# Particle-Associated Systemic Microvascular Dysfunction

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Abstract Number: 722
Last modified: April 16, 2009

Preference: Poster Presentation
Working Group: Health Related Aerosols

**Abstract**
Tremendous attention has been paid to the health effects of exposure to particulate matter (PM). It is not only because of the increased application and use of industrial PM, but also due to concern(s) regarding the association between ambient PM and an increased risk of cardiovascular morbidity and mortality. Exposure to certain types of PM cause changes in the vascular reactivity of several macrovascular segments. However, no studies have focused upon the systemic microcirculation, which is the primary site for the development of peripheral resistance, as well as the site of origin for numerous vascular pathologies. Ultrafine PM has been suggested to be more toxic than its larger counterpart by virtue of its increased surface area. The purposes of the study were to determine if PM size affects the severity of post-exposure microvascular dysfunction and to elucidate potential mechanisms related to the bioavailability of nitric oxide (NO). In this study, Sprague-Dawley rats were exposed to fine or ultrafine TiO2 aerosols at concentrations of 1.5-16 mg/m3, for 4-12 hours, to produce pulmonary loads of 7-150 mg/rat. Twenty-four hours after exposure, microvascular function was evaluated via intravital microscopy. Endothelium-dependent and -independent arteriolar functions were tested by exposure to various vasoactive agents. The role of local reactive species and circulating neutrophils was also evaluated. The results of these experiments indicate that: 1) particle surface area dictates the intensity of systemic microvascular dysfunction; 2) dysfunction is characterized by a decreased bioavailability of endogenous NO; 3) loss of bioavailable NO after exposure is partially due to elevations of local oxidant stress; and 4) circulating neutrophils appear to be involved in the microvascular dysfunction following particle exposure. Taken together, these mechanistic studies support the hypothesis that suggests peripheral microvascular effects associated with PM exposure occur simultaneously with the activation of inflammation at the microvessels.