Influence of Arterial Damage and Wall Shear Rate on Platelet Deposition

Ex Vivo Study in a Swine Model

Lina Badimon, Juan-Jose Badimon, Angel Galvez, James H. Chesebro, and Valentin Fuster

To study the influence of blood flow on platelet interaction with selected biological surfaces, we have developed an ex vivo perfusion chamber system. In the present experiments, deendothelialized pig aorta and collagen Type I bundles from Achilles tendon were exposed to either native or heparinized pig blood for periods of time ranging from 1 to 30 minutes, and for flow rates corresponding to wall shear rates of 106 to 3380 sec⁻¹. On the deendothelialized vessel wall, platelet deposition increased with both exposure time and wall shear rate, reaching a maximum value between 5 and 10 minutes of perfusion. At high shear rates and long exposure time (over 10 minutes), platelet deposition decreased from maximum values, indicating that some platelets were embolized by the flow. Ultrastructure analysis of the specimens showed platelet activation, spreading, and degranulation. Collagen induced a progressive accumulation of platelets following a power type curve of aggregate growth with exposure time without reaching a saturation level, even after long perfusion times (30 minutes) and high wall shear rates (3380 sec⁻¹). In conclusion, the reactivity of the exposed materials and the local shear rate, defined by the blood flow and the patent luminal cross section, regulate platelet deposition to injured vascular wall. (Arteriosclerosis 6:312–320, May/June 1986)

It is well known that hemodynamic parameters of blood flow, such as diffusion, convection, velocity, shear rate, and shear stress, determine the interaction of the formed elements with vessel walls and prosthetic implants in the cardiovascular system. Such parameters are therefore important in the platelet reaction to artificial or biological surfaces in the circulatory tree.

The substrate itself also may act as stimulus for the activation of the platelet and may play an important role in the final outcome of the platelet response. In our experimental model of carotid angioplasty, we have shown that as soon as the procedure, mural thrombus formation is directly related to medial tear; the exposed media stimulates platelet aggregation and thrombus formation, even in fully heparinized animals. Conversely, in areas of deendothelialization without medial rupture, only discrete mono- or bilayers of platelets were seen. Deeper rupture of vascular surfaces exposes collagen fibrils normally not present on subendothelial surfaces; thus the major distinction in this model may be related to the surface stimulation.

In this study, we have investigated the effect of blood flow on platelet deposition: 1) to mildly injured vessel wall, as may occur in the early phases of arterial disease; and 2) to collagen Type I, a model of fibrillar collagen that may occur in severe arterial injury such as in disrupted advanced atherosclerotic plaque.

Methods

Experimental Model

The animals studied were normal pigs, Yorkshire albinos (n = 45; body weight = 23 ± 4 kg) obtained from local farmers. All procedures performed in this study were approved by the appropriate institutional guidelines for animal research.

Deendothelialized Vessel Wall

We used a modification of Fischman’s method⁶ to produce deendothelialization. Each animal was deeply anesthetized by an intramuscular injection of 25 mg/kg of ketamine (Ketalar, Parke Davis, Morris Plains, New Jersey) plus 1 mg/kg of xylazine (Rompun, Miles Laboratory, Shawnee, Kansas) and was intubated. The aorta was exposed, and all branches were ligated. The animal was then euthanized by an overdose of pentobarbital sodium solution (Fort Dodge Laboratories, Fort Dodge, Iowa). Simultaneously, a cannula was inserted in the aortic arch and at
the trifurcation of the abdominal aorta. A buffer solution, Tris HCl 0.01 M, was perfused to clear the vessel of blood, and an airstream was then passed through the aorta at a rate of 1000 ml/min for 10 minutes. The aorta was immediately removed and placed in ice-cold Tris buffer. This procedure induced selective endothelial injury without damaging the basement membrane. The absence of endothelium was demonstrated by "en face" staining with silver nitrate.

Pieces of aorta 3 cm in length and 2 cm in width were prepared for use in the perfusion chamber. The aortas, stored in Tris buffer with antibiotics (penicillin and streptomycin) at 4°C, were used within 3 weeks of harvesting.

Collagen Strips

Collagen strips from pig Achilles tendon Type I collagen bundles were obtained after the sacrifice of normal animals. The tendons were dissected, cleaned of surrounding connective tissue, and stored in divalent ion-free Tyrode's buffer. Immediately prior to an experiment, strips 3 cm in length were separated to be placed in the chamber.

Perfusion Chamber

Several cylindrical plexiglass chambers were designed to mimic the tube-like shape of the vascular system. The cylindrical channel of the flow chamber through which blood circulates was machined so that a portion of the circumferential wall (25 mm in length, 1 mm in width) was removed. The resulting "window" permitted direct exposure of the test surface. The substrate was held in place by the pressure of the upper lid on the lower core. The superfusion chamber was immersed in an outer chamber (water bath) through which water at 37°C was continuously circulating (Figure 1). Two chambers of different internal diameters (1.0 or 2.0 mm) were constructed to obtain a broad range of wall shear rates on the substrate with moderate changes in average blood flow rate.

Experimental Procedure

The pigs were anesthetized by injecting a mixture of ketamine (25 mg/kg) and xylazine (1 mg/kg), and the carotid artery and contralateral jugular vein were cannulated. Blood samples were collected to determine hematocrit (29% ± 1%) and platelet count (444, 276 ± 44, 791/μl) (x ± se), and then the pigs were intravenously heparinized (300 U/kg) (Liquemin 10,000, Roche Laboratories, Nutley, New Jersey). The cannulated carotid artery was connected by polyethylene tubing (20 cm in length, Clay Adams PE 200, Cole-Palmer, Chicago, Illinois) to the input of the plexiglass chamber. The output of the chamber was connected to a peristaltic pump (Masterflex Model 7013) (Figure 2). Blood that passed through the chamber was recirculated back into the animal by the contralateral jugular vein. At the beginning of the experiment, a deendothelialized vessel wall or a collagen strip was mounted in the chamber. The specimens were perfused with Vassar saline solution, at 37°C for 60 seconds. After the preperfusion period, blood entered the chamber at a preselected flow rate for times ranging from 1 to 30 minutes. At the termination of blood flow, buffer was again passed for 30 seconds through the chamber under identical flow conditions. The changes from buffer to blood and vice-versa were achieved by a switch valve without the introduction of stasis in the chamber. The selected flow rates were 5, 10, and 20 ml/min in the small and large chamber. These blood flows gave theoretically calculated average blood velocities from 2.65 to 42.3 cm/sec, and local shear rates from 106 to 3380 sec⁻¹, that is, shear rates ranging from those of large arteries to those of terminal arterial branches and the microcirculation. Within these shear rates, blood can be considered as having Newtonian fluid properties with constant viscosity. Shear conditions at the vessel wall were calculated from the expression for shear rate given for a Newtonian fluid in tube flow.

Figure 1. Photograph of the perfusion system. Blood flows from the carotid artery through the chamber, which is immersed in a 37°C water bath, regulated by a distal pump (not shown).

Figure 2. Unassembled plexiglass superfusion chamber. A. Chamber with cylindrical channel for blood circulation. B. Lid of the chamber. C. Holder of the chamber. D. Outer water bath.
Using the method we previously described, we calculated the number of platelets deposited on each specimen from the platelet count and the \(^{111}\text{In}\) activity on the perfused area and in blood. Results were normalized by area of exposed surface.

**Radioactive Labeling of Platelets**

Approximately 24 hours before the perfusion experiments, autologous platelets were labeled with \(^{111}\text{In}\) (tropolone)\(_3\) by a modification of our previously described technique. In brief, \(^{111}\text{In}\)-tropolone was prepared from \(^{111}\text{In}\)-chloride (Medi-Physics Incorporated, South Plainfield, New Jersey) by the addition of 50 \(\mu\)g of tropolone dissolved in 50 \(\mu\)l of saline to 500 \(\mu\)Ci of \(^{111}\text{In}\)-chloride. This solution was mixed with 1 ml of platelet-free plasma (PPP). Platelets were harvested from 43 ml of blood and were collected by venipuncture into 7 c.c. of modified ACD-solution. The isolated pellet of platelets was resuspended in 2 ml of plasma (PRP). The \(^{111}\text{In}\)-tropolone complex was added to the PRP mixture and the solution was incubated at 37\(\circ\)C for 20 minutes. Free \(^{111}\text{In}\) was removed by washing with 4 ml of PPP. The final pellet of labeled platelets was resuspended in 4.5 ml of PPP and was injected into the animal after a low spin centrifugation to remove any microaggregates. The labeling procedure required approximately 2 hours. The average efficiency (platelet incorporated activity/initial activity added \(\times 100\)) of platelet labeling in plasma was 55\(\%\) \(\pm\) 0.5\(\%\) (\(x \pm se\)). An average indium plasma activity of 3.7 \(\pm\) 0.7\(\%\) (\(x \pm se\)) was measured just before injection of the platelet concentrate. The injected activity was 212 \(\pm\) 12 \(\mu\)Ci (\(x \pm se\)), and 3 \(\times\) \(10^6\) \(\pm\) 2 \(\times\) \(10^5\) per \(\mu\)l of \(^{111}\text{In}\)-labeled platelets (\(x \pm se\)) were injected in a volume of 4.5 ml of plasma.

**Ultrastructural Analysis of Specimens**

The specimens, vessel wall and collagen strips, were fixed in a mixture of 3% glutaraldehyde in 0.2 M cacodylate buffer (pH 7.4) immediately after removal from the chamber. For scanning electron microscopy, specimens were dehydrated by processing through a series of ethanol solutions and dried with carbon dioxide by the critical point method. The dried tissue was coated with 100 \(A\) of gold-palladium and carbon and examined under an ETEC Autoscanning electron microscope. Representative sections were photographed with Polaroid 55 P/N film.

For transmission electron microscopy, specimens were fixed in 1% OsO\(_4\), were stained in block with 2% aqueous uranyl acetate, were dehydrated with ethanol, and were embedded in Epon 812. The specimens were examined under a Philips 201 transmission electron microscope, and representative sections were photographed with Kodak electron microscope film 4463.

**Biodistribution of Indium-111-Labeled Platelets**

At the end of the perfusion experiment, approximately 24 hours after the intravenous injection of \(^{111}\text{In}\)-labeled platelets, the animals were euthanized and the heart, lungs, liver, spleen, kidneys, and blood were isolated and weighed. The radioactivity of weighed portions of these organs was measured (Beckman, Gamma 800) and the organ biodistribution was determined. The percentage of injected radioactivity in the viscera was then calculated. Blood volume was considered as 8.2\% of the body weight.

**Statistical Analysis**

The results were statistically analyzed for the best bivariate data model fitting and the unpaired t test when applicable. Variance about the mean is given as \(\pm 1\) se (standard error of the mean).

**Results**

Blood was exposed to deendothelialized vessel wall and fibrillar Type I collagen for flow rates of 5, 10, and 20 ml/min in a small (0.1 cm) and large (0.2 cm) diameter perfusion chambers for exposure times ranging from 1 to 30 minutes. The shear rates at the test surfaces (wall shear rates) corresponded to 1690 to 3380 sec\(^{-1}\) in the small chamber and 106 to 212 sec\(^{-1}\) in the large chamber. The values of platelet deposition on the two surfaces were determined by radioactive evaluation of the total test surfaces and by electron microscopy.

**Platelet Deposition on Deendothelialized Vessel Wall**

The exposure of deendothelialized vessel wall to blood flow at a low shear rate, 106 and 212 sec\(^{-1}\), induced platelets to adhere to the exposed vessel. The deposition of platelets reached a maximum within 5 to 10 minutes of exposure, after which platelet accumulation remained relatively constant (Figure 3). At the maximal deposition, the number of platelets on the vessel ranged from 7 \(\times\) \(10^6\)/cm\(^2\) to 10 \(\times\) \(10^6\)/cm\(^2\).

At the high wall shear rate, 1690 sec\(^{-1}\), initial platelet deposition rate was higher than at the lower shear rate. Maximum platelet deposition was also observed at 5 to 10 minutes of exposure. However, at longer exposure times (20 to 30 minutes), platelet deposition decreased to values not significantly different from those at the lower shear rates for the same exposure times. At the maximum platelet deposition the number of platelets deposited ranged from 12 \(\times\) \(10^6\)/cm\(^2\) to 16 \(\times\) \(10^6\)/cm\(^2\) (Figure 3).

![Figure 3. Platelet deposition on deendothelialized vessel wall versus exposure time at different wall shear rates. Wall shear rates (sec\(^{-1}\)): △ = 1690; ⋄ = 212, and ○ = 106.](image-url)
Table 1. Regression Lines of Platelet Deposition vs Time of Superfusion of Collagen at Different Shear Rates

<table>
<thead>
<tr>
<th>Shear rate (sec⁻¹)</th>
<th>Intercept</th>
<th>Slope</th>
<th>r</th>
<th>p</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>3380</td>
<td>203</td>
<td>0.909</td>
<td>0.848</td>
<td>&gt;0.01</td>
<td>8</td>
</tr>
<tr>
<td>1690</td>
<td>12.8</td>
<td>1.456</td>
<td>0.810</td>
<td>&gt;0.001</td>
<td>18</td>
</tr>
<tr>
<td>212</td>
<td>3.9</td>
<td>1.22</td>
<td>0.963</td>
<td>&gt;0.001</td>
<td>16</td>
</tr>
</tbody>
</table>

Values are expressed as \( y = bx^n \).

At short exposure times (1 to 10 minutes), platelet deposition increased with respect to the local shear rate of the circulating blood on the vessel (Figure 4). At longer exposure times, the accumulation of platelets appeared to reach a plateau and be unaffected by shear rate; presumably the platelets that had accumulated at shorter superfusion times had been dislodged by the blood flow (Figure 4).

**Platelet Deposition on Type I Collagen**

Platelet deposition on collagen fibers (Type I) was considerably increased compared with that observed on the vessel wall (Figure 5). The number of platelets deposited was more than two orders of magnitude greater than in subendothelium \(10^6\) to \(10^9\)/cm². The bivariate best fitting equation for the growth rate of platelet deposition versus exposure time followed a power curve \( y = bx^n \), with statistically significant regression coefficients (Table 1). Even at a very high wall shear rate, 3380 sec⁻¹, platelet thrombi on the superfused area were not dislodged but remained adherent to the surface. Platelets accumulated monotonically on the tendon as a function of exposure time and wall shear rate (Figure 6). Occasionally, platelet thrombi completely spanned the lumen of the chamber, without being removed by the blood flow.

**Ultrastructure of Superfused Specimens**

Transmission electron microscopy of deendothelialized aortic wall indicated that the basement membrane was not overtly damaged by the deendothelialization procedure. Platelet deposition was dependent on shear rate and time.
At low shear rates (102 sec\(^{-1}\), 212 sec\(^{-1}\)) and short exposure time (1 to 5 min), platelets were scattered on the subendothelial surface; at longer times (10 to 30 min), platelets formed patchy deposits of mono- or bilayers but without complete activation, as indicated by the absence of pseudopodia formation and the presence of granular material. At high shear rates (812 sec\(^{-1}\), 1690 sec\(^{-1}\)) and short exposure time, a similar pattern was observed, but platelet degranulation and spreading were more extensive. At 10 to 15 minutes of exposure, more platelets were seen and they were completely spread, uniformly covering the subendothelium (Figure 7).

Scanning electron microscopy of platelet deposits on collagen showed platelet aggregates at all shear rates and exposure times. Platelets showed complete activation, shape change, and pseudopodia (Figure 8). Transmission electron microscopy showed platelet thrombi with extensive degranulation and even lysis of platelets which contacted the collagen fibers, and some granulated platelets toward the outer parts of the thrombi (Figure 9).

**Organ Distribution of Indium-111**

To check if the recirculation of blood produced any substantial platelet damage, we studied the platelet distribution in different circulatory beds. \(^{111}\)Indium-111 platelet distribution in different organs was studied postmortem, 24 to 30 hours after \(^{111}\)Indium-labeled platelets were injected. About 48% of radiolabeled platelets were found in the systemic circulation; the remainder was localized in liver, spleen, lungs, kidneys, and heart (Table 2). These results were also compared with a group of animals sacrificed between 24 and...
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30 hours after $^{111}$In-labeled platelet injection but which were not used for perfusion experiments (i.e., their blood was not exposed to foreign materials in an extracorporeal circuit). The results were not significantly different from those of the test animals (Table 2).

Hematologic and Labeling Parameters

The platelet count and hematocrit did not change throughout the experiment (Table 3). Indium plasmatic activity was also unchanged. Some samples were evaluated pre- and postpump, and no difference in platelet lysis or platelet count was found. The gamma emission of the cannula inserted in the carotid artery of the animal was not significant.

Discussion

We have investigated the interaction of pig platelets with deendothelialized vessel wall and collagen both obtained from swine in a tubular perfusion chamber designed to simulate intravascular flow conditions. We have quantified platelet deposition on the surfaces by $^{111}$In-labeling of autologous platelets 24 hours before the ex vivo exposure of heparinized pig blood to the test surfaces. We observed that the platelet response to a damaged vessel wall is the result of two important factors: the nature of the exposed wall components and the hemorheological conditions to which the wall is exposed.

Table 2. Organ Distribution of Indium-111 Platelets

<table>
<thead>
<tr>
<th>Pig group</th>
<th>Liver (%)</th>
<th>Spleen (%)</th>
<th>Lung (%)</th>
<th>Heart (%)</th>
<th>Kidney (%)</th>
<th>Blood (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test (n = 21)</td>
<td>27.5</td>
<td>14.8</td>
<td>9.8</td>
<td>6.2</td>
<td>0.19</td>
<td>47.5</td>
</tr>
<tr>
<td>Control (n = 21)</td>
<td>25.5</td>
<td>14.9</td>
<td>9.8</td>
<td>6.4</td>
<td>0.21</td>
<td>49.1</td>
</tr>
</tbody>
</table>

Values are means ± SE.

Table 3. Control Testing throughout the Perfusion

<table>
<thead>
<tr>
<th>Time of test</th>
<th>Platelet count ($\times 10^9/\mu l$)</th>
<th>Hematocrit (%)</th>
<th>$^{111}$In-plasmatic activity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preheparin</td>
<td>421 ± 42</td>
<td>30 ± 0.7</td>
<td>4.6 ± 0.6</td>
</tr>
<tr>
<td>Postheparin</td>
<td>408 ± 46</td>
<td>30 ± 0.2</td>
<td>—</td>
</tr>
<tr>
<td>Beginning</td>
<td>432 ± 114</td>
<td>29.4 ± 1.2</td>
<td>5.3 ± 1.4</td>
</tr>
<tr>
<td>End</td>
<td>432 ± 73</td>
<td>31 ± 1.2</td>
<td>3.3 ± 0.6</td>
</tr>
</tbody>
</table>

*Sequential samples were analyzed at different time intervals subsequent to the initiation of the perfusion up to its completion, and these measurements were at no time significantly different from baseline values.

Values are means ± SE.
Platelet Deposition

Platelet deposition on deendothelialized vessel wall is a shear-dependent event (Figure 3 and 4). Platelet deposition increased with wall shear rate. However, at high shear rates and long exposure times, platelet deposition decreased from that measured at short times, indicating that some platelet deposits had been dislodged by the flow. At long times, the remaining platelet layer was similar in magnitude to that observed in vessels exposed to low shear rates. Consequently, when collagen fibrils were exposed to blood platelets, deposits continued to increase with increasing exposure time, indicating that the rate of platelet removal was always considerably less than the attachment rate. On the fibrils, the aggregates developed into large platelet thrombi. The net platelet deposition rate was also directly related to the wall shear rate and the increase in platelets followed a power-type curve (Figures 5 and 6).

Surface Factors

In these experiments, the predominant effect on the deposition of blood platelets was due to the nature of the surface. Type I collagen developed a deposit of platelets that was two orders of magnitude greater than that observed on deendothelialized vascular wall. On the collagenous surface, platelets were seen to spread, degranulate, and attach to other platelets, and these attachments were resistant to removal by shear forces for exposure times up to 30 minutes. Conversely, platelet attachment to the deendothelialized vessel segments was more limited in nature. Aggregates of platelets that formed at high shear were dispersed with prolonged exposure time; however, a layer of platelets was always present on the surface.

A comparison of platelet response to subendothelium and a-chymotrypsin digested vessel has been reported by Baumgartner et al. in a citrated blood annular perfusion system in vitro. The platelet deposition on the digested vessels, which consist primarily of collagen fibrils, was much greater than that on the subendothelium in which amorphous collagen is normally exposed, as we have observed in the present study.

A factor that might influence the difference between the collagen Type I fibrils and deendothelialized vessel segments is the level of platelet inhibitory postanoid substances produced by the vessel smooth muscle cells. Pig vessel wall, as well as human, rabbit and rat vessel walls, produce a significant amount of prostacyclin (measured as 6-keto-PGF\(_1\alpha\)) when freshly removed; however, the quantity produced rapidly decays with storage at 4°C in Tris buffer (unpublished observations). Although all vessels used in this study were stored from 5 to 21 days before usage, a small but measurable level of 6-keto-PGF\(_1\alpha\) was present in the deendothelialized vessels and may contribute to the reduced deposition of platelets on the surface of mildly injured normal vessel wall.

Blood Flow Factors

Blood flow conditions directly influence the arrival and removal rates of platelets at the surface. In our perfusion system, the flow conditions are well-defined and platelets deposit on both deendothelialized vessel wall and collagen fibrils in quantities that increase with local shear rate (Figures 3 to 6). Our methodology does not distinguish between attachment and removal, and, in general, the influence of flow in removing platelets from surfaces is relatively unexplored. However, we have observed on deendothelialized vessel wall that the direct attachment, or adhesion, of platelets to the vascular surface (platelet-subendothelial interface) is apparently irreversible, but platelet-platelet interactions (aggregates) formed at high wall shear rate and short exposure time are dislodged or embolized by the flow. Collagen, however, does not show the same rheological behavior. High shear rates are unable to dislodge significant quantities of platelet thrombi, and deposits continue to increase with exposure time (Figure 5).

Perfusion System

Perfusion Chamber

In our system, flow rate is controlled by a distal peristaltic pump that produces at the test surface a wide range of shear rates under laminar flow conditions. The lateral exposure of the biological test material to the blood that flows through a tube-like channel is intended to simulate the intravascular conditions in vivo. The design allows the exposure of both prosthetic rigid materials (unpublished results) and seeded matrices in addition to biological surfaces. Blood exposure to foreign surfaces other than the chamber is minimal in this system. Measurements indicate that there is no quantitative change in platelet count, hematocrit, or platelet \(^{111}\)In-release due to passage through the extracorporeal circuit. The organ distribution of \(^{111}\)In-platelets after the experiment also was not significantly different from animals not used in such perfusion experiments, indicating that there is no gross irreversible platelet microaggregate formation due to the recirculation of blood in the system (Table 2).

Autologous Platelet Labeling

Platelet labeling with \(^{111}\)Indium, the maintenance of platelet function after the labeling process and the experimental and clinical application of the procedure have been previously reported. Labeling of platelets in plasma has been performed to eliminate passage of the platelet pellet to buffered medium, thereby reducing the manipulation of the platelets. By labeling platelets, we have been able to objectively quantify the results of platelet deposition on the test surface. Since this determination does not distinguish between adhesion and aggregate or thrombus formation, we have performed morphologic studies of the platelet deposits by electron microscopy.

Anticoagulant

The setting of an extracorporeal circuit required the use of an anticoagulant. We used heparin, the most commonly used anticoagulant for in vivo procedures. We did not observe any thrombocytopenic effect (Table 3). Results reported by Baumgartner and in our laboratory (unpublished observations) with native blood, without anticoagu-
lation, indicate that platelet deposits in native or heparinized blood are more similar than those obtained in citrated blood, the most common in vitro anticoagulant.

**General Considerations**

Our results suggest that platelet deposition, and consequently the growth of platelet thrombi, may be regulated both by the exposure of the fibrillar collagen, which will act to irreversibly aggregate platelets, and the potent luminal cross-sectional area of the vessel, which will regulate the local shear conditions. Both factors may play an important role in certain clinical conditions. When an atherosclerotic plaque is disrupted spontaneously or by angioplasty, fibrillar collagen and connective tissue are exposed to the circulating blood. In addition, the luminal cross-sectional area patent to the blood flow, will be variable. It appears from our studies that the nature of the surface will determine the overall stability of the thrombus, whereas the local flow conditions will influence the rate of growth of the platelet deposits. In any case, it can be expected that a layer of platelets will remain firmly adherent to any injured area. These platelets, either directly (platelet thrombosis) or through release of growth factors, may be responsible for the accelerated rate of restenosis observed in certain angioplasty studies.

Hamodynamic forces and disturbed flow conditions are indeed factors favoring the thrombotic process as a complication of advanced atherosclerosis. It seems they are also of considerable importance in both the initiation and localization of early atherosclerotic lesions. It has been suggested that there is a causative relation between arterial hemodynamics and the development of vessel injury which produces the platelet response. Hemodynamics is consequently a significant aspect of atherogenesis as well as of the complications of developed atherosclerosis.

This experimental model, which simulates physiological conditions in defined areas of the vasculature, may be of importance in evaluating the potency of various anti-thrombotic agents and platelet-inhibitory drugs.

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