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Deep vein thrombosis (DVT) related to air travel is emerging as a major health problem. The condition may be entirely symptomless and resolve on its own or it may lead to pulmonary embolism and possible death. Estimates of the incidence of the condition vary widely from 1 to 10% of airline travellers. Considering that scheduled airlines carried well over one billion passengers in 2001 it is clear that DVT needs to be taken very seriously. In this issue our New Zealand correspondent, Maurice Mckeown, PhD takes a close look at what we know about DVT and, equally important, what can be done to prevent it. A must read for anyone planning a trip by airplane.

Also in this issue – magnesium helps abort severe asthma attacks, latest cancer trends in the US, some recent, important information about breast cancer prevention and treatment, and confirmation that vitamin C improves iron absorption.

Enjoy!

*Yours in health,
Hans Larsen, Editor*

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Magnesium helps abort severe asthma attacks

WELLINGTON, NEW ZEALAND. Asthma is an increasingly common disease especially among children. The disorder is allergic in nature and manifests itself as spasms of the airway tubes leading to often-severe difficulties in breathing. The severity of an asthma attack is determined by measuring the forced expiratory volume in one second (FEV₁) and comparing it to the normal FEV₁.

An FEV₁ of 50% or less of normal is a severe attack while a FEV₁ of 30% or less is life-threatening.

A magnesium deficiency has been implicated in chronic asthma and intravenous injections have been found useful in alleviating severe attacks. Researchers at the University of Otago now report that a combination of the asthma drug salbutamol and an isotonic magnesium solution applied as a spray (nebulized) is highly effective in helping asthma patients recover from an attack. Their clinical trial involved patients who had come to the emergency department because of a severe asthma attack. Upon admission all patients were given 100 mg hydrocortisone intravenously as well as 2.5 mg of salbutamol applied by jet nebulization. At least 30 minutes later the FEV₁ of the patients was measured and if it was less than 50% of normal they were randomized to either the magnesium group (28 patients) or the placebo group (24 patients). The placebo group received 3 nebulized doses of 2.5 mg of salbutamol plus saline solution spaced 30 minutes apart before their FEV₁ was measured again. The magnesium group received similar treatment except that their nebulizer solution

contained 150 mg of magnesium sulphate as well as the 2.5 mg of salbutamol in an isotonic solution.

At 90 minutes the average FEV₁ of the magnesium group was 1.96 L as compared to 1.55 L in the placebo group or 51.2% and 41.3% of normal capacity respectively. Twelve of the patients in the magnesium group (43%) were admitted to hospital after the trial as compared to 17 in the placebo group (71%). The beneficial effect of the magnesium was found to be greater in patients with

life-threatening asthma (FEV₁ less than 30%). The researchers conclude that adding magnesium to the salbutamol solution normally used in the treatment of asthma greatly enhances its effect, especially in severe and life-threatening attacks.

Hughes, Rodney, et al. Use of isotonic nebulised magnesium sulphate as an adjuvant to salbutamol in treatment of severe asthma in adults: randomised placebo-controlled trial. The Lancet, Vol. 361, June 21, 2003, pp. 2114-17

Selenium absorption by prostate tissue

BRISBANE, AUSTRALIA. There is considerable evidence that selenium may be protective against prostate cancer and there are currently several large clinical trials underway to determine definitively if selenium supplementation decreases the incidence of prostate cancer. Selenium is an important constituent of the body's naturally produced antioxidant, glutathione peroxidase, and its cancer preventive effect may be associated with increased glutathione levels.

If selenium proves to be cancer preventive it is clearly important to know whether selenium levels as measured in a blood sample correlates with actual selenium levels in prostate tissue. Researchers at the University of Queensland recently set out to answer this question. Their clinical trial involved 51 men who had been scheduled for transurethral resection for prostate enlargement. The men were randomly assigned to serve as controls or to receive selenium yeast tablets daily for one month prior to surgery. The

tablets provided a total of 200 micrograms/day of selenium. Blood samples were taken at the beginning of the 30-day trial and on the day of surgery and the selenium content of red blood cells was compared to the selenium content of prostate tissue removed during surgery.

The researchers found that the red blood cell level of selenium had increased from 173 ng/mL to 209 ng/mL in the supplemented group with no significant change among controls. The selenium level in prostate tissue from supplemented men was significantly higher than among controls (241 ng/g versus 196 ng/g). The researchers conclude that selenium supplementation is effective in raising selenium levels in both prostate tissue and red blood cells, but conclude that selenium values from blood testing do not correlate with values obtained from testing of prostate tissue.

Gianduzzo, TRJ, et al. Prostatic and peripheral blood selenium levels after oral supplementation. Journal of Urology, Vol. 170, September 2003, pp. 870-73

UK doctors' knowledge of radiation exposure

READING, UK. A team of medical doctors from several hospitals in the UK has performed a survey of their peers to gauge their knowledge of the amount of radiation exposure their patients receive when subjected to various types of x-ray examinations. One hundred and thirty practicing medical doctors were involved in the survey. The results were, to put it mildly, disappointing. Not one of the respondents know the approximate dose a patient is exposed to during a chest x-ray let alone the unit of measurement used to quantify x-ray exposure. A chest x-ray exposes the patient to approximately 0.02 mSv of radiation. The doctors were also asked to provide an estimate of the

radiation exposure in other procedures in terms of the equivalent number of chest x-rays. Only 1.5% of the doctors knew that one abdominal x-ray is equivalent to 75 chest x-rays and only 6% were aware that a CT scan of the abdomen is equivalent to 400 chest x-rays. None of the doctors knew that a leg arteriogram exposes the patient to a radiation dosage equivalent to that of 400 chest x-rays. The researchers conclude that most doctors have no idea as to the amount of radiation received by patients undergoing common x-ray examinations. They estimate 100 to 250 deaths occur each year in the UK as a result of cancers caused by medical radiation exposure.

Shiralkar, S, et al. *Doctors' knowledge of radiation exposure: questionnaire study*. **British Medical Journal**, Vol. 327, August 16, 2003, pp. 371-72

Editor's comments: I think perhaps the investigators in this study are being a little harsh on their fellow physicians. From what I can glean from the literature estimates of the radiation exposure from a chest x-ray varies between 0.02 milliSievert (2 millirem) and 0.08 mSv (8 millirem). Similarly, estimates of exposure from a CT scan vary between 1.1 mSv and 8 mSv. It is interesting that very few medical sites on the Internet actually give values for

exposure. Most couch the exposure risk in very vague terms like "don't worry, be happy!" The Canadian Centre for Radiation Safety limits maximum annual exposure from medical x-rays to 1.0 mSv. So having more than one CT scans in a year could be problematical down the road. I think the problem of doctors not knowing how much radiation they are causing their patients to be exposed to goes much deeper. Do the radiation experts really know and, perhaps more important, do they really know the associated long-term cancer risks?

Cancer trends in the USA

ATLANTA, GEORGIA. The annual report on the status of cancer in the United States has just been released. The report is a joint effort of the American Cancer Society, the Centers for Disease Control and Prevention, the National Cancer Institute, and the North American Association of Central Cancer Registries. Overall cancer incidence rates were essentially stable between 1995 and 2000, but may be increasing slightly if allowing for reporting delays. Overall cancer death rates have remained steady from 1998 to 2000. More than half of all cancer diagnoses and deaths involve lung cancer, breast cancer, prostate cancer or colorectal cancer (cancer of the colon or rectum).

Lung cancer

Lung cancer incidence and mortality have been declining among men since 1991, but have increased among women. This is no doubt due to the fact that smoking control programs have been far more effective among men than among women. The average annual death rate from lung cancer was 56.8 per 100,000 for men and 40.7 for women (1996-2000). Lung cancer rates were lowest in Utah, the state with the lowest adult prevalence of smoking (13%) and the highest in Kentucky, the state with the highest adult smoking prevalence (31%).

Breast cancer

The incidence of female breast cancer has increased continually since 1986 particularly among white women. Death rates, however, have decreased steadily since the early 1990s possibly due to the more extensive use of mammography screenings. The average annual death rate from breast cancer (1996-2000) was 27.7/100,000 with slightly higher rates observed among black women.

Prostate cancer

The incidence of prostate cancer has increased by 2.3% per year since 1994 and more recently by 3.0% per year among white men and by 2.3% per year among black men. Death rates, on the other hand, have been steadily declining and now stand at 32.9/100,000 (30.2 among white men and 73.0 among black men). Some experts argue that the increased use of PSA testing is responsible for the decline in mortality; however, the subject of screening for cancers is a highly controversial one. Dr. M.J. Quinn of the UK National Cancer Intelligence Centre points out that the use of the prostate specific antigen (PSA) test for screening purposes is not recommended by the US Preventive Services Task Force or in the European Code Against Cancer. He is clearly opposed to the use of PSA testing for screening purposes and points out that it may lead to unnecessary biopsies and dangerous treatments without any proven reduction in mortality.

Cancer of the colon and rectum

The incidence of colorectal cancer has stabilized since 1995 for both men and women and death rates have declined. Overall mortality rate for the period 1996-2000 was 21.2 per 100,000, but was particularly high among black men at 34.6/100,000.

The report concludes that overall cancer incidence and death rates began to stabilize in the mid to late 1990s, but have lately shown signs of increasing again.

Weir, Hannah K, et al. Annual report to the nation on the status of cancer, 1975-2000, featuring the uses of surveillance data for cancer prevention and control. Journal of the National Cancer Institute, Vol. 95, September 3, 2003, pp. 1276-99

Folic acid and B vitamins help prevent breast cancer

BOSTON, MASSACHUSETTS. Researchers at the Harvard School of Public Health have released the results of a major study aimed at evaluating the association between blood (plasma) levels of folate (folic acid), vitamins B6 and B12 and the risk of breast cancer. The study involved 32,826 female nurses who had blood samples drawn during 1989 and 1990. At the end of 1996 712 of the participants had developed breast cancer.

The researchers found the women with the highest plasma levels of folate (greater than 14 ng/mL) had a 27% lower risk of breast cancer than did women with a lower level (less than 6.4 ng/mL). The protective effect of folic acid was found to be even more pronounced in women who regularly consumed alcohol (one drink per day or more). Here those with the highest folate levels had an 89% lower risk of breast cancer than did women with low levels.

High plasma levels of vitamin B6 (greater than 95.3 pmol/mL) were associated with a 30% risk reduction as compared to low levels (less than 28.5 pmol/mL). High vitamin B12 levels were associated with a lower breast cancer risk among premenopausal women, but not among postmenopausal women. This finding contradicts that of earlier studies which found a protective effect only among postmenopausal women. It is interesting that no correlation was observed between the intake of vitamin B12 from food and plasma levels; a significant correlation was noticed between vitamin B12 intake from supplements and plasma levels. Plasma homocysteine levels were not associated with breast cancer risk. The researchers conclude that folic acid and vitamin B6 may help prevent breast cancer and that ensuring an adequate intake of these vitamins either from food or supplements may reduce breast cancer risk.

Zhang, SM, et al. *Plasma folate, vitamin B6, vitamin B12, homocysteine, and risk of breast cancer*. **Journal of the National Cancer Institute**, Vol. 95, March 5, 2003, pp. 373-80

Mastectomy versus lumpectomy – No survival difference

WASHINGTON, DC. There are two major alternatives for the surgical treatment of breast cancer. One, mastectomy, involves removal of the entire involved breast while the other, breast conservation therapy (BCT), involves removing just the tumour (lumpectomy) and subsequent radiation therapy. If the lymph nodes in the armpits (axillary lymph nodes) are found to be affected they are usually removed as well.

Researchers at the National Cancer Institute undertook a study between 1979 and 1987 to evaluate the survival rate of women who had undergone mastectomy as compared to women who had been treated with BCT. The 237 study participants have now been followed up for a median of 18.4 years. The survival rate for mastectomy patients over this period was 58% versus 54% in the BCT group – a difference that was not statistically significant. The disease-free

survival rate was 67% for the mastectomy group and 63% for the BCT group – again a difference that was not statistically significant. There was no statistically significant difference in the number of women who developed cancer in the previously unaffected breast (7 in the mastectomy group and 5 in the BCT group). There was also no difference in the number of women who developed cancer at sites other than the breast (10 in each group).

The researchers conclude that there are no statistically significant differences in the survival rate or in the incidence of the development of new cancers between women treated with mastectomy and those treated with breast conservation therapy. Poggi, MM, et al. *Eighteen-year results in the treatment of early breast carcinoma with mastectomy versus breast conservation therapy*. **Cancer**, Vol. 98, August 15, 2003, pp. 697-702

Zinc status difficult to measure

DAVIS, CALIFORNIA. A zinc deficiency has been linked to retarded growth, impaired immune function, and poor pregnancy outcome and infant health. A team of American and Mexican researchers now reports that the accurate determination of an individual's zinc status is difficult as zinc concentrations in blood samples vary significantly depending on when the blood sample is drawn (morning, afternoon or evening) and whether the patient had been fasting or not prior to the

sampling. An elevated white blood cell count, the use of oral contraceptives, hormones or steroids, or the presence of diarrhea can also influence zinc levels as does age and gender. The researchers conclude that serum or plasma zinc level cannot be considered a reliable indicator of zinc status in an individual. For population studies they propose the following cutoff levels (in micrograms/dL) for zinc (levels below which a deficiency would be indicated):

	<u>Morning Fasting</u>	<u>Morning Non-fasting</u>	<u>Afternoon</u>
Women aged 10-70 years	70	66	59
Men aged 10-64 years	74	70	61
Men older than 65 years	72	61	56

Their cutoff points are based on data from the NHANES survey carried out among 14,770 participants between 1976 and 1980.

Hotz, Christine, et al. Suggested lower cutoffs of serum zinc concentrations for assessing zinc status. American Journal of Clinical Nutrition, Vol. 78, October 2003, pp. 756-64

Vitamin C improves iron absorption

QUERETARO, MEXICO. It is estimated that 2.5 billion people worldwide suffer from iron deficiency and about 1.2 billion have iron deficiency anemia. The problem is particularly acute in countries such as Mexico where the normal diet contains large amounts of cereals and legumes (poor sources of absorbable iron) and limited amounts of meat, poultry and fish (good sources of heme or absorbable iron). Forty per cent of school-age children and 29% of women of childbearing age in Mexico suffer from iron deficiency anemia.

It is well known that ascorbic acid (vitamin C) improves the absorption of iron. Now researchers at the University of Queretaro and Baylor College of Medicine in Houston report that consuming a lime drink (limeade) containing 25 mg of ascorbic acid markedly increases iron absorption. The clinical trial involved 15 non-pregnant, non-lactating, iron-deficient women (ferritin less than 12 micrograms/L). The women were fed a traditional Mexican diet (maize tortillas and beans with

vegetables) to which 0.25 mg of a stable isotope of iron had been added. After 2 weeks a blood sample was taken and iron level measured. For the following 15 days the women were fed the same diet, but also consumed limeade to provide an additional 25 mg of ascorbic acid at breakfast and lunch. Iron absorption increased more than 3-fold when limeade was added – from 6.6% to 22.9%. A follow-up test performed 2 months after the beginning of the experiment showed that the average ferritin levels had increased about 33% (from 6.3 to 8.4 micrograms/L). The researchers conclude that consuming 25 mg of ascorbic acid as limeade twice daily with meals improves the absorption of iron and may improve iron status in iron-deficient women over the longer term.

Diaz, Margarita, et al. The efficacy of a local ascorbic acid-rich food in improving iron absorption from Mexican diets: a field study using stable isotopes. American Journal of Clinical Nutrition, Vol. 78, September 2003, pp. 436-40

NEWSBRIEFS

Electrical stimulation helps alleviate prostatitis pain.

Prostatitis is the most common urinary system complaint among men between the ages of 18 and 50 years. Prostatitis can be either acute or chronic. Only 5-10% of patients with chronic prostatitis actually have a bacterial infection so treatment with antibiotics is often ineffective. Not all cases of chronic prostatitis are inflammatory in nature and are classified as non-inflammatory pelvic pain syndrome. Researchers at the Zurich University Hospital in Switzerland recently developed and tested a novel electrical device that stimulates the prostate via electrodes placed in the prostatic urethra and the anal channel. Chronic pelvic pain decreased significantly in 10 out of 12 patients (83%) who used the device twice a week for 30 minutes over a 5-week period. The device can be used by patients in their homes.

Journal of Urology, Vol. 170, October 2003, pp. 1275-77

Don't mix warfarin and cranberry juice. The British Committee on Safety of Medicine warns patients on warfarin (Coumadin) not to drink cranberry juice. The Committee has received 5 reports of severe interactions, one fatal, between warfarin and cranberry juice. Because warfarin is metabolized by cytochrome P450 and certain antioxidants in cranberry juice inhibit the activity of P450, the combination of the two can lead to very high warfarin levels (INR of 50 or higher), which can cause severe internal bleeding.

Reuters Health Information, September 18, 2003

Dark chocolate better than milk chocolate.

Researchers at the National Institute for Food and Nutrition Research in Rome report that eating dark chocolate raises the level of antioxidants in blood plasma. Their trial involved 12 healthy volunteers who consumed 200 g of milk chocolate, 100 g of dark chocolate or 100 g of dark chocolate with milk on different days. Only the dark chocolate increased antioxidant levels, particularly the level of the flavonoid epicatechin. The researchers speculate that milk may impair the absorption of epicatechin and point out that an increase in plasma antioxidant level may help protect against heart disease.

Nature, August 28, 2003, p. 1013

Cancer research suspect. Much advanced cancer research is done using cultures of known cancer cells. There is now growing evidence that 20-40% of research done with these cells may be

suspect. The problem is that cancer cell cultures are easily contaminated with other cancer cells. The most notorious "rogue" cell is the "HeLa" cell or cervical cancer cell, which was first used in cancer research in 1952. One single HeLa cell can completely outgrow a colony of prostate cancer cells or other cancer cell in very short order and thus make results meaningless. Unfortunately, this is often covered up. Says David Lewis, manager of the European Collection of Cell Cultures, "If people have spent 3 years working on the wrong cells, they are not likely to tell other people about it". Dr. Adrie van Bokhoven at the University of Colorado Health Sciences Center says that DNA fingerprinting should be mandatory to confirm the identity of all cell cultures prior to research results being published.

New Scientist, September 20, 2003, pp. 8-9

Heart cells do regenerate. It has long been thought that heart cells (myocytes) are unable to repair and regenerate themselves. Researchers at the New York Medical College in Valhalla now report that this assumption is incorrect. They have discovered that the human heart contains stem cells. Stem cells are unspecialized cells and are unique in that they can renew themselves through many cell divisions and, under certain conditions, can be induced to become special purpose cells such as myocytes or insulin-producing cells in the pancreas. The researchers took stem cells from healthy rat hearts and injected them into damaged rat hearts. They found that the cells regenerated the damaged myocardium and formed new blood-carrying vessel and myocytes with the characteristics of young myocytes. They conclude that the discovery of the existence of stem cells in the heart opens up new opportunities for repairing damaged hearts.

Cell, Vol. 114, September 19, 2003, pp. 763-76

Pregnancy and NSAIDs don't mix. Researchers at Kaiser Permanente in Oakland, CA report that women who use NSAIDs (ibuprofen or naproxen) or NSAID-containing products (Advil, Motrin, Naprosyn) during pregnancy have an 80% higher risk of having a miscarriage (natural abortion before 20 weeks of gestation) than do women who do not use NSAIDs. Aspirin has a similar detrimental effect, but acetaminophen (Tylenol, Paracetamol) use was not associated with an increased risk of miscarriage. The risk of miscarriage was

particularly high if the NSAIDs were used around the time of conception and if usage lasted longer than 1 week.

British Medical Journal, Vol. 327, August 16, 2003, pp. 368-72

Deep Vein Thrombosis in Air Travellers

**by Maurice Mckeown, BDS, PhD
(Our New Zealand correspondent)**

The problem of deep vein thrombosis (DVT) after airline travel rises to public consciousness from time to time as the popular press report stories about healthy young travellers succumbing to the condition, or provide details of high profile cases going to court.

What is deep vein thrombosis?

In deep vein thrombosis a blood clot forms in one of the veins deep inside the leg. It can occur at any age but is much more common in older people. It can be caused by a wide variety of factors other than air travel. The clot may break away from its position and travel through the heart to the lung where it may cause severe symptoms which can result in death.

What are the risks of developing DVT after air travel?

Are we all becoming more and more unjustifiably fearful in a stressful world? My own perception is that the average airline passenger is much more concerned that the plane will crash than the possibility that they could develop a life-threatening medical condition. Yet the chances of the former are miniscule compared to the latter. The airlines have done little to help. Many have now put general flight-health advice on their websites and placed information pamphlets on in-flight health in the pocket in front of our seats, the ones with the exercise advice that almost never mention the words 'deep vein thrombosis'. One suspects that their motive is to forestall litigation rather than help their customers avoid the condition. The airlines are clearly in denial but a growing body of research is pointing to a major health problem.

There are a number of important questions to ask ourselves. How common is the problem? How susceptible are we to developing the condition and what can be done to minimise the risk?

We now have a rough estimate of the frequency of DVT and some indication of which groups of individuals are in a higher risk category. Unfortunately, the categories of individuals who are at greater risk are quite long. One is left with the impression that the majority of travellers on any particular flight fall into a high-risk category. High-risk groups include older people (probably those over 60 years), travellers with a variety of known medical conditions, pregnant women, those who have recently had surgery and women taking oral contraceptives or hormone replacement therapy.

The risk of developing DVT, which can of course occur quite independently from air travel, is very strongly linked to age. It is very uncommon in young people and very common in the elderly. If we consider air travel in isolation, studies have shown that 3-5% of travellers develop clots in veins. Some are, of course, asymptomatic or occur with mild symptoms. Thus a precise statistical analysis of the incidence of the condition is very difficult. In other words the traveller is unaware that they have suffered a clot. In 2001 *The Lancet* published an analysis estimating that 1 million cases of DVT related to air travel occur in the US every year and that 100,000 of these cases result in death (*Lancet, September 8, 2001, p. 838*).

However imprecise these figures may prove to be; they do suggest that the risks posed by air travel may be dramatically greater than commonly perceived. One analysis has concluded that frequent business travellers have a 5% risk of contracting DVT in any one year; data which ought to bring the matter to the attention of their companies' medical department, not to mention their health insurers.

What can be done to minimise risk?

The popular press have dubbed the condition – “economy class syndrome”, in the belief that the cramped seating arrangements, particularly with respect to legroom, are the prime cause. But is this really true? Recent analysis of the frequency of the condition suggests that it is equally prevalent in all classes of passengers and even aircrew. (The possible exception being cabin attendants who move around all the time - if on duty.) It seems that cramped conditions may not be the only precipitating cause. It appears more likely that lack of movement is much more important. On a recent round trip from New Zealand to Europe I formed the distinct impression that diligent exercisers were in a very distinct minority on board my flight.

People at risk

It is best to consider risk in the context of those who are apparently healthy and in those who have a known medical problem. If the healthy individual seeks advice from their doctor they may be told that they have little to fear, particularly if they are young and healthy. They may be advised that if they are really concerned they should take plenty of in-flight exercise, drink lots of water and even take an aspirin before takeoff.

The exercise advice appears to be excellent and it should of course include a warning not to go to sleep! (Difficult on flights of 8 -14 hours or more.) Perhaps the doctor might prescribe an amphetamine!! Advise on regularly drinking of plain water may be misplaced.

Is it of value to drink large amounts of water?

There appears to be no evidence that it is. In fact a study in Japan by Hamada et al, published in the *Journal of the American Medical Association* found that subjects who drank one cup of water per hour during a nine-hour flight experienced increased blood viscosity. Interestingly the study found that those who drank an electrolyte fluid (similar to a good quality sports drink) in the same manner, had no increase in blood viscosity and no increase in urinary output. Hamada used an electrolyte drink containing 110 mg (per 8 oz cup) of sodium and 30 mg of potassium (*JAMA, February 20, 2002, pp. 844-45*).

Advice is also commonly given to avoid caffeinated beverages because of their diuretic effect. Despite the fact that research has shown that coffee and other caffeinated beverages do not increase dehydration. (Armstrong: *International Journal of Sport Nutrition and Exercise Metabolism June 2002*)

Alcohol Consumption

Travellers are also advised to avoid alcohol because of its dehydrating effects. Yet red wine consumption is not particularly diuretic and is known to be beneficial to the health of blood vessels and has the effect, in moderation at least, of reducing the stickiness of blood platelets. A Polish research group last year found that the resveratrol present in the human diet (red wine carries significant amounts) may be an important compound responsible for the reduction of platelet adhesion and changed reactivity of blood platelets in the inflammatory process. (Olas et. al. *Thrombosis Research 15 August 2002*)

It remains to be determined what effect a moderate amount of red wine might have for the flying public. It is an impending research study which ought to have no lack of volunteers.

Does aspirin prevent blood clots?

I have been unable to unearth any definitive research that says it does. Medical opinion is divided. There is no doubt that it confers certain benefits on the arterial side of the cardiovascular system since it reduces the incidence of first heart attacks if taken daily for long periods. It should be pointed out that the arterial side of the cardiovascular system can also be affected by thrombosis, although to a much lesser extent than the venous part of the system. Arterial clotting has been closely linked to platelet adhesion. Aspirin and other natural substances can help reduce this. Some medical researchers feel that aspirin's beneficial influence in the venous system is minimal. A study of 300 high-risk passengers recorded a 4.8% incidence in the control group and a

3.6% incidence in those taking aspirin. Clearly aspirin had some value in this instance. (Belcaro et al: *Angiology Vol 230, 2002.*)

Are only long haul passengers at risk?

A study by the UK-based Aviation Health Institute found that 17% of flight-related DVT cases occurred in association with short flights. It has also been demonstrated that the duration of travel is not linked to the severity of the thrombosis suffered. (Parsi et. al. *Australian and New Zealand Journal of Phlebology June 2001*).

The British Independent newspaper has just published interim findings on the incidence of DVT in high-risk passengers as a result of a short-haul flight (London-Rome), which is of less than 3 hours duration. The authors released the preliminary results prior to journal publication because of their potential significance. The authors found that 4.3% of 568 passengers developed clots, which were detected by ultra sound. Two of the victims went on to suffer a pulmonary embolism. The lead researcher Professor Gianni Belcaro, of G d'Annunzio University in Italy said that their research suggested that most blood clots develop in the first two to three hours of a journey and grow larger and more dangerous with time. Unfortunately, we shall have to wait for the completion of the project and publication of the final report in order to find out full details, such as who was deemed to be at high risk.

What groups of healthy people are at risk?

It is now clear that aircraft cabin altitude, determined by the pressure within, appears to be the key-precipitating factor for an increased risk of blood clotting. Altitude, not immobility, is the primary problem. The information below suggests that we are all at risk. The degree of risk is determined primarily by our own physiological/genetic make-up.

A Norwegian study published by Bendz et al in *The Lancet* put 20 young men in a hypobaric chamber, which simulated usual aircraft cabin altitude.

Cabin pressures simulated an altitude of 5000-8000 feet in various aircraft types; reducing oxygen pressure from 98 to 79 mmHg as calculated for a Boeing 747. It has also been calculated that this can lead to 90% saturation of haemoglobin with oxygen; a figure that may be reduced even further by sleep and the effects of cramped conditions on respiratory mobility. Other environmental factors, notably humidity levels are also being investigated. Cabin humidity falls rapidly after take off. Its potential effect on factors like dehydration is currently controversial. In individuals with other respiratory problems, reduced oxygen saturation can lead to a chain of events in their blood which favours clotting.

It was found in the Norwegian study that a substantial hour-by-hour increase in blood clotting factors occurred in all of the healthy subjects. There was a 2-8 fold increase in clotting factors. The implication is that all flyers are subject to this increased risk, suggesting that those who succumbed to DVT have a variety of risk factors deriving from their own genetic and physiological make-up, and their environmental circumstances (*Lancet, November 11, 2000, pp. 1657-58*).

Enhanced likelihood of coagulation has also been demonstrated by Wolfgang Schobersberger et. al. in a study measuring coagulation factors on an actual long-haul flight. The effects were observed in all test subjects. He concluded, "Long-haul flights induce a certain activation of the coagulation system. This activated coagulation could be a risk factor for VTE during long-haul flights mainly when other risk factors are present." (*Thrombosis Research October 2002*).

It has been established that people carrying the Factor V Leiden variant are much more likely to suffer DVT than those without the variation. Caucasians populations can have a 5% incidence of the gene variant. The mutation does not appear to be present in Black or Asian populations, although it is present to a limited extent in Afro-Americans. Factor V Leiden increases the risk of venous thrombosis 3-8 fold for heterozygous (one bad gene inherited) and by 30-140 fold, for homozygous individuals (two bad genes inherited). Risk is dramatically increased beyond that if the individual is also suffering high blood homocysteine levels. The Wellman clinic in London (UK) has developed a series of tests to identify the Factor V Leiden variant and a number of other

genetic variants related to increased clotting risk. It is estimated that the Factor V Leiden variation is responsible for 40% of all cases of thrombosis. Interestingly, it increases the risk of DVT for men by 8-fold and in women by 80-fold. Women therefore appear to be at much greater risk.

Women taking oral contraceptives are also much more vulnerable to DVT, although the risk for those on estrogen replacement therapy is higher because they are older and face a greater base-line risk. Women who have recently given birth are also at increased risk. There are those who believe that pregnant women are at such increased risk that they should not fly at all, since preventative anticoagulant therapy can have serious consequences for the foetus. If they do fly it is advisable that they scrupulously follow the preventative advice at the end of this article.

Conventional wisdom says that the young, fit and healthy have little to be concerned about. Unfortunately, this may not be the case. In fact they may be at much greater risk than the young and unfit! This applies particularly to athletes, especially endurance athletes, who show a high incidence of the condition according to some researchers. This may be partly due to their very efficient cardiovascular systems pumping blood around more slowly.

It has recently been reported that at least two international soccer teams wear compression stockings on long haul flights, as a number of studies have shown that wearers of compression stockings are dramatically less susceptible to DVT than those not wearing the hose. One study has shown a complete elimination of the risk in stocking wearers (*Lancet*, May 12, 2001, pp. 1485-88). It has been claimed that 85% of flight DVT victims fall into the athletic category.

Airhealth.org, an organization dedicated to the dissemination of information concerning DVT estimates that 100,000 deaths due to air travel related DVT occur in the US every year (*Lancet*, September 8, 2001, pp. 838). This would make the condition the 5th leading cause of death overall after heart disease, cancer, stroke, and respiratory disease.

According to the US National Center for Health Statistics at the Center for Disease Control and Prevention the following four are the most common causes of death in the 20 to 44 year age group (*National Vital Statistics Report*, Vol. 49, No. 11, Deaths: Leading Causes for 1999):

Accidents	34,540
Cancer	21,404
Heart disease	16,767
Suicide	13,727

Air travel related DVT, however, may well be the most important cause of death among people in the 20 to 44 year age group. Airhealth.org reports that 47% of the victims in their registry were in this age group corresponding to 47,000 deaths out of the total 100,000 deaths (www.Airhealth.org).

Older Individuals

A substantial number of people, commonly in older age groups, have a variety of medical problems which require special attention e.g. those who have recently had surgery*, those already taking anticoagulant medication, people with cancer, heart disease or diabetes or a family history of DVT. They all need medical advice about preventative measures, which might include anti-coagulant therapy.

* Some authorities recommend that patients who have undergone surgery – particularly orthopaedic surgery, should not fly for 90 days after their operations.

What are the symptoms of DVT?

It should be pointed out that symptoms may arise many days after the end of a flight. One symposium concluded that a two-week post-flight risk period is likely. You may not therefore immediately associate any ill effects with your trip. Most patients report symptoms within one week of the end of their trip however.

LEG SYMPTOMS

- Sudden swelling in one lower leg. The left is much more commonly affected. (A little swelling in both legs is very common in flight.)
- Cramp or tenderness in one lower leg. (Healthy athletes may mistake this for cramp)
- A bruise or swelling behind the knee.

CHEST SYMPTOMS

- Shortness of breath
- Rapid breathing
- Cramp in your side, painful breathing
- Chest pain, sometimes accompanied by shoulder pain
- Fever
- Coughing up blood
- Fainting (often the first sign, especially in older people)

How can a diagnosis be made?

Leg clots can be readily diagnosed with ultrasound. A clot, which has moved to the lung, is more difficult to diagnose. A measure of your blood oxygen concentration usually taken with a simple attachment to your finger, can help. If it is low for no obvious reason further testing is required. It is sobering to note that one US research study has shown that 50% of DVT cases have no symptoms and 50% of those will progress to pulmonary embolism. In the study forty seven percent of fatal pulmonary embolisms were not diagnosed before death. (Zamula: *FDA Consumer Nov. 1989*).

Preventative measures

If you have long legs you may want to choose an airline with the largest seat pitch possible. (The seat pitch is the horizontal distance between similar points on two seats situated one behind the other.) Comparative seat pitch information for major airlines is available on the Internet on various websites. For a general comparison of airlines see www.aviation-health.org For more detailed information related to different aircraft types try www.simplyquick.com

It is probable, but not proven, that DVT is much more likely to occur in people with specific risk factors, notably inherited genetic clotting abnormalities. It has been estimated that up to one third of the population have some degree of thrombophilia – an enhanced tendency to form blood clots. Since most of us are unaware of these latent tendencies it would seem prudent to take all reasonable precautions. Little is usually said about nutritional supplements but there is good theoretical reason to believe that they may help.

Likely helpful substances are:

Vitamin E (400-800 IU) daily for some days on either side of the trip. Consult your doctor if already taking anti-coagulant medication.

Pycnogenol or Grape Seed Extract Both contain the active bioflavonoid called proanthocyanidins (OPC's), which helps strengthen capillaries, and enhances blood flow.

Vitamin B6 (in the form of pyridoxine hydrochloride), which has been shown to reduce platelet stickiness. (www.yourhealthbase.com/database/a124m.htm).

Pinokinase This is a new commercially available pill, which has recently become available. It is an oral pro-fibrinolytic anticoagulant. It is made from fermented extracts of pine bark and soybeans. A study just published in Angiology journal shows that it was 100% effective in preventing clots. Info at www.flighttabs.com

A small amount of aspirin (junior size) may help, if tolerated. People eating diets very high in fruit and vegetables may have as much salicylates in their blood as that provided by a pill according to a study of Buddhist monks in Scotland. (Blacklock et.al. *J of Clinical Pathology* 2001 Vol 54)

Resveratrol Available in the form of supplement capsules for those who do not drink red wine.

Other nutrients of possible value are ginkgo biloba, niacin, vitamin C, and vitamin B12.

Other important measures

- Wear properly fitting flight hose designed to be tight around the ankle, pressure gradually reducing further up the calf. **This is the single most effective preventive measure.**
- Flight stockings differ from ordinary hose. They have special elastic threads that are utilized to apply a precise amount of pressure to specific areas of the leg. They are available in a number of different strengths that are prescribed for a variety of medical conditions. Compression stockings exert maximum pressure at the ankles and gradually reduce that pressure up the length of the stocking. The pressure exerted at the ankle reduces by approximately 50% at the top of the stocking. This compression is scientifically designed to force blood from the secondary venous system near the skin into the primary deep vein system. The value of the stocking has been demonstrated by a study of flyers who wore flight hose on only one leg. This resulted in negligible swelling in the stocking clad leg, while the leg without the stocking experienced significant increases in volume. Thus flight hose can also relieve simple swelling of the lower extremity.
- If you have varicose veins it may be necessary to wear stockings above the knee. Please seek professional advice.
- Do leg flexing exercises while seated as studies have demonstrated that a variety of foot flexion movements result in substantial increases in blood flow in the leg.
- One authority recommends flexing of foot and calf muscles, while seated, for two minutes every half hour. If you are an avid armchair exerciser you might like to visit the Qantas airlines website. In the in-flight health section you can look at pictures of recommended exercises which ought not to injure the passenger seated next to you!
- Avoid sleeping if at all possible. If your jet lag is worse as a result try melatonin. (A prescription drug in many countries) It works miracles for me!
- Keep hydrated but do not drink pure water. Drink an electrolyte-balanced solution, available in a good quality sports drink. You may have to take some powder on board and add it to the water provided, if your baggage limit is in jeopardy.
- Do not drink large amounts of dehydrating beverages.
- Wear loose comfortable clothes.
- Take suggested supplements before, during and after your trip.
- If you are in a high risk category talk to your doctor and above all familiarise yourself with the symptoms of DVT, the diagnostic procedures necessary and possibly learn a little about what treatments might be applied.
- If the worst happens and you suspect that you have a clot seek immediate medical attention.

NOTE: Flight hose (socks) specifically designed for air travel are available at major airports and pharmacies or can be purchased online at www.scholflightsocks.com

BOOK REVIEW

- ***Textbook on EDTA Chelation Therapy***, Edited by Elmer M. Cranton, M.D., Second Edition, 2001. Hampton Roads Publishing Company, Charlottesville, VA.
- ***Bypassing Bypass Surgery***. Elmer M. Cranton, M.D., 2001. Hampton Roads Publishing Company, Charlottesville, VA.

Chelation therapy has been practiced for over 40 years and today there are chelation clinics worldwide as well as physicians treating patients on an individual basis. Aside from its FDA approved use for lead poisoning, which was the first medical application, mainstream medicine is almost universally opposed to chelation therapy, holding there is no evidence that meets their scientific and evidence-based standards for pronouncing treatments effective. The mechanism of alleged action is viewed as unknown, and the treatment is considered a waste of money and even dangerous. The majority of physicians routinely and strongly discourage their patients from initiating chelation for the treatment of stable angina, carotid artery occlusion, untreatable restenosis (recurrence of blockage) after coronary bypass surgery, impaired peripheral circulation, or for the prevention of amputation due to diabetes related severe peripheral vascular problems with lower extremity gangrene, to mention only some of the conditions for which chelation is supported by more than thirty years of anecdotal evidence and a number of clinical studies. In spite of the strong opposition from mainstream medicine, there have recently been roughly as many individuals who have undergone chelation therapy as have received coronary bypass surgery. According to chelation experts, the therapy has a forty-year record of safety. In Ontario, physicians are permitted to use chelation therapy without harassment or disciplinary action from the College of Physicians and Surgeons thanks to a private member's bill passed in the provincial legislature several years ago.

The therapy involves intravenous (IV) infusion of a common metal binding chemical, ethylene diamine tetracetic acid (EDTA), generally combined with a magnesium salt and a variety of other compounds to create an IV fluid that is well tolerated. It appears important that each treatment be done over a period of about three hours to infuse 3 grams of disodium EDTA. As many as 30-50 treatments are frequently required, although many individuals report symptom reduction after 5 to 10 treatments. EDTA is not metabolized, but binds a large number of metals and rapidly eliminates them in the urine.

An oversimplified description of what is *thought* to be the mechanism of action is related to this metal (ion) removal and the attendant decrease in the oxidative load, which results in the healing, over a long term, of oxidative damage, especially to the circulation system, and allows a redistribution of metals in the body and in enzymes that is closer to normal. The notion that the therapeutic action of EDTA is mainly due to calcium binding and elimination is no longer believed by most researchers in this field and was never believed by the critics of the therapy.

Dr. Cranton's textbook is actually a collection of articles, each with references, by medical scientists and physicians associated over the years with chelation therapy. It has sections on the scientific rationale of the therapy, twenty chapters on clinical trials, and sections on safety, the modern protocol for administration, and laboratory methods associated with EDTA plasma level measurements, monitoring of renal function, and data on urinary toxic and trace element excretion. This second edition has been updated to include some recent studies and additional anecdotal evidence, and includes the present-day protocol that has become standard for the IV administration of EDTA. While this book is perhaps mostly of interest to physicians practicing or contemplating practicing chelation therapy, some of the chapters should be of great interest to the layman since countless successful case studies are presented. Individuals with coronary heart disease, failed bypass surgery, cardiovascular or peripheral circulation problems, end-stage occlusive peripheral arterial disease with gangrene (the diabetic's nightmare since amputation is generally the only solution offered by mainstream medicine) etc., will find patients described with symptoms and problems to which they can relate.

Bypassing Bypass Surgery is written by the editor of the book discussed above and is intended for the layman, although it should also provide a useful introduction to physicians interested in the subject. The title is misleading, since this is in fact a

comprehensive book on chelation. The sub-title reads "Chelation Therapy, a Non-Surgical Treatment for Reversing Arteriosclerosis, Improving Blocked Circulation, and Slowing the Aging Process." Elmer Cranton is a graduate of Harvard Medical School. For a time he served as chief-of-staff of a U.S. Public Health Service Hospital. He has authored many books and scientific articles in the field of medicine and is certified as a fellow and diplomat of the American Board of Family Practice. At present, he oversees the operation of two clinics. The book begins with five endorsement letters regarding chelation therapy from cardiac surgeons and medical school professors which provide evidence that not all of mainstream medicine is against chelation. In the seventeen chapters that follow, virtually all aspects of chelation therapy are explored, including the early history, modern views as to the mechanism of action, a discussion of the clinical research, a comprehensive risk vs. reward analysis of bypass surgery and angioplasty (Chapter 16), a discussion of other conditions than heart disease where chelation is indicated, and a disturbing history of the politics of chelation. While no informed person would have grounds for suggesting that bypass surgery or angioplasty is unnecessary in some clinical situations, there are many instances where the evidence described by Dr. Cranton would suggest that there are sound reasons for considering chelation as either an alternative or as a therapy to try initially in the hope that surgery or angioplasty could be avoided.

For diabetic patients facing the amputation of toes or a foot because of gangrene, serious attention should be given to the anecdotal evidence quoted in this book as well as in the *Textbook on EDTA Chelation Therapy* (Chapter 11, "Effect of EDTA Chelation Therapy: Treatment of Peripheral Arterial Occlusion, an Alternative to Amputation"), since the reported success for complete reversal of this peripheral circulation problem and the concomitant saving of a foot (and ultimately probably a leg) seems compelling. When a person starts chelation in a wheelchair after being told that immediate amputation is a necessary and in fact lifesaving operation, and a few months after chelation therapy can walk normally, play golf, and has pink rather than blue feet with no evidence of seriously impaired peripheral circulation, one can only wonder what more evidence mainstream medicine wants, given that these patients were pronounced hopeless and offered life-altering amputation as the only

solution. By now, practically every chelation clinic in the world can probably provide a number of case histories of this particular application. Only the most ardent believer in the power of the placebo would dismiss these anecdotal results for end-stage occlusive peripheral arterial disease as unrelated to EDTA chelation, and demand double blind, randomized placebo controlled studies. In addition, placebo effects do not generally result in permanent alleviation of symptoms, nor are they consistent with the common observation that the benefits of chelation often fully appear only several months after the end of treatments. It can be argued that such studies would be highly unethical, given the nature and weight of the anecdotal evidence. It is also doubtful if many individuals would be interested in a study where they were hooked up to an IV for 3 hours per treatment for perhaps 60 treatments over 20-60 weeks without knowing if they were getting EDTA or just a drip containing everything but EDTA. If they were in a room with patients nearing the completion of their course of treatments and experiencing great improvement, it would be even more difficult to maintain the condition of a blind or double blind study, since everyone would probably soon want or even demand the EDTA treatment.

In view of the opposition from mainstream medicine, clearly the reader must make up his or her own mind as to the merits of chelation. Reading one or both of these books should help. Two quotations presented at the beginning of *Bypassing Bypass Surgery* seem appropriate to end this review (page x-xi, paperback edition):

"...I now achieve more lasting results with less risk, enhancing the benefits of surgery, and often avoiding surgery, by providing chelation therapy for my patients." Peter J. van der Schaar, M.D., Ph.D. Cardiac Surgeon and Director, International Biomedical Center, The Netherlands.

"...Bypassing Bypass is a book that will help patients to take responsibility for their own health, and it must be considered required reading for every serious student of preventive medicine, physician and patient alike." H. Richard Casdorff, M.D., Ph.D. Assistant Professor of Clinical Medicine, University of California, Irvine.

Reviewed by William R. Ware, PhD

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