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Type 2 diabetes is reaching epidemic proportions in the Western world despite the fact that this disease is almost entirely preventable through proper diet, exercise, and lifestyle. It is highly likely that the excessive consumption of sugar, processed and fast foods, and unhealthy fats, and the high carbohydrate diet promoted by the American Diabetes Association, the American Heart Association, the American Cancer Society and the US Department of Agriculture is largely responsible for today's diabetes epidemic. Researchers at the Centers for Disease Control and Prevention estimate that 1 in 3 Americans will develop diabetes during their lifetime, place a huge burden on the healthcare system, and shorten their lifespan by 12 to 14 years. To put the 1 in 3 in perspective, consider that the lifetime risk among women of developing coronary heart disease is also 1 in 3 while the lifetime risk of developing breast cancer is only 1 in 8.

Researchers at the Veterans Affairs Medical Center and the University of Minnesota recently confirmed that diet is extremely important in diabetes management. They found that a diet containing 30% protein (as % of energy), 40% carbohydrates, and 30% fat was significantly superior to a high carbohydrate diet in maintaining glucose control in patients with mild, untreated diabetes. For more on how to prevent and deal with insulin resistance and type 2 diabetes, please see Bill Ware's "Diet Zoo" articles and my research report at www.yourhealthbase.com/diabetes.htm

In this issue we present the second part of Bill Ware's "The Diet Zoo", this time dealing with the individual constituents of the diet – protein, carbohydrates and fats – and how they impact on our health. And to top it off, we cover new research into the benefits of magnesium, glutathione, and the emergence of fo-ti as a possible estrogen replacement. Read on!

Wishing you good health,
Hans Larsen, Editor

February Highlights

Magnesium helps prevent heart disease

CHARLOTTESVILLE, VIRGINIA. A team of researchers from the University of Virginia, the University of Hawaii, and the Japanese National Institute for Longevity Sciences has found a strong association between a low magnesium intake and the risk of coronary heart disease (CHD). Their study involved 7172 men who were enrolled in the Honolulu Heart Program between 1965 and 1968. The men were between the ages of 45 and 68 years and free of heart disease at time of enrollment. All participants provided information about their nutrient intake through a 24-hour dietary recall questionnaire administered by a dietician. During 30 years of follow-up 1431 cases of incident CHD (non-fatal myocardial infarction [heart attack], fatal heart attack, sudden cardiac death, and death from congestive heart failure associated with CHD) occurred in the group. The researchers noted that men with a high dietary intake of magnesium (340-1138 mg/day) had half the risk of developing CHD

during the first 15 years of the study than did men whose intake was low (50-186 mg/day). The association was only slightly attenuated after adjusting for other nutrients (potassium, calcium, sodium, energy intake, dietary fiber, protein, and saturated fat) and known risk factors for CHD (age, cholesterol, diabetes, hypertension, body mass index, smoking, alcohol intake, and physical activity). The researchers note that the average daily magnesium intake in the group was only 268 mg/day. This compares to 342 mg/day for the general US population and the Recommended Daily Allowance of 420 mg/day.

Abbott, Robert D, et al. Dietary magnesium intake and the future risk of coronary heart disease. **American Journal of Cardiology**, *Vol. 92, September 15, 2003, pp. 665-69*

Vitamin C and kidney stones

DALLAS, TEXAS. Ascorbic acid (vitamin C) is metabolized to oxalate in the body. Most kidney stones are formed from calcium oxalate, so not surprisingly warnings have been issued to the effect that high intakes of vitamin C may promote kidney stones. Several studies have questioned the validity of these warnings. Now researchers at the University of Texas Southwestern Medical Center weigh in with new evidence to the effect that daily vitamin C intakes of 2000 mg or less do not increase the risk of forming kidney stones. Their randomized, placebo-controlled clinical trial involved 12 participants with no history of kidney stones and 12 who were known to form calcium oxalate stones. The participants were given 1000 mg of ascorbic acid with breakfast and dinner or matching placebo for two 6-day study periods.

The researchers conclude that supplementing with 2000 mg/day of vitamin C does not change urinary pH (a key factor in stone formation) in neither normal subjects nor in known stone formers. Both stone formers and non-stone formers did, however, show a moderate increase in urinary oxalate excretion. The researchers recommend that daily vitamin C supplementation be limited to 2000 mg among people known to have a tendency to form kidney stones. They also point out that no correlation linking vitamin C consumption to risk of kidney stone formation has ever been reported in published studies involving vitamin C supplementation.

Traxer, Olivier, et al. Effect of ascorbic acid consumption on urinary stone risk factors. **Journal of Urology**, *Vol. 170, August 2003, pp. 397-401*

Glutathione helps protect heart disease patients

MAINZ, GERMANY. Glutathione peroxidase is the body's most important internally-generated antioxidant; it is synthesized from glutamate, cysteine and glycine, and its activation requires the presence of adequate amounts of selenium. Glutathione is effective in neutralizing hydrogen peroxide, lipid peroxides, and peroxynitrite – all powerful free radicals that have been implicated in the progression of atherosclerosis and other cardiovascular diseases. Superoxide dismutase (SOD) is another important internally-generated antioxidant that is effective in neutralizing the superoxide anion by converting it to hydrogen peroxide.

A group of Canadian, French and German researchers recently set out to determine if levels (activity) of glutathione and SOD in coronary heart disease patients were indicative of their long-term prognosis. Their study involved 636 patients with symptoms of stable angina (79% of group) or unstable angina. The participants were followed for an average of 4.7 years during which time there were 64 deaths from cardiovascular causes, 21 deaths from other causes, and 19 non-fatal heart attacks. The researchers found that patients with high baseline activity levels of glutathione peroxidase 1 in their red blood cells (greater than 56.31 units per gram of hemoglobin) were three times less likely to have suffered a cardiovascular event than were patients with low activity levels (less than 42.0 units per gram of hemoglobin). The magnitude of the risk reduction was not significantly altered after adjusting for other risk factors for cardiovascular events. Being older, diabetes, low left ventricular ejection fraction, and high blood levels of C-reactive protein, homocysteine and creatinine were all associated with a higher risk whereas a high blood level of HDL (high density lipoprotein) cholesterol and selenium showed a

protective effect. The red blood cell level of SOD was not associated with the risk of a future cardiovascular event.

The researchers conclude that a low level of activity of red-cell glutathione peroxidase 1 is independently associated with an increased risk of cardiovascular events in patients with coronary artery disease. They also suggest that increasing glutathione peroxidase 1 activity might lower the risk of cardiovascular events.

Blankenberg, Stefan, et al. Glutathione peroxidase 1 activity and cardiovascular events in patients with coronary artery disease. **New England Journal of Medicine**, *Vol. 349, October 23, 2003, pp. 1605-13*

Editor's comment: It is probably not too great a leap of faith to suggest that if high glutathione peroxidase activity levels are beneficial for heart disease patients they may also help the rest of us. The simplest way of increasing red blood cell levels of glutathione is to supplement with vitamin C. As little as 500 mg/day has been shown to increase glutathione by as much as 50%[1]. In order to ensure adequate glutathione activity it is also a good idea to ensure a selenium intake of 200 micrograms/day.

[1] Johnston, CS, et al. Vitamin C elevates red blood cell glutathione in healthy adults. American Journal of Clinical Nutrition, Vol. 58, July 1993, pp. 103-05

High protein diet benefits diabetics

MINNEAPOLIS, MINNESOTA. Type 2 diabetes is characterized by high and highly variable levels of glucose in the blood. The most serious consequence of long-term high glucose levels is that the excess glucose tends to bind to proteins and cause them to become "sticky". This process is called glycosylation and is a major factor in atherosclerosis and other diabetes complications. The extent of glycosolation is reflected in the blood level of glycosylated hemoglobin.

Diet is an important factor in the prevention and treatment of diabetes. Current dietary recommendations promoted by the American Diabetes Association, the American Heart Association, the American Cancer Society, and the US Department of Agriculture call for a diet containing 55% carbohydrate (in % of energy) with an emphasis on starch-containing foods, 15% protein, and 30% fat (10% monounsaturated, 10% polyunsaturated and 10% saturated fat).

Researchers at the Veterans Affairs Medical Center and the University of Minnesota now report that a high protein diet (40% carbohydrate, 30% protein and 30% fat) is superior to the recommended high carbohydrate diet in keeping glucose levels under control. Their clinical trial of the two diets involved 12 patients (10 men and 2 women) with mild, untreated diabetes. The study participants consumed the two diets for 5 weeks separated by a 2-5 week washout period. The daily distribution of calorie intake was 21% for breakfast, 27% for lunch, 13% for an afternoon snack, 34% for dinner, and 5% for a snack at 9 p.m. At the end of the 5-week test period the researchers observed a significant reduction in glucose levels with the high protein diet, particularly in the evening. They also noted a highly significant decrease in glycosylated hemoglobin in both diets, but it was substantially more pronounced after the protein diet than after the standard diabetes diet (0.8% versus 0.3%). Mean fasting triglyceride concentrations were significantly lower in the protein diet group and decreased by 20% over the 5-week period. There were no significant differences in cholesterol levels nor were any changes in weight or blood pressure observed in the two groups. The researchers conclude that adhering to a high protein diet (protein=30% of energy intake) improves glucose control in patients with mild, untreated diabetes.

Gannon, Mary C., et al. An increase in dietary protein improves the blood glucose response in persons with type 2 diabetes. **American Journal of Clinical Nutrition**, *Vol. 78, October 2003, pp. 734-41*

Eckel, Robert H. A new look at dietary protein in diabetes. **American Journal of Clinical Nutrition**, *Vol. 78, October 2003, pp. 671-2 (editorial)*

Mercury sources and toxicity

ROCHESTER, NEW YORK. Mercury is a highly toxic metal associated with damage to the kidneys and central nervous system. Mercury vapour is emitted from volcanoes, coal-burning power

stations, and municipal incinerators and returns to the earth through rain contaminated with metallic mercury. Metallic mercury is methylated to methyl mercury in oceans and lakes and enters the food chain via fish and other seafood. Long-lived predator fish such as shark, swordfish, tilefish, king mackerel, and pike and bass in fresh water are the main sources of methyl mercury. Dental amalgams are an important source of mercury vapour and the vaccine preservative thimerosal is a significant source of ethyl mercury.

Researchers at the University of Rochester School of Medicine recently published a review of what is currently known about mercury toxicity. Among the highlights:

- Mercury vapour, methyl mercury and ethyl mercury all target the central nervous system and mercury vapour and ethyl mercury also target the kidneys. Inorganic (metallic) mercury primarily targets the kidneys and stomach.
- Chelators such as DMSA are effective in removing all forms of mercury from the body, but cannot reverse central nervous system damage.
- The allowable or safe intake of mercury has recently been reduced to 0.1 microgram/day per kilogram of body weight.
- The concentration of mercury in the brain, blood and urine correlates with the number of amalgam fillings in one's mouth. The concentration increases markedly with increased chewing. Long-term use of nicotine gum by people with amalgam (silver) fillings may increase levels by a factor of 10, thus approaching occupational safety limits.
- There is concern, but no clear evidence, that mercury emitted from amalgam fillings may cause or worsen degenerative diseases such as ALS, Alzheimer's disease, multiple sclerosis, and Parkinson's disease.
- Ethyl mercury (thimerosal) is used as a preservative in vaccines. Recent concerns about its toxicity have caused US authorities to take steps to remove it by switching from multi-dose vials to single-dose vials that do not require a preservative.
- A recent move by power companies to replace mercury containing pressure-control devices for domestic gas supplies has led to numerous spills of mercury in homes. Some 200,000 homes were affected in one recent incident. The liquid mercury is difficult to remove and gives off highly toxic vapours, which are particularly harmful to infants and children.
- Several studies have found an association between mercury exposure and cardiovascular disease, but other studies have failed to confirm the connection.

Clarkson, Thomas W., et al. The toxicology of mercury – current exposures and clinical manifestations. **New England Journal of Medicine**, *Vol. 349, October 30, 2003, pp. 1731-37*

Editor's comment: The review makes it clear that exposure to mercury is detrimental, but hard to avoid. Nevertheless, avoiding the placement of new amalgam dental fillings and gradually replacing old ones with composite fillings, avoiding gum chewing if amalgam fillings are present, and limiting the intake of fish with high mercury levels are all steps that can be taken by everyone. It is important to realize that consuming just one 7 oz (198 grams) can of tuna per week translates into a mercury intake of 0.1 microgram/day of mercury per kilogram of body weight – equivalent to the currently recommended maximum daily intake.

High pulse rate associated with increased mortality

JERUSALEM, ISRAEL. Researchers at the Hadassah University Hospital report that elderly women with high pulse (heart) rates have an increased risk of dying, particularly from cardiovascular disease. Their study involved 193 women and 229 men 70 years of age at entry to the study in 1990-91. During 6 years of follow-up 20 women (10%) and 48 men (19.4%) died. The researchers found a strong correlation between heart rate (as measured as pulse rate or through an ECG) and mortality in women. Women with a resting heart rate above 77 bpm had a 3 times higher mortality than did women with a rate of 77 bpm or slower. When women on beta-blockers were excluded a heart rate above 77 bpm conferred an 8-fold increase in mortality. A heart rate above 77 bpm was associated with a 14-fold increase in death from cardiovascular disease, but not

significantly associated with death from cancer. Men generally had a 2-3 times higher death rate than women at comparable pulse rates, but higher pulse rates as such were not significantly associated with increased mortality among men. This finding is in sharp contrast to the findings of several other studies which concluded that high heart rates in men are associated both with increased overall mortality and, specifically, with death from cardiovascular disease. It is possible that the generally high mortality in men over 70 years of age may have masked the effect of heart rate in the Israeli study.

Perk, Gila, et al. Sex differences in the effect of heart rate on mortality in the elderly. **Journal of the American Geriatrics Society**, *Vol. 51, September 2003, pp. 1260-64*

Editor's comment: Women with a resting heart rate of 68 bpm or lower would seem to be at quite low risk according to this study. These women had a 6-fold lower risk of death than did women with a heart rate above 77 bpm and a 4-fold lower risk than men with a heart rate of 68 bpm or lower.

Fo-ti – A possible estrogen replacement

SAN DIEGO, CALIFORNIA. The standard hormone replacement therapy for menopausal women (estrogen plus medroxy progesterone acetate) has fallen out of favour since it was discovered that it is associated with an increased risk of cardiovascular disease, breast cancer, and stroke. Recent studies have, however, shown that ultra-low doses of estrogen (0.25 mg/day) may help reduce bone loss and thus prevent osteoporosis and hip fractures. It is not known whether these lower doses are still associated with a higher risk of cardiovascular disease, stroke, and breast cancer.

The finding that ultra-low doses of estrogen (estradiol) may be beneficial has rekindled the interest in certain herbs that mimic estrogen in their action. Researchers at the University of California have developed an accurate method for determining *in vitro* estrogen bioactivity of these herbs. They tested red clover (*Trifolium pretense L*.), dong quai (*Angelica sinensis*), black cohosh (*Cimicifuga racemosa*), soy, licorice (*Glycyrrhiza glabra*), chaste tree berry (*Vitex agnus-castus L*.), fo-ti (*Polygonum multiflorum*), and hops (*Humulus lupulus L*.). They found that soy, clover, licorice, hops and fo-ti had significant estrogen bioactivity, while chaste tree berry, black cohosh and dong quai did not. Black cohosh, soy and chaste berry have, nevertheless, been found useful in relieving certain menopausal symptoms. Fo-ti had the highest estrogen bioactivity at 1/300 (0.33%) of that of pure estradiol followed by soy at 1/330, red clover at 1/400, and licorice at 1/1650. Removing a glycone group in soy resulted in a compound with an estrogen bioactivity of 1/80 (1.25%) of that of pure estradiol. Clinical studies are now underway to determine the actual estrogen bioactivity in women using supplements containing the active herbs.

Oerter Klein, Karen, et al. Estrogen bioactivity in fo-ti and other herbs used for their estrogen-like effects as determined by a recombinant cell bioassay. **Journal of Clinical Endocrinology & Metabolism**, *Vol. 88, September 2003, pp. 4077-79*

Prestwood, Karen M. The search for alternative therapies for menopausal women: estrogenic effects of herbs. **Journal of Clinical Endocrinology & Metabolism**, *Vol. 88, September 2003, pp. 4075-76 (editorial)*

Editor's comment: The finding that as little as 0.25 mg/day of estrogen may be beneficial in preventing bone loss might, unless I am misinterpreting the results, mean that as little as 75 mg/day (0.25 x 300) of fo-ti extract may have a similar beneficial effect.

Fat intake and stroke risk

BOSTON, MASSACHUSETTS. There is strong evidence that saturated fat and *trans* unsaturated fat increase the risk of coronary heart disease while monounsaturated and polyunsaturated fats decrease it. There is also some evidence that a high intake of long chain omega-3 fatty acids from seafood is associated with a lower risk of ischemic stroke (stroke caused by a blood clot), but not with the risk of hemorrhagic stroke (stroke caused by a burst blood vessel).

Researchers at the Harvard School of Public Health now report that they have found no association between fat intake and stroke risk. Their study

involved 43,732 male health professionals who were enrolled in 1986 and followed for 14 years. The men completed food frequency questionnaires in 1986, 1990 and 1994. They were between the ages of 40 and 75 years and free of diabetes and cardiovascular disease in 1986. By January 2000 455 ischemic strokes, 125 hemorrhagic strokes, and 145 strokes of unknown type had occurred in the group. The researchers found no statistically significant correlation between stroke risk and the intake of total fat, animal fat, vegetable fat, saturated fat, monounsaturated fat, polyunsaturated fat, *trans* unsaturated fat or cholesterol. They also found no correlation between stroke risk and consumption of red meats, high-fat dairy products, nuts and eggs.

He, Ka, et al. Dietary fat intake and risk of stroke in male US healthcare professionals: 14 year prospective cohort study. **British Medical Journal**, *Vol. 327, October 4, 2003, pp. 777-82*

Editor's comment: A total of 725 strokes among 43,732 men followed for 14 years gives a total incidence of 0.1% per year. This is considerably lower than the usually-quoted figure of about 1% for the US population in general. The lead author of the study, Dr. Ka He, MD, ScD, kindly provided the following explanation for the seeming anomaly (personal communication to me, November 30, 2003):

The annual incidence of new and recurrent stroke in the US is about 700,000 according to the American Stroke Association. Based on a population of 270,000,000 the annual rate is 0.26 per 100 person-years or 0.26% per year. Stroke risk, of course, increases with age so it would clearly be higher if, for example, only people over 50 years of age were considered. Says Dr. He, "In our study, we only count the first event not recurrent stroke. Also, the participants are all healthcare professionals. They are health-conscious and relatively healthy (they were free from any CVD and diabetes). I would not be surprised if there is relatively low rate of stroke in our cohort".

NEWSBRIEFS

Diabetes epidemic in the USA. The US Centers for Disease Control and Prevention has just issued a sobering report concerning the rapidly growing incidence of type 2 diabetes in the United States. They estimate that a 40-year-old man or woman now has about a 30% chance of developing diabetes in their lifetime. For individuals born in the year 2000 the lifetime risk is now 33% for men and 39% for women. Individuals with diabetes have a shorter average lifespan than non-diabetics. It is estimated that a man diagnosed with diabetes at age 40 years will lose about 12 years of life compared to a non-diabetic, while a diabetic woman will lose about 14 years. The 1 in 3 risk for developing diabetes during a lifetime can be put in perspective by comparing it to the 1 in 8 lifetime risk of breast cancer and the 1 in 3 risk of coronary heart disease among women and the 1 in 2 lifetime risk of coronary heart disease among men.

Journal of the American Medical Association, October 8, 2003, pp. 1884-90

Tai chi and osteoarthritis. South Korean researchers report that tai chi is effective in ameliorating several symptoms of osteoarthritis. Their recent study involved 43 middle-aged women who had been diagnosed with osteoarthritis. The women were randomized to serve as controls or to participate in 20-minute tai chi sessions at least 3 times a week for a 12-week period. At the end of the study women in the tai chi group reported significantly less pain and stiffness in their joints and improved overall physical functioning. Women in the control group, on the other hand, showed no improvement or even deterioration in physical functioning. Women in the tai chi group also showed significant improvement in balance and abdominal muscle strength. The researchers conclude that the women were able to safely perform the 12 forms of Sun-style tai chi exercise for 12 weeks and that this was effective in improving their arthritis symptoms and physical functioning.

Journal of Rheumatology, September 2003, pp. 2039-44

Good vibes may help prevent falls. Staying upright involves a complicated interaction between input to sensory receptors and activation of motor neurons resulting in compensatory muscle activity. The sensitivity to sensory input (somatosensation) decreases markedly with age and this decrease is associated with an increased likelihood of falling. A group of American and Israeli researchers reports that applying subtle vibrations to the soles of the feet significantly improves somatosensation, particularly in elderly subjects. Their experiment involved 15 young men and women (average age of

23 years) and 12 elderly men and women (average age of 73 years). The participants were exposed to non-discernible (subsensory) vibrations to their feet for 30-second periods while standing still with their eyes closed and hands at their side. The researchers measured the degree of sway exhibited by the participants and found that it was significantly less when vibrations were applied than when they were not. The improvement in "sway control" was particularly impressive among the elderly participants. The researchers conclude that, "… randomly vibrating shoe insoles, might be effective in enhancement of performance of dynamic balance activities (eg. walking), and could enable older adults to overcome postural instability caused by age-related sensory loss".
The Lancet, October 4, 2003, pp. 1123-24

Perils of chicken farming. Approximately 49 billion chickens are consumed worldwide every year. Thirty years ago it took nearly 3 months to grow a broiler chicken to slaughter weight (2 kg) – today it takes 41 days and the stated goal of the chicken industry is to reduce this period by 1 day a year. How is this achieved? By extreme selective breeding. Today 98% of all broilers are descended from birds supplied by just 3 companies. The rapid growth translates into poor skeletal strength and often results in lameness. Lame chickens have been observed to prefer feed laced with painkillers and the Compassion in World Farming (CIWF) group believes this indicates that they are in pain. The fast-growing chickens have also been found to have a substantially higher incidence of cardiovascular disease and liver damage. The CIWF is now challenging the UK government's policies on broiler farming on the basis that they are in direct contravention of the European Union directive of 1998, which prohibits farming methods that have a detrimental effect on the animals' health and welfare.
New Scientist, November 15, 2003, p. 19

Lead in city gardens. Researchers at Northwestern University in Illinois tested lead levels in vegetables and herbs grown in 17 gardens in Chicago. Onions, radishes, and rhubarb often had lead levels above 10 micrograms/gram and dried coriander from one garden contained over 39 micrograms/gram of lead. The researchers express concern that consuming vegetables and herbs from city gardens could result in a lead intake exceeding the current safe limits of 15 micrograms//day for children and 75 micrograms/day for adults.
New Scientist, November 8, 2003, p. 17

Rye bread is easier on the pancreas. A high carbohydrate meal stimulates the pancreas to release insulin. If the pancreas is stimulated often enough insulin is repeatedly released and, ultimately, type 2 diabetes is likely to develop. Researchers at the University of Kuopio in Finland now report that rye bread is a lot easier on the pancreas than is refined wheat bread. Their experiment involved 19 healthy, postmenopausal women who consumed refined wheat bread or one of three rye breads with differing fiber contents. For the first 2 hours after the breads were eaten glucose levels were not significantly different among the breads; however, after 2.5 and 3 hours the glucose level in the women eating wheat bread had fallen below fasting levels, while the glucose levels in the rye bread consumers remained elevated. Insulin response was considerably lower (a desirable state) when consuming rye bread than when consuming wheat bread. The researchers conclude that structural differences between the breads rather than fiber content is what is responsible for the reduced insulin response.
American Journal of Clinical Nutrition, November 2003, pp. 957-64

The Diet Zoo: Does Science Provide Guidance? – Part II

by William R. Ware, Emeritus Professor of Chemistry, University of Western Ontario

You are what you eat. You buy what you eat. Therefore you are what you buy. (unknown source)

THE PROTEIN QUESTION. The amount of protein needed each day is the subject of much debate which unfortunately appears to occur in the absence of hard scientific data. There is no question that protein is an essential component of the human diet. The body gets the amino acids required for its own protein, enzyme and hormone synthesis from the amino acids derived from the protein in food. Some amino acids the body can make, others must come from food, which is a concern for pure vegetarians. The Establishment promotes a figure of 0.8 grams per day per kg of body weight (55 g for

a weight of 150 lbs, 73 g for a weight of 200 lbs), but compelling evidence in favor of this number appears lacking. Most low-carb advocates feel this is too low and suggest 1 to 1.2 grams per day per kg or even higher.

Low-carb diets generally involve increased protein consumption, and the critics almost always raise the spectre of serious health problems associated with bone loss, decreased bone mass density, increased rates of heart disease and the risk of kidney stones or kidney damage. While there is no question that individuals with kidney problems or a tendency to form stones should be careful of high protein intake and should work with their physicians if altering their diets in this direction, there appears to be very little modern scientific evidence that increasing the protein intake to 1.2 g/kg or even somewhat higher is associated with any of the risks to the general population that the critics enumerate. The following is a short list of recent studies that relate to these criticisms.

- In a review of recent epidemiological studies, Kerstetter et al [46] found that reduced bone density and increased rates of bone loss were observed in individuals consuming *low* protein diets, not high protein diets.
- In a study published in 2003, Layman et al [47] found that increasing the proportion of protein to carbohydrate in the diet of adult women had a positive effect on body composition, blood lipids, glucose homeostasis and satiety during weight loss.
- In a study also published in 2003, Roughead et al [48] found that calcium retention was not reduced when subjects consumed a high protein diet from common dietary sources such as meat.
- Layman et al [49] found in a recent study that a diet with increased protein and a reduced carbohydrate/protein ratio stabilizes blood glucose during non-absorptive periods and reduces the post-meal insulin response, both of which are generally viewed as desirable effects.
- In a prospective study published in 1999 based on the Nurses' Health Study data, Hu et al [50] found no support for the hypothesis that high protein intake increases the risk of ischemic (occlusive) heart disease. In fact, their findings suggest that replacing carbohydrates with protein may be associated with lower risk of ischemic heart disease.
- According to a study published in 2003, Farnsworth et al [51] found that replacing carbohydrate with protein from meat, poultry, and diary foods had beneficial metabolic effects and no adverse effects on markers of bone turnover or calcium excretion.
- The importance of calcium intake in promoting the favorable effect of increased dietary protein intake is discussed in two recent papers. Dawson-Hughes and Harris discuss supplementation with calcium citrate and vitamin D [52]. Dawson-Hughes [53] reviews studies that also deal with this aspect.
- Rapuri et al [54] found that the highest quartile of protein intake was associated with higher bone mass density in elderly women only when calcium intake exceeded about 400 mg/day. Over a three-year follow-up, no association was seen between protein intake and the rate of bone loss.
- A study reported by Kerstetter et al [55] in 2000 concluded that for young healthy women consuming a well-balanced diet moderate in nutrients known to influence calcium metabolism, the recommended daily allowance (RDA) for protein of 0.8 g/kg body weight does not support optimal calcium nutrition. They suggest at least 0.9 g/kg are need to normalize calcium metabolism.
- Appel [56] has recently reviewed the question of the effects of protein intake on blood pressure and CVD. His summary is of interest: "Recent evidence suggests that an increased intake of protein, particularly plant protein, may lower blood pressure and reduce the risk of cardiovascular disease"
- Knight et al [57] in 2003 reported that high protein intake was not associated with renal function decline in women with normal renal function, but a high intake of non-dairy animal protein may accelerate renal function decline in women with mild renal insufficiency.

With millions of people worldwide adopting the low-carb way of life and therefore eating more protein, if the critics were correct one might have expected a worldwide epidemic of kidney stones, but the critics of these diets appear unable to come up with evidence of such an epidemic.

Those who advocate consuming only protein from plant sources on occasion argue that our ancestors during and prior to the Stone Age were vegetarians, but modern research suggests otherwise and indicates that they were hunter gatherers who derived 30-40% of their calories from lean meat, bone marrow and animal brain [58] . Cordain et al [59] estimates that the worldwide average protein consumption of hunter-gathers was in the range of

19-35% of total energy. The tentative conclusion from this research is that our genetic makeup, which is virtually unchanged since the Stone Age, is suited to a diet that includes considerable protein and fat from animal sources.

Thus the criticism of low-carb diets that they contain too much protein does not appear justified except for individuals with special medical problems or who eat huge amounts of meat. Red meat and processed meats (bacon, ham, etc.) constitute a special case to be discussed below. However, no really long-term studies on the safety of *very* high protein diets are available (Willett's criticism, [27]), but the high score prudent diet quintile in the Nurses' study [60] had a daily consumption of 100 g, which for a 150 lb woman is about 1.5 g/kg, almost twice the Establishment number, and this was a long-term study.

CARBOHYDRATES. Before the advent of agriculture, which originated about 10,000 years ago, humans obtained their carbohydrate principally from leaves, roots, berries, nuts, and occasionally honey. Cordain et al [59] estimate that our Stone Age ancestors obtained 22-40% of their energy from carbohydrates. These carbohydrates were mostly of the type that were slowly digested and presumably did not result in large swings in insulin and blood glucose. With agriculture came the cultivation of grains, which assumed an ever-increasing role as an important food source. Moving forward to the present, the treatment of grains has become highly sophisticated and commercialized. The fine grinding of grains along with the removal of the outer covering which contains many nutrients and fiber has resulted in flour that is rapidly digested, can produce huge swings in both blood sugar and insulin, and is mainly starch. The feeding of grain and corn to animals raised for meat has changed dramatically the distribution of the various types of fat in the meat, especially in animals fattened in feed lots, as compared to free range or wild animals. Today, the typical North American consumes 50-55% of total energy in the form of carbohydrates, which translates to over 200-300 grams per day. This is in total harmony with the USDA food pyramid. More about this pyramid later.

The terms *complex* and *simple* are frequently used to describe carbohydrates, and those labeled complex have tended to be regarded as superior health-wise. Sugars such as sucrose and fructose were labeled simple, whereas the carbohydrates in bread and starchy foods such as potatoes are considered complex. In fact, starch is just sugar molecules strung together, and the digestive process rapidly breaks down these links to generate sugars, so the distinction between complex and simple is deceiving and misleading. The effect on blood glucose, the principal end result of carbohydrate digestion and absorption, is similar whether the source is sugar, white bread or potato. An average sized potato is equivalent to about ¼ cup of sugar. Over the last century the consumption of sugar in North America has constantly increased, reaching about 150 pounds per person per year, which is an astounding figure considering many people eat far less. A lot of this sugar is hidden in prepared foods such as baked goods, canned food, low-fat foods, etc. There are those who consider this huge sugar consumption to be a serious health issue [61].

Today the terms complex and simple have been largely replaced by a new nomenclature—high and low glycemic index carbohydrates [62]. The glycemic index (GI) indicates the effect, for normal, healthy individuals, of a measured amount of the food on the rise and subsequent fall of blood sugar. This generates a scale which uses as a reference point for comparison the effect of either white bread or pure glucose. Another yardstick, which is also gaining popularity, especially in nutritional epidemiology, is the glycemic load (GL), defined as the glycemic index times the amount of carbohydrate. The basic idea is that eating a small amount of a high GI food can be equivalent to eating a large amount of a low GI food, and that the glycemic load is an appropriate measure of the influence of a typical serving of a carbohydrate containing food. The GI is a useful guide to food selection if the goal is to reduce swings in blood sugar and insulin, since eating significant amounts of high GI foods with a meal, even in the presence of fat and protein, will generally elevate the blood glucose levels more than will a low GI mix of carbohydrates with the same protein and fat meal.

There is a growing consensus, even it would appear among the experts advising The Establishment, that it is wise to limit high GI foods and emphasize low GI foods. Thus the frequently and recently seen recommendation to eat vegetables, fruit, and whole grains, beans and legumes, and avoid potatoes, sugar, and foods made from refined flour such as bread, cookies, muffins, other baked goods, flour tortillas, and most pasta. This recommendation is inconsistent with the guidelines contained in the USDA food pyramid or in the standard recommendations from nutritional experts or even

the American Diabetes Association a few years ago. Interested readers should consult Dr. Walter Willett's new book, *Eat, Drink and be Healthy, the Harvard Medical School Guide to Healthy Eating* [27], for a scathing criticism of the USDA pyramid and a discussion of the important question of what carbohydrates to eat. This book was reviewed in IHN, April 2003.

Eating foods with a high GI or large amounts of foods with a low GI, i.e. a high GL, can result in significant blood glucose elevation after eating, so-called postprandial hyperglycemia, which is accompanied by elevated insulin levels. In the presence of insulin resistance, there may be what is called compensatory hyperinsulism, i.e. abnormally high insulin levels to compensate for the lack of insulin sensitivity as the body attempts to regulate the blood glucose levels. Thus questions have arisen as to the possibility of health problems associated with postprandial hyperglycemia and hyperinsulinemia. A number of studies have provided strong evidence that the consumption of high GI and GL meals contributes significantly to the risk of CHD, CVD and diabetes [63,64,65]. The other area of interest involves the connection with cancer. Both of these concerns have recently been reviewed in the journal *Nutritional Reviews* by Janette Brand-Miller [66]. There have been a number of case-control studies (See [1] for a discussion of the various types of epidemiologic study) of the question of a connection between cancer and a high dietary glycemic load and the consumption of high GI foods. Studies involving colorectal cancer [67], breast cancer [68] and endometrial cancer [69], have all indicated enhanced risk even after correcting for confounding factors. However, the evidence from large prospective studies of breast cancer [70] and colorectal cancer [71] have not confirmed these findings, although a prospective study based on the Nurses' Study data found that impaired glucose metabolism may play a role in pancreatic cancer [72]. Thus there remains considerable uncertainty regarding the GI-GL cancer connection [66]. In spite of this, the evidence regarding the enhanced risk of CHD, CVD and diabetes should be sufficient to raise real concerns about this aspect of diet, quite independent of the ultimate resolution of the cancer risk question.

There is a certain irony in the fact that the widespread adoption of the low-fat dogma resulted in many cases in the substitution of fat with carbohydrates, many of which were from high GI foods. Dr. Gerald Reaven, in a recent paper regarding the effect of high-carb diets on triglyceride-rich lipoproteins, HDL cholesterol and the risk of CHD (Abbasi et al [73]), comments that "Given the atherogenic potential of these changes in lipoprotein metabolism, it seems appropriate to question the wisdom of recommending that all Americans should replace dietary saturated fat with carbohydrates." Dr. Walter Willett takes the same position [27] and recommends replacing saturated fat with unsaturated fat rather than carbohydrate.

DIETARY FIBER. There seems little doubt as to the health benefits of consuming adequate amounts of dietary fiber [74], which consists of the structural and other polysaccharides and lignin in plants that are not digested in the human stomach and small intestine. An added benefit of a diet adequate in fiber containing foods is that they are usually rich in micronutrients in addition to nonnutritive components that have health benefits. It is common practice today to classify fiber as either insoluble or soluble. Foods rich in soluble fiber include oats, beans and psyllium, whereas wheat bran is rich in insoluble fiber. Prospective, case-control and intervention studies that have investigated the relationship between fiber consumption and various diseases have not always yielded consistent or statistically significant results. The early hope, kindled in the early 70s by the observation that a high fiber diet was protective against colorectal cancer in Africans, has not withstood the scrutiny of modern epidemiology, although the American Dietetic Association still holds that position [74], based on a 1992 meta-analysis of case control-studies. However, when this analysis was refined by restricting it to studies that used validated dietary questionnaires, the risk became nil [75]. This is consistent with the recent prospective study [75] based on the Nurses' Health Study data as well as five other large prospective studies where the inverse relationship between fiber intake in the risk of colon cancer was weak or nonexistent [75].

On a more positive note, an inverse association between high fiber and whole-grain intake and the risk of diabetes has been recently reported [76], a result that is consistent with seven other prospective studies. Also, a higher intake of dietary fiber, particularly water-soluble fiber, has been associated with reduced risk of CHD [77]. In addition, Liu et al [78] found that higher intake of dietary fiber was associated with lower risk of both CVD and heart attacks, but the association was not statistically significant when adjusted for confounding. Nevertheless, the authors suggest that their data and that of others generally supports the current

dietary recommendations to increase the consumption of fiber-rich whole grains, fruits and vegetables for the primary prevention of CVD. These recommendations typically suggest consuming amounts and types of foods that translate into >25 g/day of fiber which is about twice the current national average of 14-15 g/day [79]. A problem with some studies is that the cohort in question had a rather high level of overall fiber consumption, which makes it difficult to assess the risk as a function of fiber intake. For example, in [78] the median intake in the lowest quintile was 18 g/day and in the highest quintile 26 g/day, whereas in [77], which found a stronger association, the total fiber intake in the lowest quartile was only 5.9 g/day.

The mechanism of the action of fiber in relation to health is no doubt complex, but dietary fiber has been shown to delay the absorption of carbohydrates after a meal and thus decrease the insulin response to carbohydrates, and higher insulin levels have been linked to blood lipid disorders, hypertension, abnormalities in clotting factors, and atherosclerosis. Water-soluble fiber decreases total and LDL cholesterol, but the effect is small unless huge amounts of fiber are consumed. Dietary fiber has also been associated with other CVD risk factors such as fasting insulin, and levels of triglycerides and fibrinogen [74,77].

DIETARY FATS AND RED AND PROCESSED MEAT. In the great diet debate, fats get most of the attention and generate most of the controversy and animosity. It is clear from reading dietary recommendations in the popular press as well as in medical and nutritional journals that the notion is still common that fat is bad and low-fat diets are the way to go. This subject was reviewed recently in three issues of the IHN [1] and by Gary Taubs in two articles, one titled “The Soft Science of Dietary Fat” in the journal Science [2] and the other titled “What If It Has Been A Big Fat Lie,” the cover story in a recent issue of the New York Times Magazine [3]. Dr. Walter Willett has a chapter devoted to this subject titled “The Surprising News About Fat” in his book *Eat, Drink and Be Healthy.* A very recent review in *JAMA* by Hu and Willett [4] is highly recommended in connection with the question of dietary fat and heart disease, as is the review by Hu et al on types of dietary fat and the risk of CHD [80]. For the past several decades, low-carb diets that were high in fat and protein were condemned because they violated the First Commandment of health, i.e. avoid all fat as much as possible because fat is bad for you. Since it was never possible for The Establishment, no matter how hard they tried [2,3], to provide an evidence based case against all fat, over the past decade or so the position has shifted to the condemnation of only saturated fat and *trans*-fat. The evidence that the mono- and polyunsaturated fats had many healthy attributes could no longer be ignored!

Saturated fat increases LDL *and* HDL cholesterol in many individuals. Since LDL is considered bad and HDL good, one can argue that the outcome is more or less neutral rather than a bad mark against saturated fat. However, this is definitely not the Establishment view. And in addition, attention must be paid to the triglyceride (TG) levels. Elevated TG levels are considered to be an independent cardiovascular risk factor [81,82], and high TG levels coupled with low HDL levels are also a significant risk factor for CVD [83]. Elevated levels of triglycerides are also associated with increased blood viscosity, also a predictor of CVD [84]. There is also considerable evidence that elevated TG levels combined with high total or LDL cholesterol levels yield enhanced risk of CVD [85]. It is worth repeating that low-fat high-carb diets rich in rapidly digested carbs tend to elevate TG and reduce HDL in many individuals, but this is still an area with many unresolved issues [86]. This is one of the principle arguments used by opponents of low-fat diets [27]. Favorable changes in these two blood lipids are generally seen when individuals on low-fat diets switch to low-carb diets. This dietary change generally results in moderate to large decreases in fasting triglycerides, with only a small increase in total cholesterol which are prevented or reversed if significant weight loss occurs. Increases in HDL are also seen in some studies of low-carb diets.

Epidemiologic studies aimed at determining the effect of saturated fat on the risk of CHD have been limited in number and inconsistent. In the most recent reviews of this question [4,80], only two studies are quoted where total fat and thus presumably saturated fat was reduced. One gave an increase, one a decrease in CHD risk. In a number of studies, however, where saturated fat was replaced by unsaturated fat, it was observed that there was a very significant decrease in the incidence of the first adverse coronary event or that there was protection from secondary adverse events. These studies are the principal basis for the commonly encountered recommendation today that saturated fat should be replaced by unsaturated fat rather than by carbohydrate, this latter action being the normal reaction to advice to reduce fat consumption. These studies, while providing important guidance, do not prove that saturated fat

is bad, but merely that changing the ratio of saturated to unsaturated is important. *Two variables were changed at once.* The Lyon Heart Study [87] which addressed the question of diet and secondary prevention of adverse cardiovascular events, found a large increase in the consumption of omega-3 fatty acids plus a Mediterranean type diet relatively high in fat (~30% of energy) produced a 73% reduction in new events compared to the "prudent Western diet" which was significantly lower in omega-3 fats. Also, a study from Harvard published in October, 2003 reports finding no support for associations between intake of total fat, cholesterol, or *specific types of fat* and the risk of stroke in men [88].

A 2001 paper from the Harvard School of Public Health by Hu et al [80] reviewed the relationship between the types of dietary fat and the risk of CHD. Their comment on the results from the Nurses' Study merits quoting. *"The association between saturated fat and CHD observed in the Nurses' Health Study was much weaker than predicted by international comparisons, but is consistent with the possibility that the proportional increase in plasma HDL concentration produced by saturated fat somewhat compensates for its adverse effects on the LDL level."* Note that the principal reason The Establishment condemns saturated fat is that it raises LDL. This review (free full text at www.jacn.org/) contains an excellent discussion of the importance of omega-3 fatty acids and many other issues related to fat and heart disease. Their conclusion section includes the following statement. *"It has been increasingly recognized that the widely promoted low-fat concept is too simplistic and not compatible with available scientific data."* Hung et al [89] also provide a good review of the arguments in favor of diets higher in monounsaturated fatty acids, fiber and low GI foods in the context of insulin resistance, glycemic and blood lipid control.

A recent study by Sacks and Katan [90] is directly related to the question of the level of dietary fat that is beneficial. They examine three diets which were compared with the standard Western diet: (a) the AHA step 1 diet with 30% fat, 55-60% carbohydrate, and 10% saturated fat; (b) a low-fat diet with 20% fat, 65% carbohydrate, 7% saturated fat and (c) the Mediterranean diet estimated at 38% fat and rich in unsaturated fats. The standard Western diet was taken to contain 38% fat, 42% carbohydrate, and 17% saturated fat. All numbers are percentages of total energy. These diets were analyzed on the basis of estimates of the effects of diet composition, including the intake of unsaturated fats, on HDL, LDL and TG levels, available from epidemiologic data, and the associated changes in the risk calculated. As compared to the Standard Western diet (38% fat), the 30% fat diet gave a 0% increase in CHD risk for men, and an 8% increase for women. The 20% fat diet yielded a 1% increase for men and a 21% increase for women. The Mediterranean diet with its high level of unsaturated fat gave a 19% *decrease* in risk for men and a 16% *decrease* for women as compared to the Western diet. Examination of their data reveals the interaction between the postulated changes in risk due to the elevation of TG, the decrease in HDL and the decrease in LDL as the fat content of the diet was reduced. The predicted effects in men suggest the futility of the low-fat intervention. The predicted adverse effect of low-fat intervention in women, in the words of the authors, "*raises further questions about safety.*" The Mediterranean diet produced results that compare favorably with drug interventions for hyperlipidemia.

The bottom line is that the case against saturated fat as being bad in the context of heart disease appears very weak, but that the advice to decrease saturated fat and increase unsaturated fat should be taken seriously because there is a reasonable amount of evidence based justification for such a dietary modification. Thus the criticism of the low-carb diets as regards saturated fat contains an element of "evidence based truth." The results of large prospective epidemiologic studies support the hypothesis that CHD risk depends on the type rather the quantity of dietary fat, and that the adverse effects of *trans*-fats extend beyond their adverse influence on the LDL/HDL ratio. Consumption of linoleic and particular α-linolenic acid (an omega-3 fatty acid) appear to reduce the risk of CHD [91].

There are many health problems aside from the above mentioned elevation of TG and suppression of HDL that are associated with a very low-fat or "almost zero fat" diets which are heavy in high GI carbs. A good source for a discussion of low-fat diets based on modern endocrinology can be found in Dr. Diana Schwarzbein's book *The Schwarzbein Principle.* She has treated countless patients over a number of years suffering the ill and sometimes near fatal effects of such diets. For diabetics, Dr. R. K. Bernstein provides a modern discussion of fat in the context of blood sugar control [92].

The connection between dietary fat and cancer and in particular meat and red meat and cancer has

been a subject of great interest since early studies indicated a strong connection, even prompting the National Academy of Sciences to suggest in 1982 that decreased fat intake might result in decreased rates of breast, colorectal and prostate cancer. Since that time, analytic epidemiologic studies have generally failed to substantiate these early findings [93], and in the case of breast cancer it is now generally accepted that total dietary fat intake is not significantly related to risk. [93]. But a pooled analysis of prospective studies found a weak positive association between breast cancer risk and saturated fat among both pre- and postmenopausal women, but no association with other fats [94]. Also, in a very recently published prospective study [95] that concentrated on premenopausal women (age 25-33 at the start of the study, the Nurses' Health Study II), it was found that the intake of animal fat during the premenopausal years, mainly from red meat and high-fat dairy foods, was associated with an increased risk of breast cancer. Disagreement with other studies that found no association, especially with red meat, was attributed to the age distribution in the groups studied. Both cancer of the colon and prostate appear to carry positive risk associated with red meat intake [93]. It is unclear whether it is a fat component or some other factor related to drugs or chemicals present in the meat or to the method of preparation. In the case of colon cancer, studies suggest that fat intake per se is not a risk factor [93]. Also, not all studies are consistent. Hill [96] reviews a number of studies that suggest rejecting the connection between colorectal cancer and meat. Case-control studies related to pork consumption and colorectal cancer, for example, vary widely and are inconsistent with odds ratios ranging from 0.39 (very protective) to 3.3 (very risky) [93]! Processed meats such as ham and bacon are well known to contain chemicals that are transformed on cooking into chemicals that are carcinogenic in animals. Finally, there is no modern epidemiologic evidence implicating vegetable fats in the etiology of cancer.

Frequently encountered advice encourages individuals to limit their intake of dairy products. Norat and Riboli [97] have recently reviewed studies that address the question of the connection of dairy products and colorectal cancer. Their findings indicate that cohort studies consistently found a protective effect of total dairy products and milk intake. No relationship was found with cheese or yoghurt intake. However, as mentioned above, a very recent study linked high-fat dairy products to breast cancer in premenopausal women.

The role of fat in the etiology of diabetes has been the subject of much debate in recent years. Two recent studies, one based on the Nurses' Health Study [98], and the other on the Health Professionals Follow-up Study [99], find essentially no association between fat intake and the risk of developing diabetes. For women, neither total fat, saturated fat or monounsaturated fatty acids intakes were associated with an increased risk of type 2 diabetes, but trans-fatty acids increased the risk and polyunsaturated fatty acids reduced the risk. For men, the association between total and saturated fat intake and an elevated risk for type 2 diabetes was eliminated when BMI was taken into account. Frequent intake of processed meats was found to perhaps increase the risk. However, Schulze et al [100] have recently reported a large study that implicates diets high in processed meats as increasing the risk for type 2 diabetes in women. A relative risk of 1.91 was obtained when less than once a week consumption was compared with five times a week. The authors suggest nitrites and advanced glycation end products may be implicated.

Therefore it appears prudent when considering sources of fat for a low-carb diet to limit the intake of red meat and processed meats, and high-fat dairy products, and to emphasize mono- and polyunsaturated fats over saturated fat. Thus there is some justification for the criticism leveled by the critics of low-carb diets and especially the Atkins Diet, as regards unlimited and indiscriminate meat and high-fat dairy food consumption. Also, the low-carb dieter has a wide choice of fat sources such as fish, poultry, and nuts, and oils. There is essentially universal agreement as to the potentially adverse effects of consuming *trans*-fats (See [1] for a review of this subject).

DIETARY PATTERNS. We rarely eat individual macronutrients in isolation, but rather eat meals consisting of a variety of foods with complex combinations of nutrients, *both macro and micro*, that are quite possibly either interactive or synergistic. We are now seeing studies that attempt to address this problem by examining the relationship between whole dietary patterns and the incidence or risk of disease [101,102]. Dietary pattern analysis is viewed as complementary to more traditional analysis and as well can be used to determine if the effect of a specific nutrient is independent of overall dietary patterns, and the pattern approach can also be used to evaluate dietary guidelines. Most importantly, it can identify types of diets that carry low risk for particular

diseases such as cancer, diabetes or CHD without dealing in detail with the relative merits of the individual components. Two popular methods, factor analysis and cluster analysis are by their very nature *a posteriori*, since the eating patterns are derived through statistical modeling of dietary data. The results so far have been quite interesting.

- Two recent studies, one based on the Nurses' Health Study [60], the other on the Health Professionals' Follow-Up Study [103], identified two major dietary patterns. One, called the "prudent" pattern," was characterized by higher intake of fruits, vegetables, fish, whole grains and legumes. The other, called the "Western Pattern" was characterized by higher intake of red and processed meat, high-fat dairy products, refined grains, French fries, sweets and desserts. In both men and women, the prudent diet was associated with decreased risk of CHD whereas the Western diet provided increased risk. For example, when women in the highest prudent diet quintile and the lowest Western quintile were compared to those with the opposite extreme pattern, the relative risk of CHD was 0.64, a dramatic reduction. Similar results were obtained in the men's study.
- A recent study, from Harvard [104] where no association was found for breast cancer risk when a Western diet (red and processed meat, refined grains, fat and sweets) was compared to a 'healthy" diet (fruit and vegetables, fish and poultry, low-fat dairy and whole grains). Alcohol was found to increase the risk. These results are consistent with a recent pooled analysis of cohort studies by Missmer et al [105]. It is interesting that the pattern analysis found no risk with the Western pattern in spite of the recent study [95] quoted above that linked animal fat and high-fat dairy food with breast cancer.
- In another study from Harvard [106] based on the Nurses' Study data, which yielded on factor analysis the two major dietary patterns described above, the "Western" and the "Prudent," no significant positive association between the Western dietary pattern and the risk of colorectal cancer was observed, and the protective nature of the prudent pattern for colon cancer was not statistically significant.
- The Harvard group [107] found that a "Western" type diet pattern was associated with a substantially increased risk of type 2 diabetes in men. This is particularly interesting in connection with the hypothesis discussed above that type 2 diabetes is a vascular disease, since the Western diet also carried a higher risk for CHD. When low physical activity and obesity were also included in the analysis, the relative risk was 11.2, a particularly high risk.

The researchers at Harvard and their collaborators suggest that the relationship between CHD risk and dietary patterns, which appear to apply to both men and women, may act through biochemical factors. In an earlier study [108] they had found the prudent pattern in men was associated with lower levels of insulin, and the Western pattern was associated with higher levels of tissue plasminogen activator, fasting insulin, leptin and homocysteine, markers consistent with increased risk of CHD. Also, the women with the higher prudent-pattern score had higher intake of protein, folate (folic acid) and fiber. In connection with protein consumption and the "protein question" discussed above, Appel [56] in his review points out that in the prudent diet, the highest score went with the highest protein consumption (100g/day) whereas the highest Western diet pattern score had the lowest protein consumption of 90 g/day.

COMBINING LIFESTYLE AND DIET. While such aspects of lifestyle as exercise and smoking have not been discussed, they are very important modifiable aspects of risk for both diabetes and heart disease. The following studies leave no doubt.

- In a 16-year follow-up [7] over 84,000 women in the Nurses' Study, free at baseline of diagnosed CVD, diabetes or cancer, were studied to determine the incidence of type 2 diabetes. As compared to the rest of the cohort, women in the upper 40% of the dietary score who exercised 30 min/day, had a BMI <25, did not smoke but consumed alcohol had a risk factor of 0.09, that is, 91% of the cases of diabetes in this cohort could be attributed to habits and forms of behavior that did not conform to the low risk pattern. Just including diet, exercise and BMI gave a risk factor of 0.12, still sensationally low. The low risk diet was defined as low in *trans*-fats and GL and high in cereal fiber with a high ratio of polyunsaturated to saturated fat.
- In a study [5] of men and women, average age 51, with IGT (impaired glucose tolerance) and IFG (impaired fasting glucose) and a BMI equal or greater than 24, diet and lifestyle modifications were introduced to determine the effect on the progression to type 2 diabetes. The modest goals were at least a 7% reduction

in weight and at least 150 minutes of physical activity per week. The dietary recommendations involved a low-calorie low-fat diet. The result was a 58% reduction in the progression of IFG and IGT to diabetes, as compared to the placebo group (there was also a drug intervention arm of this study).

- In a recent study [6] 522 men and women, mean age 55 with IGT were randomly assigned to an intervention or control group. The intervention group received individual guidance on increasing physical activity. The intervention diet had a weight reduction goal of only 5% minimum and involved a diet with less than 30% fat, l0% saturated fat, fiber intake of at least 15g/1000 cal, frequent ingestion of whole-grain products, vegetables, fruits, low-fat milk and meat products, soft margarines, and oils rich in monounsaturated fat. The risk of type 2 diabetes was reduced by 58% in the intervention group as compared to the control group.
- In a study [8] of primary prevention of CHD in women using the Nurses' Study data, diets were scored according to a 'low risk" diet low in *trans*-fats and GL, high in cereal fiber, marine omega-3 fatty acids, and folate with a high ratio of polyunsaturated to saturated fat. During follow-up of 14 years, women in the upper 40% of the diet score, non-smoking, BMI<25, 30 minutes of exercise per day, and alcohol consumption of equal to or greater than 5 g/day had a sensational reduction in risk of CHD for a relative risk of 0.17. Eliminating alcohol raised the risk factor to 0.34, and in addition removing the BMI restriction, raised it to 0.43.

CONCLUSION. The summary given in Chapter 11 of Walter Willet's book *Eat, Drink and be Healthy* nicely summarizes the conclusions that arise from the scientific studies discussed above. He suggests [27]:

- maintaining a stable, healthy weight;
- replacing saturated and *trans*-fats with unsaturated fats;
- substituting whole-grain carbohydrates for refined-grain carbohydrates;
- choosing healthier sources of proteins by trading red meat for nuts, beans, chicken and fish
- eating plenty of vegetables and fruits; and
- using alcohol in moderation.

In other words, adhere to the "prudent diet" and avoid the "Western diet," as defined by the diet pattern studies from Harvard and supported by extensive prospective studies involving huge cohorts and long follow-up. It also seems clear that concerns over protein consumption exceeding the Establishment recommendation are unwarranted, that fat, except for *trans*-fat, is by and large good for one with the qualification that excessive saturated fat, especially at the expense of unsaturated fat, may not be healthy and that red and processed meats may carry some risk. Willett's recommendation of avoiding refined grains is equivalent to the emphasis of low-GI sources of carbohydrates, as is his recommendation regarding fruits and vegetables, although some fruits carry a rather high GI.

So far, it seems that nutritional epidemiology has identified only a handful of macronutrients that it might be wise to minimize or avoid in making dietary decisions. These include red meat, processed meats such as bacon, ham, sausage etc, saturated fat, high-fat dairy products, as well as the high GI foods such as starchy foods and those made from highly refined grains, white rice, sugars, and of course anything containing any *trans*-fats. Considering the variety of foods available in this age of plenty, simply avoiding or limiting the consumption of these questionable food sources should not present a serious hardship, should not result in the failure to consume adequate amounts of important nutrients, and may well yield substantial health rewards.

See Part I for references*

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