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From Olympians to Mere Mortals

The Indiscriminate, Global Challenges of Air Pollution

Beijing won its bid to host the 2008 Olympics while promising to substantially improve its air quality, spending in excess of 10 billion dollars to implement pollution control measures (1). Based on substantial and growing evidence that air pollution impacts cardiac and respiratory health (2), Olympic athletes and the public were concerned that notoriously poor air quality in Beijing might have detrimental impacts on athletes. Even after substantive (13–60%) reductions in individual air pollutant concentrations during the 2008 Games as reported in this issue of the *Journal* (pp. 1150–1159) by Huang and colleagues (3), daily average levels of pollutants such as fine particulate matter in Beijing remained four to nine times higher than in large metropolitan cities in the United States during the same time period (4). Athletes remained concerned about potential health impacts, some deferred competing in the Games (5), and Olympic teams set up training camps away from Beijing to avoid intense air pollution exposures (6).

Over several years just prior to the 2008 Olympics, epidemiological studies reported that patterns of associations between fine particulate air pollution and cause-specific mortality were consistent with the hypothesis that air pollution exposure contributes to pulmonary and systemic oxidative stress, inflammation, and associated increased risk of atherosclerosis and ischemic cardiovascular and obstructive pulmonary diseases (2, 7). Recent reviews of the expanding literature (8) and emerging evidence from the Multi-Ethnic Study of Atherosclerosis (9) suggest that there are likely multiple, complex, interdependent mechanistic pathways linking air pollution to cardiopulmonary disease, but also provide growing evidence that pulmonary and systemic oxidative stress and inflammation play important roles.

Against this backdrop, in this issue of the *Journal*, Huang and coworkers (pp. 1150–1159) report results of a Beijing Olympics–based study investigating the relationship between air pollution and exhaled breath and urinary biomarkers of pulmonary and systemic oxidative stress and inflammation (3). This quasiexperimental study evaluated 125 young and healthy medical students before, during, and after the 2008 Beijing Olympics. Huang and colleagues demonstrated substantial decreases in these biomarkers tracking with reductions in air pollution, followed by subsequent increases in these biomarkers after return toward typical levels of air pollution in Beijing. These results add to previously reported evidence, from the same research team, that these Olympics-related changes in air pollution in Beijing were also associated with changes in systemic inflammation, thrombosis, blood pressure, and heart rate (10). Also, a third study using the Beijing Olympics–related changes in air pollution (with a focus on black carbon) found that the reductions in air pollution were also associated with exhaled nitric oxide, a biomarker of acute respiratory inflammation (11).

These studies have several important strengths. For example, Huang and colleagues (3) took advantage of the sharp reductions in pollutant levels achieved through intense restrictions on industrial operations and traffic in the Beijing area during the Olympics, followed by a rapid return to usual practices and more typical pre-Olympic pollutant concentrations after the Games. The use of quasiexperimental design in this panel study to estimate the effect of air pollution on the outcomes reduces the potential for confounding by long-term trends in health. Such confounding by trends in both the health outcomes of interest and air pollution levels over time has been a common challenge in air pollution health effects research.

Furthermore, quasiexperimental studies of air pollution health effects are relatively unique, with a few notable exceptions. In the 1980s in Utah Valley, a labor dispute resulted in the intermittent operation of the local steel mill, the primary single source of air pollution in the valley, demonstrating significant associations between air pollution and hospital admissions for respiratory disease (12). A ban on coal sales in Dublin Ireland in 1990 resulted in an immediate and large reduction in particulate matter air pollution and corresponding significant reductions in respiratory and cardiovascular death rates (13). An initial analysis of the 1996 Atlanta Olympics took advantage of transiently reduced traffic levels and found some evidence of associations between changes in ozone and childhood asthma emergency room visits (14). However, compared with conditions in 2008 Beijing, the changes in air pollution were very small, and subsequent analyses were unable to disentangle the combined effects of meteorological conditions, reduced traffic, and intervention-related health effects (15). Related natural experiment studies also include studies of public smoking bans and evidence of related reductions in cardiovascular disease (16).

Randomized experimental designs (including controlled exposure human studies) conceptually may be ideal for understanding the underlying mechanisms of air pollution–induced cardiac and pulmonary disease in humans, but obvious practical and ethical concerns significantly limit who can be exposed and the duration and intensity of exposure in such studies. Quasiexperimental designs with high pollution variability, such as the study in this issue of the *Journal*, allow important mechanistic inferences to be made about longer-term exposures under "real-world" conditions.

Collectively, these recent Beijing Olympics studies lend support to the hypothesis that exposure to particulate matter induces inflammation and oxidative stress in the lungs and perhaps other tissues, which increases the tendency toward thrombosis and activates the sympathetic nervous system to increase the risk of cardiovascular death. These studies also suggest that even young and healthy individuals without pulmonary or cardiac disease may be susceptible to these effects of particulate matter, and provide additional promising novel biomarkers for investigating the mechanisms of air pollution–induced disease.

Although this study measured multiple pollutants in an effort to understand how individual components of the complex air

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pollution mixture may impact disease, significant correlations between pollutants and the more general reduction of pollution that occurred during the Beijing Olympics limit the ability to make compelling inferences regarding the individual effects of specific pollutants on these markers.

China and other rapidly industrializing nations face tremendous challenges over the next decades, with rapid development often competing with adverse environmental impacts, including increased levels of air pollution. Without serious efforts to control pollution, "business-as-usual" practices are likely lead to dramatic increases in concentrations not only in China, but worldwide. Although the emissions control policies that China has planned to implement may help to avert some of the public health impacts associated with air pollution exposures both locally and globally, many uncertainties remain (17). A recent global atmospheric chemistry model estimates that, without new legislation to prevent growth in air pollution, the average global citizen in 2050 will experience nearly the same air quality as the average East Asian citizen in 2005 (18). Although this model is hopefully a pessimistic scenario, it underscores the need for serious preventive action.

This challenge of pollution control in the context of population and economic growth is not limited to developing nations like China. All nations bear the burden of controlling pollutants, which do not respect national borders. From countries with rapid expansion of industry to more established economies, and from Olympic athletes to "mere mortal" healthy young adults such as those evaluated in the study reported in this issue of the *Journal*, to individuals with preexisting health conditions—all face substantial challenges from air pollution now and in the future.

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Using MicroRNAs to Inform Clinical Decision Making in Lung Cancer

Ready for Prime Time?

Given that we have now reached the era of targeted therapeutics in lung cancer, defining histological subtypes of disease and evaluating the genomic landscape of the tumor has become essential to lung cancer management. A number of tyrosine kinase inhibitors (e.g., epidermal growth factor receptor inhibitors), for example, have demonstrated clinical efficacy among subsets of patients with lung cancer harboring epidermal growth factor receptor mutations (1, 2). Many of these targeted therapies are currently limited to adenocarcinoma of the lung, although recent characterization of the mutational landscape of squamous cell lung carcinoma promises to bring the era of personalized therapy to this subtype of the disease (3). Despite such paradigm-shifting