

Leukocyte Adherence Initiation in Skeletal Muscle Capillaries and Venules

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In vivo leukocyte adherence has many physiological implications but the effect of vessel size and hemodynamic parameters on adherence initiation remains unclarified. The early phases of adherence, defined to include (1) attachment of previously freely moving leukocytes to endothelium or (2) leukocytes which roll along the vessel wall, are the focus of this report. Blood velocity and diameter in 121 capillaries and venules in the cremaster of 13 rats were measured. The hemodynamic and vessel size difference characterizing vessels in which either initial leukocyte wall attachment or leukocyte rolling occurred (termed "adherent vessels"), as distinguished from vessels in which neither transient stoppage nor cell rolling was observed (termed "nonadherent vessels"), was then determined. Fifty-seven percent of the vessels observed were adherent vessels. These vessels were characterized by a larger diameter, a smaller blood velocity, and a smaller calculated wall shear rate than the nonadherent vessels. The results show that leukocyte adherence can be initiated in capillaries and postcapillary vessels with diameters that are equal to and less than the leukocyte size. Within vessels less than 11 μm , adherence or nonadherence appears dependent on local hemodynamics with the possibility of a critical shear rate threshold of about 400 sec^{-1} . In vessels with shear rates greater than this value only 7% were observed to have adherence. In vessels greater than 11 μm the absence of hemodynamic differences between adherent and nonadherent vessels suggests the presence of other adherence-initiating mechanisms. It is thought that in these larger size vessels both local erythrocyte effects and adherence initiation within upstream capillaries affect observed adherence. © 1987 Academic Press, Inc.

INTRODUCTION

It is an ubiquitous observation, in almost all microcirculatory preparations with adequate resolution, to see leukocytes rolling along the endothelium of microvessels. The rolling is thought to be a prelude to ultimate firm adherence and, under appropriate conditions, to leukocyte emigration to adjacent extravascular tissue, although other functions of the rolling cells cannot be ruled out. Classically, such adherence is viewed as being related to inflammation, but numerous links between leukocyte adherence, dynamics, and several clinical entities have been suggested. Areas in which leukocytes have been implicated as a contributing

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factor include lung dysfunction (O'Flaherty *et al.*, 1978; Shasby *et al.*, 1982; Suttorp and Simon, 1982), atherosclerosis (Jorgensen *et al.*, 1972; Jouris *et al.*, 1983; Trillo, 1982), myocardial infarction (Flynn *et al.*, 1980; Friedman *et al.*, 1974; Prentice *et al.*, 1982; Romson *et al.*, 1983; Zalokar *et al.*, 1981), and cancer cell metastasis (Wood, 1958). Manifestations of the leukocyte component in these entities undoubtedly require initial cell adherence, but the initiating mechanisms are almost as poorly understood now as they were over a century ago.

A potentially important feature is that vessels of a given type and size, in close proximity to one another (100 μm and less), can differ markedly with regard to observed leukocyte adherence, some having extensive adherence and others being free of observed adherence. This suggests that during a particular observation interval, two classes of vessels exist: those in which leukocytes adhere and those in which they do not. If one can uncover key features which distinguish one from the other, then a clarification of the factors which affect initial leukocyte adherence may follow. Because the adherence process likely begins when freely moving cells either become transiently stopped against the endothelium or begin to roll along the vessel wall, we have focused on these initial aspects of the leukocyte-wall interaction process. We have pursued this line of inquiry by observing and measuring vessel diameter and blood velocity in capillaries and postcapillary venules in the rat cremaster microvasculature. Our aim was to determine if vessel diameter or hemodynamic parameters could distinguish between vessels that had transient leukocyte stoppage or cell rolling (arbitrarily termed adherent vessels) from those vessels with neither of these events (arbitrarily termed nonadherent vessels).

MATERIALS AND METHODS

Cremaster Preparation

Male spontaneously hypertensive rats, SHR ($n = 13$, age = 41 ± 3 days, weight = 100 ± 14 g), of the Okamoto and Oaki strain (Okamoto and Oaki, 1963) supplied by Charles River Laboratory were used in this study. This animal strain was selected for intensive study because of its widespread use and its importance as an experimental model. Each animal was initially anesthetized with a single dose of pentobarbital sodium (6.0 mg/100 g body wt ip), placed on a heated mat, and the trachea was cannulated. Systemic blood pressure was monitored via a carotid cannula coupled to a Gould P23 ID pressure transducer. The technique used to prepare the cremaster muscle for microscopic study was adapted from the method reported by Baez (1973) and described in detail elsewhere (Mayrovitz and Roy, 1983). Briefly, the cremaster muscle was separated from the scrotal sack by blunt dissection and kept moist by a constant flow of Krebs solution maintained at 34° . The solution was bubbled with a gas mixture of 95% N_2 -5% CO_2 to control the pH at 7.40. The cremaster was spread over an optically clear heated pedestal, which was thermostatically controlled to maintain the muscle at $34 \pm 0.1^\circ$. The upper portion of the pedestal formed an open chamber that permitted the muscle to be superfused with the Krebs solution at a rate of 2 ml/min. Following these procedures the animal, already secured to a mounting board, was placed on the stage of a Leitz Laborlux 12 HL trinocular microscope

equipped with a 150 W xenon light source for transillumination. All microscopic observations were done using a 50 \times , 1.0 numerical aperture water objective and 16 \times eyepieces. Measurements were begun 30 min after the animal was placed on the microscope stage.

Experimental Protocol

A microvessel was selected by moving the microscope stage until a capillary or postcapillary venule was located which met the conditions that both walls of the vessel could be visualized and the vessel was not obscured by overlying larger vessels. Following completion of measurements in this vessel, another vessel was selected by defocusing the microscope, moving the stage, and then restarting the entire process. These procedures were carried out successfully in 13 animals yielding determinations in 121 separate vessels.

If the selected vessel was a capillary, the entire length of the capillary was microscopically scanned so as to define its most proximal and distal sites. During this scanning procedure a determination was made as to the presence of (a) leukocytes rolling along the vessel wall and (b) leukocytes which were freely flowing and abruptly stopped in contact with the vessel wall. The events (a) or (b) will subsequently be referred to as leukocyte "adherence." The capillary was scanned for 2–3 min. If no leukocyte adherence was noted during this interval, the most distal site of the capillary (just before its venous confluence) was studied in detail. This procedure entailed the video recording of this segment of the vessel, which typically had the largest diameter within the capillary, for not less than 5 min. Simultaneously with the video recording, blood velocity was measured. Continued observation of this site was made during the entire measuring interval for the presence of leukocyte adherence. If during the initial 2 to 3-min scan of the capillary, adherence was observed, then the site at which the adherence first occurred was identified and vessel diameter and blood velocity were measured at sites just proximal and distal to the initial adherence site. In addition, counts of rolling leukocytes were made at the adherent site. All measurements were made continuously for 5–10 min.

If during the searching process for a vessel, the first vessel encountered was a postcapillary venule then all observations and measurements were carried out at the site along the vessel which was first intercepted in the microscopic field. Measurements of vessel diameter, blood velocity, and rolling leukocyte count were made at this site for 5–10 min.

At the conclusion of each experiment two blood samples were drawn by direct cardiac puncture. From one sample a CBC, including white blood cell differential, was obtained. From the other sample whole blood viscosity was determined at 37° using a cone-in plate viscometer (Wells-Brookfield Micro Viscometer).

Blood Velocity Measurement

Blood velocity in individual microvessels was measured using dual photo-optic sensing and on-line cross correlation of these signals (Intaglieta *et al.*, 1970; Wiedeman *et al.*, 1980). This method dynamically determines the delay between upstream and downstream signals generated by moving red blood cells as they interrupt the light path impinging on the photo-sensors. The sensors were positioned in the center of the vessel image and aligned along the vessel length at a known

distance apart. The vessel image was projected and displayed on a ground glass screen and the photo-optic signals were preamplified, bandwidth limited to 2 kHz and ac coupled before being fed into a commercially available velocity tracking device (IPM, Model 102). Signals obtained and processed in this fashion correspond to a velocity V in the center of the observed blood vessel. The velocity signals were displayed using an ink-writing polygraph (Grass, Model 7WC8PA) and recorded for later analysis. Previous work has shown that this velocity measurement method is capable of *in vivo* errors of less than about $\pm 5\%$ (Roy and Mayrovitz, 1982).

During all velocity measurements the image of the vessel was televised through a binocular viewing tube (MTI-65 Newvicon camera with 16 mm, 1:1.6 Cosmicon lens and $2\times$ electronic magnifier), video recorded (JVC, Model CR-6060U), and continuously observed on a TV monitor ((RCA, Model TC1119). The exact site of blood velocity measurement was registered on the video tape for later analysis using an electronic cross hair from a video analyzer (CVI, Model 321) which was superimposed and recorded on the image of the vessel. Blood velocity data were recorded on an audio channel of the tape recorder by frequency modulating the velocity signals with a commercially available device (Vetter, Model 2). This same device was used for signal demodulation during off-line analysis when required.

Vessel Diameter

Vessel diameters, D , were measured off-line by processing the recorded images. This was accomplished by first calibrating the coordinates of the video image on the monitor using the manually controlled video cross hairs. The intersection of the horizontal and vertical cross hairs defines a unique voltage characterizing each x - y coordinate. Calibration of the region of the image field used for analysis was established using a calibrated stage micrometer with $10\text{-}\mu\text{m}$ line spacing (Leitz, Model M9). Horizontal and vertical calibration factors were determined and thereafter used for the *in vivo* measurements of vessel diameter. Accuracy of the dimension measuring system was evaluated with a calibrated standard having opaque and transparent line widths varying from 3.0 to $12.0\ \mu\text{m}$ with an absolute error guaranteed to be within $\pm 0.10\ \mu\text{m}$ (Gold Arc Precision Linewidth and Calibration Standard No. 1562). Multiple measurements of the standard indicated that we could routinely obtain the stated value within $\pm 0.12\ \mu\text{m}$.

Calculations

Volume flow rate was calculated as the product of measured velocity (V) and vessel cross-sectional area assuming cylindrical vessel geometry. Shear rate at the vessel wall was calculated as $4V/D$ which assumes Poiseuille flow. Total leukocyte flux in cells per minute passing through an observed vessel was estimated as the product of the animal's systemic leukocyte count and the blood flow. Granulocyte flux was similarly calculated using the animal's granulocyte count. When statistical comparisons were made, the standard t test was used.

TABLE 1
SYSTEMIC BLOOD DATA SUMMARY

Leukocytes	
Total count (No./ μ l)	3450 \pm 682
Granulocytes (%)	51.6 \pm 2.7
(No./ μ l)	1941 \pm 254
Lymphocytes (%)	41.9 \pm 2.8
(No./ μ l)	1293 \pm 142
Monocytes (%)	2.2 \pm 0.7
Band (%)	3.8 \pm 0.8
Erythrocytes	
Total count (No./ μ l)	6655 \pm 190
Hematocrit (%)	37.2 \pm 1.2
Hemoglobin (g/100 ml)	13.7 \pm 0.2
Viscosity	
Shear rate (sec ⁻¹)	cP
23	6.4 \pm 0.3
46	5.6 \pm 0.2
115	4.8 \pm 0.1
230	4.5 \pm 0.1

Note. Data are expressed as means \pm SEM; cP is the whole blood viscosity value in centipoise.

RESULTS

General Data Summary

Table 1 is a summary of data which characterizes pertinent systemic blood parameters of the animal population used in this study. Blood pressure (mean \pm SEM) in these animals was 141.4 \pm 2.8 mm Hg. The total leukocyte count (3450/ μ l) is larger than reported for 8- to 12-week-old SHR (2458/ μ l) and WKY rats (2758/ μ l) but is less than the count of 5845/ μ l for normal Wistar control rats (Mayrovitz *et al.*, 1982) and less than the value of 6100/ μ l reported for 16 to 17-week-old SHR (DeClerck *et al.*, 1980). In all cases the total leukocyte count is characterized by a large standard error. The differential count of the present animal population revealed a slightly greater percentage of granulocytes (51.6%) than lymphocytes (41%). Though a larger fraction of granulocytes (55%) as compared with lymphocytes (40%) is generally seen in men (McGrath *et al.*, 1982), the reverse ratio is generally seen in rodents (Mitruka *et al.*, 1977; Charles River, 1982]. The other hematological values shown in Table 1 are within normal limits. The whole blood viscosity shows that the anticipated increase with decreasing shear rate and the mean viscosity of 4.5 cP obtained at 230 sec⁻¹ is close to the value of 4.4 cP previously found on a sample of 25 SHR aged 8 to 12 weeks (Mayrovitz *et al.*, 1982).

Microvascular Data Summary

Table 2 summarizes results relevant to the overall group microvascular measurements. Leukocyte adherence was observed in 69 vessels (57%). These vessels had a larger diameter, a lower mean blood velocity (470 vs 740 μ m/sec, $P =$

TABLE 2
MICROVASCULAR DATA SUMMARY

	All vessels	Adherent	Nonadherent
Number	121	69	52
Diameter (μm)	9.8 ± 0.3	10.5 ± 0.4	$8.9 \pm 0.4^*$
Velocity ($\mu\text{m}/\text{sec}$)	586 ± 43	470 ± 31	$740 \pm 86^*$
Flow (pl/sec)	48 ± 4	47 ± 5	49 ± 6
Wall shear rate (sec^{-1})	257 ± 19	187 ± 11	$346 \pm 38^{**}$
$D_{\text{vessel}}/D_{\text{cell}}$	1.20 ± 0.03	1.29 ± 0.04	$1.08 \pm 0.04^*$
Total flux (cells/min)	9.7 ± 1.2	8.8 ± 1.4	10.8 ± 2.3
Granulocyte flux (cells/min)	5.2 ± 0.8	4.6 ± 0.9	6.1 ± 1.5
Adherent flux (cells/min)		4.2 ± 0.3	

Note. Data are presented as means \pm SEM.

* $P < 0.01$ compared with Adherent vessels.

** $P < 0.001$ compared with Adherent vessels.

0.005), and a lower shear rate (187 vs 346 sec^{-1} , $P = 0.0001$) than those vessels in which no adherence was observed. Based on the *in vivo* size of rolling leukocytes of $8 \mu\text{m}$ in this species (Mayrovitz, R. A., *et al.*, 1986), the computed ratio of vessel to cell diameter is 1.29 and 1.08 in adherent and nonadherent vessels, respectively.

Overall Relationship to Vessel Diameter

To more closely examine the factors which distinguish vessels in which adherence is observed from vessels in which adherence is absent, comparisons using equivalent diameter ranges were carried out. In Fig. 1 the number of vessels within each diameter range in which adherence was observed is compared with the number

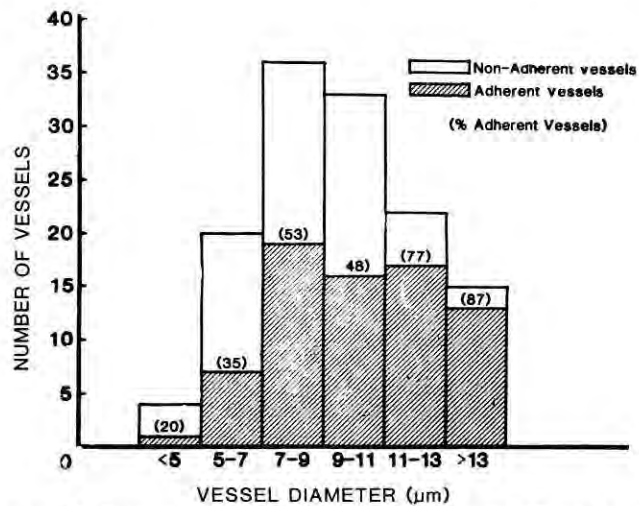


FIG. 1. Distribution of adherent and nonadherent vessels by diameter. The designation (% Adherent Vessels) denotes the percentage of the vessels within each range that were observed to have adherent leukocytes.

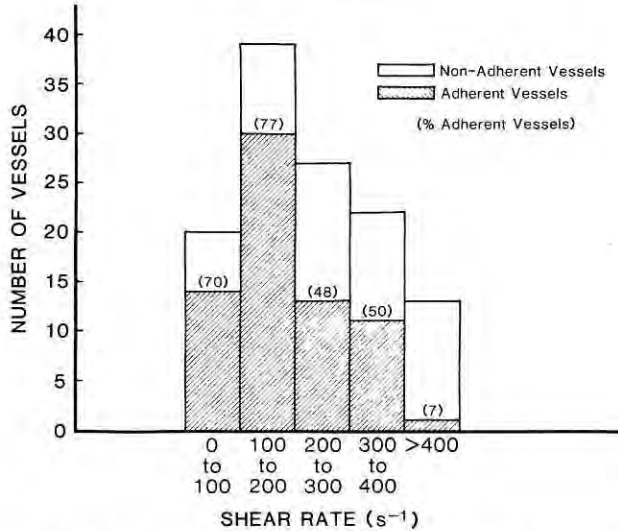


FIG. 2. Distribution of adherent and nonadherent vessels by calculated wall shear rate.

of vessels in the same diameter range in which no leukocyte adherence was observed. It may be seen that the percentage of adherent vessels tends to increase with vessel diameter, with 87% of the vessels greater than 13 μm being observed to have adherent leukocytes. For vessels with a diameter between 7 and 11 μm , adherent and nonadherent vessel percentages are about equal.

Overall Relationship to Blood Shear Rate

In Fig. 2 adherent and nonadherent vessels are compared with regard to calculated blood shear rate. The frequency of adherence is seen to be substantially greater in vessels characterized by the lower shear rate ranges. For example, 77% of observed vessels in the 100 to 200-sec⁻¹ range had adherent cells whereas only 7% of the vessels with a shear rate greater than 400 sec⁻¹ had adherent cells. By contrast, within the range of 200–400 sec⁻¹ approximately equal numbers of adherent and nonadherent vessels were seen. The shear rates embodied in Fig. 2 do not differentiate between vessel diameters. It is therefore instructive to determine if, within equivalent shear rate ranges, there are significant differences in the diameters of adherent and nonadherent vessels. Calculations of the mean diameter corresponding to each of the progressive shear rate ranges of Fig. 2 reveal the following values in μm for the adherent and nonadherent groups, respectively: 12.4 vs 12.6, 10.5 vs 8.4, 9.2 vs 8.9, 9.8 vs 8.1, and 8.2 vs 7.9. None of these differences were statistically significant, but a trend for the adherent vessels to have the larger diameter is suggested.

Overall Relationship to Blood Velocity

In Fig. 3 adherent and nonadherent vessels are compared with regard to measured blood velocity. The frequency of adherence is seen to be substantially greater in vessels characterized by the lower velocity ranges. For example, 69% of observed vessels in the 0.2–0.4 mm/sec range had adherent leukocytes whereas

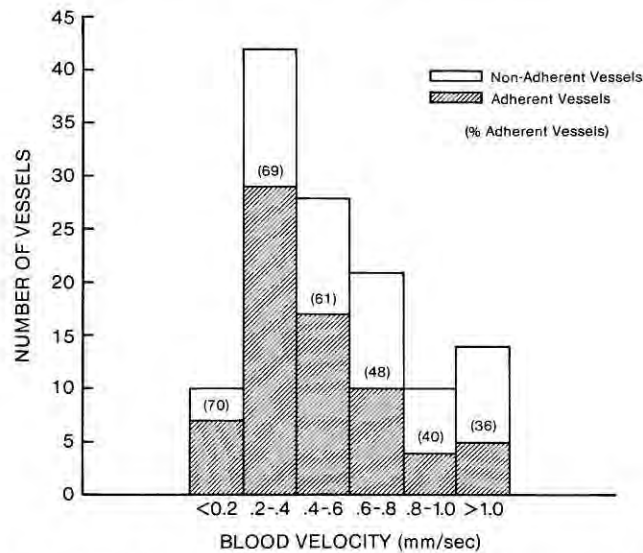


FIG. 3. Distribution of adherent and nonadherent vessels by measured blood velocity.

36% of the vessels with a velocity greater than 1.0 mm/sec had adherent cells. By contrast, within the range of 0.6–0.8 mm/sec approximately equal numbers of adherent and nonadherent vessels were seen. As with the previously described shear rate ranges, the velocity ranges embodied in Fig. 3 do not differentiate between vessel diameters. It is therefore again instructive to determine if, within equivalent velocity ranges, there are significant differences in the diameters of adherent and nonadherent vessels. Calculations of the mean diameter corresponding to each of the progressive velocity ranges of Fig. 3 reveal the following values in μm for the adherent and nonadherent groups, respectively: 10.7 vs 14.0, 10.0 vs 8.3, 10.3 vs 7.3, 11.2 vs 9.2, 10.8 vs 8.7, and 12.0 vs 9.8. The general trend of this data suggests that with the exception of the lowest velocity range the adherent vessels tend to have the larger diameter. However, statistical significance ($P < 0.01$) was found only in the 0.4–0.6 mm/sec range. A comparison of Figs. 2 and 3 shows similar trends in adherence with increasing shear rate and velocity, respectively. However, it should be noted that even in the highest velocity range there still remain 36% of the vessels which were adherent whereas only 7% are adherent in the highest shear rate range.

Within Discrete Diameter Ranges

Possible interplay between vessel diameter and local hemodynamics as they may affect adherence vs nonadherence was examined by comparing, within equivalent diameter ranges, blood velocity, volume flow, and shear rate. Results are summarized in Table 3. Each of the parameters was found to be significantly greater in the 7–9 and 9–11 μm ranges of the nonadherent vessels. It is these diameter ranges for which there were approximately equal numbers of adherent and nonadherent vessels. The number of adherent cells observed per minute (adherent leukocyte flux) is shown in Fig. 4 as a function of vessel size range.

TABLE 3
COMPARISON OF HEMODYNAMIC PARAMETERS WITHIN EQUAL DIAMETER RANGES

Diameter range (μm)	Velocity ($\mu\text{m}/\text{sec}$)		Volume flow (pl/sec)		Wall shear rate (sec^{-1})	
	ADH	NON-ADH	ADH	NON-ADH	ADH	NON-ADH
5-7	396 \pm 41	514 \pm 52	12 \pm 1	15 \pm 2	260 \pm 31	348 \pm 37
7-9	381 \pm 42	1033 \pm 217*	20 \pm 2	61 \pm 14*	188 \pm 20	480 \pm 97*
9-11	470 \pm 56	974 \pm 143*	36 \pm 4	73 \pm 9*	190 \pm 23	402 \pm 63*
11-13	535 \pm 78	352 \pm 157	59 \pm 9	38 \pm 9	182 \pm 27	120 \pm 32
>13	543 \pm 71	599 \pm 450	101 \pm 14	116 \pm 70	145 \pm 21	155 \pm 98

Note. ADH, adherent vessels; NON-ADH, nonadherent vessels. Data are presented as means \pm SEM.

* $P < 0.01$ compared with ADH vessels.

These data suggest a trend for adherent flux to be greater in the larger size vessels.

DISCUSSION

Central to the issues dealt with in this study is the concept of *in vivo* leukocyte adherence. Though adherence has been seen in virtually every microvascular preparation, systematic quantitation of this ubiquitous phenomenon began little more than a decade ago (Atherton and Born, 1972) and an understanding of the *in vivo* leukocyte dynamics is beginning to emerge (Schmid-Schönbein *et al.*, 1980; Mayrovitz, 1982; Mayrovitz and Rubin, 1985). In the present study we have focused on the initial phases of the leukocyte-wall interaction process: the transition of freely flowing cells into cells attached to endothelium as assessed by light microscopy and by the cells rolling along the vessel wall. Either of these events was termed leukocyte adherence. Mechanisms associated with leukocyte firm adherence and subsequent emigration were not addressed.

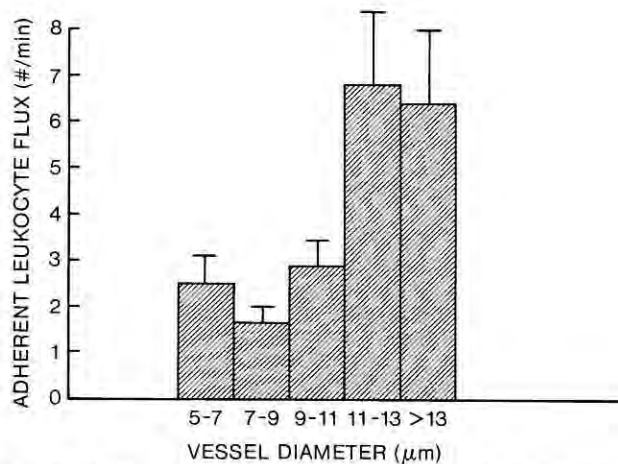


FIG. 4. Distribution of leukocyte adherence by vessel diameter.

The simplest physical accounting for the initial adherence process would require wall proximity of the leukocyte for a time interval sufficient for adherence to develop. How close to the wall the cell must get and how long it must be there are not known. Given that these necessary conditions are satisfied, observable adherence probably depends on the presence of some form of energy or force interaction between vessel wall and leukocyte (Schmid-Schönbein *et al.*, 1975; Mayrovitz *et al.*, 1977a, b, 1980; Nobis *et al.*, 1985) and on the dynamics of the blood flow. Schmid-Schönbein and co-workers (1980) have shown that the ratio of vessel diameter to leukocyte size is an important determinant of adherence initiation via hydrodynamic interactions. These authors report that passage of leukocytes through capillaries does not result in their attachment unless the vessel diameter is about $11 \mu\text{m}$ or larger, which occurs in the divergent channel leading to the venule. Under these conditions, erythrocytes speed by granulocytes and displace them to the vessel wall. Their data show that essentially no erythrocyte passing occurs when the ratio of vessel to cell diameter is less than 1.3. For a leukocyte diameter of $8 \mu\text{m}$ this means that erythrocyte passing would not account for adherence in vessels smaller than $10.4 \mu\text{m}$. However, in the present work, substantial adherence in vessels with diameters less than this value was observed, indicating that other factors are involved. The present results which focus on the capillaries and postcapillary venules suggest that shear rate or the related quantities, shear stress and force, acting in the vicinity of the wall also are factors affecting adherence initiation. An examination of the overall relationship between shear rate and the presence or absence of leukocyte adherence (Fig. 2) reveals a trend for leukocyte adherence to diminish with increasing shear rate. At a shear rate greater than about 400 sec^{-1} only one vessel out of a total of 14 was observed to have adherent leukocytes. The sharp decrease in adherent vessels when shear rate changes from 300 to 400 sec^{-1} to a value greater than 400 sec^{-1} may suggest a critical threshold. The concept of a critical shear rate is consistent with previous *in vivo* assessments in venules (Atherton and Born, 1973) and arteriolar vessels (Mayrovitz and Wiedeman, 1976). The present work extends this concept to capillaries and venules of a different tissue.

That shear rate cannot be the only parameter which separates adherent from nonadherent vessels is demonstrated by the fact that within the shear rate ranges of 200 – 300 and 300 – 400 sec^{-1} (Fig. 2) there is approximately an equal number of adherent and nonadherent vessels. When categorized by vessel size, the dominant role of local hemodynamics on leukocyte adherence initiation is found to be restricted to vessels $< 11 \mu\text{m}$. For a given measured centerline velocity V , the actual wall shear rate when a leukocyte passes by is likely to be considerably higher in the smaller vessels where all the velocity gradient is concentrated in the very thin lubricating plasma layer between the cell and the endothelium. This may be one of the reasons that the percentage adherence in vessels having $D < 7 \mu\text{m}$ is smaller, because once a leukocyte is deformed in order to negotiate the lumen of a capillary having $D < 7 \mu\text{m}$ it may flow rapidly through. For vessels with diameters $> 11 \mu\text{m}$, wall shear rate and velocity in adherent vessels are similar to those found in all other diameter ranges, but the frequency of adherence is substantially greater. In these larger size vessels there may be a greater likelihood of leukocytes being in sufficiently close proximity to the vessel wall thereby increasing the probability of adherence initiation. The mechanism of

erythrocyte passing and hydrodynamic interaction between erythrocytes and leukocytes could account for such events. Alternatively, or possibly in concert with this mechanism, closer wall proximity of the leukocyte may result from rheological factors affecting the leukocytes' normal radial position (Nobis *et al.*, 1982; Vejlens, 1938), although we did not observe red cell aggregation.

An additional factor that we believe to be of importance relates to the topographical aspects of the microvascular field under study. Vessels within the larger diameter classes are those which serve as the termination of capillaries. When these venules are observed at randomly selected sites the presence or absence of adherence in them depends on whether there was adherence in the vessels feeding them. There is a strong tendency for the leukocyte adherence in the feeding vessels to continue into the collecting vessel (Bagge and Karlsson, 1980). Thus, rolling initiated in a capillary continues on the contiguous wall of the collecting vessel. Within this framework it is likely that there will be a greater percentage of the larger size vessels which will have leukocyte adherence in spite of similar local hemodynamics as present in smaller vessels without adherence.

In summary, the present results show that leukocyte adherence can be initiated in capillaries and postcapillary vessels that have diameters that are equal to and less than the leukocyte size. Within the diameter range of 7–11 μm adherent and nonadherent vessels are observed with about equal frequency. Within vessels less than 11 μm , adherence or nonadherence appears dependent on local hemodynamics, and the presence of a critical shear rate threshold of about 400 sec^{-1} is suggested. Above this threshold leukocyte adherence is rare. In vessels greater than 11 μm the absence of hemodynamic differences between adherent and nonadherent vessels suggests the presence of other adherence-initiating mechanisms. It is thought that in these larger size vessels both local erythrocyte effects and adherence initiation within upstream capillaries affect observed adherence.

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