Scientific efforts to understand the health effects of air pollution and public policy efforts to control air pollution have a fascinating history. The early “killer smog” episodes in Meuse Valley, Belgium (1930), Donora, Pa (1948), and London, UK (1952) provided stark evidence of deleterious respiratory and cardiovascular health effects of severe air pollution exposure. This evidence motivated early public policy efforts to improve air quality. In the United States, Britain, and elsewhere, legislative, regulatory, and related efforts to control air pollution were initiated. Ambient air quality standards and guidelines were established. Severe air pollution episodes were largely mitigated, and concern about adverse air pollution–related health effects abated. Nearly all air pollution researchers agreed that air pollution at very high concentrations posed serious health hazards. By the late 1970s and through the 1980s, however, it was argued by many that air pollution, at levels then common to the United States and Britain, was no longer a significant threat and that adverse air pollution exposure has also been linked with changes in a variety of subclinical physiological end points that relate to cardiovascular health, including enhanced systemic inflammation, blood coagulation, and thrombosis; vascular dysfunction and atherosclerosis; and impaired cardiac autonomic function. In general, the evidence suggests that long-term exposure (years or decades) to air pollution contributes to pulmonary and systemic oxidative stress, inflammation, atherosclerosis, and increased risk of ischemic heart disease and death; and that short-term exposures (a few days or weeks) contribute to triggering acute ischemic heart disease events by increasing the risk of atherosclerotic plaque rupture and thrombosis. There is additional evidence that air pollution is associated with heart failure, stroke, and cardiac arrhythmia and arrest.

For most individuals, the excess cardiovascular risks associated with air pollution exposure are small, but given the ubiquitous and involuntary nature of the exposure across large populations, the public health implications are substantial. It is estimated that urban air pollution is the 13th-leading cause of global mortality and is responsible for >700,000 cardiopulmonary deaths per year.

Pollutants Responsible for Adverse Health Effects

Air pollution consists of a complex combination of gaseous pollutants and particulate matter. Particulate matter air pollution is a mixture of particles suspended in the air that vary in size, shape, surface area, chemical composition, solubility, and origin. Air pollutants most strongly implicated in contributing to adverse cardiovascular health effects includes fine particulate matter (commonly defined as particulate matter with an aerodynamic diameter ≤2.5 μm, or PM 2.5). The primary sources of fine particulate matter air pollution include combustion of various fossil and bio fuels and high-temperature processes such as coal-fired power plants and the operation of gasoline and diesel vehicles and smelters. Fine particulate matter also includes secondary particles from atmospheric transformation products, including sulfate and nitrate particles. There is some evidence that coagulable pollutants (including sulfur dioxide, nitrogen dioxide, carbon monoxide, and ozone) also contribute to adverse health effects.

Although the specific components and characteristics of air pollution most responsible for pollution-related health effects are not fully understood, in nearly all communities traffic is a primary source of pollution and is often the principle source. Residential proximity to roadways with relatively heavy traffic density is an important source of air pollution exposure.
variability that can be exploited in epidemiological studies. There is growing evidence that traffic-related pollution contributes to cardiovascular disease and death. As examples, very recent studies have found traffic-related air pollution to be associated with systemic inflammation and platelet activation, atherosclerosis, incidence of coronary heart disease, and cardiovascular mortality.

**Does Air Pollution Contribute to Risk of Deep Vein Thrombosis?**

Recently, Baccarelli and colleagues reported the results of a case-control study from the Lombardy region of Northern Italy. They found that long-term exposure to particulate matter air pollution was associated with increased risk of deep vein thrombosis (DVT). As noted in an accompanying editorial, this was a well-conducted, detailed, and reasonably large case-control study that substantially expanded the realm of observed pollution-related adverse health effects to include venous thrombosis. A primary concern relative to this first report of air pollution contributing to venous thrombosis was the size of the estimated effect. Every 10 μg/m³ elevation in inhalable particulate matter was associated with a 70% (95% confidence interval, 30 to 123) increased risk of DVT. This large excess risk seemed improbable, especially in areas with high average concentrations, which can exceed 50 μg/m³. It also seemed improbably large when compared with other studies of air pollution and cardiovascular disease and when compared with other well-established risk factors.

In the current issue of *Circulation*, Baccarelli and colleagues also report evidence that living near major traffic roads is associated with increased risk of deep vein thrombosis even after controlling for community-level particulate matter air pollution. These new results are based on an expansion of the previous analysis using primarily the same research cases and controls from the Lombardy region of Italy. The analysis used 663 enrolled patients with DVT of the lower limbs and 859 age-matched controls using standardized protocols. The distance from residential addresses to the nearest major traffic road was assessed using geographic information system methodology. The risk of DVT associated with living closer to major traffic roads was assessed using conditional logistic regression models while adjusting for various clinical and environmental covariates including background levels of particulate pollution. DVT risk was significantly greater for those living closer to major traffic roads.

Baccarelli et al. report that for the 10% of the subjects who lived closest to major traffic roads versus the 10% of subjects who lived farthest away from these roads, there was an estimated 47% (95% confidence interval, 11 to 96) increase in DVT risk. On the basis of statistical models that fit a relatively flexible penalized spline for distance to major road, the association with DVT risk was nearly linear over the observed distance range (0 to 718 meters). The association was relatively weaker in women than in men and was absent in women using oral contraceptives. Residential distance from roadways with heavy traffic density has been shown to reflect exposure to traffic-related air pollution. However, it is unclear in this study what the actual differences in exposure were, making it difficult to compare effect estimates. Furthermore, proximity to major traffic roads is associated with other potential risk factors such as noise. A recently reported cohort study from the Netherlands found that the significant associations between cardiovascular mortality and traffic-related pollution were insensitive to adjustment for traffic noise.

Venous and arterial thromboses, until recently, have been considered as distinctly different conditions. But growing evidence suggests that there are pathophysiological links between arterial and venous thrombosis and that they share common risk factors such as age, obesity, diabetes mellitus, hypertension, hyperlipidemia, cigarette smoking, and potential exposure to air pollution. Given the evidence that exposure to air pollution can contribute to pulmonary and systemic inflammation and blood coagulation, an epidemiological link between air pollution and both arterial and venous thrombosis is plausible.

These results presented by Baccarelli and colleagues are certainly intriguing and have potentially important public health and medical implications. They extend the potential role of air pollution, including traffic-related exposures, on cardiovascular disease. Nevertheless, although the evidence that air pollution contributes to arterial diseases is substantial, evidence that it plays a role in venous diseases is currently meager and is limited primarily to these 2 analyses of the same subjects from a single study area. There is a clear need for additional high-quality studies of air pollution and DVT to help corroborate these results, to provide more precise estimates of the effects, and to better understand the contribution of pollution from traffic and other sources.

**Disclosures**

None.

**References**


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The Expanding Role of Air Pollution in Cardiovascular Disease: Does Air Pollution Contribute to Risk of Deep Vein Thrombosis?

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