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Effects of Stasis on Leucocyte Activity in Microvessels

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Leucocyte adherence to the walls of microvessels and their appearance in interstitial space indicating emmigration through walls is a common observation in living animal preparations amenable to microscopic study. These phenomena are strikingly similar to those accompanying tissue injury (ZWEIFACH, 1973) and are a hallmark of the inflammatory process (GRANT, 1973). The Clarks, (CLARK and CLARK, 1935) in reporting on their extensive studies using the rabbit ear chamber, noted that transient inadvertent compression of the vessels by an overlying cover slip would produce an increase in leucocyte sticking. If the duration of blood flow arrest was sufficient, leucocyte emmigration resulted. Since neither the pre and post occlusion values of leucocyte sticking or blood flow were quantified in these studies, definitive statements concerning the role of blood stasis as a mediator of leucocyte adherence can not be made. In 1972, ATHERTON and BORN counted the observed number of leucocytes rolling along the walls of vessels in the mouse mesentery and hamster check pouch and showed that this parameter is suitable for quantifying the degree of the leucocyte-wall interaction process. Using this method, MAYROVITZ and WIEDEMAN (1975) showed that in arterial vessels of the bat wing the magnitude of leucocyte adherence is critically dependent on hemodynamic forces related to blood velocity. In the present study the effect of blood stasis on the leucocyte-wall interaction process is investigated by determining simultaneously the change in leucocyte adherence and blood velocity following arterial occlusion.

Methods: The bat wing was prepared for microscopic observation by placing the unanesthetized animal in a tubular chamber, extending its wing over a large optical flat and securing the wing in position using small spring loaded clips. To enhance visibility, a small amount of mineral oil was put on the undersurface of the wing. In one series of experiments (7 animals) a second layer of mineral oil was placed on toe top surface. A branch of the supplying artery to the wing (main artery) was observed at a magnification of 1200 x before and after occlusion of the main artery. Pre and post occlusion observation times ranged from 30 to 120 minutes. The duration of flow stasis ranged from 1 to 25 minutes. In four animals of this series, localized occlusion

in part on the frequency with which this phenomena was observed and on the relatively slight stimuli required to produce it. GRANT (1973) has suggested that perhaps all preparations employed in the study of leucocyte sticking have a built-in artifact which renders leucocyte sticking omnipresent in "normal" circumstances. Use of the bat wing preparation which required neither anesthesia, surgical intervention, vessel exposure, or trauma to study this phenomena shows that leucocyte sticking is an extremely rare occurrence in arterial vessels. Since systematic study of the venous vasculature has not yet been carried out under these conditions, no definitive statement can be made regarding veins. The present findings also demonstrate that while blood flow stasis by itself is not a sufficient stimulus to provoke leucocyte adherence, stasis does augment pre-existing leucocyte-wall interactions as shown by transient increases in leucocyte flux in the peeled preparation. The interrelationship between the leucocyte adherence phenomena and local hemodynamic factors is complex. For a given vessel diameter, an increase in the blood velocity will increase the number of leucocytes per minute available for random collisions with the vessel wall. In a situation where leucocytes are adhering, this will tend to increase the observed leucocyte flux. Contrastingly, an increased velocity will cause the shear stresses to which the leucocytes are exposed to be larger. This will tend to reduce leucocyte adherence by overcoming the leucocyte-wall interaction force and tend to reduce leucocyte-vessel wall contact time. In the present study, increases in leucocyte flux following occlusion release were seen when blood flow (calculated as average velocity times vessel cross-sectional area) increased, decreased or remained unchanged. This finding argues for the possibility that, though hemodynamic factors play a role in the leucocyte-wall interaction process, the increase in leucocyte flux produced by stasis is mediated by factors which enhance the affinity of the endothelial cell of the wall for leucocytes. The mechanism responsible for this augmentation is unknown. However, the time course of the response, which is characterized by a substantial increase in leucocyte flux during the first minute following flow resumption with a rapid return toward pre-occlusion levels, provides information about its properties. By way of speculation, such a temporal response would be seen if endothelial cells experienced transient alterations of their membrane properties due to changes in the local chemical environment during the stasis period. Return of blood flow would subsequently reverse the chemical derangement and permit leucocyte flux to return to preocclusion levels.

REFERENCES can be obtained by writing the senior author.