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EDITORIAL

Air Pollution, Exercise, and Cardiovascular Risk

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There is mounting evidence that exposure to higher levels of air pollution is associated with adverse cardiovascular consequences. A recent scientific statement from the American Heart Association concluded that transient changes in air pollution are associated with a short-term increased risk of cardiovascular disease and death.[1] There is also convincing evidence for an association between air pollution and myocardial ischemia and infarction, ventricular arrhythmia, heart failure exacerbation, and stroke.[1-5] Mechanisms that have been proposed as possible explanations for these associations include direct effects from agents that cross the pulmonary epithelium into the circulation, including gases and the soluble constituents of particles such as transition metals.[1] Activation of pulmonary reflexes may lead to alterations in autonomic balance that may in turn alter coronary tone and result in a higher risk of arrhythmia and the disruption of vulnerable plaque.[6] The heightened risk that begins early after exposure to high levels of particulate air pollution appears to persist over days and may be related to pulmonary oxidative stress leading to enhanced systemic inflammation and altered hemostatic–fibrinolytic balance.[7-9] These putative pathways may act separately or in concert, be associated with different outcomes, and be activated by different components of ambient pollution. These acute and transient effects of particulate air pollution should be distinguished from the heightened long-term, chronic risk of adverse cardiovascular outcomes associated with living in areas with higher mean levels of air pollution; this long-term risk has been demonstrated in several large cohort studies, including a recent report from the Women's Health Initiative.[10]

In this issue of the *Journal*, Mills and colleagues[11] report the results of a double-blind, randomized, crossover study of 20 men with a history of myocardial infarction exposed to either dilute diesel exhaust — at a level similar to what might be routinely experienced when driving in traffic — or filtered air. During each exposure period, subjects exercised on a bicycle ergometer to a target of 5 to 7 metabolic equivalents for two 15-minute periods separated by 15-minute rest periods. The researchers found that although the heart-rate response to exercise was not different across exposure periods, myocardial ischemia, which was detected in all patients, was associated with significantly greater ST-segment depression and a greater ischemic burden during exposure to diesel exhaust than during exposure to filtered air. Interestingly, Mills and colleagues did not find that exposure to dilute diesel exhaust had an effect on the degree of endothelium-dependent or endothelium-independent vasodilatation in response to provocative testing performed 6 hours after exposure. In addition, exposure to dilute diesel exhaust had no effect on the basal concentration of plasma tissue plasminogen activator (t-PA) or plasminogen activator inhibitor type 1 at 6 hours after exposure, although exposure did significantly suppress net t-PA release in response to bradykinin infusion, indicating a proclivity to impaired fibrinolytic activity.

The pathways linking air pollution exposure to the increased severity of exercise-induced ischemia observed in this study are unclear. One potential mechanism is decreased myocardial oxygen supply, perhaps related to vasoconstriction or transient thrombus formation. Another is decreased oxygen-carrying capacity caused by higher levels of carbon monoxide or by increased demand reflected in a higher rate-pressure product or altered

myocardial energetics. Mills and colleagues found no effect on peripheral vascular reactivity measured 6 hours after exposure; however, this does not preclude an effect on the coronary vasculature during exposure. It is unlikely that the observed effect was a result of carbon monoxide exposure, since its level in the dilute diesel exhaust was quite low. Increased myocardial oxygen demand also seems unlikely because no significant difference in heart-rate response was observed during either exercise period. Still, this possibility cannot be excluded, since data on other relevant hemodynamic measures, such as blood pressure and rate-pressure product, were not provided. Mills and colleagues did not directly assess the propensity for transient intracoronary thrombus formation or altered myocardial energetics that may have occurred during exposure.

This study may provide insight into the mechanism responsible for the reported association between transient exposure to higher levels of ambient air pollution and the onset of acute cardiovascular events. Furthermore, the study suggests that the risk of exertion-triggered acute cardiovascular events[12] may be heightened when vigorous exertion is undertaken in the presence of high levels of air pollution. For example, the susceptibility to more severe exercise-induced ischemia, regardless of the pathway, may be one mechanism leading to acute decompensation among patients with heart failure as well as to the onset of ventricular arrhythmias. Whether this is related to the onset of myocardial infarction is less clear, but the changes in t-PA release may create a predisposition to occlusive thrombus formation when vulnerable atherosclerotic plaque is disrupted, and short-term effects on coronary tone have not been ruled out.

The study was specific in evaluating the effects of dilute diesel exhaust, an extremely complex mixture of particles and gases; it is not possible to glean which constituents of diesel exhaust were responsible for the observed effects. Complicating matters further, ambient air pollution is a heterogeneous mixture of gases and particulate matter, of which diesel exhaust is only one of many components.[1,13] There is a growing body of evidence that other mobile and stationary sources of combustion-related pollution are likely contributors to adverse cardiovascular effects. Identifying the specific sources and constituents responsible for the reported acute cardiovascular effects of air pollution is an important goal for future investigations.

There are some important limitations to the study with respect to generalizability. For example, different engines, fuels, and loads will result in different outputs. In addition, the study does not directly address the cardiovascular consequences of air pollution from sources other than diesel combustion. Furthermore, the findings can be directly applied only to men with a history of myocardial infarction and evidence of inducible ischemia on exertion. Nonetheless, if such exposures are causal, these findings may represent the tip of an iceberg constituting the effects of transient changes in exposure to elevated levels of air pollution on cardiovascular risk. It is likely that patients with established coronary disease who have not experienced a myocardial infarction would respond similarly to transient exposure to air pollution. More speculative are the effects of exposure in the vast numbers of people with risk factors for coronary disease, many of whom have subclinical disease and perhaps vulnerable plaque that may serve as a substrate for acute coronary events.

The evidence from Mills and colleagues suggests that the risk of having an acute cardiovascular event triggered by vigorous exertion[13,14] may be heightened with exposure to high levels of air pollution. Considering the unequivocal benefit of habitual exercise,[14] including its established role in decreasing the risk that isolated episodes of exertion may trigger the onset of an acute cardiovascular event, the risk–benefit ratio may be optimized if people exercise away from traffic when possible.

No potential conflict of interest relevant to this article was reported.

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