identification of important new genome–environment interactions in DCM pathogenesis (3) and also have implications for the clinical management of DCM patients.

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REPLY

We appreciate the interest in our recent review (1) of the genetic basis of dilated cardiomyopathy from Drs. Poller, Schultheiss, and Kühl. We agree with the first point that the screening of healthy, unselected populations is always important to more fully understand genetic variation. We also agree with the general premise of the second point that understanding gene/environment interactions can be helpful, and at times essential, for understanding the pathogenesis and progression of genetic disease.

We also suggest that the first point of Drs Poller and colleagues (“. . . unless representative healthy populations are screened . . .”) may be even more important for their work (2) to ascertain any role of viruses in causing idiopathic dilated cardiomyopathy (IDC). In their study only myocardial samples from patients with IDC were examined for virus, but no myocardial samples from any control group (e.g., ischemic cardiomyopathy, or a “representative healthy population”) were reported. This raises the question of whether viruses, ubiquitous in all living organisms and perhaps equally so in control myocardium, are relevant for IDC.

Although it is likely that environmental influences affect penetrance and phenotype, it is also clear that a great deal of phenotypic variation can be attributed to epigenetic variation independent of environmental influence. Transcriptionally competent retrotransposons likely number in the thousands in mammalian genomes, and, for example, have been shown to cause the considerable phenotypic variation that is routinely observed in isogenic mice strains (3). Understanding the genetic, epigenetic, and environmental factors that cause or modify human disease will require a great deal of careful effort supported by the most robust controls possible.

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Cardiovascular Manifestations of Carbon Monoxide Poisoning

We read with interest the report by Satran et al. (1) on the cardiovascular manifestations of carbon monoxide (CO) poisoning. In the Hospital Río Hortega of Valladolid (Spain), we followed CO poisonings prospectively for two years (2). The protocol included, among other parameters, carboxyhemoglobin (COHb) levels, electrocardiogram (ECG), creatine kinase (CK) and CK-MB. During the study period studied, 154 patients were included, of whom 20% (n = 31) presented sinusal tachycardia, 5% (n = 8) arrhythmias (mainly auricular fibrillation), and 4% (n = 6) ischemic changes, including one patient in whom cardiac catheterization was carried out without findings of coronary artery disease. Eight (7.2%) adult patients and 25.6% (n = 10) of patients under 10 years of age had elevated CK levels. Similarly, CK-MB levels were elevated in 1.8% (n = 2) of adults and in 12.7% (n = 5) of children (p < 0.01) (2). In our series, the percentage of patients with cardiovascular manifestations is inferior to that described by Satran et al. (1). We suggest that this is because our study population included all CO poisonings, of which 40% were mild (COHb <25%), whereas Satran et al. (1) included only moderate or severe poisonings. The fact that elevated CK and CK-MB levels occur more frequently in children than in adults suggests a greater toxicity or affinity of CO for the pediatric musculature, although this hypothesis remains to be verified.

Satran et al. (1) report that, in an unspecified number of patients, the etiology of the CO poisoning was fire exposure, and that eight patients died owing to burn injuries (1), but they make no reference to plasma lactate concentrations. Lactate is the principal marker of cyanide (CN) in the blood of patients who inhale fire smoke, and levels greater than 10 mmol/l suggest that, in these patients, CN plays a more important role than does CO (3,4). We suggest that a percentage of the myocardial ischemias described by Satran et al. (1) may be due to fire smoke inhalation syndrome and not solely to CO poisoning. Smoke from fires contains a mixture of gases, but of these it is CO and CN that provoke tissue hypoxia and may lead to death (5). Although the protagonism of CO in the multifactorial hypoxia of fire smoke inhalation syndrome is well known, the role of CN is less so (4).
We suggest that CN may have had a synergetic effect with CO in the cellular hypoxia and myocardial ischemia seen in the cases reported by Satran et al. (1). We consider that in patients affected by the inhalation of fire smoke, plasma lactate concentrations are as important as COHb levels, especially where there is myocardial injury.

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REPLY

We read with interest the letter of Dr. Dueñas-Laita and colleagues regarding our study, “Cardiovascular Manifestations of Moderate to Severe Carbon Monoxide Poisoning.” The Italian investigators found 7.2% (8 of 110) of adults and 25.6% (10 of 39) of children had elevated creatine kinase (CK) levels, whereas 1.8% (2 of 110) of adults and 12.7% (5 of 39) of children had elevated CK-MB levels in a series of patients with acute carbon monoxide (CO) poisoning (1). We found 37% of patients had myocardial injury based on elevated cardiac enzymes and electrocardiogram (ECG) (2). We agree with the investigators that the major difference between our study and their own can be attributed to the severity of CO poisoning. Our study focused on more critically ill patients: 187 (81%) experienced loss of consciousness, 106 (46%) had an abnormal Glasgow Coma Scale (<14), 116 (50%) were intubated, and 14 (6%) required blood pressure support. Another important difference between the two studies is the use of troponin, which is a more specific and sensitive indicator of myocardial injury and would be expected to increase the percentage of patients found to have myocardial injury. Myocardial injury determined by troponin has been shown to be an important indicator of both short- and long-term mortality (3–5). In fact, we recently reported preliminary data the long-term outcomes of our cohort and found patients with myocardial injury had 31.9% mortality compared to 16.3% in patients without myocardial injury at a median follow-up of 6.6 years (6).

Dr. Dueñas-Laita and colleagues suggest that cyanide poisoning from fire exposure contributed to a higher percentage of patients with myocardial injury in our study. We believe this is unlikely. In our series of 230 patients, 42 had CO poisoning from fire exposure and 12 (28%) had myocardial injury. By comparison, 188 patients had CO poisoning from other etiologies (faulty furnace, automobile exhaust, and so on) and 73 (39%) sustained myocardial injury. One patient exposed to fire did have confirmed cyanide poisoning, although our data are otherwise limited in this area. We agree with the researchers that testing serum lactate is reasonable in any patient with CO exposure from fire.

Finally, the data from Dueñas-Laita and colleagues indicate myocardial injury from even mild CO poisoning is frequent and adds to the literature regarding the myocardial effects of CO poisoning.

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