THE THREAT posed by coronary vasospasm for the initiation of myocardial ischemia or infarction is assumed to depend on the degree to which the reduction in transmural diameter results in the interference with coronary blood flow. Further, it is thought that the thrombosis that may accompany vasospasm is a result of the grossly reduced blood flow secondary to a critical vascular constriction and that the interaction of platelets with a damaged vascular wall, with the ensuing release reaction, may further potentiate the coronary spasm. In the present report we present evidence from scanning electron microscopic (SEM) studies that indicates that marked endothelial damage, extensive platelet deposition and thrombus formation may occur at the site of a focal arterial constriction even when the reduction in transmural diameter is insufficient to alter flow substantially.

Methods

Fifteen New Zealand white rabbits (3.1 ± 0.4 kg, mean ± SD) were anesthetized with sodium pentobarbital (30–35 mg/kg, administered intravenously) and both common carotid arteries exposed. Four adult mongrel dogs were anesthetized as above and artificially ventilated with a Harvard positive-pressure respirator. After a median sternotomy, the pericardium was incised and the proximal portion of the left anterior descending coronary artery (LAD) exposed. After occlusion of side branches, when necessary, an electromagnetic flow probe (model EP 406, Carolina Medical Electronics) was placed on the right common carotid artery (RCCA) (external diameter 2.0 ± 0.1 mm) of each of the rabbits of groups 1 and 2 (fig. 1) at the level of the second to third tracheal ring and on the proximal portion of the LAD of each dog (external diameter 2.3 ± 0.2 mm).

Group 1

The RCCA of five rabbits and the LAD of two dogs were focally constricted 1 cm proximal to the probe by partial ligation with suture thread (0-cotton) to achieve a 50% reduction in transmural diameter (fig. 1). The desired degree of luminal constriction was achieved by the apposition of two points on the suture thread; the distance between these points was calculated from the vascular circumference, with the wall thickness (0.1 mm) considered negligible. The diameters were confirmed during SEM examination and varied from 40–60% luminal reduction.

Group 2

In a second group of five rabbits and two dogs, a second ligature was placed 1 cm proximal and immediately before the first (fig. 1). This second ligature
was applied to achieve an 80% reduction of luminal diameter (later confirmed as varying between 70 and 90%).

Group 3

In five additional rabbits, the partial ligation of the RCCA was preceded by total proximal occlusion of the artery with a Heifetz clip9 for 1 hour (fig. 1). The Heifetz clip was used to achieve a 100% reduction of luminal diameter and a total obstruction of blood flow, using a device that is easily removable to permit adequate perfusion fixation.

The partial constriction was maintained for 1 hour in all animals.

Blood flow was continuously monitored with a Carolina square-wave electromagnetic flow meter (model 501 D). Before each experiment, the flow probe and meter were calibrated using the internal electronic calibration system and by comparison with a system of known flow rate. Aortic blood pressure and heart rate were monitored by way of a cannula inserted into the descending aorta via the femoral artery. Carotid or coronary blood flow and aortic blood pressure were recorded simultaneously beginning 15 minutes before constriction. Arterial Po2, Pco2 and pH were determined from blood withdrawn just before terminating each experiment using a Corning 175 Automatic pH/Blood Gas System.

For SEM study, the carotid and coronary arteries were fixed in situ by perfusion of 1.6% glutaraldehyde in 0.08 M Sørensen’s phosphate buffer (pH 7.4, 320 mosmol/l, room temperature, 110 mm Hg) without prior exsanguination. Perfusion of the rabbit carotid arteries was achieved by way of a cannula inserted via the left ventricle into the ascending aorta, and the coronary arteries were perfused by way of a cannula inserted retrogradely through the ascending aorta into the sinus of Valsalva. At the onset of perfusion, the right atrium was opened and drained throughout the perfusion. In group 3, the Heifetz clips were removed immediately before the onset of perfusion. Both common carotid arteries, the LAD, and the circumflex coronary arteries were then excised, immersed in 2.5% glutaraldehyde in 0.1 M phosphate buffer for at least 24 hours, and processed for SEM studies by the critical point drying technique.4 The arteries were then opened longitudinally into three or four parts, mounted on aluminum studs, coated with gold palladium, and examined with a Cambridge S-180 scanning electron microscope.

The structural integrity of the endothelial lining was assessed for each segment of the RCCA and LAD (fig. 1) as well as the contralateral control left carotid and circumflex coronary arteries.

The frequency of occurrence of crater- and balloon-like vesicular defects was determined for each segment as follows: To maintain homogeneity of data, only segments of the rabbit carotid arteries were considered for this analysis, and only these data are included in table 1. Craters and balloons were counted in a series of 30 random SEM fields of equal area at 1000 × magnification for each of the arterial segments shown in figure 1. These fields were selected at 100 × magnification, which is below that which permits detection of these endothelial alterations. Fields that contained areas of desquamation were disregarded for this analysis. Craters and balloons were grouped together for this analysis on the basis of previous SEM and transmission electron microscopic studies, indicating that craters actually represent balloons whose limiting membrane had collapsed or ruptured.6 Comparisons between the total number of craters and balloons between arterial segments of the same group or between corresponding arterial segments of
Table 1. Average Number of Craters and Balloons for Each Arterial Segment Indicated in Figure 1

<table>
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<th>Distal slope of CA</th>
<th>Distal slope of CA</th>
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*Constriction A.
†Constriction B.
‡Control, left common carotid artery.
§Mean ± SD of total number of craters and balloons in 30 random scanning electron microscopic fields (magnification × 1,000) for five rabbits. Each microscopic field at this magnification reflects an endothelial area of 5,110 μm² (0.012 mm²).

Analysis of arterial blood samples withdrawn before and after balloon inflation in each animal indicated that the mean arterial blood pressure in the control group was 80.9 ± 6.3 mm Hg, and the mean blood pressure in the experimental group was 80.9 ± 6.3 mm Hg.

Results

Scanning Electron Microscopic Studies

Endothelial craters and balloons were found in greatest concentration on the proximal slope of the arterial constriction. Unlike endothelial desquamation, however, craters and balloons were also found in adjacent segments of these vessels, even in arterial segments that were not subjected to arterial constriction. In these experiments, the degree of arterial constriction was assessed by measuring the diameter of the lumen at various points along the artery before and after the balloon was inflated.

In each case, there was a significant reduction in lumen diameter, accompanied by an increase in the number of craters and balloons. In addition, the degree of arterial constriction ranged from 40% to 60%, with the mean constriction rate being 50%. The decrease in lumen diameter and the increase in the number of craters and balloons were statistically significant (p < 0.001).

The frequency of occurrence of craters and balloons in the arterial segments subjected to arterial constriction (table 1) was significantly greater than that of craters and balloons in the arterial segments subjected to balloon inflation (figs. 2 and 3). At these sites, marked endothelial damage was evident, with platelet aggregation, subendothelial cell damage, and platelet adhesion to exposed subendothelial structures. These changes were not evident in the arterial segments subjected to balloon inflation (figs. 2 and 3). The degree of arterial constriction ranged from 40% to 60%, with the mean constriction rate being 50%. The decrease in lumen diameter and the increase in the number of craters and balloons were statistically significant (p < 0.001).

In each case, there was a significant reduction in lumen diameter, accompanied by an increase in the number of craters and balloons. In addition, the degree of arterial constriction ranged from 40% to 60%, with the mean constriction rate being 50%. The decrease in lumen diameter and the increase in the number of craters and balloons were statistically significant (p < 0.001).
FIGURE 2. Luminal surface of one of four longitudinal sections of the right common carotid artery of a rabbit subjected to 50% reduction in transluminal diameter for 1 hour (see figure 1, group 1). (A) Low-magnification micrograph of the site of constriction. White arrow indicates the point of maximum constriction. Note thrombus formation (T) just proximal to this site. Black arrow shows direction of blood flow. PS = proximal slope of constriction, depicted in higher magnification (×110) in figure 2C. (B) Higher magnification (×1300) of area of thrombus formation in figure 2A showing a microthrombus, with its component platelets and erythrocytes, attached to exposed subendothelial tissue (CT). (C) Higher magnification (×1400) of area of proximal slope of constriction shown in figure 2A showing numerous endothelial craters (C) and balloons (B). (D) Luminal surface of the nonconstricted portion of the vessel depicted in figure 2A showing normal, well-organized endothelium. Normal endothelium illustrated in this figure was also seen consistently throughout all contralateral control carotid arteries. Arrow shows cell borders; N = nuclear protrusions. Magnification ×1400.

Group 2

In this group, blood flow to the site of the constriction was reduced by application of a proximal ligature (figs. 1 and 4A). Unlike group 1, endothelial desquamation was found (on the proximal slope, segment 7) in only one of seven animals of group 2; in the other six animals, endothelial desquamation was not found at, or in any of the segments adjacent to, the site of constriction (segments 5–8) (figs. 4A–C). However,
endothelial desquamation and secondary platelet attachment were found at the site of the proximal ligature in four out of the five rabbits and in both dogs (figs. 1, 4A, 4D and 4E). At the proximal ligature, the endothelial damage was found routinely at the site of maximum constriction and in adjacent portions of the proximal and distal slopes (segments 10 and 9). In one of the four rabbits, the site of the proximal ligature was totally obliterated by thrombus formation.

The frequency of occurrence of craters and balloons on the proximal slope of the constriction of the vessels in group 2 (fig. 1, segment 7) was markedly less than the corresponding segment of group 1 (segment 3) (p < 0.001) (table 1). In fact, the number of craters and balloons on the proximal slope (segment 7) approached very closely that of the distal slope (segment 6), with the number in the latter segment being less by half (although not statistically significant) than the distal slope of group 1 (segment 2). Nonetheless, the number of craters and balloons on the proximal or distal slope (segments 7 and 6) was still greater, although of borderline statistical significance, than the adjacent, nonconstricted, proximal segment (segment 8; p < 0.1, p < 0.05, respectively) or distal segment (segment 5; p = 0.2, p < 0.1, respectively); and greater than the contralateral control vessels (p < 0.05, p < 0.025, respectively). The number of alterations on the proximal slope of the constriction (segment 7) was also much lower than the corresponding segment of the proximal constriction site of these vessels (segment 10) (p < 0.05), and the numbers of lesions on the proximal slopes of the proximal constriction site (segment 10), where the vessel was constricted by 70–90%, were fewer than the number of lesions in the corresponding segments of the constriction site in group 1 (segment 3) where the diameter was reduced by only 40–60% (p < 0.05). On the other hand, no significant difference was seen between any of the distal slopes in these groups.

**Group 3**

Endothelial desquamation was not found on the proximal slope or in segments adjacent to the site of constriction (segments 12–15) of any of the vessels in group 3 where blood flow was totally obstructed by proximal occlusion with a Heifetz clip. Similarly, the number of craters and balloons on the
proximal slope (segment 14) of these vessels was significantly less than the corresponding segment of group 1 (segment 3), where flow to the site of constriction was not substantially reduced \((p < 0.025)\) (table 1). On the other hand, the number of alterations in the proximal slope segment was greater than that of the corresponding segment of group 2 (segment 7), where flow was substantially reduced but not totally obstructed \((p < 0.05)\).

The number of craters and balloons in the proximal slope segment (segment 14) was greater than that of the distal slope segment (segment 13) \((p < 0.001)\), the
adjacent, nonconstricted segments (segments 12 and 15) \((p < 0.001; p < 0.001, \text{ respectively})\), and the contralateral, control segments \((p < 0.001)\). However, the number of craters and balloons in the nonconstricted segments (segments 12 and 15) of this group (where blood flow was totally obstructed) was also significantly greater than corresponding segments of group 1 (segments 1 and 4), where blood flow was not interrupted at all \((p < 0.025 \text{ and } p < 0.025, \text{ respectively})\), and greater (although of borderline significance) than corresponding segments (segments 5 and 8) of group 2, where blood flow was substantially reduced but not totally interrupted \((p < 0.1 \text{ and } p < 0.05, \text{ respectively})\). This generalized increase in the number of craters and balloons in all segments of the vessels of group 3 compared with corresponding segments of group 2 is consistent with the results of earlier studies that showed that total temporary arterial occlusion for periods of 5 minutes to 2 hours results in numerous endothelial craters and balloons distal to and, to a lesser extent, proximal to the site of the obstruction but without endothelial desquamation or thrombus formation.\(^6\text{ – }^7\)

Flow Studies

**Group 1**

No substantial reduction in blood flow was detected after the 40–60% reduction in transluminal diameter. The mean flow rate before application of the constriction was 17.4 ± 1.0 ml/min (fig. 5) and the flow immediately after constriction was 16.7 ± 0.9 \((p > 0.3)\). The average mean flow rate for the entire hour after constriction was 17.5 ± 2.2 \((p > 0.45)\). In general, only minor fluctuations in blood flow were detected over the course of the 1-hour constriction, but in two animals, single episodes of a rapid transient reduction in flow of 6.0 and 8.0 ml/min were recorded, followed by a rapid return to normal. The time course of these transient reductions in flow was less than 1 minute. The mean aortic pressure and heart rate remained close to control levels throughout the period of constriction (fig. 5).

Similar patterns appeared in flow measurements of the LAD of two dogs subjected to 40–60% reduction in luminal diameter. In the first dog, the mean flow rate of 56.0 ml/min before constriction was virtually unchanged (52.5 ml/min) upon application of the ligature. This flow was maintained until 45 minutes after the constriction, when a slight rise, followed by a rapid drop to 35.0 ml/min, was detected (fig. 6), followed by a second drop 2 minutes later, to 22.5 ml/min. After returning to 32.5 ml/min, flow declined steadily to 17.5 ml/min by the end of the hour. The mean aortic pressure and heart rate before constriction (125 mm Hg, 108 beats/min) remained relatively constant for the entire hour of constriction (122 ± 1 mm Hg, 111 ± 5 beats/min). Similarly, in the second dog, the flow rate of 40.0 ml/min before constriction was virtually unchanged upon application of the ligature (38.5 ml/min), but again, at 30 minutes, it dropped rapidly by 20.0 ml/min and then rapidly returned to normal. This was followed by a steady decline to 25.0 ml/min by the end of the hour. As with the first dog, the mean aortic pressure and heart rate before constriction (105 mm Hg and 100 beats/min) remained relatively constant throughout the hour of constriction (113 ± 4 mm Hg and 97 ± 6 beats/min).

In both dogs, where blood flow was reduced to 30% and 40% of control levels, respectively, by the end of the hour, large thrombi were found during SEM examination on the proximal slope close to the point of maximum constriction (fig. 3).

**Group 2**

Measurements of blood flow through the rabbit carotid arteries subjected to 40–60% reduction in transluminal diameter only after application of a proximal ligature (70–90% luminal reduction) (fig. 1, group 2) revealed a 95% reduction in flow from control levels (fig. 7). The control flow rate of 17.2 ± 2.6 ml/min was reduced to 3.1 ± 1.8 ml/min upon application of the proximal ligature \((p < 0.001)\), with no additional reduction after application of the distal ligature. The mean aortic pressure and heart rate remained at control levels throughout the hour after constriction (fig. 7), indicating that the recorded drop in flow rate was not due to changes in these measurements.
Similar results were obtained from the coronary vessels of two dogs. In the first dog, the flow rate of 35.0 ml/min was reduced to 5.0 ml/min upon application of the proximal ligature (70%-90% constriction).

This flow rate was maintained throughout the hour of constriction (5.2 ± 0.9 ml/min). Similarly, in the second dog, the flow rate of 36.0 ml/min was reduced to 3.0 ml/min immediately after constriction, with the average flow rate for the entire hour remaining at 4.2 ± 0.9 ml/min. In both cases, the aortic pressure of control levels (130 and 112 mm Hg, respectively) was maintained for the entire hour after constriction (130 ± 2 and 102 ± 7 mm Hg, respectively).

**Discussion**

We have shown that a focal partial arterial constriction results in marked endothelial damage at the site of constriction, followed by extensive platelet deposition and thrombus formation when the reduction in transmuralial diameter is insufficient to substantially alter the rate of distal blood flow. This endothelial damage appears as cellular fragmentation and desquamation with exposure of subendothelial tissues or as the "less severe" endothelial craters and balloons. We have shown previously that injury appearing as craters and balloons on SEM represents protruding blebs and vacuoles as seen with transmission electron microscopy. These alterations have been reported after a wide variety of injurious stimuli as well as "spontaneously" at branch orifices, suggesting that these alterations represent a nonspecific reaction of endothelial cells to injury.

We have demonstrated that the carotid or coronary arteries that were subjected to 40-60% reduction in luminal diameter (resulting in no substantial change in the rate of distal blood flow) showed endothelial desquamation and thrombus formation only on the proximal slope (fig. 1, segment 3), particularly in the area just proximal to the point of maximum constriction.
(figs. 2 and 3). The frequency of occurrence of endothelial craters and balloons was also significantly greater on the proximal slope of these constriction sites than on the distal slopes, with the number of craters and balloons in adjacent nonconstricted segments approaching that of the contralateral control. In groups 2 and 3, where a second ligation was placed proximal to and before the first in order to substantially or totally reduce blood flow to the distal constriction site, endothelial desquamation was found in only one of 14 animals, and the number of endothelial craters and balloons was dramatically reduced. This virtually excludes the possibility that the endothelial damage seen at the site of constriction of the vessels of group 1 might be the result in any large measure of mechanical damage associated with the string itself or to specimen handling.

This predilection of endothelial desquamation as well as crater and balloon formation for the proximal slope of the constriction sites of these vessels, and the virtual absence of desquamation and the marked reduction in number of craters and balloons when blood flow was significantly reduced, is suggestive of the mechanical effect of the blood associated with the acutely narrowed arterial segment. This is supported by several reports of functional and structural changes in the endothelial lining associated with areas such as arterial curvatures and "flow dividers" of branch orifices. These sites are normally subjected to increases in magnitude of wall shear stress (force parallel to luminal surface and independent of turbulence) and/or wide variations in the direction of these forces. This suggestion is further supported by studies by Fry, in which an intravascular grooved plug was used to narrow the arterial lumen acutely. Fry reported that when the shear force of the blood approaches $379 \pm 85$ dyn/cm$^2$, the "acute yield stress of the endothelial surface," rapid cellular deterioration occurs and results in focal or widespread endothelial desquamation.

That shear forces of this magnitude might be possible in the present experimental system can be estimated as follows: By applying Poiseuille’s law, shear stress ($\sigma$, in dyn/cm$^2$) may be expressed by $\sigma = 4Q\eta/\pi r^4$ where $Q$ = flow in ml/sec, $\eta$ = viscosity in poise (0.03), and $r$ = luminal radius in cm. For the vessels in group 1, assuming the average luminal radius of the carotid arteries (as confirmed by SEM) to be 0.5 mm at the point of maximum constriction, with the mean flow for all animals after constriction being 16.7 ml/min, the shear stress approaches 85 dyn/cm$^2$. For the coronary arteries, these calculations resulted in shear forces of 231 and 228 dyn/cm$^2$, respectively. These calculations assume steady, laminar flow. Accurate calculations of the shear forces in highly pulsatile arterial systems like these are virtually impossible without knowing the precise velocity profile across the arterial lumen. However, the marked blunting of the velocity profile in circumstances of pulsatile flow leads to a much greater velocity gradient at the arterial wall, especially at sites of arterial constriction, to the extent that it would be reasonable to expect a five- or even 10-fold increase in shear stress in pulsatile flow over that for the same mean flow rate in steady flow. By contrast, the average shear stress at the site of maximum constriction of the vessels in group 2, where blood flow was reduced to a mean of 3.1 ml/min by application of a proximal ligation, and where endothelial desquamation was found in only one out of seven animals, is calculated to be only 15.7 dyn/cm$^2$, with corresponding values for the coronary arteries being 22 and 17.8 dyn/cm$^2$. That endothelial damage was found in one case is not surprising in view of the possibility that a small fluctuation in luminal radius during the experiment could still raise the incident shear force from any of these values to "yield stress" levels.

These observations are of particular significance in view of calculations that forces at or exceeding the yield stress of the endothelial lining may indeed occur in vivo at flow divider areas of branch orifices and at points of arterial curvature or constriction, particularly in areas of the vascular system such as coronary arteries that are frequently subjected to an increased demand for flow. Although desquamation of the endothelium was not found on the distal slope of the arterial constriction, the frequency of craters and balloons was still greater (although of marginal statistical significance, $p < 0.1$) than adjacent nonconstricted segments of these vessels. This increase in endothelial damage on the distal slope of the arterial constrictions is worthy of note because of evidence that, whereas outflow regions of arterial constrictions are usually areas of low wall shear, these sites are nevertheless subjected to increased turbulence.

Turitto and Baumgartner determined that the rate and extent of formation of platelet microthrombi on exposed subendothelium actually increase with increasing shear rate up to the highest shear rate tested of 10,000 sec$^{-1}$. This shear rate is equivalent to a shear force of approximately 200-400 dyn/cm$^2$, which approaches the reported value for the yield stress of the endothelial lining. It is not certain whether shear rates in excess of these studied would continue to favor increased rate and extent of thrombus formation and at what point such shear forces might favor embolization. Nonetheless, the latter report further supports the suggestion that a focal partial arterial constriction is a much favored site for marked endothelial damage, platelet deposition, and thrombus formation, even, and possibly particularly, when the reduction in luminal diameter is insufficient to alter the rate of flow.

In a previous study of cerebral vessels, spasm was induced in the basilar artery of the cat by either mechanical stroking with a blunt probe, by stimulation with bipolar electrodes or by introduction of autologous blood into the adjacent subarachnoid space. As confirmed by SEM, the response to these spasmogenic stimuli was also close to a 50% reduction in transluminal diameter which is equivalent to that achieved by design in the present study. Examination of the luminal surface of these vessels revealed, routinely, marked endothelial cell damage, with platelet deposition and thrombus formation similar in
nature and distribution to that found in the present study.

The results of the present studies are further supported by the report of Folts et al. in which cyclical reductions in blood flow were demonstrated in coronary arteries which were constricted (60–80%) by a circumferentially placed plastic cuff. In the latter study, evidence was presented indicating that these cyclical reductions in blood flow were due to the accumulation of platelet aggregates that further obstructed the already narrowed artery and then were washed free. Although the very regular, cyclical pattern seen by Folts et al. was not detected in the present studies, rapid, transient reductions in flow were seen in four out of the seven animals in group 1 at the frequency of one or two for the hour. Significantly, the platelet deposition and thrombosis at the site of partial arterial constriction in the present study were, with the aid of the SEM, found to be associated with marked endothelial damage in every case.

Considerable evidence has accumulated implicating coronary vasospasm as a major, if not the principal, causative factor in variant angina and as a contributory factor to classic angina pectoris and acute myocardial infarction. It has been assumed that the threat posed by vasospasm for the initiation of myocardial ischemia depends on the degree to which the reduction in luminal diameter results in the interference with distal coronary blood flow. However, the results of the present study suggest a modification of this assumption. We suggest that coronary vasospasm may result in myocardial ischemia and/or infarction as a result of a “critical” vascular constriction, when coronary flow would be dangerously reduced and also as a result of marked endothelial damage that may occur even when the reduction in luminal diameter is not sufficient to substantially alter the rate of distal coronary flow. Such endothelial damage may result in thrombus formation at the site of spasm followed by partial or total arterial occlusion at that site (especially if superimposed upon preexisting arteriosclerosis), or occlusion of smaller coronary vessels distally after platelet shower or embolization.

It has further been assumed that the thrombosis that may accompany vasospasm is a result of the grossly reduced blood flow secondary to the marked vascular constriction. Maseri et al. reported that in two patients with spasm at the onset of infarction, postmortem examination revealed fresh thrombi at the site of spasm. They concluded that sometimes, blood stagnation caused by vasospasm may result in thrombus deposition at the site of damaged intima. Nonetheless, spasm is frequently associated with a reduction in luminal diameter of less than the “critical” level. Moreover, the present studies, considered with those of Fry and Turitto and Baumgartner, suggest that the site of coronary vasospasm may be susceptible to thrombus formation even, and perhaps particularly, when the reduction in vascular diameter is insufficient to alter the rate of distal coronary flow.

That coronary vasospasm might cause episodes of myocardial infarction, which are considered to occur in the absence of angiographically demonstrable coronary pathology, was challenged by Arnett and Roberts. They suggested that, among the possible explanations for the occurrence of myocardial infarction in patients who are subsequently shown to have a “normal” coronary tree, an occluding embolus (rather than spasm) appears to be the most likely explanation. However, the results of the present study support an earlier suggestion that the hypothesis that implicates thrombosis or embolization need not exclude coronary vasospasm as the pathogenetic precursor to those episodes of myocardial infarction that are considered to occur in the presence of “normal” coronary arteries.

Finally, on the basis of the results of the present study and studies of cerebral vasospasm, it is necessary to confirm whether this sequence of increased shear forces, marked endothelial damage and thrombus formation might also occur at sites of arteriosclerotic stenosis, suggesting another cause for a sudden compromise of coronary perfusion. Arterial spasm might itself contribute to the initiation of atherogenesis, again as a consequence of this marked endothelial damage; this possibility should be investigated. This would expand considerably the role of coronary vasospasm in the pathogenesis of classic angina pectoris and acute myocardial infarction.

Acknowledgment

The authors gratefully acknowledge the technical assistance of Iris Sharon, Shmuel Boudin, Dorit Gurfel, Nathan Orgal, and Louise Perez.

References

Endothelial cell damage and thrombus formation after partial arterial constriction: relevance to the role of coronary artery spasm in the pathogenesis of myocardial infarction.

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doi: 10.1161/01.CIR.63.3.476

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