Endothelial, Not Hemodynamic, Differences Are Responsible for Preferential Leukocyte Rolling in Rat Mesenteric Venules

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At the onset of the inflammatory process, leukocytes roll along venular but not arteriolar walls before they firmly attach and emigrate. To test whether differences in hydrodynamic flow conditions are responsible for the preferential occurrence of leukocyte rolling in venules, we varied wall shear rate, $\gamma_w$, between 30 and 2,000 sec$^{-1}$ by selective micro-occlusion of side branches in venules and arterioles (diameter, 20–37 μm) of the exposed mesentery of anesthetized rats. In venules, 39% (range, 6–77%) of all passing leukocytes were found interacting with the endothelium (rolling), whereas this fraction was only 0.6% in arterioles. The fraction of rolling leukocytes in venules decreased from 49±13% at $\gamma_w<100$ sec$^{-1}$ (N=12) to 24±13% at $\gamma_w>400$ sec$^{-1}$ (N=12). Mean leukocyte rolling velocity in venules increased with $\gamma_w$, but the most frequent rolling velocity class was 20–40 μm/sec at all shear rates. In arterioles, even prolonged (up to 90 minutes) conditions of reduced flow ($\gamma_w<150$ sec$^{-1}$) did not induce leukocyte rolling. Radial distribution of freely flowing leukocytes was not different in arterioles and venules. The data indicate that hemodynamic factors are not responsible for the difference of leukocyte adhesion between arterioles and venules. The venular endothelium appears to be specialized to support leukocyte adhesion during inflammation. This finding correlates with reports on preferential expression of various endothelial-leukocyte adhesion molecules on venular endothelial cells. (Circulation Research 1991;69:1034–1041)

Leukocyte rolling is observed in the venules of most tissues exposed for intravital microscopy.1–7 By contrast, leukocyte rolling in arterioles is rarely reported and appears to occur only with considerable trauma.8 The velocity of rolling leukocytes has been observed to range around or below 50 μm/sec,3,7 which is at least an order of magnitude lower than the blood flow velocities typical for venules. Although leukocyte margination, a phenomenon that might be considered to induce leukocyte rolling, occurs predominantly in venules because of rheological reasons,9–11 it is not sufficient to explain the leukocyte rolling phenomenon. Even fully margined leukocytes will travel at about 50% of the centerline velocity in 30-μm venules12 and thus substantially faster than rolling cells, which are retarded by an adhesive interaction between the leukocyte and the endothelium. This adhesive interaction has been the subject of several investigations.4,7,13

Recent investigations suggest that leukocyte rolling results from a specific receptor–ligand interaction between leukocytes and the endothelium.13,14 Various adhesion molecules have been shown to be preferentially or exclusively expressed on venular but not arteriolar endothelium, among them the leukocyte endothelial adhesion molecule ELAM-115,16 and another lectinlike adhesion molecule, GMP-140,17 MECA-79 antigen,18 which probably is involved in lymphocyte homing to high endothelial vessels in lymph nodes, is found exclusively on venules. Distinct distribution of endothelial adhesion receptors may account for preferential leukocyte adhesion to venular endothelium in vivo.

Alternatively, it has been proposed that the observed differences between arterioles and venules may be attributable to different hemodynamic conditions.3,4,7 Usually, mean blood flow velocity and hence wall shear rate is about twice as high in arterioles compared with venules of the same size.19 In earlier studies, leukocyte adhesion has been reported to be confined to venules even after chemotactic stimulation with the formylated bacterial peptide f-MLP.6 Reduction of blood flow and hence wall shear rate increases the fraction of rolling leukocytes in venules of the rat mesentery.7 So far, however,
leukocyte rolling has not been studied with systematic variation of wall shear rates in both arterioles and venules.

We therefore undertook the present study to investigate whether hemodynamic differences between arterioles and venules account for the restriction of leukocyte rolling to venules. To this end, we manipulated blood flow velocities in individual arterioles and venules with diameters around 30 μm by selectively micro-occluding side branches. With this approach, we studied the velocity and frequency of rolling leukocytes over a wide range of wall shear rates in arterioles and venules of the exposed rat mesentery using stroboscopic fluorescence microscopy.

Materials and Methods

Ten female Sprague-Dawley rats (body mass, 250–300 g) were anesthetized with ketamine (Ketanest, 75 mg/kg i.m.) after premedication with pentobarbital (Nembutal, 20 mg/kg i.m.) and atropine (0.1 mg/kg i.m.). Polyethylene tubing catheters of appropriate size were placed in the trachea, the right carotid artery, and the right jugular vein, and arterial blood pressure and heart rate were recorded continuously. Blood samples (20 μl) were taken from the carotid catheter at approximately 30-minute intervals, hematocrit was measured with heparinized microhematocrit tubes, and leukocyte concentration was determined with an electronic cell counter (Coulter DNI, Herts, UK). The animals were thermo-controlled to 36.5–37°C with a heating pad controlled by a rectal thermistor. The peritoneal cavity was opened by a midline incision with a thimberauter to prevent local bleeding. A few loops of ileum proximal to the appendix were exteriorized onto a Lucite stage and superfused with thermostated (37°C) bicarbonate-buffered saline (millimolar composition: NaCl 132, KCl 4.7, CaCl₂ 2, MgCl₂ 1.2, NaHCO₃ 18, equilibrated with 5% CO₂ in N₂ to adjust pH to 7.35). Throughout the experiment, the animals received two infusions: acridine red solution (−1 mg/ml) at 4 ml·kg⁻¹·hr⁻¹ and physiological saline containing pentobarbital (0.2 mg/ml) at 40 ml·kg⁻¹·hr⁻¹. The resulting concentration of acridine red was sufficient for fluorescent staining of leukocytes and did not interfere with systemic leukocyte concentration or leukocyte rolling in venules, as observed by intravital microscopy.

Observations started approximately 20 minutes after exteriorization of the mesentery with the use of a Leitz intravital microscope (objective, SW 25/0.60) modified for televised imaging.²⁰ Both freely flowing and rolling leukocytes were observed with stroboscopic (50 sec⁻¹), Strobex 236, Chadwick Helmhut, Mountain View, Calif.) epi-illumination and were recorded on 3/4-in. videotape (Sony U-matic) with an SIT camera (Bosch TYC 9A, FRG). The size of the resulting field of view was approximately 300×250 μm, limiting maximum measurable cell velocity to ~10 mm/sec at the video framing rate of 50 sec⁻¹.

Venules and arterioles with diameters of approximately 30 μm were selected, because pilot experiments using blood-perfused glass tubes and an earlier in vivo study¹³ had shown that in these vessels all leukocytes can be detected with acridine red labeling and epifluorescence. Arterioles were identified as vessels with divergent bifurcations, whereas conflu-ent branches defined venular segments. Microvascular flow rate was modified by permanent occlusion of selected side branches with a blunt glass microprobe, resulting in a variation of blood flow velocity over a 50-fold range. Blood flow velocity in arterioles and venules was reduced by occlusion of downstream and upstream side branches, respectively. In venules, velocity also was increased by up to 56% by occlusion of parallel venous pathways. At each blood flow velocity (two to eight flow states per vessel), video scenes of 1–2-minutes duration were recorded and evaluated with a PC-based interactive digital image processing system developed for microcirculatory applications.²¹ Within each scene, the velocities of ~30 consecutive leukocytes (average, 32±6; range, 20–66) were determined by measurement of the distance traveled between two or more successive video frames. The highest cell velocity, v₃₅₅, was used to calculate mean blood flow velocity, v̄, using a relation given by Gahtgens et al²²:

\[ \bar{v} = v_{\text{max}}/(2 - e^2) \]  

(1)

where \( e \) is the ratio of the leukocyte diameter (assumed to be 7 μm²) to vessel diameter. Alternative models²⁴,²⁵ for estimating \( \bar{v} \) from \( v_{\text{max}} \) assume different shapes of the velocity profile in the presence of the particle. They yield results within 3% of those obtained using Equation 1 at the pertinent vessel and cell diameters.

At the sample size used (~30 leukocytes), the velocity of the fastest leukocyte detected is only slightly lower (by less than 5%) than that of the fastest leukocyte in a large sample (75 leukocytes), as had been observed in previous pilot experiments (data not shown). To additionally validate this estimation of \( \bar{v} \), we measured centerline blood flow velocities by temporal cross-correlation (velocity tracking correlator, model 102, IPM, Inc., San Diego, Calif.) of signals obtained from a photodiode pair on which the microscopic image was projected. Centerline velocities were larger than \( \bar{v} \) by an average factor of 1.7±0.6, which is in quantitative agreement with previous studies²⁶ and is thought to result from the spatial averaging characteristics of the photosensors. From \( \bar{v} \) (Equation 1) and vessel diameter, \( d_{\text{vessel}} \), blood flow rate, \( Q_{\text{v}} \), was calculated, and Newtonian wall shear rate, \( \gamma_w \), was estimated as

\[ \gamma_w = 8 \cdot \bar{v} / d_{\text{vessel}} \]  

(2)

Total leukocyte flux, \( \dot{N}_{\text{WBC}} \), was determined by dividing the number of leukocytes passing the vessel by the elapsed time. Leukocyte discharge concentration, \( [\text{WBC}] \), was calculated as
Rolling leukocytes were identified with a velocity criterion derived from the assumption of a paraboloid velocity profile in the microvessel. The velocity of a freely flowing cell traveling close to the wall will be smaller than that of the fluid traveling at the same radial position in an undisturbed flow profile. Hence, the estimate of \( v_{\text{crit}} \) given earlier has been modified by an arbitrary factor of one half to obtain a conservative (lower) estimate of \( v_{\text{crit}} \). The modification was introduced to account for additional drag exerted on the marginated but nonadherent cell by the vessel wall and also for variations in leukocyte diameter and temporal fluctuations of blood flow velocity.

\[
\nu_{\text{crit}} = \bar{v} \cdot \epsilon \cdot (2 - \epsilon)
\]

Any cell that travels below the critical velocity is likely to be retarded by an adhesive interaction with the vessel wall.

The flux fraction of rolling leukocytes was calculated for each recording by dividing the number of rolling leukocytes by the total number of leukocytes (\( N_{\text{WBC}} \)) passing the vessel. The volume fraction of rolling cells, that is, the number of rolling leukocytes expressed as percent of all leukocytes present in a given volume of microvessel at any time, was calculated by dividing the sum of the transit times of rolling leukocytes by that of all passing leukocytes. Correspondingly, the average velocity of rolling leukocytes passing each vessel (flux-weighted average) was calculated as the arithmetic mean, whereas the average velocity of all rolling leukocytes present in each vessel segment (volume-weighted average) was obtained as the harmonic mean of the velocities of all passing rollers.

The radial position of freely flowing (noninteracting) leukocytes within the microvessel was estimated from their velocities, assuming that leukocytes with an average diameter of 7 \( \mu \)m travel at the velocity prevailing at the radial position of their center of mass in a parabolic velocity profile. The number of leukocytes passing within each of a series of concentric rings (width, 1 \( \mu \)m) was calculated and divided by the cross-sectional area of each ring to obtain relative concentrations. All experimental sequences containing at least 15 freely flowing leukocytes (33 of 52 venular sequences, all 45 arteriolar sequences) were included in this analysis to avoid possible bias due to small sample size.

Data are expressed as arithmetic mean \( \pm 1 \) SD of \( N \) vessels or \( n \) leukocytes. Differences and regressions were regarded significant with a value of \( p < 0.05 \) using Student’s \( t \) distribution.

**Results**

Leukocyte rolling was investigated in rats surgically prepared for intravital microscopy of the mesentery. During the experimental period of 130-20 minutes (range, 90-155 minutes), blood pressure, heart rate, and systemic hematocrit remained constant, whereas systemic leukocyte counts increased from 4,050 \( \pm \) 1,500 to 10,500 \( \pm \) 3,700 \( \mu \)L\(^{-1}\). Leukocyte discharge concentrations measured in the microvessels averaged 118 \( \pm \) 54\% (range, 47-249\%) of the systemic leukocyte concentrations determined at the respective time points. In 52 recordings of 10 individual venules (mean diameter, 28 \( \pm \) 3 \( \mu \)m; range, 20-32 \( \mu \)m), 1,645 leukocytes were observed, of which 648 (39\%) were identified as rolling cells because they traveled at velocities below \( v_{\text{crit}} \). In 45 scenes of eight arterioles (mean diameter, 28 \( \pm \) 5 \( \mu \)m; range, 22-37 \( \mu \)m), the velocity of only nine of 1,483 leukocytes (0.6\%) was less than \( v_{\text{crit}} \).

In the control situation before micro-occlusion, blood flow velocity \( v \) as calculated from the velocity of the fastest leukocyte (Equation 1) was considerably lower in venules (1.3 \( \pm \) 0.8 mm/sec; range, 0.4-2.7 mm/sec) than in arterioles (3.6 \( \pm \) 1.2 mm/sec; range, 1.1-5.1 mm/sec). Blood flow was manipulated over a wide range by permanent occlusion of selected side branches of the investigated vessels with a blunt microprobe. Resulting blood flow velocities ranged from 0.1 to 2.9 mm/sec in venules and from 0.1 to 5.1 mm/sec in arterioles. Correspondingly, calculated wall shear rates varied between 30 and 1,000 sec\(^{-1}\) in venules and between 40 and 2,000 sec\(^{-1}\) in arterioles. The distribution of individual leukocyte velocities was quite different in arterioles and venules, as shown in Figure 1 for two representative flow states in a single arteriole and venule. Some leukocytes traveled at velocities below \( v_{\text{crit}} \) in the venule, but all leukocytes appeared to be flowing without wall contact in the arteriole.

The flux fraction of rolling leukocytes varied between 6\% and 77\% of the total number of passing leukocytes (average, 40 \( \pm \) 18\%) in the investigated venules and between 0\% and 7\% (average, 0.7 \( \pm \) 1.5\%) in the arterioles. The flux fraction of rolling leukocytes in venules was independent of systemic leukocyte count and was negatively correlated with wall shear rate (\( N = 52, p < 0.01 \)), decreasing from 49 \( \pm \) 13\% at \( \gamma_{w} < 100 \) sec\(^{-1}\) (\( N = 12 \)) to 24 \( \pm \) 13\% at \( \gamma_{w} > 400 \) sec\(^{-1}\) (\( N = 12 \)) (Figure 2). In arterioles, the fraction of rolling leukocytes was low and independent of wall shear rate over the whole range from 40 to 2,000 sec\(^{-1}\). Even during prolonged situations with reduced flow rates, which were induced in four arterioles for 48-91 minutes at flow velocities between 0.13 and 0.40 mm/sec (\( \gamma_{w} < 150 \) sec\(^{-1}\)), no rolling leukocytes were detected. The volume fraction of rolling leukocytes in venules, that is, the number of rolling leukocytes expressed as a percent of all leukocytes present in a microvascular segment, was higher than the flux fraction, owing to the low velocity of rolling cells. Rolling leukocyte volume fraction in venules was independent of wall shear rate, averaging 85 \( \pm \) 14\% at \( \gamma_{w} < 100 \) sec\(^{-1}\) and \( 81 \pm 14\% \) at \( \gamma_{w} > 400 \) sec\(^{-1}\) (Figure 2).

The mean velocity of rolling leukocytes passing the venules (flux-weighted average) increased almost linearly from 42 \( \pm \) 16 \( \mu \)m/sec at \( \gamma_{w} < 100 \) sec\(^{-1}\) to
Figure 1. Velocities of successive leukocytes observed in a mesenteric arteriole (top panels) and venule (bottom panels); critical velocity, \( v_{cm} \), indicated by broken line. Arteriole: diameter, 28.9 \( \mu \)m; mean blood flow velocity, \( \bar{v} \), 1.38 before (left) and 0.52 mm/sec after (right) micro-occlusion (wall shear rate, \( \gamma_{ws} \), 382 and 144 sec\(^{-1}\), respectively); no rolling leukocytes. Venule: diameter, 29.6 \( \mu \)m; \( \bar{v} \), 1.40 and 0.67 mm/sec; \( \gamma_{ws} \), 378 and 181 sec\(^{-1}\); 13 and 11 rolling leukocytes, respectively. Note three rapidly rolling cells at the higher flow velocity.

248 \pm 166 \mu m/sec at \( \gamma_{ws} > 400 \) sec\(^{-1}\) (\( p < 0.01 \)) (Figure 3, top panel). The mean velocity of rolling leukocytes present in each venule (volume-weighted average) was lower for all shear rate classes because of a stronger representation of slow rollers. It increased with wall shear rate from 34 \pm 15 \mu m/sec at \( \gamma_{ws} < 100 \) sec\(^{-1}\) to 110 \pm 74 \mu m/sec at \( \gamma_{ws} > 400 \) sec\(^{-1}\) (\( p < 0.01 \)) (Figure 3, bottom panel). Conspicuously, standard deviations increased more than mean values, elevating the coefficient of variation from 37\% to 67\%, which indicates an increasing heterogeneity of rolling leukocyte velocities with increasing wall shear rate.

This was analyzed in more detail by pooling the velocities of rolling leukocytes into four shear rate classes: \( \gamma_{ws} < 100 \) sec\(^{-1}\), 100–200 sec\(^{-1}\), 200–300 sec\(^{-1}\), and >300 sec\(^{-1}\). The resulting velocity histograms (Figure 4) indicate a remarkably similar distribution of rolling leukocyte velocities in all \( \gamma_{ws} \) classes. Even at high wall shear rates, rolling leukocytes most frequently traveled at velocities between 20 and 40 \mu m/sec. At higher wall shear rates (\( > 200 \) sec\(^{-1}\)), an additional population of leukocytes appeared, which were rapidly rolling (cell velocities>300 \mu m/sec) or possibly jumping along the vessel wall. These cells are responsible for the increase of mean leukocyte rolling velocity with wall shear rate.

To investigate the possibility that the extent of hydrodynamic leukocyte margination might be quantitatively different in arterioles and venules, we analyzed the velocities of freely flowing leukocytes. The observed velocity distribution, normalized with respect to maximal cell velocity \( v_{max} \) in each vessel, was similar in arterioles and venules (Figure 5, top panels) and in vessels with high and low velocities (\( \bar{v} \) above and below 1 mm/sec, data not shown). Likewise, the calculated radial positions of freely flowing leukocytes were similar (Figure 5, bottom panels): In 45 arteriolar sequences, 309 of 1,474 freely flowing leukocytes (21\%) traveled within 1 \mu m of the endothelial wall, that is, with their center of mass at a calculated position of less than 4.5 \mu m from the endothelial surface. This was not different from the fraction of hydrodynamically margined but not rolling leukocytes in venules: In 33 venular
sequences containing at least 15 freely flowing leukocytes each, 145 of 780 cells (19%) approached the vessel wall to 1 μm or less.

Discussion

Leukocyte rolling in the rat mesentery is restricted to venules and does not occur in arterioles, irrespective of wall shear rate. Intentional variation of vessel perfusion induced wall shear rates covering the physiologically relevant range between less than 50 and more than 1,000 sec⁻¹ in both arterioles and venules. Low shear rates, even when maintained for up to 90 minutes, did not cause leukocyte-endothelial interaction in arterioles.

Preferential leukocyte rolling in venules has been described in earlier studies in different tissues²⁻⁴,⁶,⁷ under conditions of unrestricted flow. The fraction of rolling leukocytes in a given venule was found to increase with reduced shear rate accomplished by graded micro-occlusion. However, low flow states in arterioles were not investigated in these studies. Mayrovitz et al.⁰ have observed leukocyte rolling in arterioles of the bat wing on laser-induced trauma. Most authors²,⁴,⁷ attribute the absence of rolling leukocytes in arterioles to the higher flow velocities and hence higher wall shear rates prevailing in these vessels. This assumption is not supported by the present data because the marked difference between arterioles and venules persists even at identical shear rates in both vessel categories.

In venules of the rat mesentery, we find a moderate decrease of the fraction of rolling leukocytes with increasing wall shear rate, reaching 24±13% at γw>400 sec⁻¹. In the same tissue, Firrell and Lipowsky⁷ reported a more pronounced decrease, reaching less than 10% of rolling leukocytes at γw>400 sec⁻¹. This quantitative disagreement probably can be attributed to the different methods used: Slowly rolling leukocytes are well detected by conventional transillumination,⁷ but the fraction of fast (or intermittently) rolling cells may remain undetected unless stroboscopic fluorescence microscopy is used. This assumption is supported by the velocity distribution of rolling leukocytes measured in the present study. At γw>300 sec⁻¹, almost 20% of the leukocytes clearly interacting with the vessel wall travel at a velocity greater than 300 μm/sec and probably are invisible with transillumination and conventional video techniques. For the very same reason, the present data show an increase of mean leukocyte rolling velocity with increasing wall shear rates, whereas earlier studies⁴,⁷ reported a relatively constant velocity of rolling leukocytes at shear rates above ~100 sec⁻¹. This apparent discrepancy is reconciled by the finding that in the present study, the most frequent velocity of rolling leukocytes was found to be 20–40 μm/sec independent of prevailing shear rates, which is in agreement with the earlier reports.⁵,⁷

The induction of leukocyte rolling involves several steps. First, the cells need to acquire a marginal position in the flowing blood. In small postcapillary venules with diameters just above leukocyte diameter, red cells push the leukocytes toward the wall while overtaking.⁹ This effect depends on the entry condition of the leukocytes, because it is operative only when leukocytes travel in vessels slightly exceeding their own size. In larger venules, red blood cells may form aggregates at low shear rates, which occupy the axial flow portion in the vessel, displacing leukocytes to the marginal regions.¹⁰,¹¹ This mechanism is operative if the composition of the blood plasma permits red cell aggregate formation. However, in rats, aggregation tendency is weak and undetectable with standard aggregometry.²⁷ Both mechanisms of leukocyte margination are more likely to be important in venules than in arterioles. It has been speculated that this difference may favor leukocyte rolling in venules.⁹,¹¹ In the rat microcirculation, we found similar numbers of hydrodynamically margined but noninteracting leukocytes in arterioles and venules: 21% of freely flowing leukocytes traveled within 1 μm of the vessel wall in arterioles; 19% did so in venules. The presence of marginated but noninteracting leukocytes in both arterioles and venules does not rule out the possibility that margination in small postcapillary venules,⁹ which were not investigated in

![Figure 3](http://circres.ahajournals.org/)

**FIGURE 3.** Average velocity of rolling leukocytes (WBC) as a function of wall shear rate in venules. Small symbols: Average rolling leukocyte velocity in each individual venule; large symbols: group averages±SD. Top panel: Average velocity of all rolling leukocytes passing the venules (flux average); bottom panel: average velocity of all rolling leukocytes present in the vessels (volume average).
the present study, may be responsible for the initiation of leukocyte rolling. In view of the finding that flow reversal in small networks of the rat mesentery fails to induce significant leukocyte rolling in arterioles,29 a crucial importance of this entry effect appears unlikely: With flow reversal, the leukocyte enters an arteriole from a small capillary, as it normally does in a postcapillary venule. These findings suggest that although hydrodynamic initiation of leukocyte margination may be a prerequisite, it is not a dominating factor limiting the number of leukocytes interacting with the endothelium.

Because hemodynamic differences have been ruled out as major factors explaining the restriction of leukocyte rolling to venules, endothelial differences between arterioles and venules represent an obvious alternative hypothesis. A variety of endothelial adhesion molecules have been found to be exclusively or preferentially expressed on venular endothelium. GMP-140 (LECAM-3), a member of the LECAM family of calcium-dependent lectinlike cell adhesion receptors, is predominantly expressed in venular endothelium of a variety of tissues and organs.17 Another endothelial member of the same family of adhesion molecules, ELAM-1 (LECAM-2), is preferentially expressed in venules of the skin on induction of delayed hypersensitivity reaction15 and in cytokine-stimulated human skin.16 MECA-79 antigen, which probably represents a ligand for the leukocytic adhesion molecule LECAM-1 (gp90MEL) in high endothelial vessels of peripheral lymph nodes, is found exclusively in venules.18 These findings support the concept of a specialized venular endothelium directing leukocyte adhesion to venules.

Recently, LECAM-1 has been demonstrated to mediate leukocyte rolling in rat mesenteric venules by showing a blocking effect of recombinant soluble LECAM-1.14 The important role of the interaction between LECAM-1 and its endothelial ligand is emphasized by the finding that the recombinant soluble receptor blocks leukocyte recruitment to an inflammatory site.29 In view of these findings, the present data suggest that an as yet unidentified (carbohydrate) ligand for LECAM-1 may be preferentially or exclusively expressed in venules. Leukocyte rolling is known to be absent in mesenteric venules in situ in the absence of inflammation but is rapidly induced (within 1–3 minutes) on mild trauma as associated with exteriorization.30 Earlier studies have demonstrated that the extent of leukocyte rolling decreases after an initial peak at −20 minutes of exteriorization, suggesting that endothelial ligand expression may be regulated.

In conclusion, the present study demonstrates that the restriction of leukocyte rolling to venules is not caused by the existing hemodynamic differences between arterioles and venules. The venular endothel-

FIGURE 4. Velocity histograms of rolling leukocytes, grouped in four shear rate ($\gamma_s$) classes as indicated in each panel. Number of leukocytes ($n$) and venules ($N$) indicated. Most frequent rolling velocity is 20–40 $\mu$m/sec at all shear rates.
lium appears to be particularly prone to supporting leukocyte rolling and adhesion in vivo.

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