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In this issue we present the 2nd part of Professor Ware's article on the connection between dietary fats and coronary heart disease. Dr. Ware convincingly explodes the myth that a low fat, high carbohydrate diet is healthy. He also discusses good and bad eicosanoids and sheds new light on the connection between cholesterol levels and atherosclerosis. A must read!

Also in the issue we report that American researchers have found that an adequate intake of potassium is a vital ingredient in stroke prevention. This is especially true for people taking diuretics for hypertension. PC-SPES, the much touted and then reviled herbal combination for prostate cancer, has made news again with the finding that it is highly effective in preventing the initiation and progression of colon cancer. Lorenzo's oil, a mixture of oleic and euricic acids developed by the concerned parents of a boy with adrenoleukodystrophy, has been endorsed by neurologists as the standard treatment for the disease. All this and more in this our 132nd issue of IHN.

I will take this opportunity to wish you and your family all the best for the Holiday Season.

Yours in health,
Hans Larsen, Editor

December Highlights

LETTERS TO THE EDITOR

I would like to know the mercury content of canned tuna and canned salmon versus established safe levels of serum mercury. Also, is there a consensus among experts as to the relative safety and health benefits of wild versus farmed fish?

RF, USA

Editor: *The mercury level of canned tuna, according to Health Canada, is less than 0.5 ppm, the maximum allowable level. The levels in fresh and frozen tuna can be as high as 1.5 ppm. Canned salmon is also below 0.5 ppm. According to Dr. Barry Sears, author of "The Omega RX Zone", farmed salmon has a much higher content of arachidonic acid than does wild salmon. This alone would make farmed fish less healthy than wild salmon.*

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I read that coenzyme Q10 is very beneficial for those who have low ventricular ejection fraction or congestive heart problems. I discussed this with my doctors and they did not feel it to be important, but do not discourage taking it. Why the low acceptance that CoQ10 may be an important medicine?

LSW, USA

Editor: *There is quite a lot of literature on the benefits of CoQ10 supplementation in ventricular dysfunction (congestive heart failure). You can find a summary of the research in the July 2001 issue of "Pharmacotherapy"[1]. I should think the low acceptance is caused by the fact the CoQ10 is not a drug, cannot be patented, and therefore, cannot be marketed to generate exorbitant profit. L-carnitine is also an excellent supplement for congestive heart failure.*

[1] Tran, M/T., et al. Role of coenzyme Q10 in chronic heart failure, angina, and hypertension. Pharmacotherapy, Vol. 21, July 2001, pp. 797-806

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I am 75 years of age and have been diagnosed with Parkinson's disease. I recently found that there could be a link to carbon monoxide, which caused me to recall that, by accident, I passed out from carbon monoxide poisoning when I was 10 years old. The fire department gave me oxygen, but I was physically restricted for about 2 weeks. Is there any connection?

CM, USA

Editor: *Carbon monoxide poisoning often results in the development of parkinsonism. However, the time gap between exposure and symptom development is usually much shorter than 65 years and most patients probably recover within a year or two of the exposure[1].*

[1] Sohn, Y.H., et al. The brain lesion responsible for parkinsonism after carbon monoxide poisoning. Archives of Neurology, Vol. 57, August 2000, pp. 1214-18

ABSTRACTS

Potassium deficiency linked to stroke

HONOLULU, HAWAII. Several studies have observed that low potassium levels are associated with a greater mortality from stroke. Now American researchers report that the incidence of stroke also increases with low potassium levels. Their study involved 5600 men and women over the age of 65 years who were free of stroke at enrollment in 1990-93. All participants underwent a thorough medical examination at baseline, completed a food frequency questionnaire and had blood serum potassium level determined.

After 4 to 8 years of follow-up a total of 473 strokes (404 ischemic) had occurred in the group. The researchers found that participants on diuretics had a 2.5 times increased risk of stroke if their serum level of potassium was below 4.1 mEq/L. The highest number of potassium-deficient individuals (71.9 per cent) was found among those taking thiazide diuretics. Using potassium-sparing diuretics lowered the risk slightly while taking potassium supplements with the diuretic brought it down to 1.4 times the risk of diuretic users with a serum potassium level above 4.0 mEq/L. Participants who were not taking diuretics were found to have a 50 per cent (1.5 times) increased risk of stroke if their dietary potassium intake was less than 2340 mg/day. Participants who were on diuretics and also had low potassium levels and atrial fibrillation had a 10 times greater risk of stroke than did diuretic users in normal sinus rhythm whose potassium levels were above 4.0 mEq/L.

Green, D.M., et al. Serum potassium level and dietary potassium intake as risk factors for stroke. **Neurology**, *Vol. 59, August 2002, pp. 314-20*

Levine, Steven R. and Coull, Bruce M. Potassium depletion as a risk factor for stroke. **Neurology**, *Vol. 59, August 2002, pp. 302-03 (editorial)*

Editor's comment: This study clearly shows that an adequate potassium intake is a vital ingredient in stroke protection, especially for users of diuretics. Potassium is best obtained from the diet - tomato paste, beet greens, raisins, prunes, bananas, and sockeye salmon are all good sources.

The demise of PC-SPES

LAJOLLA, CALIFORNIA. The herbal compound, PC-SPES, was touted as an effective prostate cancer cure in the mid- to late 1990s. Many patients and alternative medicine practitioners reported excellent results with it. By the summer of 2001 reports began to appear on the Internet of possible contamination with diethylstilbestrol, a synthetic form of estrogen. The California Department of Health Services tested several lots of PC-SPES and found that they were contaminated with diethylstilbestrol and warfarin. In February 2002 the Health Services issued a warning about the product and its manufacturer, BotanicLab, voluntarily recalled it. BotanicLab went out of business in June 2002 and PC-SPES is no longer available.

Researchers at the University of California obtained several lots of PC-SPES manufactured between 1996 and 2001. They tested them and found that they, particularly the early lots, were effective in killing prostate cancer cells. They also found that the early lots were heavily contaminated with diethylstilbestrol and the anti-inflammatory drug indomethacin (Indocin). In July 1998, warfarin, an anticoagulant began to appear in the product in quantities that could affect blood clotting.

The researchers conclude that phytochemical (herbal) compounds may well have a place in the treatment of prostate cancer, but that manufacturing practices and quality control procedures need to be vastly improved before such compounds can be reliably tested in clinical trials.

Sovak, Milos, et al. Herbal composition PC-SPES for management of prostate cancer: identification of active principles. **Journal of the National Cancer Institute**, *Vol. 94, September 4, 2002, pp. 1275-81*

White, Jeffrey. PC-SPES: a lesion for future dietary supplement research. **Journal of the National Cancer Institute**, *Vol. 94, September 4, 2002, pp. 1261-63 (editorial)*

PC-SPES reborn?

LOS ANGELES, CALIFORNIA. A team of University of California (San Diego) researchers recently reported that PC-SPES, a much touted herbal remedy for prostate cancer, had been found to be heavily contaminated and had been taken off the market. Nevertheless, researchers at the UCLA Center for Human Nutrition in Los Angeles now report that they have found PC-SPES to be highly effective in preventing the initiation and progression of colon cancer. They evaluated PC-SPES *in vitro* using three different colon cancer cell lines. They found that the herbal compound caused a 95 per cent inhibition of cell proliferation in all three lines. In contrast, estradiol did not stop cell proliferation at all. Thus it is unlikely that the observed effect of PC-SPES is due to possible contamination with diethylstilbestrol, another estrogenic compound.

The researchers also evaluated PC-SPES (250 mg/kg/day) in laboratory mice genetically engineered to develop multiple tumours in the gastrointestinal tract within a few weeks after birth. They found that mice treated 5 times a week for 10 weeks with PC-SPES developed 58 per cent less tumours than did control mice. They conclude that the components of PC-SPES, either independently or in combination, act to produce a drastic reduction in tumour initiation and progression in the gastrointestinal tract.

Huerta, Sergio, et al. PC-SPES inhibits colon cancer growth in vitro and in vivo. **Cancer Research**, *Vol. 62, September 15, 2002, pp. 5204-09*

Soy products and stomach cancer

GIFU, JAPAN. Japanese researchers report that a high intake of non-fermented soy products (tofu, soybeans, soymilk, okara) reduces the risk of dying from stomach cancer. Their study involved over 30,000 people aged 35 years or older. During a 7-year period (1992-99) 121 of the study participants died from stomach cancer. The researchers found that men who consumed 112 grams/day (on average) of non-fermented soy products had half the risk of dying from stomach cancer than did men who consumed 37 grams/day (on average). This 50 per cent risk reduction held true even after adjusting for other variables known to affect stomach cancer. Women with a high daily intake of soy products (both fermented and non-fermented) also reduced

their risk by 50 per cent, but this reduction was of marginal statistical significance.

The researchers also observed that men with a high rice intake had an 81 per cent higher mortality from stomach cancer than did men with a low intake. A similar, but only marginally significant, association was found among women. They conclude that the high rice consumption in Japan may contribute to the high mortality from stomach cancer found in that country. Smoking and obesity were also found to be significant risk factors for stomach cancer death.

Nagata, C., et al. A prospective cohort study of soy product intake and stomach cancer death. **British Journal of Cancer**, *Vol. 87, July 1, 2002, pp. 31-36*

Exercise prevents glucose intolerance

BILTHOVEN, THE NETHERLANDS. There is considerable evidence that regular, vigorous exercise can help prevent type 2 diabetes. Now Dutch researchers report that activities like gardening and bicycling, when done on a regular basis, can help prevent glucose intolerance, the precursor of diabetes. Their study involved 424 men between the ages of 69 and 89 years who were known to be non-diabetic. Glucose intolerance was diagnosed if the fasting glucose reading was greater than 7 mmol/L (126 mg/dL) or the 2-hour post-load concentration was greater than 7.8 mmol/L (140 mg/dL).

The researchers found that men who engaged in at least 30 minutes of moderate-intensity physical activity every day had a 3 times lower incidence of impaired glucose tolerance than did more sedentary men. This correlation held true even after adjusting for smoking, a family history of diabetes, alcohol intake, body mass index, and dietary factors. Men who had reduced their physical activity level during the 5 years prior to the glucose test had a greater risk of being glucose intolerant than did men who had maintained their level. Bicycling and gardening were the most popular activities among the men. The researchers found no correlation between daily walking and a reduced risk of glucose intolerance, but caution that this could be because relatively few men walked regularly or because their walks were not brisk enough.

Van Dam, Rob M., et al. Physical activity and glucose tolerance in elderly men: the Zutphen Elderly study. **Medicine & Science in Sports & Exercise**, *Vol. 34, July 2002, pp. 1132-36*

New test helps predict Alzheimer's disease

CARLTON, AUSTRALIA. Alzheimer's disease is preceded by the development of a mild cognitive impairment that can appear as much as 10 years prior to Alzheimer's becoming apparent. The impairment can be detected by testing patients over a period of years. Australian researchers have just discovered that it is possible to determine the presence of mild cognitive impairment (MCI) in a single day. Their study involved 20 older people who had been tested every 6 months for 2 years and were known to have MCI. They were matched by age, gender, and education level with 40 people without MCI. The study participants completed a series of cognitive tests (CogState) on 4 occasions within a 3-hour period. The computerized tests were designed to evaluate working memory, episodic learning, attention and psychomotor speed. The researchers found that normal subjects improved their performance with each test while MCI patients did not improve or plateaued early. The test accurately predicted the presence of MCI in 80 per cent of the subjects actually diagnosed with MCI (80 per cent sensitivity) and correctly assigned participants to the normal category in 95 per cent of cases (95 per cent specificity). The researchers emphasize that the high degree of specificity is particularly important as studies have shown that 50 per cent of all people classified as having MCI during a single assessment were found not to have MCI on subsequent assessments. In other words, they just happened to have a "bad" day on the day they were tested.

Darby, D., et al. Mild cognitive impairment can be detected by multiple assessments in a single day. **Neurology**, *Vol. 59, October 2002, pp. 1042-46*

Bypass surgery and brain damage

BALTIMORE, MARYLAND. Bypass surgery (coronary artery bypass grafting) is associated with a significant risk of subsequent stroke and brain damage (encephalopathy). Researchers at the Johns Hopkins University report a stroke rate of 2.7 per cent and an encephalopathy rate of 6.9 per cent in 2711 patients who underwent bypass surgery during the period January 1, 1997 to December 31, 2000. Patients with encephalopathy (delirium, confusion, coma, and seizures) had an average hospital stay of 15.2 days and a mortality of 7.5 per cent. Patients with stroke stayed in the hospital for an average of 17.5 days and had a mortality of 22 per cent. Patients with neither of these conditions had an average stay of 6.6 days and a mortality of 1.4 per cent.

The researchers attempted to correlate the pre-operation state of the patients with their risk of surgery-induced encephalopathy or stroke. They found that the risk of encephalopathy increased with age, a history of past stroke, and the presence of hypertension, diabetes or carotid bruit (carotid artery blockage). The risk of stroke could be predicted by a history of past stroke, hypertension and diabetes. Time spent on the cardiopulmonary bypass machine during the operation was found to be another important variable. The risk of encephalopathy or stroke increased by 30 to 50 per cent for each additional 30 minutes spent on the machine.

The researchers conclude that their models may be useful when discussing the risk of bypass surgery with patients and their families. They also suggest that surgery without a bypass pump may be an option for high-risk patients.

McKhann, Guy M., et al. Encephalopathy and stroke after coronary artery bypass grafting. Archives of **Neurology**, *Vol. 58, September 2002, pp. 1422-28*

Sugar, glycemic load and pancreatic cancer

ROCKVILLE, MARYLAND. Although pancreatic cancer is relatively rare (an estimated 29,700 cases in the US in 2002) it is almost always fatal with a 5-year survival rate of only 4 per cent. Cigarette smoking, obesity, and diabetes increase the risk of pancreatic cancer. Researchers at the Harvard Medical School and the National Cancer Institute now report that a high intake of fructose (found in juices and soft drinks) and a diet with a high glycemic load are potent risk factors for pancreatic cancer in sedentary, overweight women. The glycemic load of a meal is the product of the amount of available carbohydrate in a standard serving of the food and the glycemic index of the food (divided by 100). Recent research has shown that a high glycemic load diet increases the risk of heart disease and diabetes.

The researchers evaluated the results of the Nurses' Health Study begun in 1980 and found that 180 nurses had developed pancreatic cancer over an 18-year follow-up period. They found that women with a high fructose intake (in 1980) had a 57 per cent increased risk of pancreatic cancer while women with a high glycemic load diet had a 53 per cent increased risk. None of these observed increases were statistically significant. However, when the analysis was limited to sedentary, overweight (BMI equal to or greater than 25) women a clear, statistically significant association was found. Nurses with a high fructose intake (greater than 33 grams/day) had 3 times the risk of developing pancreatic cancer than did nurses with a low intake (less than 17 grams/day). Similarly nurses with a high glycemic load diet (greater than 100/day*) had a 2.7 greater risk than did nurses with a low glycemic load diet (less than 70/day*). The researchers conclude that their findings support the hypothesis that high insulin levels and abnormal glucose metabolism promotes pancreatic cancer.

* Based on a glycemic index for glucose of 100.

Michaud, Dominique S., et al. Dietary sugar, glycemic load, and pancreatic cancer: risk in a prospective study. **Journal of the National Cancer Institute**, *Vol. 94, September 4, 2002, pp. 1293-1300*

NEWSBRIEFS

Another "winner" from genetic engineering. Researchers at the Weizmann Institute of Science in Israel have genetically modified a fungus to make it more deadly to the weeds that it normally blights. The fungus was specifically designed to target the velvetleaf weed that infests cotton fields. Fortunately, it was carefully tested before it was released. It was found that the fungus also kills tomato and tobacco seedlings. This particular GM fungus never made it out of the experimental greenhouse, but the incident highlights the very real danger of genetically-modified bioorganisms to make them more lethal to some plants - it could result in some very unintended effects.
New Scientist, September 28, 2002, p. 7

Our environment takes another beating. The 1987 Montreal Protocol agreed to phase out the use of chlorinated fluorocarbons (CFCs), the main destroyers of the ozone layer. In 1994, another ozone "eater", methyl bromide, was added to the list. Almost 70 million kilograms of this chemical are used every year primarily to fumigate soils and kill pests in grain mills and silos. The USA accounts for about 40% of total worldwide use. The Protocol specified that methyl bromide could no longer be used after the year 2005. Emboldened by the US Government's decision not to sign the Kyoto Protocol on global warming American grain millers are now lobbying the government to renege on the Montreal Protocol claiming that here is no "technically and economically feasible alternatives" to the use of methyl bromide. The US Environmental Protection Agency has yet to decide whether to allow an exemption on the use of methyl bromide by grain mills.
New Scientist, October 5, 2002, p. 11

Lorenzo's oil vindicated. Seventeen years ago young Lorenzo Odone was diagnosed with adrenoleukodystrophy, a progressive disease that is usually fatal within 2 years. Lorenzo's parents began a desperate search for a cure. They came up with a mixture of oleic and erucic acids (Lorenzo's oil) and scrupulously gave it to the boy every day. Seventeen years later he is still alive. Just last week, Dr. Hugo Moser of the Kennedy Krieger Institute in Baltimore told an international meeting of neurologists that Lorenzo's oil is highly effective in dealing with adrenoleukodystrophy and that all boys with the genetic defect leading to the disease should routinely be given the oil. His conclusions are based on a 10-year clinical trial of 104 boys with the defect. The disease involves a progressive loss of the myelin sheath that insulates nerve fibers. It is believed that Lorenzo's oil blocks the enzymes that produce some very long chain saturated fatty acids involved in the myelin sheath loss.
New Scientist, October 5, 2002, p. 7

Bedbugs make a comeback. Bedbugs were largely eradicated in the Western world during the 1950s and 1960s. The bedbug (*Cimex lectularius*) bites humans and gorges itself on blood whereupon it crawls back to its favourite hiding place to digest its meal. They dwell in furniture, bed frames, hi-fi equipment or telephone handsets – anything with a dark, hard-to-clean crevice. The massive increase in trade and tourism has reintroduced the bedbug to the Western world where it now spreads itself around through garage sales and other venues where used furniture and electronic equipment change hands. Dr. Ian Burgess of the University of Cambridge points out that bedbugs have never been known to spread disease, but are a nuisance and are becoming increasingly resistant to the pesticides used to kill them.
New Scientist, October 5, 2002, p. 10

DIETARY FAT AND CORONARY HEART DISEASE. IS THERE A CONNECTION? – Part II

by William R. Ware, Ph.D., Emeritus Professor of Chemistry, University of Western Ontario, London, Ontario, Canada

FATS AND CHOLESTEROL

Aside from the indication that it is beneficial to replace saturated fat with unsaturated fat, the cohort and intervention studies fail to provide much guidance. It is instructive to turn to the relationship between fat consumption and serum (blood) cholesterol levels. It appears to be an uncontested fact that the consumption of saturated fat increases the levels of low-density lipoprotein (LDL) cholesterol, which is regarded as the bad lipoprotein. However, life is never simple, since saturated fat also increases the high-density lipoprotein (HDL) cholesterol fraction as well, and HDL is considered very beneficial. The extent to which this results in a draw, so to speak, is not clear, but the conventional wisdom ignores the increase in HDL, focuses on the increase in LDL, and thus concludes that saturated fat as bad. However, if an individual had a normal level of LDL and a low level of HDL, raising the HDL might on balance be beneficial even if the LDL level also went up. The percentage decrease in risk is 3% for every 1% increase in HDL, whereas there is only a 1% increase in risk for each 1% increase in LDL (8). The changes in both LDL and HDL with the ingestion of saturated fat will depend on the nature of the fat, that is, the actual saturated fats involved, and as well, will depend on the individual, since there is considerable variation. Perhaps it is because of the combination of good and bad effects of saturated fats, coupled with individual variation, that the studies discussed above provided no definitive guidance as to the question of saturated fat increasing the risk of CHD, but only inconsistent findings.

Both monounsaturated fats (olive oil is high in monounsaturates) and polyunsaturated fats turn out to be beneficial in the context of cholesterol levels. They raise HDL and lower LDL. The interplay between diet and HDL, LDL, total cholesterol, and the other important blood lipids, the triglycerides, merits further discussion, not only since it relates the "bad" label attached to saturated fat and the "good" label associated with the mono- and polyunsaturates, but also because it relates to the question of high vs. low fat diets which can modify these blood lipid levels.

Studies far too numerous to list have established, probably beyond reasonable doubt, that high levels of total cholesterol and LDL cholesterol present a risk for the development of CHD. Since LDL cholesterol represents typically more than 50% of the total cholesterol, this total is considered a surrogate for LDL. Thus the studies that measured only total cholesterol remain valid today and are part of the case for high serum cholesterol being a risk factor. Four quite different and more or less independent approaches to lowering both total cholesterol and LDL produce reduced risk of CHD (surgery, sequesterant drugs, statin drugs and diet). This is one of the cornerstones of the argument that LDL is bad and that lowering it represents a beneficial intervention. There is also considerable literature indicating that low HDL carries added risk for CHD and that raising HDL decreases the risk (9-12).

However, there are some disturbing aspects to this picture. In fact, Ravnskov (4,7) and a few others have been very vocal critics of the hypothesis connecting cholesterol, fat and CHD, but their views are perhaps a bit extreme. Nevertheless, as any doctor involved with heart patients will tell you, something like 50% of all heart attacks occur in individuals who have a normal blood lipid profile, i.e. LDL is not elevated and HDL is not low. In addition, there is frequently no correlation between the extent of LDL lowering and the decrease in risk, and the decrease in risk in some studies is independent of the level of risk in the subjects studied (13,14). This latter phenomenon is also seen in the diet intervention studies, as discussed above. In addition, a significant decrease in CHD risk is found by lowering LDL in individuals that are already at low risk as judged by their blood lipid profile (15,16).

It does not help that the details of the mechanism of the adverse action of LDL is poorly understood, as is the overall mechanism of the formation of atherosclerotic plaques, from their beginnings as fatty streaks in arteries to large, unstable plaques, the rupture of which is thought to be related to heart attacks. In fact, the conventional wisdom that atherosclerosis is caused by high cholesterol has recently been challenged by Ravnskov in the *Quarterly Journal of Medicine*. He documents the following points (17):

- Serum cholesterol does not predict the degree of atherosclerosis at autopsy.
- Serum cholesterol does not correlate with the degree of coronary atherosclerosis on angiography.
- Serum cholesterol does not correlate with the degree of coronary calcification.
- Serum cholesterol does not correlate with the degree of peripheral atherosclerosis.
- Changes in serum cholesterol concentrations are not followed by parallel changes in atherosclerosis growth--i.e. there is no exposure response.

Thus an important question: why does high cholesterol predict cardiovascular disease if LDL levels and changes in LDL do not correlate with the degree of atherosclerosis or with atherosclerosis growth? As Ravnskov points out, there can be many reasons for these observations. One is that high LDL or total cholesterol may be secondary to other factors that promote cardiovascular disease (17). On-going research will no doubt eventually produce a more satisfactory picture.

It seems clear that LDL is bad cholesterol and HDL is good cholesterol. Saturated fat consumption raises both and might be viewed as neutral. Eating mono- or polyunsaturated fat decreases LDL and raises HDL. From this one might conclude that it is pointless to worry about fat. However, to not worry about fat at all would be to ignore the apparently beneficial effects of the unsaturated fats and the studies that demonstrated a significant decrease in the risk of CHD when saturated fat is replaced with unsaturated fat--a benefit that does not appear to prove that the reduction of saturated fat was indeed beneficial, but that merely the combined action has merit. In this context, it is important to understand that if one merely increases the consumption of unsaturated fat and does not decrease the saturated component, there may be a risk of adversely disturbing the energy balance with an associated weight gain, unless other macronutrients such as protein or carbohydrate are decreased.

LOW-FAT DIETS

Once the "fat is bad" religion was firmly established and supported by the US government, the medical profession, the nutritionist community, the media, and, with great enthusiasm, the food industry, the so-called low-fat or very low-fat diet was a natural result. Since most people tend to maintain a certain level of caloric intake, low fat in fact meant a dietary change that involved replacing fat with carbohydrate. Protein in general was not viewed as a candidate since most common protein sources contained lots of fat. Carbohydrate has roughly half the calories per gram as compared to fat (4 vs. 9 kcal/gram), so the low fat diet was also a high carbohydrate diet, and this was embraced by millions as the path to health and longevity. Lack of knowledge among the general public as to the various types of carbohydrates and their relative effects on blood glucose, insulin, and the development of insulin resistance led to the indiscriminate consumption of increased amounts of carbohydrates, in many cases carbohydrates from sources such as potatoes, white rice, ordinary pasta, white bread, bagels, baked goods, sugar-rich deserts, non-diet soft drinks and juices, etc. Much of the carbohydrate that replaced fat was of the type that was rapidly digested to yield large increases in post-meal (called postprandial) blood glucose and insulin, which frequently leads to insulin resistance and eventually the so-called metabolic syndrome or Syndrome-X (18). Carbohydrate not needed for energy was turned into fat and stored--something the general public was probably not aware of, since the "fat is bad" religion did not include information on the metabolism of carbohydrates. The notion that eating fat made one fat, and avoiding fat therefore would result in weight stability or weight loss, was part of the conventional wisdom of the masses.

The replacement of fat with carbohydrate has been studied a great deal since the "fat is bad" religion became commonplace. In many individuals, such a change in diet results in a significant decrease in serum HDL, an equally significant increase in serum triglycerides, and eventually the development of insulin

resistance, where the body requires larger and larger amounts of insulin to manage the load of serum glucose that arises from the heavy carbohydrate component of the diet. Insulin resistance frequently leads to type 2 diabetes, which in turn results in a whole host of serious health problems and a well documented huge increase in the risk of heart disease. Most diabetics in fact die of heart disease. The above-described changes in HDL and triglycerides also are in the direction of increasing the risk of CHD. It actually turns out to be difficult to separate the effects on CHD risk of high triglycerides and low HDL, since these two conditions frequently occur together, but there are studies that indicate that high triglycerides can be viewed as an independent risk factor (19). Suffice to say that there are a number of studies in the recent literature that indicate a very high level of increased risk when HDL is low and triglycerides are high (9-12). Interestingly enough, men with conventional risk factors for CHD actually have low risk if they have low triglycerides and high HDL (11). Some investigators think that in fact low HDL and high triglycerides can present a greater risk than either high total cholesterol or high LDL (8). In some individuals, low HDL and high triglycerides are accompanied by a change to smaller LDL particles. There is considerable evidence that these are more dangerous in the context of heart disease than large, less dense LDL particles (20). In fact, this is one of the frequently encountered arguments against the low-fat high-carbohydrate diet. However, not all studies find that CHD risk higher when the serum concentration of small, dense LDL particles predominates (21).

ESSENTIAL FATTY ACIDS

By restricting fat consumption, there also arises the risk of a deficiency in the essential fatty acids, which are critical to health. The omega-3 and omega-6 (n-3 and n-6) polyunsaturated fatty acids require a more detailed discussion. They are critically important because they are involved in the production of what are called *eicosanoids*, which are transient hormones that play key roles in human biochemistry. There are a large number of different eicosanoids, and a detailed discussion (22) is beyond the scope of this review. Suffice to say that the subject can be simplified by thinking in terms of two classes of eicosanoids, which are frequently called "good" and "bad" although this simple pair of labels conceals the fact that good and bad eicosanoids are both necessary. It is thus not a matter of minimizing the bad and maximizing the good, but of keeping the two classes in balance. How they complement one another can be seen from the following table:

"Good" Eicosanoids	**“Bad” Eicosanoids**
Reduce pain	Promote pain
Prevent blood clots caused by platelet aggregation	Cause blood clots initiated by platelet aggregation
Cause dilation of blood vessels	Cause constriction of blood vessels
Enhance immunity	Depress immunity
Improve brain function	Depress brain function

These lists are far from complete but nevertheless illustrate the complementary nature of the two classes as well as the central role they play in essential biochemical processes. The connection with cardiovascular disease is also evident. The relationship between the n-3 and n-6 polyunsaturated fatty acids and the eicosanoids is that the n-3 fats are involved in the production and regulation of the good eicosanoids whereas the n-6 fats come into play with the bad eicosanoids. Since balance is the name of the game, it is important not only to get enough of each type of fat, but also to get them in roughly the correct proportion for optimum functioning of all the systems that depend on eicosanoids and the hormones derived from them. One school of thought on this subject maintains that the n-3 to n-6 ratio should by around 1:2 to 1:4. There is some evidence that our genetic makeup evolved on a diet that had a ratio in this range (23). While the optimum ratio is debatable (24), what is clear is that the typical Western diet is very heavy in the n-6 fats and very light in the n-3s. This is due to the high consumption of vegetable oils that are rich in n-6 fatty acids and the low consumption of fish, nuts, and the oils that are rich in n-3s. There is a great deal of literature on the beneficial effects of increasing the intake of n-3 fats, and most of this is in the context of cardiovascular disease. The typical Western diet has been estimated to have an n-3 to n-6 ratio of 1 to 20. Thus there seems to be little risk associated with dietary modifications that reduce n-6 consumption, and there appears to be considerable room to increase the n-3 content of diets, a move that should prove beneficial.

An interesting twist to the n-3 story is that the parent acid, *alpha*-linolenic acid, is converted with variable efficiency in humans into two critically important n-3 fatty acids, EPA and DHA. Fish, however, are rich in these two n-3 fats, and they can be found in concentrated form in fish oil. There are dozens of studies that have shown that n-3 fatty acids from fish and other sources are active in preventing heart attacks and sudden cardiac deaths by preventing erratic heart rhythms, reducing the tendency of blood to clot inside arteries (a cause of heart attacks), improving the blood lipid profile (total cholesterol, HDL, LDL, and triglycerides), and favorably influencing inflammation which is thought to play an important role in the development of atherosclerosis (plaque formation). By far the strongest connection between the n-3 fatty acids and heart disease is the reduction of sudden deaths, presumably because of the strong anti-arrhythmic effects of these fats (25). This is very important since for a significant number of victims, sudden death is the first indication of heart disease. It is clear from the above that by reducing the dietary fat content to a very low value, there is a significant danger of insufficient n-3 essential fatty acids and of having a very high ratio of n-6 to n-3, because what fat there is in the low-fat diet will generally be rich in the omega-6 fats.

In the above discussion of the connection between dietary fat and CHD, one study was mentioned that produced an astounding 73% reduction in risk of a second adverse coronary event as compared to the control group in patients who had already experienced one heart attack. The dietary approach in this study was to switch the treated group to a Mediterranean style diet and to add supplementary alpha-linolenic acid in the form of an enriched margarine (free of *trans*-fats) thus increasing the n-3 content of the diet. This study, known as the "Lyon Diet Heart Study" underscores the importance of the n-3 essential fatty acids in connection with heart disease (26,27).

In summary, many experts in nutrition, who base their views and recommendations on the recent literature, are suggesting that the popular movement to replace fat with carbohydrate was in fact a serious mistake in the context of public health, that the recommendation in fact has no basis in valid scientific studies, and that the general public would be well advised to instead replace some saturated fat with unsaturated fat and limit the consumption of rapidly digested (high glycemic index) foods (24). The consumption of the right mix of fat, protein and slowly digested carbohydrates such as are found in many vegetables, as well as low-glycemic index fruits, is recommended as a prudent approach to a diet that is more in tune with current knowledge regarding the prevention of CHD than the low-fat high-carbohydrate diet.

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