A Simple Experiment and a Weakening Paradigm

The Contribution of Blood to Propensity for Thrombus Formation

Yale Nemerson

For many years, arterial thrombosis was considered a result of vascular injury combined with a "normal" response of circulating coagulation factors and formed elements. Indeed, the original articles describing tissue factor in atherosclerotic lesions implied that rupture or erosion of the plaque that results in contact of the circulating blood with plaque-bound tissue factor is sufficient to result in thrombus formation. These formulations ignore the fact that thrombi have been observed to occlude an artery within minutes of formation. These formulations neglect the fact that thrombi can rapidly grow to macroscopic sizes that are observable within minutes of their formation.

This reasoning led us to examine more closely the participation of blood components in thrombus propagation. Using ex vivo and in vitro techniques, we were able to demonstrate the participation of blood-borne tissue factor in the formation of thrombi on collagen-coated surfaces and on arterial media. The article by Karnicki and colleagues significantly expands the previous results inasmuch as they performed a simple but revealing quantitative experiment. The fundamental question they addressed is the relative contribution of blood elements and arterial surfaces to formation of thrombi on arterial segments perfused with heparinized blood. The experimental design enabled these investigators to conclude that, in an all-porcine system, the thrombotic mass was more regulated by the blood than by the particular arterial segment used. The experiments were straightforward: blood was obtained from 25 pigs and perfused over arterial segments derived from a single donor aorta. The atheroexperiments in which blood derived from 8 different donors was perfused over segments obtained from 12 donors was also performed. Importantly, the thrombotic mass was much more influenced by the blood as compared with the arterial wall.

This interesting and important result clearly indicates the importance of circulating elements in thrombogenesis. Thus, the speculations arising from the identification of circulating tissue factor--containing microparticles and elevated levels of tissue factor antigen noted in patients with acute coronary syndromes now has experimental verification. The mechanism underlying this phenomenon has yet to be clearly elucidated. Karnicki et al unexpectedly found that thrombus mass correlated with the lymphocyte count. Although the leukocyte count has been suggested as a risk factor for myocardial infarction, the current data could be explained by an unknown mechanism, even viral infection, as suggested by these authors. Whatever the explanation, these studies warrant a considerable effort to establish the way in which blood regulates thrombus growth. While porcine thrombosis resembles the human condition, we note the obvious differences between pigs and man.

See pages 1495

This reasoning led us to examine more closely the participation of blood components in thrombus propagation. Using ex vivo and in vitro techniques, we were able to demonstrate the participation of blood-borne tissue factor in the formation of thrombi on collagen-coated surfaces and on arterial media. The article by Karnicki and colleagues significantly expands the previous results inasmuch as they performed a simple but revealing quantitative experiment. The fundamental question they addressed is the relative contribution of blood elements and arterial surfaces to formation of thrombi on arterial segments perfused with heparinized blood. The experimental design enabled these investigators to conclude that, in an all-porcine system, the thrombotic mass was more regulated by the blood than by the particular arterial segment used. The experiments were straightforward: blood was obtained from 25 pigs and perfused over arterial segments derived from a single donor aorta. The atheroexperiments in which blood derived from 8 different donors was perfused over segments obtained from 12 donors was also performed. Importantly, the thrombotic mass was much more influenced by the blood as compared with the arterial wall.

This interesting and important result clearly indicates the importance of circulating elements in thrombogenesis. Thus, the speculations arising from the identification of circulating tissue factor--containing microparticles and elevated levels of tissue factor antigen noted in patients with acute coronary syndromes now has experimental verification. The mechanism underlying this phenomenon has yet to be clearly elucidated. Karnicki et al unexpectedly found that thrombus mass correlated with the lymphocyte count. Although the leukocyte count has been suggested as a risk factor for myocardial infarction, the current data could be explained by an unknown mechanism, even viral infection, as suggested by these authors. Whatever the explanation, these studies warrant a considerable effort to establish the way in which blood regulates thrombus growth. While porcine thrombosis resembles the human condition, we note the obvious differences between pigs and man.

References


From the Department of Molecular Medicine, Mount Sinai School of Medicine, New York.

Correspondence to Dr Yale Nemerson, Division of Thrombosis Research, Department of Medicine, Mount Sinai School of Medicine, 1 Gustave Levey Pl, Box 1269, Annenberg, New York, NY 10029-6504. E-mail Yale.Nemerson@mssm.edu

(ARTERIOSCLER THROMB VASC BIOL. 2002;22:1369.)
A Simple Experiment and a Weakening Paradigm: The Contribution of Blood to Propensity for Thrombus Formation

Yale Nemerson

doi: 10.1161/01.ATV.0000034020.52348.61
Arteriosclerosis, Thrombosis, and Vascular Biology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2002 American Heart Association, Inc. All rights reserved.
Print ISSN: 1079-5642. Online ISSN: 1524-4636

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://atvb.ahajournals.org/content/22/9/1369

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Arteriosclerosis, Thrombosis, and Vascular Biology can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Arteriosclerosis, Thrombosis, and Vascular Biology is online at:
http://atvb.ahajournals.org//subscriptions/