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**Experimental studies on the pro-thrombotic effect of particles of particles**

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Particulate air pollution is associated with cardiovascular morbidity and mortality. To help finding a plausible explanation for these epidemiological observations we have conducted experimental studies to assess whether and how particles deposited in the lung influence the formation of thrombi in the peripheral circulation. We used an *in vivo* animal model that allows a quantification of the intravascular thrombus that arises when a localized endothelial injury is produced (photochemically, using Rose Bengal and illumination by a laser light) in a peripheral vein or artery.

Thrombus formation in a femoral vein was enhanced 1 h after a single intratracheal (i.t.) administration, to hamsters, of amine-modified (positively charged) polystyrene particles of 60 nm diameter, while this did not occur with particles of 400 nm, nor after administration of unmodified or carboxyl-modified particles of 60 nm. Similarly, i.t. administration of diesel exhaust particles (DEP, 50 µg/animal) led, 1 h later, to an enhanced thrombus formation in the femoral vein or artery. These prothrombotic effects of DEP could be explained by platelet activation (demonstrated *ex vivo* and *in vitro*) and they persisted at 6 h and 24 h after instillation. They could be mitigated by pretreatment with diphenhydramine (an H1-histamine receptor antagonist), dexamethasone (a corticosteroid), or sodium cromoglycate (a mast cell stabilizer).

I.t. administration of silica particles also led to a prothrombotic effect in the systemic circulation after 24 h. This effect was abolished by depletion of either pulmonary macrophages (pretreatment with clodronate in liposomes) or circulating neutrophils (pretreatment with cyclophosphamide), indicating that cross-talk between these inflammatory cells is instrumental in the pathogenesis of particle-induced prothrombotic effects in the vasculature.

Our results provide plausible mechanistic explanations for the epidemiologically established link between air pollution and acute cardiovascular effects. The early effects (at 1 h) are compatible, at least in part, with translocation of particulates from the lungs into the blood circulation, whilst the late effects (at 24 h) are dominated by pulmonary inflammation.

*Further reading:*

Articles by NEMMAR *et al.*, including a review in *Toxicology Letters*, 2004, 149, 243-253

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