

## ALTERNATIVE MEDICINE

AN EVIDENCE-BASED APPROACH

## Pycnogenol for Preventing Traveler's DVT

## History of Use

According to naturopath Michael T. Murray of Bastyr University, Seattle, the earliest recorded medicinal use of pine bark extracts was in 1534, when French explorer Jacques Cartier became trapped in ice during an expedition up the St. Lawrence River. His crew subsisted on salted meat and dry biscuits but began showing signs of scurvy, the cause of which was not then known. Local Native Americans recommended that the explorers consume tea made from pine bark and needles, and the men survived the ordeal.

In the 1970s, Jacques Masquelier, a professor at the University of Bordeaux (France), heard of Cartier's story and concluded that pine bark must contain vitamin C and other antioxidants. He subsequently analyzed the active proanthocyanidin components, which are similar to those in grape seed extract, and termed them collectively pycnogenol. Today, pycnogenol, formulated from extracts of the French maritime pine tree *Pinus pinaster*, is a registered trademark of Horphag Ltd., Guernsey, England.

## Rationale for Use

Like grape seed extract, green tea, and other polyphenol-flavonoid compounds, pycnogenol is a powerful antioxidant. It interferes with cell proliferation, modulates chronic inflammation, and inhibits xanthine oxidase. It acts in a capillary-protective fashion via effects on the lysosomal enzyme system.

Pycnogenol also inhibits platelet aggregation, which suggests that it may have potential for prevention of blood clots. Smokers tend to have elevations in platelet activity levels, and a German study found that smoking-induced platelet reactivity was prevented by the intake of 500 mg aspirin or 125 mg pycnogenol (Thromb. Res. 1999;95:155-61).

## The Economy Class Syndrome

Much attention has been paid in recent years to the economy class syndrome, in which passengers in cramped conditions on long flights have subsequently developed deep vein thrombosis (DVT) and pulmonary embolism.

A report from the emergency medical service of the Paris airports found that, of the 70 cases of acute thromboembolism treated between 1984 and 1998, 77% were in patients who had been on flights lasting longer than 12 hours (Bull. Acad. Natl. Med. 1999;183:985-97). This report also acknowledged that it reflected only acute, symptomatic cases, such as patients who fainted upon leaving the airplane.

The true scope of the problem was highlighted by the LONFLIT study, which showed that 3% of travelers developed clots on long flights, most of which were silent or asymptomatic but still potentially dangerous (Angiology 2001;52:369-74). With some 600 million Americans flying each year—50% on flights longer than 4 hours—one estimate is that up to 1.8 million travelers may develop clots (Phytother. Res. 2004;18:687-95).

Routine advice for travelers at risk for these conditions, such as those with varicose veins

and chronic venous insufficiency, has included the use of compression stockings and prophylaxis with low-molecular-weight heparin or aspirin. Travelers are also advised to drink non-alcoholic fluids, avoid salty food, and stand and stretch frequently, but exercising can be difficult on a crowded airplane. Advocates of the use of pycnogenol suggest that it is safer than aspirin, as it does not increase bleeding time or cause GI side effects.

## Clinical Study Findings

A group of Italian researchers recently reported their data comparing pycnogenol to placebo for the prevention of edema and venous stasis in a group of 169 asymptomatic subjects at mild to

moderate risk of thrombosis following flights lasting 7-12 hours. The study involved ultrasound scans of the legs before and within 12 hours after the flights to evaluate the femoral, popliteal, and tibial veins. Assessment of edema was done on an analog scale, with composite scores ranging from 0 to 12. The rate of ankle swelling was measured with a strain gauge.

Participants received two capsules of 100 mg pycnogenol or placebo 2-3 hours before their flight, with two more capsules 6 hours later and one the next day.

After the flights, patients in the pycnogenol group had an increase in edema score of 17.9%, compared with an increase of 58.3% in the placebo group, a difference that was statistically significant (Clin. Appl. Thromb. Hemost. 2005;11:289-94).

The change in ankle circumference from before to after the flight also was significantly smaller in the active treatment group, at 6%, compared with 11% in the placebo group. The rate of ankle swelling, evaluated in a subgroup of 45 patients, increased an average of 91% in the placebo group but only 36% in the pycnogenol group.

No patients in the study reported side effects from the treatment.

The researchers noted a number of factors that may contribute to flight-associated edema and release of thrombogenic factors, including compression of the popliteal vein on the edge of the seat, immobility, decreased fluid intake, water loss in the dry atmosphere, decreased air pressure, and relative hypoxia. They also pointed out that edema is not limited to the visible lower limbs. "The effects of edema could be more important than expected as retinal and brain edema have been episodically described and can be associated with vision problems and ... sleep and behavioral pattern alterations, which may be associated or confused with jet-lag symptoms. Actually, in our experience, in several subjects and patients with high levels of edema after long flights, the presence of subclinical edema has been detected with cerebral MRI or CT scans." The subclinical cerebral edema was, in some cases, associated with severe alterations in speech and sleep. This phenomenon should be studied more specifically, particularly in older patients who are prone to the development of edema, they said.

—Nancy Walsh

▶ Travelers on long flights are at risk for the "economy class syndrome," involving edema, venous stasis, and possible deep vein thrombosis.

▶ Extracts of the French maritime pine tree exhibit antioxidant and antiplatelet effects, and have been shown to reduce edema following air travel.

## Echo Data Help Predict Chest Pain Outcomes

BY DIANA MAHONEY  
New England Bureau

BOSTON — A novel risk score, comprising measures of wall motion and myocardial perfusion from contrast echocardiography and clinical variables, is a sensitive predictor of 1-year outcome in patients presenting to the emergency department with chest pain prior to obtaining troponin data, reported William Foster, M.D.

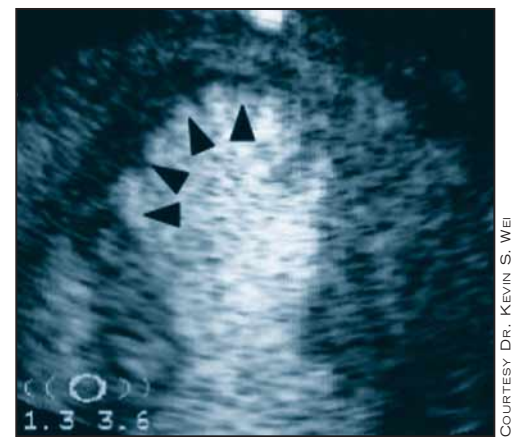
In the risk score development model and a subsequent validation model, the tool proved to be more effective for risk stratification than did the use of cardiac troponin measures and clinical variables without the ultrasound data, said Dr. Foster in a poster presentation at the annual meeting of the American Society of Echocardiography.

Dr. Foster and colleagues at the University of Virginia in Charlottesville developed the risk score using clinical and myocardial imaging data from 973 patients presenting to the emergency department (ED) with chest pain that could not easily be attributed to a noncardiac cause and who did not have ST-segment elevation on their admission ECG.

The risk score stratifies the like-

The researchers developed an alternative risk score model that includes troponin levels in the clinical variables.

With respect to echocardiographic variables for risk prediction, regional function was characterized as normal or abnormal using a 14-segment model, including 6 segments in each of the basal and midpapillary muscle levels and 2 segments in the apex. Myocardial perfusion was evaluated using the same segmented model and was



Arrowheads demonstrate presence of a resting perfusion defect in the septum.

deemed abnormal if there was no evidence of maximal opacification within a segment by five cardiac cycles. An echocardiographic study was considered abnormal if at least one segment was abnormal for either regional function or myocardial perfusion, Dr. Foster noted.

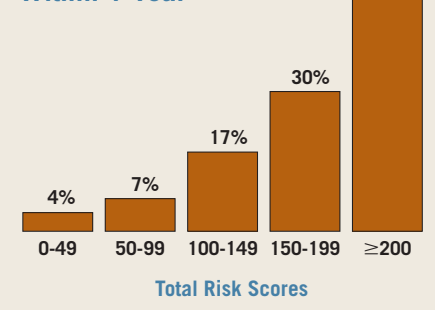
Each of these predictors is associated with a score between 0 and 100, based on estimates developed using logistic regression models.

Among the 973 patients in the development sample, the model showed "excellent discriminatory capacity," with an 86% probability of correct prediction, said Dr. Foster.

Approximately 60% of those with total risk scores of 200 or higher, and 30% of those with scores of 150-199, experienced a primary or secondary cardiac event at 1 year. About 17% of patients with scores of 100-149, 7% of those with scores of 50-99, and 4% of those with scores of 0-49 had events within 1 year.

To validate the sensitivity of the scores as potential indicators, Dr. Foster applied the risk score model prospectively in 232 patients who were followed for up to 1 year. "We saw the same pattern in the validation sample, with a similar prognostic discriminatory capacity between the validation and development samples," said Dr. Foster.

## Chest Pain Patients Who Had a Cardiac Event Within 1 Year



likelihood of developing primary or secondary events within 1 year of chest pain presentation in the ED. Primary events include all cause mortality and myocardial infarction; secondary events include unstable angina, revascularization, and heart failure.

The clinical predictive factors considered in the risk score include age older than 60 years, the presence of three or more coronary disease risk factors, known coronary luminal diameter narrowing of more than 50%, ST-segment deviation on ECG, two or more angina events in the past 24 hours, and aspirin use in the past 7 days.