was found to be at 18-fold higher risk for a heart attack than the latter group! Note that the risk factors in the former group are all typical components of the insulin resistance syndrome.

Insulin resistance is a key component of type 2 (so-called “mature-onset”) diabetes, and people who are insulin resistant are at greatly increased risk of becoming diabetic, even though they may not yet show impaired regulation of blood sugar. Insulin resistance and most type 2 diabetes appear to arise from a common problem – excessive exposure of the body’s tissues to fat (fatty acids).\textsuperscript{31-38} Insulin resistance syndrome and type 2 diabetes are hardly ever encountered in Third World societies where people eat very-low-fat diets and remain lean for life. Conversely, people who are overweight – especially those that have an increased depot of abdominal fat – are known to be at greatly increased risk for insulin resistance and diabetes. This probably reflects the fact that their swollen fat cells are constantly spewing out excessive amounts of fatty acids into the circulation; moreover, these cells do an inefficient job of trapping the fatty acids derived from recent fatty meals. After a fatty meal, absorbed fat circulates in the bloodstream; properly functioning fat cells, in response to the hormone insulin, take up this fat and store it, so they can release it back to the blood later when glucose (and thus insulin) levels are low and the body’s tissues need fat for metabolic fuel. But when fat cells become overstuffed with fat (as they do in people who are overweight), they become resistant to the action of insulin, and as a result don’t efficiently trap and store meal-derived fat. This “homeless” fat is thus more likely to end up in other tissues, at a time when they don’t need fat for
fuel. Since these tissues aren’t ready to burn this fat, they store it (as triglycerides) and also convert it to other chemical compounds.

Moreover, bloated fat cells that are poorly responsive to insulin tend to spew out fat into the circulation throughout the day, since they are insensitive to the insulin signal. (Insulin tells fat cells to take up fat and hold onto it – which is why excessive insulin activity tends to promote obesity.) So blood levels of free fatty acids tend to be constantly elevated in overweight people, even when glucose and insulin levels are high and fat isn’t needed as fuel. This problem is exacerbated following fatty meals.

As a result, skeletal muscle, the endothelial linings of arteries, and other tissues experience chronic excessive exposure to fat, even when they don’t need it. If they rapidly convert this fat to stored triglycerides, little immediate harm is done. But they can also convert this fat to certain chemical compounds that can cause metabolic havoc – in skeletal muscle, these compounds impede the efficiency of insulin signaling; in the endothelial cells that line the arteries, they cause oxidative stress and inflammation, which play a key role in the induction of atherosclerosis, including coronary heart disease.39-42 (LDL particles likewise have a pro-inflammatory effect on the arterial lining – which is largely why high blood levels of LDL cholesterol (or of apolipoprotein B) promote atherosclerosis.)

The notion that “fat poisoning” is at the root of insulin resistance and vascular damage associated with insulin resistance syndromes has received support from recent studies showing that the extent to which skeletal muscle is insulin resistant correlates directly with the amount of fat stored as triglyceride in the skeletal muscle fibers themselves.43-47 In point of fact, the triglyceride per se is not the problem – rather, it is a marker for the fact that skeletal muscle has been exposed to too much fat at the wrong time. (Curiously, the correlation between muscle triglyceride levels and insulin resistance breaks down in people who are endurance athletes; in such people, triglycerides levels in muscle fibers often are high even though the fibers are usually insulin sensitive. This presumably reflects the fact that, owing to a high fuel requirement, the muscle fibers of endurance athletes are adapted to do a very efficient job of converting fat to stored triglycerides – which means that relatively little of this fat is converted to the alternative compounds that cause insulin resistance.)

The reason why different types of fat have differing impacts on risk for insulin resistance, diabetes, and atherosclerosis – aside from the well-known fact that they have differing effects on LDL cholesterol levels – is that they vary in their ability to give rise to chemical compounds that create metabolic problems. In rat studies, a high dietary intake of fat of any type (with the notable exception of omega-3 fats such as those in fish oil) usually leads to insulin resistance and weight gain. Olive oil is not an exception to this rule; some strains of mice become obese and diabetic if you feed them olive-oil-rich diets (whereas they remain lean and insulin sensitive on a carbohydrate-rich diet).48 Nonetheless, saturated fats induce insulin resistance and endothelial inflammation more efficiently than other types of fat.49 In particular, the prominent saturated fat palmitic acid, unlike unsaturated fats, can give rise to the compound ceramide, which works in
various ways to compromise insulin function and promote arterial inflammation.\textsuperscript{50-54} Saturated fats can also be converted to diacylglycerol, another compound which promotes insulin resistance, oxidative stress, and inflammation. Not surprisingly, a number of studies have concluded that people whose tissues have a relatively high proportion of saturated fat, or whose diets are estimated to be relatively high in saturated fat, tend to have poorer insulin sensitivity.\textsuperscript{55, 56} Thus, reduction of LDL cholesterol may not be the only reason why the low saturated fat content of vegan diets protects the vascular system. The inordinate contribution of saturated fats to the insulin resistance syndrome may help to explain why vegetarians have been found to be at substantially lower risk for diabetes, even when compared to omnivores of comparable body size.\textsuperscript{57}

Excessive tissue exposure to unsaturated fats – oleic acid is the most common of the monounsaturated fats, and linoleic acid the most common of the “omega-6” polyunsatures – can also compromise insulin function and promote inflammation under certain circumstances, presumably because they also can also promote the synthesis of the chemical mediator diacylglycerol.\textsuperscript{58, 59} However, as contrasted with saturated fats, they are more likely to be converted to innocuous triglycerides, so they typically have a less harmful impact.\textsuperscript{52, 60, 61} And oleic acid can sometimes exert a favorable effect by agonizing the conversion of palmitic acid to ceramide.\textsuperscript{52, 60} Some researchers conclude that oleic acid is less likely than linoleic acid to compromise insulin function or promote arterial inflammation\textsuperscript{62-64} – though contrary results have also been reported.\textsuperscript{65} As contrasted to linoleic acid, oleic acid has the further advantage that it is not readily peroxidized by oxidative stress; thus, when oleic acid is the predominant component of cellular membranes, oxidative stress has a somewhat less harmful effect on cellular function. For these reasons, many nutrition researchers now commend monounsaturated-oil-rich oils and nuts (such as virgin olive oil and almonds) as more compatible with health than other sources of dietary fat\textsuperscript{66-68} – consistent with the relatively good vascular health observed in populations which traditionally followed an oleate-rich “Mediterranean” diet.\textsuperscript{69}

If insulin resistance does in fact reflect “fat poisoning”, then it would be reasonable to expect that a very-low-fat diet would tend to have a corrective impact on this syndrome. In fact, this is precisely what has been demonstrated in clinical studies – diets in which fat provides no more than 10-15% of calories, even when high in sugars or rapidly digested starches, tend to produce notable improvements in insulin sensitivity.\textsuperscript{70-72} The experience of the Pritikin Clinics provides a dramatic illustration of this principle: in patients whose baseline fasting serum insulin is high (indicative of insulin resistance, as the body manufacturers increased amounts of insulin to compensate for the poor responsiveness of the body’s tissues to this hormone), serum insulin tends to fall by an average of 40\% during 3 weeks of the Pritikin regimen.\textsuperscript{4} (While daily walking exercise no doubt contributes to this benefit, other studies not incorporating exercise have similar shown the insulin-sensitizing efficacy of very-low-fat diets.)

To understand current scientific controversies, it is important for you to know that lesser degrees of fat restriction – e.g. the 25-30\% fat diets recommended by official bodies like the American Heart Association and the American Diabetes Association – do not seem to
have much of an impact on insulin resistance. In other words, when it comes to dietary fat restriction, half-way measures seem to be of little benefit. Indeed, modulating the amount of dietary fat in the range of 20-40% of calories appears to have little impact on insulin sensitivity (although in the longer term it may influence one’s ability to achieve and maintain leanness). It’s important to realize that a very-low-fat diet, as implemented by the Pritikin and Ornish clinics, has no more than half as much fat as the “low-fat” diet recommended by the American Heart Association; bear this in mind the next time you hear the media report that a “low-fat diet” has failed to achieve benefits.

As noted, obesity – or at least an excess accumulation of abdominal adipose tissue – can be a major contributor to insulin resistance. It is thus relevant to observe that, in the long-term, very-low-fat vegan diets that emphasize whole foods tend to be associated with substantial reductions in body weight and body fat. The experience of Dr. Ornish’s heart patients is illustrative: during the first year of the study – during which the subjects were allowed to eat as many calories as they wished – weight loss averaged 22 pounds! (This despite the fact that most of the patients weren’t consciously trying to lose weight.) Dramatic rapid weight reduction is also the typical experience of the Pritikin Clinics. While regular walking exercise presumably contributes to this weight loss, it is pertinent to note that almost equally dramatic weight loss was seen in a recent clinical study in which type 2 diabetics were placed on a very-low-fat whole-food vegan diet, without explicit exercise advice. These reports are paralleled by the observation that American vegans tend to be much lighter than either omnivores or lacto-ovo-vegetarians – even when their diets are not exceptionally low in fat. (Thus, reduced fat intake does not seem to provide a complete explanation for the relatively low body mass of vegans.) The exceptional leanness of the macrobiotic vegans surveyed by Sacks presumably reflects the fact that their diets are both vegan and low in fat. It is of course well known that Third World peoples whose traditional diets are quasi-vegan and low in fat tend to be very lean throughout life; studies in rural China show that this phenomenon is not primarily attributable to reduced calorie intake. The long term favorable impact of a low-fat vegan diet on body fat levels no doubt reinforces its shorter-term favorable impact on insulin resistance syndrome.

( Believe it or not, the weight loss achieved with the Ornish and Pritikin regimens has been used to denigrate the value of their dietary recommendations. More than one “health expert” has noted that it is difficult to evaluate the inherent merits of the diets which Pritikin and Ornish recommend because their regimens “include weight loss”. This objection might have some force if these regimens included extra gimmicks, such as conscious caloric restriction or appetite-suppressant drugs, intended to accelerate weight loss – but of course they don’t. The weight loss is the natural consequence of the diet and daily walking exercise.)

Why do vegans tend to be so much leaner than omnivores? I suspect that part of the explanation is that a vegan diet tends to provoke lesser amounts of insulin secretion following a meal. This is because protein – especially animal protein – while, by itself a relatively weak stimulus to insulin secretion, can dramatically potentiate the insulin response to co-ingested carbohydrate. Recent studies examining urinary C-peptide
and serum sex hormone-binding globulin – two clinical parameters that can be used to estimate daily insulin secretion – suggest that, even in the short term before substantial weight is lost, daily insulin secretion tends to be relatively low on vegan diets;\textsuperscript{79, 80} in one of these studies, addition of 32 grams of fat-free egg protein to a moderately low-protein vegan diet (substituted for 14 grams of fat) boosted urinary C-peptide output by a dramatic 60% - suggesting a major increase in daily insulin secretion. Even though there is not much difference in the glycemic indices of wheat flour and the “sticky” white rice consumed in the Orient, the insulin response to wheat flour is much higher – likely because the protein content of wheat is twice that of rice.\textsuperscript{81} (It’s a very good bet that the macrobiotic vegan diet – banning wheat flour and sugars, and stressing intact whole foods – is associated with very low daily insulin secretion.) And the propensity of plant proteins to evoke greater secretion of glucagon than animal proteins do\textsuperscript{21} may also contribute to leanness in vegans – glucagon promotes fat burning in the liver.

Insulin is the hormonal signal that tells the body to store and retain fat, rather than burn it. If you manage to keep your insulin levels relatively low while minimizing your ingestion of fat - a trick which very-low-fat whole-food vegan diets seem to accomplish – it is reasonable to expect a progressive loss of body fat until your body fat stores equilibrate at a lower set-point – precisely what is observed clinically with diets of this type.\textsuperscript{82} It stands to reason that your benefit in this regard will be even greater if you emphasize whole, low-glycemic-index carbohydrate foods in your diet, that, by definition, provoke less insulin secretion. Recent studies are demonstrating that dietary glycemic index does indeed have an impact on weight control, whether or not you are consuming a vegan diet.\textsuperscript{83-85}

Much of the reduction in daily insulin secretion associated with vegan diets reflects the favorable impact of such diets on the insulin sensitivity of skeletal muscle. Even when vegan diets aren’t notably low in fat, the fact that such diets feature a notable predominance of unsaturated over saturated fat alleviates “fat poisoning” and promotes efficient insulin function in skeletal muscle. The body necessarily compensates for this by decreasing daily insulin secretion (thereby preventing hypoglycemia). This phenomenon doubtless contributes importantly to the characteristic leanness of vegans. In this regard, it should be noted that people who follow “Mediterranean diets” – in which fish is the chief flesh food, dairy products are consumed sparingly, and olive oil is the predominant source of fat – likewise have been found to be leaner, on average, than those eating a more typical Western diet replete with fatty animal products.\textsuperscript{86-90} Like a vegan diet, a Mediterranean diet is associated with a predominance of unsaturated over saturated fat, and a favorable impact on insulin sensitivity.\textsuperscript{89-91}

In addition to the favorable impacts of low-fat, whole-food vegan diets on blood fat profiles and insulin function, such diets may beneficially affect other risk factors as well. For example, there is preliminary evidence that blood viscosity – another heart disease risk factor – is lower on such diets – in other words, your blood becomes more fluid.\textsuperscript{92}

The rapid improvement in angina symptoms reported by heart patients attending the Pritkin and Ornish clinics is not likely to reflect re-opening of clogged coronary vessels;
although this happens to a modest degree, symptomatic improvement is of much more rapid onset. Rather, it may reflect a lessening of endothelial inflammation (improving the efficiency of homeostatic vasodilator mechanisms which boost blood flow to oxygen-deprived regions of the heart), as well as the fact that carbohydrate is a more efficient fuel than fat when tissue oxygen levels are low; it takes more oxygen to derive a given amount of biochemical energy (ATP) from fat than from glucose. (Which is why – incredibly – pharmaceutical companies have been trying to develop drugs that inhibit fat burning as treatments for angina; one would think that the short-term symptomatic benefits of these drugs would be offset by a long-term adverse impact on obesity and “fat-poisoning”. Very-low-fat diets, as well as high supplemental intakes of the dietary cofactor carnitine, likewise have the potential to promote selective use of carbohydrate in poorly-oxygenated heart tissues – while promoting leanness.)

**Bringing Heart Disease to a Halt**

Dr. Caldwell Esselstyn, a distinguished surgeon at the Cleveland Clinic, has devised a simple lifestyle regimen that appears to stop serious coronary heart disease in its tracks. He began with the provocative observation by his friend Dr. William Castelli that, in the massive Framingham study, people whose total cholesterol remained under 150 (mg/dl) were virtually immune to heart attack. Similarly, cholesterol levels are typically below 150 in the Third World societies where heart disease is very rare. Although many factors contribute to the coronary atherosclerosis that gives rise to heart attacks, an excess of the LDL particles that carry most of the cholesterol in the blood appears to play an obligate role in this regard. This is because LDL particles promote inflammation of the endothelial lining of the arteries while also inducing the formation of “foam cells” beneath the endothelial surface; foam cells are immune cells (macrophages) which ingest oxidized LDL particles and in the process are stimulated to release pro-inflammatory hormones. When the level of LDL particles is low – as it typically is in people whose total cholesterol level is below 150 – significant atherosclerosis of coronary arteries is rarely encountered.

Dr. Esselstyn reasoned that, by recommending a very-low-fat whole-food vegan diet, he could usually reduce cholesterol dramatically; nonetheless, the experience of Ornish and of the Pritikin Clinics suggests that, in heart patients, such a regimen on average reduces cholesterol to about 170 – good, but possibly not good enough. So, in patients whose cholesterol didn’t fall below 150 with diet alone, he implemented aggressive drug therapy – usually the drug lovastatin, sometimes in conjunction with cholestyramine – to push the cholesterol below 150.

In 1985, Esselstyn recruited 24 patients with serious symptomatic heart disease who were willing to try his diet-drug regimen. He found that, in every case, he could reduce cholesterol below the 150 barrier with this approach. After about a year, he found that he had to exclude 6 patients from the study owing to their failure to comply with the dietary advice, but the remaining 18 patients were very compliant for a number of years. After 5 years, he could report that his compliant patients had achieved modest regressions of coronary blockages similar to the experience of Ornish, and that symptomatic angina was
substantially improved. But the results of the recent 12-year follow-up are the most impressive. Of these 18 patients, one patient, who had been in heart failure on entrance to the study, experienced a serious cardiac arrhythmia (heart electrical failure) and died—though autopsy showed that he had not experienced a heart attack. One other patient elected to have an angioplasty because, although his angina had substantially improved, it had not gone away altogether. With these exceptions, there were no other serious cardiac events in the 18 compliant patients over 12 years of follow-up—this despite the fact that these patients had experienced a total of 49 serious cardiac episodes in the 8 years prior to their enrollment in the study! In other words, even in patients with serious pre-existing heart disease, the Esselstyn regimen seems to have brought the progression of coronary disease to a halt! For practical purposes, coronary heart disease may be essentially “curable” with the proper diet/drug regimen, despite the fact that only a modest regression of coronary blockages is achieved; this regimen evidently alleviates the inflammatory process in the endothelial cells lining the coronary arteries, such that the arterial lining becomes much less prone to rupture and trigger blood clots.

These findings are all the more impressive in light of the fact that, except in patients who have a degree of heart failure or have very severe multi-vessel occlusions, the very expensive and somewhat risky surgical procedures currently used to treat coronary disease (bypass surgery or angioplasty) do not reduce subsequent risk for a heart attack—they are only of symptomatic benefit in patients with angina. (Think about that next time you hear about the ever-escalating medical costs that are burdening our economy.) This reflects the fact that, more often than not, heart attacks are triggered by inflammatory rupture of small coronary arteries—whereas surgical procedures only alleviate the strictures in large coronary arteries (which contribute to anginal pain during exercise). In contrast, with a lifestyle/drug regimen whose modest cost involves prescribing and monitoring some relatively inexpensive off-patent drugs, Esselstyn has demonstrated that heart attack can be almost totally prevented! (To learn more about Dr. Esselstyn’s work, go to www.heartattackproof.com, or read his excellent new book Prevent and Reverse Heart Disease.)

You had better not make the assumption that you can live your life precisely as you wish, and then, when you develop heart disease, go on the Esselstyn regimen and save your life. The flaw in this strategy is that, in about half of all cases, the first symptom of coronary heart disease is sudden death! (Not even Dr. Esselstyn resurrects the dead!) And, unfortunately, common diagnostic tools like treadmill tests and angiograms do a far less than perfect job of assessing risk for heart attack. (There are numerous cases of people who passed an EKG stress test with flying colors—and then dropped dead the next day; noted newsman Tim Russert is a case in point. These stress tests, while they can reveal blockages in large coronary arteries, tell us little about the health of smaller coronary arteries.) The safest strategy is to assume that you are in the process of developing coronary heart disease—most Americans are—and put yourself on the Esselstyn program now. This will entail going on the very-low-fat, whole-food vegan diet recommended here, monitoring the subsequent course of your serum cholesterol, and then taking whatever drugs or supplemental nutrients may be required to get your cholesterol below 150 if the diet alone does not suffice.
Another assumption you shouldn’t make is that, by getting your cholesterol under 150 with drugs alone, you can expect the same degree of protection as that achieved by the Esselstyn regimen. Although Dr. Esselstyn has emphasized the impact of his regimen on cholesterol levels, his very-low-fat approach can also be expected to have a very favorable impact on fatty acid-induced arterial inflammation and on insulin resistance syndrome, which markedly boost coronary risk; very likely, this phenomenon contributed importantly to the protection enjoyed by Dr. Esselstyn’s patients. I am unaware of any studies using cholesterol-lowering drugs that have succeeded in virtually eliminating future heart risk. Even though a lifelong cholesterol level below 150 may imply very low coronary risk, reducing cholesterol below 150 once you already have severe coronary atherosclerosis may not by itself be sufficient to achieve complete protection. However, I should also point out that a diet/lifestyle approach by itself may be insufficient for optimal benefit – the longterm results of Dr. Ornish’s regimen, which eschews cholesterol-lowering drugs, while impressive, are not nearly as impressive as those of Dr. Esselstyn.

Statins Have Versatile Benefits

Statins are particularly appropriate, as there is recent evidence that they can directly dampen the inflammation of arterial endothelial cells, independent of their impact on serum cholesterol. They also can reduce elevated blood levels of C-reactive protein, which, like elevated LDL, is a risk factor for atherosclerotic disease that exerts a pro-inflammatory effect on the arterial lining; in patients with “normal” cholesterol levels but elevated C-reactive protein, statin therapy prevents heart attacks. Elevated C-reactive protein is a feature of insulin resistance syndrome, and, like “fat poisoning”, acts on the arterial wall to provoke oxidative stress and inflammation.

Some statins occur naturally in a special strain of yeast, and high-statin strains of red yeast rice, a traditional Oriental food, are now available as cholesterol-lowering supplements that don’t require a prescription. However, a note of caution: in a very small percentage of cases, statin therapy can induce a dangerous muscle damage syndrome – although this has not yet been reported in people using red yeast rice (possibly because the statin dose provided by recommended doses is less than 10 mg, which is half as high as the lowest prescribed dose of lovastatin), you should promptly discontinue your use of this supplement if you notice unexplained persistent muscle pain or weakness, and see your physician. Furthermore, statins can decrease your body’s synthesis of the protective antioxidant coenzyme Q10, so supplemental intakes of this nutrient might be warranted when you use statins – although there isn’t clear evidence that such compensatory supplementation improves health outcomes. In particular, coenzyme Q10 deficiency does not appear to be responsible for the muscle damage syndrome occasionally evoked by statins. However, in light of evidence that supplemental coenzyme Q10 can be therapeutically beneficial in congestive heart failure, and that low serum levels of this cofactor predict increased mortality in this syndrome, it might be wise for statin users who also have heart failure, or who are at risk for heart failure, to supplement with coenzyme Q10; hopefully, future clinical studies
will evaluate this strategy. Coenzyme Q supplementation can also be useful in the control of elevated blood pressure, whether it might be more useful for this purpose in statin-users than in non-users has not been studied.

Statins may confer health benefits that extend beyond the vasculature. Recent evidence suggests that, in addition to improving endothelial function and lowering dangerous blood fats, statins may help to maintain bone density and lower fracture risk, and possibly even decrease risk for Alzheimer’s disease. These are precisely the reasons why many women choose to use prolonged estrogen replacement therapy following menopause. However, unlike estrogen, statins do not increase risk for female cancers or induce the pro-coagulant effects that render estrogen’s vascular benefits somewhat equivocal.

Natural Aids for Cholesterol Control

If your cholesterol remains in the 150-200 range after you adopt a low-fat vegan diet, it would be prudent to reduce it further. However, since medicine considers this range “normal” (despite the fact that coronary care units are filled which patients whose cholesterol is in this range!), it may be difficult for you to find a doctor willing to give you a prescription for a statin under these circumstances. Red yeast rice and other natural aids for cholesterol control can be used as an alternative. In one controlled clinical study, 2.4 grams daily of a standardized preparation of red yeast rice decreased elevated LDL cholesterol by an average of nearly 20%.

Berberine, a commercially-available natural compound derived from several Chinese herbs, has recently been shown to complement the cholesterol-lowering activity of natural or synthetic statins. Like statins, berberine increases the liver’s production of LDL receptors (which remove LDL particles from the circulation, thereby lowering LD cholesterol levels) – but it does so by a mechanism that is different from, and complementary to, to effect of statins in this regard. So concurrent use of berberine may potentiate the efficacy of red yeast rice for cholesterol control. Moreover, berberine can aid blood sugar control in diabetics, working in a manner analogous to the widely-prescribed drug metformin. Unfortunately – as is the case with metformin – about a third of people using barberine initially experience some gastrointestinal upset – but this effect is often transitory. A dose of 500 mg, three times daily, has been reported to aid control of blood sugar and cholesterol in diabetics.

Other natural agents which have the potential to lower elevated LDL cholesterol at least modestly (they aren’t likely to work as well as statins in this regard) include supplemental soluble fiber – glucomannan may be of particular merit in this regard – phytosterols, and tocotrienols. Since phytosterols work by inhibiting intestinal absorption of cholesterol, their efficacy will likely be greater in omnivores than in vegans; however, some efficacy would be expected, as vegans can reabsorb cholesterol secreted in the bile. Tocotrienols are natural fat-soluble antioxidant compounds, structurally closely allied to vitamin E, that are richly supplied by palm oil and rice oil. Whereas statins directly inhibit the rate-limiting enzyme for cholesterol synthesis (HMG-
CoA reductase), the tocotrienols act to suppress the production of this enzyme by cells.\textsuperscript{131} The limited clinical literature on tocotrienols suggests that these compounds are not as consistently or as potently effective for lowering blood cholesterol levels as statins are;\textsuperscript{132-134} nonetheless, some clinical and animal research studies suggest that tocotrienols can inhibit atherogenesis to a degree that is disproportionate to their cholesterol-lowering activity.\textsuperscript{132, 135} I suspect that tocotrienols have the same favorable impact on the function of vascular endothelial cells that statins do – which would be expected if they succeed in reducing the activity of HMG-CoA reductase in endothelial cells. If this is the case, their health benefits may be quite parallel to those of the statins. A total daily intake of 200 mg appears to have clinically useful effects. These compounds also have potential cancer-preventive or –retardant activity, as documented in rodent studies.\textsuperscript{136}

The Nay-Sayers – Are Carbohydrates Bad for You?

In the very-low-fat diets recommended by Pritikin, Ornish, and Esselstyn, at least 70% of the calories are provided by carbohydrate. This is also true of the macrobiotic vegan regimen, and of the diets practiced by most rural Asians. In societies where the traditional diet is predominantly carbohydrate, coronary heart disease is rarely encountered. It may thus strike you as more than a bit odd that a number of prominent medical authorities are now maintaining that high-carbohydrate diets are harmful to heart health!\textsuperscript{137-142}

The scientists making this assertion are comparing what they call “low-fat diets” with diets that are lower in carbohydrate and higher in monounsaturated fat (e.g. olive oil). The key point to recognize is they are not testing the sort of very-low-fat whole-food vegan diet that has shown such a favorable impact on heart disease and insulin sensitivity, but rather the “low-fat diet” advocated by the American Heart Association, which provides 25-30% of calories as fat, is omnivore, and does not place any special emphasis on whole or low-glycemic-index foods. As far as I can tell, the only merit of such a diet – as contrasted to the slightly higher fat diets typically consumed by average Americans – is that it produces a very modest decrease in serum LDL cholesterol. But similar reductions can be achieved with diets that are equivalently low in saturated fat, but which are lower in carbohydrates and higher in monounsaturated fats. A number of investigations have shown that, when these two types of diets are compared, the diet higher in monounsaturates is associated with lower fasting triglyceride levels, higher HDL cholesterol, and larger, less dense LDL particles – all suggestive of lower cardiovascular risk.\textsuperscript{137-139} Note that the favorable shifts in blood fat profile associated with the monounsaturate-rich diet would tend to reverse some of the risk factors associated with insulin resistance syndrome. Nonetheless, there is no evidence that such diets improve insulin sensitivity as contrasted to the effects of a 25-30% fat diet – they appear to ameliorate some of the risk associated with insulin resistance without getting to the root of the syndrome itself, which is fat poisoning. Yet neither does a 25-30% “low-fat” diet improve insulin sensitivity – and, since it is omnivore and only modestly lower in fat, it doesn’t have much long-term impact on body fat either.
What is the metabolic basis for these effects? Daily insulin secretion is likely to be higher on a 25-30% fat diet than on a diet lower in carbs and higher in monounsaturates—in part because the former diet does not improve insulin sensitivity and thus does not tend to lower fasting insulin levels. Although skeletal muscle has the capacity to break down and take up the triglycerides circulating in the blood (via an enzyme known as lipoprotein lipase), insulin acts to inhibit this capacity—so triglycerides levels tend to be higher because muscle does a poorer job of clearing them from the circulation. The chronic elevation of serum triglycerides associated with high-insulin-response diets, in turn, has metabolic effects that tend to reduce the number of protective HDL particles, decrease the size of LDL particles, and boost the capacity of blood to clot—changes suggestive of increased cardiovascular risk. In addition, slow removal of circulating triglycerides after fatty meals results in higher levels of particles known as chylomicron remnants; some experts suspect that these chylomicron remnants contribute to the progression of atherosclerosis.

An obvious implication is that, if you emphasize low-glycemic-index carbohydrates in your diet, while avoiding animal protein—or take other steps to moderate daily insulin secretion—the tendency of high-carbohydrate diets to raise fasting or post-meal triglycerides levels will be blunted. Thus, scientists have often noted that the carbohydrate-rich diets have little impact on triglycerides if high-fiber foods are chosen. You will recall that triglyceride levels of the Boston macrobiotic vegans were considerably lower than those of the control subjects whose diets were undoubtedly lower in carbohydrates—evidently a function of the low daily insulin secretion of these vegans. Aerobic exercise training and supplemental fish oil—both of which I strongly recommend—have also been show to blunt the impact of increased carbohydrate intake on blood triglycerides; exercise accomplishes this by increasing muscle’s capacity to take up triglycerides, whereas fish oil decreases the liver’s synthesis of triglycerides.

There is another issue that the advocates of high-monounsaturate diets fail to address. Free fatty acid levels are almost certainly higher following high-fat meals than lower-fat meals. There is some reason to believe that the exposure of tissues to high levels of free fatty acids following meals contributes to the insulin resistance syndrome and cardiovascular risk. Recent studies show that the healthful protective function of the vascular endothelium is impaired for several hours after a fatty meal—even a meal rich in monounsaturates—possibly owing to free fatty acid excess. This effect may counterbalance to some degree the more favorable impact of high-monounsaturate diets on fasting blood fat levels. Thus, it really isn’t a “slam dunk” to predict that a monounsaturate-rich diet will result in lower overall cardiovascular risk than the 25-30% fat diets to which it has been compared.

What is the relevance of these concerns to the very-low-fat, whole-food vegan diet recommended here? Not much! In practice, fasting triglycerides often fall on such a regimen—particularly if exercise is also recommended. This may reflect the fact that fiber-rich vegan meals provide a relatively modest stimulus to insulin release, even though carbohydrate intake may be high. Furthermore, in the longer term, people on such diets tend to lose substantial amounts of body fat—and this ultimately translates into
reduced triglyceride synthesis in the liver and thus lower blood triglycerides. With respect to concerns about post-meal triglyceride levels and chylomicron remnants, the fat content of very-low-fat meals (10% fat) is so low that there will be very little post-meal rise in triglycerides – this essentially becomes a non-issue. Even when fasting triglycerides rise slightly, as they did in Ornish’s study, this increase in triglycerides was accompanied by a regression of coronary stenosis, marked symptomatic improvement, and increased survival; evidently, whatever modest adverse effect the rise in triglycerides exerted was overwhelmed by the overall positive impact of the regimen.

Fasting triglyceride levels are also modestly elevated in the Tarahumara Indians\textsuperscript{159} – the people whose virtual freedom from coronary disease motivated Pritikin to initiate his diet-based clinical program for heart patients.

In this regard, it should be noted that the increased cardiovascular risk associated with elevated triglycerides in the general American population in part reflects the fact that high triglycerides are often associated with the insulin resistance syndrome – in other words, this syndrome may be the main mediator of the increased risk, rather than the triglycerides themselves. The increase of blood triglycerides induced by high-carbohydrate diets arises by a completely different mechanism, and does not imply insulin resistance - in fact, such diets tend to improve insulin sensitivity if they are sufficiently low in fat - so it is by no means certain that this rise in triglycerides has the same negative significance for cardiovascular health.\textsuperscript{147,160} Moderate rises in triglycerides per se probably have a modestly negative impact on vascular health – they can catalyze a decrease in HDL level and a reduction in LDL size - but they are unlikely to represent the health disaster that some would suggest.

It should be noted that the formal clinical studies comparing 25-30\% fat diets with high-monounsaturate diets have attempted to maintain steady calorie intakes on these diets so that the tendency of low-fat diets to provoke weight loss is negated; this obviously would tend to make the long-term effects of low-fat diets seem worse than they actually would be when people consume them in \textit{ad libitum} amounts.\textsuperscript{161,162}

Nonetheless, one is now constantly confronted with pronouncements by medical authorities and self-proclaimed health experts that high-carbohydrate diets are potentially harmful to heart health, particularly in people with insulin resistance syndrome or diabetes. Indeed, some popular authors claim that high-glycemic-index high-carbohydrate diets are the \textit{chief cause} of insulin resistance syndrome. (This latter claim is truly remarkably inane when you consider that the rural Chinese are virtually immune to insulin resistance, obesity and diabetes as long as they continue to eat their 70\% carbohydrate traditional diet featuring high-glycemic-index sticky rice! More generally, the societies which have the highest carbohydrate intakes – and thus the lowest fat intakes – are the least likely to develop insulin resistance.)

Why is it that the advocates of high-monounsaturate diets persist in comparing such diets with the rather half-witted recommendations of the American Heart Association, as opposed to the very-low-fat approach of Pritikin et al that has documented dramatic
efficacy in heart patients? Possibly because they consider such a diet too impractical to merit testing. Dr. Gerald Reaven, a firm proponent of monounsaturates who has made a classic contribution to our understanding of insulin resistance syndrome, states that “increased carbohydrate intake...within the boundary of menus that can be followed in the free-living state have not been shown to decrease insulin resistance directly, by enhancing insulin sensitivity, or indirectly, by producing and maintaining fat loss.”137 (My emphasis added.) In other words, he discounts the practicality of very-low-fat vegan diets – which demonstrably do improve insulin sensitivity and promote weight loss. This will come as news to the patients of Ornish and Esselstyn who managed to maintain compliance to such diets for many years – or to the patients in Dr. Neal Barnard’s recent study (to be described below) who staged a “patient insurrection” and refused to go back to their former fatty diets when the study protocol demanded it!80

Although I disagree with Dr. Reaven with respect to the practicality of the diet I recommend, I nonetheless must commend him for qualifying his comments so that people will know that they do not pertain to the very-low-fat approach. The popular pundits currently denigrating “high-carbohydrate” diets generally take no such pains, with the result that many lay people are left to conclude that Pritikin, Ornish and Esselstyn are killing their poor patients with those lethal carbohydrates!

Ironically, Dr. Reaven was one of the first scientists to demonstrate conclusively that insulin sensitivity improves substantially on a very-low-fat, high-carbohydrate diet. In work conducted during the 1970s, Reaven and colleagues recruited healthy non-obese middle-aged volunteers and compared the effects of two formula diets, one of which supplied only 10% fat calories and 75% carbohydrate, and the other, 42% fat calories and 43% carbohydrate; the volunteers were started on the higher-fat diet, and then were switched to the very-low-fat diet. The carbohydrate provided in these formula diets was primarily maltodextrin – which has a very high glycemic index – and dairy protein was the protein source, so the high-carbohydrate diet in particular was guaranteed to provoke heavy insulin release following meals. The researchers found that, after 2 weeks on the high-carbohydrate diet, a phenomenon known as “insulin receptor down-regulation” had occurred – the number of insulin receptors on the body’s tissues had decreased, presumably in response to the high insulin secretion associated with the high-carbohydrate diet. Yet, despite the fact that there were fewer receptors to transmit the insulin “signal”, insulin’s ability to promote glucose uptake and storage by muscle was dramatically increased by the high-carbohydrate diet.71 Evidently, even though there were fewer insulin receptors, each receptor did a much more efficient job of accomplishing insulin’s metabolic mission – unencumbered by the fat over-exposure induced by fatty diets. (Very likely, the improvement in insulin function would have been even more dramatic if the insulin receptor down-regulation had been avoided by using lower glycemic index carbohydrate and plant protein in the formula diets.) I have yet to see this study – or any of the other studies demonstrating a marked insulin-sensitizing effect of very-low-fat diets – cited in the treatises that blame carbohydrates for the modern epidemic of insulin resistance and diabetes. Yet they commonly refer to insulin receptor down-regulation as the mechanism whereby high-carb diets allegedly induce insulin resistance.
The take-home lesson is this: if you are only willing to make very modest changes in your current diet, then cutting back on foods high in saturated fat and compensatorily increasing your intake of monounsaturate-rich foods, *may* give you a slightly better outcome than replacing saturated fats with high-glycemic-index carbohydrates. (Whether this is true or not might hinge on whether you would lose some weight on the lower fat diet.) On the other hand, if you are willing to take the pains to do something more definitive for your heart health (and, I would argue, your overall longevity), then a very-low-fat whole-food vegan diet has remarkable documented efficacy in this regard, and can render you virtually “heart attack proof” if you take such adjunctive steps as are needed to keep your cholesterol below 150.

I must register a strenuous objection to the notion that, operating on the presumption that most people are ill-disciplined and a bit dense, health experts should be dispensing watered-down advice that presumably will be more acceptable to the public – pablum for the masses, so to speak - rather than informing people about the lifestyles that provide *truly optimal* health benefits. This is the mind-set that resulted in the virtually useless current dietary recommendations of the American Heart Association - which now serve as such a convenient target for the ridicule of the monounsaturate clique. In point of fact, a goodly proportion of the public is at least as bright and self-disciplined as the pompous medical authorities who are talking down to them.

And what precisely is so difficult about a low-fat whole-food vegan diet? It is very easy to understand: Avoid animal products – flesh foods, dairy and eggs. Go easy on the few high-fat plant foods – olives, avocados, seeds, nuts, and the oils and butters derived therefrom – and eat to your heart’s content from fruits, vegetables, beans, and whole grains, preferably in structurally intact form. Unlike diets where you attempt to count calories and measure out portion sizes of fatty meats – diets that are cumbersome in practice and have poor long-term compliance (in part because their results are so paltry) – the low-fat vegan approach is simple and discrete: there are foods that you can eat, and foods that you don’t eat – period. I’ve done this for a number of years, and, if you set your heart and mind to it, you can too. After you’ve lost the first ten or twenty pounds – without ever once counting a calorie – your cholesterol has plummeted, and you’ve trashed your blood pressure medication, you’re likely to be so enthusiastic that you’ll have found your new lifestyle!

What would be the outcome if Ornish and Esselstyn encouraged their patients to eat large amounts of monounsaturates? My guess is that the high fat intake would compromise the ability of their regimens to promote insulin sensitivity and weight loss. However, it would be preferable to replace such speculation with hard results from well-designed clinical studies – hopefully, such studies will be forthcoming. One recent study has demonstrated that, when women adopt a diet that is near-vegan (animal protein intake was cut by 75%) and that emphasizes low-glycemic-index whole foods – yet that allows use of olive oil, seeds, and nuts (fat content averaged 30% of calories) – weight loss averages 9 pounds over 4 months, and this is associated with a worthwhile improvement in insulin sensitivity. Thus, whole-food vegan diets need not be exceptionally low in
fat to provide some benefit. Of course, these benefits might have been even better with a very-low-fat regimen – but why not resolve this issue with clinical studies?

**Going Nuts**

The observant reader will recall that, whereas I do not recommend a high-fat diet of any kind, I do recommend a modest daily intake – up to an ounce – of monounsaturated-rich nuts, particularly almonds or hazelnuts. (These nuts are distinguished by the fact that their monounsaturate content is over twice as high as the sum of their saturated fat and omega-6 content; an ounce of these nuts provides about 10 grams of oleic acid.) In the context of a very-low-fat diet, this will help to insure that oleic acid is the predominant fatty acid in your body’s tissues, and in circulating LDL particles. (Under ordinary circumstances, humans synthesize little fat - most of the fat in our bodies is diet-derived – so you can determine the nature of your body fat by modulating your dietary fat.) Unlike polyunsaturated fats, oleic acid is not readily oxidized, and thus does not encourage oxidative stress. Indeed, feeding almonds has been shown to have a favorable impact on blood markers for oxidative stress. Since oxidative damage to LDL particles is thought to increase their toxicity to the vascular system, a diet in which monounsaturates predominate may make these particles less pathogenic. The fact that monounsaturate-rich oils are less atherogenic than polyunsaturate-rich oils in cholesterol-fed hamsters may reflect this phenomenon, albeit – perplexingly – other researchers have found monounsaturates to be more atherogenic in rodents!

Moreover, there is now strong and consistent epidemiological evidence that regular consumption of nuts (tree nuts as well as peanuts) is associated with a marked reduction in heart attack risk. (Peanut butter does not always emerge as protective, possibly owing to the additives – including hydrogenated oils – added to most commercial peanut butter.) In particular, nuts (like omega-3 fats) appear to reduce risk for sudden-death heart attacks, precipitated by cardiac electrical disturbances. The fatty acid profile of nuts does not offer an adequate explanation for this phenomenon – evidently there is something else protective in nuts. Nuts are rich in essential minerals, fiber, plant protein, and phytochemicals; which of these might be primarily responsible for the observed protection is not yet clear. Frequent nut consumption has also been linked to reduced risk for type 2 diabetes – possibly reflecting the fact that monounsaturates have a less negative impact on insulin sensitivity than do saturated fats, and may act as a functional antagonist of saturated fats in this regard. Also, oleic acid increases the ability of the intestinal tract to produce a hormone, glucagon-like peptide-1, which may aid in control of blood glucose and in diabetes prevention.

A further consideration is that, even if you eat a very-low-fat diet and are lean, you will still have body fat, and fatty acids will circulate in your bloodstream. Since, aside from the omega-3 fats, oleic acid seems to provoke less “fat poisoning” than other fats, won’t raise LDL cholesterol, and is resistant to oxidation, it makes sense to insure that oleic acid is the predominant fatty acid stored in your body. This can be achieved by adding a modest amount of nuts, nut butters, or olive oil to a very-low-fat diet. In other words, I am arguing, not for a high-fat diet rich in monounsaturates, but rather for a very-low-fat...
diet in which monounsaturate predominance is achieved by regular intentional consumption of modest amounts of monounsaturate-rich foods. Almonds or hazelnuts may be the best choices in this regard, since the health impact of nuts emerges as very favorable in epidemiological studies – and these particular nuts are exceptionally high in oleic acid, and low in both saturated and polyunsaturated fats. If you add up to an ounce of nuts or nut butter to a plant-based daily diet that is otherwise devoid of fatty foods, your daily fat intake is not likely to be more than 15% of total calories. Dr. David Jenkins, a Toronto-based researcher who happens to be a vegan, has conducted numerous studies of almond-supplemented diets, and the effects he has observed are often favorable, and no worse than benign. And perhaps I should mention the fact that almonds are delicious!

In regard to olive oil, however, caution is in order. One study has demonstrated that consuming 50 grams of olive oil with a meal can acutely provoke arterial inflammation. Olive oil contains a modest but meaningful fraction of saturated fat, and even oleic acid can exert a pro-inflammatory effect in excess. Dr. Esselstyn tells the story of a pastor who adopted a wholly plant-based diet after quadruple bypass surgery – a diet, however, which included large amounts of olive oil. After his angina returned, Dr. Esselstyn convinced him to lay off the oil, and his angina remitted. And I have heard anecdotes from people who gained unwanted weight after they began to lace their previously very-low-fat diets with copious amounts of “heart healthy” olive oil. Recall also the mice who became fat and diabetic on an olive oil-drenched diet. So if you elect to include olive oil in your diet, it may be wise to use it only occasionally and in small amounts (like a teaspoon). And heart patients who choose to follow the clinically-proven recommendations of Drs. Esselstyn and Ornish and avoid all fatty foods, have my full respect. Nonetheless, I am unaware of any evidence that modest intakes of nuts can harm arterial health – and I doubt that such evidence will be forthcoming.

**Spirulina vs. Oxidative Stress**

Spirulina is a lot less delicious than almonds – but it may be even more protective. Here’s why:

One of the key reasons why elevated levels of LDL particles, fatty acids, C-reactive protein, glucose, and also elevated blood pressure promote atherosclerosis is that they induce arterial oxidative stress by activating an enzyme complex known as “NADPH oxidase”. Excessive activity of NAPDH oxidase also plays a key role in the progression of congestive heart failure, in hypertension and hypertensive complications, in the development of aortic aneurysms, and in the tissue damage provoked by a heart attack or stroke. Thus, many experts on cardiovascular medicine view NADPH oxidase as a key target for cardiovascular-protective pharmaceuticals. Indeed, one reason why statins may confer such versatile protection is that they can modestly reduce the activity of this enzyme complex.

Fortunately, nature has an answer for excessive NAPDH oxidase activity. Our body’s cells make increased amounts of a compound known as bilirubin when they are subjected
to high oxidative stress; bilirubin provides feedback inhibition of NADPH oxidase.\textsuperscript{191-194}

People who inherit a variant gene that causes them to have chronically elevated blood levels of free bilirubin, are known to be at greatly reduced risk for coronary disease.\textsuperscript{195, 196}

While this suggests the utility of bilirubin as a protective nutraceutical, there are no concentrated natural sources of this compound (aside from ox bile!), and it is very expensive to synthesize. But microalgae, including notably spirulina, are very rich in a compound known as phycocyanobilin (PhyCB - about 0.6% of the dry weight of spirulina) that is a close chemical relative of bilirubin. Inside human cells, PhyCB is rapidly converted to phycocyanorubin,\textsuperscript{197} which is even closer in structure to bilirubin, and which likewise is a very potent inhibitor of NADPH oxidase activity.\textsuperscript{198} This probably explains why oral administration of spirulina (or of phycocyanin, the chief protein in spirulina, which contains PhyCB as a component) has exerted such a remarkable range of anti-inflammatory and antioxidant effects in rodent studies.\textsuperscript{198, 199}

Very recently, French researchers have observed that oral administration of spirulina or of phycocyanin nearly completely prevents the early signs of atherosclerosis in cholesterol-fed hamsters.\textsuperscript{200}

Although efforts are now underway to develop PhyCB-enriched spirulina extracts as a nutraceutical, nothing prevents you from using spirulina now as a food. Extrapolating from rodent studies, it has been estimated that 1-2 rounded tablespoons daily (15-30 grams) might be likely to reproduce the potent antioxidant effects observed in rodents.\textsuperscript{198}

Although it would be premature to declare spirulina a “wonder food” for cardiovascular protection – the available clinical literature is sparse, and generally employs very low doses – it would be perfectly reasonable to use this food now instead of waiting for “all the evidence to be in”. Indeed, spirulina was used as a dietary staple by the Aztecs, and has been found to be very safe in rodent toxicology studies.\textsuperscript{201} One recent clinical study observed worthwhile reductions of blood pressure and LDL cholesterol – accompanied by a significant rise in HDL cholesterol - in healthy volunteers consuming 4.5 grams daily.\textsuperscript{202} Although it doesn’t taste very good – and smells decidedly worse! – it can be rendered reasonably palatable by including it in smoothies.

I should add that excessive activation of NAPDH oxidase is believed to play a mediating role in a wide range of other disorders – including insulin resistance and the complications of diabetes, neurodegenerative conditions such as Alzheimer’s and Parkinson’s diseases, hepatic cirrhosis, asthma, osteoarthritis, erectile dysfunction, periodontal disease, and sun-induced skin damage – to name just a few.\textsuperscript{203} If spirulina and PhyCB live up to their promise as safe, natural inhibitors of NADPH oxidase activity, the future implications for health may be extraordinary.

(By the way, in case you are wondering why certain nutritional antioxidants - such as vitamins E and C - have failed to benefit cardiovascular risk in controlled clinical studies: their antioxidant activity is selective, and they don’t influence the main adverse metabolic effects of NADPH oxidase activity.)
III. Obesity and Diabetes – Preventable and Reversible

As noted above, the typical response to a very-low-fat whole-food vegan diet – without any conscious effort to count or restrict caloric intake – is rapid and substantial weight loss (at least in people who have significant body fat stores). Owing to the fact that a low-fat vegan diet usually has a relatively low caloric density, you can find yourself eating a greater volume of food – while progressively losing weight! Hence the title of Dr. Ornish’s diet book – *Eat More – Weight Less*. Studies which compare the body masses of vegans with those of omnivores or lacto-ovo-vegetarians consistently find that, at any given height, vegans weigh less.

A rational strategy for getting lean and staying lean is to keep daily insulin secretion as low as feasible within the context of a very low fat intake. Insulin is the body’s signal to store fat; it inhibits the burning of fat while promoting use of carbohydrate. Keeping insulin low therefore tends to increase the rate at which stored fat is burned – and this fat will not be wholly replaced by dietary fat if fat intake is kept very low. Bear in mind that a very-low-fat vegan diet has only about half as much fat as the “low-fat diet” recommended by many health authorities. It is easy for vegans to achieve this level of fat restriction, because their diets lack fatty animal products. Of course, you won’t go on losing fat indefinitely with such a strategy; as you get leaner, fat will become less available for use as fuel, and your daily rate of fat burning will decline until it equals the rate at which you ingest fat. At that point, you will have achieved a new leaner equilibrium that you should maintain as long as you stick with your lifestyle.

A very-low-fat vegan diet can be expected to reduce daily insulin secretion because it improves the insulin sensitivity of muscle (which necessitates a compensatory reduction in insulin production), while minimizing the potentiating impact of dietary protein on meal-evoked insulin secretion. The tendency of “poor quality” plant protein to promote glucagon secretion more avidly than animal protein does may also aid fat loss, since glucagon acts on the liver to promote fat burning and appetite control.

To optimize the decrease in meal-induced insulin secretion, it is important to emphasize lower-glycemic-index foods – in other words, lay off the wheat flour products (other than pasta) and baked potatoes, and emphasize structurally intact whole foods that are gradually digested. Recent studies show that if you eat a meal that produces a sharp spike in insulin levels, you are likely to be quite hungry several hours later (as your blood sugar bottoms out in response to the insulin spike) – whereas meals which produce gentle sustained rises in blood sugar and insulin promote satiety for hours to come. There is now evidence that, even in the context of diets that are neither vegan nor low fat, selecting meals that moderate the postprandial insulin rise tends to aid weight loss. Dr. Marthinette Slabber coined the phrase “low-insulin-response diet” to characterize diets of this sort; she proceeded to show that, even when the calorie content and the macronutrient profile of the diet (its relative proportions of fat, protein and carbohydrate) were kept constant, dieters lost more weight with a low-insulin-response diet than on a higher insulin response diet. Slabber achieved low insulin response by emphasizing low-glycemic-index starchy foods and banning the co-ingestion of animal protein and
significant amounts of carbohydrate – in other words, the volunteers could eat both meats and starches, but they had to be segregated into separate meals. (As you will remember, protein – particularly animal protein – potentiates the insulin response to carbohydrate.) Vegans achieve the same benefit by simply omitting the animal protein altogether. However, since low-fat vegan diets are quite high in carbohydrates, it is all the more important for vegans to choose low-glycemic-index starchy foods if they wish to achieve the best weight control benefits.

(Incidentally, the idea of banning co-ingestion of animal protein and starch did not originate with Slabber – this has been a cardinal principle of “food-combining” regimens for years, like that set forth in the best-seller *Fit for Life*. The rationales offered for these regimens have been folkloristic and frankly rather inane – inviting the withering ridicule of academic nutritionists – but the fact of the matter is, the dietary advice most likely does help people to achieve weight loss.)

**Exercising for Optimal Fat Loss**

It virtually goes without saying that regular exercise – both aerobic and resistance – can substantially potentiate the weight control benefits of a prudent diet. Several surveys have examined the strategies of people who have succeeded not only in losing large amounts of weight, but in keeping the weight off for several years. The great majority of these people report that they are doing at least two things – trying to avoid fatty, calorie-dense foods, and exercising regularly.

Dr. Jean-Pierre Flatt has noted that, when done in the proper manner, aerobic exercise and a low-fat diet can synergize in promoting fat loss. The key is to exercise in a way that promotes selective utilization of stored fat. This can be achieved by exercising on an empty stomach (first thing in the morning is an excellent time), and doing an aerobic exercise that is moderate in intensity and prolonged in duration. If you eat carbohydrate before you exercise, the resulting spike in insulin will tend to keep your fat in your fat cells while your exercise does a wonderful job of burning the carbohydrates you have just ingested – which really misses the point! A moderate intensity is important because highly intense exercise can only be sustained by rapidly drawing down your stored glycogen; furthermore, a moderate pace enables you to sustain exercise for a longer period of time; the longer you exercise, the more selectively you burn fat.

Flatt recognised that, after you have exercised, your body will eventually feel the urge to reload the glycogen stores depleted by the exercise. If you do this with a meal that is quite low in fat, and if you have exercised in a way that achieves substantial oxidation of stored fat, then the amount of fat ingested with the meal will be less than the amount of fat you have just burned – your body fat content will be a bit lower, but your glycogen stores will be repleted. Repeat this strategy on a daily basis, and you will inevitably get leaner, until a new leaner set-point is reached. Evidently, the very-low-fat whole-food vegan diet recommended here should be an ideal complement to a fat-burning aerobic exercise program – and vice versa.
The relatively selective fat burning induced by a prolonged session of aerobic exercise can persist for several hours if no food is ingested during this time. And this is actually more practical than it might sound, since the hepatic fat burning triggered by aerobic exercise tends to suppress hunger. Certain nutraceuticals – carnitine, hydroxycitrate, and pyruvate salts – may have the potential to amplify the liver’s capacity to burn fat in the post-exercise period, thereby aiding hunger control.

These considerations have given rise to a novel lifestyle strategy for fat loss which can be described as “mini-fast with exercise”. In this protocol, each session of exercise is nested within a 12-14 hour “mini-fast”, achieved by skipping one meal. For example, instead of eating breakfast, one does morning exercise and doesn’t eat until lunchtime. I have been using this strategy for over a decade – in conjunction with a low-fat vegan diet – and this has helped me keep my body fat in the 5% range. Dr. Babak Bahadori has generalized this strategy so that exercise can be done at mid-day or in the evening, as desired. A clinical study which evaluated this regimen with overweight volunteers at Oasis of Hope Hospital found that, on average, 25% of initial body fat was lost after 12 weeks – without calorie counting, and without significant supervision. For a more detailed explanation of this strategy, see the appendix: The NutriGuard “Learn to Burn” Leanness Program.

Although medical experts commonly recommend exercise training as an aid for weight control, it is more than a little odd that almost no attention is devoted to the context within which exercise is done. Exercising after a carb-rich meal or snack, or eating right after exercise, insures that you will burn relatively little stored fat. It is the proper integration of exercise and eating habits that promotes optimal leanness.

Although aerobic training, in the long term, can have a favorable impact on insulin sensitivity because it promotes loss of excess body fat, exercise also has an acutely favorable impact on the insulin responsiveness of the muscles that are exercised. Therefore, aerobic exercise or resistance training that involves large muscle groups can achieve an acute improvement in insulin sensitivity. However, this benefit lasts for no more than 48 hours after the last exercise session. This implies that, if you want to use exercise training to optimize your insulin sensitivity, you shouldn’t go two consecutive days without exercise. Thus, it is advisable to do significant exercise at least four days per week.

**Type 2 Diabetes is Reversible**

As noted earlier, there is good reason to believe that insulin resistance syndrome as well as most cases of type 2 diabetes reflect “fat poisoning”. Muscle insulin resistance plays a fundamental role in both syndromes. Insulin, whose release is triggered by the increase in blood sugar that follows meals, acts on muscle fibers to promote their efficient uptake and storage of meal-derived glucose. In skeletal muscle, the insulin signaling mechanism can be impaired by exposure to excessive levels of free fatty acids, at times when these fats aren’t needed as fuel; chemicals synthesized from these unneeded fatty acids are responsible for the resulting impairment of insulin signaling. The offending fatty acids
are derived from bloated insulin-resistant fat cells, fatty meals, as well as from excessive triglycerides stored in the skeletal muscle fibers themselves. The longer-chain saturated fatty acids found in fatty animal products and palm oil are especially potent in their adverse impact on insulin signaling, whereas monounsaturated and omega-6 polyunsaturated fatty acids have an intermediate impact, and omega-3 fatty acids are not harmful. (This helps to explain why insulin resistance and diabetes are less common in vegans – even those who aren’t notably lean or whose diets are not especially low in fat.\textsuperscript{57}) Fat poisoning also impairs the insulin sensitivity of the liver, which, like skeletal muscle plays a key role in glucose metabolism. The liver stores and synthesizes glucose, and releases glucose continually to the bloodstream at a rate which insures that glucose levels remain high enough to fuel the brain and other vital organs. Insulin acts on the liver to slow its release of glucose, insuring that blood sugar doesn’t go inappropriately high.

Despite inefficient insulin function, most people who are developing insulin resistance manage to maintain reasonably normal blood sugar levels owing to a compensatory increase in insulin secretion by the beta cells of the pancreas. Their insulin levels remain elevated throughout the day, and blood glucose rises after meals may be on the high side, but glucose eventually returns to a normal fasting level. Despite relatively normal glucose levels, chronic fat poisoning of the endothelial lining of the arteries means that people with compensated insulin resistance are at increased risk for atherosclerosis, heart attack, and stroke.

Unfortunately, chronic excessive exposure of pancreatic beta cells to joint elevations of glucose and fatty acids can induce a phenomenon known as “glucolipotoxicity”.\textsuperscript{218} Marked elevations of blood sugar after meals, provoked by ingestion of high-glycemic index carbohydrates, can contribute to this excessive glucose exposure. Glucolipotoxicity decreases the capacity of beta cells to detect rises in blood sugar, with the result that insulin secretion doesn’t increase appropriately after a meal, and insulin levels may be inadequate to slow glucose release from the insulin-resistant liver. The failure of beta cells to respond to elevated glucose with adequate increases in insulin secretion can result in blood sugar levels that are continuously elevated, even during fasting metabolism. Moreover, fat poisoning is exacerbated, since insulin does an inefficient job of promoting fat storage and retention in adipose tissue at times when glucose is elevated and fat is not needed for fuel. As a result, exposure of beta cells to glucose and fatty acids is further enhanced, and glucolipotoxicity is reinforced; hence, once beta cell glucolipotoxicity is in force, it tends to be sustained by a vicious metabolic cycle.

Glucolipotoxicity not only impairs the function of beta cells – it also hastens their death.\textsuperscript{219} In all tissues in which cells are proliferating, the birth of new cells is compensated by programmed cell death – a “cell suicide” phenomenon known as “apoptosis”. (That’s why our organs don’t continually expand as we age.) In the pancreas, new beta cells continuously arise by cell division – but this is matched by an equal rate of cell death via apoptosis. Glucolipotoxicity does not influence the rate of beta cell multiplication, but it boosts the rate at which beta cells die via apoptosis. As a
result, the total mass of beta cells tends to fall gradually in diabetics, such that, when diabetes is in an advanced stage, they may have less than half as many beta cells as normal healthy people do. Thus, failure of physiologically appropriate insulin secretion in diabetics reflects not only not only improper function of beta cells, but also a deficit of total beta cell mass.

The key role of hyperglycemia (elevated blood glucose) in the genesis of glucolipotoxicity helps to explain why, as demonstrated by epidemiological studies, diets that have a high glycemic index tend to increase risk for diabetes. Conversely, measures which slow the absorption of carbohydrate following meals, such as the drug acarbose, have been shown to help prevent or postpone the onset of diabetes. However, a high dietary glycemic index alone doesn’t seem to provoke beta cell failure unless it is also accompanied by fat overexposure; this explains why diabetes is rare in lean Asians whose dietary staple is high-glycemic-index short-grain rice, but whose diets are low in fat.

**Eliminate the Fat!**

Fat poisoning is the fundamental problem that underlies both insulin resistance syndrome and type 2 diabetes. The evident remedy is to minimize dietary fat (particularly saturated animal fat), decrease body fat, and burn off the triglycerides stored in muscle. The very positive results of the Pritikin Clinics with diabetic patients suggests that a very-low-fat whole-food vegan diet, coupled with substantial daily walking exercise, does a good job of accomplishing these goals. The relatively low glycemic index of the whole foods employed by these Clinics may likewise have a beneficial impact on glucolipotoxicity in diabetics, and thereby aid recovery of their beta cell function.

Doctors at the Pritikin Clinic have published their experience with 652 type 2 diabetic patients who went through their 3-week diet/exercise program. 71% of the patients taking oral medication and 39% of those taking insulin were able to discontinue their medication – and, despite this reduction in medication, fasting blood sugar dropped by an average of 15%. Blood fat levels and blood pressure also tend to decline to a very worthwhile extent, often enabling other medications to be reduced. (With respect to concerns regarding the impact of high-carbohydrate diets on serum triglycerides, it should be noted that, on average, triglycerides fell 33% in these patients – a reduction even more striking than the accompanying 22% decline in LDL cholesterol – so much for “high-carbohydrate” diets being bad for diabetics!)

As noted previously, the Pritikin Program likewise achieves a substantial improvement in the insulin sensitivity of non-diabetics with insulin resistance syndrome – as indicated by an average 40% reduction in fasting insulin levels.

No doubt, some scientific skeptics will call into question the genuine benefits of the Pritikin diet by noting that the patients were engaged in regular exercise (as if daily walks could be expected to produce benefits anywhere near this great!) So it is of particular interest to look at a more recent study in which type 2 diabetics were treated with a low-
fat whole-food vegan diet, without caloric restriction and without explicit exercise advice. Dr. Andrew Nicholson and colleagues have reported that, in type 2 diabetics consuming such a diet for 12 weeks, fasting blood sugar dropped by an average of 28% and the average weight reduction was an impressive 16 pounds.73

These impressive clinical results are entirely consistent with the fact that, in societies whose traditional diets are low in fat and quasi-vegan, obesity, insulin resistance, and type 2 diabetics are very rarely encountered – even when calorie intakes are ample.

There are also indications that, independent of its impact on blood sugar, a vegan diet may reduce risk for some the crippling complications of diabetes. A high intake of animal protein puts a stress on kidney function that tends to accelerate the kidney failure associated with diabetes and various kidney diseases. Conversely, a relatively low-protein vegan diet appears to be protective in this regard.225-227 Furthermore, there are anecdotal reports that a program incorporating a low-fat whole-food strictly vegan diet and daily exercise often leads to rapid improvement in the painful and annoying symptoms associated with diabetic nerve damage (diabetic neuropathy);228, 229 if these reports are confirmable, it is an important development, because these symptoms are usually very hard to control with standard therapy.

Finally, we shouldn’t lose sight of the fact that the chief reason why type 2 diabetics die prematurely is accelerated coronary heart disease. Variations of serum cholesterol, even within the so-called normal, healthy range (150-200) have a substantial impact on this risk230. Although Dr. Esselstyn did not enroll diabetics in his landmark study, it is only commonsensical to expect that his strategy – lowering cholesterol dramatically with a low-fat vegan diet and potentiating this benefit with cholesterol-lowering medication as needed – will likewise have a major impact on the heart disease risk of diabetics.

A word about the value of low-glycemic-index foods in the management of diabetes is in order. Such foods may help diabetics to control their weights, but they have the added advantage of moderating the rises in blood sugar produced by meals.251-253 In diabetics, excessive blood glucose levels act like a toxin on the body’s tissues – safe dietary measures which help to keep these glucose levels down can be expected to reduce risk for future complications, and can also help beta cells to recover from glucolipotoxicity if concurrent measures are taken to reverse fat poisoning.

The Monounsaturate Alternative?

In light of the demonstrable dramatic benefits of a low-fat, high-carbohydrate whole-food vegan diet in type 2 diabetics, it is particularly distressing to read, both in the popular media and the scientific literature, the repeated claim that high-carbohydrate diets are bad for diabetics, and that the ideal diabetic diet should provide 45-50% of its calories from monounsaturate-rich fat.234, 235

In light of the fact that fat poisoning is at the root of insulin resistance and type 2 diabetes, what rationality can there be in recommending a high-fat diet of any type for
diabetics? The high-monounsaturate alternative only looks good in comparison to the virtually pointless recommendations of the American Diabetes Association - a 25-30% fat omnivore diet that does not improve insulin sensitivity, has minimal impact on body weight, and only modestly lowers cholesterol. As compared to this diet, the high-monounsaturate alternative has a somewhat more favorable impact on the blood fat profile but it is no more successful in restoring insulin sensitivity, controlling fasting blood sugar, or in promoting weight loss. Nonetheless, since it doesn’t cause a further deterioration in insulin sensitivity, and is lower in carbohydrates, blood sugar levels after meals tend to rise less markedly, so it probably does provide some modest benefit in regard to glucose toxicity. On the other hand, it is likely that free fatty acid levels after the fattier meals will be higher on the monounsaturate regimen, which potentially could exacerbate the impairment of endothelial function associated with diabetes. Thus it is not entirely clear whether the monounsaturate regimen would be preferable in regard to coronary risk, but lower post-meal glucose levels suggest that it would be preferable from the standpoint of the complications of diabetes induced by hyperglycemia.

But, even if the monounsaturate enthusiasts are correct in their contention that a high-monounsaturate approach is better for diabetics than is the “high-carbohydrate” ADA-recommended diet – so what? Neither of these regimens addresses the fundamental, underlying problem in type 2 diabetes – the continual excessive exposure of the body’s tissues to fat. A very-low-fat, whole-food vegan diet, especially when complemented by exercise training designed to burn stored fat, does address this issue – in part because, in the longer run, it promotes substantial fat loss.

**Strategies for Reversal – the Fasting “Cure”**

The inherent reversibility of type 2 diabetes is revealed by the experience of surgeons who treat severely obese diabetics with stomach stapling operations. In the majority of instances, as patients gradually lose massive amounts of weight, the diabetes simply goes away – normal blood sugar control is achieved without drugs. While it isn’t feasible to treat the average diabetic with this draconian and expensive approach (such surgery is only considered appropriate for grossly obese patients; it entails a measure of risk, often leads to unpleasant side effects – and many patients ultimately regain the weight), the medical treatment of diabetes should strive for the same outcome – getting to the root of the syndrome by getting the fat out of the diet, achieving and sustaining a substantial reduction in body fat, reducing the fatty acid and triglyceride content of the blood, and minimizing the fat content of muscle fibers.

There is some reason to suspect that fasting – when used in conjunction with proper low-fat diet and exercise – may have a role in a “cure” for diabetes. Although fat overexposure – fatty diets feeding fatty bodies - seems to be the fundamental cause of most type 2 diabetes, many diabetics fail to completely normalize their control of blood sugar even after they have adopted a very-low-fat diet and lost substantial body fat. This may result, at least in part, from a vicious cycle in which persistent hyperglycemia and fatty acid overexposure induce glucolipotoxicity in beta cells – impairing their function so that glucose and fatty acids remain elevated, and glucolipotoxicity is reinforced.
A possible way around this vicious cycle may be offered by prolonged fasting.\textsuperscript{240} During a fast, blood sugar tends to fall into the normal range even in type 2 diabetics, giving the beta cells a respite from glucose overexposure and enabling them to gradually improve their function. (Although fatty acid levels tend to be high during a fast, they don’t harm beta cell function unless glucose levels are concurrently elevated.) Indeed, many research groups have noted that, following a prolonged fast, the glucose control of diabetics tends to be improved to a greater degree than could be attributed to the weight loss achieved by the fast; these researchers have pinpointed improved beta cell function as perhaps the key reason for this “excessive” improvement in diabetic control.\textsuperscript{241-244} Unfortunately, this benefit usually has proved transitory, as still-overweight diabetics go back to eating the fatty foods that made them diabetic in the first place, and glucolipotoxicity is rapidly re-established.

But Dr. Joel Fuhrman, a strong advocate of very-low-fat, whole-food vegan diets for prevention and treatment of diabetes, reports that, if a fast of 2-3 weeks duration is preceded by a months of proper eating and exercise that achieves substantial weight loss and improved diabetic control, and if the fast is followed up by resumption of proper diet and exercise, glucose control is often normalized, without medication, when the fast is discontinued; moreover, this “cure” of diabetes persists as long as the prescribed diet and exercise program is maintained.\textsuperscript{245} Dr. Fuhrman does not take primary credit for this discovery – he notes that this technique was used successfully to “cure” type 2 diabetics by clinical researchers at the Rockefeller Institute for Medical Research in New York who published their findings in 1915!\textsuperscript{246} These researchers emphasized that lasting benefit could only be achieved if the patients remained “below weight” and if dietary fat was rigorously avoided; they note that “the addition of some quantity of butter or olive oil to the diet will bring back the glycosuria, ketonuria and other symptoms immediately or within a short time.” (So much for the miracle of olive oil in diabetes!) Presumably, the remarkable insights of the Rockefeller researchers were virtually forgotten when insulin was developed as a diabetes treatment in subsequent years.

A couple of cautions are in order. First, the reports by Fuhrman and the Rockefeller researchers require further independent verification before they can be considered adequately proved. Secondly, it is highly advisable to have the guidance and supervision of a properly-trained physician when embarking on prolonged fasts – particularly the water-only fasting that Dr. Fuhrman practices. A so-called protein-sparing fast may be inherently safer, and would seem likely to have a comparable beneficial impact on diabetes, but even with this strategy a physician’s guidance is very desirable. For example, insulin and certain oral medications must be discontinued when diabetics fast, to avoid induction of hypoglycemia; a doctor’s guidance in this regard is crucial.

One potential “fly in the ointment” which may trip up efforts to re-establish normal pancreatic function in type 2 diabetics is the fact that, as noted above, the total number of pancreatic beta cells tends to decline by about 50% or more in diabetics, owing to an elevated rate of cell death induced by glucolipotoxicity.\textsuperscript{247} This loss of beta cell mass tends to become more severe as diabetes persists over years. Even if prolonged fasting manages to normalize the function of a diabetic’s beta cells, the loss of beta cell mass can
not be rectified in this comparatively brief time, so the remaining beta cells will evidently have to “work harder” to re-establish normal glucose control. If the remaining mass of beta cells is large enough, and if virtually normal beta cell function is restored, this may be feasible, but under less favorable circumstances it may not prove feasible to completely reverse glucolipotoxicity. This may be one key reason why diabetes appears to be more inherently reversible in patients whose diabetes was recently diagnosed, as opposed to patients who have been diabetic for many years. The take-home lesson is this: if you have been diagnosed with type 2 diabetes, take aggressive measures now to reverse it – don’t wait until your beta cell mass has further declined.

We thus have the option of attempting to “manage” diabetes – trying to postpone its horrendous complications and the premature cardiac death which awaits most patients – or we can try to reverse it, restoring normal glucose control and alleviating the insulin resistance syndrome largely responsible for the excess coronary risk. If you were diabetic, which would you prefer? Pritikin has pointed the way to a definitive resolution of this devastating disease – but we must accept the challenge of carrying his work further.

**Spirulina vs. Diabetic Complications**

As I mentioned earlier, increased oxidative stress produced by activated NADPH oxidase is one of the key mechanisms by which persistent hyperglycemia and fat poisoning lead to the characteristic long-term complications of diabetes – blindness (retinopathy), kidney failure, nerve damage (neuropathy), and the accelerated atherosclerosis that leads to heart attacks and strokes. Bilirubin, in its free form, functions physiologically as an inhibitor of NADPH oxidase. Dr. Toyoshi Inoguchi, who has devoted much of his career to defining the fundamental role of NADPH oxidase overactivity in the genesis of diabetic complications, recently did an intriguing epidemiological study in which he assessed the risk for major diabetic complications in diabetics who also have Gilbert syndrome; you may recall that people with this syndrome are characterized by chronically elevated blood levels of free bilirubin. He found, that, as compared to comparable diabetics not known to have Gilbert syndrome, diabetics with Gilbert syndrome were only about one-third as likely to develop retinopathy, kidney failure, or coronary disease!

Since the chief phytonutrient in spirulina, PhyCB, can mimic the inhibitory effect of its chemical relative bilirubin on NADPH oxidase activity, there is reason to suspect that regular consumption of ample amounts of spirulina (or of PhyCB derived from spirulina) will have a very favorable impact on risk for diabetic complications. Potentially, this could be of benefit not only to type 2 diabetics, but also to type 1 diabetics whose diabetes is inherently irreversible (at least until beta cell transplantation is perfected). So adding spirulina to a very-low-fat, whole-food vegan diet may be a very smart move for diabetics – though clinical confirmation of this strategy may still be many years away.

Overactivation of NADPH oxidase is also suspected to play a mediating role in the induction of insulin resistance, as well as the beta cell failure caused by
Thus, regular consumption of spirulina may also aid the prevention and reversal of type 2 diabetes.

**High Protein for Weight Loss**

High protein approaches to weight control have received more media attention over the last decade than low-fat strategies – although thankfully the heyday of the Atkins craze appears to have passed. Although I recommend the vegan approach, there is indeed reason to believe that high-protein diets can promote weight loss.

I tend to divide high-protein diet regimens into two categories – those that are reasonably responsible, and those that aren’t. In the latter category belong those diets – like the Atkins diet – that exhort their adherents to eat as many fatty animal products as their hearts desire. Pile on the steak, the omelets, the cheese, the bacon, the butter and cream – just avoid the carbs, and the weight will drop off. This approach appeals to beef addicts whose only real concern is achieving (temporary) cosmetic weight loss. Naturally the weight loss will only last as long as the dieter manages to stay off the carbohydrates.

In point of fact, such a diet often does work to achieve weight loss. In people whose usual diets are high in fatty animal products (which is true of a high proportion of fat Americans), switching to a low-carb Atkins regimen often does not lead to a major increase in animal product intake. And since the carbohydrates have been dropped, the net effect is a substantial reduction in daily calorie intake and steady weight loss (for awhile). This is possible because the fat-burning ketogenesis unleashed by such diets can have a major impact on appetite control. In effect, at Atkins diet is just a vulgarized version of the protein-sparing modified fast – a well-documented temporary strategy for achieving rapid weight loss. Such modified fasts provide sufficient pure protein to avoid loss of lean mass, while avoiding carbohydrates and fats altogether. Atkins modifies this by providing protein from fatty animal products – implying a concurrent high intake of animal fat – as well as the token low-calorie salad. But whereas advocates of protein-sparing fasts have never represented them as more than temporary expedients that must be followed up by effective maintenance regimens, the Atkins diet masquerades as a sustainable lifestyle.

The inherent problem with such strategies is that, in the long run, your equilibrium body composition will be determined by the effectiveness of the maintenance regimen – so you might as well go right to the maintenance regimen! The common experience with protein-sparing fasts is that patients tend to gain back the lost weight once they go on the “maintenance regimen” – many maintenance regimens have little inherent efficacy, or the patients are poorly compliant once ketosis is no longer suppressing their hunger. The logical way to salvage such strategies is to repeat the fasting phase at regular intervals, so that weight is never allowed to rebound to baseline levels. In effect, the “mini-fast” strategy described above takes this insight to its logical limit, integrating short-term fasting into daily lifestyles.
The ability of an Atkins regimen to promote rapid weight loss is not in question. Much of the initial weight loss reflects loss of water weight resulting from glycogen depletion; although this is of no benefit to health, it gives immediate positive feedback to the dieter, and doubtless accounts for much of the faddish popularity of this regimen.

Despite the fact that the Atkins diet has been around for several years, pertinent published clinical data regarding its longer-term health effects are scarce – presumably because few people manage to continue such drastic carb avoidance in the long term. Of particular interest in this regard is a study published recently by Dr. Richard Fleming, a cardiologist who uses drug therapies to address a wide range of risk factors in his patients. He also asks these patients to eat a low-fat diet that allows a moderate intake of lower-fat animal products. However, some of his recent patients have been resistant to his dietary advice, preferring instead to adopt the Atkins approach. Fleming compared the clinical course of those patients who followed his dietary advice with those who went the low-carb route; note that all patients in the study benefited from similar drug therapies. What he found was that, after one year, coronary artery disease had regressed significantly and heart blood flow had improved in those on low-fat diets, whereas these parameters had worsened significantly in those who had adopted low-carb diets. (Which brings to mind a personal experience: a friend of a friend of mine was doing very well on the Atkins program – the weight was really coming off – until he suffered his heart attack!)

A careful reading of Fleming’s paper shows that, after one year, those who had tried low-carb diets were no lighter than at baseline; evidently, they hadn’t remained faithful to these diets. Presumably, Atkins could contend that Flemings’ study wasn’t a fair test of his strategy. But this raises the issue of compliance – how many people are capable of remaining on a very-low-carb diet indefinitely? Human beings, unlike cats, are not strict carnivores, and I question whether lean active humans can function well and feel well on a very low carbohydrate intake. My suspicion is that, as excess weight is lost and stored fat becomes less available as a metabolic fuel, people become hungrier on such a diet, and eventually increase their intake of carbohydrate. This would terminate the ketosis that promotes appetite control, likely triggering gorging and rebound weight gain. The burden of proof should be on the advocates of these diets to demonstrate otherwise. There’s no doubt that many people can lose weight quickly on an Atkins regimen – the real question is whether they can keep up this regimen for years – and if so, what are its health consequences? With respect to low-fat diets, the evidence is plain – in societies whose traditional diets are low in fat, people tend to remain lean for a lifetime.

A related concern is whether the Atkins diet is consistent with the sort of vigorous and prolonged aerobic exercise that has such a commendable impact on overall health - and that is so helpful for maintaining weight loss. Glycogen – stored carbohydrate – is usually crucial for fueling such exercise; when endurance athletes run low on glycogen, they experience a burn-out popularly known as “hitting the wall”. Ultra-endurance athletes eating high-fat diets develop metabolic adaptations which enable them to make better use of stored fat; we don’t know whether the same can be said for Atkins’ patients. But my suspicion is that exercise is the last thing on their minds – they want a quick and
easy fix that won’t interfere with their psychological addiction to greasy animal products. In fact, a recent clinical study compared response to aerobic exercise in people consuming either a ketogenic very-low-calorie diet or a reduced-carbohydrate, high-protein regimen (similar to “the Zone”, as discussed below). Not surprisingly, those on the ketogenic diet reported more fatigue and negative moods during exercise.254

The more responsible advocates of high-protein regimens typically recommend lower-fat cuts of meat, poultry and fish, and permit reasonable intakes of lower-glycemic-index starchy foods. (The “Zone” diet falls into this category.) As compared to the very-low-carb Atkins approach, these regimens are much more sustainable as continuing lifestyles, and perhaps could be useful as maintenance regimens for those who have lost weight with an Atkins diet. There is reason to believe that these regimens do have a favorable impact on appetite control that can promote gradual weight loss. Even though protein potentiates the insulin response to starch, the carbohydrate intake on these regimens is relatively low – only about 40% of calories when protein and fat each supply 30% – and thus, if the carbohydrates have a moderate glycemic index, the insulin response to meals tends to be modest.84 But it seems likely that high protein intakes promote satiety by other mechanisms as well.

Danish scientists recently published a fascinating clinical study in which they evaluated the impact of two “low-fat” ad-libitum diets on body weight – one providing 12% of calories as protein, the other 25%.255 Both diets contained no more than 30% fat calories (in fat-drenched Denmark, this qualifies as radically low-fat!) The overweight participants were allowed to eat as many calories as they wished, but a clever experimental design insured that each group consumed protein, fat, and carbohydrate in the specified proportions. After the six-month study was concluded, the results were dramatic. Both groups had lost substantial weight – presumably because their baseline diets had been very high in fat – but the high-protein group had lost substantially more weight – an average of 20 pounds, as compared to 11 pounds in the lower-protein group; fat loss showed a similar disparity. The reason? Analysis of food intake records indicated that the subjects eating the high-protein diet had chosen to consume about 20% fewer calories than the lower-protein group! This clearly indicates that, at least in people who are overweight, high protein intakes can quell appetite. Some years previously, a study conducted with rhesus monkeys had reached the same conclusion.256

So there is definitely some method to the madness of the high-protein advocates – these diets are popular because they do tend to promote weight loss. It seems that the average American diet contains just enough animal protein to promote maximal obesity! If you either eliminate the animal protein altogether, or you double it, you are likely to lose weight.

My chief objection to this high-animal-protein strategy is that the long-term health impact of such a regimen is terra incognita. These diets typically contain a fair amount of animal fat – and of course animal protein – so their impact on vascular risk factors is likely to be less favorable than that of a low-fat vegan regimen.257 The impact of such diets on diabetes has not been reported – although the associated weight loss is likely to
be of some benefit, the relatively high fat content of these regimens suggests that they won’t be as effective as the low-fat vegan approach. As we will note subsequently, the quasi-vegan nature of rural Asian diets may be primarily responsible for the very low incidence of “western” cancers in these societies; there is little reason to believe that high-protein diets would be comparably effective for preventing cancer (though a leaner physique and decreased insulin secretion would presumably be of some merit in this regard). The possible adverse impact of high-protein diets on bone health (as discussed below) is a matter of concern to many nutritionists. Finally, from an ecological standpoint, no more than a small proportion of the world’s population could feasibly indulge in such diets – the livestock industry is vastly inefficient in its use of land and water, and effectively deprives us of the land needed to raise crops for underfed humans.

Despite these telling objections, I am willing to admit that, for people unwilling to adopt the vegan alternative, a high-protein diet may be better for your health than staying fat on an ordinary American diet. And it is at least theoretically feasible to eat a high-protein vegan diet by making heavy use of soy products. (Thus, Dr. Barry Sears has recently introduced The Soy Zone.) The health impacts of relatively high protein vegan diets remain to be explored. As we shall see, high intakes of “poor quality” plant proteins appear unlikely to increase cancer risk – yet possibly could aid appetite control. In particular, frequent servings of beans may be helpful to dieters, as they are low in glycemic index, and high in both fiber and plant protein.

Although I can’t recommend a high-protein diet as a continuing lifestyle, I think we owe a debt of gratitude to the advocates of these diets for stressing the importance of the glycemic index concept and of the post-meal insulin surge. Although Pritikin always emphasized the desirability of whole foods, I can’t recall that he ever had anything bad to say about whole-wheat bread or baked potatoes (sans the grease). This really isn’t his fault - the term “glycemic index” hadn’t even been invented when he did his most important work. Now, however, we have a stand-off in which the Ornishites stress the dangers of dietary fat, whereas the Zonies blame high-glycemic-index carbs for all our health ills. Perhaps the proper resolution is (as it often is in acrimonious disputes between men of good will): they’re both right! If we manage to avoid both fat and high-glycemic-index carbohydrates – like the macrobiotic vegans have long advocated - our health and our waistlines should be all the better for it.

Several years ago I had occasion to recommend a low-fat vegan diet to an acquaintance who had some health concerns. A few months later, he called me back, with the rueful news that his cholesterol had gone up since following my advice! I began to question him about his diet. Did he eat a lot of pasta? No, didn’t particularly like pasta. Did he eat a lot of beans? No, not fond of beans. How about rice? No, never was a rice person. By now I was starting to catch on. I’ll bet you eat a lot of bread. Yes, an awful lot of bread. And I bet that you like baked potatoes, don’t you? Yes, I eat a lot of those. Clearly, his insulin was going sky-high after every meal. The moral of this story is: if you’re a bread-and-potatoes vegan, don’t expect health miracles!
IV. Avoiding Hypertension, Stroke – and Dementia?

Hypertension (high blood pressure) is associated with increased risk for heart attack, and if your heart muscle has been damaged by previous heart attacks, it increases risk for heart failure by increasing the work load on the heart. But hypertension has an even more dramatic impact on risk for stroke – both ischemic (blood clot-induced) and hemorrhagic stroke. And there is recent evidence that high blood pressure in mid-life increases your risk for Alzheimer’s disease later in life. Elderly hypertensives tend to experience a more rapid decline in cognitive function with age, even when they do not progress to dementia. And one recent clinical study suggests that pharmacological control of hypertension in the elderly may reduce their risk for developing Alzheimer’s. So keeping your blood pressure low-normal throughout life may be the best strategy for insuring that your intellect remains sharp during your retirement years.

Studies comparing the blood pressures of vegetarians and omnivores – even when the two groups are matched for body size – usually observe lower blood pressure in the vegetarians. The recent celebrated DASH study confirmed that diets relatively low in saturated fat and high in potassium-rich fruits and vegetables tend to reduce blood pressure – most substantially in hypertensives. Since vegetarian diets are often high in fruits and vegetables, and relatively low in saturated fat, these factors may explain at least part of the impact of vegetarian diets.

When Dr. Frank Sacks and colleagues assessed the blood pressures of the Boston macrobiotic vegans that I mentioned previously, the average values he observed were astoundingly low. Among those under the age of 30, the average blood pressure was 106/60 – an outstandingly protective value. Among the older people, average blood pressure wasn’t much worse: about 112/67. One of the most intriguing observations was made when Dr. Sacks stratified that group into those that stringently avoided animal products (less than 5% of calories from animal products) and those that were slightly more liberal in this regard: blood pressure was consistently lower in the strict vegans.

Obesity and insulin resistance – typically associated with high blood insulin levels - are risk factors for hypertension; insulin promotes salt retention by the kidneys and boosts the activity of the sympathetic nervous system (even in people who are “insulin resistant”), effects which tend to raise blood pressure. Nature probably “intended” these effects of insulin to compensate for the fact that insulin also vasodilates arteries feeding muscle to promote efficient glucose storage – but this vasodilatory response is impaired in insulin resistance; thus, insulin resistance and the associated increase in insulin secretion appear to collaborate in raising blood pressure. As I’ve noted above, macrobiotic diets tend to be low in glycemic index (wheat flour is banned), and macrobiotics are usually quite lean and insulin sensitive; their daily insulin secretion is thus probably quite low. These factors doubtless play a role in the exceptionally low blood pressures of young macrobiotics. It should be noted that macrobiotic diets – and those of vegetarians in general – are not notably low in salt, and about half of the vegans in the Sacks study indicated that they salted their meals at the table.
The vascular risk associated with a given blood pressure tends to increase with increasing blood pressure throughout the normal range. (In this respect, it is similar to the impact of LDL cholesterol on coronary risk.) Thus, it is likely that the exceptionally low (but physiologically adequate) blood pressures of macrobiotics are associated with greater vascular protection than would be a so-called normal value of 120/70.

Most low-fat whole-food vegan diets are relatively rich in potassium – particularly if they are high in fruit, vegetables, tubers, and beans. Studies have repeatedly demonstrated that, in people eating their usual salty diets, a substantial increase in potassium intake causes a reduction in blood pressure. In part, this reflects the fact that potassium acts on the kidney to increase its capacity to rid the body of salt. Additionally, the modest increase in blood potassium levels typically seen when potassium intakes increase can have a direct favorable impact on the endothelial lining of the blood vessels, boosting its capacity to generate the protective vasodilator nitric oxide. Whether or not this leads to a reduction in blood pressure, it is likely to reduce your risk for heart attack or stroke; nitric oxide helps to ward off atherosclerosis and blood clots – it is virtually nature’s antidote to vascular disease. These considerations may rationalize the epidemiological finding that, independent of any impact it might have on blood pressure, a high potassium diet greatly decreases your risk for stroke.

Another dietary factor which has emerged in recent studies as beneficial for blood pressure control is protein. In epidemiological studies, people who have relatively high protein intakes tend to have lower blood pressure and to be at lower risk for an increase in blood pressure. In some studies conducted in the U.S., plant protein appears to be more protective in this regard. It is not clear whether this reflects some inherent property of plant protein (for example, a decreased propensity to promote insulin secretion?), or perhaps simply reflects the fact that diets rich in animal protein tend to also be high in saturated fat, which boosts insulin levels by compromising insulin sensitivity. Why protein should have a favorable influence on blood pressure is not yet well understood, but it should be noted that the amino acid arginine and the sulfur-containing amino acids can be metabolized to yield two hormone-like factors which promote vasodilation: nitric oxide and hydrogen sulfide. Regular ingestion of beans, soy products, and nuts may therefore aid blood pressure control in vegans; indeed, each of these foods has been linked to decreased risk for hypertension.

**Salt – The Fundamental Cause of Essential Hypertension**

Dietary salt appears to be the most profound determinant of risk for hypertension. Terrestrial animals have evolved in an environment in which sodium was scarce and potassium was plentiful; our kidneys therefore became adept at holding on to sodium and excreting potassium. Since humans rather recently learned how to mine salt and use it as a seasoning – and even more recently developed the art of stripping our food of potassium by refining grains and lacing our meals with refined sugars and oils – our kidneys must now accomplish the reverse feat, retaining potassium while getting rid of
sodium. The physiological shifts which this has entailed evidently have not had an entirely benign impact on our health.

Medical anthropologists, examining tribal groups not yet “blessed” with the bounty of modern civilization, have repeatedly observed that essential hypertension (the most common type of high blood pressure, not attributable to kidney damage or hormone-producing tumors) is literally absent in societies that don’t add salt to their food. The age-related rise in blood pressure seen in most Americans – even those who don’t become hypertensive – is also absent in these populations. But as soon as these cultures acquire salt, hypertension and the age-related rise in blood pressure have followed in its wake.

Skeptics have suggested that some other changes – increased body fat, more psychological stress, or reduced dietary potassium – may have been the real cause of the onset of hypertension in these groups. This view has been put to rest by a classic study in chimpanzees conducted by Dr. Derek Denton and colleagues. These researchers worked with a captive chimpanzee colony in West Africa, dividing it into two well matched groups. All the chimps continued to get the potassium-rich, salt-free fruit and vegetable diet they were use to, but they also received a special liquid formula. For half of the chimps, this formula was laced with salt. For 20 months, the scientists gradually raised the salt content of the formula, making sure that total salt intakes remained within the usual human dietetic range. Sure enough, average blood pressures progressively rose in the chimps receiving salted formula; the pressure increases were dramatic in some chimps and small or nonexistent in others – much as one would expect in humans. In contrast, blood pressures remained stable in the chimps not receiving salt. After 20 months, the salt was removed from all formulas, and the elevated chimp blood pressures gradually fell back down to the normal range. Since chimps are almost genetically identical to humans, this study constitutes very strong evidence that the introduction of salt was a major factor in the onset of hypertension in acculturated Third World societies. Of course, other factors such as onset of obesity and insulin resistance, a more sedentary lifestyle, and depletion of dietary potassium are likely have played an ancillary role in this regard.

Ecologic epidemiological studies – those in which lifestyle factors in various populations are correlated with disease risks in those populations – suggest that salt is an important risk factor for stroke and cardiac hypertrophy, to some degree independent of its impact on blood pressure. (Except when it is an adaptive response to healthful exercise, cardiac hypertrophy – an increase in the mass of the left ventricle of the heart – is associated with increased risk for congestive heart failure and for potentially lethal disorders of the heart’s electrical rhythm.) In other words, even if salt doesn’t notably raise your blood pressure, it may still be raising your risk for stroke and heart failure. Salted diets, for reasons that are still obscure, also tend to increase loss of calcium in the urine – which in the long term can be expected to have a negative impact on bone density, while increasing risk for painful kidney stones. Such diets also seem to increase the intensity of asthma, at least in males. And the societies that have the highest salt intakes are also those with the highest incidence of gastric pathology – gastric
Scientists are currently attempting to determine whether salt has an impact on the virulence or pathogenic impact of Helicobacter pylori, the microorganism that seems to be the chief mediator of gastric disease.

Clearly, the common notion that dietary salt is something you need to be concerned about only if you have hypertension, is simply mistaken.

Why does salt have such a plethora of adverse effects? Salt seems to be most toxic to those peoples whose kidneys have a diminished capacity to excrete it. The resulting increase in vascular fluid volume triggers compensatory hormonal mechanisms which boost the kidney’s capacity to excrete salt and thereby correct the fluid retention – but these hormones apparently have some adverse health impacts. In particular, salted diets evoke the production of certain hormonal compounds structurally related to the heart drug digitalis in susceptible individuals. These hormones inhibit the “sodium pump” in the kidney tubules, thereby aiding sodium excretion. But these sodium pumps are found on cells throughout the body – including the vascular endothelial cells that play a major role in determining whether we develop hypertension, heart attack, or stroke. I suspect that a hormone-mediated disruption of endothelial function is at the root of the vascular risk associated with salted diets, and that the endothelium of the small resistance arteries of the cerebral vasculature is particularly susceptible to this adverse hormonal influence.

Lessons from Kitava

About a decade ago, Swedish medical scientist Dr. Staffan Lindeberg and colleagues did a survey of the population of the island of Kitava – a Melanesian culture off the coast of Papua New Guinea – to test an interesting hypothesis. The Kitavans are one of the few cultures remaining that still does not add salt to food. They cook some of their meals in sea water, so they do get some salt in their diet – about 2.5 grams of salt daily (corresponding to 1 gram of sodium), about one-quarter as much as most Americans get. And their diets are extremely rich in potassium, owing to the fact that they get the majority of their calories from potassium-rich tropical tubers (yams, sweet potatoes); I estimate that they get about 8 grams of potassium daily – about triple the average American intake. In other words, their intake of salt and potassium is very similar to that of our paleolithic forbears. The Kitavans remain very lean and insulin sensitive throughout life – their diet is near-vegan (they get a small amount of fish) and their chief foods are low in glycemic index and caloric density. Yet they have a fairly ample intake of saturated fat from coconuts, and as a result their cholesterol levels are not all that low – about 180 in the men and 220 in the women. (Presumably, the Kitavans maintain good insulin sensitivity, in part, because the saturated fat in coconut milk is of medium chain length and, unlike the longer-chain saturated fats found in fatty animal products, does not impair insulin sensitivity.) And almost all of the adults smoke tobacco – this is virtually the only Western habit they have adopted, a stunning tribute to the addictive powers of nicotine!
Dr. Lindeberg was able to confirm that, like other salt-free cultures that have been examined, the Kitavans were free of essential hypertension. But he wanted to take this a step further and see whether this translated into a low risk for stroke. So he conducted physical exams on dozens of elderly Kitavans, and also sought to determine whether any members of the tribe had ever seen or heard of symptoms suggestive of a stroke in other members of the tribe. He also looked into risk for coronary heart disease and heart attack by doing EKG studies and asking appropriate questions.

His conclusions were stunning: he was unable to uncover any evidence that anyone in the tribe had ever suffered a stroke, heart attack, or angina. The closest that he could come in this regard was a report that a 70-old man had suddenly fallen dead on the beach for no apparent reason – during the late nineteenth century! Yet, with 2500 residents, a fair proportion of whom were elderly (a few in their nineties), this absence of vascular disease could not be attributed to a lack of elderly Kitavans. (More generally, the common idea that Third World societies with relatively short average life expectancies lack elderly citizens, is bunk – once a person in these societies reaches the age of forty, he may have a better chance to achieve an advanced old age than a 40-year-old American does, owing to low risk for the degenerative diseases that typically kill us; the low life expectancy in these societies typically reflects high infection-mediated mortality in infancy and childhood.)

The apparent absence of stroke is quite a stunning finding, because stroke is reasonably common in many lean Third Word cultures in which heart attack is very rare (cultures which salt their food, of course). On its face, the absence of coronary disease in Kitava is less striking, because this disease has been rare in many Third World cultures – but this should be viewed in the context of the fact that cholesterol levels in Kitava are not low and most adults are tobacco addicts! Lindeberg’s findings strongly suggest that an unsalted, high-potassium diet, in conjunction with excellent insulin sensitivity, has an extraordinarily protective impact on vascular health.

But Lindeberg noted something even more remarkable. He was unable to find any evidence, either from direct physical examination or report, that anyone on Kitava had ever suffered from senile dementia! Senile dementia was a concept absolutely foreign to the Kitavans. Lindeberg found a couple of mentally retarded young Kitavans, but onset of dementia with age was unheard of. Consider the fact that full-blown senile dementia is not subtle – if a person couldn’t recognize his own children, it wouldn’t be long before virtually everyone on the island knew about it.

But Lindeberg may not have been the first to note this phenomenon. Dr. Hugh Trowell, an expert on the diseases of Africa, recounts the experiences of a British psychiatrist practicing in Nairobi in the 1930s. At this time, the use of salt among average black Kenyans was still rare, and stroke was very rarely seen. This psychiatrist noted that the psychiatric ward where he practiced displayed the full range of mental disorders common in Western society – with the exception that “senile dementia was a notably absentee.”
Could senile dementia – including Alzheimer’s disease – be a disease of civilization made possible by salted diets?!

This possibility is not altogether far-fetched. A growing number of scientists – myself included - have independently postulated that a healthy cerebral vasculature may somehow minimize risk for Alzheimer’s disease (and, of course, the so-called vascular dementia that results from strokes). Many risk factors for stroke and vascular disease are likewise risk factors for Alzheimer’s. The recent striking discovery that therapy with statin drugs may greatly diminish risk for this disease fits this hypothesis, as it is known that statins have a protective impact on the vascular endothelium and can reduce stroke risk. Perhaps maintaining effective brain blood flow somehow dampens the process that gives rise to Alzheimer’s. Or perhaps some diffusible product of the healthy cerebrovascular endothelium – such as nitric oxide – functions to prevent the self-perpetuating inflammatory process involved in Alzheimer’s from gaining a foothold.

Whatever the answer to this riddle may be, it is not unreasonable to posit the following: if you keep your cerebral vasculature so healthy that it is virtually immune from stroke, you may also greatly diminish, if not eliminate, your risk for Alzheimer’s.

Recent discoveries suggest that salty diets might also increase Alzheimer’s risk by promoting oxidative stress in the brain. Excessive oxidative stress produced by brain scavenger cells known as “microglia” is believed to be a key cause of the neuronal death and dysfunction that characterizes Alzheimer’s disease. In certain salt-sensitive strains of rats (prone to develop hypertension on salty diets), a salty diet leads to an increase in brain sodium content that in turn leads to increased brain activity of the hormone angiotensin-II. This increase in cerebral angiotensin-II activity results in the development of hypertension in these rats – but this hormone can also act on microglia to boost their production of oxidant stress. More specifically, angiotensin II does not activate microglia directly, but rather potentiates their response to other activating signals. Thus, it would be reasonable to postulate that salty diets could make some sensitive individuals prone to Alzheimer’s by exerting a “priming” effect on microglia, increasing their propensity to produce oxidants. In this regard, it is intriguing that hypertension in one’s middle years is a strong risk factor for Alzheimer’s; conversely, treatment with anti-hypertensive drugs that antagonize angiotensin II activity has been linked to a marked decrease in risk for Alzheimer’s, and a slowing of its progression. While the protection seemingly afforded by these drugs might be attributed to favorable effects on vascular function, some researchers suspect that inhibition of angiotensin II activity in the brain also contributes in this regard – in part because drugs which can penetrate the blood-brain barrier seem to be more effective for dementia prevention. It should be noted, however, that it is not yet known whether salty diets can increase angiotensin-II activity and microglial activation in those specific regions of the brain where Alzheimer’s neurodegeneration occurs – much further research will be required to determine whether salty diets can promote the oxidative stress that kills and disables neurons in Alzheimer’s disease.
Prevention of Alzheimer’s is an extremely important challenge. The incidence of this horrible disorder – possibly more horrible for the victim’s family than for the victim himself – increases progressively with increasing age, until its prevalence in people over 85 is said to be about 50%. What would be the point of taking elaborate precautions to protect yourself from killer diseases like heart attack, diabetes, and cancer, if your reward is to spend your “Golden Years” in a state of imbecility, while your children cope with heartache and ruinous expenses?

Current evidence suggests that the most fundamental key to keeping your cerebral vessels healthy into old age is a low-salt diet. Other factors which minimize stroke risk include a high potassium intake, good insulin sensitivity, regular aerobic exercise, keeping blood pressure low (through dietary and/or pharmaceutical measures), and statin therapy (despite the fact that LDL cholesterol is not an important stroke risk factor). The diet and exercise strategies which I recommend should help to accomplish many of these aims. Even if the alleged connection between vascular health and Alzheimer’s ultimately proves to be a red herring, the worse that you could expect from following these guidelines is a greatly diminished risk of stroke – in itself, no mean blessing!

A cautionary note: don’t assume that these measures will be useful for treating Alzheimer’s once it is already firmly established. The inflammatory process, once it builds up a head of steam, may be self-perpetuating and very hard to slow or stop. If simple dietary measures could halt Alzheimer’s, we’d almost certainly know about it by now. So don’t wait until the horse is already out of the barn to shut the door!

By the way, in light of the fact that fish oil has anti-inflammatory effects and Alzheimer’s is in essence a low-grade chronic inflammatory disorder of the brain, it is not unreasonable to speculate that omega-3s may decrease Alzheimer’s risk\(^\text{316}\) – and a limited amount of epidemiology suggests that this disorder may indeed be somewhat rarer in fish-eating cultures.\(^\text{339}\) You will recall that Kitavans eat a modest amount of fish, which conceivably could contribute to their protection in this regard.

**Dangers of Salt Restriction?**

By now you have probably figured out that no piece of dietary advice, no matter how seemingly benign and laudatory, goes unchallenged in the modern media. And so it goes with the advice to restrict salt.

To help the kidney retain sodium on a low-sodium diet, the body manufactures increased amounts of the hormones renin and angiotensin II.\(^\text{340}\) (Curiously, a high-salt diet boosts angiotensin II activity within the brain, whereas a low-salt diet increases angiotensin II production in the systemic circulation.) Potentially, this can have adverse consequences; angiotensin II in excess can promote constriction of blood vessels – thus raising blood pressure – and can also promote the process of atherosclerosis, as it is a growth factor for vascular smooth muscle. (The vasoconstrictive activity of angiotensin II presumably reflects the fact that it evolved to help animals survive hemorrhage; its sodium-retaining...
activity is also useful in this regard, as this helps to maintain vascular volume.) The rise in angiotensin II production during salt restriction is triggered by a concurrent rise in the hormone renin; several studies have concluded that people with relatively high renin levels are at increased risk for heart attack.341, 342

This increased production of angiotensin II evoked by low-sodium diets may be largely responsible for an odd phenomenon known as “salt resistance”: although most people achieve at least a modest reduction in blood pressure when dietary salt is reduced, in some people blood pressure doesn’t fall at all or may even rise slightly; these people are characterized as “salt resistant”, whereas those who respond favorably to the salt reduction are call “salt sensitive”. Studies show that salt-resistant people tend to experience above-average increases in angiotensin II when put on low-sodium diets.343, 344 We thus have a bit of a paradox: although salted diets seem to be a sine qua non for development of essential hypertension, many people with elevated blood pressure fail to achieve a reduction in this pressure when they cut back on dietary salt. Evidently, the hypertension genie is not always easy to put back in the bottle! It seems that years of exposure to a heavily salted diet can have long-lasting effects on the structure and function of the vascular system that are not readily reversible.

An illustration of this principle is provided by a study in infants.345 Dutch pediatricians conducted a clinical study in which half of a group of newborn infants were given a low-sodium diet for their first six months of life, whereas the other half received the amount of salt ordinarily given to Dutch infants. It didn’t surprise anyone that blood pressures were lower in the low-salt group after the six months were up. The real surprise came 15 years later, when the insightful investigators had the idea of measuring blood pressure again in the now teenage participants in that study: they found that the blood pressures of the teens who had been in the low-salt group were still significantly lower than those who hadn’t been sodium restricted as infants – this despite the fact that both groups presumably had been eating the same salty diet after 6 months of age! Evidently, salt restriction at an early age has long-lasting effects on blood pressure regulation. Conversely, it is clear that many years of a high-salt diet has effects that cannot be immediately reversed by cutting way back on dietary salt.

Studies of severe and sudden salt restriction in salt-addicted Western populations have noted another potential adverse effect: an impairment of insulin sensitivity;346-350 there is disagreement as to whether more moderate salt restriction is harmful in this regard.351-354 This effect is most dramatic when people’s salt intake it cut to very low levels – i.e., only about half of the salt intake of Kitavans. (As you will recall, the Kitavans have excellent insulin sensitivity on a salt intake low enough to prevent hypertension and stroke.) There is some indication that the magnitude of this effect tends to wane with time.349 Furthermore, when more realistic levels of salt restriction are tested – for example, cutting current salt consumption in half – the effect is modest and in some studies non-existent. The physiological basis of this effect is still unknown. (I have a suspicion that a reduction in the level of the hormone bradykinin may play a role; this hormone promotes insulin sensitivity, and there is a recent report that its blood levels decline during salt restriction.355 Alternatively or additionally, increased activity of the sympathetic nervous
system – the “fight or flight” neural activity evoked by stress or hemorrhage – may be responsible for this effect.\(^{356-358}\)

If salt restriction can impair insulin sensitivity and raise angiotensin II production, why are low-salt societies like Kitava almost universally characterized by good insulin sensitivity and a near absence of vascular disease? Conceivably, the extreme leanness of these groups acts as a compensatory factor – this clearly plays a role in their good insulin sensitivity. Furthermore, it is now known that the nitric oxide produced by healthy vascular endothelium acts to blunt the actions of angiotensin II;\(^{359}\) conceivably, the leanness and excellent insulin sensitivity of low-salt cultures aids this production of nitric oxide and thus renders them resistant to the potentially adverse impact of elevated angiotensin II levels. The high potassium intakes of most low-salt cultures may also provide some protection in this regard.

In any case, the fact that some of the physiological effects evoked by salt restriction can potentially have an adverse impact on vascular health, has led some medical scientists to question the wisdom of recommending salt restriction for everyone.\(^{340,360}\) This point of view has been further encouraged by the fact that epidemiological studies attempting to correlate the habitual salt intakes of Americans with their subsequent risk for heart attack have had conflicting outcomes. Such studies are hampered by the fact that it is very difficult to get an accurate assessment of people’s habitual salt consumption by analyzing a single sample of urine or a short food diary. Furthermore, unless a person is aggressively avoiding salt, it is almost impossible for a modern American to achieve a salt consumption as low as that of Kitavans – so the findings of such studies may not be very germane to assessing the benefits of a lifelong diet that is truly low in salt. It should be noted that one study – much ballyhooed in the popular press for its conclusion that people eating diets relatively low in salt were at increased risk for heart attack\(^{361}\) – has been thoroughly discredited, as the technique for assessing salt intakes was clearly very flawed.\(^{290,362}\) A more recent and more credible study has concluded that lower-salt diets are associated with decreased mortality from heart attack and stroke in overweight subjects, but not in lean subjects.\(^{363}\) Yet another recent study found that overall mortality and cardiovascular mortality were somewhat greater in people eating saltier diets.\(^{364}\) (Ironically, the popular media presented this latter study as evidence that low-sodium diets increase risk for mortality, since the data indicated that low daily sodium intakes correlated with increased mortality. However, this finding reflected the fact that people who are sickly and inactive tend to consume fewer calories, and thus less sodium; when the data were analyzed on a sodium-per-calorie basis, saltier diets were found to confer greater risk. This is a good example of how sensationalist media often misrepresent scientific evidence in pursuit of a “hot” story.)

A Role for ACE Inhibitors – Drugs and Peptide Nutraceuticals

I will readily admit that, whereas lifelong salt restriction in lean Third World populations with minimal atherosclerosis appears to be remarkably protective, it is not necessarily the case that institution of salt restriction in middle-aged salt-addicted, overweight, atherosclerotic Americans will be equivalently beneficial. Nonetheless, I believe that,
under the right circumstances, moderate salt restriction is highly recommendable. For one thing, the impairment of insulin function associated with moderate salt restriction is at most modest (if not non-existent), and certainly can readily be compensated by other lifestyle measure that promote good insulin sensitivity – such as those discussed above. Secondly, there are drugs as well as nutrients that can directly antagonize the adverse effects of angiotensin II on the vascular system. In particular, so-called ACE inhibitor drugs, commonly used to treat hypertension, inhibit the production of angiotensin II. (ACE – the acronym for “angiotensin-I converting enzyme” – is a protease enzyme that generates angiotensin II by cleaving a short precursor protein.) Dr. Graham McGregor, a forthright and compelling advocate of moderate salt restriction for control and prevention of hypertension, has demonstrated that, in so-called salt-resistant patients whose blood pressure fails to decline during salt restriction, concurrent treatment with an ACE inhibitor enables salt restriction to achieve its intended favorable effect on blood pressure. This therapeutic combination – salt restriction plus ACE inhibitor – produces substantial reductions in the blood pressure of most hypertensive patients, regardless of their salt sensitivity status. Of related interest is the fact that ACE inhibitor therapy has been shown to prevent the negative effect of severe salt restriction on insulin sensitivity (possibly because these drugs boost bradykinin levels).  

ACE inhibitors are generally well tolerated, and, rather like statins, have a versatile protective impact on vascular health. If you have high blood pressure, I suggest that you discuss with your physician the advisability of using an ACE inhibitor in conjunction with salt restriction. However, ACE inhibitors cannot be used by a small percentage of people, in whom they induce a chronic cough; a new type of drug that inhibits the angiotensin receptor may be more appropriate for them. Furthermore, for the majority of people who are normotensive and who would like to enjoy the health benefits of salt restriction, it is not feasible to use a prescription drug. Fortunately, there is a natural alternative – the omega-3 fats found in fish oil somehow act as antagonists to angiotensin II activity – which is one reason why they often help to lower elevated blood pressure. In analogy to the synergism of ACE inhibitors and salt restriction in control of hypertension, there is limited clinical evidence that the combination of supplemental fish oil and salt restriction can have a more substantial favorable impact on blood pressure than either measure alone. (And it may be germane to note that the Kitavans obtain fish omega-3s from their moderate consumption of fish – the only significant animal product in their diet.) Thus, especially if you have hypertension or pre-existing coronary disease, it may be wise to supplement with fish oil when you institute salt restriction. As little as 3 grams of fish omega-3 per day appear to be beneficial in this regard.

Yet another intriguing possibility looms on the horizon. Over a decade ago, scientists discovered that when they partially hydrolyzed certain food proteins with special enzymes, some of the resulting short proteins (peptides) were potent inhibitors of ACE; furthermore, they found that some of these ACE-inhibitory peptides were immune to destruction by digestive enzymes, and thus could be absorbed intact after oral administration. Scientists, particularly in Japan, have been working to develop food-derived partially hydrolyzed proteins as ACE-inhibitory nutraceuticals, and their efforts are now reaching fruition with a product manufactured from bonito – a sort of cat-
food-grade tuna that the Japanese traditionally use as the condiment “katsuobushi”.

In oral daily doses as low as 1.5 grams, a "katsuobushi peptide" product has been shown to act effectively as an ACE inhibitor and to lower elevated blood pressure – by an average of 10 points systolic, 6 points diastolic in a recent controlled study recruiting patients who were mildly hypertensive. This product emerges as very safe in toxicology tests, and so far has not been linked to chronic cough when used clinically; in part, its safety reflects the fact that, like other food proteins, it is simply metabolized to the amino acids your body requires. It is currently being sold as a nutraceutical in Japan, and is now becoming available to nutritional distributors in the U.S. Efforts to produce products with comparable efficacy from plant proteins – such as soy, buckwheat, and wheat germ – are in progress. It can be anticipated that the use of such products in conjunction with moderate dietary salt restriction will have a very favorable effect on elevated blood pressure in almost every hypertensive.

However, one reason why the advent of natural food-peptide ACE inhibitors is so exciting, is that there is growing evidence that, even in people who have “normal” blood pressure, ACE inhibitor therapy is likely to slow the progression of atherosclerosis, and reduce risk for heart attack and stroke. This benefit is at least partially attributable to the fact that, as mentioned above, ACE inhibitors boost the level of bradykinin, a hormone-like compound that has a favorable effect on arterial health as well as insulin sensitivity. This latter effect may rationalize recent evidence that ACE-inhibitor therapy seems to decrease risk for type II diabetes. The availability of nutraceutical ACE inhibitors will mean that all of us will have access to this protection, whether or not we are hypertensive or can afford expensive prescription drugs.

Arguably, the statins and the ACE inhibitors have become the “superstars” of cardiovascular medicine; these usually-well-tolerated drugs have demonstrated considerable efficacy for prevention of heart attack and stroke. For example, a study using cholesterol-fed hamsters examined the ability of a statin and an ACE inhibitor, alone or in combination, to prevent early arterial damage; either drug alone reduced the damage by about a third, while the combination reduced it by two-thirds (and note that the ACE inhibitor was protective even though the hamsters had normal blood pressure).

**Additional Nutraceutical Strategies**

In addition to nutraceutical ACE inhibitors and fish oil, there are several other supplemental nutrients that have potential for aiding blood pressure control. These include the amino acid arginine, the “metavitamins” taurine and coenzyme Q10, and cocoa flavanols. The latter are of particular interest. The Kuna Indians of Panama are known to be free of hypertension as long as they follow their traditional diet – which is as salty as American diets! They also appear to be at very low risk for stroke. What distinguishes the Kuna is their heavy daily intake of flavanol-rich raw cocoa. The ability of cocoa flavanols to reduce elevated blood pressure has been demonstrated in recent studies, and appears to reflect the fact that these flavanols can act directly on the
arterial lining to provoke increased production of the vasodilator nitric oxide. Spirulina and its key phytonutrient PhyCB may also have potential for blood pressure control, inasmuch as excessive activity of NADPH oxidase, both in the vasculature and the brain, appears to play a key role in the induction and maintenance of hypertension. (You will recall that PhyCB can inhibit NADPH oxidase.) Moreover, NADPH oxidase is an important mediator of the adverse effects of angiotensin II – so spirulina might function as an angiotensin antagonist. In a recent open clinical study which enrolled healthy volunteers, ingestion of 4.5 grams of spirulina daily for 12 weeks was associated with average reductions of 10 points in systolic pressure and 7 points in diastolic pressure – a very large effect given that most of the participants were not considered hypertensive.

(Since we have touched on dementia in this chapter, it is also appropriate to note that NADPH oxidase in the brain is believed to be the major source of the oxidative stress that kills and disables brain neurons in Alzheimer’s disease. Ingested PhyCB likely has access to the brain, as suggested by rodent studies in which spirulina feeding has prevented chemically-induced brain damage. So it’s reasonable to suspect that spirulina may have potential for preventing Alzheimer’s disease, as well as other common neurodegenerative conditions linked to cerebral oxidative stress, such as Parkinson’s disease and ALS.)

The possible utility of nutraceuticals for managing hypertension – and for reducing stroke risk independent of blood pressure – is an area that deserves far more clinical investigation, particularly since it is not feasible to put half the adult population on expensive prescription drugs.

**Restricting Chloride?**

*Sodium* gets a lot of bad press as a contributory factor in hypertension. But in fact, sodium *chloride* is the toxin that makes hypertension possible – other forms of sodium, like sodium bicarbonate or sodium citrate, appear to be harmless. It is the combination of sodium and chloride that is harmful – sodium without the chloride – or chloride without the sodium – doesn’t adversely affect blood pressure. In other words, to avoid hypertension and other complications of a salted diet, we need to restrict sodium or chloride – but not necessarily both. Several researchers have found that, when people are put on a low-salt diet, concurrent administration of sodium citrate can prevent the induced rise in angiotensin II levels. The sodium citrate also prevents an increase in the activity of the sympathetic nervous system that could be potentially harmful to heart patients. Yet, unlike sodium chloride, sodium citrate does not raise blood pressure or increase loss of calcium in the urine. So far, no one has looked at the impact of sodium citrate on the insulin resistance evoked by salt restriction; such research seems advisable. These considerations suggest that the adverse hormonal responses to salt restriction represent the body’s effort to conserve sodium, not salt or chloride. At present, there is no clear evidence that relying on the modest amounts of chloride occurring naturally in whole-food diets has any adverse hormonal consequences. Thus, by adding non-toxic organic sources of sodium to a low-salt diet – while keeping chloride...
consumption low - it is conceivable that salt restriction would have a more unequivocally positive impact on heart health. People often thoughtlessly equate sodium with salt – in fact, the most protective strategy might be to restrict *chloride*, rather than sodium.

However, it is clear that more clinical research is needed on this issue before definitive conclusions can be drawn or recommendations made; one disquieting note is that serum potassium levels are reported to decline when people on low-salt diets are given sodium citrate. Another study reports that dietary sodium citrate, like sodium chloride, increases the potency of certain hormones for triggering rises in blood pressure – even though it didn’t increase blood pressure in the absence of hormone infusions. The fact that sodium citrate supplementation doesn’t raise blood pressure and has a favorable impact on angiotensin II and activity of the sympathetic nervous system, doesn’t necessarily mean that it couldn’t influence vascular health negatively in other respects.

**Salt Restriction – Key to Cerebrovascular Health**

Even if we assume that – as suggested in a recent major study – the impact of moderately low salt intakes on heart attack risk in lean people is equivocal, doesn’t this somewhat miss the point? We have already discussed how hearts attacks can be almost totally prevented – even if you have pre-existing heart disease – and rigorous salt restriction is not necessary to achieve this protection. The main point of salt restriction should be to prevent *stroke* and optimize your *cerebrovascular* health. A salted diet appears to be a *sine qua non* for hypertension and – as suggested by studies in Kitava and East Africa – stroke as well; its impact on cerebral health is thus parallel to that of LDL cholesterol on heart health. The real question that remains is, how low do you have to get your salt intake to achieve substantial protection in this regard – and how early in life do you need to start? Current evidence suggests that, if you are overweight, moderate restriction provides substantial protection, whereas more substantial restriction (closer to the salt intake of Kitavans) may be required in lean people. While optimal protection may require consuming a low-salt diet from infancy, it seems most likely that an adequate degree of salt restriction initiated later in life will provide at least some benefit to most people, and thus is recommendable. The prospect of achieving virtually total protection from stroke and perhaps even dementia is exciting indeed, and we shouldn’t allow the quibbling about salt’s impact on heart risk to distract us from this fundamental goal.

Many vegans are rather smug about their vascular health, presuming that their low cholesterol levels make them invulnerable in this regard. So it is important to stress that, with respect to strokes that result from occlusion of small cerebral arteries, LDL cholesterol is not clearly established as a risk factor – and low LDL cholesterol is actually associated with *increased* risk for hemorrhagic stroke. In quasi-vegan Third World societies where heart attack is rare – and dietary salt intakes are commonly high – stroke is a leading cause of death. So vegans would be well advised to insure that their diet is rich in potassium, and moderately low in salt.
Bear in mind that, even if salt restriction doesn’t have a major impact on your blood pressure, the protective impact of low-salt, high-potassium diets on stroke risk, heart hypertrophy, bone health, and quite possibly dementia are in large measure independent of any impact on blood pressure per se. And, even when salt restriction doesn’t have much effect on your current blood pressure (which is likely to be the case if your current pressure is relatively low), remember that low-salt diets tend to prevent the typical age-related rise in blood pressure. These facts are usually conveniently ignored by the pundits who claim that salt restriction often has minimal impact on blood pressure and has unknown long-term health effects. All in all, the potential health benefits of a low-salt, high potassium natural diet are so substantial and versatile – especially if such a diet is instituted at an early age – that I am inclined to recommend it with minimal if any reservations. In particular, if you want to maximize your chances for maintaining healthy brain function when you achieve an advanced age, a low-salt, potassium-rich diet is the way to go!

The Genie Back in the Bottle - A Way Around the “Salt Paradox”?

The fact that many people don’t achieve a really useful reduction in elevated blood pressure when dietary salt is reduced – what I call the “salt paradox” – encourages skeptics to question the role of salt in the genesis of hypertension, and to doubt the wisdom of recommending universal salt restriction. “Salt resistance” may often reflect structural changes in small arteries – a thickening of the artery walls known as medial hypertrophy – that are induced by long-term hypertension, and that can maintain excessive resistance to blood flow even after salt is removed from the diet. But it is likely that certain metabolic vicious cycles also play a role in this phenomenon. In other words, salted diets may trigger some maladaptive patterns of metabolic activity that become self-sustaining, and work to keep blood pressure elevated even when salt is withdrawn from the diet. Could there be a way to break these metabolic vicious cycles so that a low-salt diet could then “cure” essential hypertension?

Work by Dr. Alan Goldhamer suggests that there may indeed by quite a simple way to put the hypertension genie back in the bottle. It has been known for many years that, during prolonged fasting, blood pressure tends to drop – and it drops most dramatically in people who are hypertensive, often coming all the way down to the normal range. Of course, most people go back to their old eating habits after a fast, and – unless they’ve lost a lot of excess weight during the fast – their blood pressure goes right back up. But what if people were to adopt a low-salt vegan diet when they terminate the fast – could the reductions in blood pressure be sustained?

Goldhamer and his colleagues have been testing precisely this strategy. He puts his hypertensive patients on a water-only fast for about 10 days – or however long it takes for blood pressure to fall back into the normal range. Then his patients are transitioned to a diet that is entirely consistent with that which I am recommending here – a vegan diet that is low in salt, low in fat, and emphasizes lower-glycemic-index whole foods (i.e. no wheat flour products). Goldhamer has summarized the results achieved with 174 hypertensive patients treated with this regimen. The most encouraging observation is that
the blood pressure of his patients tends to fall a bit further after they terminate their fast and start to eat the low-salt vegan diet – which suggests that it may be possible to conserve the blood pressure reductions achieved by the fast. On average, this regimen slashed the blood pressure of the patients from an initial value of 159/89 to a very satisfactory 122/76, well within the so-called normal range. In fact, only 11% of his patients failed to achieve “normal” blood pressure. This benefit is all the more striking in the context of the fact that Goldhamer discontinues any anti-hypertensive medications during the fast.

The chief problem with Goldhamer’s remarkable study is that he doesn’t have long-term follow-ups on most of his patients – so we don’t know for sure how well the benefits are conserved in the longer term. A high proportion of his patients come from out-of-state, spend several week’s at Goldhamer’s clinic, and then go back home – making it hard for the doctor to determine how well they are doing. Nevertheless, Goldhamer has been able to monitor the long-term progress of 42 of the patients in the study, who live near Goldhamer’s clinic. He reports, that, an average of 27 weeks after the fasting regimen was completed, the blood pressure in these 42 patients averaged 123/77 – despite the fact that these patients were using no anti-hypertensive drugs. This sounds to me a lot like a “cure” for essential hypertension – though it seems likely that this “cure” will persist only as long as the patients persist with their low-salt vegan diet. Dr. Goldhamer informs me that, thanks to an agreement with a local labor union, he is now planning a study that will have the thorough-going long-term follow-up required to provide decisive proof of the value of his therapy.

It’s important to realize that most of Goldhamer’s hypertensive patients are not obese, and the primary intent of the fast is not to achieve weight loss. It is of course well known that obese people who manage to lose large amounts of weight on therapeutic fasts or other diets tend to achieve sustained reductions in elevated blood pressure – but that is not what Goldhamer is trying to do. The modest amount of fat loss his patients achieve during about 10 days of fasting may be modestly beneficial for their blood pressure control – but can hardly explain the massive reductions in systolic pressure – on average, a remarkable 37 points, about triple the reduction seen with most drug therapies – achieved with his regimen. The most likely explanation is that fasts of sufficient duration can break some of the vicious cycle mechanisms that act to sustain hypertension in salt-resistant subjects. I suspect that the substantial reductions in insulin secretion achieved during a fast435 – reductions that are sustained to some degree by the low-fat, whole-food vegan diet the patients adopt afterwards – have a lot to do with the dramatic impact of Goldhamer’s regimen. Perhaps medial hypertrophy accounts for the fact that a small minority of patients fail to normalize their blood pressure during the fast.

Dr. Goldhamer uses water-only fasting – a technique that, in the longer term, can induce a substantial loss of lean mass, and can be potentially hazardous without the careful supervision of a physician – so his fasts are conducted on an in-patient basis in his clinic. (If you would like to learn more about Goldhamer’s Center for Conservative Therapy, its website is www.healthpromoting.com.) However, I think that it is likely that a protein-sparing modified fast (PSMF)436-438 – a fast which is modified by administration of high-
quality protein (from flesh foods or powders), potassium salts, vitamins, and minerals – would be as effective, or nearly as effective, as the water-only fasting that Goldhamer endorses. The PSMF was developed to enable obese people to fast safely for many months at a time, while maintaining most of their lean mass and preserving good nutritional status – but it is also safe and appropriate for shorter-term fasts in people who are not massively overweight, and can be conducted on an out-patient basis (though it is prudent to have a doctor’s supervision during any type of therapeutic fasting) So, for people who would prefer to control their high blood pressure naturally with a health-protective diet - rather than just relying on drugs to provide mediocre control – a PSMF of 10-14 days duration, followed by a low-salt, low-fat, whole-food vegan diet, may perhaps be the key to success. In any case, a modified fast of moderate length is unlikely to hurt you – and will shed a few pounds of fat that you probably don’t really need.

I should however emphasize that this “fasting cure” of high blood pressure still needs more clinical documentation before we can be sure that it works; while there is no doubt that fasts tend to lower blood pressure, the ability of low-salt vegan diets to preserve this benefit requires further verification. Nevertheless, though this approach is still “unproven”, it’s not likely that you will hurt yourself trying it – particularly if your doctor is willing to supervise your fast.
V. Preventing and Controlling Cancer

You may have read about a hyperexpensive clinical study, sponsored by the National Cancer Institute, which attempted to determine, once and for all, whether “low-fat, high-fiber” diets would reduce risk for colon cancer - or more accurately, the benign colon tumors (adenomas) that often give rise to cancer; the subjects chosen for this study had previously experienced such adenomas. Half of the participants in the study were asked to cut back on fatty meats and increase their intake of fiber-rich plant foods, whereas the other half were asked to maintain their habitual food intake. To the considerable consternation of the study’s authors, the findings of this ambitious four-year study were entirely negative – the dietary recommendations had no impact on the subsequent occurrence of colon adenomas.439

In a letter responding to the published study, Dr. Dean Ornish was scathing regarding the fact that the study’s participants had achieved only rather trivial modifications of their diets – saturated fat intake, on average, was reduced only about 20% in the “low-fat” group, and fiber intakes were increased only modestly.440 Nonetheless, I don’t think that Ornish’s critique, although accurate, cuts to the heart of the issue. The real crux of the matter, I believe, is that “low-fat, high-fiber diets” per se do not prevent colon cancer – low-fat vegan diets do!

The protocol of this colon cancer prevention trial had mandated that the participants asked to cut back on fatty meats should simultaneously increase their intakes of lower-fat poultry, fish and dairy products – thus, their intake of animal products and animal protein did not decline at all. Presumably, the scientists who designed the study buy into the popular notion that ample intakes of dietary protein – especially “high quality” animal protein – are crucially important to good nutrition and health. (The popularity of this view – encouraged for many decades by propaganda sponsored by dairy and livestock interests - is such that vegan advocates are constantly questioned as to how one could possibly get an adequate protein intake with a vegan diet.)

You probably are aware that the incidence of many of the chief types of cancers prominent in Western society, including cancers of the breast, colon, prostate, pancreas, ovary and uterine endometrium – cancers which, in conjunction with lung cancer, are responsible for the bulk of our cancer mortality – are relatively rare throughout rural Asia and Africa. These cancers are rare not only on an absolute, but also on an age-adjusted basis – in other words, at any given age, people in these societies are far less likely to develop these cancers than we are. For many of these cancers, it is clear that genetic factors are not primarily responsible for this rarity, since these cancers are reasonably common in Asian-Americans and African-Americans. And the disparity in risk for these cancers is large and important; we are talking about manifold variations in risk - up to tenfold or more in the case of prostate cancer. In other words, if we could figure out why these cancers are comparatively rare in the Third World and institute the necessary corrective measures in the West, the impact on cancer mortality would be astounding.
By the 1970s, as medical scientists became better aware of the stark international disparities in age-adjusted cancer incidence and mortality, the first efforts were made to explain this remarkable phenomenon. Suspicion first fell on dietary fat, since the average daily dietary fat intake in various countries throughout the world was found to correlate quite nicely with the incidence of the “western” cancers in these countries. Seemingly consistent with this hypothesis was the fact that fat-enriched diets (with the notable exception of fish-fat) could markedly increase the yield of carcinogen-induced cancer in many animal studies. With respect to colon cancer specifically, dietary fiber was suspected to be protective; it was thought that dietary fiber might bind to putative carcinogens or cancer-promotional agents, lessening their access to the cellular lining of the colon.

Unfortunately, these neat theories soon began to fall apart. Closer examination showed that international incidences of these cancers tended to correlate with saturated or animal-derived fat intake, but showed no correlation whatever with fats derived from plants sources. And yet, in animal studies, the polyunsaturated omega-6 fats (as found in many vegetable oils) were more effective than saturated or other types of fat in promoting cancer induction. Furthermore, so-called case-control epidemiology in Western populations – studies which compare the diets of people who come down with a disease to the diets of roughly comparable people who don’t – are only partially confirmatory of a link between these cancers and dietary fat; in the case of breast cancer, no such link is found, even when saturated fat is considered separately.  

Meanwhile, the fiber hypothesis of colon cancer has received little support from animal studies, and equivocal support from epidemiological surveys. And scientists in Africa have noted that, as crude maize meal has been progressively replaced by refined low-fiber maize meal as a dietary staple in rural African populations, the incidence of colon cancer has remained low. The N.C.I. study cited above, as well as a large companion study that specifically examined the impact of supplemental wheat-fiber on colon adenoma incidence and found no effect, appear to have delivered the coup de grace to the fiber theory of colon cancer prevention.

I myself was in quite a quandary on this issue, which had fascinated me since my medical school days. Back in the 1970s, I had made some of my own correlations between dietary fat and “western” cancer incidence, and had become convinced that dietary factors were at the root of the vast international disparities in risk. But over the course of time it became apparent that the fat and fiber hypotheses didn’t hold a lot of water.

**Vegan Diets vs. Growth Factors**

A few years ago, I became interested in nutritional determinants of growth factor activities. One growth factor in particular, IGF-I (insulin-like growth factor-I) appears to have an important influence not only on lean mass (it promotes the synthesis and retention of protein in muscle, mediating the influence of growth hormone in this regard), but on cancer induction. It turns out that genetically altered cells that are prone to give rise to cancer – cells that have sustained certain heritable mutations in their DNA that can
potentially disrupt their growth control mechanisms – have mechanisms that somehow “sense” that these cells are genetically flawed, and that then often direct these cells to “commit suicide” in a natural process known as apoptosis. It is now known that apoptosis is a crucial regulator of the cell population in most tissues; the number of cells in a tissue is determined by the balance between cell multiplication and apoptosis, which must proceed at roughly equal rates if the cell number in adult tissues is to remain constant. Apoptosis plays an essential role in embryonic development (we wouldn’t have discrete fingers if the tissue between them didn’t die off in planned apoptosis), and it is becomingly increasingly clear that effective apoptosis is crucial for prevention of both cancer and autoimmune disease.\textsuperscript{444,446}

A number of hormonal growth factors are capable not only of promoting cell multiplication, but also of suppressing apoptosis in various tissues. Of key importance in this regard is IGF-I, which appears to suppress apoptosis in most tissues. Most of the IGF-I in the blood is produced in the liver, which secretes it into the bloodstream; however, other normal tissues as well as certain tumors can make enough of this hormone to influence their own growth. Most types of multiplying cells express receptors for IGF-I during some stage of their cell cycle, and activation of these receptors by IGF-I not only promotes cell replication, but also usually makes these cells less susceptible to apoptosis.\textsuperscript{447-449} In particular, this appears to apply to many pre-cancerous tissues, in which apoptosis provides crucial protection from cancer induction.\textsuperscript{446,447} The versatile activity of IGF-I in blocking apoptosis in many tissues thus suggests that IGF-I may be a nearly universal “cancer promoter”. IGF-I does not directly induce mutations in cellular DNA – these may arise as a result of free radical damage or attack by carcinogens – but it may increase the rate at which mutations occur by boosting the rate of cellular proliferation; risk of mutagenic DNA damage is greatest during DNA replication, which is necessary for cell proliferation. Moreover, once a cell has sustained dangerous pre-cancerous mutations (which becomes more common as we age and our cells progressively accumulate mutations), high IGF-I activity will increase the chances that that cell and its progeny will survive to give rise to a cancer.

Not surprisingly, one strategy that mutant cells adopt to avoid apoptotic death is to increase their production of IGF-I receptors, so that they will be more sensitive to the available IGF-I. It has recently been discovered that one of the prime purposes of many so-called “tumor suppressor” genes is to decrease expression of the IGF-I receptor.\textsuperscript{450,451} When these suppressor genes are rendered non-functional by mutation, increased amounts of this receptor are produced, making the cells less vulnerable to apoptosis. Heritable mutations of the BRCA1 suppressor gene are linked to increased risk for breast and ovarian cancers; a key role of this gene in breast and ovary cells is to suppress production of the IGF-I receptor. Researchers thus surmise that “activation of the overexpressed receptor by locally produced or circulating IGFs may be a crucial step in breast and ovarian cancer progression.”\textsuperscript{451} A likely implication is that women who carry this mutation could lower their cancer risk by diminishing their IGF-I activity.

You have probably heard or read that underfeeding rodents – giving them 20-40% fewer calories than they would consume spontaneously when given free access to food –
literally slows their aging process and increases their maximal achievable longevity by
25% or more. One reason why these rodents tend to live longer is that they are less
susceptible to cancer – although their lifelong risk for cancer may not be low, their age-
adjusted risk (their incidence at any given age) is substantially decreased. Recent studies
pinpoint a decrease in IGF-I activity as the likely mediator of this effect. Caloric
restriction markedly depresses both the levels and the activity of IGF-I in the
bloodstream; if calorie-restricted rodents are given a concurrent infusion of IGF-I to
prevent a reduction in IGF-I activity, the calorie-restricted diet fails to prevent cancer.\textsuperscript{452, 453}

Beginning with the pioneering study of Dr. June Chan, who found that risk for prostate
cancer was several-fold higher in men with moderately elevated IGF-I levels,\textsuperscript{454} epidemiological studies have begun to look at the impact of circulating IGF-I levels on
risks for various cancers. So far, relatively high blood levels of IGF-I have been linked to
significantly increased risk for prostate, colon, and pre-menopausal breast cancer.\textsuperscript{455-459}
(Note that these are some of the most important “western” cancers.) Actually, to be a bit
more accurate, it is the level of free IGF-I in the blood that is emerging as a risk factor.
Most of the IGF-I in the blood is bound to certain proteins (not unreasonably known as
“IGF binding proteins”) that prevent it from exerting its activity; only the IGF-I that
breaks free from the grasp of these proteins has biological activity.

Which leads us to a rather obvious question: how do dietary factors regulate IGF-I
activity? The impact of dietary restriction in this regard makes it clear that diet can have
an important impact in this regard. And this makes a good deal of sense: when calorie
availability is low, what sense would it make for animals to have high anabolic growth
factor activity (e.g. high IGF-I activity) if sufficient calories aren’t available to support the
growth and maintenance of an enlarged tissue volume? Thus, calorie-restricted animals
tend to be small and lean (not unlike the rural Asian populations at low risk for “western”
cancers!)

Calorie intake appears to regulate IGF-I activity primarily by modulating insulin
secretion. High insulin secretion – as is seen when animals eat large amounts of calories
and/or are fat – acts on the liver to promote IGF-I synthesis and to inhibit production of a
factor (known as IGF binding protein-1, or IGFBP-1 for short) that binds to IGF-I,
suppressing its activity.\textsuperscript{460-463} Thus, the low daily insulin secretion associated with low-
fat, whole-food vegan diets (or other low-insulin-response diets) would presumably
decrease circulating IGF-I activity. Furthermore, the fact that dietary saturated fat has a
particularly obnoxious impact on muscle insulin sensitivity – and thus tends to provoke a
compensatory increase in insulin secretion – may help to explain the adverse impact of
dietary animal products on cancer risk. Insulin sensitivity is also compromised in
obesity, but is improved by exercise – thus offering a satisfying explain for the fact that a
great many cancers are more common in people who are overweight,\textsuperscript{464} and less common
in those who exercise regularly.\textsuperscript{465} The characteristic leanness of vegans is evidently an
advantage in this respect.
But another primary determinant of IGF-I activity is the availability of essential amino acids – the nutritionally essential building blocks of protein that are richly supplied by most dietary animal protein.\textsuperscript{466-468} Thus, it is not surprising that diets low in protein, or in which the protein is provided by plant proteins relatively low in certain essential amino acids (such as soy!) have been found to have an effect somewhat similar to underfeeding in decreasing cancer yields in carcinogen-treated rats.\textsuperscript{469-473} One scientist, cognizant of the fact that soy protein tends to be a bit deficient in the essential amino acid methionine, wanted to see what would happen if a supplement of methionine was added to the soy-based diets of carcinogen-treated animals; sure enough, the addition of methionine largely abrogated the ability of soy-based diets to reduce cancer yield,\textsuperscript{473} (It is ironic that many nutrition experts have suggested that methionine be added to dietary soy products to improve the “quality” of their protein!)

Plant proteins, as opposed to animal proteins, tend to be relatively low in certain essential amino acids – most notably methionine and lysine. Since vegan diets also tend to be lower in total protein than omnivore diets are, it is apparent that essential amino acid nutrition tends to be somewhat poorer in vegan diets – albeit sufficient to support a healthy life and normal development. You will also recall that, in lean long-term vegans, daily insulin secretion tends to be relatively low despite high carbohydrate intakes – in part because of their good insulin sensitivity, but also owing to the absence of dietary animal protein. (This latter effect can be amplified by choosing whole foods that are low in glycemic index.) There is thus a logical basis for predicting that IGF-I activity will be lower in vegans.

Recent surveys in British vegans indicates that their blood IGF-I levels in fact are about 10\% lower than those observed in omnivores or ovo-lacto-vegetarians.\textsuperscript{474, 475} But this underestimates the true disparity in IGF-I activity, as vegans were also found to have elevated levels of the IGFBP-1, an antagonist of IGF-I activity. Studies examining the IGF-I activity of the very lean vegans of rural Asia have yet to be done, and are urgently needed.

An intriguing aspect of this British work is that higher intakes of “poor quality” plant protein (non-soy plant protein) were found to correlate negatively with IGF-I – suggesting that plant protein can actually suppress the liver’s production of IGF-I. This may reflect the fact that the non-essential amino acids in plant protein provide a highly effective stimulus to secretion of the pancreatic hormone glucagon,\textsuperscript{476-478} which acts on the liver to boost the metabolic breakdown of amino acids, including methionine.\textsuperscript{479} Thus, ingestion of “poor quality” protein may actually decrease liver levels of some essential amino acids by promoting their metabolic disposal. In effect, “poor quality” protein can act as a functional antagonist of essential amino acids – thereby reducing IGF-I synthesis. (This raises an interesting possibility – could supplementation with non-essential amino acids be used to decrease IGF-I production in omnivores?\textsuperscript{477}) These considerations suggest that the dietary ratio of essential to non-essential amino acids may be as important a determinant of IGF-I levels as the absolute amount of essential amino acids is.
Another interesting finding by the British researchers was that, among vegans, frequent soy milk consumption was associated with a considerable increase in IGF-I. This may reflect the fact that soy protein is of relatively high quality compared to many other plant proteins; it’s a relatively good source of the lysine that is poorly supplied by grain proteins. While adding soy products to an omnivore diet may tend to reduce its protein quality, this would tend to enhance net protein quality in vegans – while of course also increasing essential amino acid intake. So vegans might be well advised to avoid heavy consumption of soy. (Yet soy isoflavone supplements may be warranted, as there is evidence that these phytoestrogens may reduce risk for prostate, breast, and colon cancer, as discussed below.)

Greek physicians performed a study of related interest in type 1 diabetics, who lack the capacity to make their own insulin. Type 1 diabetics are at high risk for kidney failure, but, as we noted above, vegan diets appear to be protective in this regard. The physicians therefore studied the impact of two different diets on their diabetic patients; each diet had moderate yet fully adequate protein content (around 1 gram per kilogram of body weight per day), but one diet was omnivore whereas the other was vegan. While they confirmed the expected favorable effects of the vegan diet on kidney function, they also determined that IGF-I levels were nearly 20% lower on the vegan diet than on the omnivore diet. Since the respective diets were not modulating insulin secretion in these patients, these results may be directly reflective of the impact of protein “quality” on liver function.

Moreover, there is evidence that low-fat, whole-food vegan diets may reduce blood sex hormone activities. As you know, steroid sex hormones (estrogens, androgens) act as growth factors for certain tissues, and can influence the induction and growth of various cancers. The reduction in daily insulin secretion associated with diets of this type would be expected to boost the liver’s production of the sex hormone-binding globulin (SHBG), a protein which circulates in blood and reduces the effective activities of steroid sex hormones by binding tightly to them. Moreover, IGF-I acts in various ways to promote sex hormone synthesis, so a decrease in IGF-I activity might be expected to decrease this synthesis. These two mechanisms are likely responsible for the decrease in blood levels of free estrogen that has been repeatedly observed in women who adopt low-fat vegan diets. Increased fecal excretion of estrogens has been observed during consumption of fiber-rich vegetarian diets, and may also contribute to this effect.

The impact of such diets on free testosterone in men is less clear. The recent study examining British vegans reported that their free testosterone levels were no lower than those of omnivores, despite the fact that their SHBG levels were higher. On the other hand, studies from the Pritikin Clinic indicate that total blood testosterone levels do not change during the Pritikin program, yet SHBG levels increase by about 30%. Taken together, these observations imply a reduction in free testosterone; unfortunately, the measurements of testosterone and of SHBG were made in two separate studies on two different groups of men, so this conclusion is a bit shaky. (Bear in mind that Pritikin patients differ from many free-living vegans in that they eat a very-low-fat diet and exercise daily – their insulin sensitivity is thus likely to be superior.) Other studies
comparing vegetarians with omnivores have reported that total or free blood testosterone levels are lower in the vegetarians.\(^489, 490\) Evidently, more clinical research is needed on this issue. It will also be of interest to determine whether vegan diets influence the conversion of testosterone to its more active derivative dihydrotestosterone. Blood levels of the chief metabolite of dihydrotestosterone - androstanediol glucuronide – are reported to be decreased in vegetarians and in Chinese;\(^489, 491\) however, one recent study found no such decrease.\(^474\) Some Japanese dermatologists have noted that Japanese men prone to male-pattern baldness seem to be balding at an earlier age than in past generations; conceivably this could be indicative of an increase in testosterone activity as the Japanese diet has changed from quasi-vegan to one much higher in fatty animal products.

In some tissues, IGF-I and sex hormone activity seem to interact synergistically as cancer promoters. For example, in estrogen-responsive breast cancers – and presumably healthy breast tissue as well – estrogen acts to greatly potentiate the response to IGF-I by increasing the availability of IGF-I receptors and of certain proteins that are crucial for effective transmission of the IGF-I “signal” (most notably the protein IRS-1).\(^492-496\) Thus, estrogen and IGF-I interact synergistically in promoting proliferation and blocking apoptosis in cancerous and pre-cancerous breast tissue. Conversely, it would seem to follow that the moderate reductions in both estrogen and IGF-I achieved by a low-fat, whole-food vegan diet would likewise interact synergistically to provide protection from breast cancer. It is not unlikely that similar reasoning applies to certain other cancers arising from sex hormone-responsive tissues. For example, in an androgen-responsive prostate cancer, IGF-I only has growth factor activity if an androgen is simultaneously present.\(^497\)

Although insulin can function indirectly as a growth factor by acting on the liver to boost circulating IGF-I activity, there is credible speculation that it may also have direct growth factor activity in some circumstances. In regard to risk for pancreatic cancer – one of the most inerorably lethal of cancers – the proximity of at-risk pancreatic cells to the insulin-secreting beta cells means that these cells are exposed to far higher concentrations of insulin than other tissues see; at these high concentrations, insulin can activate the receptor for IGF-I – in effect, mimicking IGF-I activity.\(^498\) There is also evidence that many pancreatic tumors express high levels of insulin receptors that promote cell growth when activated.\(^499\) In other tissues, although physiological concentrations of insulin have little direct growth factor activity, they have the potential to potentiate response to other growth factors.\(^500-503\) Considerable evidence now links elevated insulin secretion to increased risk for colon cancer;\(^504, 505\) perhaps colonic insulin receptors help to mediate this phenomenon. For all of these reasons, keeping daily insulin secretion low appears to be a very rational strategy for reducing cancer risk.

**Clinching Evidence from China**

My thinking about vegan diets, IGF-I, and cancer risk really crystallized when I encountered the fascinating findings of Dr. Colin Campbell and the China Health Project, the most massive epidemiological study yet attempted. This study has characterized a wide range of dietary, lifestyle, and blood parameters in a large number of rural provinces
of mainland China, and has attempted to correlate these with the pattern of disease in these provinces. Most of the people in these provinces are quite poor, and although they are not ethically or intellectually committed to veganism, they are usually too poor to incorporate animal products into their diets except on an occasional basis. Nonetheless, the provinces vary in the extent to which animal products are eaten.

Since a strictly vegan diet is cholesterol-free, whereas all animal products (other than non-fat dairy) contain cholesterol, the addition of animal products to a vegan diet typically leads to an increase in serum cholesterol level. For this reason, serum cholesterol can be used as a marker for animal product ingestion in rural China. Also of rough utility in this regard is serum urea, a metabolic product of protein breakdown. Campbell reports that, in rural China, risk for the entire range of “western” diseases – including coronary disease, diabetes, and a number of prominent cancers (including those of the breast, colon and prostate) – correlates positively with serum levels of both cholesterol and urea. This strongly suggests that the extent to which animal products are included in rural Chinese diets is a chief determinant of their risk for “western” diseases, including the “western” cancers. Campbell notes that there does not appear to be a threshold below which animal products are no longer dangerous – minimal risk was found in those provinces that were most strictly vegan.

(Actually, vegan diets also appeared to offer protection from cancers of the stomach and liver – cancers more common in Third World cultures where sanitary conditions are often poor; this is an important point, since some scientists have questioned whether vegan or high-carbohydrate diets might be partially responsible for high rates of these cancers in Third World cultures. In fact, endemic infectious hepatitis and heavy consumption of salt and of microbially-contaminated salt-preserved or fermented foods – typical of societies that lack refrigeration - appear to be the chief environmental causes of these cancers. There does not appear to be any notable excess of these cancers in American vegetarians, and these cancers are comparatively rare in economically advanced countries.)

One key finding in Campbell’s China research is that, by and large, rural Chinese are not undernourished from the standpoint of calorie intake. Indeed, rural Chinese typically have a calorie intake that is substantially higher, per pound body weight, than that of Americans, even if they are not engaged in vigorous manual labor. This should put to rest the common notion that rural Asians have low cancer rates simply because they periodically undergo involuntary caloric restriction.

**Vegan Diets Prevent Cancer – More Evidence**

Campbell’s observations were by no means unprecedented. Several previous (and subsequent) international epidemiological studies, attempting to correlate characteristic dietary intakes in various countries with their age-adjusted cancer incidence or mortality, have noted that estimated intakes of animal protein correlate just as tightly with “western” cancer risk as animal fat (or saturated fat) intake does. A reasonable interpretation of this is that when scientists demonstrated correlations between total fat or saturated fat intake and cancer risk, the fat intakes were just serving as markers for
animal product intake. Other studies have looked at the rising incidence of “western” cancers throughout Asia (especially urban Asia) over the last several decades; several studies have shown that increases in animal product consumption correlate nicely with the cancer incidences observed about ten years later. Increased animal product consumption has likewise been linked to increasing cancer rates in Mediterranean countries whose diets used to be predominantly plant-based.

It is a little known fact that the age-adjusted death rate from total cancer tripled in African-American males during the twentieth century; only about half of this increase can be attributed to the smoking epidemic. This cancer holocaust occurred despite the fact that access to competent medical care presumably increased for African-Americans during this period. I suspect that this phenomenon is mechanistically similar to that now being observed in Asia, where “western” cancer rates are rising steadily wherever economic status is improving. Whenever people emerge from Third World status – whether in Asia or in the rural South – their increased economic power translates into greater consumption of (relatively expensive) animal products – and rates of “western” cancers soon climb commensurately.

Physicians practicing in sub-Saharan Africa during the last century frequently noted that risks for “western” cancers seemed to be extremely low among black Africans – even prostate cancer, to which African-Americans are particularly prone. These impressions square well with the fact that traditional diets in this region were quasi-vegan.

Unfortunately, the lack of reliable cancer registries in most of sub-Saharan Africa have made it difficult to compare the cancer rates of Africans with those of black Americans. The Third World is not the only place where rates of “Western” cancers have been comparatively low. These rates were relatively low in Crete during the middle of the last century, when the residents of this island were practicing the prototypical “Mediterranean diet”: low in animal products (except for fish, which provides cancer-retarding omega-3 fats), and high in fruits, vegetables, and olive oil. Although insulin sensitivity was probably not optimal on this relatively high-fat diet, the residents of Crete at that time were physically active and relatively lean, which would have a compensating impact in this regard. Furthermore, the meal-induced stimulus to insulin release was presumably rather low owing to the paucity of animal protein and the moderate carbohydrate content of meals; thus, daily insulin secretion was probably much lower than in most other Western societies. The low intake of animal protein might have been associated with a modest reduction in IGF-I production, and the increased phytochemical intake provided by a diet rich in fruits and vegetables would have also been protective. These considerations thus provide a satisfying explanation for the relatively low rates of cancer which the people of Crete used to enjoy. (Unfortunately, Crete and the rest of the Mediterranean world have been gravitating toward diets richer in fatty animal products over the last few decades – and this is reflected in their climbing cancer rates.)
Prostate Cancer

Let’s now take a closer look at the many types of cancer that appear to flourish wherever people adopt diets rich in fatty animal products. These include major killers such as cancers of the prostate, breast, colon and (with an essential assist from tobacco!) lung - jointly responsible for well over half of all cancer mortality in the U.S. - as well as a number of other malignancies that are somewhat less common but no less deadly.

The case of prostate cancer is particularly illuminating. In 1998, Dr. James Hebert and colleagues of the University of Massachusetts Medical School published an intriguing paper that provides the age-adjusted death rates for prostate cancer (circa 1985-1989) and estimated average daily food intakes (circa 1979-1981) for 59 countries, based on data provided by the World Health Organization and Food and Agriculture Organization of the United Nations.\(^{523}\) I arbitrarily defined as “quasi-vegan” those countries for which estimated intake of animal product calories was 10% or less of estimated total calorie intake; six countries – Egypt, Guatemala, Honduras, South Korea, Sri Lanka, and Thailand – fell into this category. I averaged their age-adjusted prostate cancer death rate and came up with a figure of 1.96 (per 100,000 male population). In contrast, this death rate in the U.S. was 32.19 – over sixteenfold higher! (And the death rate in black Americans is much higher than this.) Skeptics might note that total calorie intakes were relatively low in some of these countries, but the estimated intakes in Egypt and Korea (with death rates of 2.75 and 0.90, respectively) were not. I then averaged the death rates in the 20 countries whose estimated daily intake of animal products exceeded 1,000 calories, and came up with a figure of 29.91 – just about fifteen-fold the rate of the quasi-vegan countries. (Evidently, the high rate in the U.S. was no fluke.) Among these heavy consumers of animal products, the lowest prostate cancer death rate was in Poland – 22.46.

Since these figures deal with death rates, and it is probably reasonable to presume that the relatively poor people in quasi-vegan countries get poorer quality medical care than people in richer omnivorous countries do, the disparity in the incidence of clinically significant prostate cancer is probably considerably greater than fifteen-fold! The fact that international risk for prostate cancer varies so substantially may be largely attributable to the fact that several different hormonal activities – presumably IGF-I, testosterone, and possibly insulin, all of which would usually be lower in vegans – interact in a multiplicative fashion to promote prostate cancer development.

Bear in mind that, among non-smoking American males, prostate cancer is the leading cancer killer. These large international disparities in prostate cancer death rates are thus hugely significant in regard to human suffering and premature death.

But the pertinent scientific findings offer a ray of hope. Migrant studies show that middle-aged men who come to the U.S. rapidly assume the high risk of prostate cancer typical of the U.S.\(^{524}\) This presumably means that hormonal activities prevalent in mid-life or late-life have a major impact on prostate cancer risk. Conversely, it would be reasonable to presume that, if you don’t yet have clinically apparent prostate cancer, by
lowering those key hormonal activities with a protective diet and lifestyle, you can rapidly decrease your risk for this cancer.

**Breast Cancer**

Dr. Hebert and colleagues did a very similar analysis of the determinants of the large international variations in breast cancer mortality. Though not quite as impressive as the huge disparities in prostate cancer mortality, these variations in breast cancer mortality are important: age-adjusted breast cancer death rates vary by a factor of about six-fold, with North American and Western European rates near the top – this despite the fact that the availability of early detection programs makes breast cancer a frequently curable disease in the technologically advanced countries. Using complex statistical methods (multiple regression analysis), Hebert concluded that consumption of calories from animal products was likely to be the chief determinant of risk, whereas consumption of fish, cabbage, and grain products appeared to be protective; a high population growth rate was associated with an additional measure of protection, probably because early pregnancy is known to reduce a woman’s subsequent risk for breast cancer. (The statistical analysis made it clear, however, that the seeming impact of animal product calories was not just a trivial consequence of the fact that animal product consumption tends to be low in poverty-stricken societies with high fertility rates.)

The protection associated with fish intake has emerged in other international studies examining breast cancer rates. This is likely to reflect the fact that the omega-3 fats found in fish can help to prevent breast cancer; diets high in fish oil have been shown to suppress the induction and slow the growth rate of breast cancer (including human breast cancers) in rodents. Once again, we are led to the conclusion that, whereas a vegan diet may be highly protective, a vegan diet supplemented with fish oil (or the omega-3 fats found in fish oil) may be even more protective. And bear in mind that a given intake of omega-3 fats should be all the more protective in the context of a diet that is overall quite low in fat.

Nutrition at an early age may have a decisive impact on breast cancer risk. In Third World populations at low risk for breast cancer, girls typically have a late menarche – they may not become fertile until age 17 or 18. The trend in Western society – and more recently, in parts of Asia that have become economically advanced, like Japan – is for a steady decline in the age of menarche; not uncommonly, girls in the U.S. now can conceive by age 12 or even earlier. An increase in effective IGF-I activity, dependent on a sufficient increase in body fat, appears to play a role in triggering menarche; thus, increased intakes of animal products and calorie-dense foods may be keys mediators of the downward trend in the age of menarche. The relevance of this is that late menarche is known to be associated with a substantial reduction in subsequent breast cancer risk.

Case-control studies of breast cancer – that is, studies in which women who develop breast cancer are compared to somewhat similar women who haven’t - have been especially perplexing, because, at least in Western countries, they by and large have
failed to incriminate saturated fat or animal product consumption as a risk factor for breast cancer. In this respect, breast cancer has been notably different from prostate and colon cancer.) I suspect that, in order to enjoy the rather substantial protection from breast cancer seen in rural Asia, it is necessary to consume a vegan or near-vegan diet throughout life - and particularly in childhood, such that menarche is substantially delayed. The fraction of American women who would satisfy this criterion is vanishingly small, and thus the protection afforded by such a regimen will not emerge in American epidemiological studies. (A study which examined breast cancer risk in Seventh-Day Adventists, only a small fraction of whom are strict vegans, reported that women describing themselves as vegans had about one-third the risk for breast cancer as that seen in other women, but that this difference failed to achieve statistical significance because the number of vegans was so low.) The extent to which Americans are infatuated with dietary animal products can be gauged by examining the massive Nurses’ Health Study: in the bottom quintile of animal protein consumption (the 20% of women consuming the least animal protein), animal protein accounted for 12% of total calorie consumption – an amount which may well be sufficient to support maximal IGF-I production.

A crucial role of early nutrition in breast cancer risk is borne out by migrant studies. As noted above, when Asian men migrate to the U.S. in mid-life, and their diet shifts to a more typically American pattern, their risk for prostate cancer rapidly climbs toward that experienced by American-born Asian-Americans. In contrast, when adult Asian women migrate, their breast cancer risk remains more characteristic of their place of birth. The practical implication of this is that we shouldn’t expect adoption of a vegan diet in middle age to have a really dramatic impact on subsequent breast cancer risk. If you would like to protect your daughter from this all-too-common cancer, initiating a strict vegan diet early in childhood (or even in utero?) may be the most effective strategy.

The thesis that a diet must be rather rigorously vegan to provide important protection from breast cancer also appears to be consistent with trends in cancer mortality in African-Americans during the last century – whereas death rates from many cancers tripled during this time, the death rate from breast cancer increased by only one-third. This suggests that animal product intake among American blacks during the early decades of the twentieth century, while low by today’s standards, may have been sufficient to confer a substantial risk for breast cancer, such that subsequent further increases in animal product intake did not have a really dramatic impact on this risk.

Although much research attention has been directed to the possibility that dietary fat influences breast cancer risk – as it certainly does in rodent studies – most epidemiology conducted in the U.S. or other Western countries has failed to observe a notable effect of total fat consumption on breast cancer risk. And yet, in the China Health Project, increased dietary fat per se (that is, independent of animal product intake) was found to be a risk factor for breast cancer. More recently, a case-control study in Indonesia – where fat intake still averages only about 15% of total calories – has found that breast cancer was dramatically more frequent in women whose fat intake was relatively high; in the total group studied, women whose pre-marriage fat intake was in the upper 25% were
8-fold more likely to have breast cancer than the women whose pre-marriage fat intake was in the bottom 25%! (Post-marriage fat intake also was associated with breast cancer risk in this study, albeit somewhat less dramatically.)

Why is it that studies in East Asia indict dietary fat as a notable risk factor for breast cancer, whereas Western studies generally do not? You will recall from a previous chapter that diets very low in fat (under 15% fat calories) typically have a very favorable impact on insulin sensitivity – associated with a marked reduction in insulin secretion; in contrast, varying fat intakes within the range commonly encountered in the U.S. appears to have little influence on insulin sensitivity. There is good evidence that, even within Western populations, insulin sensitivity (independent of body weight) impacts breast cancer risk – women who are insulin sensitive are at lower risk. A recent study conducted in Shanghai concluded that women whose insulin secretion was relatively high during morning fasting metabolism were almost three times more likely to have breast cancer than women with relatively low insulin secretion. These findings seem to be quite reasonable in light of the fact that elevated insulin secretion can boost the effective activities of growth factors and sex hormones. A possible resolution of our seeming paradox is now at hand: in Asian communities where fat intake is traditionally quite low, an increase in dietary fat tends to impair insulin sensitivity – whereas no such effect in seen in the West, where virtually everyone consumes a fatty diet. Within the West, however, there is a slight trend toward reduced breast cancer risk in subjects who eat less saturated but more monounsaturated fat – which parallels the fact that monounsaturates are less harmful to insulin sensitivity than are saturates.

Dietary choices can influence breast cancer risk via their impact on obesity. Overweight women are at increased risk for post-menopausal breast cancer, and also have poorer prognosis when they develop this disease. At least in part, this may reflect the fact that overstuffed fatty tissue has an increased capacity to convert circulating androgens (yes, women make them too!) to estrogen, which of course is a breast cancer promoter. This fat-produced estrogen is the chief source of estrogen activity after menopause. (By the way, this also explains why overweight men sometimes develop enlarged breasts!) Moreover, this estrogen would be expected to have greater bioactivity, since sex hormone-binding globulin levels would tend to be lower in overweight women who are insulin resistant. Additionally, obesity is associated with fat cell overproduction of leptin, a hormone which may act directly on breast tissue to boost breast cancer risk and to promote the progression of pre-existing breast cancer. Evidently, achieving and maintaining leanness – with a low-fat vegan diet, exercise, or other measures – is a smart way to decrease breast cancer risk.

In overview, the available data are reasonably consistent with the proposition that a very-low-fat vegan diet, consumed throughout life – in particular, during the childhood and teen years, when the breasts are developing – will notably decrease risk for breast cancer. To the extent that such a diet promotes lifelong leanness, it will lessen breast cancer risk postmenopausally by diminishing breast exposure to certain fat-produced hormones. On the other hand, efforts to reduce breast cancer risk in middle-aged Western women by instituting moderately-low-fat omnivore diets are likely to be abject failures.
Colon Cancer

Let’s return for a quick look at colon cancer. Risk for colon cancer (and for the benign adenomas that give rise to them) appears to correlate with the extent to which cells in the colonic mucosa (the epithelial lining of the colon) are undergoing replication. This can be quantified by careful observation of biopsy specimens, and is known as the “proliferative fraction”. One of the growth factors which can increase the proliferative fraction is IGF-I; thus, it is not surprising that increased blood levels of IGF-I (or of free IGF-I) have been shown to be a risk factor for colon cancer. Some years ago, scientists at Loma Linda University (which is affiliated with the Seventh-Day Adventist Church, and thus has a special interest in vegetarianism) compared the proliferative fraction of the colon of vegetarians with that of omnivores. Nearly half of the vegetarians they examined in this study were strict vegans. Can you guess what they found? The proliferative fraction of the vegetarians was about half that of the omnivores!

Perhaps the heavyweight intellects at the NCI who designed the recent colon cancer prevention trials should have taken this evidence into account. It’s rather remarkable that scientists can look at the diets practiced by Third World groups at low risk for colon or other “western” cancers and see only “low fat” or “high fiber” – the fact that these diets are quasi-vegan appears to escape them. One gets the impression that most Americans are so biased toward viewing protein as health-promoting that it simply never occurs to them that a needlessly high intake of protein or of essential amino acids might be as grave a risk to health as an excess of fat or of calories.

Increased insulin secretion emerges as a potent risk factor for colon cancer in recent studies – consistent with evidence that obesity increases, and exercise diminishes, colon cancer risk. Increased insulin exposure has been shown to promote colon carcinogenesis in rodents. These findings are not surprising in light of the fact that high insulin levels increase effective IGF-I by suppressing the liver’s production of IGFBP-1. However, it is conceivable that insulin has a direct impact on colon epithelial cells. Furthermore, inasmuch as insulin acts on the brain to stimulate activity of the sympathetic nervous system (which, as we have seen, is one reason why fat people tend to be hypertensive), it is interesting to note that, in rodents, sympathetic activity increases the incidence of colon tumors in carcinogen-treated animals, apparently because it somehow boosts the proliferation of the colonic epithelial cells. Whether this phenomenon occurs in humans does not seem to be known, but such an effect might explain the increased risk for colon cancer in chronic heavy smokers (since nicotine activates the sympathetic nerves.)

In epidemiological studies examining the international variations in colon cancer mortality, calorie intake from animal products and saturated fat – as in the cases of breast and prostate cancer – correlates strongly with risk. However, in studies focusing on American or European populations, in which animal protein intake is almost uniformly high, some interesting distinctions emerge; most notably, consumption of red meat emerges as a strong risk factor, the impact of poultry or fish is more neutral, whereas dairy products appear to be protective in some though not all studies. This latter
finding has lent some fuel to speculations that dietary calcium may lower colon cancer risk – as suggested by recent controlled studies\textsuperscript{558, 559} - by lessening the exposure of colon epithelial cells to certain irritative fat-soluble compounds (namely fatty acids and bile salts) that have the potential to increase the proliferation of these cells.\textsuperscript{557, 560, 561} In the colon, calcium binds to these compounds, sequestering them in a way that renders them harmless. On the other hand, colonic exposure to these irritants is boosted by fatty diets; fatty meals stimulate bile acid secretion, and of course directly increase the free fatty acid content of the colon. Whether chronic colonic exposure to fatty acids and bile acids does indeed play a significant role in human colon carcinogenesis is still unclear. The nature of the apparent “toxic” influence of dietary red meat on the colon is likewise unclear, though there is evidence that heme iron, which imparts the distinctive color to red meat, can exert an irritant pro-oxidant effect on the colon lining that stimulates proliferation of colonic epithelial cells and induces formation of carcinogenic nitrosamine compounds.\textsuperscript{562-566}

In any case, it is not unreasonable to speculate that a low-fat vegan diet, featuring lower-glycemic-index starches and supplemented with calcium, could minimize colon cancer risk by two distinct yet complementary mechanisms: decreasing the activity of the key growth factors IGF-I and insulin, and minimizing the exposure of the colonic epithelium to certain irritative compounds that likewise can promote epithelial proliferation.

If the IGF-I thesis of cancer risk has validity, dietary animal protein is unlikely to be the only culprit. High-glycemic-index and high-caloric-density carbohydrate foods (especially those designed by food manufacturers to be addictively delicious), as well as dietary fat, can play a role in promoting the excessive insulin secretion and weight gain that can likewise boost IGF-I activity. The unholy triumvirate of animal protein, high-glycemic-index carbs, and fat – most notably, saturated fat - undoubtedly collaborate in the induction of a number of “western” diseases. (Nonetheless, in the absence of fat or animal protein, the relatively high-glycemic-index sticky rice that predominates in most rural Asian diets doesn’t seem to do much harm, cancer-wise.)

In regard to glycemic index, Dr. Campbell informs me that risks for certain cancers tend to be higher in regions of rural China where wheat is the staple crop, as compared to regions where rice predominates. As noted above, the insulin response to wheat flour is particularly strong, possibly because wheat flour not only has a high glycemic index, but also has a relatively high protein content – whereas the insulin response to rice is more moderate; this is reflected in the fact that levels of sex hormone-binding globulin tend to be higher in the rice-consuming provinces.\textsuperscript{567} Dietary glycemic index may well be a determinant of cancer risk,\textsuperscript{568} a view consistent with the findings of a recent Italian study.\textsuperscript{549}

**Smoking-Linked Cancers: Lung, Pancreatic, Bladder, and Renal**

Now that American women “have come a long way, baby”, lung cancer is the chief cancer killer in both sexes in the U.S. I don’t need to remind you that cigarette smoking is the chief cause of the twentieth century lung cancer epidemic; it has been estimated
that, in U.S. men, smoking avoidance would prevent 90% of lung cancer (which was an uncommon malignancy before machine-rolled cigarettes were popularized during World War I). Nonetheless, there is considerable evidence that certain dietary factors can modulate risk for lung cancer in smokers.

The first attempts to correlate international human cancer rates with typical dietary fat intakes pinpointed lung cancer as one of the tumors which showed such a correlation. More refined subsequent analyses concluded that this correlation was specific to animal fat (vegetables oils didn’t appear to increase risk), and that this correlation was independent of, and complementary to, the impact of cigarette smoking. One of the scientists chiefly responsible for linking lung cancer risk to animal fat intake – the late Dr. Ernst Wynder – is notable for having conducted the definitive epidemiological studies that firmly established cigarette smoking as the primary cause of lung cancer (at a time when mainstream medical opinion was severely skeptical of this connection, and doctors were doing cigarette ads!)

Wynder drew particular attention to the fact that, whereas men in Japan are now about twice as likely to be smokers as men in the U.S., and Japanese smokers tend to smoke more heavily than American men (albeit they tend to start smoking a bit later in life), their age-adjusted mortality rate from lung cancer is only about half that of American men. Wynder thought that a far lower intake of saturated fat was protecting the Japanese from lung cancer. (Arguably, a greater intake of fish oil also contributes to their protection.)

By and large (though not invariably), studies in Western nations comparing the typical diets of lung cancer patients with those of healthy controls (matched for age and smoking habits) have found a higher dietary intake of saturated fat and/or cholesterol in the lung cancer patients – consistent with the results of the international studies. Conversely, a high intake of fruits and vegetables emerges as protective in these studies.

Several epidemiological studies have looked at the possible impact of IGF-I activity on lung cancer risk; the results have been inconsistent, but several do conclude that high circulating levels of IGF-I or free IGF-I are associated with increased lung cancer risk. This would not be unexpected, as lung tissue is known to respond to this growth factor.

In light of these considerations, I propose that, in the many studies linking saturated fat and/or cholesterol intake to lung cancer risk, the fat and cholesterol have in effect just been serving as markers for increased animal product intake, and it is the global impact of dietary animal products on effective IGF-I activity that is the primary mediator of this association. If this is indeed the case, then smokers who choose a low-fat vegan diet high in fruits and vegetables should be able to lower their lung cancer risk to a very worthwhile degree. (Supplemental fish oil and selenium might also be useful in this respect.)
However, I would be remiss not to note that by far the most effective way to prevent lung cancer is to avoid cigarettes (as well as second-hand tobacco smoke). I wish I could say that the diet I recommend would make it easier to break nicotine addiction, but I don’t have any reason to think that this is true. If you are a nicotine addict and smoking cessation programs haven’t worked for you in the past, you might consider doing what a friend of mine has done – become a nicotine gum addict! While nicotine per se is probably bad for your vascular health, it’s not likely to be injurious to your lungs when you obtain it from gum rather than cigarettes.

Another cancer linked to smoking is pancreatic cancer; although not one of the most common of cancers, its rapid and inexorable lethality now make it the #4 cancer killer in the U.S. Smoking approximately doubles risk for this malignancy. Although little is known at this point regarding the role of IGF-I as a risk factor for this cancer, international epidemiology shows a clear correlation between animal product consumption and pancreatic cancer risk. However, recent evidence that insulin resistance (or, more accurately, glucose intolerance, which is usually associated with insulin resistance) is an important risk factor for pancreatic cancer has focused attention on the possibility that increased insulin secretion plays a role in the induction of this cancer – particularly because insulin levels are exceptionally high in the immediate environment of the pancreatic cells that give rise to cancer. This suggestion is consistent with evidence that type 2 diabetics – in whom fasting insulin levels are often elevated – are at increased risk for this malignancy, whereas treatment of rats with drugs that destroy their capacity to make insulin (effectively turning them into type 1 diabetics) inhibits the induction of pancreatic cancer. Furthermore, insulin has been shown to act as a growth factor for many human pancreatic cancers.

Between 1950 and 1995, the age-adjusted pancreatic cancer death rate (which, sadly, is virtually equivalent to pancreatic cancer incidence) rose nine-fold in Japan; a five-fold increase in the death rate during the middle decades of the last century was observed in African-Americans. Since smokers approximately double their risk for this cancer, the smoking epidemic can account for only a modest portion of these stark increases. It is reasonable to suspect that marked increases in the consumption of animal products and of high-glycemic-index carbohydrate were largely responsible for the surge in pancreatic cancer deaths. Conversely, it is likewise reasonable to expect that long-term consumption of a low-fat, whole-food vegan diet that avoids higher-glycemic-index starches and sugars would keep insulin secretion low and thus minimize pancreatic cancer risk.

Yet another prominent cancer linked jointly to smoking and diet is bladder cancer. Smoking appears to at least double risk for this malignancy, and may be responsible for about a third of the bladder cancer incidence in the U.S. However, in international epidemiology, bladder cancer emerges strongly as one of the “Western” cancers associated with high intakes of fats and animal products. Fortunately, Dr. Hebert has published an analysis of bladder cancer mortality analogous to his studies of prostate and breast cancer. I used his data to make some calculations similar to that reported above for prostate cancer – in other words, I determined the average age-adjusted bladder...
cancer mortality of males in the countries with the lowest animal product intake – in this case, Guatemala, Honduras, Korea, and Thailand – with that of the 18 countries with the highest intake of animal product calories. For the quasi-vegan countries, this average mortality was 2 (per 100,000 population per year), whereas it was 17 in the countries with high animal product intakes. It is evident that differences in smoking habits can’t possibly explain this huge disparity in mortality. And most likely the gap in incidence is even broader, because bladder cancer is reasonably curable in advanced societies with good quality medical care (its incidence in the U.S. is about 5 times higher than the mortality rate).

Hebert’s analysis showed that bladder cancer mortality correlated most tightly with total fat consumption. Although animal fat correlated much more tightly than vegetable fat, the latter nonetheless correlated better than tobacco intake. The correlations with intakes of animal protein, meat, and milk products were only slightly less tight than those with total or animal fat. Hebert’s statistical calculations led him to conclude that total fat intake was likely to be the most important determinant of bladder cancer risk. A similar conclusion emerges from a study which lumped together the results from a number of studies comparing the dietary habits of bladder cancer patients with those of healthy controls.591 This latter analysis also concluded that a high intake of fruits and vegetables was likely to be protective in this regard. A study examining bladder cancer risk in Seventh-Day Adventists – a substantial proportion of whom are vegetarian, and very few of whom smoke – reported that consuming flesh foods 3 or more times weekly was associated with a 2.6-fold increase in risk.592

One study has reported that IGF-I levels tend to be higher in patients with bladder cancer than in matched control subjects.593 Furthermore, two studies have reported that all human bladder cancers examined express functional receptors for IGF-I, and that, to a greater or lesser degree, their proliferation is stimulated by this growth factor.594, 595 Moreover, the most aggressive cancers tend to express the highest level of this receptor. Thus, it is reasonable to suspect that increased IGF-I activity encourages the development of bladder cancer, and that, to the degree that low-fat vegan diets lower IGF-I activity, they will be protective with respect to bladder cancer risk. However, the strong correlations with total dietary fat suggest that fat per se may have some additional role in the induction of bladder cancer (independent of its effect on IGF-I activity). If a high fat intake can act directly on skeletal muscle to impair insulin sensitivity, it presumably could have direct metabolic effects on the bladder or other tissues as well that might influence cancer risk. Alternatively, it has been suggested that high-fat diets might increase the absorption of fat-soluble mutagens.590 Regardless of how this issue is resolved, it seems highly likely that you could minimize your risk for bladder cancer by eating a low-fat vegan diet rich in fruits and vegetables – and of course not smoking.

Yet another smoking-linked “Western” cancer is renal (kidney) cancer; a two-pack-a-day habit roughly doubles risk. This cancer is virtually untreatable once it spreads beyond the kidney, so, despite the fact it gets little media attention, it kills about 11,000 Americans annually.596 When back in 1975 noted epidemiologists Bruce Armstrong and Richard Doll published a truly classic analysis correlating cancer rates with estimated food intakes
in the world’s nations, they included a chart showing a remarkably linear correlation between daily intake of animal protein and renal cancer incidence in men. This incidence ranged from no more than 1 (per 100,000/year) in Japan, Jamaica, and Nigeria, to over 10 in the U.S., Nordic countries, and New Zealand. The correlation of renal cancer incidence with total protein intake was much looser, and the correlation with intake of beans and nuts was strongly negative. A case-control study in Shanghai found that men whose meat intake was in the bottom 25% were less than a third as likely to develop renal cancer as those with higher meat intakes – whereas high intakes of fruits and vegetables were associated with low risk. (Fruits and vegetables appear to be strongly protective with respect to both renal and bladder cancer; conceivably, this reflects the fact that the kidney and bladder are exposed to relatively high concentrations of water-soluble mutagens in urine, and various phytochemicals offer protection from these mutagens by inducing detoxifying enzymes.) Some case-control studies in Western populations likewise correlate high intakes of animal protein or total protein with increased renal cancer risk, although one such study found that calorie intake seemed to be the true determinant.

Obesity and diabetes have been clearly established as strong risk factors for renal cancer. Although these conditions are associated with increased IGF-I activity (owing to suppression of IGFBP-1), it is conceivable that the increased insulin levels typically seen in overweight people have a more direct cancer-promoting effect on the kidney (similar to the likely role of insulin in pancreatic cancer induction. High levels of functional receptors for both IGF-I and insulin are expressed by renal cancers, and for some unknown reason these receptors appear to be hyperactive – though whether insulin might have growth-promoting activity for these cells has not been established. The involvement of IGF-I in the development of renal cancer, however, seems to be highly likely; a heritable gene mutation (“von Hippel-Lindau syndrome”) associated with high risk for renal cancer, has been shown to boost some of the key effects of IGF-I in renal cells; and in fact about 70% of renal cell cancers harbor a mutant form of this gene. One recent study shows that administration of IGF-I stimulates the growth and spread of a human renal cancer implanted in immunodeficient mice; curiously, however this effect is lost once the cancer reaches an advanced established stage.

**Gynecological Malignancies: Ovarian and Endometrial Cancers**

Ovarian cancer is rather akin to pancreatic cancer in that it is difficult to detect before it has spread beyond the point of surgical curability. This is the malignancy that deprived us of two of our most brilliant comedienes – Gilda Radner and Madeleine Kahn – at far too young an age. The international incidence of ovarian cancer tends to parallel that of breast cancer – high in the developed world and relatively low in Japan and the Third World. However, the incidence of this cancer in Asia and southern Europe has been rising in the last several decades – in parallel to increased dietary intakes of animal products – whereas it has remained stable in most economically advanced countries during this time. Not surprisingly, the international incidence of ovarian cancer has been reported to correlate with intakes of saturated fat and/or animal products, and some but not all studies comparing the habitual diets of ovarian cancer patients with
those of healthy control subjects report increased intake of saturated fat, cholesterol, and/or various animal products in the cancer patients.

As in the case of breast cancer, reproductive factors have an important impact on risk for ovarian cancer, independent of nutritional factors. Ovarian cancers usually arise from the epithelial covering of the ovary, and this epithelium is breached every time an ovulation occurs, thus in effect inducing a wound that is repaired by epithelial proliferation. It is therefore easy to understand why a woman’s risk for ovarian cancer tends to be proportional to the number of ovulatory cycles during her reproductive years. Thus, some circumstances which block ovulation – such as pregnancy or use of oral contraceptives – tend to reduce risk for ovarian cancer; for example, prolonged use of oral contraceptives cuts risk approximately in half. Although frequent pregnancy may explain part of the reduction in risk for ovarian cancer noted in the Third World, the use of oral contraceptives is more common in economically advanced countries, so reproductive factors do not adequately account for the international variations in risk for this cancer.

The limited available epidemiology on IGF-I and ovarian cancer risk suggests that increased blood levels of IGF-I may increase risk in younger women (under 55), but not in older women. However, a high proportion of ovarian cancers make their own IGF-I, and tumors which show the greatest expression of this growth factor tend to behave more aggressively. Almost all human ovarian cancers examined have been shown to express IGF-I receptors, which appear to be functional and indeed necessary for proliferation of the tumors. IGF-I receptors have also been detected in the normal epithelium from which most ovarian cancers arise. A heritable mutation of the BRCA1 gene, which is associated with greatly increased risk for both breast and ovarian cancers, results in increased expression of IGF-I receptors in the ovary and in ovarian cancers.

There is suggestive evidence that increased activity of estrogens as well as of androgens may also increase ovarian cancer risk. Thus, a recent study indicates that women who use estrogen replacement postmenopausally may nearly double their risk for this cancer. Previous studies suggest that the impact of estrogen replacement may be less dramatic than this, but the balance of evidence is now in favor of estrogens increasing risk somewhat. This appears consistent with recent evidence that estrogens can increase the proliferation of normal ovarian epithelium. There is also reason to believe that increased androgenic activity (believe it or not, women make larger amounts of androgens than of estrogens!) likewise boosts ovarian cancer risk. Insulin and possibly IGF-I act on the ovary to promote androgen synthesis, and these androgens tend to be more active in women with high insulin because insulin concurrently suppresses the liver’s production of sex hormone-binding globulin. Women who are obese or have previously suffered from polycystic ovary syndrome – conditions typically associated with insulin resistance and a compensatory increase in insulin levels – are known to be at increased risk for ovarian cancer. Postmenopausally, obesity may also contribute to ovarian cancer risk by increasing the body’s production of estrogens – fat...
cells are capable of converting other circulating steroid hormones to estrogens, and this effect is more substantial in women who are overweight.

High intakes of the dietary sugar galactose are toxic to the ovaries of rodents, and women with a genetic abnormality of galactose metabolic are prone to ovarian dysfunction.\(^624, 625\) This has given rise to the speculation that diets high in the dairy sugar lactose – which, when digested, yields galactose – might be associated with risk for ovarian cancer. Despite promising initial findings,\(^626\) epidemiological studies have generally failed to confirm that lactose-rich diets confer an increased risk for this cancer, though some studies suggest that a very high intake of lactose might have some impact in this regard.\(^627, 628\) Suffice it to say that the jury is still out on this association – the possibility that very high intakes of lactose might increase ovarian cancer risk in genetically susceptible women remains open.

These considerations enable us to predict that a low-fat, low-glycemic-index vegan diet, by working in various ways to keep insulin secretion low, promoting leanness, and moderating the activities of IGF-I, estrogens, and androgens, would lower risk for ovarian cancer. This supposition is certainly consistent with the low risk for ovarian cancer noted in societies that derive most of their calories from plant foods.

The most common gynecological malignancy is endometrial cancer – cancer arising from the endometrial lining of the uterus. Although the high incidence of this cancer has remained fairly steady in the U.S. over the last half-century, mortality has declined markedly owing to earlier detection and effective use of surgery and radiation for treatment; thus, mortality from endometrial cancer is now only about half of that from ovarian cancer. Increased exposure to estrogen boosts risk for this cancer, whereas the hormone progesterone helps to prevent it. For this reason, women who experience chronic elevations of progesterone activity – for example, those who have multiple pregnancies or use oral contraceptives – are at decreased risk; conversely, postmenopausal estrogen replacement therapy can substantially boost risk, but most of this excess risk is alleviated if progestins (compounds with progesterone-like activity) are included in the regimen. The hormonal environment associated with obesity and type 2 diabetes also greatly increases risk.\(^629, 630\) In part, this reflects the aforementioned fact that, postmenopausally, an enlarged adipose mass promotes increased synthesis of estrogen. However, these conditions are also associated with increased blood levels of insulin, which seems to work both directly and indirectly to increase endometrial cancer risk.

Cancer of the uterine endometrium is clearly one of the “Western” cancers, much more common in societies where animal products make up a substantial portion of the diet;\(^606, 631\) the higher incidence of obesity and type 2 diabetes in economically advanced societies obviously contributes to, but does not entirely explain this phenomenon. In some studies comparing the habitual diets of endometrial cancer patients with those of controls, an increased intake of animal products emerges clearly as a risk factor – although not all such studies agree on this point. The most dramatic findings in this regard have been reported from Shanghai – presumably because animal product intake remains relatively
low among a significant portion of the population. The Shanghai researchers found that, even after making statistical corrections for differences in body size, women whose caloric intakes from fat or protein were in the upper 25% of the population, experienced 4-fold and 3-fold higher risk (respectively) for endometrial cancer; more careful analysis revealed that “the association of fat and protein with endometrial cancer risk was confined to foods of animal origin in the diet….These results suggest that diets rich in animal fat and protein may play an important role in the etiology [cause] of endometrial cancer.” Understandably, this relationship does not emerge as strongly in societies where nearly everyone obtains a substantial proportion of daily calories from animal products; nonetheless, studies from Hawaii and Northern Italy likewise indict fatty animal products, while noting that starchy foods, fruits, and vegetables appear to be protective.

In light of these findings, you won’t be unduly surprised to learn that IGF-I plays an important role as a growth factor both for normal endometrium and endometrial cancer cells. This accords well with the findings of a recent Japanese study comparing endometrial cancer patients with healthy control subjects; serum IGF-I levels were significantly elevated and IGFBP-1 levels were significantly diminished in the cancer patients, implying a substantial excess of IGF-I activity in the patients.

Furthermore, the impact of sex hormones on endometrial proliferation and on endometrial cancer risk appears to reflect modulation of IGF-I activity. Thus, estrogen induces the endometrium to make more of its own IGF-I, and promotes increased expression of the IGF-I receptor in some endometrial cancer cells. Conversely, progesterone inhibits proliferation of endometrial tissue – and reduces cancer risk – by inducing endometrial tissues to release IGF-I’s functional antagonist, IGFBP-1.

Insulin has just the opposite effect, suppressing endometrial production of IGFBP-1, just as it does in the liver. Thus, we would expect elevated insulin to work in multiple ways to increase endometrial cancer risk – suppressing production of IGFBP-1 both in the liver and endometrium, while increasing estrogen activity by suppressing the liver’s production of sex hormone-binding globulin. The drug tamoxifen, which acts as an estrogen antagonist in the breast and thus is useful for preventing and treating breast cancer, has the unfortunate side effect of increasing risk for endometrial cancer; there is recent evidence that tamoxifen therapy boosts synthesis of IGF-I in uterine tissue, while concurrently suppressing production of IGFBP-1. In aggregate, these findings go a long way to rationalize the facts that elevations of insulin, free IGF-I and free estrogen – as well as tamoxifen therapy - constitute risk factors for endometrial cancer, whereas progesterone and progestins are protective in this regard.

**Hematological Cancers: Leukemias and Lymphomas**

Cancers arising from the white blood cells – the leukemias and lymphomas – appear to fall into the category of “Western” cancers, although they have received fairly little attention in this regard. Some statistics published by Dr. Wynder illuminate this point. Back in 1955, the age-adjusted mortality from adult leukemias in Japanese males was about 3 (per 100,000/year), whereas among U.S. males it was 11; with respect to the
lymphomas, the death rate among Japanese males was 5, as opposed to 14.5 in U.S. men. Similar disparities were seen among women. These death rates rose steadily in Japan over the next 30 years, whereas they remained relatively stable in the U.S.

Wynder’s perceptive analysis also provides data on dietary intakes. In the early 1950s, the estimated per capita daily intake of red meat in Japan was 8 grams (as opposed to 231 grams in the U.S.), and of eggs was 7 grams (as opposed to 60 grams in the U.S.). Japanese dairy product intake was negligible, whereas fish intake was significant but not very high – 53 grams. Japanese intake of added fats and oils was also quite low – 5 grams daily – as was sugar and fruit intake. Thus, the characteristic Japanese diet in the early 1950s consisted primarily of starchy foods – primarily white rice and tubers – with modest amounts of vegetables, soy products and fish (no doubt copiously laced with salt!) Of their daily protein intake of 61 grams, only about 16 grams came from animal sources, and all but about 3 grams of this came from fish (rich in protective omega-3 oils). So the Japanese at that time might be aptly characterized as pesco-vegan. Wynder’s data show that animal product intakes rose steadily and substantially over the next 30 years; daily red meat intake averaged 105 grams in 1985 – still far lower than U.S. intakes, but a long way from veganism. (In addition to data on mortality from leukemia and lymphoma, he provides statistics on a number of other cancers – I have assembled the data pertaining to “Western” cancer mortality circa 1955 in Figure 1.)

There are several reasons for suspecting that IGF-I activity has an impact on risks for leukemias and lymphomas. For one thing, these cancers derive from cell lines for which IGF-I is a growth factor, and many of these cancers are themselves IGF-I responsive.\textsuperscript{642, 643} The ability of caloric restriction to slow the induction or growth of leukemias in rats has been traced to a reduction in IGF-I activity.\textsuperscript{644, 645} Furthermore, surgical removal of the pituitary gland – which abolishes secretion of growth hormone and, consequently, minimized hepatic IGF-I production – prevents the induction or growth of leukemias in rats.\textsuperscript{646, 647} Another key point is that children who were heavy at birth are known to be at increased risk for childhood leukemias; boys are also more likely to develop this cancer than girls.\textsuperscript{648-650} Greek researchers analyzed the IGF-I and IGFBP-3 levels of a large group of healthy children ranging in age from infancy to 14 years; they found that birthweight was strongly predictive of IGF-I levels, and that girls tended to have higher levels of the IGF-I antagonist IGFBP-3. Thus, risk for childhood leukemia seemed to correlate with effective IGF-I activity.\textsuperscript{651} These researchers also did a case-control study comparing leukemic children with children of identical age hospitalized for acute non-malignant diseases; they found that lower levels of IGFBP-3 were associated with increased risk for leukemia – again pinpointing IGF-I activity as a leukemia risk factor.\textsuperscript{652}

There is also a report that children who develop the most common type of childhood leukemia (acute lymphoblastic) tend to have greater height for their age than the general population of children.\textsuperscript{653} Of related interest is the fact that leukemia is more likely to develop in children from families of upper socioeconomic status.\textsuperscript{654} These findings appear consistent with the possibility that post-natal over-nutrition may also have a significant impact on childhood leukemia risk.
Aside from studies demonstrating that various types of leukemias or lymphomas do (or do not) express IGF-I receptors and respond to IGF-I, there so far is little published literature examining the impact of IGF-I activity on adult risk for these malignancies. A number of reports indicate that multiple myeloma – a type of cancer that arises from antibody-producing B lymphocytes – is dependent on IGF-I as a growth factor, and one of these studies showed that injections of IGF-I doubled the growth rate of a human multiple myeloma cell line transplanted into immunodeficient mice; it would therefore be reasonable to expect that dietary or pharmaceutical measures which reduce a person’s IGF-I activity might therefore retard the induction or growth of multiple myeloma. One intriguing report describes a T-cell lymphoma which lacks IGF-I receptors but responds avidly to insulin as a growth factor. In any case, the relatively low incidence of these cancers in quasi-vegan cultures – and the steady increase in their incidence in Asian
societies gradually adopting a more Westernized diet – is consistent with the possibility that relatively low IGF-I activity helps to prevent the white cell-derived malignancies.

A final relevant point – as noted below – is that there are a couple of venerable clinical reports suggesting that low-protein vegan diets may have some cancer-retardant efficacy in the treatment of childhood leukemias. If that is indeed the case, would it not be reasonable to suspect that such a diet during childhood might lower risk for leukemias? The typically slower growth and sexual maturation of children raised as vegans is presumably indicative of decreased growth factor activities. It is also of interest to speculate whether women who are vegans and follow a vegan diet during pregnancy might be less prone to deliver high-birth-weight infants. In this regard, gestational diabetes – a common cause of high-birth-weight deliveries – would seem to be less likely in long-term vegans, who tend to be relatively lean.

The other common malignancies of early childhood – Wilm’s tumor and neuroblastoma – have likewise been shown to occur more commonly in children with high birth weight, suggesting that these cancers may also be promoted by high growth factor activities. It is quite conceivable - though admittedly still speculative - that if you allow your children to overeat a fatty, over-refined omnivore diet that “optimizes” their growth, you may be increasing not only their long-term risk for many adult disorders, but also their more immediate risk for pediatric malignancies.

Ancillary Cancer-Preventive Benefits of Vegan Diets

To recap, I propose that low-fat, whole-food vegan diets are usually associated with decreased blood levels of insulin and of the free active forms of IGF-I and sex hormones. If this thesis is correct, it may go a long way toward explaining the low risk for “Western” cancers enjoyed by quasi-vegan societies.

A simple way to look at this is that the body regulates the activities of key anabolic (tissue-building) hormones – as well as sex hormones, which effectively are anabolic if they lead to pregnancy – to reflect the “perceived” availability of the food calories (from meals, or stored as fat) and essential amino acids that are required to build and sustain an increase in body mass. Boosting your anabolic activity at a time when the availability of fuel and structural materials is low would make about as much sense as building a big chain of luxury hotels in the middle of a prolonged recession – when times are lean, resources need to be conserved so that the structure and function of the body’s vital organs can be preserved. The body relies on insulin as a key indicator of fuel status; insulin secretion reflects both the quantity and the glycemic index of dietary carbohydrate, the concurrent intake of protein, and the availability of stored fat. The liver acts as a sensor – it monitors the availability both of carbohydrate and of essential amino acids, while concurrently monitoring insulin levels, and uses this information to regulate its production of IGF-I as well of the binding proteins that suppress IGF-I and sex hormone activities. When people eat a low-fat, low-glycemic-index vegan diet in the long term, the low glycemic response to meals, the moderate intake of “low quality” plant protein, and low body fat stores all collaborate to keep daily insulin secretion low and to
convince the liver that essential amino acids are in short supply. In effect, such a diet represents a way of tricking your body into “thinking” that you are slightly underfed – without having to endure the hunger pains or energy deficit associated with genuine caloric restriction. As a result, IGF-I and sex hormone activities are kept relatively low – and with less hormonal support to drive proliferation and suppress apoptosis, pre-cancerous tissues are less likely to give rise to cancer.

Consideration should also be given to the possibility that a low-fat, whole-food vegan diet may also influence production of “autocrine” hormones by pre-cancerous tissues. Although tissues commonly respond to hormones circulating in the bloodstream, they also often make hormones to which they are self-responsive – known as autocrine hormones - and some of these hormonal activities may act as cancer promoters. For example, some tissues manufacture their own IGF-I – or other hormones with growth-promoting activity, such as epidermal growth factor. Whether nutritional factors might modulate these autocrine hormonal activities so far has received little study. Furthermore, it is not impossible that nutritional conditions (such as essential amino acid availability) could directly influence the behavior of pre-cancerous tissues independent of any effect on hormone production, in such a way as to modulate cancer risk. In this regard, there is growing evidence that increased activity of an enzyme known as “mammalian target of rapamycin” – or “mTOR” – which supports cell multiplication by boosting the efficiency of protein synthesis, plays a role in the induction of many cancers by supporting proliferation and blocking apoptosis in pre-cancerous tissues; conversely, inhibition of mTOR activity has been shown to decrease cancer incidence in rodents. mTOR activity decreases in cells that experience a relative deficiency of one or more essential amino acids; thus, independent of circulating levels of insulin or IGF-I, it is conceivable that the relatively low intakes of methionine or lysine that characterize most vegan diets could modestly decrease mTOR activity in at-risk tissues, thereby helping to prevent cancer. (It should be noted that one way that IGF-I and insulin boost cancer risk in some tissues is by activating mTOR.)

No doubt, the mechanisms by which dietary factors influence risk for Western cancers are complex and only partially understood at this time. While epidemiology points to elevated levels of free IGF-I and insulin as key factors in the induction of many Western cancers, it is also quite clear that these are not the only mediators of the impact of diet and lifestyle on Western cancer incidence.

One way in which vegan diets might afford cancer protection is by limiting the production or activation of mutagens that play a role in cancer induction. In particular, attention has been drawn to the fact that surface charring of flesh foods during cooking causes chemical reactions that produce potent carcinogens known as heterocyclic amines. (These aren’t formed in plant products because the compound creatine – found only in animal flesh – is a key precursor to these carcinogens.) Heterocyclic amines readily give rise to mutations and cancers in animals. The extent to which they play a role in inducing cancer in omnivores is still a matter of speculation, but in any case it is unlikely that these compounds are entirely innocuous in humans, whether or not they are having a large impact on cancer risk. Their possible role in induction of colon cancer has attracted particular interest. One recent study demonstrated measurable levels of
heterocyclic amines in the breast milk of human omnivores – whereas these agents were not found in the breast milk of a vegetarian; the authors suggest that these carcinogens may play a significant role in induction of human breast cancer.  

The heterocyclic amines have been shown to induce lymphomas – cancers arising from immune cells known as lymphocytes – in rodents, the most common type of human lymphoma, non-Hodgkins lymphoma (NHL), has been linked to increased intakes of animal fat and protein in epidemiological studies, both in international studies, and in case-control studies in the U.S. Unlike most other major cancers not clearly linked to tobacco, the age-adjusted incidence of NHL in the U.S. has been sky-rocketing, rising 73% between 1973 and 1991, such that it is now our fifth leading cancer killer. (The incidence of prostate cancer has also gone up dramatically, but this is thought to reflect the fact that physicians are now much more adept at detecting prostate cancer at a very early, non-aggressive stage.) The relatively stable incidence of most cancers over the last 50 years in the U.S. suggests that environmental exposure to man-made mutagens does not play a major role in their genesis. However, there is considerable reason to suspect that the striking increase in NHL might in fact be attributable to such mutagens; particular suspicion falls on certain pesticides, herbicides, and organic solvents, as workers who use these products have often been found to be at greatly increased risk for NHL. If you don’t have high occupational exposure to these fat-soluble toxins, your exposure will come primarily through ingestion of fatty animal products; farm animals ingest these toxins in their feed or forage, and store them in their fat cells. To the extent that fat-soluble mutagens do indeed play an important role in the induction of NHL and perhaps other cancers, you can evidently minimize your exposure by eating a vegan diet.

Dr Eldon Savage and colleagues assessed the content of a number of organic pollutants in the breast milk of women who were longtime vegans, in comparison to the levels found in the general U.S. population. Although the level of polychlorinated biphenyls (PCBs) did not differ, the levels of the 6 pesticides and herbicides assessed were vastly lower in the vegans – only about 1-2% of the levels found in the general population, if detectable at all. These researchers concluded that “diet may indeed be a major predictor of chemical pollutants in the body.” A subsequent Scandinavian study comparing the breast milk of lacto-ovo-vegetarians with that of omnivores reached similar conclusions, although the disparities in pollutant levels were not so dramatic, presumably because many of the vegetarians ate fatty dairy products and eggs; however, in this study, PCB levels were significantly lower in the vegetarians.

Because vegetarian diets are devoid of heme iron – a type of iron found in flesh foods (most notably red meats) whose absorption is high and poorly regulated – the body iron stores of vegetarians tend to be only about half as high as those of omnivores. (Nonetheless, the great majority of vegetarians make adequate amounts of red blood cells and are not anemic; vegetarian diets typically contain ample amounts of non-heme iron, and the body absorbs enough of this to prevent iron deficiency.) Free iron atoms can bind to chromosomes and, by interacting with the oxidant hydrogen peroxide, can generate the vicious hydroxyl radical capable of inflicting mutagenic damage on
The extent to which iron is a catalyst for the “spontaneous” mutagenesis which contributes to human cancer induction is not yet clear, but many scientists believe that iron plays an important role in this regard. Several epidemiological studies have found increased cancer risk in people with above-average body iron stores; such studies are hard to interpret, since iron stores tend to be higher in people who eat flesh foods that likewise have been linked to increased cancer risk.

More definitive evidence on this point has been provided by a recent epidemiological study and two controlled clinical trials. The epidemiological study concluded that, among a large group of blood donors, those who had donated the most blood (and thus had depleted themselves of the most iron) were at significantly lower risk for cancer than those who had donated the least blood. But perhaps the most provocative evidence on this point stems from a controlled clinical trial which attempted to determine whether regular phlebotomy (blood drawing) would reduce risk for heart attack in patients who had peripheral arterial disease. During a follow-up period averaging 4.5 years, the researchers were disappointed to learn that the phlebotomy therapy did not significantly influence heart attack risk – but it was associated with a significant 30% reduction in the incidence of new serious cancers! Phlebotomy therapy has also been shown to quite markedly reduce risk for liver cancer in patients with chronic hepatitis C. These findings suggest that the relatively low (but usually adequate) iron status of vegetarians may indeed reduce their cancer risk.

In summary, we see that a vegan diet helps to minimize exposure to at least three categories of agents with mutagenic/carcinogenic potential: heterocyclic amines, fat-soluble environmental toxins, and iron.

Another key point is that vegan diets are often high in phytochemicals – especially if these diets emphasize whole foods that are rich in potassium. Certain phytochemicals have shown cancer-preventive activity in rodent studies, either because they modulate enzyme activities in ways that lessen carcinogen activation, or because they have “anti-promotional” effects that increase the rate of apoptosis in pre-cancerous tissues. Many epidemiological studies suggest that a high intakes of fruits, vegetables, or legumes are linked to lower cancer risk – and phytochemicals may be important mediators of this effect. The isothiocyanates derived from cruciferous vegetables (such as cabbage and broccoli), the polyphenols found in green tea, and the lycopene found in tomato products, are currently attracting particular attention as putative cancer-preventive factors. Many of these compounds are so-called “phase 2 inducers”, which boost cellular expression of the antioxidant glutathione and of a number of enzymes that aid antioxidant defense and promote detoxification of carcinogens.

Another category of phytochemicals with cancer preventive potential are the phytoestrogens, most notably the isoflavones found in soy. Although estrogens are usually thought to act as cancer promoters, at least for breast and endometrial cancer, the safety of soy isoflavones reflects the fact, that in blood concentrations that can be achieved by ordinary dietary intakes of soy, these agents selectively activate the beta-form of the estrogen receptor. There are two different forms of estrogen receptor;
the alpha receptor is responsible for the feminizing effects of estrogen, and mediates the adverse impact of estrogen exposure on breast and uterine cancer risk. In contrast, the beta estrogen receptor does not have feminizing effects (which is why men can eat soy without growing breasts!), and in fact appears to have cancer preventive activity in many of the tissues in which it is expressed. In particular, there is reason to suspect — stemming from epidemiology, animal studies, and theoretical considerations — that frequent consumption of soy isoflavones may reduce risk for cancers of the prostate, colon, and breast. Although there are a few studies reporting that isoflavone administration can boost mammary cancer growth in rodents, a careful examination of these studies reveals that they employ extraordinarily high isoflavone doses that couldn’t possibly be obtained from a natural diet; at these very high levels, activation of the cancer-promoting alpha receptor could be expected.

I should also comment briefly on the cancer-preventive potential of olive oil. Some case-control studies focusing on Mediterranean populations where olive oil is in common use have noted decreased risks for certain cancers — most notably breast cancer — associated with increased intakes of this oil. I suspect that this may reflect the fact that, within the context of diets that are not notably low in fat, substituting olive oil for other sources of calories may not have a major adverse impact on either insulin sensitivity or body weight, and may thus act to lower daily insulin secretion while decreasing dietary protein content — effects that could be expected to lower blood growth factor activities. There is also speculation that antioxidant phytochemicals in extra-virgin olive oil might provide some cancer protection. Nonetheless, I must reiterate that adding large amounts of olive oil to a very-low-fat whole-food vegan diet would appear likely to compromise the ability of such a diet to improve insulin sensitivity and promote appropriate weight loss. In light of the fact that such low-fat diets have demonstrated a really profound cancer-preventive potential in Asian and African cultures — corresponding to “Western” cancer rates much lower than those seen in any Mediterranean country — I am not inclined to recommend high-fat diets of any kind. Nonetheless, if you are unwilling to make the often substantial dramatic dietary changes necessary to minimize your dietary fat intake, current evidence suggests that increasing your intake of olive oil is not likely to increase your risk for cancer, and indeed might even lower it.

**What About the “Third World” Cancers?**

Scientists who are inclined to skepticism (or nihilism) occasionally point out that the international correlation studies that relate high-carbohydrate, quasi-vegan diets to low risk for “Western” cancers, also demonstrate high rates of certain “Third World” cancers in societies consuming those diets. In particular, rates of gastric, hepatic, esophageal, and cervical cancer are often high in these societies. As an example, the low cancer mortality rates for 1955 Japan displayed in Figure 1 do not imply that mid-century Japan enjoyed an Edenic freedom from this dreaded disease — death rates from gastric, hepatic, esophageal, and cervical cancers were substantially higher in Japan than the U.S. at that time. However, a strong case can be made that the true correlate of these cancers is not high-carbohydrate diets, but rather poverty.
The chief causes of “Third World” cancers appear to be preventable endemic infections and/or foodstuffs that are microbially contaminated and/or excessively salty. For example, hepatitis B infection – usually preventable by appropriate hygiene – appears to be at the root of most of the world’s liver cancer; it is certainly responsible for most liver cancer in Japan and China. Chronic infection of the stomach lining with the bacterium Helicobacter pylori is now known to underlie most gastric pathology – both stomach cancer and stomach ulcers. And most cervical cancer now appears to be a late complication of venereal infection with human papillomavirus. (In medical school, I was impressed by the fact that nuns are at low risk for cervical cancer, but high risk for endometrial cancer; you will remember that the latter is prevented by multiple pregnancies and oral contraceptives.)

Mutagens such as nitrosamines present in microbially-contaminated foods also play a role in the induction of “Third World” cancers, most notably esophageal and gastric cancer. Such contamination usually reflects poor access to refrigeration; gastric cancer rates have plummeted around the world as effective refrigeration became more widely available during the twentieth century. The use of heavily salted foods – a second-best alternative to refrigeration for food preservation – is typical of societies at high risk for gastric cancer. How such foods promote gastric cancer is not yet entirely clear – they may be more prone to microbial contamination than refrigerated foods (and thus contain gastric mutagens), the nitrite content of the crude salts used for such purposes may promote mutagen formation, and/or their concentrated salt content may somehow increase the propensity of Helicobacter pylori to colonize the stomach and promote stomach cancer. In any case, now that refrigeration is readily available, the use of salt for food preservation is now unnecessary, and, as noted above, there are many other good reasons to keep your salt intake low. In Asian cultures, certain fermented foods (a case of intentional microbial contamination!) are known to contain mutagens, and may contribute to risk for esophageal and gastric cancers. High intakes of fruits and fresh vegetables rich in antioxidants – notably vitamin C – appear to be protective with respect to gastric cancer, possibly because the antioxidants block the intra-gastric formation of mutagens from food-borne precursors; societies at the highest risk for gastric cancer are characterized by high intakes of salt and low intakes of vitamin C.

I am unaware of any cogent evidence – or any credible theoretical grounds for suspecting - that high-carbohydrate diets featuring lightly-salted fresh foods can increase risk for any “Third World” cancer. There are no reports indicating that Western vegetarians are at increased risk for these cancers. Indeed, as noted above, the provinces of China with the lowest intakes of animal products appear to be at lowest risk for gastric and hepatic cancer – suggesting that, not surprisingly, the growth factors which promote induction of “Western” cancers can also promote the development of certain cancers prevalent in the Third World. Indeed, the best evidence that diets low in animal protein can reduce cancer risk in rodents comes from studies focusing on liver cancer. Dr. Campbell’s research indicates that low-protein diets not only prevent liver cancer, but also impede the progression of hepatitis B infection in rats. His interest in dietary protein as a stimulant to cancer induction had its origins in his experiences as a young epidemiologist investigating an epidemic of liver cancer among Philippine children; these
children were found to have ingested peanut butter contaminated with aflatoxin, a potent hepatic carcinogen produced by a species of mold that can grow on improperly stored peanuts. Campbell noticed that the children whose diets were being “enriched” with donated U.S. surplus milk appeared to be at increased risk for this cancer; a subsequent literature search turned up previous work by Indian scientists showing that a diet high in milk protein boosted the ability of aflatoxin to induce liver cancers in rats.\textsuperscript{713}

Although esophageal cancer is prominent in many relatively poor societies, it is also a prominent type of cancer in the West, primarily because smoking combined with heavy drinking (especially hard liquors with a high concentration of alcohol)\textsuperscript{716} greatly increases risk for this cancer. As in the case of gastric cancer, a low intake of fruits, vegetables, and vitamin C markedly increases esophageal cancer risk.\textsuperscript{703, 717, 718} In the U.S., risk for the most common type of esophageal cancer – squamous cell cancer - is concentrated in smokers of lower socioeconomic status who are prone to alcohol abuse and whose diets are low in fruits, vegetables, and vitamins.\textsuperscript{719}

The incidence of a sub-type of esophageal cancer – esophageal adenocarcinoma – has been increasing rapidly over the last several decades, and, in the U.S., is now the type most commonly seen in white males.\textsuperscript{720} It occurs in the lower part of the esophagus near the junction with the stomach, and arises from tissue that has been repeatedly damaged by acid reflux.\textsuperscript{721} Obesity increases risk for this cancer by about three-fold, which explains some but not all of the recent increase in incidence. Smoking is also a risk factor, but the impact of alcohol is less clear. Case-control studies show that people who develop this cancer tend to eat diets that are low in fruits, vegetables and fiber; some but not all studies incriminate dietary fat as a risk factor.\textsuperscript{722-725} One large recent case-control study conducted in the U.S. squarely indicts diets rich in saturated fat, animal protein, and cholesterol – whereas polyunsaturated fat intake was not associated with risk.\textsuperscript{726} There is little published information regarding the possible role of IGF-I in the genesis of this cancer. Staying lean with a low-fat, whole-food vegan diet rich in fruits and vegetables appears quite likely to minimize your risk for esophageal adenocarcinoma. If you suffer from chronic heartburn, you may be at increased risk for this cancer, and might be well-advised to consult your doctor on this issue.\textsuperscript{727} The only known cure for this cancer is prompt surgical excision of the tumor at its earliest stage.

A Brief Overview

Our discussion thus far has touched on nearly all of the cancers that cause over 10,000 deaths annually in the U.S. – the exceptions being cancers arising in the oral cavity, larynx, and brain, as well as the most lethal type of skin cancer, malignant melanoma. Risk for cancers of the oral cavity or larynx are dramatically increased in people who smoke, drink heavily, and have a low intake of fruits and vegetables\textsuperscript{728} – in other words, these cancers are substantially preventable by a prudent diet and lifestyle, whether or not modulation of IGF-I activity has a marked influence on their induction.

With respect to malignant melanoma – which arises from special pigment cells in the skin known as melanocytes – it is known that IGF-I is a crucial growth factor for melanocytes,
for the pre-cancerous “pigmented nevi” that can give rise to melanoma, and for a high proportion of melanomas. Antigodies to the IGF-I receptor suppress the growth of many but not all human melanomas in cell culture and in immunodeficient mice. Treatment with human growth hormone – which boosts the liver’s production of IGF-I – has been reported to stimulate the growth of pigmented nevi in children, and researchers have noted that the tendency of pigmented nevi to appear during adolescence may reflect the increase in effective IGF-I activity that occurs during puberty. Thus, although the limited relevant epidemiology does not clearly implicate dietary factors in the induction of melanoma, there are reasons to suspect that the lower IGF-I activity associated with low-fat, whole-food vegan diets might confer a measure of protection from this cancer. In any case, the most effective way to prevent this cancer is to avoid bad sunburns, particularly during childhood.

The chief theme that emerges from studies examining the dietary determinants of brain cancer risk, is that frequent consumption of cured (nitrite-treated) meats such as bacon may increase this risk, whereas fruit and vegetable consumption is protective; these findings thus suggest that carcinogenic nitrosamines found in foods or produced in the digestive tract may play an important role in the induction of many brain cancers. Nonetheless, the current evidence indicting cured meats as a major risk factor for brain cancer is by no means airtight – more definitive studies will be required to firm up this association before it can be generally accepted. In any case, you don’t have to worry about this if you avoid meat altogether!

My point in taking you through this possibly rather tedious laundry list of the most prominent human cancers is to stress the fact that almost all cancers are substantially preventable by a prudent diet and lifestyle. You can achieve this protection:

- by keeping key growth factor activities relatively low with a vegan diet that is low in fat and emphasizes lower-glycemic-index whole foods - complemented by regular exercise that promotes insulin sensitivity and leanness;
- by increasing your intake of protective cancer-fighting phytochemicals with a high intake of fruits and vegetables;
- by minimizing exposure to mutagens or mutagenic infectious agents by practicing sound hygiene and safe sex, making appropriate use of refrigeration for food preservation, avoiding foods that are heavily salted or nitrite-cured, avoiding charred flesh foods that contain heterocyclic amines and fatty animal products that may harbor environmental mutagens, avoiding sudden excessive sun exposure, keeping alcohol intake moderate, and of course not smoking;
- by using nutritional supplements that can boost your daily intake of nutrients and phytochemicals likely to decrease cancer risk - such as vitamin D, selenium, fish oil omega-3 fats, green tea polyphenols, and soy isoflavones (I’ll touch on supplementation in the final chapter);
- and by availing yourself of your doctor’s ability to detect cancerous or pre-cancerous tissues when they are still in an early, surgically-curable stage.

Take another look at Figure 1. Those marked disparities in cancer mortality correspond to a tremendous amount of potentially preventable human suffering. In my first year of
A Role in Cancer Therapy?

Many though not all types of cancer are still responsive to the growth-promoting actions of IGF-I and of sex hormones; moreover, IGF-I supports the growth of new blood vessels (angiogenesis) that is critically important to the expansion of solid tumors and development of metastases. It is thus logical to expect that dietary measures which decrease the blood levels of these hormones, or that increase the level of proteins that block their activities, will have utility for slowing the growth and spread of certain cancers. In other words, it is logical to inquire whether a low-fat, whole-food vegan diet can have a palliative role in cancer treatment.

As we have noted, the macrobiotic vegan diet is low in fat and relatively low in glycemic index (owing to the fact that it bans wheat flour products and emphasizes whole foods); thus, it very likely would decrease IGF-I and sex hormone activities in the blood. The founder of macrobiotics, Michio Kushi, encouraged the use of his diet for managing cancer. For this reason, the powers-that-be in the cancer establishment have been at pains to stigmatize macrobiotics as an “unproven therapy” tantamount to quackery. Yet Dr. James Carter, who is quite interested in the health impacts of vegetarianism, decided that it would be of interest to quantify the survival of patients with pancreatic or metastatic prostate cancer who had decided to adopt a macrobiotic vegan diet as part of their therapy; he then compared their survival statistics with those of “historical controls” – cancer patients from the same area whose cancers were in comparable stages of development, but who had not elected to become vegans. He found that, with respect to both pancreatic and prostate cancer, the patients who became vegan were surviving significantly longer. Even though historically-controlled studies of this sort are less-than-definitive medical evidence, Carter’s observations are both provocative and credible, and merit replication in studies that are more rigorously designed (prospective controlled studies).
Back in the 1960s, two clinical groups reported favorably on their experience with a low-protein vegan diets in the treatment of childhood leukemias. Although this diet was not curative, it did seem to prolong remissions. Presumably, these observations were forgotten as more effective chemotherapeutic regimens for childhood leukemias became available. These reports accord well with more recent evidence that increased IGF-I activity represents a risk factor for this cancer, which is more common in children who are tall and had a high birthweight.

The Pritikin Clinic has provided striking evidence of related interest. Dr. James Barnard of UCLA obtained serum samples from 13 overweight men enrolling in the Pritikin program, both prior to their entering the program, and again after they had been on the diet/exercise regimen for only 11 days. He also obtained serum from 8 Pritikin “veterans” who had been following the Pritikin lifestyle regimen for an average of 14 years. He then used this serum as the growth medium for a cell line derived from a human prostate cancer, LNCaP; these cells are known to be responsive to both IGF-I and testosterone. Barnard measured the growth rate of the LNCaP cells in the various sera; as compared to cells grown with sera obtained prior to the Pritikin program, the cells grown in the sera obtained after 11 days of the Pritikin program grew 30% less rapidly. Furthermore, cell growth was depressed by 45% when sera from the long-term Pritikin veterans was used. Conversely, the rate of spontaneous cell death (apoptosis) was markedly higher when cells were incubated with the 11-day Pritikin serum or the serum from Pritikin veterans.

Clearly, a low-fat, whole-food vegan diet, coupled with daily exercise, can have a marked effect on the growth factor activity of the blood. Direct measurements showed that the Pritikin regimen lowered IGF-I levels while boosting that of IGFBP-1 – thereby decreasing effective IGF-I activity; in addition, free testosterone declined owing to an increase in sex hormone-binding globulin. These findings nicely rationalize the impact of the sera on the growth of the LNCaP cells. Furthermore, in conjunction with previous reports from the Pritikin Institute, these findings confirm that a low-fat whole-food near-vegan diet, complemented by insulin-sensitizing exercise, can decrease blood levels of insulin, free IGF-I and free sex hormones – as suggested above.

In light of the fact that insulin is a major determinant of the effective activities of IGF-I and of sex hormones, and can function directly as a growth factor for some cells, a recent study correlating fasting insulin levels with cancer recurrence and survival in early-stage breast cancer patients is of great interest. When the researchers compared those women whose insulin levels were in the bottom 25% with those whose insulin was in the top 25%, the latter group was twice as likely to experience a cancer recurrence, and three times as likely to die from their cancer. This doesn’t necessarily mean that high insulin makes breast cancer more lethal – arguably, high insulin levels might just be an indicator of some other factor which is responsible for the poorer outcome – but it’s a reasonably safe bet that insulin does indeed have some direct role in this regard. Since we have just mentioned the Pritikin Institute, it is worth recalling that, in cardiac patients whose serum insulin levels were initially relatively high, these insulin levels dropped by an average of 40% after only 3 weeks of the Pritikin diet-exercise regimen.
Dr. Dean Ornish is currently conducting a controlled study to determine whether a strictly vegan version of his regimen, originally developed for heart patients, can favorably influence the clinical course of patients with early-stage prostate cancer; the patients recruited were in the so-called “watchful waiting” period, in which the tumor is confined to the prostate and it is initially unclear whether surgical treatment or radiation therapy will be warranted. His preliminary results indicate that, after one year, the prognostic marker PSA fell by an average of 4% in patients using this lifestyle program, whereas it rose by an average of 6% in the control group.\textsuperscript{762, 763} After two years, 13 of the 49 control patients had decided to go forward with definitive therapy (surgery or radiation), while only 2 of the 43 patients in the lifestyle group had made this choice.\textsuperscript{764} Since prostate cancer therapy itself can have undesirable complications, any strategy which can decrease the need for such therapy is quite worthwhile. Hopefully this and other future studies will further clarify the role of optimal diet in cancer management. So as not to raise false hopes, it should be noted that nutritional measures are extremely unlikely to have a curative impact on cancer, or to markedly reduce tumor size (objective remission). The extent to which feasible dietary measures can modulate blood growth factor activities is limited, and moreover many cancers are no longer dependent (or can be expected to eventually achieve independence) from blood-borne growth factors. A more realistic expectation is that an appropriate diet could slow the spread of many tumors to a useful degree, such that patients could look forward to extra months or perhaps even years of useful life. (The remarkable experience of Dr. Anthony Satillaro, recounted in his book \textit{Recalled by Life}, may represent one of those very rare incidences in which a macrobiotic diet does indeed achieve marked sustained tumor regression.)

Perhaps a vegan diet might have a more definitive impact on survival when it is used in conjunction with potentially curative measures such as surgery, radiation, or effective chemotherapy; if these latter strategies succeed in eradicating visible tumors, it is reasonable to hope that instituting a vegan diet might reduce the chance that small remaining nests of cancer cells will survive to induce a recurrence of the cancer.

Furthermore, it is reasonable to expect that a vegan diet will prove to be a useful complement to novel anti-angiogenic strategies as these become clinically available. There is good reason to hope that the advent of measures for slowing or stopping the tumor-evoked growth of new blood vessels will make metastatic cancer susceptible to long-term control. (By way of analogy, the development of insulin injections turned type 1 diabetes into a chronic treatable disorder, rather than the rapid death sentence it had previously been.) Harvard scientists have recently reported that, in immunodeficient mice injected with the LNCaP human prostate cancer, a soy protein diet resulted in a suppression of angiogenesis (and of tumor growth) associated with - and possibly mediated by - a reduction of circulating IGF-I levels.\textsuperscript{765} These same scientists had previously shown that caloric restriction – which markedly suppresses IGF-I activity – likewise inhibits angiogenesis in this tumor model.\textsuperscript{766} Whether IGF-I suppression can impede cancer-evoked angiogenesis in only some tumors, or rather has broad general efficacy in this regard, remains to be seen. IGF-I acts on some tumors to boost their production of VEGF (vascular endothelial growth factor), a potent stimulus to
angiogenesis,\textsuperscript{749, 750} and it also makes endothelial cells more responsive to this growth factor;\textsuperscript{748} thus, tumors which rely on production of VEGF to promote development of the new blood vessels required for sustained tumor growth may be particularly dependent on IGF-I activity.
VI. Preventing and Treating Autoimmune Disorders

Autoimmune disorders are diseases in which the body’s immune cells become “confused” and cause inflammatory damage to the body’s own tissues. Some prominent examples are rheumatoid arthritis, ulcerative colitis, lupus erythematosus, multiple sclerosis, and type 1 diabetes (in which the insulin-producing beta cells are destroyed by immune cells). Although these disorders are rarely thought of as “western” diseases or diseases of civilization, Dr. Hugh Trowell has summarized a large number of reports indicating that most of these disorders used to be remarkably rare among sub-Saharan black Africans, but are now becoming more common among urbanized Africans who have adopted a more westernized lifestyle. Furthermore, it is pertinent to note that the incidence of these diseases in African-Americans is generally no lower than that in American whites – the incidence of lupus is actually higher; thus, genetic factors cannot account for the remarkable rarity of autoimmune syndromes among black Africans during the first half of the twentieth century. With respect to rheumatoid arthritis, it was noted that, not only was this disorder rare among Africans, but that when it occurred, it was generally much less severe than the disorder encountered in the West. Working on the opposite side of the continent, British physician Dr. B.M. Greenwood made very similar observations regarding the rarity of the whole range of autoimmune disorders in Nigerians, and the mildness of clinical rheumatoid arthritis.

As might be expected, the urbanization and westernization of segments of the black African population over the last few decades has been associated with a substantial increase in autoimmune disorders. A report on ulcerative colitis illustrates this point nicely. Up until 1975, only 18 cases of this disorder had been diagnosed among blacks in all of sub-Saharan Africa. In the next four years, 13 cases were diagnosed in a single large hospital serving blacks near Soweto, South Africa. Notably, all 13 of the victims were educated, urbanized, and ate a westernized diet rich in animal products.

I have attempted to find pertinent comparable data from Asia, where many rural societies are quasi-vegan. Unfortunately, Asia did not give rise to a Hugh Trowell, and information on the incidence of autoimmune disorders in most parts of Asia is spotty at best. However, I was able to find several intriguing reports from Thailand, which – at least until recently – appears to have been one of the most vegan of societies, as assessed by United Nations food disappearance data. (Incidentally, Hebert reported that the age-adjusted death rate from prostate cancer in Thailand was one-sixtieth of that in the U.S!) Thai physicians have reported that both rheumatoid arthritis and type 1 diabetes are far rarer in Thailand than in Western countries, and that the disorder systemic sclerosis, when it occurs, is much milder in its manifestations. Since we don’t know what the incidence of these disorders is in Thai-Americans, these findings are not too meaningful in themselves - we can’t rule out the possibility that genetic factors are primarily responsible; however, viewed in the context of the data from Africa, these reports are satisfyingly consistent with the thesis that a vegan diet may reduce risk for autoimmunity.
Of related interest are recent international epidemiological studies correlating typical diets with risk for type 1 diabetes and multiple sclerosis. The incidence of type 1 diabetes in a country tends to correlate with the extent to which animal products are included in the typical diet; with respect to multiple sclerosis, international studies suggest a link to saturated fat or animal fat consumption. Shanghai is noted for a remarkably low rate of type 1 diabetes – about only 2% as high as the incidence in Finland; unfortunately, since there are no available data on the incidence of type 1 diabetes in Chinese-Americans, it is not clear to what extent environmental factors are responsible for this low incidence. As of 1960, not a single case of multiple sclerosis had been diagnosed in a black sub-Saharan African, and as of 1975 no cases had been identified in the Bantu population of 15 million. From 1932 to 1952, Trowell worked in busy pediatric wards in East Africa without diagnosing or observing a single case of type 1 diabetes; a handful of cases appeared during the late 1950s prior to his retirement. Yet black Americans are by no means immune to these disorders.

A recent American study, utilizing data from the Nurses’ Health Study, has failed to find any link between saturated fat intake and subsequent risk for multiple sclerosis. As we have noted, since almost all Americans consume substantial amounts of animal products during all or most of their lives – even American vegetarians, who typically are quite fond of dairy products and eggs – this study cannot invalidate the thesis that lifelong consumption of a vegan diet tend to prevent multiple sclerosis and other autoimmune disorders.

Vegan diets may also have a role in the treatment of autoimmune disorders. Scandinavian clinics have demonstrated that uncooked (“living food”) vegan diets – preceded by a one-week juice fast - are genuinely beneficial in the management of various autoimmune or inflammatory disorders, most notably rheumatoid arthritis; the arthritis does not go into complete remission, but the symptoms and related laboratory indices are substantially improved in a high proportion of patients. (These findings are a bit hard to interpret owing to the fact that, after the fast, vegan foods are introduced gradually, and any food that appears to provoke a flare-up in symptoms is thenceforth excluded from the diet; in other words, the regimen incorporates efforts to deal with specific food sensitivities. Nonetheless, since most authorities believe that food hypersensitivity plays a role in, at best, only a small percentage of cases of rheumatoid arthritis, it is unlikely that food exclusion is primarily responsible for the clinical benefits achieved by these protocols.) The utility of a low-fat vegan diet for controlling symptoms in rheumatoid arthritis has also been confirmed by an American study. Another common disorder which appears to respond to these techniques is fibromyalgia.

These results are paralleled by the experience of Dr. Roy Swank, who for half a century has been treating multiple sclerosis with a diet that minimizes animal fat and saturated fat, while increasing polyunsaturate intakes. He reports that, in his experience, patients who adopt this regimen within two years of first appearance of symptoms have a very favorable response – although the disease does not remit entirely, it generally fails to progress, so that 20 or 30 years later they are alive and functioning at a relatively high
level. In the great majority of cases, MS follows a relapsing but inexorable downward course which eventually leaves the patients severely crippled and precipitates their premature deaths. Swank claims that this slow downward spiral can be prevented altogether in patients who are treated promptly, and considerably slowed in patients who adopt his diet at a more advanced stage of the disease. It is unfortunate that other neurologists haven’t taken up the challenge of replicating Swank’s work – until this happens, Swank will no doubt be relegated to “crank” status in the neurological community. (Perhaps after his death they will erect the requisite monuments!) It will be of great importance to determine whether it is avoidance of saturated fat per se, or rather of the animal products which supply this fat, that is responsible for the claimed benefit.

One other report merits mention. A young lady in Japan, afflicted with the potentially lethal disorder systemic lupus erythematosus (SLE), decided – against the advice of her physicians, but egged on by her parents – to discontinue her steroid therapy and instead adopt a low-calorie fully vegan diet. Her disorder rapidly improved, and, at the time her case was reported by her red-faced physicians, had been in total remission for 5 years. Perhaps this was merely a coincidence – and perhaps not!

**In Search of a Mechanism**

It is well accepted that fasting leads to rapid symptomatic improvement in patients with rheumatoid arthritis. This isn’t necessarily of much practical significance, because sooner or later a person needs to go back to eating normal amounts of calories – at which point symptoms usually return with a vengeance (assuming the patient doesn’t adopt a vegan diet). But it may be practical importance to understand why fasting has this anti-inflammatory effect. The fact that fasting very markedly decreases blood IGF-I activity may be an important clue. Blood white cell levels drop dramatically during a fast, and it is known that IGF-I is a crucial growth factor for the body’s production of white cells. These white cells are mediators of inflammation in many inflammatory disorders. Less dramatic reductions in circulating white cells are seen when people adopt whole-food vegan diets. Trowell commented on the fact that, in the African populations in which autoimmunity was so rare, blood white cell levels typically were much lower than in Europeans (though Africans could respond appropriately to infections with a rise in white cell levels). These findings encourage the hypothesis that a whole-food vegan diet helps to control inflammation by decreasing the levels and possibly the activity of white cells that mediate inflammation – owing in part to a suppression of IGF-I activity.

However, this is not an adequate explanation for the former virtual absence of most autoimmune disorders in sub-Saharan black Africans. This absence seems to imply that the crucial mechanisms which prevent the body’s immune cells from becoming “confused” and recognizing the body’s own tissues as “the enemy” simply work more effectively in the context of a whole-food vegan diet. These mechanisms are highly dependent on the process of apoptosis: during their early development in the thymus gland, juvenile immune cells which are capable of attacking the body’s own tissues are identified and then “instructed” to commit suicide by apoptosis.
Guess what can protect the body’s immune cells from apoptosis. Did anybody say….IGF-I?! In fact, there is suggestive, though not yet definitive, evidence that high IGF-I activity can interfere with the process whereby self-attacking immune cells are “strangled in their cradle” via apoptosis. Indeed, some researchers have expressed concern that therapeutic administration of IGF-I might increase “the potential for the development of autoimmune disease or lymphoid malignancy by allowing self-reactive or transformed lymphocytes to escape programmed cell death.” These considerations might provide at least part of the explanation for the apparent rarity of autoimmunity in certain quasi-vegan populations – relatively low IGF-I activity may aid the efficiency of the process that eliminates rogue immune cells. Conversely, high rates of both cancer and autoimmunity in Western society may reflect the fact that high growth factor activities evoked by rich diets impair the efficiency of protective apoptosis – we simply do a poor job of eliminating the deranged cells that can give rise to chronic inflammatory damage or cancer.

Of course, alternative or adjunctive explanations can be entertained. Some scientists believe that exposure to partially absorbable antigens derived from animal proteins (like milk protein) play a role in triggering certain autoimmune reactions. However, it is not immediately obvious why animal proteins, and not plant proteins, would be offenders in this regard. It is reasonable to imagine that a specific food protein might help to induce a specific autoimmune disease – indeed, this phenomenon has been demonstrated in animals, and the thesis that milk protein helps to trigger type 1 diabetes has generated a great deal of controversy - but it would seem unreasonable to suggest that animal proteins are uniquely nefarious in this respect and thus are responsible for the full range of autoimmune disorders in omnivore societies.

Taking another tack entirely, Dr. Greenwood suggested that chronic parasitic infections were primarily responsible for low African rates of autoimmunity. While this is an intriguing suggestion, I would be more likely to suspect that the antigenic exposures entailed by chronic infection would increase risk for autoimmunity. Moreover, I doubt that the prevalence of parasitic infections was so uniform throughout black Africa as to make this a tenable explanation for the virtual absence of autoimmunity there. Nonetheless, this view merits further exploration.

In any case, there is reason to suspect that autoimmune disorders are substantially preventable, and that a whole-food vegan diet can make a worthwhile contribution in this regard. There is less doubt that such diets have anti-inflammatory properties that are useful for the management of rheumatoid arthritis, fibromyalgia, and possibly multiple sclerosis.

A role for growth factor activities in autoimmune syndromes is also supported by reports that chronic caloric restriction has a favorable impact on several autoimmune conditions in genetically-susceptible rodents. Although this strategy may not be clinically practical, fasting or restricting calories on alternative days is now being studied in humans as a health-promoting regimen; compliance is reported to be good in well motivated overweight subjects, and is said to be beneficial in rheumatoid arthritis.
Controlling Asthma

Allergy is a type of immune hypersensitivity that is fundamentally different from the autoimmune disorders considered above, in that it reflects an excessive response to foreign proteins – proteins not made by your body. Thus, it does not result from a failure to eliminate autoreactive immune cells. Allergy occurs in people who, for unknown reasons, make high amounts of IgE antibodies. This particular type of antibody is bound to the surface of inflammatory cells known as mast cells; when this IgE binds to its target foreign protein, the mast cells are stimulated to release histamine and other inflammatory substances that can lead to the sneezing, wheezing, and itching characteristic of an allergic response. I know of no evidence that a vegan diet influences your risk for allergies one way or another – with one qualification.

One of the most serious manifestations of allergy is asthma, which results from spasm and inflammatory congestion of the narrow breathing tubes of the lung (bronchioles); a serious attack can be life threatening if not promptly controlled. Allergy attacks are often triggered by allergic reactions in the lungs, but exercise can also trigger or exacerbate attacks in some people. The same Swedish doctors who report success with whole-food vegan diets in rheumatoid arthritis, report that their regimen is also often successful for alleviating chronic asthma. If this is true (more study is obviously needed, as no controlled clinical trials have been published on this), my best guess is that the diet is not influencing the allergic activation of mast cells, but rather the lung’s response to this chronic inflammatory insult. Repeated bouts of asthma often cause the linings of the bronchioles to thicken – a phenomenon known as “airway remodelling”; this narrows the air passages, much like atherosclerosis constricts blood flow by narrowing the lumen of arteries. It is now known that IGF-I is an important growth factor for the bronchial cells whose multiplication leads to this remodelling – epithelial cells, smooth muscle cells, and fibroblasts. One the the main inflammatory mediators involved in asthma, leukotriene D4, is now known to boost IGF-I activity in the bronchioles by inducing smooth muscle cells to release an enzyme that breaks down an inhibitory IGF-I binding protein made in the lung. It is reasonable to expect that a decrease in blood-borne IGF-I activity, achieved with a low-fat, whole-food vegan diet, could reduce the IGF-I activity in the lung’s bronchioles and thus help to prevent or reverse airway remodelling. While there is currently no experimental evidence supporting this view, I think that it deserves consideration. In any case, it would be worthwhile for asthma researchers to evaluate the impact of vegan diets on chronic asthma.

Alternate-day caloric restriction has recently been reported to benefit patients with moderate asthma. Since this would be expected to induce an episodic reduction in growth factor activities, the benefit observed here may be mechanistically related to that achieved with vegan diets.

A low-salt diet may also be useful for controlling asthma. Doctors had noted that, when African children migrated from their villages to cities, their susceptibility to asthma seemed to increase rapidly and dramatically. Yet this migration did not influence their reactivity on allergy skin tests, suggesting that urbanization was making their
airways more sensitive to the inflammatory compounds released during an asthma attack. Dr. Peter Burney may have been the first to propose that salt was at the root of this phenomenon. Subsequent investigations have shown that, in asthmatic subjects – particularly males – a high-salt diet does indeed make the airways more sensitive to bronchoconstrictive agents, and worsens the clinical course; conversely, a low-salt diet is protective in this regard. More recent evidence indicates that dietary salt also influences the severity of exercise-induced asthma.

My suspicion is that the sodium pump inhibitors evoked by salted diets, that make blood vessels more sensitive to vasoconstrictors, likewise can make the bronchioles more sensitive to bronchoconstrictors; indeed, other researchers have recently raised this possibility. There is conflicting evidence as to whether inhalation of the drug ouabain – a drug that inhibits the sodium pump – sensitizes humans to bronchoconstrictors, however, this drug may conceivably be an inefficient inhibitor of the type of sodium pump expressed in the lungs. One intriguing recent study assessed blood levels of the circulating sodium pump inhibitor, and showed that these levels correlated directly with lung responsiveness to a bronchoconstrictor – a finding quite consistent with my proposal.

Finally, it should be noted that supplemental fish oil may have some utility for controlling asthma – presumably because it can inhibit production of the most active forms of certain inflammatory mediators (the aforementioned leukotrienes) that promote bronchoconstriction and airway remodelling in asthma. A number of studies examining this application have had negative outcomes, but this may simply reflect the fact that the supplementation regimen used did not achieve an adequate enrichment of omega-3 fats in body membranes. To achieve the best anti-inflammatory benefits of fish oil, you need to take an ample dose of the fish oil omega-3s (at least 4 grams daily) for a long period of time, in the context of a diet that is relatively low in total fat and especially omega-6 fats. This has been illustrated nicely with respect to psoriasis: many investigators have concluded that fish oil is of minimal or no benefit in this disorder, but a study which administered an ample dose of omega-3 while asking the subjects to minimize dietary fat found a very nice response. One insightful study has shown that supplemental fish oil benefits asthma only in those subjects whose leukotriene metabolism is significantly influenced. Since I recommend a very-low-fat diet anyway, supplemental fish oil could be expected to be relatively effective within the context of that recommendation. (I shouldn’t neglect to mention that the anti-inflammatory activity of fish oil is useful for treating rheumatoid arthritis and various other autoimmune disorders, and thus would make a useful complement to a low-fat whole-food vegan diet in the treatment of these syndromes.)

In summary, there is reason to expect that a low-fat, low-salt vegan diet supplemented with ample amounts of fish omega-3 fats could have a very favorable clinical impact on asthma, attacking the problem from several angles simultaneously. Given the fact that asthma seems to be reaching epidemic proportions, especially among inner-city children, this possibility merits clinical evaluation.
VI. Bones and Joints – Staying Intact

If you are planning and hoping to live to a ripe old age, it’s important to keep your bones reasonably strong, and your joints functional. How would the diet that I suggest influence the health of these connective tissues? With respect to maintenance of bone density, the diet that I recommend has some definite advantages, but also potentially some drawbacks.

Vegan diets tend to be lower in protein than omnivore diets. Protein is a source of sulfur amino acids – methionine and cysteine – that are eventually metabolized by the body to yield sulfuric acid (ouch!). The body can buffer this acidity by drawing on the phosphate in bone mineral, breaking down the bone mineral in the process; some of the calcium released in this process ends up in the urine rather than back in bone. On the other hand, the acid generated by protein metabolism can be buffered by the carbonate generated when certain negatively-charged organic compounds are metabolized – compounds like citrate, for example. Generally, foods that are rich in potassium are a good source of such compounds. Thus, a diet high in natural-food potassium tends to protect your bones from the calcium-leaching potential of dietary protein – and a potassium-rich diet of moderate protein content seems to be optimal for bone health, at least from the standpoint of acid-base balance. 838-842

(Vegetarian advocates are fond of stating that the sulfur content of animal protein has a bone-leaching acidifying effect on the body. What they usually fail to state is that the sulfur content of plant protein is virtually as high as that of animal proteins: plant proteins tend to be lower in the sulfur amino acid methionine, but higher in the sulfur amino acid cysteine. Thus, any inherent advantage of vegan diets in this regard stems from the fact that they usually are lower in total protein than omnivore diets.)

It is ironic that the calcium-rich foods most recommended for preservation of bone health – dairy products – are high in protein, and thus have a countervailing acidifying metabolic effect that promotes bone breakdown. This is especially true for cheese – a real disaster for bone health, regardless of propaganda to the contrary. 843 On the other hand, milk contains compounds that can be metabolized to carbonate, and thus has a somewhat less unfavorable effect in this regard. But if your intent is to protect your bones by increasing your calcium intake, it makes much better sense to take a supplement such as calcium carbonate or calcium citrate, that not only provides calcium, but also generates alkaline buffering power to protect your bones. (No, every body does not need milk!) In fact, the Nurses’ Health Study revealed that women who ate the most dairy products had the highest subsequent risk for fracture. For example, risk for hip fracture was increased by 45% in women who drank two or more glasses of milk a day. 844 Since this wasn’t a randomized trial, it doesn’t constitute truly cogent evidence that high dairy consumption is bad for your bones – but these results are consistent with this possibility, and in any case they hardly support the heavily financed propaganda of the dairy industry.
A salty diet also has an adverse effect on bone health, owing to the fact that, for reasons that remain obscure, salt promotes loss of calcium in the urine. On the other hand, a high intake of potassium helps to offset this adverse effect of salt, possibly because it promotes urinary excretion of sodium chloride. So a low-salt, potassium-rich diet should help you to maintain your bone density.

However, there are several respects in which a vegan diet might not be absolutely ideal for maintaining dense bones. For one thing, IGF-I has an anabolic effect on bone; dietary protein supplements have been shown to promote better fracture healing in the elderly, possibly because they boost circulating levels of IGF-I. Some studies report that circulating IGF-I levels are relatively low in fracture patients - though, conceivably, the low IGF-I could just a marker for the low calorie intake associated with feebleness. Furthermore, the fact that free estrogen levels tend to be lower in vegans (both pre- and post-menopausally), while beneficial in regard to cancer risk, would not be expected to promote optimal bone density.

Another problem is that vegan diets, lacking dairy products, often don’t supply truly optimal intakes of calcium and vitamin D. (Vitamin D is an artificial additive to dairy products – the only natural foods truly rich in this vitamin are fish liver and fish liver oils.) When children are raised on a vegan diet without supplementation, I suspect that relatively low intakes of calcium and vitamin D, in conjunction with reduced IGF-I activity, will conspire to blunt the increase in bone density that children normally achieve. There are some reports regarding children raised on macrobiotic diets which support this supposition. On the other hand, once people reach adulthood, I suspect that a low-salt, potassium-rich vegan diet will tend to slow the gradual loss of bone density that is a natural feature of aging. If vegan children are given calcium/vitamin D supplements, it seems likely that this will enable them to achieve a higher bone mass in their youth, and if they maintain their vegan diet throughout adulthood, this bone mass might decline more gradually. Thus, a supplement-assisted diet of the sort recommended here seems quite consistent with maintaining adequate bone density into old age.

An additional potential hazard of a vegan diet for bone health is the fact that a diet exceptionally low in protein can somehow impair the efficiency of calcium absorption. So if you choose the vegan approach, make sure that your regular diet features some beans and/or soy products; any adverse impact of this protein on acid-base balance can be offset by a high potassium intake - provided that your total protein intake remains moderate (don’t make a fetish of soy protein products!) As we have seen, increased intakes of “low-quality” plant protein seem unlikely to increase IGF-I levels or cancer risk; lentils, which are very low in methionine, may be a smart choice for boosting the protein content of a vegan diet. There is growing evidence that soy isoflavones may be beneficial to bone health – presumably owing to activation of beta-type estrogen receptors in bone.

Finally, the fact that vegans tend to be quite lean – an evident advantage with respect to many health risks – will actually work against optimal bone density. People who are fat tend to have denser bones, in part because weight-bearing exercise will put a greater
mechanical stress on bones; this stress acts as a signal for bones to increase their density. If you are a lean, light person – whether or not you are a vegan – you can compensate for your lack of heft by simply doing more weight-bearing exercise – brisk walking or stair climbing, for example.

What does epidemiology suggest about vegan diets and bone health? Two studies have attempted to correlate the age-adjusted risk for hip fracture in various nations which their characteristic food intakes; they each conclude that, the higher the intake of animal products, the higher the risk of hip fracture.\textsuperscript{862,863} Ironically, quasi-vegan societies with relatively low calcium intakes are thus seen to have much lower risk for fractures than countries such as ours which make a fetish of dairy calcium! Critics will be quick to cast doubts on the significance of these findings by claiming that people in quasi-vegan cultures do more physical labor, or may have distinctive genetic inheritances that play an important role in their lower fracture risk. While such criticisms are not without merit (Chinese, for example, appear to be at lower risk for hip fracture owing to a genetic difference in hip structure), it is of interest that fracture rates are now climbing in Hong Kong and other parts of the Orient as diets become more westernized.\textsuperscript{864}

In any case, I believe that an overall survey of relevant findings is consistent with the view that a low-salt, potassium-rich vegan diet, complemented by calcium/vitamin D supplementation – particularly during youth, when bone mass is being built – and adequate in protein content, is likely to increase your chances for maintaining adequate bone density into old age. Regular exercise will further increase this protection.

I should comment briefly on the current controversy regarding the possible impact of dietary calcium on prostate cancer risk. High-calcium diets tend to decrease your body’s production of activated vitamin D (calcitriol) - a reflection of the fact that you don’t need to absorb calcium as efficiently if your calcium intake is high. Pharmacological doses of calcitriol have been shown to retard the growth of many prostate cancers, and some epidemiology suggests that good sun exposure – which improves vitamin D status - is associated with lower prostate cancer risk.\textsuperscript{865-867} These considerations have given rise to the suspicion that high-calcium diets might increase risk for prostate cancer by suppressing production of calcitriol.\textsuperscript{868} Several epidemiological studies support this view,\textsuperscript{869-871} but others do not\textsuperscript{872-878} – or only do so after drastic statistical manipulations of the data.\textsuperscript{879} (One of these studies reported significant protection associated with high calcium intake!)\textsuperscript{873} I am somewhat skeptical of this thesis primarily because, in most studies that have examined serum calcitriol levels in large numbers of men, a relatively low calcitriol level has \textit{not} been associated with a subsequent increase in prostate cancer risk – a finding that doesn’t seem to support the proposition that \textit{blood-borne} calcitriol plays a physiological role in prostate cancer prevention.\textsuperscript{880-882} However, the prostate cells which can give rise to cancer are capable of manufacturing their own calcitriol, and this production is not influenced by dietary calcium.\textsuperscript{883} Perhaps the calcitriol circulating in the blood only becomes truly relevant to prostate cancer prevention when the prostate’s own capacity for making calcitriol is compromised by poor vitamin D status.\textsuperscript{884} If this is the case, then any impact of calcium nutrition on prostate cancer risk should be minimized by taking ample but safe doses of supplemental vitamin D. Furthermore,
good vitamin D status replicates the beneficial impact of dietary calcium on bone health, since both vitamin D and calcium support bone density by suppressing production of the bone-dissolving parathyroid hormone. So perhaps the smartest approach when supplementing is to take ample doses of vitamin D (e.g. 2,000-5,000 IU daily) and moderate doses of calcium (500-1,000 mg). In the Physicians Health Study, greatest risk for aggressive cancer was seen in men with estimated daily calcium intakes in excess of 1,500 mg; moderate calcium supplementation in the context of a vegan (i.e. dairy-free) diet is unlikely to yield a daily calcium intake in excess of this limit. Those tempted to minimize calcium intakes in an effort to reduce their prostate cancer risk should bear in mind that good calcium status not only aids bone health, but may also reduce risk for colorectal cancer.885, 886

Many vegan advocates tend to over-react to the propaganda of the dairy interests by trying to minimize the importance of dietary calcium for bone health. In particular, they point to the low risk of fractures in quasi-vegan societies where calcium intakes are low. I would counter by noting that, whereas, at least under certain circumstances, a low-calcium diet can be compatible with the maintenance of good bone health, this is not inconsistent with the possibility that insuring an ample calcium intake will promote even better bone health – especially if the calcium is provided as a nutritional supplement (rather than in protein-rich dairy products) and is accompanied by vitamin D, another nutrient with great potential for promoting maintenance of bone density.887, 888 However, I will agree with the calcium critics that the importance of dietary calcium has been somewhat overemphasized relative to other protective factors such as an appropriate acid/base balance and a low salt intake. Furthermore, vitamin D and calcium aren’t the only supplemental nutrients that might be protective in this regard; there is evidence that supplemental vitamin K, as well as other minerals such as magnesium, zinc, manganese, and copper – all of which play important roles in bone metabolism - can aid maintenance of bone density.889-897 In particular, Japanese clinical studies suggest that high doses of vitamin K may markedly reduce fracture risk, even though only a modest impact on bone density is observed.898 For this reason, I believe that a well designed “nutritional insurance formula” (as described below) may be particularly helpful for keeping your bones healthy. Supplemental calcium alone, at least postmenopausally, provides rather modest benefit – perhaps a 2% increase in bone density in the first year or so of supplementation, after which steady loss of bone mineral resumes. This modest benefit may be enough to postpone your date with a serious fracture – but don’t let the advertising hype of calcium pushers lull you into thinking that calcium supplements alone will provide definitive protection for your bones.

However, supplementation is not always favorable to bone health. Recent evidence suggests that dietary intakes of pre-formed vitamin A (retinol, retinyl palmitate) – whether from foods or supplements – may promote loss of bone density and increase fracture risk.899-901 Even relatively modest intakes – barely higher than the amount long regarded as the “recommended daily intake” by the U.S. government – are associated with increased risk of fracture. Apparently, this reflects the ability of retinol (or rather its metabolic product retinoic acid) to increase the activity of osteoclasts, the bone cells that dissolve bone mineral.902, 903 The good news is that beta-carotene, which the body can
convert to retinol to provide adequate vitamin A activity, has not been linked to loss of bone density; evidently, the amount of vitamin A activity derived from dietary beta carotene is sufficiently high to promote adequate nutrition, but sufficiently low that it represents no threat to bones. Food sources of pre-formed vitamin A include fish, fish oils, liver, eggs, and certain dairy products and breakfast cereals that are “vitamin fortified”; retinol does not occur naturally in any vegan foods. So you can avoid dietary retinol altogether if you eat a vegan diet, avoid “enriched” breakfast cereals, and choose supplements in which the vitamin A activity is provided entirely by beta carotene. Once manufacturers have revised their products to exclude pre-formed retinol, vitamin-mineral supplements should be exceptionally beneficial for bone health.

A Comment on Kidney Stones

Although kidney stones are rarely life-threatening these days (thanks to the availability of good surgeons), they can be excruciatingly painful. Most such stones consist of calcium salts (e.g. calcium oxalate), so an effective way to prevent them is to minimize the amount of calcium that the kidneys allow to pass into the urine. We have already noted that a salty diet, as well as a diet high in protein, promotes loss of calcium in the urine – whereas the alkalinizing effect of a potassium-rich diet is protective in this regard. In other words, a low-salt whole-food vegan diet of moderate protein content (i.e. that isn’t high in soy protein products) should be just about ideal for preventing kidney stones.

The other key ways to reduce your risk for kidney stones is to moderate your intake of vegetables (such as spinach) that are rich in the compound oxalic acid, and to increase your intake of fluids. In susceptible individuals, very high supplemental intakes of vitamin C may cause the body to make significant amounts of oxalic acid; however, in most people this is not a significant concern. (Earlier studies suggesting a more general effect of vitamin C on urinary oxalate levels proved to be technically flawed.) Conversely, supplemental vitamin B6 tends to decrease oxalic acid production in people who make excessive amounts of this compound, and thus may be useful for reducing kidney stone risk in such individuals. Ample intakes of magnesium – from whole grains, beans, or supplements – also appear to reduce kidney stone risk.

Surprisingly, unless your diet is exceptionally high in calcium (say, over 2,000 mg per day), dietary calcium seems to have relatively little influence on the amount of calcium that is excreted in the urine. An increase in dietary calcium acts to suppress the production of certain hormones that induce calcium absorption – the net effect being that net calcium absorption does not rise significantly; this protective mechanism is overridden only when calcium intake becomes exceedingly high. Ironically, supplemental calcium has actually been found to reduce kidney stone risk in some individuals, owing to the fact that dietary calcium tends to form an insoluble precipitate with dietary oxalic acid, such that the oxalic acid cannot be absorbed. Yet the conventional medical wisdom for years has been to have kidney stone patients cut back on calcium – which does little to prevent these stones, while putting bone health at risk!
In one recent Italian clinical study, patients who previously had experienced kidney stones were randomly assigned to either a low-calcium diet or a diet with a reduced intake of salt and animal protein. During the next five years, recurrent kidney stones were only half as common in those patients restricting salt and animal protein, as in those restricting calcium. Hopefully this highly publicized study will help to change medical practice for the better.

**Keeping Your Joints Healthy**

If you want to enjoy the health-promoting advantages of regular aerobic exercise into a vigorous old age, is it also of great importance to keep your weight-bearing joints in good shape. Staying lean and choosing aerobic exercises that are low impact – power walking, stair climbing, elliptical gliding, or cycling in preference to running or bouncing aerobics – will be beneficial in this regard. The weight loss achievable with a low-fat, whole-food vegan diet accompanied by exercise may be of particular benefit to overweight people who are starting to experience hip or knee problems. However, how such a diet will influence cartilage health in other respects is not clear. There does not appear to be any evidence that quasi-vegan societies enjoy special protection from osteoarthritis.

There is recent evidence from two 3-year controlled studies that the natural supplement glucosamine – a biosynthetic precursor of the mucopolysaccharides that constitute a high proportion of the dry weight of cartilage, and of the hyaluronic acid that lubricates your joints – can slow or halt the loss of cartilage in people suffering from osteoarthritis of the knee. Moreover, when the participants in this study were followed up five years later, those who had received glucosamine during the study were found to be 57% less likely to have undergone a surgical knee replacement. There is considerable evidence – albeit not entirely consistent - that glucosamine supplementation can provide symptomatic benefit in osteoarthritis, easing pain and improving joint mobility – without the potential toxicity associated with many anti-inflammatory drugs. These considerations suggest that, in people who still enjoy healthful joint function, glucosamine supplementation might have utility for preventing the onset of osteoarthritis and keeping your joints structurally intact. It will probably be many years before this supposition is adequately evaluated in clinical studies, but I am following my instinct and incorporating glucosamine into my supplementation program while my joints are still in good shape.
VIII. Coda – A Few Odds and Ends

To wrap up, I will address a few relevant topics that somehow didn’t make it into the preceding discussions:

Prostates and Periods

Prostatic hyperplasia – as distinct from prostate cancer, which usually arises in a different part of the prostate – rarely kills men, but it can make one’s “golden years” more annoying than they ought to be. I have a strong suspicion that the reduction of growth factor and sex-hormone activity associated with whole-food vegan diets may slow the onset of this disorder.\textsuperscript{925} It is intriguing to note that symptomatic prostatic hyperplasia used to be considered quite rare in China – but has become increasingly more common in recent years.\textsuperscript{926-928} The fact that it is now more common in urban China than in rural China is consistent with the possibility that quasi-vegan diets are indeed protective in this regard. Furthermore, there are recent reports that increased serum levels of free IGF-I and of insulin may be associated with increased risk for clinically significant BPH, whereas the IGF antagonists IGFBP-1 and IGFBP-3 may be protective in this regard.\textsuperscript{929-932} Regular exercise, as well as moderate alcohol consumption – both of which promote improved insulin sensitivity, and thus tend to lower blood levels of insulin – have also been linked to reduced risk for this disorder.\textsuperscript{933, 934} Thus, an overview of the admittedly limited relevant evidence that is currently available encourages the view that the relatively low growth factor activity (low blood levels of free IGF-I and of insulin) associated with low-fat whole-food vegan diets would tend to prevent or postpone symptomatic overgrowth of the prostate.

Women have their own set of problems – including the pre-menstrual tension syndrome, menstrual cramping, and the side effects associated with onset of menopause. Since free estrogen levels are lower on whole-food vegan diets, the hormonal shifts which precipitate these syndromes are less dramatic in the context of such a diet. A recent controlled study by Dr. Neal Barnard and colleagues has demonstrated that the annoying symptoms often experienced premenstrually, as well as menstrual cramping, are less severe when women are eating a low-fat, whole-food vegan diet.\textsuperscript{80} (In fact, the symptomatic benefit was so substantial that it interfered with the experimental design – the women who were supposed to switch back to an ordinary omnivore diet refused to do so!) There is also an impression that in quasi-vegan societies like China, the hot flashes and other symptoms associated with onset of menopause are less troubling; whether vegan diets might have preventive or therapeutic benefit in this regard has not been assessed in clinical studies.

Health Benefits of Fiber

Although the idea that dietary fiber lowers colon cancer risk may not hold water after all, there are plenty of other respects in which an ample intake of dietary fiber – which you will surely achieve with a low-fat, whole-food vegan diet – can aid your health. Aside from the obvious fact that you will avoid constipation, the incidences of appendicitis,
diverticulitis, hemorrhoids, varicose veins, hiatal hernia, and gallstones are anomalously low in cultures whose traditional diets are high in fiber. Dr. Hugh Trowell and his eminent colleague Dr. Denis Burkitt did much to document this point in their insightful writings promoting fiber-rich whole-food diets. They popularized the motto: “hard in, soft out” – meaning that, if you eat “hard” fiber-rich foods, you will have a soft stool that will protect you from the many potential health problems associated with hard stools. Hard stool can lead to impactions that promote both appendicitis and diverticulitis; and the straining associated with the need to evacuate hard stools is suspected to be a factor in the origin of hemorrhoids, varicose veins, and hiatal hernia.

The impact of dietary fiber on risk for appendicitis is now however a bit less clear than we formerly suspected. Studies in South Africa indicate that risk of appendicitis in black South Africans is remaining quite low despite the fact that dietary fiber consumption has declined quite substantially and is now not much higher than that of whites. However, dietary fat intake – and thus presumably intake of animal products – remains low in most black South Africans. So perhaps it is a low-fat or quasi-vegan diet that mediates the protection from appendicitis. There is evidence that a vegan diet can have an impact on the types of bacteria that populate the lower intestinal tract. Furthermore, as we have seen, a vegan diet influences the rate of cell multiplication in the colon lining. Conceivably, such factors could influence risk for appendicitis. Epidemiology in Britain suggests that British vegetarians have only about half as high a risk for this disorder as do omnivores.

An association of high fiber intake with reduced risk for diverticulitis and hemorrhoids appears to be more solid, inasmuch as high-fiber diets have shown utility for treating these syndromes.

The rarity of varicose veins in rural Africa was once quite extraordinary. I can quote Dr. Denis Burkitt on this: “During 1958 in an area of Uganda where at that time western culture had little impact, I specifically looked for varicose veins in over 4,000 adults during an inspection of an entire community for trypanosomiasis. Only five cases were found, an incidence of 0.12%, which is about one-hundredth of the incidence in Britain or the U.S.A.” This rarity of varicose veins goes hand-in-hand with a rarity of deep venous thrombosis, a frequent complication of surgery that can lead to fatal pulmonary embolism. (This is what killed Andy Warhol, for example.) Several British surgeons have claimed that the incidence of deep venous thrombosis has plummeted in their practices after they started to give bran supplements to their patients; unfortunately, I am not aware of any controlled clinical studies that have attempted to validate these observations.

With respect to gallstones, dietary fiber, by speeding the transit of food through the intestines, decreases the ability of gut bacteria to transform bile acids into less soluble metabolites that are linked to increased gallstone risk, such as deoxycholate. These metabolites, after being reabsorbed, inhibit the liver’s production of an enzyme (7-alpha-hydroxylase) that converts cholesterol to bile acids; as a result, bile tends to have an excess of cholesterol that may crystallize out to form gallstones. This key liver enzyme is
also suppressed by insulin\textsuperscript{950, 951} – implying that good insulin sensitivity and low-insulin-response diets should be protective. Low-fat whole-food vegan diets are typically rich in fiber, tend to promote leanness and insulin sensitivity, and provoke relatively low insulin secretion – so they are ideal for preventing gallstones.

To show how effective this protection can be, I will quote gallstone expert Dr. Kenneth Heaton: “Denis Burkitt recalls that in 17 years’ surgical practice in East Africa he operated on only two patients with gallstones, one of whom was a queen. At the time of writing, figures from replies to questionnaires received by D.B. amply confirm personal impressions. Twelve hospitals in Uganda have supplied 109 monthly returns and have not reported a single case of gallstones. The same is true for Malawi after 102 hospital months. In Tanzania, 207 hospital months have yielded only two cases and in Kenya 67 hospital months have turned up just one case. In West Africa, 13 Nigerian hospitals have seen only two patients with gallstones in a total of 109 months.”\textsuperscript{952}

Contrast these figures with the estimate that, as of 1970, about one-third \textit{million} gallbladders were removed \textit{annually} in the U.S!\textsuperscript{953} And lest there be any be any suspicion that blacks are at low genetic risk for gallstones, Heaton cites a survey in Philadelphia noting that African-Americans accounted for 42\% of all admissions for treatment of cholesterol gallstones.

Native American women – and women with significant Native American genetic heritage, such as mestizo Mexicans and Mexican-Americans – are at greatly increased genetic risk for gallstones, and their risk for this disorder is extremely high if they grow up eating the fatty, over-refined omnivore foods popular in the U.S. Although having symptomatic gallstones usually only entails physical discomfort and the inconvenience of undergoing surgery, it can also have a more sinister outcome; in about 2-3\% of cases, a surgically-removed gall bladder is found to harbor a gallbladder cancer – which is almost invariably rapidly fatal if not completely removed by the initial surgery. Presumably, the inflammation often induced by gallstones markedly increases the chance that a cancer will arise in the gallbladder; gallbladder cancer is associated with gallstones in about 80-90\% of cases. A survey of the records of the New Mexico Tumor Registry during the 1970s indicated that gall bladder cancer was the third most common cancer diagnosed in Native American women, trailing only cancers of the breast and uterine cervix.\textsuperscript{954} To the extent that proper diet can minimize gallstone risk in Native Americans, adopting such a diet may thus be expected to proportionately lower risk for one of their most prominent killer cancers.

Evidently, if you want to minimize your need for the services of a surgeon and stay out of the hospital (which is where the really bad antibiotic-resistant germs are!), a high-fiber whole-food diet is a really smart idea.

While I am on the topic of fiber, I shouldn’t neglect to cite some recent intriguing epidemiological studies, making use of the huge Nurses’ Health Study data base, indicating that a relatively high consumption of \textit{whole} grains (not grains per se) is associated with significantly decreased risk for heart attack, stroke, and diabetes.\textsuperscript{955-957}
The authors of these studies used sophisticated statistical analyses to try to pin down the components of whole grains that were primarily responsible for this protection, but the protection appeared to be largely independent of fiber per se, or of specific nutrients such as B vitamins, vitamin E, or magnesium. Nor is reduced glycemic index a likely explanation: in an American population, whole wheat flour is the predominant whole grain – and this has virtually as high a glycemic index as white flour. Thus, there appears to be a “mystery factor” in whole grains that provides important and versatile health protection. I would like to see the neglected trace mineral silicon examined in this regard\textsuperscript{958, 959} – but that is a mere hunch. The “take-home lesson” is that at every opportunity you should choose whole grains over refined grains if at all possible – consistent with the advice to eat a whole-food diet. Whole-wheat pasta is a great way to get your whole wheat, as is bulgur wheat (a dish popular in the Mediterranean); “flourless” breads featuring sprouted grains or partially intact grain kernels are a better choice than breads made from finely-ground flour. Macrobiotic vegans place great emphasis on brown rice, which in any case is more flavorsome than white rice. Health food stores usually offer a wide range of rather exotic whole grains.

**Adverse Effects of Veganism?**

It is common sense to suspect that the reduction in IGF-I activity associated with a vegan diet will not be favorable to optimally efficient wound healing\textsuperscript{960, 961} As noted above, there is evidence that protein supplements can boost circulating IGF-I levels and accelerate the healing of fractures in the elderly. Theoretically, a reduction in IGF-I levels might also compromise the ability of the body’s immune cells to multiply aggressively in response to invasion by pathogenic microorganisms.\textsuperscript{962} However, there currently is little evidence that vegans have a compromised immune status or are at increased risk for infection.\textsuperscript{963} If you are faced with a severe trauma or a persistent infection and would like to boost your IGF-I activity temporarily, adding some low-fat dairy products to your diet would be a rational strategy.

In regard to risk of infection, inadequately cooked flesh products are the most common source of staphylococcal “food poisoning” and other food-borne infectious illnesses. Presumably, this is because the infectious organisms that thrive in animals - including humans - are fundamentally different that those that infest plants. The harm that arises from eating microbially contaminated plant products generally results, not from infection, but from ingestion of carcinogens or other toxins produced by the contaminating organisms. (The recent episode of E. coli-contaminated spinach stemmed from water polluted by livestock waste.) Yet even proper cooking doesn’t seem to deter transmission of “mad cow disease”. (Fortunately for vegans, “mad broccoli disease” is unlikely to make an appearance!) The popular furor over the European “mad cow” epidemic and the occasionally lethal outcomes of food-borne E. coli infections in children have motivated many people to take a more serious look at vegetarianism or veganism (though I’m a mite perplexed that fear of heart disease, diabetes, or cancer hasn’t already provided sufficient motivation!)
There is some evidence that, in people who are hypertensive, a low intake of saturated fat and of animal protein – as well as low blood cholesterol levels - may increase risk for hemorrhagic stroke; this has been reported in Japan, and, more recently, in the U.S. Conceivably, the cerebral vasculature may be thinner and more prone to rupture when growth factor activities are low; smooth muscle cells of the artery wall are protected from apoptosis by IGF-I, which also promotes production of the protein elastin. This is a very minimal risk if your blood pressure is on the low side – hemorrhagic stroke is quite rare even in Japanese when their systolic blood pressure is under 120 – and it should be noted that so-called ischemic stroke (the type resulting from blood clots) is much more common in the U.S. Nonetheless, if your blood pressure is very high (despite your best effort to control it with diet and drugs) and your doctor thinks that hemorrhagic stroke may be a major risk for you, cutting the animal protein out of your diet may not be a wise idea. Theoretically, fish oil, which I have often recommended for a wide range of health-protective benefits, has the potential to increase risk for hemorrhagic stroke owing to the fact that, much like aspirin, it can stabilize the blood clotting cells (platelets); however, there is currently little direct evidence in support of this concern, whereas there is good reason to believe that fish oil provides protection from the much more common thrombotic type of stroke.

The epidemiological correlations between low serum cholesterol and hemorrhagic stroke risk are just one aspect of a broader phenomenon that has led many to question the wisdom of striving for low cholesterol levels. Epidemiological studies have often found that people with relatively low serum cholesterol are at increased risk for death from a number of non-vascular disorders, including many types of cancer, respiratory diseases, digestive diseases, cirrhosis, trauma, and suicide. It is important to note that, when people in Western society have a low cholesterol level, this is hardly ever attributable to a consumption of a quasi-vegan diet – their cholesterol is usually low despite consuming a fatty, over-refined diet. Low cholesterol under these circumstances implies a peculiarity of metabolism or lifestyle that in many cases may be harmful to health, or that reflects an ongoing disease process. Thus, a low cholesterol may be a reflection of a low food calorie intake in people who are depressed, demented, feeble, or addicted to drugs or alcohol; such people are evidently at increased risk for death from a number of causes – and serum cholesterol clearly has nothing to do with it. The reduction in calorie intake may itself pose a risk by compromising the intake of protective vitamins, minerals, and phytochemicals. Chronic inflammation also typically lowers cholesterol, and it has been shown that cholesterol tends to decline in the 4-6 years prior to death from cancer – a phenomenon that, in the opinion of many experts, largely accounts for correlations between low cholesterol and cancer risk. Some cancer cells remove cholesterol-rich LDL particles from the bloodstream, whereas others can lower cholesterol through inflammatory mechanisms. No one has ever proposed a credible mechanism whereby low serum cholesterol could increase cancer risk, or demonstrated that low cholesterol increases cancer yields in rodent studies.

Analyses that take these factors into account have concluded that, with the likely exception of the low cholesterol/hemorrhagic stroke connection (which still lacks a clear explanation, but emerges quite consistently in epidemiological studies), low cholesterol
itself is unlikely to be the cause of the increased non-vascular mortality associated with low cholesterol levels. The most definitive analysis in this regard – by British epidemiologist Dr. M.R. Law and colleagues - divided epidemiological studies into two kinds: those in which the enrollees were employees of a large company, and so-called community-based studies that enrolled a large cross-section of the general public. Law reasoned that, in the employee-based surveys, the subjects were very likely to be healthy at baseline (when blood samples were taken), whereas in community-based surveys a far higher proportion of the subjects would have pre-existing medical conditions that could lower cholesterol. Sure enough, Law found that none of the employee-based studies linked low cholesterol to increased mortality from any cause, whereas all of the community-based studies correlated low cholesterol with increased non-coronary mortality. Law concluded that this was definitive evidence that low cholesterol was the result, rather than the cause, of lethal diseases or of medical conditions that promote lethal disease. (The studies in question did not specifically note the incidence of hemorrhagic stroke, so they did not provide insight into its link to low cholesterol – but on other grounds Law concluded that the link between low cholesterol and hemorrhagic stroke was genuine.) Another insightful study showed that increased risk was seen only in people whose cholesterol declined substantially; people whose cholesterol was steadily low for a number of years were not at increased risk. The authors of this study concluded that their “results add strength to the reverse-causality proposition that catabolic diseases cause total cholesterol to decrease.” In other words, the reduction in cholesterol is usually a marker of a dangerous health problem – rather than a mediator of it.

This is borne out by studies looking at mortality risk in people who use cholesterol-lowering drugs – these studies show that cholesterol reduction has a dramatically protective impact on vascular risk, without increasing risk of mortality from cancer or any other major cause. With respect to dietary impacts on cholesterol, it is comforting to note that in the Oxford Vegetarian Study – a long-term follow-up of the health status of 6,000 British vegetarians (a significant proportion of whom are vegans) – the vegetarians were at substantially and significantly lower risk for all-cause mortality, as well as for death from heart disease or cancer specifically. You will also recall that, in the China Health Project, the provinces in China that had the lowest cholesterol levels were also those that had the lowest risk for cancer – presumably owing to the fact that, in China, a low cholesterol is a marker for low animal product consumption. Thus, there is little reason to suspect that either low cholesterol, or a reduction in cholesterol, acts to increase cancer risk. It bears repeating that the correlations noted in epidemiological studies very frequently do not reflect causation; for example, the fact that heart disease is more common in societies that have safe drinking water does not imply that safe drinking water causes heart disease! Similar logic may apply to the association between low cholesterol and non-vascular mortality.

A major problem with the hypothesis that low cholesterol tends to increase mortality is that, by and large, no one has offered any credible mechanism whereby moderately low cholesterol levels could exert dire effects. However, some scientists still suspect that a correlation between impulsive or violent behavior and low cholesterol may in fact reflect
some impact of circulating cholesterol levels on brain function;\textsuperscript{981, 982} a limited amount of animal data appears to support this possibility, whereas other animal studies do not. Law did not find any association between suicide or other violent death and low cholesterol in the employee-based studies. Furthermore, he cites evidence that depression can lower cholesterol levels – via anorexia or inflammatory mechanisms – whereas successful treatment of depression is typically followed by an increase in serum cholesterol.\textsuperscript{976}

Suffice it to say that there is presently no evidence that vegan diets render people more violent or impulsive, nor has the world yet been terrorized by roving bands of hopped-up vegans! Indeed, the relatively low intake of branched-chain amino acids and high intake of carbohydrates that characterizes most vegan diets would be expected to promote brain synthesis of the neurotransmitter serotonin – a deficit of which is often a factor in violent behavior or depression.\textsuperscript{983} Nonetheless, it should be noted that many vegan diets are poor sources of omega-3 fatty acids, and a low intake of these has recently been linked to increased risk for depression.\textsuperscript{984, 985} This once again argues that vegans would be well advised to supplement with fish oil – though plant sources of omega-3 such as flax oil are also likely to be useful with respect to optimizing brain function.

Vegans are usually lean and thin. You should be aware that, if you want your son to become a star linebacker, a vegan diet may make it harder for him to acquire the large muscle mass required. It is a common belief among body builders that, no matter how much soy protein a person consumes, a vegan diet is not consistent with achieving maximal lean mass. This is probably just the flip side of the reduction of growth factor activity that is so protective from a health standpoint. For vegans attempting to build a larger muscle mass, supplemental creatine (about 3 grams daily) as an adjunct to vigorous resistance training may be particularly helpful, as vegan diets contain no creatine at all, and vegetarians typically have a slightly lower body pool of creatine.\textsuperscript{986, 987} Supplements of the essential amino acid leucine – as well as of its natural metabolite beta-hydroxy-beta-methylbutyrate (HMB) – have also demonstrated some potential for increasing muscle protein synthesis and/or slowing the rate of muscle protein breakdown,\textsuperscript{988-990, 990-1000} apparently without adverse effects,\textsuperscript{1001} there is no evidence that supplemental leucine or HMB influence IGF-I activity. A simple way to look at this is that skeletal muscle tries to maintain a relatively constant level of free leucine; when this level is low (as it often is immediately after strenuous exercise or in certain diseases associated with loss of lean mass) muscle fibers attempt to normalize this level by increasing the rate of protein breakdown and slowing the rate of protein synthesis. Conversely, an increase in muscle levels of free leucine has the opposite effect, inducing an increase in protein synthesis coupled with a reduction in protein breakdown – precisely what you would want if you are trying to increase your lean mass. Muscle may also monitor the level of the leucine metabolite HMB as an index of free leucine levels, and the utility of HMB supplements (3 grams daily) for slowing muscle breakdown and building lean mass is now well documented; remarkably, there is also preliminary evidence that such supplementation may even slightly lower serum cholesterol and blood pressure.\textsuperscript{1001} Thus, for vegans who would like to beef up their muscle mass without having to resort to androgenic hormones (anabolic steroids) or measures that increase blood-borne IGF-I activity, supplements of creatine, leucine, and HMB, complemented by resistance training, may offer a safe and effective alternative.
A further proviso – if you wish to raise an infant on a vegan diet, by all means make sure that he/she gets human breast milk (if at all possible) during the first months of life; there is more and more evidence that breast feeding provides important health advantages. (In other words, human milk should not be viewed as a health-destructive animal product - at least in infants!) Once the infant is eating solid food, don’t go overboard on restricting fat – growing infants require a fair amount of fat for proper formation of their central nervous systems. And of course make sure that your child takes a supplement providing vitamin B12 – this nutrient plays an important role in supporting tissue growth. Supplements of calcium and vitamin D may also be advisable, albeit less crucial. It may interest you to learn that, in the final edition of his classic book on child rearing, Dr. Benjamin Spock advised that all children over the age of 2 be raised on a low-fat vegan diet (much to the consternation of his publisher, I might add!). A vegan diet had saved Dr. Spock from a severe health problem in his eighties; he went on to live another decade, and became a staunch advocate of veganism in his later years.

The Paleolithic Persuasion

I would be remiss not to take at least a little time to address the increasingly popular notion that humans are evolutionarily adapted to a high meat diet such as that which they practiced in pre-agricultural times. Whatever the merits of this view, it has great appeal to people who want to be told that the flesh products they like to eat are actually good for them!

After the invention of stone tools and weapons, which made hunting much more effective, and prior to the invention of agriculture, humans did indeed get a high proportion of their calories from game animals. Foliage, fruit, wild tubers, and nuts supplied the remainder of their calories – grain products and beans were not dietary staples prior to agriculture. Many aspects of this diet doubtless were laudatory. The plant foods were whole, rich in potassium, fiber, and phytochemicals, and low in both glycemic index and caloric density. Refined salt was not available. The meat of game animals was usually quite lean – not at all like the marbled steaks that modern man enjoys – yet was comparatively rich in protective omega-3 fats. Dairy products were unknown, and eggs were only an occasional treat. Quite a lot of energy was expended in the pursuit of not that many calories – implying that obesity was probably a rare problem (as is certainly the case with the few remaining hunter-gatherer cultures).

However, I refuse to buy into the argument that the thousands of years that our paleolithic ancestors spent as hunger-gatherers implies that we are adapted to require a high intake of flesh products to maintain good health. Although certain useful nutrients such as carnitine, creatine, and taurine are supplied primarily by flesh foods, humans did not lose their capacity to synthesize these compounds during their paleolithic years (in stark contrast to the fact that cats have become obligately dependent on flesh as a source of taurine). Very small dietary intakes of animal products can meet the need for vitamin B12...
(which these days can be readily provided in supplements). There is no reason to believe that high protein intakes are vitally important to health and, as we have seen, relatively low protein vegan diets can protect us from a wide range of disorders.

Vegan advocates could counter (and often do) by claiming that, in the millions of years prior to the development of stone weapons, our hominid ancestors were quasi-vegan, like the current great apes – and that we thus are adapted to require a vegan diet; they note that our dentition and digestive tracts are much more akin to those of herbivores than carnivores. Or they could claim that thousands of years of reliance on agriculture have made us dependent on grains for good health. Frankly, I think that these views are just as specious as the contrary view that we are adapted to require lean meat. Throughout their evolution, man’s ancestor have eaten whatever they could get their hands on to stave off starvation. There is no compelling reason to believe that any particular pre-modern dietary pattern guarantees an Edenic state of lifelong good health. The sober fact is that, rather than falling back on a comfortable myth about an ideal bygone diet, we need to resort to scientific analysis of a broad range of evidence in order to define the diets and lifestyles that can best protect us from the degenerative disorders of aging. I applaud the anthropologists who are helping us to better understand the dietary patterns of our ancestors – their work serves to expand our awareness of the wide range of dietary choices open to us – but I categorically reject the notion that their findings constitute a blueprint for an ideal future diet.

Furthermore, trying to implement a “paleolithic” diet in the modern age – doing one’s “hunting and gathering” in modern supermarkets, I suppose – is of questionable practicality. Flesh foods that are truly low in fat have a very low net calorie yield, with the result that, lacking grain products, you will need to eat huge amounts of flesh just to avoid starvation. Consider that, during the Lewis and Clark expedition, the men consumed an average of 8 pounds of meat a day! If you had access to a lot of fruit and nuts, your dependence on massive amounts of flesh foods would be alleviated somewhat, but most paleolithic people probably didn’t have this luxury. If modern-day people pretending to be paleolithic get by on much lesser amounts of meat, it’s undoubtedly because the meat they are eating is a lot higher in fat than is half-starved wild game - or they are eating a lot more fruit and nuts than most paleolithic people had access to. (In this regard, it is interesting to note that, when Plains Indians killed a buffalo, if the animal was quite lean, they often wouldn’t even bother to butcher it – too much trouble for too few calories!)

Advocates of the paleolithic diet are fond of recounting the remarkable study by Dr. Kerin O’Dea, who convinced 10 diabetic Australian aborigines to return to their traditional hunter-gatherer lifestyle for a period of 7 weeks. Not surprisingly, their diabetic control improved to a remarkable degree, and, on average, they lost 8 kilograms of weight. What is often left unsaid is the fact that these people were consuming an average of 1200 calories (kcal) per day – in other words, they were virtually starving. As long has they had stored fat to burn, I presume that this was reasonably tolerable – but if the study had gone on much longer, the participants would have started to lose lean mass and would not have been happy campers! Despite the fact that they were getting
64% of their calories from animal products, the wild game they were eating was so low in fat that their total diet derived only 13% of its calories from fat – even Pritikin would have been impressed! They were eating over a pound of flesh daily – and yet starving.

Good luck finding any farm flesh even approximately that lean in a supermarket – the grain-fed farm animals you’ll find there have severalfold higher fat content. The “leanest” beef is about 29% fat calories, and skinless white meat poultry about 23%. The only flesh you’ll find that is paleolithically lean is wild fish. So unless you choose pescovegetarianism, high flesh diets will be high fat diets – or at least higher in fat than is optimal for insulin sensitivity.

There are also important political and ecological issues to address. Hunting and gathering made a fair amount of sense as a lifestyle when there were no more than a few million humans on the entire earth to share the wild game. It makes no sense whatever when the human population – thanks to agriculture – has swollen to multiple billions. As matters stand now, humans devote substantially more arable land to grazing livestock, and to growing the feed for livestock, than they do to raising crops for human consumption - in a world where millions of children starve to death every year! Furthermore, the demand for land to graze cattle and other livestock is one of the chief factors driving the progressive destruction of the world’s rain forests. One can just imagine the consequences if pampered, rich Americans decided to give up grain products and increase their flesh consumption severalfold!

Thus, while many aspects of the diets practiced by our paleolithic forebears may have favorable health consequences and are worthy of emulation, the notion that modern man should give up grains and get a high proportion of his daily calories from low-fat flesh foods – not as a temporary strategy to achieve weight loss, but as a continuing lifestyle – is impractical and, moreover, socially irresponsible. Furthermore, what would be the consequences for long-term bone health of a diet so high in protein? Eskimos, whose traditional diets are quite high in protein (and only rendered practical by the fact that they consume large amounts of blubber), are noted for a very high incidence of early-onset osteoporosis.1004

**Paleolithic Vegans**

A very different – and, to my mind, much more commendable – way of emulating our Paleolithic forebears is to eat a vegan diet that features fruits, vegetables, tubers, and nuts, and omits grains and legumes (which became part of our diet during the agricultural era). A popular variant of this is the raw-food vegan diet; this likewise excludes grains and legumes, which aren’t edible unless cooked. Diets of this type are exceptionally rich in micronutrients and phytochemicals. They tend to be rather high in fat (as nuts are the only really concentrated sources of calories in such diets), but any negative effects in this regard on insulin sensitivity or body fat would likely be mitigated by the fact that such diets tend to be of low caloric density overall. Indeed, overweight people typically lose large amounts of weight on such diets.1005 Not surprisingly, IGF-I levels tend to be low in raw-food vegans, as they are in other vegans.1006 A potential disadvantage of raw food
diets to people who are highly physically active – and thus have high caloric requirements – is that an inordinate amount of time would have to be spent in eating! So I am not likely to abandon my whole grains and beans any time soon – but I will acknowledge that the Paleolithic vegan strategy is likely to have a very favorable impact on health (assuming that B12 is supplemented), and is compatible with a healthy planet and a well-fed human species – so Paleolithic vegans have my blessing.

A Word on Alcohol

Although I didn’t include a mention of alcohol in the “6 dietary commandments” that begin this essay, I was tempted to do so. It seems that every other week there is another story about a new health benefit related to moderate alcohol consumption. (By moderate I mean, in women, 1 drink daily and maximally 2; in men 1-2 drinks daily, maximally 3. Note that women are more sensitive both to the beneficial and harmful effects of alcohol, owing to the fact that they usually have lower body mass, and moreover tend to absorb alcohol more efficiently; in men, a significant proportion of ingested alcohol is metabolized by the stomach lining before it can reach the bloodstream.)

Studies suggest that regular moderate use of alcohol reduces risk for heart attack, stroke, diabetes, osteoporosis, and – in women, though not men – weight gain and obesity.1007, 1008, 1008-1010 Moderate drinkers tend to be much more insulin sensitive than non-drinkers, suggesting that alcohol somehow promotes the insulin sensitivity of muscle.1010-1013 The ability of alcohol to increase protective HDL cholesterol has long been known. More recent studies show that transient exposure of vascular endothelial cells to physiological levels of alcohol greatly improves their ability to break down blood clots;1014-1016 “acute phase” risk factors (such as C-reactive protein) are lower in moderate drinkers.1017 The ability of alcohol to prevent heart attack appears to be especially dramatic in diabetics: in a couple of recent reports, risk of heart attack was 60-80% lower in diabetics who drank moderately!1018-1020

An insulin-sensitizing effect of alcohol may perhaps explain another intriguing and surprisingly little known impact of moderate alcohol consumption – preventing weight gain in women.1010 Analysis of data from the Nurses’ Health Study revealed that, at any given height, women who drank moderately were, on average, 15% lighter than teetotalers – despite the fact that they consumed slightly more calories!1021 Similar, in a large British study, women who drank regularly were only half as likely to be obese as non-drinkers.1022 One recent study suggests that moderate alcohol consumption is at least as effective as regular exercise in preventing weight gain in women.1023 The analogous observation in men is that men drinkers consume substantially more calories, and yet are no heavier than men who don’t drink.1024 These strange observations are known as “the alcohol paradox”, and have not yet received an adequate explanation. I suspect that decreased daily insulin secretion in drinkers may play a role in mediating this effect.1010 This phenomenon is of much more than just cosmetic interest – it no doubt contributes to the marked reduction of diabetes risk in women drinkers.1025 It is ironic that the impact of alcohol on weight gain in women appears to be considerably greater than than of smoking1021 – and yet many teenage girls now take up smoking to keep their weight
down! Fortunately, 1-2 drinks daily appear to optimize this impact of alcohol, so there is no need to resort to alcoholism.

There of course are some drawbacks. Even moderate alcohol use appears to be associated with a very modest increase in risk for both breast and colon cancer. More recent careful analyses suggest that this increased risk is seen only in people whose folic acid nutrition is mediocre, giving rise to the hypothesis that alcohol increases the risk of these cancers by interfering with folic acid metabolism; if this is the case, then supplemental folate should eliminate this risk in moderate drinkers. In one study, the lowest rate of breast cancer was seen in regular moderate drinkers who had excellent folic acid status. At more abusive levels of intake, alcohol – especially in the high concentrations found in hard liquor – is associated with increased risk for esophageal cancer, and can potentiate the ability of smoking to induce head and neck cancer. Frank alcoholics are of course at high risk for liver failure and disorders of the pancreas, heart, and other tissues. Thus, the relationship between alcohol intake and mortality is a U-shaped curve – for best health, you need just enough, but not too much.

We shouldn’t lose sight of the fact that beer and wine are whole foods which provide nutrients and well as protective phytochemicals. Although resveratrol and other polyphenols in wine come in for special attention, the phytochemical content of beer is not negligible, as it reflects the flavonoid content of the whole grains from which it is manufactured. I have a less charitable attitude toward distilled hard liquors, which I consider refined foods analogous to refined sugars. Furthermore, hard liquors make it easier to grossly overconsume ethanol (the kids who occasionally die of acute ethanol poisoning at frat parties were not drinking beer!), and the high concentration of ethanol in these products has greater potential to damage the upper digestive tract and promote cancer. Nonetheless, the chief protective component of alcoholic beverages (in moderation) is clearly ethanol per se.

Most physicians and health experts appear to be loath to recommend alcohol; they obviously don’t want to cause new cases of alcoholism, but I have a suspicion that they are also often are afflicted by an excessive puritanism or a fear of lawsuits. The fact of the matter is, most adults already have enough experience with alcohol to know whether they can control it – or whether it controls them. If you are the type of person who can’t have one drink without having six drinks – or if you’ve never used alcohol and have a family history of alcoholism - then you had better stay away from alcohol altogether. But if you know that you can handle alcohol, then in my opinion you’re missing a big opportunity to protect your health if you don’t drink moderate amounts of alcohol on a regular basis. The health benefits are too great and too versatile to pass up!

I have a personal anecdote that may be of interest. Back in the 1950s, my grandmother, then in her fifties, had a serious heart attack. Her doctors were of the opinion that she would be lucky to live another year. But her folksy Texas family physician had one simple prescription: “Mrs. McCarty, every day I want you to drink three shots of alcohol. Alcohol is a blood thinner.” I can testify by first-hand experience that she was faithful to this prescription – and she lived another 30 years! (And the latest research on alcohol
and endothelial cells shows that – alcohol is a blood thinner. Never underestimate the wisdom of folksy Texas physicians.)

**Health Benefits of Coffee**

Another common drink worthy of comment is coffee. The “mental energizing” impact of this beverage reflects the fact that, in physiological concentrations, caffeine can inhibit brain receptors for the hormone-like compound adenosine. However, adenosine receptors influence the function of cells throughout the body. In particular, they appear to have a pro-inflammatory impact in various neurodegenerative disorders, and also play a mediating role in the fibrotic response (leading to cirrhosis, liver failure, and increased risk for liver cancer) that often complicates chronic hepatic disorders such as hepatitis, fatty liver, or alcoholism. This probably explains why recent studies show that people who make heavy use of (caffeinated) coffee are at decidedly lower risk for Parkinson’s disease, Alzheimer’s disease, cirrhosis, and hepatic cancer. In particular, a Finnish study found that people who drank 3-5 cups of coffee daily during midlife were over 60% less likely to develop dementia in later life than coffee non-drinkers. Given the high prevalence and devastating impact of dementia among the elderly, this finding – which is roughly consistent with that of previous smaller studies – is of extraordinary practical importance if borne out in future research.

Moreover, heavy users of coffee – caffeinated or decaffeinated - enjoy a much lower risk for type 2 diabetes; men who drink about 6 cups a day appear to decrease their risk by about 50%! Obviously, something in coffee beans other than caffeine is responsible for this benefit. Suspicion now centers on chlorogenic acid; there is fragmentary evidence that this compound can slow the absorption of ingested carbohydrate and also boost intestinal production of a hormone that promotes the proper function of pancreatic beta cells. Regardless of the mechanism involved, there is no serious doubt that heavy use of coffee lowers diabetes risk.

Like beer and wine, coffee is rich in phytochemicals, some of which may have protective potential. In particular, the compounds cafestol and kahweol can act as phase 2 inducers, promoting the detoxification of certain carcinogens. Perhaps this explains the trend toward a modest reduction in risk for colorectal cancer observed in coffee drinkers.

In people who haven’t ingested caffeine in the recent past, caffeine typically raises the heart rate and the blood pressure. This has encouraged the common presumption that caffeine usage should increase risk for heart attack or vascular disorders. But, in fact, the acute cardiovascular response to caffeine tends to wear off over time in people who ingest it regularly; in fact, after several weeks of steady use, caffeine usually fails to raise heart rate or blood pressure. That presumably explains why long-term use of caffeinated beverages has been found to have little impact on cardiovascular risk.

There is also concern that coffee and other caffeinated beverages may have an adverse effect on calcium absorption and bone density. In fact, the negative impact of caffeine on
calcium absorption appears to be quite modest, and unlikely to be of physiological significance in people who achieve the recommended intake of calcium. Many studies fail to observe any impact of coffee drinking habits on bone density or fracture risk, and some studies which do find an effect conclude that it is only significant in those whose calcium intakes are low. So including calcium in your daily supplementation program – which in any case is appropriate if you are concerned about your bone health – would likely alleviate any potential adverse impact of coffee intake on your bone density.

So heavy regular use of coffee can be expected to decrease our risk for type 2 diabetes, hepatic fibrosis or cancer, and some common devastating neurodegenerative disorders – without however increasing cardiovascular risk. And its favorable impact on alertness may modestly improve intellectual performance. Unless caffeinated coffee unduly impairs your capacity to get restful sleep, or makes you too anxious, enjoying it regularly and frequently – 3 cups or more daily - may be a smart idea.

Tea, although not as potent a source as coffee, also supplies caffeine. Green tea has occasioned particular interest owing to its high content of catechin polyphenols – most notably EGCG – that can act as phase II inducers and prevent carcinogen-induced cancers in rodents. Epidemiological studies suggest that regular drinkers of green tea may be at lower risk for certain cancers, notably those of the breast, lung, and prostate.

These considerations thus suggest that ample intakes of coffee and green tea, coupled with moderate regular use of wine or beer, can confer a diverse array of health benefits. Also recommendable are (unsalted or lightly-salted) fruit or vegetable juices, as these are excellent sources of potassium and antioxidant phytochemicals; one intriguing recent study reports a markedly lower risk for Alzheimer’s disease in Japanese-Americans who drink juices regularly. Although it may be preferable to eat fruits and vegetables in their whole fiber-rich form, juicing makes it more convenient to achieve a high volume of fruit/vegetable consumption. We have also cited the vascular protection afforded by raw cocoa – albeit the commercial cocoa preparations currently available tend to be low in protective flavanols.

**Ancillary Strategies: Exercise/Supplementation/Early Detection**

Choosing the proper foods certainly isn’t the only measure you’ll want to adopt to preserve your health. Regular exercise – both aerobic and resistance – is astonishingly versatile in the health protection it affords. In fact, almost all of the prominent pathologies we have discussed are susceptible to prevention or control, at least to some degree, by regular exercise. That includes coronary disease, obesity, diabetes, hypertension, stroke, dementia, osteoporosis, and many prominent types of cancer. Preferentially, your aerobic exercise should be done in a way that selectively burns body fat (as discussed above – see the Appendix on the NutriGuard Learn to Burn Leanness Program) so that you will get the best benefits with respect to weight control and insulin sensitivity. And low-impact exercise is highly advisable if you plan – as you should – to
still be exercising in your nineties. With respect to resistance training, there is growing evidence that this can promote glucose tolerance and insulin sensitivity, just as aerobic activity can. In the elderly, resistance exercise can have a really outstanding impact both on strength and muscle mass. (The elderly often lose substantial amounts of lean mass – this is known as “sarcopenia”, and it impairs insulin sensitivity, control of body fat, and of course physical capacity.) Arguably, resistance training is much more important for 70-year-olds than for 20-year-olds - though you’d be hard-pressed to guess this when you visit your local gym! Dr. William Evans, a pioneer in this field, aptly remarks that “there is no pharmacological intervention that holds a greater promise of improving health and promoting independence in the elderly than does exercise.”

With respect to supplementation, I maintain that it is rather ridiculous for us to expect that any natural diet, no matter how carefully and insightfully planned, can provide the optimally health-protective amounts of all essential and non-essential nutrients, phytochemicals, and food factors. For a few nutrients, optimal intakes simply cannot be feasibly or reliably achieved from natural diets – vitamin D, for an example. For others, while it may be possible to obtain an appropriate intake from natural foods, it may be a bit rash to assume that your dietary choices invariably supply this amount – particularly since the content and availability of soil minerals varies widely, and since our foods are not always prepared in a way that best preserves nutrient content. And, as Dr. Roger Williams liked to stress, biochemical individuality implies that, owing to genetic quirks influencing absorption or transport, you may need a bit more of a certain nutrient than other people might. With respect to protective phytochemicals, it really isn’t realistic to expect that we will eat enough broccoli, tomatoes, spinach, green tea, etc. to insure a consistently high intake of the key phytochemicals they provide – supplementation can insure this consistency while increasing your total intake of these protective factors. For all of these reasons, I maintain that a rational supplementation program should be a key component of a health-protective lifestyle. If you want to maximize your chances for a long, vigorous, healthy life, you need to eat right, exercise right – and supplement right!

The foundation of your supplementation program should be a good “nutrition insurance formula”, which provides at least adequate daily amounts of the essential vitamins and minerals. (A proviso is that, since excess iron stores may pose a health risk, it may be wise to choose an iron-free supplement unless you are at risk for iron deficiency.) The common one-per-day vitamin-mineral pill which many Americans take is an example of such a formula. More elaborate multiple-tablet formulations can provide higher intakes of certain crucial vitamins and minerals. It is appropriate to complement such a formula with additional supplements providing protective nutrients and phytochemicals not standardly provided in insurance formulas.

Arguably, a low-fat, whole-food vegan diet gives you an excellent chance to achieve ample intakes of most micronutrients – a much better chance than you would have with the fatty, over-refined foods consumed by most Americans. Nonetheless, as we have noted, a vegan diet is devoid of vitamin B12 and vitamin D, and possibly sub-optimal in
calcium – nutrients which are readily supplied by an insurance formula. Since such a diet lacks the long-chain omega-3 fats found in fish, an enriched fish oil supplement is advisable for vegans. In regions of the world where soil selenium is low (such as in many parts of Europe), a vegan diet tends to be a poorer source of this crucial nutrient than omnivore diets are\textsuperscript{1095} – so vegans would be wise to obtain selenium from supplements. A further consideration is that diets high in fiber and low in fat often do not promote optimal absorption of certain minerals and fat-soluble nutrients – nutritional supplementation can compensate for this problem.

(Lest I be accused of hypocrisy for questioning the ecological practicality of high-flesh diets while recommending that everyone use fish oil omega-3s, I will note that it should be technically feasible to derive these protective oils from unicellular sources – after all, the omega-3 fats in fish derive ultimately from marine algae.\textsuperscript{1096} In fact, a commercial source of unicellular DHA is currently available – although it is more expensive than fish oil omega-3; perhaps further technical advances will make unicellular omega-3 a practical alternative. Terrestrial sources of omega-3 should also be considered; although the alpha-linolenic acid found bountifully in flaxseed has limited health benefit compared to the longer-chain omega-3s found in fish oil, its metabolite stearidonic acid appears to share many of the protective properties of fish oil.\textsuperscript{1097-1100} and is produced by a wild weed known as Echium.\textsuperscript{1101} Theoretically, flax itself could produce ample amounts of stearidonic acid if it were genetically modified to express the enzyme delta-6-desaturase, the catalyst for the conversion of alpha-linolenic acid to stearidonic acid. Ecologically-aware scientists should devote much further attention to these issues.)

Certain nutrients, supplied by many animal-derived foods but not plant products, play physiologically-essential vitamin-like cofactor roles in metabolism, but are not considered nutritionally essential since our own bodies can make them. Nonetheless, tissue levels of these nutrients tend to be higher in omnivores than in vegetarians. These nutrients, which have been dubbed “carninutrients”, include carnitine, creatine, and taurine.\textsuperscript{1102} Sub-optimal taurine status may be responsible for the fact that the platelets (clotting cells) of vegetarians tend to aggregate (clot) more readily than those of omnivores – one of the few respects in which vegetarians don’t have an edge when it comes to vascular health.\textsuperscript{1102} Since creatine promotes strength and neuroprotection, carnitine is a catalyst for fat burning, and taurine has anti-inflammatory/antioxidant effects, carminutrient supplementation may be appropriate for vegans who wish to optimize their health and physiological capacities.

Recently, Oasis of Hope Hospital has developed a cutting-edge program of functional foods and nutraceutical supplements intended to promote optimal health, and emphasizing a comprehensive strategy known as “full-spectrum antioxidant therapy”. This regimen, which includes ample intakes of spirulina and flavanol-rich cocoa powder, is described in the new monograph \textit{The Oasis Executive Health Program} - please refer to this treatise for my current views regarding the potential benefits of supplemental nutrition. The strategies suggested in this new book are completely consistent with the dietary advice provided here. For more comprehensive information on nutritional supplements, I refer the interested reader to what is now arguably the most credible and
encycledic source of information on supplemental nutrition, the *Physician’s Desk Reference on Nutritional Supplements* by Dr. Sheldon Hendler, now in its second edition. Dr. Hendler is a remarkably diligent and insightful biomedical scholar whose analyses of the nutrition literature are both scientifically critical and yet highly appreciative of the health-protective potential of supplemental nutrition. (And I’d say these nice things about him even if he weren’t a longtime close friend!)

Finally, you should be aware that, no matter how carefully you plan your lifestyle, there is nothing that you can do (short of dying!) that will provide you with absolute protection from cancer. We are all gradually accumulating mutations in our body’s cells, and, if we live long enough, sooner or later an errant cell will survive to generate a cancer. (In this respect, cancer can be differentiated from certain other disorders – such as coronary disease and type 2 diabetes – which, except perhaps in a few individuals with really horrible genes, are truly unnecessary in a properly fed population.) Fortunately, some of the most common types of cancer are often susceptible to early detection, and, if caught early enough, can often be cured surgically. So follow your doctor’s guidance in regard to regular screening programs that can detect colon, prostate, breast, and uterine cancer, and any other screening measures that might be warranted in your case.

There has been some consternation in the macrobiotic vegan community occasioned by the fact that macrobiotics do in fact sometimes develop cancer; perhaps their guru had left the impression that such a diet confers mystical protective powers – rather like the “impenetrable shield” that certain toothpastes were alleged to provide in bygone TV advertising. In fact, the best that any diet and lifestyle can hope to do is *postpone* the onset of a major cancer (and even then, some unfortunates will experience cancer at a relatively early age). The hope is that you can postpone your date with cancer to such an advanced age that something else will almost certainly get you first; but there are no guarantees. The key point is: don’t get complacent – avail yourself of your doctor’s talent for spotting cancer at an early stage when it may still be curable.

Occasional monitoring of vascular or other risk factors is also advisable, just in case your healthful lifestyle fails to cope adequately with an unfavorable genetic inheritance – or you are less than completely compliant with your own best intentions. Your doctor can keep you apprised of your blood pressure, blood sugar, and standard blood fat risk factors.

**Slowing the Aging Process**

So far, I have had very little to say about aging per se, although I’ve had much to say about the diseases that can make old age miserable and short. But rodent studies show that it is at least theoretically feasible to slow the aging process itself. When rats are fed 30-40% fewer calories than they ordinarily would eat by choice, both their average and *maximal* longevity increases. An increase in average longevity is not necessarily a major achievement – preventing or slowing the onset of certain diseases can achieve that. But if humans had a magic pill that – say – prevented all vascular disease and cancer, the chances of their living beyond 120 years of age would still be negligible; in effect, 120 is
the maximal lifespan of humans. As we pass the century mark, we simply become too physiologically frail in too many ways to last much longer. So we won’t get past the 120 barrier unless we find a way to slow the aging process itself – which is what caloric restriction does in rodents. At any given advanced age, calorically restricted rats are simply more physiologically youthful – smarter, leaner, more active, more capable of fending off infections – than rats of comparable age who have been “pigging out” all their lives. The aging process, in which the maximal physiological capacity of the body’s organs gradually but inexorably declines, is literally in slow motion in rats that are underfed.

The catch is that underfed rats are hungry rats – and few humans would conciously choose to go hungry all their lives, or would be capable of abstaining when ample food is available. So caloric restriction is not likely to have much practical utility for slowing human aging.

However, certain genetic mutations have also been shown to increase lifespan in mice – by up to 60% - and these mutant mice may help us both to better understand how caloric restriction promotes longevity, and how humans might practically prolong their lifespans.

These long-lived mutant mice are all characterized by reduced growth hormone (GH) activity. In some of these strains, the pituitary’s production of GH is greatly diminished; in another strain, the GH receptor doesn’t function right. The result, in all cases, is that the liver makes very subnormal amounts of our old friend IGF-I. And perhaps you will recall that IGF-I activity is also substantially diminished by caloric restriction.

There is another dietary trick that you can play on rodents to increase their lifespans – feed them diets that are low in one specific essential amino acids. Feeding rats diets that are low in either methionine or tryptophan, while allowing them as many calories as they want, increases their maximal lifespan. Of course, a diet that is low in one or more essential amino acids can markedly decrease the liver’s production of IGF-I. Vegan diets of moderate protein content tend to be rather low in methionine; perhaps a methionine-restricted vegan diet may represent a practical strategy for modest life prolongation in humans.

Another strategy which delays aging in rodents – and protects the brain from neurotoxins – is alternate-day fasting, which has proved protective even when total calorie intake doesn’t fall owing to compensatory overconsumption on feeding days. It has been suggested that the “mini-fast with exercise” strategy, recommended for weight control, might represent a practical avenue for achieving such protection in humans. Alternate-day caloric restriction is also being studied as a potentially feasible life-extension technique.

Could IGF-I be a crucial pacesetter for the aging process? Breeds of dogs and strains of rats have characteristic longevities that differ a good deal. In general, the larger the breed of dog, the shorter its lifespan; the same thing holds for rat strains.
surprisingly, the IGF-I levels of dog breeds or rat strains tend to correlate directly with their adult weight. In other words, the lower the IGF-I level, the longer the lifespan – precisely what one would expect if IGF-I regulates the pace of aging.

Although comparable findings aren’t yet available in humans, epidemiological analyses do suggest that, barring malnutrition, people who are shorter and lighter tend to outlive people who are taller and heavier. And people who are taller and heavier tend to have higher levels and/or activity of IGF-I – that’s why they are tall and heavy. I recall hearing that the average lifespan of massive NFL players is about 55 years – I’m not sure how accurate this is, but it doesn’t surprise me. So the take-home lesson is this: while the large hunks may get the babes, skinny little wimps live longer!

A growing number of scientists who specialize in aging – gerontologists – are coming around to the view that IGF-I activity may indeed be a determinant of the rate of the aging process. In the section on breast cancer, we saw that IGF-I is a key signal for the onset of sexual maturity in teenagers – which explains why girls usually don’t get their periods until age 17 in rural quasi-vegan societies, while the overfed young ladies in this country often reach that milestone by age 12! In effect, IGF-I is signalling that enough calories, and protein and stored fat are available to support a healthy pregnancy. If IGF-I has such a crucial role in regulating this important developmental milestone, isn’t it reasonable to suspect that it could play a comparable role later in life?

We have already discussed how a low-fat, low-glycemic index vegan diet can lower your risk for cancer and inflammatory disorders by keeping IGF-I activity relatively low. It may well be that this strategy also modestly retards the aging process. Ancillary strategies which can lower daily insulin secretion – such as exercise training, supplemental chromium, or taking vinegar or glucomannan with meals – or that decrease the liver’s production of IGF-I – such as flax lignans or oral estrogen replacement – may have complementary value in this regard. With the exception of estrogen’s adverse impact on risk for estrogen-responsive tumors, these measures are all commendable from the standpoint of preventing major diseases. Wouldn’t it be a wonderful bonus if they also retarded the aging process?

To better explain what I mean by slowing aging, let’s pretend that you have an identical twin. Let’s further assume that you elect to follow a low-fat, whole-food vegan diet for most or all of your life, and to avail yourself of exercise and other healthful measures that keep IGF-I activity relatively low, whereas your twin becomes a slothful omnivore who has a real predilection for double cheeseburgers. And let’s assume that, despite your twin’s questionable health habits, you both manage to make it to age 80 without experiencing any major diseases. At that time, I predict that you would be leaner, more mentally agile, more physically spry, and possibly even younger looking than your twin – even though you were both putatively healthy. Of course, the greater likelihood is that, by age 80, your twin’s physical status would have been compromised not only by the aging process, but also by vascular disease or possibly cancer – if your twin were still alive at all!
So, if you want to be able to really enjoy life at 80, or 90, or even 100, a low IGF-I lifestyle may be just what the doctor ordered!

**Compressing Morbidity**

There is not, and will never be, a diet that can repeal mortality. Which is a good thing – we have a moral obligation to “shuffle off this moral coil” so that future generations will have room!

In the preceding discussion, I have attempted to show that it should be theoretically feasible, by lifelong use of an optimally health-protective diet, assisted at times by various ancillary strategies, to virtually totally prevent coronary disease, obesity, diabetes, hypertension, stroke, and possibly even senile dementia, and to substantially postpone the onset of (if not outright prevent) most of the prominent types of cancer. Under these circumstances, infection and trauma would likely become the chief causes of death.

Such is the case in Kitava, where there is essentially no vascular disease or diabetes, and apparently very little cancer. Infection and trauma cause most deaths; in some extremely elderly people, death comes for no apparent reason (an arrhythmia in a worn-out heart?) While Dr. Lindeberg was visiting Kitava, the only fatality was a 70-year-old man who fell out of a palm tree! (Take-home lesson: do not climb trees after age 70. In further illustration of which: noted vegan George Bernard Shaw died at age 94 – razor-sharp until the end - after falling out of an apple tree he had climbed in pursuit of apples!)

If an aged person dies of infection or trauma (or dies in his sleep for no discernible reason), he will probably do so fairly quickly. In other words, unless there are other illnesses that precipitated the infection or trauma, he won’t be in the hospital or on elaborate therapies for months or years prior to his death. If he has avoided vascular disease and dementia, and kept his bones and joints in reasonably decent shape, chances are that he will remain reasonably independent and mentally and physically active up until his death. In other words, old age won’t be the chamber of horrors that it all too often proves to be for less fortunate people. This strategy of remaining reasonably healthy to a ripe old age and then dying quickly of infection, trauma, or “old age”, is known as “compression of morbidity”. This is the type of life – and death – that sane people should wish for. I maintain that by eating right, exercising right, supplementing right, and taking advantage of your doctor’s ability to detect some illnesses at an early curable stage, you have a reasonably good chance to achieve this outcome, using foods, nutrients, and other resources that are available now.

Consider the alternatives: Being a cardiac cripple for years, unable to function normally, repeatedly requiring surgery, and in constant fear of “the big one”. Suffering strokes that leave you physically or mentally impaired – perhaps barely able to talk – during your last sad years of life. Becoming demented and spending years totally dependent, while your loved ones suffer emotional havoc and ruinous expense, or have to devote their lives to your care. Developing cancer and fighting it for years with the trauma of chemotherapy,
surgery, or radiation, until the cancer progresses and your body wastes away while you cope with chronic pain. Becoming diabetic and eventually going blind, or needing regular kidney dialysis, or suffering constant nerve pain, or requiring a below-knee-amputation because your leg circulation is shutting down and you’ve developed gangrene – all as a prelude to your premature and ultimately fatal heart disease.

Have I convinced you that staying healthy is very, very smart?!

Striving to compress your morbidity is also patriotic. With medical costs continuing to skyrocket, particularly in the U.S., the growing number of elderly Americans who require several decades of medical care for chronic metabolic ailments are imposing a near-intolerable financial burden on our society – a burden that is likely only to get larger and larger. Arguably, doing whatever you can to stay healthy for as long as you can is a lot more meaningfully patriotic that waving a flag. (Furthermore, as we’ll discuss below, choosing a vegan diet can also benefit our planet’s ecology, help to conserve finite resources, and help alleviate world hunger. It’s the way to be a “global patriot”!)

An Overview of Dietary Options

Of course, people who are attempting to learn how to stay healthy may be hard-pressed to retain their sanity amid the welter of mutually-contradictory dietary advice that the media dish out. One day we are told that a high-carbohydrate, low-fat diet is the key to cardiovascular health – the next, we are told that monounsaturated fat is the real key, and that carbohydrates can be bad for you. Then the advocates of high-protein diets weigh in with their advice – which is promptly denounced by both the olive oil advocates and the Pritikinists. Meanwhile, the conventional wisdom that people should cut back on salt is confounded by breathless media reports that low-salt diets may increase risk for heart attack – which are swept back under the rug when the latest DASH study confirms the utility of salt restriction for controlling blood pressure. What next? Is it any wonder that a high proportion of Americans now state that they are sick of all this dietary advice, and plan to eat whatever they like?

Part of the purpose of this essay has been to put these contending views in perspective. By and large, the scientific advocates of these seemingly irreconcilable views are honorable, intelligent scientists who can cite some rational arguments in support of their positions. And, as contrasted to the self-destructive diets currently being practiced by most Americans – or even the half-bright recommendations of American Heart Association - the low-fat whole-food vegan, the high-monounsaturate, and the high-protein approaches all can produce demonstrable benefits. And a large part of the reason for this is that all of these regimens lower daily insulin secretion. Which suggests to me that keeping insulin secretion low must have major merit as a health strategy.

If you can keep insulin secretion low while simultaneously minimizing fat intake, you are likely to achieve greater leanness and better insulin sensitivity. If you can keep insulin secretion low while avoiding animal protein, you are likely to reduce your cancer risk. In a nutshell, that’s why I prefer the very-low-fat vegan approach. Furthermore, the fact
that much of the Third World has been – at least until lately – following a diet of this sort gives us some very direct insight into its likely health consequences. In these cultures, coronary disease, obesity, and diabetes are virtually absent, while the incidence of “western” cancers and of many autoimmune disorders is substantially reduced. In those cultures that, in addition, avoid salt, hypertension, stroke, and possibly even dementia are rare. While high-monounsaturate and high-protein approaches may indeed have some health advantages relative to current American diets, there is simply no reason to believe that they could confer the full range of health benefits enjoyed by quasi-vegan cultures.

Thus, although I respect the many scientists who advocate alternative views, the low-fat whole-food vegan strategy seems the most protective overall and is my current choice. The burden of proof is on those who advocate high protein or high monounsaturate intakes to demonstrate that their approaches have comparably versatile protective activity. Nonetheless, I intend to keep an open mind on this issue and take careful note of future relevant research. One thing that should be quite clear is that the impact of dietary choices on health can be incredibly complex, and no one yet has all the answers!

All the same, I’m confident that your health will be well served by following the recommendations offered above, even if future research proves them to be less than ideal in some respects. As compared to the salty, fatty, high-glycemic-index omnivore diet that most Americans now ingest, the diet which I recommend will doubtless give you a far better chance to achieve a ripe old age in vigorous good health.

The Ecological and Ethical Consequences of Omnivore Diets

The intent of this book has been to define dietary patterns that are most conducive to your own long-term health. In other words, I’ve focussed on showing you where your self-interest lies; whether you choose to accept this advice, or anyone else’s advice, to protect your own health, is – and by rights should be - entirely your own decision.

However, now that there are 6 billion other people inhabiting the planet, your food choices also have ecological and ethical ramifications that are potentially profound - your own health is by no means the only consideration at stake. The Western practice of including animal products in nearly every meal – now being emulated by the emerging middle classes throughout Asia and elsewhere – is incredibly wasteful of our limited resources of fossil fuels, fresh water, and arable land. It is the chief factor behind the progressive destruction of the world’s rain forests and the remarkably diverse species which they shelter. It is directly responsible for the rape of our oceans, now being overfished to the point of ecological devastation. The high energy cost of producing farm animals contributes importantly to the carbon dioxide pollution that drives global warming – and the methane produced by ruminant livestock (most notably cattle) also makes a significant contribution in this regard. The massive quantities of waste generated by modern factory farms represent a continual threat to the health and purity of our rivers and water supplies. Overgrazing by ruminant livestock is stripping bare much of the world’s grasslands – and the wildlife indigenous to these areas are often purposely slaughtered, as they are viewed as threats to cattle (or, more bluntly, the profits of
cattlemen). But, perhaps most importantly, a progressively higher percentage of the world’s arable land is being devoted to growing crops intended to feed farm animals – at a time when hunger-related disease kills approximately 25,000 children per day worldwide. This situation is now being exacerbated by the fact that newly emerging middle classes in China and India are choosing to emulate Westerners in their high consumption of flesh foods – and by growing use of arable land for biofuels production. This situation recently has triggered major jumps in grain prices that have led to food riots and increased starvation throughout the Third World. In effect, livestock breeders are now outbidding poor humans for the available grain supply. The dollars that you elect to spend on hamburgers, steaks, fried chicken, eggs, and dairy products set in motion economic forces which effectively insure that a higher and higher proportion of the world’s poor will suffer from chronic malnutrition – or outright starvation.

If you’d like to read a devastating critique of the ecological and ethical consequences of our omnivore diet, you can’t do better than to read Part III of John Robbins’ important new book, *The Food Revolution*. Let me cite just a few of the eye-opening statistics which the author has compiled: According to specialists at the University of California Agriculture Extension, it takes 25 gallons of water to raise a pound of wheat, 49 gallons to raise a pound of apples, and 5,214 gallons to raise a pound of beef; Robbins drives this point home further by calculating that “you’d save more water by not eating a pound of California beef than you would by not showering for an entire year”. Much of the water required, directly or indirectly, for livestock production derives from non-renewable aquifers that are now in danger of depletion – most notably the crucial Ogallala aquifer in the central U.S.

The livestock industry is also immensely inefficient with respect to fuel consumption. Producing 1 calorie of protein from soybeans or wheat requires the expenditure of 2-3 calories of fossil fuel – whereas producing a calorie of beef protein requires the use of 54 calories of fuel. The energy-intensity of livestock production entails not only a wastage of limited energy resources, but also a considerable increase in carbon dioxide production. The Union of Concerned Scientists has concluded that “the two most damaging things residents of this country do to our climate are drive vehicles that get poor gas mileage and eat beef.”

It takes about 12-16 pounds of grain to produce a pound of saleable beef. That’s why 70% of the grain grown in the U.S. is fed to livestock – an amount that would be sufficient to feed 1.4 billion people. In Russia, 75% of the grain consumed is now devoted to livestock; in Brazil – where about two-thirds of the population is said to suffer from malnutrition – the figure is 50%. Over the last couple of decades, the proportion of domestic grain fed to farm animals has risen from 8% to 26% in China, from 1% to 30% in Thailand, and from 10% to 36% in Egypt. Many countries which formerly were self-sufficient or grain exporters, are now perilously dependent on grain imports; if U.S. grain production fell suddenly owing to climactic conditions or aquifer depletion, devastating worldwide famine could result. Throughout the Third World, the desire to reap greater profits is motivating landowners to expel peasants from subsistence farms, so that the land can be devoted to growing crops intended for livestock. Largely as a result, the
number of landless peasants in Central America has risen fourfold since 1960. I’m not so naïve as to believe that increased availability of arable land for human food production would automatically end hunger in the Third World – social justice and control of explosive population growth would also be required – but adequate land availability is a *sine qua non* if there is to be any hope of attaining this goal.

Meanwhile, total grain production per capita has fallen worldwide since 1984, owing to soil depletion and the exhaustion of aquifers – trends markedly accelerated by the massive demands on crop production imposed by the livestock industry – as well as continuing human population growth. Increasingly, push is coming to shove – it is estimated that over 1 billion humans are now chronically malnourished. Indulgence in animal product-rich diets by the world’s expanding middle class is not an extravagance that humans can afford at this juncture in history.

Unfortunately, we can’t turn to the oceans for salvation. The United Nations has estimated that “11 of the 15 major oceanic fishing grounds had gone into serious decline as a result of overfishing” – largely a result of sophisticated new trawling methods which literally strip the oceans bare. Worldwide annually, 16 kg of fish are caught per person – whereas 200 kg of other marine life netted along with the edible fish are simply discarded. Half of the world’s fish catch is devoted to the feeding of livestock, and fish farms are also consuming a growing proportion of this catch.

There are also ethical issues related to the care of farm animals. In the interests of economic efficiency, a high proportion of the world’s farm animals are now being raised in “factory farms”. These entail the confinement of animals in incredibly tight holding pens throughout their entire lives. You can forget about carefree livestock frolicking in verdant glades – modern “farm” animals often effectively spend their lives in fetid straightjackets. John Robbins devotes Part II of his book to this grim story – I frankly don’t have the stomach to read it. Whether or not you have moral qualms about the slaughter of animals for food – bear in mind that most farm animals would never have existed at all if it weren’t for human intervention – it is certainly morally indefensible to raise animals in grossly inhumane circumstances just so that a pork chop will be a bit cheaper.

So think about these issues next time you hear some pundit holding forth on the alleged health benefits of high-protein or “paleolithic” diets. And remember that, when you choose to indulge in a diet rich in animal products, you aren’t just making a private decision that affects your health - you effectively are voting to starve children, to deplete our limited water and energy resources, to ravage the planet’s oceans and grasslands, to accelerate global warming, and to subject farm animals to unspeakable cruelty. Of course, that wouldn’t be your *intent* – drunk drivers don’t intend to kill their victims – but that would be the net consequence of your actions.

But let’s look at the positive side – isn’t it astonishingly fortunate that the type of plant-based diet that is most suited to preserve your longterm health, is also the type of diet that is most consistent with a healthy environment, preservation of biodiversity, conservation
of our limited resources, prevention of global warming, and food sufficiency for the earth’s whole population?!

If you want to be ecologically and ethically responsible but you simply aren’t willing to go all the way to veganism, then try cutting way back on animal product usage – make much greater use of beans and soy products – and choose poultry (preferably free-range) or wild fish rather than beef or other large livestock. Although the raising of chickens places a far greater burden on limited resources than does growing crops for direct human consumption, it is a lot less offensive in this regard than the beef industry. And the poultry industry, while it poses some water pollution issues, at least can’t be blamed for the destruction of the ecology of much of the American West, or the ongoing loss of Amazonian rain forests. Above all, try to avoid beef and dairy products. There are about 1 billion cattle on the earth now, and they tend to be better fed than large segments of the human population!

Finally, a word on the ethical aspects of veganism. People who are unwilling to promote the death or abusive treatment of animals, are also unlikely to accept war or terrorism as instruments of political policy. It is no accident that the one avowed vegan member of the U.S. Congress, Dennis Kucinich, has proposed the formation of a Department of Peace dedicated to the resolution of disputes, nationally and worldwide, in a non-violent manner. The great Emperor Ashoka of India, who converted to Buddhism after experiencing the carnage triggered by his own war of conquest, was noted not only for espousing vegetarianism and establishing animal hospitals throughout his kingdom, but also for promoting the concept of “ahimsa” (non-violence), banning the needless killing of any living being, eliminating slavery, preaching universal religious tolerance and conversion by rational argument only, working in many ways to promote the welfare of his subjects and of people in neighboring lands, encouraging the development of herbal medicine, planting trees throughout his empire, and turning former enemies into well-respected allies. His era was remembered as a Golden Age in India’s history, and H.G. Wells commented that, whereas most “exalted majesties” “have shone for a brief moment, and as quickly disappeared…Ashoka shines and shines brightly like a bright star, even unto this day.” Clearly, ethical veganism has the potential not only to promote the welfare of animals, but of all humans as well. (All the more reason why the world needs a bountiful plant-derived source of stearidonic acid – so that humans can enjoy optimal omega-3 status without exploiting fish!)

For Further Reading

There are a number of well-written, informative books currently available that can give you further information on the health benefits of diets that are vegan, low in glycemic index, and/or low in salt. Many of these books provide recipes that, to a greater or lesser degree, are compatible with the dietary advice I have offered; you can use your own creativity to modify them when warranted.

There is a growing literature on the health impacts of veganism; I must confess that I certainly haven’t looked at all of it. If you are looking for biomedical information that is
both credible and meaty, the best books I’ve found are by Dr. Neal Barnard, who is the President of the Physicians Committee for Responsible Medicine (PCRM), and a highly articulate advocate for vegan diets and the ethical treatment of animals. Although he has written a number of fine books, my personal favorite is *Eat Right, Live Longer*; a more concise and more recent book along similar lines is *Food for Life: How the New Four Food Groups Can Save Your Life*. His latest work is *Dr. Neal Barnard's Program for Reversing Diabetes: The Scientifically Proven System for Reversing Diabetes without Drugs*. Under Dr. Barnard’s leadership, the PCRM has distinguished itself by promulgating the new four food groups: fruits, vegetables, legumes, and whole grains.

If you would like to explore the ethical and ecological aspects of veganism, you can’t do better than the writings of John Robbins. His first book, *Diet for a New America*, is, by common consent, the classic work of the American vegan movement; he has followed that up with *The Food Revolution*, which provides even deeper insight into the devastating global consequences of omnivore diets. His latest book, *Healthy at 100*, focuses on centenarian cultures to explain how a vegan diet, complemented by regular physical activity and a positive emotional outlook fostered by respect for the elderly, can optimize healthspan. Robbins is a fascinating character; heir to the Baskin-Robbins ice cream fortune, his growing intellectual and ethical conviction that animal-based diets entail the needless suffering of our fellow creatures and are disastrous for both the ecology and our health, led him to turn his back on his heritage and become an ardent and poetic champion of veganism. Although Robbins doesn’t have the formal biomedical training that some vegan advocates do, his discussion of pertinent scientific evidence is usually surprisingly credible and scholarly. (However, I must confess that I don’t share his fashionably negative view of genetic engineering.)

If weight loss is of particular interest to you, Dr. Dean Ornish’s *Eat More, Weigh Less* and Dr. Barnard’s more recent *Turn off the Fat Genes* can give your further insight into the weight loss benefits of low-fat, whole-food vegan diets. The Pritikin Clinics now stress the advantages of low-caloric-density whole foods for achieving weight loss, as outlined in Robert Pritikin’s *The Pritikin Principle – The Calorie Density Solution*.

If your interest is more focused on heart disease, *Dr. Dean Ornish’s Program for Reversing Heart Disease* is an excellent choice. The amazing story of Dr. Caldwell Esselstyn’s 12-year clinical study with diet-treated heart patients is described in his *Prevent and Reverse Heart Disease*. On the diabetes front, Dr. Julian Whitaker, formerly chief clinician at the Pritikin Clinics, and now director of the Whitaker Wellness Institute, offers good advice in *Reversing Diabetes*.

If you would like to learn more about the health impacts of dietary glycemic index and have access to extensive tabular information about the glycemic indices of specific foods, your best bet is *The Glucose Revolution*, by Dr. Thomas Wolever and colleagues. The authors of this book are highly credible health scientists who have done much of the formal scientific work establishing the importance of the glycemic index concept. (Note that many of the recipes in this book are not vegan and are a bit higher in fat or salt than I would approve.)
There are only a couple of recent books on health implications of dietary salt. *Salt, Diet, and Health*, by British hypertension experts Drs. Graham MacGregor and Hugh DeWardener, provides the deepest insight into the connection between salted diets and high blood pressure, and also provides a history of man’s use of salt. *The Salt Solution*, by Herb Boynton and colleagues, examines the broader health implications of salted diets while placing more emphasis on the importance of potassium-rich foods. (Another *mea culpa*: I am a co-author of this volume.)

Dr. John McDougall is a vegan practicing physician whose writings reflect the considerable success he has had in treating heart disease and obesity with a diet-based approach for over two decades. Although I can’t agree with his rather puritanical views on alcohol and caffeine, in other respects his practical recommendations are very concordant with mine. He has authored several worthy books outlining the rationale and results of his vegan health program, but his greatest contribution may be the cookbooks he has co-authored with his wife Mary – in particular, *The New McDougall Cookbook*, currently available through amazon.com. The recipes have been honed over years of practical experience, and many are delicious. All of them are vegan, virtually all are quite low in fat (except for a few sauces to be used sparingly), and salt per se is never added. High-salt condiments are occasionally called for – such as soy sauce; you can use reduced-salt soy sauce and, if the total salt intake would still be higher than desirable, you can cut back the amount or try doing without it. (Remember though that even the Kitavans get *some* salt in their diets!) Almost all ingredients used qualify as whole foods, although they aren’t always structurally intact – for example whole wheat flour, a high-insulin-response food, is used in a few recipes (albeit flours are called for far less frequently than in the typical American diet). All in all, this is a masterful piece of work of great practical value, and it is easy to modify some recipes slightly if you want to be more stringent about salt.

Dr. Colin Campbell’s work – particularly his China Health Project - has had a major impact on my thinking and on that of the vegan movement. He describes this project – and its provocative practical conclusions - in his outstanding new book, *The China Study: Startling Implications for Diet, Weight Loss, and Long-term Health*.

Dr. Ornish has also made a signal contribution to our understanding of the central role which emotions play in health – see his book *Survival and Love* for a survey of the relevant scientific literature on this often neglected topic. Negative emotions appear to increase risk, in some cases quite markedly, for a wide range of adverse health outcomes. Dr. Ornish has pioneered the inclusion of stress management techniques in the treatment of heart disease and cancer.

I apologize to other worthy authors whose relevant works may have escaped my fallible attention.
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The NutriGuard Learn to Burn Leanness Program

A Rational Strategy for Achieving and Maintaining Leanness

The basic “game plan” of the Learn to Burn leanness program is to maximize the rate at which your body burns stored fat, while consuming a diet that is low in fat. Unlike rodents, cows, and many other animals, humans rarely synthesize meaningful amounts of fat. There are exceptions – gorging on food for days at a time, in great excess of caloric requirements, will evoke fat synthesis, and chronic consumption of a fat-free diet will also lead to adaptive increase in fat production. But, under ordinary circumstances, the fat in our bodies derives primarily from dietary fat. This implies that if we boost our daily rate of fat burning, while keeping our dietary fat intake low, we should gradually drain our body’s fat stores until we gradually equilibrate at a much leaner physique. (Obviously, we can’t continue losing fat indefinitely, as our rate of fat burning will decline as our fat stores are depleted, until it equals our rate of fat ingestion and equilibrium is achieved.)
Weight control experts unanimously endorse regular aerobic exercise as a crucial key to achieving and maintaining leanness. This evidently reflects the fact that sustained exercise of moderate intensity promotes fat burning. However, relatively little attention has been paid to the metabolic context in which exercise is done – which can have a major impact on the rate of fat burning that is achieved. The most novel aspect of the Learn to Burn program is that it maximizes exercise-induced fat burning by nesting it within a daily “mini-fast”; exercising in fasting metabolism – when insulin levels are low - promotes selective use of stored fat, and fasting for several hours after the exercise prolongs the exercise-induced fat burn. When you do subsequently eat, low-fat, carb-rich food choices, moderate in glycemic index, promote satiety by re-filling your glycogen stores and promoting even blood glucose levels – but they won’t replace the fat you have just burned. This evidently implies a daily negative fat balance that over weeks and months will make you much leaner – and you’ll stay leaner as long as you stick with the program. This “mini-fast with exercise” strategy was first introduced by nutritional scientist Mark McCarty – now a consultant at Oasis of Hope Hospital – who has used it himself for over ten years, was generalized by Austrian physician Dr. Babak Bahadori in his “7 Step Program” for weight control, that has become popular in central Europe.

The Learn to Burn program provides sound advice on healthful low-fat food choices that will help you control your appetite and burn fat throughout the day. Low-glycemic-index carbohydrate foods are recommended, as they tend to promote moderate and even insulin levels. High insulin levels evoked by high-glycemic-index carbs bring fat burning to a screeching halt, and the wild swings of blood sugar often triggered by such foods can induce rebound hunger. So the Learn to Burn program stresses food choices that are both low in fat and glycemic index.

Rapid fat oxidation in the liver sends satiety signals to the brain, and also generates ketone bodies that can be used by the central nervous system as fuel. This mechanism is largely responsible for the hunger suppression that is typically achieved after days of fasting or severe carbohydrate restriction. But ordinarily it takes several days for the liver to adapt to rapid fat burning. That’s why the Learn to Burn program makes use of special dietary supplements that are intended to accelerate the liver’s adaptation to fasting metabolism, so that the daily mini-fasts are readily tolerated.

Now that you understand the simple and logical concepts that underlie the Learn to Burn leanness program, here’s how to do it:

1. **Aerobic Exercise during a “Mini-Fast”**
   - **Pick the time of day that is convenient and most congenial for you to exercise:** in the morning, mid-day, or evening.
   - **If you choose to exercise in the morning,** you should skip breakfast – no meals or snacks in the morning until lunch.
   - **If you choose to exercise in mid-day,** you should skip lunch – no meals or snacks between breakfast and dinner. (Some call this the “Ramadan option”, since during the month of Ramadan, Moslems fast between sun-up and sun-down.)
- **If you choose to exercise in the evening**, you should eat a very early dinner – by five, or as soon as you can get home from work. You should avoid any meals or snacks in the evening after your dinner. Your exercise should be done at least 2 hours after dinner, when your insulin levels have returned to a fasting level.

- **You can drink plenty of non-caloric fluids** during your mini-fasts; this will keep you hydrated for successful exercise, while also aiding hunger control.

- **You will be surprised by how well you feel during these mini-fasts.** When you exercise in line with this strategy, you will be in vigorous fat-burning metabolism for about 12 hours per day. This accelerated fat metabolism will enable you to feel energetic and hunger-free during your mini-fasts – particularly if you use the supplements, described below, that help the liver adapt rapidly to fasting metabolism. Think of it this way: you aren’t starving yourself - by burning stored fat, you are finally “eating” food calories that you ingested weeks or months ago.

- **You can be flexible** in your choice of time for exercise. For example, if you prefer to exercise in the evening during weekdays, but would prefer to go out to dinner and evening entertainment on the weekend, you can switch your weekend exercise to mid-day. Or if you ordinarily exercise at noon, but one day you wish to attend a luncheon, you can use the morning exercise option that day.

- **For your exercise, do a moderate intensity workout** (50-60% VO2max), preferably one in which you support your own weight (i.e. brisk walking, jog-walking, stair-climbing, elliptical gliders); if knee problems make this difficult, use a stationary bike. If you are exercising at the right moderate intensity, you should be able to carry on a normal conversation at the same time; high intensity exercise burns primarily stored carbohydrate rather than fat.

- After you’ve had a chance to improve your muscle tone and cardiovascular fitness, gradually increase the length of your exercise to **at least 40 minutes per session**. However, if you are very out of shape, it is prudent to start with a short duration that is comfortable for you, and then gradually increase it as your body adapts to exercise. **Don’t overdo it and injure or severely exhaust yourself** – the point is to establish a regimen that you can maintain on a regular basis.

- **Try to work out at least five times weekly.** (Once you reach your target weight, you may be able to reduce your exercise frequency a bit, but don’t exercise less than three times a week.) On your non-exercise days, eat whenever you desire – but try to follow the food guidelines outlined below.

- Prolonged moderate-intensity exercise suppresses insulin, boosts glucagon, mobilizes fat, and thus is ideal for fat burning; increased capacity for fat burning will persist for several hours after exercise if you don’t raise insulin by ingesting carbohydrate during this time.

- The people who get the best and most rapid results with HT are usually those who do the most exercise! **Exercise is crucial to achieving optimal benefit from HT.**

2. **Proper Food Choices: Low Fat/Low Glycemic Index**

- Food choices in HT are intended to **keep daily insulin secretion relatively low** and support glucagon production (aiding fat burning), while **minimizing fat intake**.
- **Avoid fatty foods** - fat should be no more than 15% of daily calories. No fatty meats, dairy products, or egg yolks. Minimize the use of oils in cooking, scan the labels of convenience foods for fat content, and be very sparing in your consumption of avocados and olives.

- A moderate daily intake of nuts or nut butters (no more than one ounce daily) is permissible, in light of evidence that these foods are markedly protective for vascular health. (Avoid nut butters that have added hydrogenated oils.)

- A very-low-fat diet, especially if accompanied by regular exercise, tends to decrease your daily insulin production by improving your body’s sensitivity to insulin – and of course also puts less new fat in your fat cells.

- The **starchy foods** in your regular diet should have a relatively low glycemic index (that is, they should increase blood sugar gradually and moderately, to avoid excessive insulin secretion or – in diabetics – hyperglycemia.)

- Pasta, rice (preferably brown, long-grain and parboiled), beans, corn (whole corn or popcorn), bulgur wheat, barley, “old-fashioned” (not instant) oatmeal, and whole fruit are recommendable. **Avoid wheat flour products** (excepting pasta, sourdough and whole-wheat pita bread), baked or mashed potatoes (boiled are better), and sugar-loaded soft drinks (diet sodas are fine).

- **Beans** – particularly home-cooked beans – have an especially low glycemic index and are great for weight control. Eat beans frequently.

- Eat foods in a **physically intact natural form** when feasible – the glycemic index of whole-kernel grains is lower than that of flours. “Flourless” breads made from sprouted grains (e.g. “Ezekiel”) or intact grain kernels are far preferable to other breads.

- A table of glycemic indices – such as you can find in the popular book *The Glucose Revolution* - can help you choose appropriate starchy foods.

- Vegetables, vegetable juices, and whole fruit are strongly recommended – they are great for your long-term health as well as for weight control. Try to eat at least one large salad every day. Whole fruit is the best dessert or snack. These foods are rich in potassium - crucial for the health of your vasculature and bones – as well as protective phytonutrients.

- With respect to **protein** intake, certain strategies in this regard can help you to minimize your insulin secretion and/or better control appetite. Both protein-rich diets and moderate-protein vegan diets can work well with the Learn to Burn program. Long-term vegans tend to be leaner than either lacto-ovo vegetarians or omnivores - possibly because their diet is quite low in the saturated fat palmitate, which may adversely affect fat burning. Vegans typically are at low risk for coronary heart disease, diabetes, and certain cancers, and vegan diets are highly desirable from an ecological standpoint. On the other hand, high-protein diets often also work well for weight control, presumably because they aid hunger control and keep daily insulin levels fairly low. If you choose a high-protein approach, make sure to choose foods that are relatively low in fat – especially saturated fat – and eat plenty of fruits and vegetables to offset the metabolic acidifying effect of a high protein intake (bad for your bones).

- **Vinegar** can lower the glycemic index of a meal. Use vinegar as a salad dressing. You can also make a tasty “vinegar cocktail” by mixing a tablespoon of apple cider
vinegar with about 2/3 cup of water, and adding a packet of artificial sweetener; take this just prior to or with your meal.

- **Alcoholic beverages**, in moderation (1 or 2 drinks daily), are permissible, and indeed may benefit your health if you can drink responsibly. However, alcohol in excess will bring fat burning to a halt, so never ingest alcohol during your mini-fasts. Remarkably, studies show that women who drink moderately but regularly are less likely to gain weight than are non-drinkers. (Sorry guys – this doesn’t work for you!)

- **Eat enough to satisfy your hunger – no calorie counting!** Make sure that you eat enough carbohydrate so that you have adequate fuel for your subsequent aerobic exercise. But use your common sense and your self-restraint – gluttony will sabotage any weight-loss program!

### 3. Supplementation for Easy Fasting

- To make the daily mini-fasts more comfortable, the Learn to Burn program offers supplements featuring the following food factors and metabolites:
  - The availability of **carnitine** is rate-limiting for fat burning in the liver, and the liver gradually accumulates carnitine during the first days of a fast to boost its capacity for fat burning. By supplementing with carnitine, this adaptation can be achieved much more quickly.
  - The natural fruit acid **hydroxycitrate**, by inhibiting the enzyme citrate lyase, helps to boost the activity of another enzyme, carnitine palmitoyltransferase, that works with carnitine to promote hepatic fat burning.
  - The natural metabolite **pyruvate**, perhaps because it boosts the production of Krebs cycle intermediates required for complete fat oxidation, appears to enhance the rate of fat loss achievable with carnitine/hydroxycitrate supplementation. In rodents studies, supplemental pyruvate has induced a marked thermogenic effect – enabling fat to be converted efficiently to CO2 and heat.
  - A recent study shows that **chromium picolinate** promotes appetite control in people who have carbohydrate cravings.
  - The supplements **Brindall Trim**, **Lipidox**, and **Lipidox Powder** can be used with the Learn to Burn program. Brindall Trim features carnitine, hydroxycitrate, and chromium picolinate; Lipidox and Lipidox Powder provide these nutrients as well as an ample dose of pyruvate.
  - Take a full dose of the supplement of your choice prior to exercise; you can take a further dose during the post-exercise fasting phase if you wish.

- Note that these supplements do not involve drugs or even herbs – just nutrients, natural metabolites and food factors, all of which appear to be health-protective.

- This supplementation is not recommended for pregnant women, who in any case should not attempt to lose weight except as instructed by their doctors.

**Does it Work?** During a twelve-week open trial of the Learn to Burn program, overweight volunteers from the staff of Oasis of Hope Hospital lost an average of 25% of their initial fat mass. One gung-ho participant lost 46 pounds of fat in this time, while
eating two meals a day and not counting calories – and even ladies in their forties or fifties, doing walking exercise, achieved substantial fat losses.

**You don’t need to do everything right all the time!** If you can manage to exercise right, eat right, and supplement right the majority of the time, you can expect good results.

**Fat Loss vs.Weight Loss:** Note that in the first few weeks of the Learn to Burn program, lean mass often increases while body fat decreases. That means that *body fat will decrease faster than body weight*, so that your initial rate of *weight* loss may not be too impressive. After a month or more of the program, lean mass begins to decline as well, and weight loss tends to catch up with fat loss. So don’t obsess about your scale weight when beginning this program. To evaluate your progress, it is best to have your *body composition* assessed periodically (by a personal trainer or physician) so that you can quantify your *fat* loss.

**A caution to diabetics:** When using the Learn to Burn program, monitor your blood sugar control as instructed by your doctor, and modify your medication usage as needed, with your doctor’s assistance. If injectable insulin or sulfonylurea drugs are active during a mini-fast and exercise, a hypoglycemic reaction could result – so work out a proper medication schedule with your doctor. **Physician supervision is mandatory for diabetics!**

That’s all there is to it! No drugs, no prolonged starvation, no calorie counting, no avoidance of health-promoting carb-rich foods. Nothing but fat-burning exercise, health-protective food choices, and safe, natural supplements. Remember:

*The Learn to Burn program is a healthful, sustainable lifestyle – not a quick-fix gimmick*

**Resources:** *Brindall Trim, Lipidox, and Lipidox Powder*, priced at a moderate mark-up over cost, are available by mail-order from: **NutriGuard Research**, 1051 Hermes Ave., Encinitas, CA. Call (800)433-2402; outside the U.S. or Canada, you can call 760-942-3223. Or order via the web: nutriguard.com.