Ambient air pollution has been linked to exacerbation of cardiovascular disease morbidity and mortality.1 These associations have been strikingly robust and range from the observation of coronary heart disease exacerbation within hours of exposure to an increased risk of ischaemic heart disease mortality for subjects chronically exposed to elevated concentrations of ambient particles.

Two main pathological processes, atherosclerosis and thrombosis, lead to acute coronary syndromes such as unstable angina and myocardial infarction. The typical atherosclerotic lesion is a fibro-lipid plaque composed of a pool of lipids covered with a connective tissue cap. Although the plaque narrows the coronary arteries, acute coronary syndromes only occur when a plaque erodes, fissures, or ruptures and a thrombus is formed, which occludes the arteries, partially or totally, and impedes blood flow. There is a strong link between inflammation and coronary heart disease, since factors involved in inflammation and infection seem to play a pro-atherogenic role and inflammation has been identified as a potent risk factor for the acute coronary syndromes. Other risk factors such as cigarette smoking, diabetes, or high body mass index have also been found to be associated with low-grade systemic inflammation, providing a further link between inflammation and acute coronary syndromes. On the other hand, factors alleviating systemic inflammation, for example moderate exercise or weight loss, reduce the risk of acute coronary events. Acute phase proteins, like C-reactive protein (CRP) or fibrinogen, have been identified as biomarkers for inflammatory processes and are important determinants of plaque rupture.3

Systemic inflammation induced by ambient air pollution is one of the potential mechanisms linking particle deposition in the lung to myocardial infarction.1,4 Initial evidence came from an air pollution episode recorded in the mid-1980s when elevated plasma viscosity was observed.5 Ambient particulate matter has been associated with systemic responses including increases in CRP and fibrinogen in healthy individuals in cross-sectional studies.6–8 In longitudinal studies, changes in ambient particulate air pollution were associated with changes in the CRP level.9–12

The study presented in this journal by Zeka et al.13 shows an association between high concentrations of traffic-related particles and increases in inflammatory and thrombotic markers. Data of this cross-sectional study are derived from the Veterans Administration Normative Aging study in Boston including 710 subjects who were examined over a 3 year period. The strength of the study is the availability of different measures of ambient particles, which characterize different properties, as well as different origins of ambient particles. Particle number concentrations in ambient air are dominated by the so-called ultrafine particles, particles smaller than 100 nm. Black carbon measurements reflect the contribution of soot particles from combustion sources to the ambient aerosols and are dominated in the Boston area by traffic-related emissions. Sulfates, in contrast, are regionally transported secondary particles, indicating the presence of aged aerosols during the warm season. Both black carbon and sulfates were moderately correlated with fine particle mass [mass of particles smaller than 2.5 μm (PM2.5)]. But PM1.0 and sulfates were not or even negatively correlated with particle number concentrations.

While PM2.5 concentrations were moderate, particle number concentrations were reaching up to levels reported for Southern Europe.14 The authors observe an association between particle number concentrations and fibrinogen levels with a lag of 48 h, and these effects were still evident if particle number concentrations were elevated for at least a week.13 None of the other indicators of ambient particle exposures were associated with elevated fibrinogen concentrations within a week’s time frame. These data may indicate an acute phase response in association with the high surface area of ultrafine particles and the related oxidative stress exhibited. However, there is also room for the speculation that translocation of ultrafine particles into the blood may be responsible for these observed associations leading to endothelial cell action and subsequent shift to a pro-thrombotic state,11 here indicated by elevated fibrinogen concentrations. Elevated concentrations of black carbon over 4 weeks before the examination, however, were also associated with increased levels of fibrinogen, and this association was additionally reflected in analyses of PM1.0 or sulfates. Prolonged elevated concentrations of ambient particles were associated with increases in erythrocyte sedimentation rate (ESR) potentially indicating an ‘increased stickiness’ of the blood.5 Surprisingly, CRP and white blood cell counts did not show an association with changes in ambient particle level as had been implicated by earlier studies.6–12

Where does this leave us? Are the associations between local particles and fibrinogen as well as ESR signs of activation of the same pathway? The analyses done by the authors assessing effect modification suggest that they are not. While the effects on ESR seem to be attributable to younger subjects with high body mass index, age and obesity seem to modify the effect observed for fibrinogen in a different manner. The data indicate that treatment with statins and diminished capability for
detoxifying oxidative stress can potentially modify associations between air pollution and inflammatory markers.

The study is important as it indicates that locally emitted particles with high surface areas and small enough to enter the circulation may be only partially responsible for the cardiovascular disease exacerbation observed. Thereby, the data highlight that potentially different particle properties impact on the vascular physiology differently, but the underlying mechanisms are only poorly understood to date. Nevertheless, it seems very reasonable that aged aerosol, which is dominated most probably by internally mixed, partially soluble particles, may have more local effects in the lung, while relatively insoluble ultrafine particles with high surface areas may directly interact systemically with vascular functions. However, it remains to be demonstrated how these small increases in fibrinogen or ESR contribute to the onset of acute coronary syndromes and whether repeated systemic inflammatory responses relate to an increased long-term risk of ischaemic heart disease associated with ambient air pollution. But, as this study demonstrates, fine particle mass alone, while established as a good surrogate measure in mortality studies, might not capture adequately the underlying properties of the particles causally related to the exacerbation of coronary heart disease.

References


