The potential importance of work-related rhinitis tends to be discounted within the discipline of occupational medicine as well as in pulmonary practice more generally. This is ill-advised. As this study shows, not only were upper airway symptoms linked to grape farming, but so too were a decrement in airflow and an increase in reversible obstruction. Moreover, asthma was indeed more common among the exposed farmers than the referent population, although the number of observations were too few to achieve statistical significance. Beyond its importance as a potential *forme furste* of occupational asthma, rhinitis in and of itself can have a substantive impact on perceived health status and work productivity, and thus should not be disregarded as a source of morbidity.

Although some of the oldest references in the history of occupational diseases have been to respiratory conditions among farmers, for too long agricultural workers have been presumed to be relatively free of the adverse health risks borne by classic industrial workers or even by other urban service or administrative employees. In terms of allergic sensitization, this idyllic view has been reinforced by recent findings that farm-reared children may be less likely to become atopic than their urban peers, even though this cannot be extrapolated to show protection against adult-onset work-related sensitization in agricultural settings. The work of Chatzi et al underscores the need to reevaluate these idyllic presumptions.

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Autonomic Function, Omega-3, and Cardiovascular Risk

The status of the autonomic nervous system, although ignored by many clinicians, is a major determinant of cardiovascular health and prognosis. Any therapy that chronically activates the sympathetic nervous system and/or diminishes parasympathetic (vagal) tone will increase the risk of cardiovascular events. In contrast, therapies that tip the autonomic balance toward parasympathetic dominance and decrease sympathetic tone will improve prognosis.

Many studies have established an elevated resting heart rate as a risk factor for cardiovascular disease and mortality. What used to be considered a “normal” sinus rhythm of 90 beats/min is more worrisome compared with a reassuringly “abnormal” sinus bradycardia of 50 beats/min. An impaired chronotropic response to exercise, defined as a failure to achieve 85% of the age-predicted maximal heart rate, is another indicator of abnormal functioning of the autonomic system and is associated with increased mortality. Heart rate recovery after exercise, which is mediated primarily by vagal tone, has also been shown to be a significant prognostic factor.

Intact heart rate variability (HRV) [beat-to-beat variability mediated by a dynamic autonomic nervous system, especially vagal tone] and baroreflex sensitivity [reflex-mediated changes in heart rate as a response to fluctuations in preload and venous re-
turn) are characteristics of a healthy autonomic system and are potent independent predictors of cardiovascular prognosis. Low HRV has been associated with increased risk of coronary heart disease (CHD) and mortality, as well as angiographic progression of coronary atherosclerosis and sudden cardiac death.

Many interventions have been found to improve autonomic function. Although nonphysiologic stresses increase the risk of adverse cardiovascular events, normal physiologic sympathetic activation (eg, during exercise or sexual activity) improves physical conditioning, mood, and cardiovascular prognosis. Exercise transiently stimulates the sympathetic nervous system, but because it strongly augments background vagal activity, it is an effective and practical means to restore a healthy balance of autonomic tone.

The Ochsner Clinic Foundation trial studied 40 patients following major CHD events, including 29 patients who underwent comprehensive phase II cardiac rehabilitation and exercise training programs and 11 control coronary patients who did not attend cardiac rehabilitation. The purpose of our study was to determine whether active training improves prognostic indexes of autonomic regulation of the sinoatrial node and whether the changes in baroreflex gain could be ascribed to the arterial or to the cardiopulmonary component of the overall arterial pressure/heart rate baroreflex. We determined that cardiac rehabilitation and exercise training were associated with significant improvements in autonomic markers of neuroregulation of the sinoatrial node and whether the changes in baroreflex gain could be ascribed to the arterial or to the cardiopulmonary component of the overall arterial pressure/heart rate baroreflex. We determined that cardiac rehabilitation and exercise training were associated with significant improvements in autonomic markers of neuroregulation of the sinoatrial node and whether the changes in baroreflex gain could be ascribed to the arterial or to the cardiopulmonary component of the overall arterial pressure/heart rate baroreflex. We determined that cardiac rehabilitation and exercise training were associated with significant improvements in autonomic markers of neuroregulation of the sinoatrial node and whether the changes in baroreflex gain could be ascribed to the arterial or to the cardiopulmonary component of the overall arterial pressure/heart rate baroreflex.

Another intervention to improve autonomic function is the intake of marine omega-3 fatty acids (FA), principally docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA). Interest in the potential cardiovascular protective effects of increasing omega-3 fats began with studies of the Inuit. These Greenland Eskimos were found to have a low risk of ischemic heart disease despite a diet that was high in fat and cholesterol. Since the 1970s, the understanding of the important physiologic benefits of dietary omega-3 FA has continued to expand. There are several possible mechanisms whereby these dietary supplements may reduce the risk of CHD. They do appear to have a modest BP-lowering effect. They also improve the lipid profile, through decreasing triglycerides and very-low-density lipoproteins and slightly raising the cardio-protective high-density lipoprotein cholesterol. Omega-3s also alter prostaglandin metabolism by inhibiting the production of thromboxane A2 and inflammatory cytokines, reducing the likelihood of acute coronary thrombosis. However, these effects of omega-3 fats have only been documented in studies using pharmacologic doses of EPA and DHA (3 to 5 g/d), and thus they may not be able to account for the major impact on the risk of fatal CHD seen with nutritional doses (<1 g/d).

Evolving as the most important mechanism whereby omega-3s protect against a fatal heart attack is the reduction of serious cardiac arrhythmias, particularly during myocardial ischemia or infarction. Omega-3s have been shown to have a potent antiarrhythmic effect in animal studies. In these experiments, intra-venous infusion of the major omega-3 fats DHA and EPA conferred almost immediate protection against ischemia-induced ventricular tachycardia and ventricular fibrillation. Similar studies have been performed in humans undergoing ventricular stimulation in the electrophysiology laboratory.

Sudden death caused by sustained ventricular arrhythmias accounts for 50 to 60% of all deaths in persons with CHD. To date, the largest, prospective, randomized controlled trial on the effects of omega-3 FA is the GISSI-Prevenzione Trial. This study included 11,324 patients with known CHD who were randomized to receive either 300 mg of vitamin E, 850 mg of omega-3 FA, both, or neither. After 3.5 years, the group receiving omega-3 FA alone had a 45% reduction in sudden death and a 20% reduction in all-cause mortality. The former observation is consistent with an antiarrhythmic effect of fish oil omega-3 FA.

In humans, an increase in HRV following a myocardial infarction is associated with a decreased risk of fatal arrhythmias. Several studies suggest that omega-3 FA (especially DHA) may improve parameters of autonomic function, including HRV and baroreflex sensitivity. Hulguin et al, in this issue of CHEST (see page 1102), published a study addressing the effects of these FA on HRV. They administered fish oil (2 g/d providing 1.7 g of EPA plus DHA) or soy oil (2 g/d providing 0.13 g of the short-chain omega-3 FA, α-linolenic acid [ALA]) to 52 residents of a Mexican nursing home. HRV was assessed with 6-min readings obtained every other day for a 2-month run-in period and a 6-month supplementation period. They reported that both supplements improved HRV, with the fish oil supplement having a somewhat greater impact than the soy capsules. These findings should be considered preliminary, however, because there was no true...
placebo arm in the study (although most researchers in the field would consider the 2 g of soy oil a placebo, given the very small amount of ALA it provided). There was no analysis of the differences in response between the groups; thus, the fish oil supplement may not have been statistically different from the soy supplement. In addition, the generalizability of the findings to the US dietary setting remains to be determined. Nevertheless, this study lends support to the hypothesis that omega-3 FA can improve autonomic function, and thus potentially decrease the risk for life-threatening cardiac arrhythmias.

Dallongeville et al.\(^\text{25}\) conducted a cross-sectional analysis of 9,758 men 50 to 59 years old without CHD to assess heart rate and CHD risk factors in relation to the quantity and frequency of fish consumption. They found that increased fish consumption was associated with decreased heart rate in men. In a clinical trial\(^\text{26}\) at the Mid America Heart Institute, we used the “GISSI dose” of omega-3 (a daily supplement of purified fish oil to supply 1 g of EPA plus DHA) to assess changes in autonomic function. This study of 18 cardiac patients showed a significant decrease in resting pulse of 4 beats/min and a strong trend for an improvement in postexercise heart rate recovery after the omega-3 period as compared to the placebo period. Because heart rate is positively associated with risk of sudden death,\(^\text{2,3}\) the heart rate-lowering effect may also contribute toward the cardioprotection noted with marine omega-3 fats.

Omega-3 FA from fish are a natural, safe, and inexpensive therapy that provide a unique and potent protection against fatal dysrhythmias that appears to be mediated, at least in part, by favorable changes in function of the autonomic nervous system. The American Heart Association has endorsed omega-3 fish oils as an important component of secondary prevention in patients with CHD.\(^\text{27}\) Although further work needs to be done to fully elucidate the optimal dose and mechanisms of action, there is little justification for not including omega-3 fish oils as part of the dietary recommendations for our patients with known or high risk of CHD. The availability of a new blood test for RBC omega-3 levels along with proposed cardioprotective cut points that we described\(^\text{28}\) now make it simpler for physicians to rationally prescribe omega-3 oils.

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To Screen or Not To Screen

Lung cancer is the number-one killer among cancers. During 2002, 550,000 Americans died of cancer. Of these cancer deaths, lung cancer killed 161,400 or 29% of the total. Of those who acquire lung cancer, only 12 to 15% will be cured. Lung cancer kills more Americans than the next three most deadly cancers (breast, colon, and prostate) combined.¹

Despite these sobering statistics, screening for lung cancer is not done. Three lung cancer screening studies²–⁴ were published in the 1980s and failed to show a decrease in the overall mortality of those screened. Since the publication of these studies, there have been advances in the detection, diagnosis, and treatment of lung cancer. Most notable, from a screening standpoint, is the availability of CT scanning for the detection of lung cancer. This has led to nonrandomized studies⁵ designed to assess the utility of screening for lung cancer with CT scans of the chest. Nonrandomized studies⁶ using low-dose CT scans have shown an ability to detect smaller lung cancers than those detected by chest radiographs. This has led some to advocate screening for lung cancer with low-dose CT of the chest.⁷

In response to those advocating screening, Patz et al⁸ and Heyneman et al⁹ analyzed data from the cancer registry of their hospitals. They did not see a stage shift when smaller tumors were compared to other tumors < 3 cm in size.⁸⁹ This led them to become advocates for the National Lung Screening Trial (NSLT). This trial is now underway. In this issue of CHEST (see page 1136), Yankelevitz et al offer a criticism of why they believe the data of these previous studies⁸⁹ were flawed, and conclude that the data supplied do not provide a rationale to perform a randomized controlled trial comparing CT scans of the chest to chest radiographs. If this is the case, should the NSLT continue or should screening for this deadly disease commence immediately?

This question is important for several reasons. Obviously, each year many thousands of Americans and others throughout the world are dying from lung cancer. While the issue is being studied, there is the potential for thousands more to die of this deadly malady. Screening now has the potential to save many if not thousands of lung cancer victims.

However, if lung cancer screening is to be done, how much will it cost? From where will the resources come to pay for such screening? As the current US budget deficit illustrates, there are limited resources even in a rich nation. If screening is done, will there be less for other health-care issues? Should more dollars be spent on screening and less on treatment? Should more be spent on prevention (smoking cessation) and less on screening? If billions are spent on screening, will research into the molecular mechanisms and treatment of lung cancer be cut? Will there even be fewer dollars to spend on the research of lung cancer screening? Will the expected result be realized or will some other unexpected outcome result? One need only look at the surprise outcome of the use of the cyclooxygenase-2 inhibitors to realize that what is good in theory does not always bear the expected fruit in practice.

Unfortunately, the answers to these questions are mostly unknown. Yet, even if screening is embraced, there are many questions still in need of answers before it can be done intelligently. The most obvious question is who should be screened? Should all former smokers be screened? What if one smoked...