

# INTERNATIONAL HEALTH NEWS

*Your Gateway to Better Health!*

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*It is with some misgivings but considerable enthusiasm that I assume the editorship of International Health News which has been so ably and professionally edited and published by Hans Larsen now for over 16 years. I will attempt to continue the traditions and philosophy Hans has established and endeavor to bring readers up-to-date and useful information derived from the peer-reviewed medical literature that directly relates to their health, both present and future. The emphasis will be on preventive medicine, the modifiable risk factors of prevalent diseases and disorders, the relationship between nutrition, lifestyle and health and finally health related news deemed of interest. Providing concise, reliable evidence-based information that will assist readers in maintaining a high*

*quality state of health and wellbeing will continue to be the goal of this publication. There should be many fascinating and perhaps even sensational developments in both the areas of conventional and alternative medicine over the next few years and it is the aim of this newsletter to keep the readers abreast of these advances and provide information they can use. There will also continue to be book reviews and research reports, and I plan to have a special quarterly section on prostate problems.*

*In this issue, several of the studies discussed involve diet or deal with issues such as the importance of omega-3 intake in the context of both heart disease and pain suppression and as well the risks of very high red meat consumption for premenopausal women. Diabetics should note the research results on oral alpha-lipoic acid for neuropathy. The News Briefs section contains a brief account of the use of pomegranate juice for slowing the progression of recurrent prostate cancer. This seemed important enough to include in the February issue rather than delay for inclusion in the upcoming quarterly review of prostate problems. Other news topics include the importance of a second opinion for breast cancer and the combined mortality risks of obesity and smoking.*

*Finally, two book reviews are presented that should be of interest not only to diabetics but to anyone with even mildly abnormal blood glucose levels, especially those with metabolic syndrome and as well anyone looking for delicious low-carb recipes.*

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*Wishing you continuing good health,*

**William R. Ware, PhD, Editor**

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## DO LOW-CARBOHYDRATE DIETS INCREASE THE RISK OF CORONARY HEART DISEASE IN WOMEN?

It is now well known that there are two extremes in diet protocols. One is the low-fat, high-carbohydrate, energy deficient diet and the other is the diet high in fat and protein and low in carbohydrate. The former has the backing of leading research and medical societies and the latter, while frequently labeled with the intentionally derogatory term “fad” has become very popular. One of the objections to the low-carb diet frequently enunciated by mainstream medicine concerns the hypothetical increase in the risk of coronary heart disease (CHD) brought about by the high fat content of this type of diet.

Researchers from Harvard and UCLA have just published the results of a large prospective follow-up study which directly addresses this question. They followed over 82,000 women for 20 years with repeated food-frequency questionnaires. From these they developed a low-carbohydrate-diet score. Intakes of fat, protein and carbohydrate as a percentage of energy were first organized into 10 strata, with each stratum assigned one score point. Those with the lowest carbohydrate stratum received 10 points, those with the highest 0 points whereas those in the highest protein or fat intake received 10 points with the lowest getting 0 points. The score was then obtained by summing points, where the higher the score, the more closely the individual adhered to the low-carb eating pattern.

When the highest vs. the lowest deciles of this score were compared, there was no significant difference in relative risk of CHD, even after correcting for various confounding factors. In addition, it was found that vegetable sources of fat and protein provided a moderate but statistically significant reduction in CHD risk. Low-carb diets tend to have carbohydrate sources that are of low glycemic index and this results in a diet with a lower so-called glycemic load. In this study, it was found that the risk of CHD almost doubled when the

highest quintile (fifth) of glycemic load was compared with the lowest, and the result was statistically significant.

As regards the effect of the low-carb diet on blood lipid levels, data were available for only a small subgroup of participants. In this group, a low-carbohydrate-score was not associated with unfavorable total cholesterol, HDL or LDL levels, and there was an inverse association (favorable) between the score and triglyceride levels. Some earlier studies had found an adverse effect of low-carb diets on total cholesterol and LDL, but these trials were criticized by the authors for having insufficient sample size and duration to be used to study the an outcome such as CHD.

When the results for risk associated with various macronutrients were adjusted for confounding (multivariate models), no statistically significant risk of CHD was found for animal fat, total fat, vegetable fat, animal protein or total protein.

*Halton, T.L. et al Low-Carbohydrate-Diet Score and the Risk of Coronary Heart Disease in Women. New England Journal of Medicine 2006 Vol. 355, No. 19 pp. 1991.*

**Editor's comment:** Opponents of the low-carb type diet frequently point to the high fat content as the source of the alleged increased risk of heart disease. The results of this very large and long-term study, when adjusted to eliminate confounding, found no statistically significant association between CHD and total fat, animal fat or vegetable fat. This suggests that short-term studies that use a surrogate marker such as LDL cholesterol to indicate CVD risk associated with fat intake may not be relevant in the context of the basic question being addressed. This study should allay some of the concerns regarding low-carb diets generated by those that oppose them.

## VITAMIN D, SUN EXPOSURE AND SEASONAL FLU—IS THERE A CONNECTION?

While classified as a review article, this paper might better be considered a wake-up call. The authors represent a wide range of expertise. Included are a highly respected expert in nutritional epidemiology

from Harvard, well known investigators in the field of vitamin D research and an expert on atmospheric research. They advance the hypothesis that the remarkable and recurrent seasonality of epidemic

influenza, i.e. its regular and predictable appearance each winter in each hemisphere, is related to vitamin D, or the lack of it, and that this is the source of the seasonal stimulus.

Humans depend almost exclusively on sunlight as their source of vitamin D. It is probably not common knowledge among the general public that above a latitude of about 30° to 40° North or South the intensity of the required wavelengths of ultraviolet light (UV) is such that little or no vitamin D production in exposed skin occurs between October and April, and vitamin D deficiency has been repeatedly documented during the winter for individuals living in the higher latitudes.

The authors develop their case by reviewing the role vitamin D plays in immunology and how it dramatically stimulates the expression of potent anti-microbial peptides which exist in the various cellular components of the immune system and as well the in the epithelial cells lining the respiratory tract where these proteins play a significant role in protecting the lung from infection. They also discuss the ability of vitamin D to suppress excessive cytokine and chemokine production related to inflammation. There follows a large amount of evidence that directly supports their hypothesis, including the observation that UV radiation from either sunlight or artificial sources reduces the incidence of viral respiratory infections, as does cod liver oil, a source of vitamin D. Also, supplementation with vitamin D has been shown to reduce the incidence of respiratory infections in children and a vitamin D deficiency predisposes children to these infections. Finally, they show dramatic graphic evidence of the seasonal variation of influenza in both hemispheres for latitudes above 30° (the so-called temperate zones) and no seasonal variation in the tropical zones (0-29° latitude).

The authors take the conservative position that it is premature to recommend vitamin D for either the prevention or treatment of viral respiratory infections, but they significantly qualify this position by saying that it is not too early to recommend that health-care providers aggressively diagnose and adequately treat vitamin D deficiency with a goal of achieving serum 25-hydroxy vitamin D (the easily measured metabolite found in blood) at summertime levels obtained by sun exposure (50 ng/mL which is equivalent to approximately 125 nmole/L). They point out that those with large amounts of melanin in their skin (dark-skinned), the obese and the aged may need up to 5000 IU per day to achieve such levels in the winter. They also point out that 3000 IU/day of vitamin D is the estimated requirement such that 97% of Americans obtain levels > 35 ng/mL.

*J.J.Cannell et al, Epidemic Influenza and Vitamin D. Epidemiology and Infection, Vol. 134, No. 6, pp. 1129-40.*

**Editor's comment:** This seems to be a very significant paper that may not receive the attention it deserves due to the somewhat specialized journal in which it was published. The case the authors make for their hypothesis seems quite strong and at the very least should prompt trials involving direct intervention with winter supplementation. Vitamin D researchers have for some time been suggesting doses of at least 1000 IU/day for individuals at risk of a deficiency, and the current U.S. government guideline gives 2000 IU/day as the safe upper limit. The authors of this paper suggests that even higher doses may be appropriate and safe for some, and they point out that even single injections of 600,000 IU have recently been recommended for the elderly to prevent vitamin D deficiency.

In Europe, the 40° latitude line runs near Madrid Spain, the heel of the Italy boot, and northern Greece. In North America, it runs near Reno, Denver, Columbus and Philadelphia, Obviously, a large number of individuals live above 40° latitude!

## SAD NEWS FOR RED MEAT LOVERS

Two studies have just been published that raise concerns regarding elevated levels of red meat consumption (and processed meats as well). One concerns breast cancer, the other colorectal cancer. The former is from Harvard and based on data acquired in the Nurses' Health Study II which enrolled and studied premenopausal women. Twelve years of follow-up which involved almost

100,000 women documented 1021 cases of invasive breast cancer. Frequent consumption of red meat (5-7 servings a week) increased the risk by 42%, while a very high consumption (1.5 servings a day) increased risk by 97% when compared to an intake of 3 servings a week or less. These increases in risk, which were corrected for confounding, were restricted to women who

developed estrogen and progesterone positive tumors and were premenopausal at diagnosis (the mean age at enrollment was 36 years). Cases of breast carcinoma in situ were not included in the analysis. No increased risk was found for those participants who developed estrogen and progesterone receptor negative tumors. The authors point out that most risk factors in this age group are not easily modified, and that their findings concerning one that is modifiable thus have potential public health implications in preventing breast cancer.

The authors suggest several biological mechanisms that might explain their results. First, cooked or processed red meat is a source of carcinogens generated during the cooking process, and there are studies indicating a connection between breast cancer risk and the degree of doneness of red meat. Second, beef may contain residues of hormones used for growth promotion, a practice which incidentally is banned in European countries but not in the U.S. Third, red meat is a source of heme iron, which is highly bioavailable and when stored has been shown to enhance estrogen-induced tumor induction. Finally, the authors mention the increased intake of fat and point to an earlier study where the intake of animal fat but not vegetable fat was related to elevated breast cancer risk in premenopausal women. The reason for this result was not clear.

*Cho, E et al, Red Meat Intake and the Risk of Breast Cancer Among Premenopausal Women. Archives of Internal Medicine, 2006, Vol. 16, Nov 13. pp. 2253-59*

**Editor's comment:** The estrogen and progesterone receptor (ER/PR) positive type of tumor is the most common. In this study, ER/PR status information was available for 77% of the cases, of which 65% were ER/PR positive and only 21% were ER/PR negative. Also, note that the comparisons of risk used 3 or fewer serving per week as the reference point, and limiting intake to this level should not pose a hardship for most individuals.

The second study is actually a study of studies (a meta-analysis) concerning meat consumption and colorectal cancer in both men and women. This Swedish analysis included 15 prospective studies of red meat and 14 prospective studies of processed meat. The risk of colorectal cancer increased by 28% when the highest vs. the lowest intakes of red meat were compared, and 20% when a similar analysis was done for processed meat. Both results were statistically significant. Almost 9000 cases were involved in the combined studies. The association with red meat was more pronounced for rectal cancer and the connection with processed meat consumption was stronger with distal colon cancer. Results were consistent for both men and women and for Europe and the U.S. The authors speculate that both carcinogens in cooked meat and heme iron may be responsible for the association and quote studies to support this hypothesis.

*Larsson, S. and Alicja Wolk. Meat Consumption and Risk of Colorectal Cancer A Meta-Analysis of Prospective Studies, International Journal of Cancer, 2006, Vol. 119, pp. 2657-64.*

## OVARIAN CANCER AND MENOPAUSAL HORMONE REPLACEMENT THERAPY

The enhanced risk of breast cancer associated with estrogen plus progestin therapy is now well known, having received extensive coverage in the media. Ovarian cancer is a significant female cancer and while the association with hormone therapy has been investigated before, this study represents one of the latest efforts to clarify the extent of the risk. A cohort of over 97,000 women aged 50-71 years was assembled between 1995 and 1996 and followed until the year 2000. Questionnaires were used to establish the extent and nature of hormone therapy used. The use of unopposed estrogen therapy for 10 or more years, when compared with no therapy, was associated with an 89% increased risk of ovarian cancer. For women with a history of hysterectomy, there was also an increase in risk but

it failed to achieve statistical significance. Compared with no hormone therapy, 5 or more years of so-called sequential estrogen-progestin therapy (progestin use for < 15 days per cycle) was associated with a 209% increase in risk and continuous use (progestin use equal or greater than 15 days per cycle) yielded an 82% increase in risk. The results for these two estrogen-progestin protocols were statistically significant. The authors comment that the actual increased absolute risks are small with the number of cases per 100,000 patient years falling in the range of 50 to 110.

*Lacey, J.V. et al. Menopausal Hormone Therapy and Ovarian Cancer Risk in the National Institutes of Health-AARP Diet and Health Study Cohort. Journal of the National Cancer Institute, 2006, Vol. 98, No. 19, pp. 1397-1405.*

## FATTY FISH REDUCES THE RISK OF KIDNEY CANCER IN WOMEN

It is estimated that in the U.S. about 40,000 individuals will be diagnosed with kidney cancer in 2006 and about 13,000 will die from the disease. A recent study from Sweden provides evidence for a simple risk reduction strategy—eat fatty fish. This study was initiated in the late 1980s and involved 90,000 Swedish women who were questioned about their dietary habits and then followed for more than a decade. Women who consumed at least one portion of fatty fish each week during the study period ending in 2004 had a reduced risk of kidney cancer of 74% when compared to those who ate no fatty fish. However, eating lean non-fatty fish produced no protection. This result is based on a subgroup of 36,664 women who provided fish consumption information at baseline and again in 1997. There were 40 incident kidney cancer cases during the 1998-2004 follow-up. In this study, fatty fish included salmon, raw (pickled) herring, sardines and mackerel. Non-fatty fish included cod, tuna, fresh-water fish, shrimp and lobster.

The authors comment that these results support the hypothesis that the lower risk of kidney cancer is possibly due to the increased intake of fish oil rich in

the two marine omega-3 polyunsaturated fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) as well as vitamin D. They discuss the evidence for the biological plausibility of this hypothesis. The authors also point out that an explanation for the null results from earlier studies of the influence of fish consumption of cancer may have been the failure to distinguish fatty from non-fatty fish intake. As regards vitamin D, they discuss studies that found a connection between kidney cancer and vitamin D deficiency as measured by serum marker levels. This epidemiologic study, according to the authors, is the first to address this dietary association.

*Wolk, A et al. Long-term Fatty Fish Consumption and Renal Cell Carcinoma Incidence in Women. Journal of the American Medical Association, 2006, Vol. 296, No. 11, pp. 1371-6*

**Editor's comment:** What seems remarkable about these results is that the intake of fatty fish found to be protective is quite low. However, one or two servings of fatty fish per week seem unlikely to maintain summertime levels of vitamin D metabolites.

## PREVENTING SUDDEN DEATH FROM CORONARY HEART DISEASE WITH OMEGA-3 FATTY ACID

For some, sudden death is the first indication of the presence of coronary heart disease and even when the existence of this disease is recognized, sudden death is not an uncommon event. Currently, prevention of sudden death focuses on three interventions: implantable defibrillators, automated external defibrillators placed in public places and the consumption of omega-3 fatty acids. This study compares the defibrillator approach with an intervention aimed at increasing blood levels of these fatty acids. The justification in part was based on a meta-analysis that found that omega-3 fatty acids from fish and fish oil (EPA and DHA) reduced all-cause mortality and various outcomes from cardiovascular disease such as sudden death, death from cardiac disease, and nonfatal myocardial infarction (heart attack).

The study found that raising omega-3 levels would have about 8 times the impact of distributing external defibrillators and twice the impact of implanting such devices. Furthermore, the authors point out that there would also be benefits from raising omega-3 levels in individuals who do not

qualify for or had not been identified as candidates for implantable devices. This study, which was based on data from the literature, used omega-3 parameters taken from two studies, one of which found a 62% decrease in risk of cardiac arrest for healthy individuals taking omega-3 supplements, and one which found a 45% decrease in risk of cardiac arrest attributable to omega-3 supplements for patients with a prior heart attack. This latter study used 840 mg/day of easily absorbable EPA + DHA.

*Kottke, T.E. et al. Preventing Sudden Death with n-3 (Omega-3) Fatty Acids and Defibrillators. American Journal of Preventive Medicine, 2006, Vol. 31, No. 4, pp. 316-23.*

**Editor's Comment:** This study could not examine the dose dependence of the protective effect of the omega-3 intervention. Two recent studies have addressed this issue by examining the relative risk of sudden death as a function of serum levels of EPA and DHA. Serum levels are frequently determined as the percentages EPA + DHA in the

total serum phospholipids. Based on the data of Siscovick *et al* and of Albert *et al* (papers cited below), Rupp *et al* found that when the EPA + DHA concentration was at the 5-6% level, the risk of sudden cardiac death fell to between 10 and 20% of the risk when the levels were 3.5%. These are obviously dramatic risk reductions. Achieving such EPA + DHA levels, according to the data discussed by Rupp *et al*, requires consumption of 1-2 g/day of EPA + DHA, a dose level easily achieved with fish oil capsules. It is possible that doses of this level would produce even greater benefit of omega-3 fatty acids vs. implantable defibrillators. Some clinical laboratories can now measure phospholipid serum levels of EPA + DHA and thus provide

important information regarding an individual's "omega-3 status." It is also important to realize that omega-3 sources that provide only alpha-linolenic acid (e.g. flax seeds) may be inadequate for building up stores of EPA and DHA since the conversion can be very inefficient. Thus fish oil or purified EPA and DHA are the frequently recommended sources.

Rupp, H. *et al*. *Risk Stratification by the "EPA + DHA Level" and the "EPA/DHA ratio."* *Herz*, 2004, Vol. 29, No. 7, pp. 673

Siscovick, D.S. *et al*, *American Journal of Clinical Nutrition*, 2000, Vol. 71 (Supplement), pp. 208S-12S

Albert, C.M. *et al*, *New England Journal of Medicine*, 2002, Vol. 346, pp. 1113-8.

## ARE OMEGA-3 FATTY ACIDS AS EFFECTIVE AS NON-STEROIDAL ANTI-INFLAMMATORY DRUGS FOR NECK OR BACK PAIN?

The highly publicized cardiovascular side effects found with the specific COX-2 inhibitors such as Vioxx and now the indication that such problems may be characteristic of other members of the general class of non-steroidal anti-inflammatory drugs (NSAIDs) has focused attention on alternatives. The omega-3 fatty acids are prime candidates. This study from the University of Pittsburgh examined patient-perceived benefits of supplementation with eicosapentaenoic acid and docosahexaenoic acid (EPA and DHA) at 1.2 g/day to 2.4 g/day for the relief of neck and back pain, mostly due to degenerative disc disease. All patients were taking NSAIDs with 75% on COX-2 inhibitors. Results were assessed after one month.

Fifty-nine percent discontinued taking their prescription NSAID medication, 60% stated that their overall pain was reduced, and a similar percentage stated that their joint pain had lessened. Eighty percent were satisfied with the improvement and 88% stated they would continue using the fish

oil supplement. No significant side effects were seen.

The authors point out that these results are similar to controlled studies that compared the over-the-counter NSAID ibuprofen with omega-3 supplements for effectiveness in reducing arthritic pain. They conclude that fish oil supplements appear to be a safer alternative to NSAIDs for the treatment of non-surgical neck or back pain.

Maroon, J.C. *et al*. *Omega-3 Fatty Acids as an Anti-inflammatory: an Alternative to Nonsteroidal Anti-inflammatory Drugs for Discogenic Pain.* *Surgical Neurology*, 2006, Vol. 65, pp. 326-31.

**Editor's comment:** While recent safety concerns regarding the use of NSAIDs have focused on adverse cardiovascular events, enhanced risk of serious gastric problems including bleeding and perforation have always been recognized as associated with both the over-the-counter and prescription members of this class of drug, and this must also be considered in any risk—benefit analysis.

## ORAL ALPHA-LIPOIC ACID FOR DIABETIC NEUROPATHY

At least 25% of diabetic patients suffer from peripheral neuropathy. The associated pain and discomfort can have a huge impact on quality of life and, in the words of the authors of this study, "pharmacologic treatment.... remains a challenge for the physician." This study follows a recent study where alpha-lipoic acid (ALA) was administered

intravenously with good results as regards to reducing pain and abnormal sensations such as burning and numbness due to diabetic neuropathy. It was designed to test the effectiveness of a once daily oral dose of 600 mg, 1200 mg or 1800 mg of ALA or a placebo for 5 weeks. The endpoint involved changes in what was termed the Total

Symptom Score (TSS) which included stabbing pain, burning pain, unusual sensations, and asleep numbness of the feet. Other neuropathy symptom measures were also employed. This was a randomized, placebo controlled multi-center trial involving 181 patients from Russia and Israel.

At baseline, the TSS did not differ significantly between the intervention and placebo groups. Treatment yielded a decrease of about 50% in TSS scores with no significant dose dependence, whereas the placebo group experienced a 32% decrease in score. For those on the lowest dose, 62% had a 50% or greater reduction in TSS score. Other measures of decreased neuropathy symptoms also indicated ALA to be more effective than the placebo. The authors believe that a reduction of at least 50% in the TSS after 3 weeks is clinically meaningful. Side effects included nausea, vomiting and vertigo, but these were dose dependent. The authors conclude that a dose of 600 mg once daily, which exhibited the lowest level

of side effects, provided the optimum risk-reward benefit. The mechanism of the action of ALA in this context is not clear. The authors suggest a combination of antioxidant activity coupled with anti-inflammatory and anti-thrombotic action.

*Ziegler, D et al. Oral Treatment with alpha-Lipoic Acid Improves Symptomatic Diabetic Polyneuropathy. Diabetes Care, 2006, Vol. 29, No. 11, pp. 2365-70.*

**Editor's comment:** This study adds considerably to the credibility of ALA therapy by being randomized, placebo controlled and involving a significant number of participants. The authors mention earlier studies both of peripheral neuropathy and mono-neuropathy of the cranial ocular nerves were very small and uncontrolled, but nevertheless also provided strong indication of benefit. The reader is referred to the book by Dr. Bert Berkson, M.D., Ph.D. titled "*The Alpha-Lipoic Acid Breakthrough*" for an introduction of the many applications of supplemental ALA. Amazon.com will suggest related books.

## NEWS BRIEFS

### **POMEGRANATE JUICE FOR THE SLOWING OF PROGRESSION AFTER RECURRENCE FOLLOWING SURGERY OR RADIATION FOR PROSTATE CANCER**

A rising prostate specific antigen (PSA) after surgery or radiation therapy generally indicates a failure of the primary treatment and renewed progression of the disease. In this study from the University of California at Los Angeles, participants had been treated for prostate cancer with either surgery or radiation, had rising post-treatment PSA with a level > 0.2 but < 5 ng/mL and a Gleason Score of ≤ 7. Participants had to have enough PSA data to calculate a doubling time, no hormonal treatment prior to entering the study and no evidence of metastatic disease. In what the authors claim is the first clinical trial of pomegranate juice in patients with recurrent prostate cancer, treatment consisted of 8 ounces of juice daily (POM Wonderful Variety which is widely available in North American grocery stores) until disease progression endpoints were reached. Data from 46 patients were used in the analysis. After 33 months of follow-up, the mean PSA doubling time significantly increased from 15 months at baseline to 54 months. In addition, 35% of the 46 patients involved actually achieved a decrease in PSA (arrested progression) during the intervention and 4 achieved a PSA decline of > 50%. The authors point out that the

PSA doubling time is increasingly being seen as an important surrogate biomarker for prostate cancer mortality, and men with greater doubling times can expect longer survival. While the mechanism of action is unknown, the authors discuss possibilities such as antioxidant and prostaglandin-inhibitory actions of the polyphenols in pomegranate juice and the ability of these polyphenols to promote tumor cell death and inhibit proliferation and invasion. *Pantuack, A.J. et al. Phase II Study of Pomegranate Juice for Men with Rising Prostate--Specific Antigen following Surgery or Radiation for Prostate Cancer. Clinical Cancer Research, 2006, Vol. 12, No. 13, pp. 4018-26*

**Editor's comment:** A preliminary report on this study is discussed (page 298-9) in our book *The Prostate and Its Problems*, where a detailed discussion of PSA doubling times and recurrence after primary treatment can also be found (the book can be ordered directly from the International Health News website). The results of the study reported above are even more impressive than those provided in the meeting abstract quoted in the book. These results should also stimulate research into the use of this fruit juice for primary prevention and prevention of recurrence. If a pharmaceutical company had a drug that could produce the above improvement in PSA doubling times there would no doubt be great excitement in the boardroom. But

this study employs an agent available at the grocery store! Critics will of course demand large randomized placebo controlled studies.

### **BLOOD SUGAR LEVELS: A GLOBAL CRISIS**

While there is no doubt an awareness among the general public that diabetes is very bad news, just how bad it is may not be fully appreciated, especially to the extent that it prompts serious and sustained attempts to avoid Type 2 disease through lifestyle changes. A study just published in *The Lancet* spells out the seriousness of the problem. The investigators examined the connection between elevated blood sugar levels and mortality from heart disease and stroke on a worldwide basis. They found that higher than optimum blood sugar levels were responsible worldwide for 21% of deaths from ischemic (directly due to blood clots) heart disease and for 13% of deaths from stroke, which when added to the deaths from diabetes itself, puts this condition in the top five causes of mortality, accounting for over 3 million deaths per year. The observed positive association between blood glucose and cardiovascular risk extends well below the usual glucose levels used for identifying diabetes or even prediabetic disorders. Prevention therefore involves interventions aimed at shifting the distribution of blood glucose concentrations downward for the entire population. The authors are unclear as to the how this is to be accomplished worldwide, given the diversity of populations, cultures and diets. However, non-pharmaceutical approaches would seem to be restricted to interventions associated with diet, energy intake, avoidance of obesity or even being overweight, and exercise and perhaps some supplements.

In an editorial, Avendano and Mackenbach point out that this study shows that mortality attributable to higher than optimum blood glucose levels is about three times greater than that attributable to diabetes as such and suggest that the effect of elevated blood glucose levels has been seriously underestimated.

*Danaei, G. et al. Global and Regional Mortality from Ischaemic Heart Disease and Stroke Attributable to Higher-Than-Optimum Blood Glucose Concentration: Comparative Risk Assessment. Lancet, 2006, Vol. 368, Nov. 11, pp. 1651-9/*

*Avendano, M and J. P. Mackenbach. Blood Glucose Levels: Facing a Global Crisis. Lancet, 2006, Vol. 368, Nov. 11, pp. 1631-2.*

**Editor's comment:** Some readers may be interested in detailed programs aimed at risk

reduction. One aggressive approach to blood sugar control is described in the two books reviewed in this issue of the Newsletter where the techniques used to control blood sugar in diabetics are directly transferable, according to the author, for the purpose of prevention in individuals with impaired or abnormal glucose tolerance. Similar approaches can be found in the following books on Syndrome-X, i.e. the Metabolic Syndrome.

*Raven, G. T., K. Strom and B. Fox. Syndrome-X. Simon & Schuster, New York, 2000.*

*Challam, J. B. Berkson and M.D. Smith. Syndrome-X. John Wiley & Sons, New York, 2001.*

### **DO PAINKILLERS INTERFERE WITH EVALUATION OF ABDOMINAL PAIN?**

This is a crucial question, at least from the point of view of an individual presenting in the emergency room with acute abdominal pain. The wheels in the ER frequently turn very slowly and it may take several hours or even more for the patient to be evaluated by the appropriate specialist. Clinicians have traditionally withheld effective pain killers until after evaluation out of concern that analgesia might interfere with diagnosis. Meanwhile, the patient may be suffering excruciating pain. A very recent paper in the *Journal of the American Medical Association* addresses this matter by describing an investigation of the impact of opiate analgesics (pain killers derived from opium, e.g. morphine) on the clinical examination and treatment decisions for patients with acute abdominal pain. They found that while opiate administration may alter the physical examination findings, these changes do not result in a significant increase in treatment errors. In the published reports they examined, no patient experienced major morbidity or mortality which could be attributed to opiate administration prior to evaluation. Thus they recommend against withholding aggressive pain relief and suggest that doing so might be considered inhumane!

*Ranji, S.R. et al. Do Opiate. Affect the Clinical Evaluation of Patients With Acute Abdominal Pain? Journal of the American Medical Association, 2006, Vol. 296, No. 14, pp. 1764-74.*

### **COFFEE CONSUMPTION AND GLUCOSE TOLERANCE IN THE ELDERLY**

This study addresses the question: does coffee consumption influence changes in glucose tolerance in elderly subjects with normal or with impaired glucose tolerance at baseline? The answer appears to be yes, but in an unexpected direction. High coffee consumption appears to be protective against the development of abnormal glucose tolerance in individuals with normal glucose



tolerance at baseline. For those who had impaired glucose tolerance, heavy coffee consumption appeared to protect against a worsening of the condition, i.e. the development of abnormal glucose tolerance. Low coffee consumption was 5 or less cups a day, whereas high consumption was 6-10 cups. In this Finish study, the commonly used cup held about 150 ml, which is a little over half the capacity of a typical North American coffee mug. However, in this population, the common mode of preparation was boiling, which may make the results less than universally applicable.

Hiltunen, L.A. *Are There Associations Between Coffee Consumption and Glucose Tolerance in Elderly Subjects? European Journal of Clinical Nutrition*, 2006, Vol. 60, pp. 1222-5.

### **DOES SMOKING INCREASE MORTALITY IN OBESE PEOPLE?**

A recently reported study from the National Cancer Institute addresses this important question. It involved over 64,000 women and 18,700 men. The combined association of body mass index (BMI) and smoking with all-cause cancer mortality and circulatory disease mortality was examined (BMI—weight in kg divided by the square of the height in meters. 25.0 to 29.9 is regarded as overweight, greater than 30 is obese, and greater than 35 very obese). It was found that for all age/gender groups, when current smoking was combined with obesity the increase all cause mortality risk was 3.5- to 5-fold for the obese and very obese respectively, compared to normal weight never smokers. For people less than 65 years of age and a high BMI (>30) current smoking increased the risk of circulatory mortality by 6- to 11-fold as compared with normal weight never smokers. Being a current smoker had a stronger positive effect on the risk of cancer mortality than did obesity and for both men and women aged < 65. BMI had little effect on cancer mortality.

Freedman, D.M. et al. *The Mortality Risk of Smoking and Obesity Combined. American Journal of Preventive Medicine*, 2006, Vol. 31, No. 5, pp. 355-362.

**Editor's comment:** These results speak for themselves. The increases in risk are very large, but given that a significant percentage of smokers who are surgically treated for lung cancer return to smoking, the addictive nature of cigarettes is clear

and the unfortunate fact is that a high risk of disease may not motivate stopping smoking.

### **BREAST CANCER—THE IMPORTANCE OF GETTING A SECOND OPINION IF AT ALL POSSIBLE**

Breast cancer can present a diagnostic challenge, especially regarding such issues as the extent and histological nature of the disease. This in turn impacts management recommendations. In many cases, the initial diagnosis will not originate at a multidisciplinary breast cancer clinic. This study reviewed the medical records of 149 consecutive (to avoid bias) patients referred to such a clinic over a 1-year period. The records were reviewed retrospectively for changes in radiologic, pathologic, surgical and medical interpretations and the effect of these alterations on recommended surgical management was examined. The review of imaging studies resulted in changes in interpretations in 45% of patients studied, and this resulted in changes in surgical management in 11% of patients. Pathological reinterpretation resulted in 9% of patients having changes made in recommended surgical management, and for 34% of the patients, changes in surgical management resulted only from the multidisciplinary discussion with the surgeons, medical oncologists and radiation oncologists. Six patients were actually downgraded to benign disease. In all, approximately half the patients had a change in management as the result of this second opinion from a multidisciplinary center and for 32% of the women, the changes were based not on a disagreement about the radiology or pathology findings but rather on a different view of what constitutes the standard of care.

Newman, E.A. et al. *Changes in Surgical Management Resulting from Case Review at Breast Cancer Multidisciplinary Tumor Board. Cancer*, 2006, Vol. 107, pp. 2364-51.

**Editor's comment:** In this study the recommended treatment changes reflected findings of both more serious and less serious disease than found in the initial diagnosis which resulted in referral to this center. Given that this second opinion was correct and represented the best advice available, then there was obvious benefit no matter which way the second opinion went.

## BOOK REVIEWS

***The Diabetes Diet. Dr Bernstein's Low- Carbohydrate Solution, by Richard K. Bernstein, M.D., Little, Brown and Co., 2005***

and

***Dr. Bernstein's Diabetes Solution, The Complete Guide to Achieving Normal Blood Sugars by Richard K. Bernstein, M.D. Revised Edition, Little, Brown and Co., 2003***

Yes, another low-carb diet book! But this one is a bit different since the primary target audience is those with Type 1 or Type 2 diabetes. However, the author regards the principles involved as generally applicable to all who wish to remain healthy or lose weight and regain their health through dietary intervention. The author is a diabetic himself (Type 1) and changed careers in midlife from engineering to medicine (endocrinology), enrolling in the Albert Einstein College of Medicine at age 45. He has a private practice in Mamaroneck, N.Y. which is devoted solely to diabetes and pre-diabetic conditions, and he treats patients from around the world. He is a fellow of the American College of Nutrition and the American College of Endocrinology. Now in his early seventies, he has become well known as a "maverick" for his views and approach to treating both Type 1 and 2 diabetics as well as prediabetics. In a profile in the *Toronto Globe and Mail* (July 29, 2006), Loren Rubenstein used the heading "The Atkins of Diabetes" which is not far off the mark considering his views on diet.

When Bernstein entered medical school he had already had over 30 years personal experience dealing with his own diabetes, initially with no success. He had been following the standard guidelines of the day. In 1969 he acquired a blood glucose meter, which at that time weighed 3 pounds and cost \$650, quite a contrast to today's highly sophisticated meters the size of a cell phone that are given away in order to sell testing strips. His wife had to purchase it since sales were restricted to physicians—an engineer could not purchase a glucose meter! At this point in his life, he was already experiencing the first symptoms of advanced kidney disease and knew quite enough about diabetes to realize that his days were numbered. In fact, statistics at that time indicated he would be dead by about 1976. Over the next few years he learned how to use diet to control swings in his blood sugar and finally achieved essentially normal blood sugars around the clock. To quote from the introduction to *Dr. Bernstein's Diabetes Solution*, "...almost overnight I was no longer

continually tired or washed out. People commented that my grey complexion was gone. After years of sky-high readings, my serum cholesterol and triglyceride levels had not only dropped, but were at the low end of the normal ranges." Even before going to medical school, he became keenly aware that mainstream medicine was hostile to his approach, his self-doctoring, his rejection of the standard of care of the day, and especially his assertion that he was actually reversing, at least for himself, the well known devastating effects of diabetes which can lead to terrible problems with kidneys, vision, peripheral circulation, a vastly increased risk of heart disease and premature death. It is not surprising that once free to practice medicine himself, he would become a maverick physician in the eyes of mainstream medicine. Nor is it surprising that he would specialize in diabetes.

Chapter 1 of *The Diabetes Diet* is titled *Why a Low-Carb Diet Is the Only Answer for Diabetics*. The argument is simple. By eating smaller amounts of fast-acting or concentrated carbs, a smaller transient increase in blood sugar occurs, and less insulin is needed (either injected or secreted) to stabilize the serum glucose levels. As average blood sugar levels decrease, insulin efficiency increases, further minimizing insulin levels. High insulin and/or high circulating glucose levels have many deleterious consequences including fat building and storage and are related to the multitude of adverse health aspects of diabetes. This normalization of blood sugar, especially the post-meal increase, he believes, is the key to dealing with diabetes. *Dr. Bernstein's Diabetes Solution* describes numerous case histories where the success of the program is not only reflected in daily blood sugar control, but also an improvement in the standard measure of long-term, average blood glucose, glycosylated hemoglobin levels (HgbA1C), as well as normalized blood lipids, and a significant improvement in general health. While mainstream medicine recognizes the merits of diabetics having daily blood glucose ranges and HgbA1C levels similar to non-diabetics, what sets him apart is his

belief, based on his own experience treating thousands of patients, that such normalization is a realistic and in many cases achievable goal rather than an unattainable and unrealistic objective of little clinical significance.

The sharp contrast between Bernstein's approach and that of mainstream medicine is clear from the following. His target blood sugar levels are 85-90 mg/dL (4.7-5.0 mmol/L) and on the low-carb diet, this target remains the same before, during and after meals. He compares this target range to that of the American Diabetes Association (ADA) which he quotes as 70-120 mg/dL (3.9-6.7 mmol/L) before meals and less than 180 mg/dL (10 mmol/L) after meals. For HgbA1c the ADA sets a target of 7% with no intervention until it reaches 8%, whereas Bernstein states that for his patients a normal range is 4.2-4.6%. The ADA takes the position, according to Bernstein, that tight control such as he strives for with his patients "isn't for everyone." He believes this to be "nonsense" and describes the ADA ranges as "out of control" and "the rape of the diabetic" (pp, 112 in *Dr. Bernstein's Diabetes Solution*). Not only are these target ranges what he also finds for normal non-obese non-diabetics but also are what he suggests would have been found by monitoring our Stone Age hunter-gather ancestors to whom we owe credit for over 99% of our genes and thus our human biochemistry.

The centerpiece in Bernstein's diet is a severe and permanent limitation of carbohydrates to 30 grams/day, and as well restrictions on the type of carbohydrate so as to avoid those that have the greatest effect on the post-meal rise in blood sugar, as determined for each patient by extensive self-monitoring. This is in sharp contrast to the 2006 ADA guidelines which explicitly state that diets restricted to less than 130 grams/day of carbohydrates are *not recommended for the management of diabetes* (*Diabetes Care*, 2006 Vol. 29, pp. 2140-57). But with a diet of 30 grams of carbohydrate per day, the bulk of the calorie requirements must be met with protein and fat. Bernstein does not believe that high levels of protein cause kidney disease in diabetics or anyone else. He also does not buy the "fat is bad for you" view which a few years ago was almost a religion. He refers the reader to Gary Taubes article in the respected journal *Science* titled *The Soft Science of Dietary Fat* (March 30, 2001, available on his website [www.diabetes-book.com](http://www.diabetes-book.com)).

In Part One, *The Diabetes Diet* devotes about 150 pages to a discussion of the basic science underlying Bernstein's approach, the guidelines for

food selection and in particular carbohydrate selection, how to customize the diet, and the special case of the overweight individual. Part Two contains recipes developed by an award-winning chef Marcia Miele, a mother of a Type I diabetic, who operates a gourmet restaurant in Williamsport, PA.

Bernstein's earlier book provides a more comprehensive discussion of the nature and treatment of diabetes and pre-diabetes. It gives an 18-page introduction to the basics of diabetes and a lengthy discussion of blood glucose self-monitoring. The central part of the book includes a more detailed discussion of all aspects of his diet than will be found in *The Diabetes Diet*. As well, he discusses the problem of weight loss, dealing with carbohydrate craving, the use of exercise to enhance insulin sensitivity, and finally the many aspects of using insulin and other medications if and when they become necessary. The last part of the book contains a number of low-carb recipes by two other chefs. More specialized topics are discussed in five appendices. The book contains much information for both Type I and 2 diabetics and also for those who are prediabetic or have the Metabolic Syndrome and are interested in halting and reversing progression to the full-blown disease.

Loren Rubenstein, in her profile of Bernstein for the *Globe and Mail* touches on the reactions of conventional practitioners to Bernstein's approach—it is impractical because most people can not adhere to such a severe low-carb regimen, and his findings are "expert opinion" rather than conclusive evidence because his patients are his study group. Evidently the patients Bernstein has successfully treated are highly motivated. Perhaps this is because they have come to realize that it is worth taking drastic action given the obviously profound influence complications from diabetes have on the quality of life, for example kidney problems which dramatically reduce their chances of survival and require dialysis, eye problems leading to blindness, circulation problems leading to amputation, and a risk of disability and dying from coronary heart disease, a risk equivalent to someone who already has heart disease. Also, one suspects that adherence to diets that are severely carbohydrate restricted is much better if the food tastes great. Both books would appear to be of interest to diabetics, pre-diabetics and those with the Metabolic Syndrome. The diet book should be of more general interest, if for no other reason, because of the low-carb gourmet recipes.

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