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TITLE: ULTRAFINE PARTICLES EXERT PROTHROMBOTIC BUT NOT INFLAMMATORY EFFECTS ON THE HEPATIC MICROCIRCULATION IN HEALTHY MICE IN VIVO.

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ABSTRACT: **BACKGROUND:** Air pollution episodes are strongly associated with increased cardiovascular morbidity and mortality. The effect of ultrafine particles (UFPs), when translocated after inhalation, on the microcirculation of extrapulmonary organs remains unclear. **METHODS AND RESULTS:** In C57BL/6 mice, either carbon black UFPs (1×10^7) and 5×10^7) or vehicle was infused intra-arterially. Two hours after infusion, platelet- and leukocyte-endothelial cell interactions, sinusoidal perfusion, endothelial fibrin(ogen) deposition, and phagocytic activity of Kupffer cells were analyzed by intravital video fluorescence microscopy in the liver microvasculature. Expression of fibrin(ogen), von Willebrand factor (vWF), and P-selectin on hepatic endothelium was determined by immunostaining. Apoptotic cells were quantified in TUNEL-stained tissue sections. Application of UFPs caused significantly enhanced platelet accumulation on endothelium of postsinusoidal venules and sinusoids in healthy mice. UFP-induced platelet adhesion was not preceded by platelet rolling but was strongly associated with fibrin deposition and an increase in vWF expression on the endothelial surface. In contrast, inflammatory parameters such as the number of rolling/adherent leukocytes, P-selectin expression/translocation, and the number of apoptotic cells were not elevated 2 hours after UFP exposure. In addition, UFPs did not affect sinusoidal perfusion and Kupffer cell function. **CONCLUSIONS:** UFPs induce platelet accumulation in the hepatic microvasculature of healthy mice that is associated with prothrombotic changes on the endothelial surface of hepatic microvessels. Accumulation of particles in the liver exerts a strong procoagulatory impact but does not trigger an inflammatory reaction and does not induce microvascular/hepatocellular tissue injury.