Clinical Digest

Cardiovascular Disease

Healthy Anger Expression and Risk of Heart Disease

Study findings have been inconsistent regarding whether or not anger has a significant impact on risk of coronary heart disease (CHD). Researchers from Columbia University Medical Center, New York, NY; Beth Israel Deaconess Medical Center, and Harvard School of Public Health, both in Boston, MA, say that while it is important for patients to express anger, they should only do so in a healthy way.

In their observational study, they randomly selected 785 adults between the ages of 46 and 92 years with no known CHD at baseline. Each participant completed a videotaped, 12-minute, stressful interview developed to measure three different forms of anger expression: (1) constructive anger (discussing anger to resolve the situation), (2) destructive anger justification (blaming others for one's anger), and (3) destructive anger rumination (brooding over an anger-inducing incident). Trained coders rated each participant's responses and related them to the patient's 10-year risk of developing CHD.

During 6,584 person-years of follow-up there were 115 CHD events, seven of which were fatal. In both sexes, higher levels of destructive anger justification were associated with a 31% increased risk of CHD. The association between constructive anger and risk of CHD varied by gender: higher scores were associated with a 41% lower risk of CHD for men, but there was no significant association for women. This gender-specific association may be due to the fact that men and women are socialized to express anger and hostility differently. For example, in this study, the inverse association between constructive anger and hostility was stronger in men while the inverse association between constructive anger and depression was stronger in women.

The researchers say that the types of anger they assessed are relatively easy to judge in a clinical situation. While discussing anger can be protective against CHD, some patients have a tendency to discuss their anger for destructive reasons, the researchers caution. They suggest teaching "men and women to decrease discussions of anger that are motivated by the desire to justify or rationalize their emotions." Further studies are needed to test the efficacy of prevention programs designed to improve anger expression.

Source: *Am Heart J.* 2010;159(2):199–206. doi:10.1016/j.ahj.2009.11.007.

Cancer

Sunlight May Protect Against Bladder Cancer

Although smoking is the most common cause of bladder cancer, nearly half of the cases have unexplained causes. Now, researchers from Sunlight, Nutrition and Health Research Center, San Francisco, CA; University of California, and Naval Health Research Center, both in San Diego, CA, suggest there is an inverse association between ultraviolet B (UVB) light and incidence rates of bladder cancer worldwide.

Results from previous studies have shown the inverse association between UVB irradiation and bladder cancer mortality rates. Others have found that people with lower prediagnostic serum 25-hydroxyvitamin D levels have substantially higher incidence of several cancers, including breast, colon, and ovarian.

In their study, researchers used the International Agency for Research on Cancer database to analyze age-adjusted incidence rates of bladder cancer in 174 countries. They calculated the total noon solar UVB irradiance at the top of the atmosphere during each country's winter solstice month. They also determined per capita cigarette consumption for 1980 (the median year of patient exposure to smoking, assuming a 20-year incubation period).

The results of their study showed that bladder cancer rates were substantially higher in countries located further from the equator at higher latitudes. Furthermore, the data indicates that UVB irradiance was independently inversely associated with incidence of bladder cancer, even after controlling for variables such as smoking, per capita health expenditures, and cloudiness.

Despite this inverse association, several countries had high incidence rates of bladder cancer regardless of the countries' sunny locations—notably, Mozambique, Zambia, and Egypt (which has the highest incidence in the world). Such results may be explained by the high prevalence of *Schistosoma hematobium* in these counties, since chronic infection with it has been shown to substantially increase risk of bladder cancer. Other inconsistent results may be explained by countries having proportionately greater populations of smokers.

The study was limited due to several factors, including incomplete

data on per capita cigarette consumption leading to 63 countries being excluded from the study. These excluded countries tended to have lower per capita health expenditure and are less likely to offer timely diagnoses of bladder cancer. Additionally, the researchers acknowledge that a country's culture, behavior, and diet (none of which were accounted for in this study) could have affected the results. For example, types of clothing absorb UVB irradiance differently, so the incidence rate of bladder cancer in a country could have been influenced by the types of clothing worn in that area.

Regardless of these limitations, the researchers believe that because vitamin D deficiency can be a potential risk factor for bladder cancer, vitamin D supplementation can help address this problem.

Source: *Am J Prev Med.* 2010;38(3):296–302. doi:10.1016/j.amepre.2009.10.044.

NEUROLOGY

Orthostatic Syndromes and Syncope

Syncope is far more common in patients with postural tachycardia syndrome than in those with orthostatic hypotension, say researchers from University Hospitals Case Medical Center and Rainbow Babies and Children's Hospital, both in Cleveland, OH.

Postural tachycardia syndrome, a disorder characterized by orthostatic symptoms such as dizziness, lightheadedness, palpitation, and blurred vision, is often accompanied by nonorthostatic symptoms, including fatigue, vomiting, nausea, constipation, diarrhea, and migraine headaches. In their study, researchers looked at 810 patients who were referred for postural tachycardia syndrome. Of these, 185 patients met the inclusion criteria for postural tachycardia syndrome, which researchers defined as "an increase in heart rate > 30 beats per minute within the first 10 minutes of upright tilt, unaccompanied by any decrease in blood pressure." A separate group of 328 patients were categorized as having orthostatic hypotension, which they defined as "a decrease in diastolic blood pressure of > 10 mm Hg within the first three minutes of upright tilt and sustained during the remainder of the tilt study."

Of those with postural tachycardia syndrome, 38% had syncope on head-up tilt, compared with 22% of those with orthostatic hypotension ($P < .0001$). Among the postural tachycardia patients who fainted, 90% had a clinical history of syncope; only 30% of patients who did not faint had a clinical history of syncope. In orthostatic hypotension patients, however, there was no visible relationship between fainting during head-up tilt and the patients' clinical history of syncope.

The researchers contend it is unlikely their findings were simply due to differences in tilt duration. If the difference in results only reflected duration of the head-up tilt, the expectation would have been a higher frequency of fainting in patients with orthostatic hypotension, as patients who fainted tended to do so early in the tilt study. Some of the findings may be explained by the fact that patients with postural tachycardia syndrome tended to be younger and female, a population in which syncope is far more prevalent.

The researchers suggest there is a "more mechanistic explanation" of their findings, however, as postural tachycardia syndrome and orthostatic hypotension differ in their physiology in major ways. Postural tachycardia syndrome is thought to involve central hypovolemia (an abnormality centered on the low-pressure venous system), whereas the fundamental defect in orthostatic hypotension is located in the arteriolar constriction bed on the high-pressure side. The low-pressure baroreceptor system implicated in postural tachycardia syndrome might confer more sensitivity to syncope than the higher-pressure system implicated in orthostatic hypotension. The higher prevalence of syncope in postural tachycardia syndrome may indicate a shared pathophysiology.

Prior to this study, expert opinion has been divided on whether postural tachycardia syndrome predisposes to syncope. The results of this study suggest that tilt syncope could be a useful predictor of clinical syncope in patients with postural tachycardia syndrome.

Source: *Am J Med.* 2010;123(3):245–249. doi:10.1016/j.amjmed.2009.09.018.

CANCER TREATMENT

Safe, Effective Breast Irradiation In Less Time

Whole-breast irradiation after breast-conserving surgery can be given safely and effectively in a larger dose in a shorter period of time, according to researchers from Canada and London, England.

Researchers enrolled 1,234 patients with invasive carcinoma of the breast with negative axillary nodes who were treated by means of breast-conserving surgery and axillary dissection. Patients were randomized into two groups: the control group (which received whole-breast irradiation at a dose of 50 Gy given in 25 fractions over 35 days) and the hypofractionated-radiation group (which received whole-breast irradiation at a dose of 42.5 Gy given in 16 fractions over 22 days). Patients were seen every six

months for five years, then yearly for a mean of 12 years.

At 10 years, local invasive recurrence of breast cancer occurred in 83 patients (42 in the control group and 41 in the hypofractionated group). In addition, there were 13 cases of noninvasive local recurrences (six in the control group and seven in the hypofractionated group). Overall, the cumulative incidence of local recurrence at 10 years was 7.5% in the control group versus 7.4% in the hypofractionated group. In an exploratory subgroup analysis, the researchers did find hypofractionation to be less effective for high-grade tumors, compared with lower-grade tumors. They say it may be a chance finding, or may reflect a different inherent radiation sensitivity of high-grade tumors.

Survival rate also was similar between the two groups: 84.4% in the control group versus 84.6% in the hypofractionated group. Although whole-breast irradiation—particularly on the left side—has been linked to higher risk of death due to coronary artery disease, few cardiac-related deaths were observed during the study.

Over the long term, radiation therapy may cause skin telangiectasia and fibrosis of subcutaneous tissue, the researchers note, which can lead to loss of volume and retraction of the breast. They did, in fact, see a worsening of cosmetic outcome over time in the hypofractionated group compared with the control group (69.8% had an excellent or good outcome versus 71.3%, respectively). This difference was not significant, however. The researchers saw no increase in toxic effects in women who received accelerated, hypofractionated-radiation therapy as compared with those on the standard regimen.

Therefore, the researchers observed no significant difference between the two groups in regard to overall survival, local recurrence, or toxic effects, and the results of the hypofractionated regimen were not inferior to those of the standard regimen. Furthermore, the accelerated regimen might be more convenient and less costly. "Its availability as a treatment option may lead to an increase in the number of women who receive breast irradiation after breast-conserving surgery."

Source: *N Engl J Med.* 2010;362(6):513–520.