

# INTERNATIONAL HEALTH NEWS

*Your Gateway to Better Health!*

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Welcome to our 12<sup>th</sup> year of publication! In this issue we present the final part of Professor Ware's article on fats and disease with a discussion of fats and cancer and recommendations regarding fat intake. I hope you have found this thorough review of the fat/disease connection as revealing as I have.

"A curry a day may well keep the doctor away" would be an easy conclusion to draw from the recent outpouring of scientific articles describing the many preventive and curative properties of curcumin, a component of the spice turmeric. Curcumin, which gives curry its characteristic colour, has been used in India for generations to treat inflammation, skin wounds, liver and gallbladder disorders, and persistent cough. In this issue we report that curcumin may also be effective against oral cancer and pancreatic cancer, but may interfere with some chemotherapy treatments.

In addition, we report that short walks are effective in reducing heart disease risk, aspirin needs to be treated with respect, and a handful of almonds a day is highly effective in lowering cholesterol levels.

Wishing you health and happiness in the New Year,

Hans Larsen, Editor

## January Highlights

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**Editor:** Folic acid can affect blood coagulation, but as far as I know, only in fairly large doses (10 mg/day). It has only been checked in people with high homocysteine levels, so I don't know if it also has a similar effect in people with normal homocysteine levels.

\*\*\*

I would like to find out if there are any negative effects if you eat 7.5 ounces of sardines a day.

JB, USA

**Editor:** I am not aware of any negative health effects of eating 7.5 oz of sardines a day. Quite the contrary, this amount would provide a daily intake of EPA of about 1 gram, DHA about 1 gram, calcium 800 mg, and selenium 100 mcg. However, it would also contribute 300 mg per day of cholesterol to your diet.

## LETTERS TO THE EDITOR

Does folic acid make ones blood thinner like aspirin does?

KAF, USA

I would like to know if phosphatidylcholine could help in prevention of mouth cancer.

AM, USA

**Editor:** *Phosphatidylcholine has been used in the prevention or treatment of elevated cholesterol levels, Alzheimer's disease, liver disorders, and bipolar depression; however, I have not heard of it being effective in the prevention of oral cancer. Very recent research has shown that curcumin, a component of the spice turmeric, may be quite effective in preventing and reversing oral cancer[1].*

[1] Rinaldi, Anthony L., et al. *Curcumin activates the aryl hydrocarbon receptor yet significantly inhibits (-)-benzo(alpha)pyrene-7R-trans-7,8-*

*dihydrodiol bioactivation in oral squamous cell carcinoma cells and oral mucosa. Cancer Research, Vol. 62, October 1, 2002, pp. 5451-56*

\*\*\*

Please advise regarding mercury levels in fish oil. I have researched the Internet and cannot find the information I want.

LE, USA

**Editor:** *Canned salmon and tuna and fresh salmon are all low in mercury. On the other hand, swordfish, fresh and frozen tuna, red snapper, and mackerel are high in mercury. Coromega ([www.coromega.com](http://www.coromega.com)) fish oil is very low in mercury. You might find others at [www.consumerlab.com/results/omega3.asp](http://www.consumerlab.com/results/omega3.asp).*

## ABSTRACTS

### Curcumin fights cancer

MIYAZAKI, JAPAN. Curcumin is a constituent of the spice turmeric. It is non-toxic and several studies have documented its anti-inflammatory, antioxidant, and anti-carcinogenic properties. Japanese researchers now report that curcumin is effective in inhibiting the growth of human pancreatic cancer cells. Pancreatic cancer cells, along with other cancer cells produce an inflammatory cytokine, Interleukin-8 (IL-8) that helps the cancer cells to grow. IL-8, in turn, needs nuclear factor kappaB (NF-KB) in order to reproduce. The researchers found that both IL-8 and NF-KB in pancreatic cancer cells are inhibited

by curcumin. This, in turn, inhibits further growth of the cancer cells.

The researchers conclude that curcumin reduces numerous IL-8 bioactivities that promote tumour cell viability and tumour progression. They suggest that curcumin may be beneficial for patients with carcinoma affected by the enhanced production of pro-inflammatory cytokines.

*Hidaka, Hideki, et al. Curcumin inhibits interleukin 8 production and enhances interleukin 8 receptor expression on the cell surface. Cancer, Vol. 95, September 15, 2002, pp. 1206-14*

### Short walks are effective

JORDANSTOWN, NORTHERN IRELAND. Conventional wisdom has it that exercise, to be an effective health measure, must be vigorous and sustained. A team of researchers from three British universities now challenges this assumption. Their study involved 21 middle-aged, sedentary, moderately overweight men and women. Sedentary was defined as having engaged in less than 20 minutes of planned exercise per week during the preceding 3 months. The study participants were randomized (in a

cross-over design) to 1 of 2 groups. The first group undertook brisk walking for 30 minutes 5 days a week for 6 weeks. The second group took 3 daily walks (separated by at least 3 hours) of 10 minutes each 5 days a week for 6 weeks. The trial was followed by a 2-week period of no walking after which the first group walked for 3 x 10 minutes while the second group walked for 30 minutes at a time.

Both protocols were effective in increasing blood levels of HDL (good) cholesterol while decreasing

levels of total cholesterol and triglycerides. They also were equally effective in reducing tension, anxiety, and diastolic blood pressure (by 1.5 mm Hg). The 10-minute walk program produced a greater increase in maximal oxygen uptake than the 30-minute program (14.2% versus 3.8%).

The researchers conclude that 3 10-minute bouts of brisk walking throughout the day for 5 days a

week are at least as effective as a daily 30-minute walk in reducing anxiety and tension, and in reducing cardiovascular risk in previously sedentary individuals.

*Murphy, Marie, et al. Accumulating brisk walking for fitness, cardiovascular risk, and psychological health. Medicine & Science in Sports & Exercise, Vol. 34, September 2002, pp. 1468-74*

## Glucosamine – Buyer beware!

EDMONTON, CANADA. Glucosamine is a natural component of glycosaminoglycans found in cartilage and synovial fluid. Several studies have concluded that glucosamine is effective in the treatment of osteoarthritis of the knee and other areas. In Europe glucosamine is regarded as a medication and is subject to strict quality control. In Canada and the US it is freely available as glucosamine sulfate (GLS) in health food stores.

Researchers at the University of Alberta recently concluded a study aimed at determining the quality of over-the-counter GLS products available in Canadian health food stores. They obtained samples of 15 products from different manufacturers and analyzed their content of GLS and the free base glucosamine, which is believed to be the active ingredient. They observed one immediate problem with the labeling. Many GLS products did not state whether the 500 mg they contained was 500 mg of GLS or 500 mg of glucosamine, the active component. This is important, as 500 mg of GLS would contain, at most, 394 mg of glucosamine.

The researchers found that the amount of glucosamine present in the samples varied widely from the amount stated on the label. Some brands claiming a content of 500 mg of GLS per capsule actually contained as little as 295 mg and only 2 out of 15 actually contained 500 mg or more of GLS. One brand had a labeled content of 1500 mg of GLS, but in actual fact contained only 800 mg. Generally, the products contained only around 50-60% of the stated amount of GLS. The researchers recommend that the exact amount of free glucosamine present in the tablets or capsules be stated on the label.

*Russell, Anthony S., et al. Active ingredient consistency of commercially available glucosamine sulfate products. Journal of Rheumatology, Vol. 29, November 2002, pp. 2407-09*

**Editor's comment:** I personally find it very disturbing and sad that 13 out of 15 of what I have, until now, considered reputable Canadian supplement manufacturers have been found to shortchange their customers by as much as 50% when it comes to the labeling and sale of GLS.

## Another aspirin warning

PHILADELPHIA, PENNSYLVANIA. Aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) are among the most commonly used non-prescription medications and are often used on a continuous (chronic) basis. These drugs, despite their public image of being safe, are not wholly benign, even at low dosages.

Researchers at the University of Pennsylvania have just completed a study to determine the incidence of gastrointestinal problems among users of aspirin and other NSAIDs. Their study involved 535 people who had used non-prescription NSAIDs on a regular basis over the past 30 days and 1068 controls who had not used

NSAIDs within the last 30 days. The NSAID users' reasons for using the medication was prevention of stroke and heart attack (43.2%), pain relief (44.2%), and relief of arthritis symptoms (24.5%). The incidence of gastrointestinal (GI) side effects among users was 19.6% versus 9.5% for non-users. The most common complaint was constipation and/or diarrhea (experienced by 9.2% of users and 3.8% of non-users). Bleeding or stomach ulcers were experienced by 0.6% of the NSAID group and 0.3% of the non-user group. Almost 50% of NSAID users took another medication to combat

their GI problem while only 20% of non-users did so.

Researchers at the University of Michigan in commenting on the findings point out that neither low-dose aspirin, enteric-coated aspirin or buffered aspirin reduce the risk of GI complications. They also emphasize that the US Preventative Services Task Force recently recommended that low-dose aspirin only be taken by people who have been specifically determined to have a greater than 3% risk of having a cardiovascular event within the next 5 years.

*Thomas, Joseph, et al. Over-the-counter nonsteroidal anti-inflammatory drugs and risk of gastrointestinal symptoms. American Journal of Gastroenterology, Vol. 97, September 2002, pp. 2215-19*

*Scheiman, James M. and Fendrick A. Mark. NSAIDs without a prescription: over-the-counter access, undercounted risks. American Journal of Gastroenterology, Vol. 97, September 2002, pp. 2159-61*

**Editor's comment:** This study confirms my own conclusion that aspirin, even baby aspirin (81 mg), should not be used on a continuous basis unless there is a valid, documented medical reason for doing so.

## Natriuretic peptides and heart disease

FRAMINGHAM, MASSACHUSETTS. Natriuretic peptides are cardiac hormones with diuretic, natriuretic, and vasodilatory properties. Atrial natriuretic peptide (ANP) and its N-terminal prohormone (NT-ANP) are produced in the atria, whereas brain natriuretic peptide (BNP) is produced in the ventricles. Both hormones are produced in response to stretching of the walls of the heart. Higher than normal levels of these hormones are found in patients with heart failure and left ventricular dysfunction (low ejection fraction).

Clinicians have long attempted to use blood levels of ANP and BNP as a means of diagnosing congestive heart failure and left ventricular dysfunction. However, this approach has, so far, not been very successful because of the lack of data required to establish normal reference ranges. Now researchers at the Harvard Medical School and the Massachusetts General Hospital have overcome this problem. The researchers evaluated 911 healthy subjects (342 men and 569 women) with an average age of 55 years. All had fasting blood samples drawn and analyzed for NT-ANP and BNP.

The researchers found that women had markedly higher levels of natriuretic peptides than did men. Older people also had significantly higher levels than younger people. A 10-year increase in age was associated with a 1.4-fold increase in BNP

levels and a 1.2-fold increase in NT-ANP levels. A high diastolic blood pressure was associated with lower BNP and NT-ANP levels as was a higher body mass index. A large left atrium, on the other hand, was associated with higher BNP and NT-ANP levels.

The researchers propose upper (97.5<sup>th</sup> percentile) limits above which left ventricular dysfunction or heart failure should be suspected. Examples are:

- Men between 20 and 49 years      BNP: 26 pg/mL      NT-ANP: 574 pmol/L
- Women between 20 and 49 years      BNP: 38 pg/mL      NT-ANP: 664 pmol/L
- Men over 70 years      BNP: 52 pg/mL      NT-ANP: 1260 pmol/L
- Women over 70 years      BNP: 71 pg/mL      NT-ANP: 1430 pmol/L

The researchers caution that natriuretic peptide levels above these reference levels do not necessarily imply that heart failure or ventricular dysfunction is present. Other conditions such as hypertension and renal failure can also cause abnormally high natriuretic peptide levels.

*Wang, Thomas J., et al. Impact of age and sex on plasma natriuretic peptide levels in healthy adults. American Journal of Cardiology, Vol. 90, August 1, 2002, pp. 254-58*

## Antioxidant protects against kidney damage

TAIPEI, TAIWAN. Cardiac angiography and angioplasty can be hard on the kidneys because of the deleterious effects of the contrast medium (iopamidol) injected in order to facilitate the

viewing of the heart during the procedure. This problem is especially serious for patients already suffering from renal (kidney) failure.

Taiwanese researchers now report that oral supplementation with the antioxidant acetylcysteine largely eliminates the worsening of existing kidney problems. Their clinical trial included 121 patients with chronic renal insufficiency (mean serum creatinine level of 2.8 mg/dl). The patients were randomized to receive either 400 mg of acetylcysteine twice a day on the day prior to the procedure and on the day of the procedure or placebo. Both groups also received saline infusions (0.45%) at a rate of 1 mL/kg body weight per hour for 12 hours before and 12 hours after angiography. An acute contrast medium-induced reduction in renal function occurred in 25% of the patients in the control group, but in only 3% of the patients in the acetylcysteine group. The average creatinine level among the control patients increased from 2.8 mg/dL to 3.1 mg/dL 48 hours after injection of the contrast agent. The acetylcysteine group, on the other

hand, saw a drop in average creatinine level from 2.8 mg/dL to 2.5 mg/dL.

The researchers conclude that acetylcysteine protects against contrast medium-induced kidney damage, not only in patients with moderate renal insufficiency, but also in those with severe renal insufficiency.

*Shyu, Kou-Gi, et al. Acetylcysteine protects against acute renal damage in patients with abnormal renal function undergoing a coronary procedure. Journal of the American College of Cardiology, Vol. 40, October 16, 2002, pp. 1383-88*

**Editor's comment:** Contrast medium injection is toxic to kidney cells and causes a marked increase in free radical production in the kidneys. Thus it would seem to me that acetylcysteine supplementation prior to and during angiography and angioplasty may also be a good idea for patients with healthy kidneys.

## Almonds reduce risk of heart disease

TORONTO, CANADA. High cholesterol levels are a risk factor for coronary heart disease (CHD). A high level of low-density lipoprotein cholesterol (LDL) is particularly deleterious with a 1% increase in LDL corresponding to a 2% increase in CHD risk.

Canadian medical researchers now report that daily consumption of almonds significantly reduces CHD risk factors in patients with high cholesterol levels (hyperlipidemia). Their crossover experiment involved 27 otherwise healthy men and postmenopausal women with an average total cholesterol level of 6.50 mmol/L (254 mg/dL). The study participants were randomized to consume (on a daily basis), in addition to their regular diet, either 73 grams of almonds, 37 grams of almonds or whole-wheat muffins supplying the same amount of calories. The almonds or muffins were added to the diet for a 4-week period. This was followed by a 2-week washout period and the participants then switched to a different "supplement" for another 4-week period.

The researchers found that addition of 73 grams of almonds to the daily diet reduced total cholesterol level by 9.4%, LDL level by 10%, LDL:HDL cholesterol ratio by 12%, and oxidized

LDL concentration by 14%. The effect of 37 grams of almonds was correspondingly less – a 4.4% reduction in total cholesterol and a 7.8% reduction in LDL:HDL ratio. Cholesterol levels were not reduced in the muffin group, but a 10.8% increase in triglycerides was observed in this group.

The researchers point out that 73 grams of almonds would also add 18 mg of vitamin E to the diet every day. They estimate that the 10% reduction in LDL levels attained on the 73 grams/day almond "diet" would correspond to a 20% decrease in the risk of coronary heart disease. They suggest that nuts should be considered for inclusion in lipid-lowering diets.

*Jenkins, David J.A., et al. Dose response of almonds on coronary heart disease risk factors: blood lipids, oxidized low-density lipoproteins, lipoprotein(a), homocysteine, and pulmonary nitric oxide. Circulation, Vol. 106, September 10, 2002, pp. 1327-32*

**Editor's comment:** 73 grams of almonds corresponds to about 1/3 to 1/2 cup or about 65 almonds. This amount would also provide a very healthy 200 mg of easily absorbable magnesium on a daily basis.

## Curcumin fights oral cancer

COLUMBUS, OHIO. Oral squamous cell carcinoma (SCC) is the 7<sup>th</sup> leading cancer in the United States. Its most likely causes are smoking and alcohol consumption. Researchers at Ohio State University now report that curcumin, a component of the natural spice turmeric, is highly effective in not only preventing, but also in halting oral SCC.

Their experiment involved the exposure of oral SCC cells to curcumin in a culture medium and the exposure of normal oral tissue to the tobacco-associated carcinogenic agent, benzo(alpha)pyrene with and without the presence of curcumin. The researchers found that curcumin in concentrations greater than 25 micromol killed existing oral SCC cells and stopped the growth of cancer. They also found that healthy oral tissue exposed to benzo(alpha)pyrene did not turn cancerous when

pretreated with curcumin. They also noted that curcumin was highly effective in conserving intracellular levels of glutathione, the body's main endogenous antioxidant.

The researchers conclude that, "the use of curcumin as an oral cavity chemopreventive agent could be clinically significant". They suggest that curcumin could be incorporated into cigarette and smokeless tobacco formulations or could be used by smokers in the form of curcumin-containing lozenges as a means of preventing or treating oral SCC.

*Rinaldi, Anthony L., et al. Curcumin activates the aryl hydrocarbon receptor yet significantly inhibits (-)-benzo(alpha)pyrene-7R-trans-7,8-dihydrodiol bioactivation in oral squamous cell carcinoma cells and oral mucosa. Cancer Research, Vol. 62, October 1, 2002, pp. 5451-56*

## Curcumin and chemotherapy

CHAPEL HILL, NORTH CAROLINA. There is growing evidence that curcumin, a component of the spice turmeric, may be effective in the prevention of breast, prostate, colon, and oral cancers. Extracts containing curcumin have been used in India for generations in the treatment of inflammation, skin wounds, liver and gallbladder disorders, and persistent coughs. It is estimated that the average dietary intake of curcumin in India and certain parts of Southeast Asia is 200 mg/day or more.

Curcumin is a highly effective scavenger of reactive oxygen species (ROS) and also inhibits the JNK (c-Jun NH<sub>2</sub>-terminal kinase) pathway. Both ROS and an activated JNK pathway are crucial elements in successful chemotherapy. Researchers at the University of North Carolina now report that curcumin may interfere with the action of several chemotherapy drugs used in the

treatment of breast cancer. Culture experiments showed that curcumin inhibited the cancer cell destroying capability of several chemotherapy drugs (mechlorethamine, Adriamycin, and camptothecin) by as much as 70%. The results were confirmed in experiments with laboratory mice. It is believed that curcumin exhibits its effect through ROS scavenging and inhibition of the JNK pathway.

The researchers conclude that more research is urgently needed to establish whether breast cancer patients undergoing chemotherapy should be told to limit their intake of curcumin and turmeric extracts.

*Somasundaram, S., et al. Dietary curcumin inhibits chemotherapy-induced apoptosis in models of human breast cancer. Cancer Research, Vol. 62, July 1, 2002, pp. 3868-75*

## NEWSBRIEFS

**Economy class stroke syndrome.** German medical doctors report three cases of ischemic stroke that occurred during long-distance air travel. All patients (aged 21, 63 and 64 years) developed their symptoms toward the end of their

9000 km flights and had no prior indication that they were at risk for stroke. The German report comes hard on the heels of a report by French physicians who also reported three cases of stroke occurring during air travel. American

physicians have also made the connection and conclude that the “economy class” stroke syndrome may be more common than currently recognized.

*Neurology, Vol. 59, September 2002, pp. 962-63*

**Editor’s comment:** Drinking lots of water during a long flight may help in two ways. Water lowers blood viscosity and a high consumption of it also leads to frequent trips to the bathroom, i.e. getting out of a cramped seat and moving around.

**Wrong prescription for myopia.** Myopia (shortsightedness) is reaching epidemic proportions in Hong Kong, Singapore, and Taiwan where 90% of young people are shortsighted as compared to 15 to 30% in the US and Europe. Optometrists have traditionally prescribed eyeglasses or contact lenses for myopia that “undercorrected” for the problem. This was done in the hope of preventing the eyeball from elongating in the constant struggle to focus on close-up work. A study involving 94 Malaysian children was recently undertaken by British researchers to prove the value of undercorrection. The study was meant to run for 3 years, but was stopped after 2 years because the eyesight of the children got worse. Says optometrist Daniel O’Leary of Anglia Polytechnic University in Cambridge, “No glasses is the worst option of all, but don’t undercorrect for myopia. Go for full correction.”

*New Scientist, November 23, 2002, pp. 6-7*

**Vitamins and violence.** A group of British researchers claim that much of the violent behaviour found in prisons, especially among young offenders, is simply due to subclinical malnutrition. An experiment involving 231 young offenders found that prisoners given a multivitamin pill and a small amount of essential fatty acids every day committed 37% fewer serious or violent offences than the placebo group. When supplementation ceased levels of violence quickly returned to normal. Other researchers point out that omega-3 fatty acids are important for the production of the mood-altering neurotransmitter serotonin. However, the idea that supplements may help curb violent behaviour is by no means universally accepted and implementation of a supplement program is not likely to happen anytime soon. Some prisons in the US actually specifically ban supplements

because they might “increase the fighting ability” of the inmates. The prison system in the UK allows a total daily expenditure for food for a young offender of \$3.00 US. It is not likely that the system would take kindly to spending an additional \$1.50/day on supplements.

*New Scientist, November 16, 2002, pp. 38-41*

**Ecstasy and Parkinson’s disease.** Evidence is mounting of a connection between the recreational drug ecstasy (MDMA) and Parkinson’s disease. Last month the journal *Science* published a paper claiming that MDMA can damage dopamine cells and thus lead to Parkinson’s. Now scientists at the University of Manchester report that MDMA may actually be a very effective drug for reducing the uncontrollable movements of arms and legs, which often afflict Parkinson’s patients who have been on the drug l-dopa for extended periods. Experiments involving marmoset monkeys clearly demonstrated that MDMA reduced the bad side effects of l-dopa without blocking its beneficial effects. The researchers do not suggest that Parkinson’s patients should take MDMA as it is illegal, dangerous, and usually impure. However, they do suggest that their findings may lead to the development of safer drugs for counteracting the debilitating side effects of l-dopa.

*New Scientist, November 9, 2002, p. 14*

**MSG may damage eyesight.** MSG (monosodium glutamate) is a flavour enhancer commonly found in oriental and processed foods. It can affect the nervous system and cause migraine-type headaches. Japanese researchers now report that habitual consumption of MSG may also damage the retina and cause normal-tension glaucoma. The researchers fed a diet rich in MSG to laboratory rats for 6 months and found that MSG tended to concentrate in the vitreous fluid bathing the retina and ultimately destroyed retinal cells. The lead researcher, Dr. Hiroshi Ohguro, says that the findings might explain why there is a high incidence of normal-tension glaucoma in Eastern Asia where MSG is widely used. Normal-tension glaucoma eventually leads to blindness. It is not known whether occasional MSG consumption will have the same detrimental effect over a period of decades.

*New Scientist, October 26, 2002, p. 11*

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

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

## EGGS AND CHOLESTEROL

In the past 25 years, eggs have been held up as a prime example of fat, cholesterol and caloric excesses in the American diet. The widespread bad publicity resulted in almost a 50% drop in egg consumption. Eggs typically contain about 200 mg of cholesterol per egg, and are a major source of dietary cholesterol in Western diets. In addition, the egg contains many other nutrients including unsaturated fats, essential amino acids, folic acid and other B vitamins. Eggs are also low in saturated fat. The so-called omega-3 eggs from chickens fed on a diet that includes flax seed in addition have a high content n-3 polyunsaturates and in fact a very favorable ratio of n-3 to n-6 essential fatty acids. How deserving of blanket condemnation eggs really are has been addressed in a number of studies. They fall into two classes. First there are the studies that examine the relationship between dietary cholesterol and serum cholesterol. The other type of study actually examines the question of an association between egg consumption and heart disease and stroke. As regards cholesterol intake and serum levels, there have been a number of studies that find dietary cholesterol raises levels of total and LDL cholesterol, but the effects are very small, especially compared to the effects of saturated and *trans*-fatty acids (28). An interesting aspect of the cholesterol feeding studies is the observation that dietary cholesterol raises both LDL and HDL with little change in the LDL:HDL ratio. This provides another argument that dietary cholesterol is unimportant, except for the small minority who adversely respond to its ingestion (29). In fact there is a large variation in individual response of serum levels to dietary cholesterol, with many showing no change at all.

There have been 10 important prospective cohort studies of the effect of dietary cholesterol on the risk of heart disease. Only two provided a statistically significant indication that there was an increased risk, and these were not controlled for confounding from total energy or fiber (30). The two studies with corrections for confounding by total energy and fat or by total energy, fat and fiber both failed to provide a statistically significant indication of increased risk associated with an increment of 200 mg cholesterol per 1000 kcal caloric intake (about 400 to 500 mg/day). These two studies involved 37,851 men and 80,082 women. The study involving these two cohorts also looked at egg consumption in excess of one egg per day, and found no significant risk (28). Also, no risk associated with egg consumption was found for ischemic or hemorrhagic stroke. It is worth remarking that the eggs in these studies were not the new omega-3 eggs. These eggs are of recent origin and the studies in question involved a number of years of follow-up. In spite of these studies, the notion that eggs are associated with heart disease persists (31).

## FAT AND CANCER

The above discussion makes it clear that it is hard to document a convincing case, in connection with heart disease, against any kind of fat other than *trans*-fat. But how about the notion that fat causes cancer? As mentioned at the beginning of this review, the same types of studies done twenty or thirty years ago that suggested a link between fat and heart disease also implicated fat with the incidence of cancer. These studies suffered from the same weaknesses as those that attempted to associate fat and heart disease. The conclusions from these early studies have not been confirmed by modern epidemiology. Unfortunately, the only extensive data relates to breast and colon cancer, although there is significant data concerning prostate cancer. Other sites have not been studied with the statistical power found in studies of cancer epidemiology of these three sites, so any discussion of diet and cancer is of necessity incomplete. As regards breast cancer, the clearest and most consistent finding is that high calorie intake, regardless of the food source, is far more important than dietary fat. In the Nurses' Health Study, which involved a large cohort studied over a long period, there was no hint of an increase in breast cancer with higher dietary fat. In fact those with a



very low intake of fat (less than 15% of total calories) had a significant increased risk of breast cancer (3,32,33).

The early studies connecting colon cancer and dietary fat have also not held up against modern studies. The only connection appears to be with red meat, but no one knows if it is something in the red meat or has to do with chemicals produced on cooking. There is on-going research that is looking at this connection, especially the degree of "doneness" associated with cooking or broiling red meat. Again, the strongest link is with too many calories in relation to the exercise level--the problem of a positive energy balance (3,24,32,33).

The situation with prostate cancer is complex. The incidence and mortality of prostate cancer shows remarkable variation across geographical and ethnic groups, and changes in risk seen among migrants has inspired a search for dietary factors that might influence the development of this common disease. Fat is one of the most extensively studied dietary factors in this context. The current status has been reviewed by Moyad (34), Schulman et al (35) and earlier by Kolonel et al (36). Moyad reviews eleven prospective cohort studies involving over 200,000 subjects. While three studies showed positive association with red meat, the association failed to reach statistical significance. The one study that found a statistically significant connection between high-fat foods and prostate cancer has been criticized for an inadequate questionnaire and for the absence of high intakes of milk and beef that prevented the comparison with low intakes.

Case-control studies, on the other hand, have shown a connection between fat or fat-type food as well as *alpha*-linolenic acid and the incidence of prostate cancer. However, these studies are viewed as suspect because of recall bias and confounding. Also, prospective studies fail to confirm the positive risk connection with *alpha*-linolenic acid. Thus it seems clear that the association between dietary fat and the incidence of prostate cancer is very weak if not totally absent. However there is a positive association with red meat and dairy products and prostate cancer in individuals who have metastatic disease (37-40). In what appears to be the most recent large prospective study in this context, intakes of red meat and dairy products were not associated with total or advanced cancer (stage A2, B, C), but consumers of red meat had a significantly elevated risk of metastatic prostate cancer (stage D and fatal). A high intake of dairy products was also associated with an increased risk of metastatic disease, but the investigators were able to explain this association by known confounders (38). This study involved over 51,000 men followed for over 10 years. However, it is not clear if the connection with red meat is due to the meat per se or something in the meat or something associated with the cooking process. The association of prostate cancer with dairy products is thought to be confounded by the positive association with calcium intake observed in some studies of this disease (39,41). There does not appear to be any link with prostate cancer and vegetable fats (33).

With regard to other cancer sites, there is no significant evidence that there is a link between fat and cancer, but the data is very sparse (33,42).

Thus, if there is a relationship between dietary fat and cancer, it is very weak, and appears to be limited to animal fat and red meat. Limiting red meat and animal fat consumption (but not eliminating it) is part of many prudent diets, since replacing saturated fat with unsaturated fat in order to reduce the risk of CHD would normally involve decreasing the consumption of red meat and animal fat. Because red meat does in fact turn up in studies as a possible risk factor for both colon and prostate cancer, it may indeed be wise to limit consumption of this type of food until more definitive information is available. Willett holds to the view that the important factors in the relationship between diet and cancer appear to be a positive energy balance, reflected in part in early height and weight gain, early onset of menstruation for women and weight gain as an adult (24).

## **FAT IS BAD BECAUSE FAT MAKES YOU FAT**

This is a popular concept that has a strong logical appeal to the layman. However, it appears to be an oversimplification of a complex subject. Viewed in its most general form, there is of course an element of truth in the statement that eating fat makes one fat. Total energy intake is related to the consumption of fat, protein and carbohydrate, and fat being more energy dense, can contribute to an energy imbalance where

excess macronutrients are stored as fat. But this is not an argument for low-fat diets. One of the highest profile opponents of the fat makes you fat dogma is Harvard's Walter Willett. He points out that there has been a significant decline in the percentage of energy obtained from fat in the US population in the past two decades, as would be expected from the success of the anti-fat movement. However, at the same time there has been a significant increase in obesity. In short-term dietary intervention trials, individuals who are assigned to a diet that had a lower percentage of energy from fat generally had a modest reduction in weight. However, compensatory mechanisms appear to come into play, since in trials lasting over a year with fat consumption in the range of 18-40% (a very wide range indeed) of total energy, there appears to be little if any effect on the ultimate degree of fatness. Thus the available evidence points to the fact that diets high in fat do not appear to be the primary cause of the high degree of excess body fat in the US population, and reductions in fat will not be the solution (24,43).

If we turn to anecdotal evidence, the most successful *long-term* weight loss programs in North America, if not worldwide, appear to involve diets that are not low in fat but low or very low in carbohydrates, especially carbohydrates that are rapidly digested with concomitant adverse swings in both serum glucose and insulin. The diet programs with the highest profile include those of Atkins (44), the Eades (45), the Hellers (46), and Sears (22). Atkins pioneered the low-carbohydrate diet. While his anecdotal evidence is extensive with over 60,000 patients treated in his Manhattan clinic, nutritional scientists simply do not like anecdotal evidence, even when it is supported by thousands of case histories from other advocates of the same protocol. But progress is being made on this front. There are now two papers presented at national meetings that provide scientific evidence for the effectiveness and safety of the Atkin's type diet (47,48). There is also one study in the context of adolescent obesity (49). The Atkins' and other low-carbohydrate diets provide a counter argument to the fat makes you fat view since these are diets that have a higher percentage of fat than is common in North American diets, and patients are losing weight, not gaining it, without, for most individuals, adverse effects on blood lipid profiles.

Obviously, weight gain and obesity are complex subjects. However, there seems little doubt that there is a strong relationship with carbohydrate metabolism, blood levels of glucose and insulin, and the development of insulin resistance, which frequently accompanies obesity or the state of being overweight (18). To focus on fat alone would appear to be a serious mistake.

## **WHAT DO THE EXPERTS RECOMMEND?**

### **Expert Panel on the Identification, Evaluation and Treatment of Overweight and Obesity in Adults (50)**

In the context of strategies for weight loss and weight maintenance, they comment:

"Reducing the percentage of dietary fat alone will not produce weight loss unless total energy intake is also reduced. Isoenergetic replacement of fat with carbohydrates will reduce the energy fraction from fat but will not cause weight loss. Reducing intake of dietary fat, along with reducing dietary carbohydrate, usually will be needed to produce the energy deficit needed for an acceptable weight loss. When fat intake is reduced, priority should be given to reducing saturated fat to enhance lowering of LDL-C levels."

Note: In this note, LDL-C is LDL.

### **Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on the Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) (51)**

"ATP III's TLC (Therapeutic Lifestyle Changes) diet generally contains the recommendations embodied in the Dietary Guidelines for Americans 2000. One exception is that total fat is allowed to range from 25-35% of total calories provided saturated fats and *trans* fatty acids are kept low. A higher intake of total fat, mostly in the form of unsaturated fat, can help reduce triglycerides and raise HDL cholesterol in persons with the metabolic syndrome."

Note: The suggestion to increase fat intake is no doubt directed at the large population of individuals on low or very low fat diets that have high triglycerides and low HDL. Metabolic syndrome is also known as Syndrome-X.

### **Heart Sense for Women. Your Plan for Natural Prevention and Treatment (52)**

"Like many cardiologists, I used to recommend low-fat, high-carbohydrate foods to my cardiac patients. I was caught up in the low-fat, high-carbohydrate craze that swept the country ten years ago. Boy, was I off the mark! Many of my patients did initially lose weight on the no-fat, low-fat diets, but over time their HDL "good" cholesterol decreased and their triglycerides shot up, and they often regained weight."

Note: Stephen Sinatra, M.D., is Director of Medical Education at Manchester Memorial Hospital and Assistant clinical Professor of Medicine at the University of Connecticut School of Medicine. He is the author of several popular books.

### **Eat, Drink and Be Healthy. The Harvard Medical School Guide to Healthy Eating (24)**

"PUTTING IT INTO PRACTICE:

- Remember that not all fats are bad--unsaturated fats protect against heart disease and other chronic conditions.
- Make decisions about dietary fats based on their proven impact on heart disease, not by their weak--if any--connection with cancer.
- Limit the amount of saturated fat in your diet, as the American Heart Association, National Cholesterol Education Program and others recommend. But there is no good evidence that replacing saturated fat with carbohydrates will lower rates of heart disease, while there is solid proof that replacing saturated fat with unsaturated fat will.
- Reduce saturated fats by limiting the amount of full-fat dairy products you eat and replace red meat with nuts, legumes, poultry and fish whenever possible.
- Use liquid vegetable oils in cooking and at the table.
- Eat one or more good sources of n-3 fatty acids every day--fish, walnuts, canola or soybean oil, ground flaxseeds or flaxseed oil."

Note: Walter C. Willet, M.D., Dr. PH. is one of the world's leading nutritional epidemiologists. He is a professor of medicine at Harvard University and chairman of the Department of Nutrition, Harvard School of Public Health. He has co-directed or directed a number of large and highly significant studies on the relationship of diet and health. He is the author of the definitive textbook on this subject (3).

## **FINAL REMARKS**

This discussion should have made it clear that conducting studies that yield clear-cut answers is not the norm in this area. In fact the attempts to examine the question of the link between fat and heart disease have been remarkably inconsistent, when viewed as a whole. There have been a very large number of studies, especially if one counts those dating back to the 50s, and yet if one searched for one word to characterize the whole lot, it would probably be "inconclusive." Also a recurrent observation is that prospective cohort studies are at odds with case-control studies. While it is suspected that this is due, in case-control studies, to recall bias and failure to correct for confounding factors, this explanation can hardly be considered well established. Even the dietary intervention studies that replaced saturated fat with unsaturated fat were in a sense inconclusive, since two variables were simultaneously changed, but in this case, the overall result was clear enough--in fact convincing enough to become a popular recommendation

from many authorities. It should also be apparent that by selecting studies, it is possible to support practically any point of view. Unfortunately, this is not a totally unknown practice(53).

As was mentioned above, there are many puzzling features of the cholesterol-fat-CHD picture, especially in the context of the initiation and progression of atherosclerosis. The most important "new vista" that has opened up in the past decade associates inflammation with atherosclerosis and the risk of heart attacks (54). This has become an exceedingly active area of research, and inflammation may well push cholesterol off its long held position at center stage. Research now suggests some association of inflammation with the adverse aspects of hypertension, diabetes, obesity and abnormal blood lipid levels as they relate to heart disease (54). In fact, the leading researchers in the field of inflammation and CHD predict that quite soon the measurement of serum C-reactive protein will become as routine as cholesterol level measurements. There are also other markers of inflammation that are currently under investigation in connection with CHD, and in addition, a lot of attention is being given to the role of chronic infections (e.g. gingivitis, prostatitis, bronchitis, etc.) in the formation and acceleration of atherosclerotic lesions.

The flip-flops in dietary advice which are evident from this discussion of fat and heart disease could very well have an adverse effect on the future public willingness to accept or even listen to the nutritional experts or health care providers when it come to dietary advice. A widespread loss of confidence in studies of all types would be a natural response of the general public to what we are witnessing, not only in the field of nutrition, but also in many other health related areas. A recent example is the change in the view of mainstream medicine toward hormone replacement therapy, a flip-flop that has received extensive coverage in the media and generated great concern among women either taking or contemplating hormone replacement therapy. The general public will probably always have trouble dealing with flip-flops, which are unfortunately a natural phenomenon in scientific research, especially when it involves human subjects and human disease.

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Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5

E-mail: [editor@yourhealthbase.com](mailto:editor@yourhealthbase.com) World Wide Web: <http://www.yourhealthbase.com>  
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