Harvard says time to end the low-fat myth

Fats and Cholesterol: Out with the Bad, In with the Good

“Eat a low-fat, low-cholesterol diet” was the mantra for healthful eating for decades. Touted as a way to lose weight and prevent or control heart disease and other chronic conditions, millions of people have followed (or, more likely, tried to follow) this advice. Seeing a tremendous marketing opportunity, food companies re-engineered thousands of foods to be lower in fat or fat free, often increasing the salt, sugar, or refined grains in these foods to make up for lost flavor and texture.

Well it’s time to end the low-fat myth. The low-fat approach to eating may have made a difference for the occasional individual, but as a nation it hasn’t helped us control weight or become healthier. In the 1960s, fats and oils supplied Americans with about 45 percent of calories; (1) about 13 percent of adults were obese and under 1 percent had type 2 diabetes, a serious weight-related condition. (2,3) Today, Americans take in less fat, getting about 33 percent of calories from fats and oils; (4) yet 34 percent of adults are obese and 11 percent have diabetes, most with type 2 diabetes. (5,6)

Why hasn’t cutting fat from the diet paid off as expected? Detailed research—much of it done at Harvard—shows that the total amount of fat in the diet isn’t really linked with weight or disease. What really matters is the type of fat and the total calories in the diet. (7-15) Bad fats, meaning trans and saturated fats, increase the risk for certain diseases. Good fats, meaning monounsaturated and polyunsaturated fats, do just the opposite. They are good for the heart and most other parts of the body.

Much more at the link. This is pretty remarkable, I think, as Harvard has been in the lead in propagating the “low-fat myth”. Truth is busting out all over, and just like the fall of Communism, we could see the low-fat myth collapse in short order.

High carbohydrate intake nearly
Relative intake of macronutrients impacts risk of mild cognitive impairment or dementia.

High caloric intake has been associated with an increased risk of cognitive impairment. Total caloric intake is determined by the calories derived from macronutrients. The objective of the study was to investigate the association between percent of daily energy (calories) from macronutrients and incident mild cognitive impairment (MCI) or dementia. Participants were a population-based prospective cohort of elderly persons who were followed over a median 3.7 years (interquartile range, 2.5-3.9) of follow-up. At baseline and every 15 months, participants (median age, 79.5 years) were evaluated using the Clinical Dementia Rating scale, a neurological evaluation, and neuropsychological testing for a diagnosis of MCI, normal cognition, or dementia. Participants also completed a 128-item food-frequency questionnaire at baseline; total daily caloric and macronutrient intakes were calculated using an established database. The percent of total daily energy from protein (% protein), carbohydrate (% carbohydrate), and total fat (% fat) was computed. Among 937 subjects who were cognitively normal at baseline, 200 developed incident MCI or dementia. The risk of MCI or dementia (hazard ratio, [95% confidence interval]) was elevated in subjects with high % carbohydrate (upper quartile: 1.89 [1.17-3.06]; p for trend = 0.004), but was reduced in subjects with high % fat (upper quartile: 0.56 [0.34-0.91]; p for trend = 0.03), and high % protein (upper quartile 0.79 [0.52-1.20]; p for trend = 0.03) in the fully adjusted models. A dietary pattern with relatively high caloric intake from carbohydrates and low caloric intake from fat and proteins may increase the risk of MCI or dementia in elderly persons.

Neuroprotective and disease-modifying effects of the ketogenic diet

Neuroprotective and disease-modifying effects of the ketogenic diet.

Gasior M, Rogawski MA, Hartman AL.
Abstract
The ketogenic diet has been in clinical use for over 80 years, primarily for the symptomatic treatment of epilepsy. A recent clinical study has raised the possibility that exposure to the ketogenic diet may confer long-lasting therapeutic benefits for patients with epilepsy. Moreover, there is evidence from uncontrolled clinical trials and studies in animal models that the ketogenic diet can provide symptomatic and disease-modifying activity in a broad range of neurodegenerative disorders including Alzheimer’s disease and Parkinson’s disease, and may also be protective in traumatic brain injury and stroke. These observations are supported by studies in animal models and isolated cells that show that ketone bodies, especially beta-hydroxybutyrate, confer neuroprotection against diverse types of cellular injury. This review summarizes the experimental, epidemiological and clinical evidence indicating that the ketogenic diet could have beneficial effects in a broad range of brain disorders characterized by the death of neurons. Although the mechanisms are not yet well defined, it is plausible that neuroprotection results from enhanced neuronal energy reserves, which improve the ability of neurons to resist metabolic challenges, and possibly through other actions including antioxidant and anti-inflammatory effects. As the underlying mechanisms become better understood, it will be possible to develop alternative strategies that produce similar or even improved therapeutic effects without the need for exposure to an unpalatable and unhealthy, high-fat diet.

Effects of dietary glycemic index on brain regions related to reward and craving

Conclusions: Compared with an isocaloric low-GI meal, a high-GI meal decreased plasma glucose, increased hunger, and selectively stimulated brain regions associated with reward and craving in the late postprandial period, which is a time with special significance
to eating behavior at the next meal.

Moral of the story: if you want to stay lean, avoid refined carbohydrates.

Also, interestingly enough, this study appears to provide support for both the insulin and reward/addiction models of obesity.

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**Chocolate improves mitochondrial function and increases mitochondrial biogenesis**

*Alterations in skeletal muscle indicators of mitochondrial structure and biogenesis in patients with type 2 diabetes and heart failure: effects of epicatechin rich cocoa.*

(-)-Epicatechin (Epi), a flavanol in cacao stimulates mitochondrial volume and cristae density and protein markers of skeletal muscle (SkM) mitochondrial biogenesis in mice. Type 2 diabetes mellitus (DM2) and heart failure (HF) are diseases associated with defects in SkM mitochondrial structure/function. A study was implemented to assess perturbations and to determine the effects of Epi-rich cocoa in SkM mitochondrial structure and mediators of biogenesis. Five patients with DM2 and stage II/III HF consumed dark chocolate and a beverage containing approximately 100 mg of Epi per day for 3 months. We assessed changes in protein and/or activity levels of oxidative phosphorylation proteins, porin, mitofilin, nNOS, nitric oxide, cGMP, SIRT1, PGC1α, Tfam, and mitochondria volume and cristae abundance by electron microscopy from SkM. Apparent major losses in normal mitochondria structure were observed before treatment. Epi-rich cocoa increased protein and/or activity of mediators of biogenesis and cristae abundance while not changing mitochondrial volume density. Epi-rich cocoa treatment improves SkM mitochondrial structure and in an orchestrated manner, increases molecular markers of mitochondrial biogenesis resulting in enhanced cristae density. Future controlled studies are warranted using Epi-rich cocoa (or pure Epi) to translate improved mitochondrial structure into enhanced cardiac and/or SkM muscle function.

Another recent paper found similar effects in mice: **(-)-Epicatechin enhances fatigue resistance and oxidative capacity in mouse muscle**
Non-technical summary

During exercise, skeletal muscle performance depends in great part on the use of aerobic metabolism to supply the energetic demand of contractions. Endurance training increases the muscle aerobic capacity, which is not only associated with enhanced exercise performance, but also with a decreased risk of cardiovascular and metabolic diseases. Recently, it has been shown that regular use of small doses of dark chocolate may result in similar health benefits to exercise training. We show here that mice fed for 15 days with (--)-epicatechin (present in dark chocolate) had improved exercise performance accompanied by: (1) an increased number of capillaries in the hindlimb muscle; and (2) an increased amount of muscle mitochondria as well as signalling for mitochondrial biogenesis. These results suggest that (--)-epicatechin increases the capacity for muscle aerobic metabolism, thereby delaying the onset of fatigue. These findings may have potential application for clinical populations experiencing muscle fatigue.

What causes heart disease

From an interview with Fred Kummerow, a 98-year-old working scientist at the University of Illinois:

[Q.] What would you consider to be the biggest achievement of your career to date?

The biggest achievement of my career to date has been the publication of my article online in the January 2013 issue of The American Journal of Cardiovascular Disease [3]. In this publication, I described my findings; namely, that atherosclerosis in modern human beings is based on the biochemistry, composition and structure of three of the five phospholipids in the cell membrane of the coronary arteries. My findings indicate fried foods, powdered egg yolk, excess vegetable oils, partially hydrogenated vegetable oils and cigarette smoke as the greatest culprits in heart disease. Fried foods and powdered food substitutes are dietary sources of oxysterols, which alter the phospholipid membranes of our arteries in ways that increase the deposition of calcium, a key hallmark of atherosclerosis. Consumption of excess polyunsaturated fats stimulates the formation of oxysterols within the human body. Cigarette smoke and trans fats from partially hydrogenated vegetable oils interfere with fatty acid metabolism, leading to the interruption of blood flow, a major contributor to heart attacks and sudden death. In my opinion, many
of these factors have been largely ignored by the medical establishment, which has focused instead on using drugs to lower cholesterol levels. I hope my recent publication in The American Journal of Cardiovascular Disease changes this and provides the answer for proper dietary advice.

Will calorie restriction work in humans?

Calorie Restriction (CR) without malnutrition slows aging and increases average and maximal lifespan in simple model organisms and rodents. In rhesus monkeys long-term CR reduces the incidence of type 2 diabetes, cardiovascular disease and cancer, and protects against age-associated sarcopenia and neurodegeneration. However, so far CR significantly increased average lifespan only in the Wisconsin, but not in the NIA monkey study. Differences in diet composition and study design between the 2 on-going trials may explain the discrepancies in survival and disease. Nevertheless, many of the metabolic and hormonal adaptations that are typical of the long-lived CR rodents did not occur in either the NIA or WNPRC CR monkeys. Whether or not CR will extend lifespan in humans is not yet known, but accumulating data indicate that moderate CR with adequate nutrition has a powerful protective effect against obesity, type 2 diabetes, inflammation, hypertension, cardiovascular disease and reduces metabolic risk factors associated with cancer. Moreover, CR in human beings improves markers of cardiovascular aging, and rejuvenates the skeletal muscle transcriptional profile. More studies are needed to understand the interactions between CR, diet composition, exercise, and other environmental and psychological factors on metabolic and molecular pathways that regulate health and longevity.

It’s been said (sorry, link not handy) that CR won’t work in humans because the way CR works is by a partitioning of biological maintenance and repair between reproductive and somatic systems. Humans devote far less of their maintenance and repair to their reproduction than do smaller mammals such as mice. Therefore it’s postulated that the CR effect would be small to negligible in humans. However, given that CR “improves markers of cardiovascular aging, and rejuvenates the skeletal muscle transcriptional profile”, it looks like CR does provide substantial benefit to humans. Furthermore, intermittent or alternate-day fasting appears to provide just as
much benefit as CR, and they’re much easier to implement.

Update: Found the link: **Caloric restriction does not enhance longevity in all species and is unlikely to do so in humans.**

Calorie restriction is known to increase lifespan in many but not all species and may perhaps not do so in humans. Exceptions to life extension have been identified in the laboratory and others are known in nature. **Given the variety of physiological responses to variation in food supply that are possible, evolutionary life history theory indicates that an increased investment in maintenance in response to resource shortage will not always be the strategy that maximises Darwinian fitness.** Additionally, for the well-studied species in which life extension is observed, there is considerable variation in the response. This suggests that it is not an ancient ancestral response, which has been conserved across the species range. Although calorie restriction does not increase lifespan in all species, it remains a fascinating and valuable tool to study ageing at the whole organism level.

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**Diet and depression**

**Association of Western and traditional diets with depression and anxiety in women.**

**OBJECTIVE:**
Key biological factors that influence the development of depression are modified by diet. This study examined the extent to which the high-prevalence mental disorders are related to habitual diet in 1,046 women ages 20-93 years randomly selected from the population.

**METHOD:**
A diet quality score was derived from answers to a food frequency questionnaire, and a factor analysis identified habitual dietary patterns. The 12-item General Health Questionnaire (GHQ-12) was used to measure psychological symptoms, and a structured clinical interview was used to assess current depressive and anxiety disorders.

**RESULTS:**
After adjustments for age, socioeconomic status, education, and health behaviors, a “traditional” dietary pattern characterized by vegetables, fruit, meat, fish, and whole grains was associated with lower odds for major depression or dysthymia and for anxiety
disorders. A “western” diet of processed or fried foods, refined grains, sugary products, and beer was associated with a higher GHQ-12 score. There was also an inverse association between diet quality score and GHQ-12 score that was not confounded by age, socioeconomic status, education, or other health behaviors.

CONCLUSIONS:
These results demonstrate an association between habitual diet quality and the high-prevalence mental disorders, although reverse causality and confounding cannot be ruled out as explanations. Further prospective studies are warranted.

Obviously, the issue of reverse causality is important because people with a tendency to depression and anxiety are likely not to care much about their diet. Higher IQ and more conscientious people make sure that what they eat is healthy. Nevertheless, the fact that junk food makes one feel literally ill leads me to believe that the association is one of causality.

Evolution and diseases of afluence

Lifestyle and nutritional imbalances associated with Western diseases: causes and consequences of chronic systemic low-grade inflammation in an evolutionary context

In this review, we focus on lifestyle changes, especially dietary habits, that are at the basis of chronic systemic low grade inflammation, insulin resistance and Western diseases. Our sensitivity to develop insulin resistance traces back to our rapid brain growth in the past 2.5 million years. An inflammatory reaction jeopardizes the high glucose needs of our brain, causing various adaptations, including insulin resistance, functional reallocation of energy-rich nutrients and changing serum lipoprotein composition. The latter aims at redistribution of lipids, modulation of the immune reaction, and active inhibition of reverse cholesterol transport for damage repair. With the advent of the agricultural and industrial revolutions, we have introduced numerous false inflammatory triggers in our lifestyle, driving us to a state of chronic systemic low grade inflammation that eventually leads to typically Western diseases via an evolutionary conserved interaction between our immune system and metabolism. The underlying triggers are an abnormal dietary composition and microbial flora, insufficient physical activity and sleep, chronic stress and environmental pollution. The disturbance of our inflammatory/anti-inflammatory balance is illustrated by dietary fatty acids and antioxidants. The current decrease in years without
chronic disease is rather due to “nurture” than “nature,” since less than 5% of the typically Western diseases are primary attributable to genetic factors. Resolution of the conflict between environment and our ancient genome might be the only effective manner for “healthy aging,” and to achieve this we might have to return to the lifestyle of the Paleolithic era as translated to the 21st century culture.

**Don’t eat tofu if you want a functioning brain**

**Brain Aging and Midlife Tofu Consumption**

Objective: To examine associations of midlife tofu consumption with brain function and structural changes in late life.

Methods: The design utilized surviving participants of a longitudinal study established in 1965 for research on heart disease, stroke, and cancer. Information on consumption of selected foods was available from standardized interviews conducted 1965–1967 and 1971–1974. A 4-level composite intake index defined “low-low” consumption as fewer than two servings of tofu per week in 1965 and no tofu in the prior week in 1971. Men who reported two or more servings per week at both interviews were defined as “high-high” consumers. Intermediate or less consistent “low” and “high” consumption levels were also defined. Cognitive functioning was tested at the 1991–1993 examination, when participants were aged 71 to 93 years (n=3734). Brain atrophy was assessed using neuroimage (n=574) and autopsy (n=290) information. Cognitive function data were also analyzed for wives of a sample of study participants (n=502) who had been living with the participants at the time of their dietary interviews.

Results: Poor cognitive test performance, enlargement of ventricles and low brain weight were each significantly and independently associated with higher midlife tofu consumption. A similar association of midlife tofu intake with poor late life cognitive test scores was also observed among wives of cohort members, using the husband’s answers to food frequency questions as proxy for the wife’s consumption. Statistically significant associations were consistently demonstrated in linear and logistic multivariate regression models. Odds ratios comparing endpoints among “high-high” with “low-low” consumers were mostly in the range of 1.6 to 2.0.
Conclusions: In this population, higher midlife tofu consumption was independently associated with indicators of cognitive impairment and brain atrophy in late life.

Geez, those with high tofu consumption were up to twice as likely to have low cognitive performance. That tofu stuff really messes you up!

The elevated prevalence of cognitive impairment we observed in the highest compared with the lowest midlife consumers of tofu was roughly of the magnitude as would be caused by a four year difference in age or a three year difference in education. In this study population, 20% to 25% of the burden of cognitive impairment appears attributable to midlife tofu consumption—an effect size of enormous public health importance, yet not readily discernable in comparisons across populations of diverse education, occupation, age distribution and genetic composition, especially when studied using different methods.

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**Ketogenic diet and bipolar disorder**

**The ketogenic diet for type II bipolar disorder**

Successful mood stabilizing treatments reduce intracellular sodium in an activity-dependent manner. This can also be achieved with acidification of the blood, as is the case with the ketogenic diet. Two women with type II bipolar disorder were able to maintain ketosis for prolonged periods of time (2 and 3 years, respectively). Both experienced mood stabilization that exceeded that achieved with medication; experienced a significant subjective improvement that was distinctly related to ketosis; and tolerated the diet well. There were no significant adverse effects in either case. These cases demonstrate that the ketogenic diet is a potentially sustainable option for mood stabilization in type II bipolar illness. They also support the hypothesis that acidic plasma may stabilize mood, perhaps by reducing intracellular sodium and calcium.
Victorians had robust health

How the Mid-Victorians Worked, Ate and Died

Analysis of the mid-Victorian period in the U.K. reveals that life expectancy at age 5 was as good or better than exists today, and the incidence of degenerative disease was 10% of ours. Their levels of physical activity and hence calorific intakes were approximately twice ours. They had relatively little access to alcohol and tobacco; and due to their correspondingly high intake of fruits, whole grains, oily fish and vegetables, they consumed levels of micro- and phytonutrients at approximately ten times the levels considered normal today. This paper relates the nutritional status of the mid-Victorians to their freedom from degenerative disease; and extrapolates recommendations for the cost-effective improvement of public health today.

Risk of depression and processed foods

Dietary pattern and depressive symptoms in middle age.

BACKGROUND:
Studies of diet and depression have focused primarily on individual nutrients.

AIMS:
To examine the association between dietary patterns and depression using an overall diet approach.

METHOD:
Analyses were carried on data from 3486 participants (26.2% women, mean age 55.6 years) from the Whitehall II prospective cohort, in which two dietary patterns were identified: ‘whole food’ (heavily loaded by vegetables, fruits and fish) and ‘processed food’ (heavily loaded by sweetened desserts, fried food, processed meat, refined grains and high-fat dairy products). Self-reported depression was assessed 5 years later using the Center for Epidemiologic Studies – Depression (CES-D) scale.

RESULTS:
After adjusting for potential confounders, participants in the highest tertile of the whole food pattern had lower odds of CES-D
depression (OR = 0.74, 95% CI 0.56-0.99) than those in the lowest tertile. In contrast, high consumption of processed food was associated with an increased odds of CES-D depression (OR = 1.58, 95% CI 1.11-2.23).

CONCLUSIONS:
In middle-aged participants, a processed food dietary pattern is a risk factor for CES-D depression 5 years later, whereas a whole food pattern is protective.

I wonder how much of this is confounded by IQ and conscientiousness, i.e. a healthy user effect. Those more prone to depression may be less intelligent, less conscientious, and less apt to care about whether their food is healthy or not. Nevertheless, a healthy diet is likely to supply the brain with proper nutrition, so a link is plausible. From the full paper:

**Plausible mechanisms**
There are several plausible mechanisms underlying the association we observed between the whole food pattern and self-reported depression. The high content of antioxidants in fruits and vegetables could be protective, as some studies have shown higher antioxidant levels to be associated with lower depression risk. The potential protective effect of the whole food diet could also come from folate found in large amounts in some cruciferous vegetables (broccoli, cabbage, Brussels sprouts), leafy vegetables (spinach), other green vegetables (asparagus, avocado) and dried legumes (lentil, chickpea). It has been suggested that low levels of folate might increase the risk of depression and result in reduced availability of S-adenosylmethionine, a universal methyl donor, which can result in impaired formation of myelin, neurotransmitters and membrane phospholipids. In line with this, a large study of Finnish middle-aged men found an increased risk of depression in participants with lower dietary intake of folate. However, some studies have found no association between folate levels and depression in elderly populations. A further plausible mechanism involves fish consumption. The whole food dietary pattern includes a high intake of fish and there is evidence suggesting an association between high levels of fish consumption and low incidence of depression. This protective effect of fish consumption has been traditionally attributed to its high content of long-chain ω-3 polyunsaturated fatty acids. These are a major component of neuron membranes and have vascular and anti-inflammatory properties. Evidence of this association has come from observational studies that have shown an inverse association between ω-3 fatty acid levels measured in blood or estimated from intake and depression. Finally, it is also possible that the protective effect of diet on depression comes from the cumulative and synergic effect of nutrients from different sources of foods rather than from the effect of one isolated nutrient.
The deleterious effect of processed food on self-reported depression is a novel finding. A previous cross-sectional study has shown a correlation between sugar consumption and the annual rate of depression in six countries. Furthermore, the processed food diet is very close to the 'Western' pattern defined in the American population, which has been shown to be associated with higher risk of coronary heart disease and inflammation. Several lines of investigation have suggested that coronary heart disease and inflammation are involved in the pathogenesis of depression. However, further studies are needed to improve our understanding of the association between processed food intake, the inflammation process and depression.

Why is celiac disease so common in Ireland?

Celiac disease (gluten sensitive enteropathy) is a condition affecting the small bowel, characterized by permanent intolerance to dietary gluten, and giving rise to varying degrees of malabsorption and diarrhea. With the advent of sensitive screening tests, the condition is being increasingly diagnosed. Celiac disease is more common in the Irish and in those of Irish descent. Simoons (1978, 1981) hypothesized that the present-day prevalence of celiac disease across Europe is related to the interaction between genetic gradients, largely determined by the advance of agriculture, and historical patterns of cereal ingestion. This essay examines Simoons’ hypothesis as it relates to Ireland, reviews the ethnic and genetic mix of those living on the island of Ireland and aspects of Irish dietary history, and considers how these factors may have combined to result in a high frequency of celiac disease.

Sugar consumption and diabetes

The Relationship of Sugar to Population-Level Diabetes Prevalence: An Econometric Analysis of Repeated Cross-Sectional Data
While experimental and observational studies suggest that sugar intake is associated with the development of type 2 diabetes, independent of its role in obesity, it is unclear whether alterations in sugar intake can account for differences in diabetes prevalence among overall populations. Using econometric models of repeated cross-sectional data on diabetes and nutritional components of food from 175 countries, we found that every 150 kcal/person/day increase in sugar availability (about one can of soda/day) was associated with increased diabetes prevalence by 1.1% (p <0.001) after testing for potential selection biases and controlling for other food types (including fibers, meats, fruits, oils, cereals), total calories, overweight and obesity, period-effects, and several socioeconomic variables such as aging, urbanization and income. No other food types yielded significant individual associations with diabetes prevalence after controlling for obesity and other confounders. The impact of sugar on diabetes was independent of sedentary behavior and alcohol use, and the effect was modified but not confounded by obesity or overweight. Duration and degree of sugar exposure correlated significantly with diabetes prevalence in a dose-dependent manner, while declines in sugar exposure correlated with significant subsequent declines in diabetes rates independently of other socioeconomic, dietary and obesity prevalence changes. Differences in sugar availability statistically explain variations in diabetes prevalence rates at a population level that are not explained by physical activity, overweight or obesity.

**Neurologic and Psychiatric Manifestations of Celiac Disease and Gluten Sensitivity**

Celiac Disease (CD) is an immune-mediated disease dependent on gluten (a protein present in wheat, rye or barley) that occurs in about 1% of the population and is generally characterized by gastrointestinal complaints. More recently the understanding and knowledge of gluten sensitivity (GS), has emerged as an illness distinct from celiac disease with an estimated prevalence 6 times that of CD. Gluten sensitive people do not have villous atrophy or antibodies that are present in celiac disease, but rather they can
Both CD and GS may present with a variety of neurologic and psychiatric co-morbidities, however, extraintestinal symptoms may be the prime presentation in those with GS. However, gluten sensitivity remains undertreated and underrecognized as a contributing factor to psychiatric and neurologic manifestations. This review focuses on neurologic and psychiatric manifestations implicated with gluten sensitivity, reviews the emergence of gluten sensitivity distinct from celiac disease, and summarizes the potential mechanisms related to this immune reaction.

Low serum cholesterol, suicide, and violence

Engelberg H.
Source
Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, California.

Abstract
Primary prevention trials which have shown that the lowering of serum cholesterol concentrations in middle-aged subjects by diet, drugs, or both leads to a decrease in coronary heart disease have also reported an increase in deaths due to suicide or violence. There has been no adequate explanation for this association. I have reviewed the relevant published work and describe a physiological mechanism that might account for this curious finding. One of the functions of serotonin in the central nervous system is the suppression of harmful behavioural impulses. When mouse brain synaptosomal membrane cholesterol is increased there is a pronounced increase in the number of serotonin receptors. Low membrane cholesterol decreases the number of serotonin receptors. Since membrane cholesterol exchanges freely with cholesterol in the surrounding medium, a lowered serum cholesterol concentration may contribute to a decrease in brain serotonin, with poorer suppression of aggressive behaviour.

The putative connection between low serum cholesterol and violence, including suicide, has spawned a large literature – one that I’m not wholly familiar with – so I can’t say how well the connection has held up. There are a number of papers disputing it, for example this one, which concludes that statin
drugs do not result in mood changes. (Whether one can trust any research on statins is another question.)

Another paper, Cholesterol and violence: is there a connection?, found that observational studies (including cohort, case-control, and cross-sectional studies) consistently showed increased violent death and violent behaviors in persons with low cholesterol levels. Some meta-analyses of randomized trials found excess violent deaths in men without heart disease who were randomly assigned to receive cholesterol-lowering therapy. Experimental studies showed increased violent behaviors in monkeys assigned to low-cholesterol diets. Human and animal research indicates that low or lowered cholesterol levels may reduce central serotonin activity, which in turn is causally linked to violent behaviors. Many trials support a significant relation between low or lowered cholesterol levels and violence (P < 0.001). CONCLUSIONS: A significant association between low or lowered cholesterol levels and violence is found across many types of studies. Data on this association conform to Hill's criteria for a causal association. Concerns about increased risk for violent outcomes should figure in risk-benefit analyses for cholesterol screening and treatment.

By the way, the author of the first-linked paper above, Hyman Engelberg, was Marilyn Monroe’s personal physician.

Alterations in mood after changing to a low-fat diet.

The effects on mood of reducing dietary fat while keeping the energy constant were examined in ten male and ten female healthy volunteers aged between 20 and 37 years. Each volunteer consumed a diet containing 41% energy as fat for 1 month. For the second month half of the subjects changed to a low-fat diet (25% energy from fat) and the remainder continued to eat the diet containing 41% energy from fat. Changes in mood and blood lipid concentrations were assessed before, during, and at the end of the study. Profile of mood states (POMS) ratings of anger-hostility significantly increased in the intervention group after 1 month on the low-fat diet, while during the same period there was a slight decline in anger-hostility in the control subjects (group F 6.72; df 1.14; P =
Tension-anxiety ratings declined in the control group consuming the higher fat diet but did not change in the group consuming the low-fat diet (group F 6.34; df 1.14; P = 0.025). There was a decline in fasting concentrations of HDL-cholesterol after the low-fat diet and a small increase in subjects consuming the medium-fat diet (group F 4.96; df 1.12; P = 0.046), but no significant changes in concentrations of total serum cholesterol, LDL-cholesterol or triacylglycerol were observed. The results suggest that a change in dietary fat content from 41 to 25% energy may have adverse effects on mood. The alterations in mood appear to be unrelated to changes in fasting plasma cholesterol concentrations.

Speaks for itself. The brain and nervous system are composed largely of fat, and if you deprive them of it, mood changes result – or at any rate, that’s how I see it. It seems similar to the mood and memory changes reported as side effects to statin use, which deprives the nervous system of much of the cholesterol that it needs.