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REVIEW ARTICLE

Air pollution and coagulation testing: A new source of biological variability?

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Abstract

Preanalytical and biological variability both have strong influences on test results of coagulation. Beyond age and gender, increasing emphasis is now being given to a variety of demographic and lifestyle variables, including ethnicity, smoking, diet, and exercise, which should be taken into account when interpreting laboratory data. However, there is strong emerging evidence that additional environmental influences, such as pollutants and environmental chemicals, might contribute in a major way to biological variability. A large body of epidemiological evidence now exists to support the view that air pollutants are responsible for shortened prothrombin time, and decreased factor VII, tissue plasminogen activator and platelet count; on the other hand, evidence also suggests that air pollutants may significantly increase fibrinogen, factor VIII, von Willebrand factor and platelet hyperactivity. Although it is impractical to develop reference ranges specific to the daily concentration of air pollutants, the potential influence of air pollution on results of coagulation testing should be recognised when interpreting laboratory findings.

Contents

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Air pollution and cardiovascular health

Air pollution is due to a heterogeneous mixture of solid and liquid particles suspended in air, continually changing in size and chemical composition in space and over time. Primary particles, such as diesel soot, are emitted directly into the atmosphere, whereas secondary particles are created through physicochemical transformation of gases, such as nitrate and sulphate formation from gaseous nitric acid and sulphur dioxide (SO_2), respectively. There are numerous natural and anthropogenic sources of air pollution; these include motor vehicle emissions, tyre fragmentation and resuspension of road dust, power generation and other industrial combustions, smelting and other metal processing, agriculture, construction and demolition activities, residential wood burning, windblown soil, pollens and moulds, forest fires and combustion of agricultural debris, volcanic emissions, and sea spray [1]. Over the last decade a growing body of epidemiological and clinical evidence has led to a heightened concern about the potential deleterious effects of ambient air pollution on health. Of special interest are specific environmental air pollutants that include carbon monoxide (CO), oxides of nitrogen (especially nitrogen dioxide, NO_2), SO_2 and particulate matter (PM) ("thoracic particles" [PM10] <10 μm in aerodynamic diameter, "ultrafine particles" <2.5 μm, and "coarse particles" [PM10 to ultrafine particles]) (Fig. 1) [1]. Although the major mechanisms are still under investigation, human exposure to urban air pollution is increasingly being associated with inflammation, oxidative stress, activation of haemostasis, autonomic dysfunction and adverse cardiovascular events [2]. The inflammation that occurs in the lungs in response to damage caused by pollutants may have systemic consequences. Thus, the lungs are not merely portals for entry of pollutants, they probably also mediate cardiovascular responses to a substantial extent [3]. The existing body of evidence is also adequately consistent, coherent, and plausible enough to conclude that short-term exposure to elevated particulate matter significantly contributes to increased acute cardiovascular mortality, particularly in certain at-risk subsets of the population [4]. Hospital admissions for several cardiovascular and pulmonary diseases acutely increase in response to higher ambient particulate matter concentrations. The evidence further implicates prolonged exposure to elevated levels of particulate matter in reducing overall life expectancy in the order of a few years [1,5].

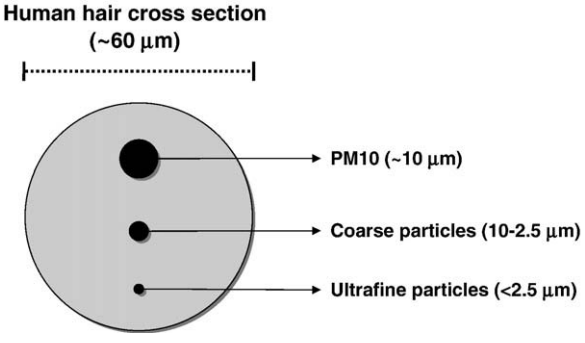

Figure 1 Size of particular matter (PM) particles as compared to a human hair.

Air pollution and haemostasis

Recent evidence indicates that air pollution is associated with remarkable changes in global haemostatic function, suggesting a tendency towards hypercoagulability even after short-term exposure [6]. In general, studies using rats and hamster models show that of ultrafine particles exert a global procoagulant effect [7] and can modulate thrombus formation [8], mostly due to enhanced Tissue Factor (TF) gene expression and production [9]. Baccarelli et al. reported that the prothrombin time (PT) becomes shorter with higher ambient air concentrations of PM10 and gaseous pollutants, especially CO and NO_2. In the 30 days before blood sampling, they also observed that PT was negatively associated with the average PM10 and NO_2, while no significant association was found between air pollutant levels and activate partial thromboplastin time (APTT), antithrombin, protein C and protein S [6]. At levels encountered in an urban environment, inhalation of dilute diesel exhaust impairs two important and complementary aspects of vascular function in humans: the regulation of vascular tone and endogenous fibrinolysis. In fact, while exposure to diesel exhaust particles and particulate matter does not aggravate pre-existing vasomotor dysfunction, it reduces the acute release of endothelial tissue plasminogen activator [10,11] and increases fibrinogen and plasminogen activator inhibitor-1 (PAI-1) [12]. Controlled human exposure studies [13–15] as well as epidemiologic studies [16,17], demonstrated positive associations between fibrinogen or plasma viscosity and air pollution. Exposure to wood smoke containing high concentrations of particulate matter increases factor VIII activity in plasma and the factor VIII/von Willebrand factor (VWF) ratio, indicating a slight effect on the balance of coagulation factors [18]. In healthy mice, increased VWF expression on hepatic endothelium was detected after application of ultrafine particles [19]. FVII activity is also significantly