It is widely believed that cardiovascular risk factors promote atherogenesis by damaging endothelium. Endothelial status has been mainly assessed by focusing the attention on the quantification of the endothelium capacity to modulate arterial vasomotion. An alternative way to get information on endothelial health is to measure products of endothelial cell injury. Quantification of circulating endothelial cells has been suggested as a method of assessing endothelial damage, given that exposure of the endothelium to most cardiovascular risk factors may cause the detachment of endothelial cells from the intimal monolayer, thus releasing mature endothelial cells in peripheral blood. More recently, there has been considerable interest in a novel marker of endothelial cell injury, namely endothelial microparticles (EMPs).1,2 Microparticles are small vesicles released from the membrane surface during cell activation, injury, or apoptosis, and display the typical surface cell proteins and cytoplasmic components of their cell origin. Endothelial cell vesiculation happens also under physiologic condition, possibly as a mechanism of endothelial cell renewal or cross-talk with other cellular targets. Elevated levels of EMPs, mostly defined as CD31+/CD42− MPs, are found in patients with a variety of vascular diseases and in subjects exposed to cardiovascular risk factors.2 In the setting of hypercholesterolemia, we had previously found that the number of circulating CD31+/CD42− microparticles was associated with aortic stiffness and that microparticles from hypercholesterolemic patients cause a significant impairment of endothelial repair in vitro.2

In this issue of the Journal, Wang et al3 explored the association between EMPs and systemic arterial stiffness in healthy humans. They found that the number of circulating EMPs was positively correlated with large and small artery stiffness indices, independent of important covariates of arterial stiffening like age and blood pressure levels. The study by Wang et al3 has the merit to demonstrate for the first time the association between EMPs levels and arterial stiffness in healthy subjects. This is relevant because it suggests that endothelial release of microparticles and vascular wall stiffness may already coexist in the early stages of vascular dysfunction.

The observational design of the present study does not allow us to give a clear answer to the question about the causal relationships between EMPs and arterial stiffness. However, at least three hypotheses are allowed in this regard (Fig. 1). Causation may be involved, whereby elevated EMPs levels may induce arterial stiffening. Accordingly, isolated EMPs induce endothelial dysfunction and reduce nitric oxide bioavailability,4 which are both important mediators of arterial compli-

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**FIG. 1.** Hypothetical role of endothelial microparticles in the pathway from endothelial injury to arterial stiffness. NO — nitric oxide; EPC — endothelial progenitor cells; WBC — white blood cells.
ance. Reverse causation might also be implicated, whereby progressive arterial stiffening expose the endothelial monolayer to an increased hemodynamic stress through imposition of an oscillatory shear regime that may contribute to endothelial activation–dysfunction, and possibly apoptosis and vesiculation. Finally, the absence of known cardiovascular risk factors among the participants to the study goes against the hypothesis that the association between EMPs and arterial stiffness might depend on confounding factors.

The present data from Wang et al., demonstrating in healthy subjects an association between endothelium-derived microparticles and arterial stiffness as an early marker of vascular dysfunction, provide the rationale and a methodologic approach to continue research in this area of vascular biology. The recognition of a role of EMPs in the stiffening of human arteries is important for our understanding of the pathophysiology of vascular disease, and may also have implications for the prevention of arterial damage.

References