

COMMENTARY

The paper by Jy and co-workers (Platelet Microparticles Bind, Activate and Aggregate Neutrophils *in Vitro*) addresses a relevant topic related to the problem of tissue injury upon reperfusion of organs rendered ischemic by vascular occlusive events. Particularly in the case of arterial thrombosis, platelet aggregates representing the predominant mass of the thrombus are a substrate onto which polymorphonuclear leukocytes and monocytes can adhere, thus becoming localized at the site of lesion. These cells can then migrate through the thrombus and the underlying vascular wall, reaching the perivascular space where they produce an inflammatory response that may lead to excessive tissue damage. Understanding the pathophysiological mechanisms responsible for these processes would undoubtedly give us a better appreciation of possible means of pharmacologic intervention to modulate the inflammatory response, when needed.

Jy and collaborators now propose the intriguing hypothesis that platelet microparticles may be efficient mediators of neutrophil activation. Microparticles, once thought to represent platelet "dust", or an epiphenomenon of activation, have received attention as a potential source of some of the procoagulant and adhesive activities usually associated with platelets. Indeed, the membrane of microparticles has many of the structural and functional features of the platelet membrane and can serve to mediate the assembly of procoagulant enzymes and cofactors. Moreover, receptors on the microparticle surface can support interactions with adhesive substrates or cells expressing appropriate ligands. Thus, it is not surprising that P-selectin (CD62P) can be implicated in supporting microparticle binding to leukocytes in a manner similar to that already shown for platelet. The potential novel finding of Jy and colleagues is that P-selectin dependent adhesion to neutrophils seems to be more efficient in the case of microparticles, and larger clusters of neutrophils are seen where microparticles rather

than platelets act as bridging elements. These observations could mean that microparticles can efficiently activate neutrophils, as well as that neutrophils can remove potentially thrombogenic microparticles from the environment where a thrombus is developing.

The data presented in the paper by Jy and colleagues appear to be based on sound techniques. Caution in interpreting the results should, however, be exerted, particularly with regard to pathophysiological significance, since the experimental conditions used by the authors can hardly mimic the vascular environment. This is a general problem for most studies looking at mechanisms relevant in thrombogenesis, mainly because the experimental models usually adopted do not consider the effects of hemodynamic forces generated in the vasculature by the flow of blood. Thus, there is no evidence at present that microparticles have any role in platelet thrombus formation. Even the more entrenched concept that microparticles may be an important source of procoagulant activity has been challenged by studies evaluating this function in relation to platelet adhesion to surfaces, a situation more likely to reflect the pathophysiological activation of the clotting system (1). Without detracting from the interest of the observed phenomena, efforts should now be directed to evaluate the hypotheses proposed by Jy and coworkers in other experimental models and, particularly, under flow conditions.

REFERENCE

1. Swords NA, Tracy, PB, Mann KG. Intact platelet membranes, not platelet-released microvesicles, support the procoagulant activity of adherent platelets. *Arteriosclerosis and Thrombosis* 13:1613-22, 1993.

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