INTERNATIONAL HEALTH NEWS

Your Gateway to Better Health!

NUMBER 111 **MARCH 2001** **10th YEAR**

Editorial

We reported in the January issue that researchers at the Harvard Medical School have concluded that current, official dietary guidelines are ineffective in reducing the incidence of major chronic diseases. In this issue we report that Harvard researchers have found that eating lots of fruits and vegetables do not, as previously thought, protect against lung and colon cancers. So what has changed? Were all the previous studies wrong? How come researchers concluded 30 years ago that eating lots of fruits and vegetables would protect against cancer and heart disease and now they don't?

Not one of the several dozen researchers involved in the recent study stopped to ask, "Could the food supply have changed? Could fruits and vegetables be less nutritious than they were 30 years ago?" Of course they could! Today's fruits and vegetables are woefully lacking in many vitamins and trace minerals. For over a hundred years they have been grown in soil that has been constantly replenished with synthetic fertilizers that contain only nitrogen, phosphorous, and potassium. Plants require many more nutrients than just these three. No wonder that a large proportion of all North Americans are deficient in magnesium and selenium. No wonder we now have to fortify grains with folic acid in order to get our daily minimum intake.

Fortunately, there is a simple way to regain the wholesome nutrition contained in "real" fruits and vegetables. Eat organic! Organically grown produce, according to the U.S. Department of Agriculture regulations, cannot be genetically engineered, irradiated or fertilized with synthetic fertilizers or sewage sludge. They also cannot be treated with synthetic pesticides and herbicides for at least 3 years before harvest. In other words, they are wholesome and healthy. Just eat one organically grown apple or one stalk of broccoli and compare their taste to that of the standard supermarket variety. You will be amazed at the difference!

Yours in health,
Hans Larsen

March Highlights

NAC benefits heart patients	p. 2
GLS combats osteoarthritis	p. 3
Chondroitin sulfate works	p. 3
Blood donors and heart attacks	p. 4
Osteoporosis drugs and stomach ulcers	p. 5
Fish oils prevent stroke in women	p. 6
Get your vitamin D from the sun	p. 6
Selenium in cancer prevention	p. 7
Mercury linked to heart disease	p. 8
Breast cancer in women under 40 years	p. 8
Newsbriefs	p. 8
The Afib Report	p. 9

LETTERS TO THE EDITOR

I found your articles on vitamin B12 most informative. I was very interested because I recently found out that gastric acid inhibitors such as Losec and Prevacid, both of which I have taken over a long period of time, can hinder the absorption of vitamin B12. For me this has led to peripheral neuropathy in my feet. Apparently the gastric acid contains "intrinsic factor" which is required for the absorption of vitamin B12. My family doctor was not aware of this nor was the neurologist I was referred to. However, I was able to find this information by a search of the Internet through articles such as yours. It was confirmed by my gastroenterologist. Surely, there

should be more awareness of the dangers of long-term use of such drugs as Losec and Prevacid, etc.

PP, USA

Editor: *Thank you for your interesting comments about gastric acid inhibitors and vitamin B12. The fact that you have been on Losec or Prevacid for a long time suggests to me that you may have a Helicobacter pylori infection. A vitamin B12 deficiency can be caused by this infection and can be eliminated by eradicating the bacteria. After eradication you may need daily or weekly B12 injections for a while followed by a daily intake of 1-2 mg of sublingual vitamin B12. If you have not been checked for Helicobacter pylori I would urge you to do so. Once it is eliminated you should no longer require gastric acid inhibitors*.

****

I am trying to find more information about the risk of breast cancer among women who have never given birth.

LR, USA

Editor: *There is a very good summary of the risk factors for breast cancer in the September 9, 2000 issue of the British Medical Journal (pages 624-28). The excess risk among women over 40 years of age who have never had children is about the same as among women who have their first child after the age of 30 years, that is, about twice the risk of women who have their first child before the age of 20 years. Early start of menstruation and late menopause (after age 54) are also additional risk factors for breast cancer with the same magnitude of risk as never having children.*

****

What types of fish do you get the good fish oil from?

JC, USA

Editor: *The best sources of fish oil are fatty, salt-water fish such as herring, sardines, salmon, mackerel, menhaden, albacore tuna, and scabbard fish. Atlantic salmon, for example, contains almost 1.5 gram of EPA+DHA (the good fish oils) per 100 grams. This compares to 0.7 gram of EPA+DHA per 100 grams for fresh-water bass, and only 0.2 gram per 100 grams for sunfish. The fish oil content of farmed fish may be substantially different.*

ABSTRACTS

N-acetylcysteine benefits heart patients

BETHESDA, MARYLAND. Nitrogen oxide (NO) is generated by the lining (endothelium) of blood vessels. A dysfunction of the endothelium involving a reduced NO availability is an early event in the development of atherosclerosis. A lack of NO tends to constrict blood vessels (reduce their diameter), increase platelet adhesion, and raise the risk of the formation of blood clots. Researchers at the National Institutes of Health now report that N-acetylcysteine (NAC) is quite effective in counteracting the effects of endothelial dysfunction and decreased NO availability.

Their clinical trial involved sixteen people, seven with coronary atherosclerosis and nine without. The researchers measured the blood flow in a coronary artery as well as its diameter and also measured the diameter of coronary arteries in the epicardium (outermost layer of the heart wall). All the participants were given an infusion of acetylcholine in order to establish baseline data. They were then given a 10-minute intracoronary infusion of NAC (48 mg/min). A 36 per cent increase in coronary blood flow was observed after the NAC infusion. The researchers also noted that the epicardial blood vessel diameter went from a 1.2 per cent constriction to a 4.7 per cent dilation after the NAC infusion. The response was similar in patients with and without atherosclerosis.

The researchers speculate that NAC either enhances the bioavailability of NO or prevents it from being prematurely inactivated through its antioxidant properties. NAC is a common supplement available in health food stores. However, the researchers make no comment as to whether oral supplementation would have

effects similar to those obtained by infusion directly into the coronary artery.

Andrews, Neil P., et al. N-acetylcysteine improves coronary and peripheral vascular function. **Journal of the American College of Cardiology**, *Vol. 37, January 2001, pp. 117-23*

Glucosamine sulfate combats osteoarthritis

LIEGE, BELGIUM. Alternative medicine practitioners have long advocated glucosamine sulfate (GLS) for the treatment of osteoarthritis. It would appear that conventional medicine is now also realizing the benefits of this safe nutritional supplement. A team of Belgian, British and Italian medical researchers report that daily supplementation with glucosamine sulfate can markedly reduce pain and other symptoms and actually repair cartilage damage in patients with osteoarthritis of the knee.

Their study involved 212 patients who were randomized to receive either a placebo or 1500 mg/day of GLS for three years in a double-blind clinical study. The researchers measured the joint space between the tibia (shin bone) and the femur (thigh bone) at the beginning and end of the study by digital x-ray analysis. They also assessed the symptoms of osteoarthritis (joint pain, stiffness, and limitation of physical function) using the Western Ontario and McMaster Universities (WOMAC) osteoarthritis index.

After three years the patients on the placebo had experienced a further narrowing of their joint space (an indicator of disease progression) of 0.31 mm. The patients in the GLS group, on the other hand, saw their average joint space widen by 0.07 mm indicating an improvement. The difference in disease progression was even more impressive when looking at the minimum joint space. Here a 0.40 mm narrowing was observed in the placebo takers as compared to a 0.11 mm widening in the GLS group. This group also reported an average 24.3 per cent reduction in the severity of their symptoms (WOMAC scale) as compared to the 9.8 per cent worsening of symptoms observed in the placebo group.

Dr. Tim McAlindon of the Boston University Medical Center calls the study a landmark in osteoarthritis research and concludes his editorial review with the remark that it is time for the medical profession to “accommodate the possibility that many nutritional products may have valuable therapeutic effects”.

Reginster, Jean Yves, et al. Long-term effects of glucosamine sulphate on osteoarthritis progression: a randomised, placebo-controlled clinical trial. **The Lancet**, *Vol. 357, January 27, 2001, pp. 251-56*

McAlindon, Tim. Glucosamine for osteoarthritis: dawn of a new era? **The Lancet**, *Vol. 357, January 27, 2001, pp. 247-48 (commentary)*

Chondroitin sulfate works

TOULOUSE, FRANCE. Chondroitin sulfate is composed of repeating units of glucosamine with attached sugar molecules. It is a rather large molecule and is relatively poorly absorbed. Although chondroitin sulfate effectively inhibits the degradation of cartilage and increases the synthesis of hyaluronic acid (a vital joint lubricant) conventional wisdom has it that it is fairly ineffective in the treatment of osteoarthritis because of its poor absorbability.

A group of French researchers now challenge this assumption. In a just released study they conclude that chondroitin sulfate is indeed effective in reducing the pain, stiffness, and disability of osteoarthritis. The double-blind, randomized, parallel group study involved 130 patients with osteoarthritis of the knee. The patients were assigned to receive either a 500 mg capsule of chondroitin sulfate twice a day or two identical looking placebo capsules daily for the duration of the three-month study. They were clinically assessed every month for the duration of the supplementation period and for the following three months.

At the end of the supplementation period the patients in the chondroitin group had decreased their algofunctional index (a composite measurement of disease severity) by 33 per cent as compared to a 19 per cent decrease in the placebo group. Self-assessed pain at rest decreased by 57 per cent in the chondroitin group versus 32 per cent in the placebo group. One month after the end of treatment the algofunctional index had decreased by 36 per

cent over baseline in the chondroitin group as compared to a 16 per cent decrease in the placebo group. Self-assessed pain scores both at rest and during activity were also substantially lower for the chondroitin group. The researchers conclude that chondroitin sulfate is safe, well tolerated, and shows efficacy in the treatment of osteoarthritis. They recommend further work to support their initial findings. **Editor's note**: Glucosamine sulfate is generally considered to be more effective than chondroitin sulfate, but is not available in France.

Mazieres, Bernard, et al. Chondroitin sulfate in osteoarthritis of the knee: a prospective, double blind, placebo controlled multicenter clinical study. **Journal of Rheumatology**, *Vol. 28, January 2001, pp. 173-81 [46 references]*

Folic acid helps heart disease patients

HALIFAX, CANADA. Several studies have concluded that high homocysteine levels are associated with coronary artery disease (CAD). It is believed that homocysteine promotes atherosclerosis through increased oxidative stress and by "encouraging" dysfunction of the lining of the arteries (endothelial dysfunction). It is generally accepted that folic acid supplementation will lower homocysteine levels, but whether folic acid supplementation will also reduce the endothelial dysfunction responsible for the initiation and progression of atherosclerosis is less certain.

Medical researchers at the Queen Elizabeth II Health Sciences Centre now report that supplementation with 5 mg/day of folic acid significantly decreases endothelial dysfunction. The extent of endothelial dysfunction is determined by measuring the blood flow through the brachial artery in the arm (flow-mediated dilation or FMD). The clinical trial included 75 patients with CAD. The patients were randomized into three groups. One group took 5 mg of folic acid daily for four months; the second group took 5 mg of folic acid plus 2000 mg of vitamin C plus 800 IU of vitamin E per day; the third group was given a placebo. At the end of the trial patients in the folic acid group had increased their blood plasma level of folate by 475 per cent (from 14 nmol/L to 80 nmol/L) and decreased their homocysteine level by about 11 per cent. FMD improved significantly as well (from 3.2 to 5.2 per cent). Patients in the folic acid plus antioxidant group increased their folate level by 438 per cent, reduced homocysteine by 9 per cent, and improved FMD from 2.6 to 4.0 per cent.

The researchers point out that the FMD improvement seen in the folic acid supplemented groups is similar to that seen with statin drugs and ACE inhibitors. They conclude that four months of folic acid supplementation is safe and significantly reduces endothelial dysfunction in patients with established coronary atherosclerosis. [61 references]

Title, Lawrence M., et al. Effect of folic acid and antioxidant vitamins on endothelial dysfunction in patients with coronary artery disease. **Journal of the American College of Cardiology**, *Vol. 36, September 2000, pp. 758-65*

Blood donors do not have fewer heart attacks

BOSTON, MASSACHUSETTS. Animal experiments have shown that an iron overload can promote atherosclerosis. Finnish researchers have also found an association between a high blood level of iron and cardiovascular disease. Iron is a powerful free radical initiator and is likely to promote lipid peroxidation. Researchers have speculated that the relatively low iron levels found in premenopausal women account for their near immunity to heart disease as compared to men and postmenopausal women. Finnish researchers recently reported that male blood donors have a substantially lower risk of having a heart attack than do non-donors. It is estimated that donating blood just once a year can reduce the iron stores in men by half.

Researchers at the Harvard Medical School now report that male blood donors do not have fewer heart attacks than non-donors. Their study involved 38,244 male health professionals who were asked about their lifetime history of blood donations in 1992. During four years of follow-up there were 328 non-fatal heart attacks and 131 coronary deaths in the group. There was no significant difference in the incidence of heart attacks or cardiac deaths among the men who

had donated blood 30 or more times during their life and those who had never donated. The researches conclude that their study does not support the hypothesis that reduced iron stores lower the risk of coronary heart disease.

Ascherio, Alberto, et al. Blood donations and risk of coronary heart disease in men. **Circulation**, *Vol. 103, January 2/9, 2001, pp. 52-57 [38 references]*

Osteoporosis drugs and stomach ulcers

HOUSTON, TEXAS. It is well known that both the osteoporosis drug alendronate sodium (Fosamax) and naproxen, a popular non-steroidal anti-inflammatory drug (NSAID), can cause damage to the stomach lining including the actual development of stomach ulcers. Researchers at the Baylor College of Medicine now report that a combination of alendronate and naproxen is considerably more dangerous than either drug on its own.

Their clinical trial involved 26 healthy volunteers (18 women and 8 men) between the ages of 30 and 50 years. The study participants were randomized to receive either 10 mg of alendronate once a day, 500 mg of naproxen twice a day or a combination of the two for a 14-day period. The presence of stomach lining damage was measured using videoendoscopy at the beginning and end of the test periods. The first test period was followed by a one-week wash-out period after which the participants were assigned to another regimen and so on until all the participants had tried all three regimens.

The researchers found that 10 mg/day of alendronate produced ulcers in 8 per cent of the participants, 500 mg of naproxen twice a day produced ulcers in 12 per cent, and 10 mg/day of alendronate plus 500 mg of naproxen twice a day produced ulcers in 38 per cent of the volunteers and significant side effects in 69 per cent. It is clear that alendronate and naproxen act synergistically in inducing stomach ulcers. The researchers conclude "it would appear prudent not to prescribe anti-inflammatory doses of traditional NSAIDs to patients receiving alendronate (and vice versa)."

Graham, David Y. and Malaty, Hoda M. Alendronate and naproxen are synergistic for development of gastric ulcers. **Archives of Internal Medicine**, *Vol. 161, January 8, 2001, pp. 107-10 [33 references]*

NIH recommend second look at vitamin C

BETHESDA, MARYLAND. It is now 27 years ago since two Scottish doctors (Cameron and Campbell) reported remarkable results from treating terminal cancer patients with high-dose intravenous vitamin C infusions. Their cause was later taken up by two-time Nobel Prize winner Dr. Linus Pauling who persuaded the Mayo Clinic to do their own study on the potential benefits of vitamin C. The study was done in 1979 and concluded that vitamin C was of no value in the treatment of terminal cancer. The Mayo researchers used 10 grams/day of oral vitamin C supplementation rather than intravenous infusions. This, says Dr. Mark Levine of the National Institutes of Health, was a crucial difference.

Dr. Levine and his colleagues have found that the body's absorption of orally ingested vitamin C decreases as the dose increases. Thus while 80 per cent of a 100 mg dose is fully absorbed less than 50 per cent of a 1250 mg dose is actually absorbed. Dr. Levine concludes that doses greater than 500 mg contribute little to plasma or tissue stores. He also estimates that even at doses of 1000 mg it is extremely difficult to achieve a blood plasma concentration much above 100 micromol/L. Intravenous infusions, on the other hand, can achieve plasma levels as high as 5000 micromol/L with a dose of 5 to 10 grams. Dr. Levine believes that these high vitamin C levels may indeed be effective in combating cancer and urges further studies and clinical trials.

Padayatty, Sebastian J. and Mark Levine. New insights into the physiology and pharmacology of vitamin C. **Canadian Medical Association Journal**, *Vol. 164, February 6, 2001, pp. 353-55*

Hoffer, L. John. Proof versus plausibility: rules of engagement for the struggle to evaluate alternative cancer therapies. **Canadian Medical Association Journal**, *Vol. 164, February 6, 2001, pp. 351-53 (commentary)*

Fish oils prevent stroke in women

BOSTON, MASSACHUSETTS. A 1995 study concluded that men who ate fish five or more times per week had a 40 per cent lower risk of having a stroke than did men who ate fish less than once a week. Researchers at the Harvard Medical School and the Brigham and Women's Hospital now report that the benefits of fish consumption are even more spectacular for women.

Their just completed study involved 79,839 female nurses who were between the ages of 34 and 59 years at the start of the study in 1980. After 14 years of follow-up a total of 574 strokes had occurred in the group. Most of the strokes (303) were ischemic, i.e. caused by a blood clot. There were also 181 hemorrhagic strokes, i.e. caused by a ruptured artery and 90 strokes of undetermined origin.

After adjusting for age, smoking and other cardiovascular risk factors the researchers concluded that women who ate fish once a week lowered their risk of having a stroke of any kind by 22 per cent and those who consumed fish five or more times per week reduced their risk by 52 per cent. They ascribe the protective effect of fish consumption to the commensurate intake of fish oils (omega-3 fatty acids). They estimate that women whose intake of fish oils is 0.5 gram/day or more have a 30 per cent lower risk of suffering a stroke than do women whose intake is below about 0.1 gram/day. There was no evidence that women with a high fish or fish oil consumption have an increased risk of hemorrhagic stroke. The researchers believe that the protective effects of fish oils are due to their ability to inhibit platelet aggregation, lower blood viscosity, suppress the formation of leukotrienes, reduce fibrinogen levels and reduce blood pressure levels and insulin resistance. They also note that the beneficial effects of fish consumption were substantially more pronounced among women who did not take aspirin on a regular basis.

Iso, Hiroyasu, et al. Intake of fish and omega-3 fatty acids and risk of stroke in women. **Journal of the American Medical Association**, *Vol. 285, January 17, 2001, pp. 304-12 [40 references]*

Get your vitamin D from the sun

BOSTON, MASSACHUSETTS. The intense publicity associating unprotected exposure to the sun with an increased risk of skin cancer has resulted in vitamin D deficiency becoming endemic in adults over the age of 50 years. Humans meet by far the majority of their vitamin D needs by exposure to the sun. Covering up or excessive use of sunscreens results in a deficiency. Danish doctors recently reported that Arab women and other ethnic Danish Moslems were vitamin D deficient even though their daily estimated vitamin D intake from dietary sources was about 600 IU. Native Danish women who do not cover up were not vitamin D deficient even though their dietary intake was only 300 IU/day. The doctors also observed that while none of the native Danes suffered from muscle cramps 72 per cent of Arab women did.

Other researchers have linked a vitamin D deficiency to an increased risk of dying from breast, colon, prostate, and ovarian cancers. Dr. Michael Holick of the Boston University School of Medicine is convinced that "The fear of vitamin D intoxication that swept Europe in the 1950s and resulted in laws forbidding fortification of milk and other products is antiquated". He recommends wider use of vitamin D fortification, but emphasizes that the optimum way of getting vitamin D is through exposure to sunlight. In the spring, summer, and autumn (in Boston) unprotected exposure of hands, arms, and face two to three times a week for 5 to 15 minutes is probably adequate. Sunbathing in a bathing suit can generate 10,000 IU of vitamin D or more within a relatively short time period. Dr. Holick points out that it is impossible to get too much vitamin D by sunbathing. Nursing home residents and other house-bound individuals can keep their vitamin D status up to par by monthly injections of 50,000 IU.

Holick, Michael F. Sunlight "D"ilemma: risk of skin cancer or bone disease and muscle weakness. **The Lancet**, *Vol. 357, January 6, 2001, pp. 4-5 (commentary)*

Selenium in cancer prevention

BETHESDA, MARYLAND. Several large studies have found a clear association between low selenium levels and an increased risk of cancer. A major clinical trial involving supplementation with 200 micrograms/day of selenium (500 mg of high selenium brewer's yeast) was carried out in the United States in 1995. This trial concluded that selenium supplementation reduced overall cancer incidence by 40 per cent and cancer mortality by 50 per cent.

Researchers from the National Cancer Institute and the Chinese Academy of Medical Sciences in Beijing now report that selenium deficient individuals are more likely to develop cancer of the esophagus and stomach than are individuals with adequate levels. Their study involved 590 patients with esophageal cancer, 402 with gastric cardia cancers (cancers located close to the junction between the esophagus and the stomach), and 87 with gastric non-cardia cancers as well as 1062 cancer-free control subjects.

All participants had provided blood samples in 1985 prior to participating in the large Linxian study that investigated the benefits of various supplements in stomach cancer prevention. The researchers found that participants with blood serum levels of selenium at or above 90 micrograms/liter had a 44 per cent lower risk of developing esophageal cancer and a 53 per cent reduction in gastric cardia cancer risk when compared to participants with levels at or below 50 micrograms/liter. There was no correlation between selenium levels and the incidence of gastric non-cardia cancers. The researchers conclude that even individuals in the highest quartile (upper quarter) of selenium levels could benefit from selenium supplementation and that a supplement of 50 micrograms/day is not enough to correct a long-term deficiency.

Mark, Steven D., et al. Prospective study of serum selenium levels and incident esophageal and gastric cancers. **Journal of the National Cancer Institute**, *Vol. 92, November 1, 2000, pp. 1753-63 [62 references]*

An apple a day may not keep cancer away

BOSTON, MASSACHUSETTS. Numerous studies done over the past 30 years have found a strong association between the consumption of fruits and vegetables and a reduced risk of cancer. Two studies just released by the Harvard Medical School now question the validity of this association. The two studies involved 80,000 female nurses and 47,000 male health professionals who were enrolled in 1980 and 1986 respectively. By 1996 the researchers had documented 519 cases of lung cancer in the women and 274 cases among the men. In addition there were a total of 937 cases of colon cancer in the two groups combined. The study participants had completed food frequency questionnaires in 1984 or 1986 in order to determine their intake of fruits and vegetables.

An analysis of the collected data showed that the women who consumed seven or more servings of fruits and vegetables daily had a 21 per cent lower risk of lung cancer than the women who consumed two or less servings a day. There was no correlation between fruit and vegetable intake and lung cancer risk in the men. Apples, pears, oranges, and cauliflower seemed to offer the most protection. The researchers found no association between a high intake of fruits and vegetables and a reduced risk of colon cancer. They do point out that the use of multivitamin supplementation and supplementation with folic acid in particular has been found to protect against colon cancer.

Cancer researchers were clearly disappointed by the results of the new studies, but says Dr. Regina Ziegler, MD of the National Institutes of Health "No one study can discount a lot of other studies" and "A lot of good studies have shown a protective effect for fruits and vegetables and we can't discount that." **Editor's note**: It is amazing that the researchers involved did not consider the possibility that commercial (as opposed to organic) fruits and vegetables may have deteriorated dramatically in nutritional value in the 30 years since the original studies were done.

Clark, Geri. Recent studies cloud link between diet and cancer. **Journal of the National Cancer Institute**, *Vol. 92, November 15, 2000, pp. 1794-95*

Michels, Karin B., et al. Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers. **Journal of the National Cancer Institute**, *Vol. 92, November 1, 2000, pp. 1740-52 [41 references]*

Feskanich, Diane, et al. Prospective study of fruit and vegetable consumption and risk of lung cancer among men and women. **Journal of the National Cancer**

Institute, *Vol. 92, November 15, 2000, pp. 1812-23 [51 references]*

Mercury linked to heart disease

ROME, ITALY. Medical researchers at the Catholic University in Rome report that patients with congestive heart failure (idiopathic dilated cardiomyopathy or IDCM) have vastly elevated concentrations of mercury and antimony in their heart tissue. They compared trace element concentrations in biopsy samples from the left ventricle among patients with IDCM and patients with valvular disorders or no heart disease at all. The IDCM patients had mercury concentrations 22,000 times higher than in the controls. Antimony concentrations were 12,000 times higher and silver, gold, chromium and arsenic levels were also highly elevated. Holter monitoring revealed frequent ectopic (premature) beats in all the IDCM patients and ventricular tachycardias in six of the 13 patients. None of the patients had had occupational exposure to the trace elements. Researchers at the University of Calgary point out that dental amalgams would be the most likely source of the mercury.

Frustaci, Andrea, et al. Marked elevation of myocardial trace elements in idiopathic dilated cardiomyopathy compared with secondary cardiac dysfunction. **Journal of the American College of Cardiology**, *Vol. 33, May 1999, pp. 1578-83 [32 references]*

Lorscheider, Fritz and Vimy, Murray. Mercury and idiopathic dilated cardiomyopathy. **Journal of the American College of Cardiology***, Vol. 35, March 1, 2000, p. 819 (letter to the editor)*

Breast cancer in women under 40 years

MILAN, ITALY. Breast cancer is relatively uncommon in women under 40 years of age (less than 10 per cent of all cases). This explains why most work on defining risk factors has centered on older women. A team of Italian researchers has released the results of a major study aimed at determining the risk factors for younger women. The study involved 579 women aged 22 to 39 years who had been diagnosed with breast cancer and 668 age-matched controls without breast cancer. The women who started menstruating at 15 years of age or older were found to have half the risk of the women who had their first period before the age of 12 years. The women who had their first child when 30 years or older had a five times greater risk of breast cancer than the women who gave birth before the age of 20 years. The women who had never given birth had about half the risk of breast cancer than did the women who had given birth to one or two children. NOTE: This association is contrary to that found for older women.

Use of oral contraceptives and abortions, whether induced or spontaneous, did not have a statistically significant impact on breast cancer risk. A family history of breast cancer, a history of benign breast disease, and higher education levels were associated with an increased risk whereas a high body mass index (overweight) conferred a decreased risk.

Tavani, A, et al. Risk factors for breast cancer in women under 40 years. **European Journal of Cancer**, *Vol. 35, September 1999, pp. 1361-67 [48 references]*

NEWSBRIEFS

Light exposure benefits elderly people. Many elderly people suffer from low melatonin concentrations and insomnia. Japanese researchers report that exposure to bright light at midday can markedly increase melatonin concentrations and improve sleep quality. They conclude that many elderly people get comparatively little exposure to bright (outdoor) light, instead spending much of their day in dimly lit indoor areas. Exposing them to bright light for four hours a day (10 am to noon and 2 pm to 4 pm) can markedly improve their sleep pattern and elevate their melatonin levels to those observed in healthy young people.

Journal of Clinical Endocrinology & Metabolism, January 2001, pp. 129-34

Vitamin E protects against bladder cancer. Researchers at the Harvard Medical School report that men who supplement with 250 mg/day

or more of vitamin E for 10 years or more reduce their risk of developing bladder cancer by more than 30 per cent. The study, which involved over 50,000 male health professionals, also found a suggestive inverse association between vitamin C supplementation and bladder cancer risk. They found no correlation between bladder cancer risk and any other dietary variables. Dietary intake of vitamin E by itself (excluding supplements) was not associated with a decrease in bladder cancer risk.
American Journal of Epidemiology, December 15, 2000, pp. 1145-53

Vitamin E derivative kills cancer cells. German researchers report that alpha-tocopheryl succinate, a derivative of vitamin E (alpha-tocopherol) effectively kills lung, breast and colon cancer cells (in cell cultures) without affecting normal cells. The more common form of vitamin E, alpha-tocopheryl acetate, and vitamin E as such do not kill cancer cells. The researchers urge large-scale trials to determine if alpha-tocopheryl succinate can be used to prevent or treat cancer in people.
British Journal of Cancer, January 5, 2001, pp. 87-89

Legionnaire's disease traced to whirlpool spa. Investigators at the Virginia Department of Health report an outbreak of Legionnaire's disease (a form of pneumonia). The victims all had in common that they had walked by a display whirlpool spa in a home improvement center. The spa was later found to be contaminated with *Legionella pneumophila*. The investigators urge increased vigilance in ensuring that whirlpool spa water is kept clean and well chlorinated.
International Journal of Epidemiology, December 2000, pp. 1092-98

Hair dyes linked to bladder cancer. Researchers at the Southern California School of Medicine believe they have found a link between the use of permanent hair dyes and the development of bladder cancer. A study of 897 men and women concluded that study participants who had used permanent hair dyes for 15 years or more had a three-fold increase of bladder cancer. The increased risk for hairdressers and barbers was five-fold. The team found no increased risk with temporary or semi-permanent dyes.
New Scientist, February 17, 2001, p. 25

A little dirt is good for you. German researchers have found that kids who get lots of colds early in life are less likely to develop asthma and other allergies later in life. A study of 1300 children born in 1990 showed that those who had at least two mild virus infections before their first birthday were only half as likely to have developed asthma by the age of seven as were kids who had only one or no infections at all. The researchers say that their findings support the "hygiene hypothesis" which claims that our ultra-clean modern lifestyles are to blame for the increase in autoimmune diseases and allergies.
New Scientist, February 24, 2001, p. 16

THE AFIB REPORT

The LAF survey is shaping up to be a major success – and a lot of work! More than 40 completed questionnaires have been returned and I am about halfway through the initial compilation of the answers. It is already clear that a thorough analysis of this almost overwhelming amount of data will not only help pinpoint the mechanisms behind LAF, but may ultimately help lead to a solution.

*In this issue of **The Afib Report** we will present some very preliminary findings from the survey and explain how antiarrhythmic drugs work and whether they are likely to be useful in the treatment of LAF.*

Preliminary Results from Survey

The typical afibber is a male college or university graduate in his early forties to late sixties who is involved in brain rather than physical work. Women also get LAF, but it would seem from our results anyway, at only 10% of the rate for men. Our typical afibber is generally healthy and fit, has no major illness other than LAF, and does not smoke. In other words a paragon of virtue. So why does he get saddled with this debilitating condition?

I originally thought that the increased stress of daily living was to blame, but the survey results show otherwise. There certainly are a few (10%?) afibbers where it is clear that the main cause of their problem is excessive stress. The vast majority of respondents is, however, either retired or describe themselves as “laid-back” or “easy-going”. So why do they get afib attacks?

The majority of afibbers is highly athletic and has been so for most of their lives. It is ironic that the individuals who chose to follow the recommendations put forth in the 60s to exercise and “be vigorous” are now reaping the rewards of following this advice in the form of LAF. The survey clearly shows this and our preliminary findings are backed up by an earlier study done at the University of Helsinki[1]. This study done in 1998 concludes that men who engage in long-term vigorous exercise have a 5 times greater risk of developing LAF than do less active men. There are compensations though, vigorous exercisers have a 5 times lower overall mortality rate and a 3 times lower risk of developing coronary heart disease than do less active men. Again, our survey supports these findings. Not one respondent, so far, has indicated that he or she has diabetes and the incidence of high blood pressure is probably about 10% as compared to the expected rate of 40-50% for a comparable sample of non-afibbers.

Perhaps one of the most intriguing observations is that the majority of attacks (75%) happen in the period between 6 PM and 8 AM. Less than 20% occur between Noon and 6 PM and so far, only one respondent reports attacks between 8 AM and Noon. It is well known that the heart (pulse) rate is fastest at about 11:30 AM and slowest at about 2:30 AM. Actually the Chinese have been aware of this circadian variation in heart rhythm for the last 2000 years. Chinese medicine recognizes that the heart qi (energy) peaks between 11 AM and 1 PM and is at its lowest between 11 PM and 1 AM. So what has this got to do with the timing of LAF attacks, you may ask?

Actually everything! It is clear that the attacks happening when the heartbeat is fastest (in the morning) are adrenergic in nature while the attacks happening at night, at rest or during digestive periods are vagal in nature. It is also evident from our survey that athletic afibbers experience their attacks between 6 PM and 8 AM. Why? The Finnish study provides some clues. Highly athletic people have large hearts (physically that is) and slow heart beats. A daytime pulse rate of 50 is not uncommon. This means that at night or during digestive periods these highly athletic afibbers’ heart rates can drop so low that a bradycardia (excessively slow heart rate) may develop. A bradycardia is a potentially serious condition so it is plausible that the autonomic control system will try to avoid it by invoking a response from the sympathetic (adrenergic) branch. If this response (release of norepinephrine from nerve endings) is a little too enthusiastic or engages foci of highly excitable cells in the atrium a LAF attack may follow. It is also possible that an excessive release of acetylcholine from the parasympathetic system in itself could initiate AF. Add to this evidence that large atria (hearts) are more likely to enter into afib and sustain it than are smaller ones and the scene is set for an exceptional vulnerability to LAF. Because women tend to have smaller and faster beating hearts they seem to be much less likely to develop vagally mediated LAF.

To summarize, attacks happening during the day (especially in the morning) are adrenergic in nature, usually initiated by physical or mental stress and involve an overactive sympathetic nervous system. Attacks that happen at night or at rest are vagally mediated and involve an overactive parasympathetic system most likely coupled with an over-enthusiastic reaction from the sympathetic branch. The distinction between the two forms cannot be over-emphasized. They have entirely different origins and mechanisms and require different treatment. This does not mean that the two forms cannot coexist in the same individual. A hard-driving, tense person who is a fanatic physical fitness enthusiast may have both types of attacks, but fortunately, as we shall see, this is not a very common condition.

So what is the answer to preventing LAF attacks? Many afibbers have been prescribed antiarrhythmic drugs so we shall begin by reviewing how these drugs work and the rationale for their use.

Antiarrhythmic Drugs: How They Work

The very first thing to realize is that no drug has ever been developed specifically for the treatment of LAF. All the antiarrhythmics available were expressly developed for the treatment of arrhythmias arising from cardiovascular disease and heart attacks. The second thing to bear in mind is that ALL arrhythmias connected with heart disease are adrenergic in nature. As a consequence there is very little research on the use of antiarrhythmics in the management of vagally mediated LAF.

Antiarrhythmic drugs are divided into 4 classes depending on their mode of action[2,3]. To understand how they work let us take a brief look at the modus operandi of an individual muscle cell (myocyte) in the heart. The membranes of myocytes act as small pumps that pump sodium, potassium and, to a lesser extent, calcium and magnesium ions in and out of the cells. When the cell is at rest the concentration of potassium is high inside the cell and the concentration of sodium is high outside the cell. At certain times the ion channels which allow entry of sodium into the cell open and sodium ions rush into the cell causing it to generate an electric charge (depolarization) and contract. The contractions proceed from cell to cell making the whole muscle fiber contract and ultimately making the whole atria contract.

Potassium leaks out of the cell during the depolarization period, but as soon as the depolarization is over it begins to flow back into the cell during what is called the rest or refractory period. Atrial fibrillation is characterized by a total lack of refractory periods. Calcium and magnesium ions follow the sodium and potassium ions respectively, but at a slower rate. Thus sodium and calcium are “excitatory” ions while potassium and magnesium can be viewed as “calming” ions. This underscores the importance of having adequate intracellular levels of both potassium and magnesium and also explains why a magnesium infusion often halts AF. It is likely that a potassium infusion would have a similar effect, but it would be far too dangerous because of the much faster action of potassium ions.

The rate of the fibrillating heart can be slowed by partially blocking the ion channels that allow the influx of sodium or calcium or the outflow of potassium. Antiarrhythmic drugs owe their effectiveness to their capability to block ion channels. Class I drugs such as quinidine, disopyramide, flecainide and propafenone primarily block the sodium channels, but also have some potassium blocking effect. Class III drugs such as sotalol, amiodarone and dofetilide primarily block the potassium channels and class IV drugs such as verapamil and diltiazem block the inward movement of calcium. Class II drugs, the so-called beta-blockers, have no direct effect on the heart cells, but slow the heart rate by blunting the stimulatory effects of norepinephrine and the sympathetic nervous system.

This then is the arsenal available to the cardiologist and electrophysiologist in the battle against arrhythmias. Do they work? Yes and no! Some of them are highly effective in the treatment of life-threatening ventricular arrhythmias, but most of them are of little use when it comes to preventing LAF, particularly LAF of vagal origin.

Beta-blockers such as atenolol and propranolol, and antiarrhythmics like flecainide, propafenone, sotalol, amiodarone, verapamil, and diltiazem are the drugs most often prescribed for LAF. Digoxin (Lanoxin) used to be widely used, but has now been totally discredited. Several clinical trials have shown that it can lengthen attacks and even cause the LAF to become chronic[4]. Verapamil and diltiazem are useful in lowering the heart rate during an attack, but do not prevent attacks or speed up the conversion to sinus rhythm. Flecainide is useful in converting afib to sinus rhythm and somewhat useful in preventing attacks. It does, however, have some rather nasty side effects including sudden death. It, like other antiarrhythmic drugs, can also cause arrhythmias.

It is easy to see why drugs like flecainide have serious side effects. Their action is not limited to the atria. They also slow down the action of the ventricles – sometimes with disastrous results. Propafenone is somewhat similar to flecainide; however, it also has slight beta-blocking properties making it a poor choice for afibbers with vagal LAF. Sotalol is not effective in converting to normal sinus rhythm, but has some preventive action. It also has beta-blocking properties. Amiodarone is used in patients with serious ventricular arrhythmias and is generally not recommended for LAF due to its potentially devastating adverse

effects. To quote the authors of the chapter on "Oral Antiarrhythmic Drugs Used for Atrial Fibrillation"[3], "The long-term efficacy of antiarrhythmic drugs for preventing a recurrence of AF is far from ideal"!!

Are these drugs useful at all in the management of LAF? The answer to this depends on what type of LAF you have. At present the adrenergic type is far easier to prevent than the vagal type.

Prevention of Adrenergic LAF

The simplest pharmaceutical method of preventing an adrenergic attack is by taking a small amount of beta-blocker (25 mg atenolol or 5 mg propranolol) when you feel an attack is imminent, before attending a stressful meeting or in general, when you know you are likely to be exposed to excessive stress. Since beta-blockers may promote vagal attacks it is best not to take them too late in the day so as to minimize the risk of a vagal attack later in the evening when vagal tone is higher.

Many doctors recommend taking 25 or 50 mg of atenolol (or the corresponding amount of propranolol) twice a day. This is probably a less than sterling idea unless you have been diagnosed with hypertension. Continuous use of beta-blockers lowers blood pressure and heart rate significantly leading to fatigue and an increased risk of vagal attacks. Getting off beta-blockers after continuous use can also be a problem as the blood pressure may rise precipitously when the drug is discontinued.

I have personally found that an 8-oz. glass of fresh, organic celery juice sipped slowly is just as effective in preventing a LAF attack as is 25 mg of atenolol.

Beta-blockers (and verapamil) can also be used to slow the heart rate during an attack. They do not speed up the conversion to normal sinus rhythm. Conversion to sinus rhythm usually occurs spontaneously within the first 48 hours. Cardioversion is sometimes effective in converting episodes of longer duration, but for some unknown reason afibbers who have been cardioverted don't stay in sinus rhythm for very long. Flecainide and propafenone are usually effective in converting to normal sinus rhythm within a few hours. They can also be effective in preventing further episodes of an adrenergic nature. However, they are both highly dangerous drugs and their use should be closely supervised by a cardiologist.

Whether you should use flecainide or propafenone on a continuous basis depends to a large extent on how often you have episodes. If just a few times a year it is probably best to just use them when needed to convert quickly – this approach would eliminate a lot of nasty, long-term side effects. On the other hand, if attacks come on every second day or every week continuous use may be indicated – assuming that celery juice and beta-blockers do not do the trick. Sotalol is another possible choice, but from all accounts the side effects are pretty bad so I would approach this drug with caution. Finally, flecainide, propafenone, sotalol, and amiodarone all share the dubious distinction of having killed more people than placebo in the clinical trials that evaluated them.

I do believe I am running out of space – and time. Next month I will discuss the pharmacological treatment options for vagal LAF and carry on with the reporting of the survey results. Also, in the next and future issues I will focus on the non-pharmacological options for the management of LAF. Yoga, qi gong, deep breathing, meditation, and certain traditional Chinese medicine approaches may well prove to be the ultimate solution. It is also possible that certain herbal combinations could be effective in preventing vagal attacks.

Until next month!

References

1. Karjalainen, Jouko, et al. Lone atrial fibrillation in vigorously exercising middle aged men: case-control study. British Medical Journal, Vol. 316, June 13, 1998, pp. 1784-85

2. Falk, Rodney H. and Podrid, Philip J., editors. Atrial Fibrillation: Mechanisms and Management. 2nd edition, 1997, Lippincott-Raven Publishers, Philadelphia, PA.
3. Saoudi, Nadir, et al., editors. Atrial Flutter and Fibrillation: From Basic to Clinical Applications. 1998, Futura Publishing Co., Armonk, NY.
4. Sticherling, Christian, et al. Effects of digoxin on acute, atrial fibrillation: induced changes in atrial refractoriness. Circulation, Vol. 102, November 14, 2000, pp. 2503-08

INTERNATIONAL HEALTH NEWS is published monthly by:
Hans R. Larsen MSc ChE, 1320 Point Street, Victoria, BC, Canada, V8S 1A5
E-mail: health@pinc.com World Wide Web: http://www.yourhealthbase.com
ISSN 1203-1933 Copyright 2001 by Hans R. Larsen

INTERNATIONAL HEALTH NEWS does not provide medical advice. Do not attempt self-diagnosis or self-medication based on our reports. Please consult your healthcare provider if you are interested in following up on the information presented.