Thrombogenicity and Procoagulant Activity of Human Mesothelial Cells


Cell seeding may decrease the thrombogenicity of implanted vascular grafts, but its application is hampered by the limited availability of autologous endothelial cells. We studied the interaction of alternate cells, human peritoneal mesothelial cells, with whole blood in a flow chamber. When titrated blood was perfused over mesothelial cells, platelet adhesion was seen on the intercellular matrix but not on the cells themselves. Perfusion with blood anticoagulated with low-molecular-weight heparin resulted in fibrin formation at the surface of mesothelial cells but not at the surface of human umbilical venous endothelial cells. At shear rates of 200 sec⁻¹ fibrin deposition on the mesothelial cell surface increased during the first 5 minutes to 5.7±1.06 µg fibrin per square centimeter, whereafter these values stabilized. The procoagulant activity of cultured mesothelial cells was higher than that of peritoneal membrane studied ex vivo. However, cultured mesothelial cells incubated with polyclonal antibodies against tissue factor showed a significant decrease in procoagulant activity. We conclude that human peritoneal mesothelial cells may be used for cell seeding procedures, provided that their tissue factor expression can be controlled. (Arteriosclerosis and Thrombosis 1992;12:1428–1436)

KEY WORDS • mesothelial cells • thrombogenicity • procoagulant activity • tissue factor • cell activation

Despite the significant improvements in prosthetic vascular grafts over the last 30 years, they still perform less well than normal arteries or autologous vein grafts, especially for small-diameter bypass procedures. One of the causes for the inferior performance of prosthetic vascular grafts is thought to be their failure to establish a blood flow-supporting cellular surface. After implantation of a graft the lumen may be reduced by deposition of proteinaceous material and aggregated platelets. Consequently, the blood flow drops and may reach a critical level at which occlusion via thrombosis occurs.

Previous workers have succeeded in seeding endothelial cells on vascular prostheses and have claimed reduced thrombogenicity of the implanted grafts. One of the major problems of endothelial cell seeding, however, is the limited availability of human endothelial cells. With current techniques, the luminal surface area of a donor vein that is needed to effectively seed a graft approximates half the surface area of that graft. In most cases it is then better to use the donor vein directly as a vascular conduit rather than as a source of endothelial cells. Alternative sources of endothelial cells have been studied and include the perinephric, subcutaneous, and omental fat; however, the identity of these cells was not truly established in those studies. Less attention has been paid to other cells that may substitute for cells lining the vascular prostheses. Mesothelial cells from the peritoneum are closely related to endothelial cells and are easily harvested in high numbers from pieces of human omentum. Mesothelial cells of animal origin produce prostacyclin, have fibrinolytic activity, and have been shown to support blood flow. We have carried out an investigation on the thrombogenicity and procoagulant activity of human mesothelial cells and its extracellular matrix under static as well as flow conditions.

Methods

Cell Isolation and Culture

Mesothelial cells were isolated from pieces of omentum obtained during abdominal surgery according to methods modified from those of Nicholson et al and Wu et al. The cells were routinely cultured in tissue-culture polystyrene flasks precoated with fibronectin (10 µg/ml, Sanbio, Uden, The Netherlands). The medium consisted of RPMI-1640 (GIBCO) with 20% pooled human serum and antibiotics. The cells were grown in a fully humidified 5% CO₂ incubator at 37°C. Morphologically, the mesothelial cells formed a confluent monolayer of polygonal cells with a typical cobblestone appearance. The identity of the mesothelial cells was regularly checked by demonstrating the presence of intracellular cytokeratins and absence of von Willebrand factor by using monoclonal antibodies.
Perfusions, Blood Collection, and Anticoagulation

Low-molecular-weight heparin (Fragmin, further abbreviated as LMWH, kindly provided by Kabi, Stockholm, Sweden) with a mean molecular weight of 4,500 and an anti-factor Xa to antithrombin ratio of 4 (165 units/mg anti-factor Xa activity and 40 units/mg anticoagulant activity, as measured by kaolin cephalin clotting time) was diluted in saline (200 anti-factor Xa units per milliliter). Ten parts of venous blood collected by clean venipuncture from healthy human donors was mixed with one part of the heparin-saline solution. Alternatively, anticoagulation was obtained by collecting blood in a 0.1 volume of 110 mM trisodium citrate. Whole blood was kept at room temperature before use in perfusions. All perfusates had a final volume of 17 ml.

Perfusates

The coverslips were rinsed with prewarmed (37°C) 10 mM N-2-hydroxyethylpiperazine-N'-ethanesulfonic acid–buffered saline (HBS, pH 7.4) and placed in the rectangular chamber. Perfusions were carried out under steady-flow conditions as described previously.25 Perfusates that had been prewarmed for 5 minutes at 37°C were circulated for 1, 3, 5, 10, 20, or 30 minutes. Different wall shear rates were obtained by varying flow rates or chamber height and were calculated with the formula used by Muggli et al.26 Exposed glass and Thermox coverslips were gently rinsed with 5 ml HBS and fixed with 0.5% glutaraldehyde in PBS. For the en face evaluation of cell morphology, cell detachment, and platelet adhesion, the coverslips were stained with May-Grünwald/Giemsa. For cross-section evaluation the Thermox coverslips with the exposed surfaces were postfixed with 2% OsO4 and dehydrated by application of increasing concentrations of ethanol. Subsequently, the exposed surface was covered with Epon according to methods published earlier.27 After heat polymerization, the Epon with the embedded matrix, cells, and adhering blood components was separated from the coverslip by thermoshock (fast change of Epon-covered Thermox from a 70°C heating plate to liquid nitrogen) and cut into 1-μm-thick sections. These sections were stained with methylene blue and basic fuchsin to study platelet aggregates and fibrin deposition.22 Flow surfaces embedded in Epon were also processed and prepared for transmission electron microscopy (TEM).

Evaluation

The en face evaluation of cell morphology, cell detachment, and adherence of platelets was performed by light microscopy at ×1,000 magnification. Cell detachment was quantified by counting the number of adherent cells per 10 high-power fields four times before and after perfusion in three separate experiments. Platelet adhesion to the submesothelial matrix was expressed as a percentage of the surface covered with platelets by using an image analyzer (AMS Ltd. 40-10, Saffron Walden, UK). The final percentage was the result of scanning 10 high-power fields in triplicate for three separate experiments.

Cross sections of the various surfaces were also studied for cell morphology, cell detachment, and fibrin deposition and for the presence and precise position of...
adherent or aggregated platelets by light microscopy at \( \times 1,000 \) magnification and by TEM.

**Quantification of Fibrin Deposition**

For experiments quantifying fibrin deposition, the fibrinogen concentration of LMWH-anticoagulated whole blood was determined according to Gauss.²⁸

**Fibrinopeptide A Assays**

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At the end of the perfusion, the coverslips were rinsed with 10 mM HBS, pH 7.35. To avoid nonspecific peroxidase activity on surfaces not exposed to flow, the nonperfused areas of Thermanox coverslips were clipped off, and the remaining parts were developed for peroxidase activity for 30 minutes at room temperature in clean 24-well culture plates (Nunc, Roskilde, Denmark) with 0.5 ml 1,2-phenylenediamine (100 \( \mu \)l of 0.4 mg/ml, 50 mM citric acid, 100 mM Na₂HPO₄, and 0.0015% [vol/vol] \( \text{H}_2\text{O}_2 \), pH 5.0). After a 30-minute incubation the reaction was stopped by addition of 0.25 ml 2N \( \text{H}_2\text{SO}_4 \), and 0.5 ml of the resulting solution was incubated for 4 hours with endotoxin (lipopolysaccharide of *Salmonella minnesota* Re595 [Re mutant], 100 ng/ml)²⁹ or in combination with polymixin B (50 \( \mu \)g/ml, Sigma). All coagulation studies were started by addition of an equal volume of control plasma. The logarithm of the clotting times showed an almost linear relation between the amounts of deposited fibrin. The data were presented in micrograms fibrin per square centimeter.²⁰

**Fibrinopeptide A Assays**

A radioimmunoassay kit (Byk, Zwanenburg, The Netherlands) was used for fibrinopeptide A (FPA) measurements. Samples of 900 \( \mu \)l were collected before and after the perfusions and added to 100 \( \mu \)l anticoagulant mixture provided in the kit. Instructions of the manufacturer were followed. FPA values are expressed in nanograms per milliliter of plasma. FPA generation was calculated from the increase in FPA level compared with the initial value just before perfusion.

**Surface Procoagulant Assays**

Procoagulant activity associated with the cell surface or the matrix was determined by a one-stage clotting assay performed in six-well polystyrene culture plates (Nunc). The cells or matrices were washed three times with PBS at 37°C. Subsequently, the surface was incubated for 1 minute with 1.25 ml Ca²⁺-Michaelis buffer (28.5 mM sodium acetate, 28.5 mM sodium barbital [pH 7.35], 50 mM NaCl, and 33 mM CaCl₂) to which 0.5 ml of thromboplastin suspension (Merz & Dade, Düdingen, FRG) in Ca²⁺-Michaelis buffer (28.5 mM sodium acetate, 28.5 mM sodium barbital [pH 7.35], 50 mM NaCl, and 33 mM CaCl₂) and after the perfusions and added to 100 \( \mu \)l of anticoagulant mixture provided in the kit. Instructions of the manufacturer were followed. FPA values are expressed in nanograms per milliliter of plasma. FPA generation was calculated from the increase in FPA level compared with the initial value just before perfusion.

Perfusions with citrate-anticoagulated blood

Perfusions with citrate-anticoagulated whole blood over confluent cells for 5 minutes at a low wall shear rate (100 sec⁻¹) resulted in a cellular detachment of 7.25±3.1% and 8.9±3% for mesothelial and endothelial cells, respectively. When endothelial and mesothelial monolayers were exposed to a high wall shear rate (1,600 sec⁻¹) for 10 minutes, likewise no significant difference in the cellular detachment (19.8±6.4% and 21.8±9.8%, respectively) was observed. After perfusion, the cell morphology was changed in comparison with unperfused cells; mesothelial and endothelial cells showed retraction and were more darkly stained (Figure 2).

**Results**

**Perfusions With Citrate-Anticoagulated Blood**

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Fibrin deposition was not observed with citrated-blood perfusions. Spread platelets and platelet aggregates were obviously present at intercellular sites of mesothelial and endothelial cells where the extracellular matrix was exposed (Figures 2C and 2D). These platelet aggregates were more prominent after a 10-minute perfusion than after a 5-minute perfusion. No differences in platelet aggregation formation were seen between wall shear rates of 600 sec\(^{-1}\) and 1,600 sec\(^{-1}\). Platelet adhesion to the surface of intact mesothelial or endothelial cells was never observed in cross sections by light microscopy or TEM.

Perfusion over the mesothelial extracellular matrix with citrated blood resulted in platelet aggregates with a longitudinal orientation parallel to the direction of blood flow (Figure 2E). After a perfusion time of 5 minutes at 600 sec\(^{-1}\), 15.4±3.2% (n=3) of the surface was covered with platelets; after 10 minutes, 28.6±6.0% (n=3) was covered. There was no significant difference in surface coverage between shear rates of 600 sec\(^{-1}\) and 1,600 sec\(^{-1}\).

Perfusions With LMWH-Anticoagulated Blood

Perfusions performed with LMWH-anticoagulated whole blood at a wall shear rate of 100 sec\(^{-1}\) for 5
A minute resulted in detachments of 1.7±0.5% and 3.6±3.0% for endothelial and mesothelial cells, respectively. At a wall shear rate of 1,600 sec⁻¹ for 10 minutes, these figures were 15.0±1.7% and 14.5±3%, respectively. In comparison with resting cells, these cells also appeared shrunken and dark but less so than was seen with the citrate-anticoagulated perfusions.

Adherent and spread platelets were rarely seen between the retracted cells after a perfusion time of 1 minute.

After longer intervals only a few platelets were observed between the cells, and aggregate formation remained rare (Figure 3A). From 3 minutes onward, fibers were observed on the surface of and in between mesothelial cells (Figure 3B). Electron microscopic evaluation of these fibers showed transverse bands characteristic of fibrin (Figure 4A). Close contact of the fibrin fibers with cellular membrane foldings was observed. Intracellular vesicles containing fibrin fibers suggest phagocytosis of fibrin fibers by the mesothelial cells. After a 30-minute perfusion, the mesothelial surface was completely covered with fibrin fibers oriented parallel to the direction of blood flow. Only a few platelets with minimal aggregate formation were adherent to the fibrin. No platelets adherent to the mesothelial cell surface could be observed in cross sections. When fibrin was situated at the mesothelial cellular surface, platelet adhesion could be observed at the top of the cell without cellular contact (Figure 4B).

Inhibition of prostaglandin synthesis by acetylsalicylic acid in mesothelial cells just before perfusion did not result in platelet adhesion to mesothelial cells. In addition, the blockade of prostacyclin production was not followed by an increase of platelet adhesion to the fibrin fibers at the mesothelial cellular surface. At the surface of perfused endothelial cells, neither adherent platelets nor fibrin formation could be detected for different perfusion times at different wall shear rates. In between the endothelial cells, adherent platelets with few aggregates were observed (Figure 3C).

FPA was generated during perfusions at 200 sec⁻¹ over mesothelial cells but not over endothelial cells, as shown in Figure 5. After 20 minutes the FPA generation during perfusions over mesothelial cells seemed to reach a plateau (563±70 ng/ml). The FPA generation during perfusions over endothelial cells remained less than 10 ng/ml at all times. Varying the wall shear rate from 100 sec⁻¹ to 1,600 sec⁻¹ did not result in a change in FPA generation (data not shown).

Fibrin deposition on the mesothelial cellular layer exposed to a shear rate of 200 sec⁻¹ increased during the first 5 minutes of perfusion to a level of 5.7±1.06 µg/cm², whereafter the values stabilized (Figure 6). A rapid increase in the FPA concentration determined in parallel was observed during the first 10 minutes of perfusion (to a level of 127±36.4 ng/ml), whereafter a plateau was reached. Fibrin deposition on the mesothelial extracellular matrix was much more pronounced.
FIGURE 4. Transmission electron photomicrographs of cross sections of perfused mesothelial cells. Perfusions were performed with low-molecular-weight heparin-anticoagulated blood at 500 sec\(^{-1}\) for 15 minutes. Panel A: Fibrin at the cellular surface. Note the fibrin fibers, which are engulfed by the mesothelial cell. Bar=0.5 \(\mu m\). Panel B: Platelet at the cell surface. Bar=1 \(\mu m\). m, Mesothelial cell; f, fibrin; p, platelet; n, nucleus.

and reached its maximum within 3 minutes of perfusion at a value of 25.93±2.95 \(\mu g/cm^2\). After this rapid increase the values stabilized. Simultaneously, FPA generation over the matrix increased during the first 10 minutes to a plateau level of 471±33.1 ng/ml.

Procoagulant Surface Activity of Cultured Endothelium, Cultured Mesothelium, and Ex Vivo Peritoneum

The procoagulant activity of cultured endothelium, cultured mesothelium, and ex vivo peritoneum was compared with the surface procoagulant assay. The results are given in Table 1. Clotting times induced by HUVECs were longer than 5 minutes, corresponding to less than 0.0011% thromboplastin expression. The procoagulant activity of confluent mesothelial cells was much higher, with corresponding thromboplastin values of 0.540±0.21%. Addition of polymixin B to the culture medium did not decrease the procoagulant activity in cultured cells (data not shown). Coagulation above the parietal peritoneum revealed a significantly lower thromboplastin value (0.0125±0.0039%, \(p=0.0352\), Student's \(t\) test). Incubation of the peritoneum with endotoxins for 4 hours resulted in a significant rise of procoagulant activity (from corresponding thromboplastin values of 0.024±0.006% to 0.111±0.018%, \(p=0.0001, n=3\)). Addition of polymixin B to the growth medium with endotoxins above the peritoneum normalized the procoagulant activity.

Tissue factor blockade with polyclonal antibodies reduced the surface procoagulant activity of cultured mesothelial cells from 0.54±0.21% to 0.140±0.109% thromboplastin (\(p=0.0473\), Table 1). Incubation of the cell monolayer after the incubation period with the polyclonal antibody revealed that more than 90% of the cells remained. Blockade of tissue factor of the mesothelial extracellular matrix also showed a reduced procoagulant activity from 0.373±0.049% to 0.021±0.017% thromboplastin (\(p=0.006\)).

Discussion

One of the major problems in small-diameter vascular grafting is the high occlusion rate during the first year. It is assumed that this is a consequence of platelet adhesion and activation. A vascular graft that is lined with living cells capable of protecting it against unintentional activation of the hemostatic response would...
sent cell damage by blood flow. Cellular detachment of endothelial cells observed after perfusion may represent the problem of the shortage of endothelial cells. Therefore, we studied the interactions between blood and cultured mesothelial cells and mesothelium ex vivo.

In perfusions with citrated blood we were able to study platelet adherence in the absence of thrombin formation. We showed that human mesothelial cells do not cause platelet adhesion at their cellular surface and in this respect are similar to endothelial cells. The shrunken and dark appearance of both mesothelial and endothelial cells observed after perfusion may represent cell damage by blood flow. Cellular detachment after exposure to flow with citrated blood was similar for mesothelial and endothelial cells and did not exceed 22% after 10 minutes at 1,600 sec\(^{-1}\). The wall shear rates that were used cover the extreme values of wall shear rates that can be expected in a 4–6-mm vascular graft. 23

Detachment of cells resulted in exposure of extracellular matrixes synthesized by these cells. Platelet adhesion and aggregation were observed on cell-free surfaces between mesothelial or endothelial cells. The extracellular matrix produced by cultured endothelial cells has previously been shown to contain von Willebrand factor; fibronectin; thrombospondin; laminin; collagen types III, IV, V, and VIII; and proteoglycans. 24 The extracellular matrix of cultured mesothelial cells has been reported to at least contain collagen types I and III; however, the presence of other matrix proteins has yet to be ascertained. Platelets rapidly adhere to purified collagen types I and III and form aggregates. 25 When the mesothelial extracellular matrix was exposed to citrated blood, 28.6% of the surface became covered with platelets and aggregates, possibly mediated by collagen types I and III in the matrix. The rather high incidence of aggregates on the matrix of mesothelial cells also pointed to an important role of collagen types I and III for platelet adhesion. Perfusion of mesothelial cells and their extracellular matrixes with citrate-anticoagulated blood demonstrated that mesothelial cells have two different surfaces, a nonthrombotic apical surface and an adhesive basal surface. A similar polarity has been reported for endothelial cells. 26

The use of LMWH to prevent anticoagulation of the perfused blood allowed us to study the role of thrombin formation in the interaction of flowing blood with cellular surfaces. Cell detachment was not significantly different between perfusions with different anticoagulated perfusates. In contrast to citrated blood, perfusions with LMWH blood resulted in fibrin deposition on the mesothelial cells. However, platelet adhesion and aggregation to the fibrin network was minimal. Fibrin, however, is a very reactive adhesive surface for platelets. 27 This observation suggests the presence of an

Table 1. Procoagulant Activity of Cultured Mesothelial Cells or Their Extracellular Matrixes, Ex Vivo Peritoneum, and Human Umbilical Vein Endothelial Cells

<table>
<thead>
<tr>
<th>Coagulation surface</th>
<th>Normal pooled plasma (%)</th>
<th>Normal pooled plasma, surface incubated with anti-tissue factor (%)</th>
</tr>
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<tbody>
<tr>
<td>HMCs</td>
<td>0.540±0.21</td>
<td>0.140±0.109†</td>
</tr>
<tr>
<td>MEMs</td>
<td>0.373±0.049</td>
<td>0.021±0.017§</td>
</tr>
<tr>
<td>Peritoneum</td>
<td>0.0125±0.0039*</td>
<td>Not tested</td>
</tr>
<tr>
<td>HUVECs</td>
<td>0.0011±0.0001†</td>
<td>Not tested</td>
</tr>
</tbody>
</table>

Procoagulant activity was determined as described in "Methods." Human mesothelial cells (HMCs) and mesothelial extracellular matrix (MEM) were preincubated for 1 hour with polyclonal rabbit antibody to tissue factor. All values represent mean±SD of three separate experiments and are given as a percentage of a standard tissue factor solution. Each experiment was performed in triplicate. HUVECs, human umbilical vein endothelial cells.

Student's t test at \(*p<0.05, \#p<0.001\) was performed as compared with human mesothelial cells.

Student's t test at \(*p<0.05, \$p<0.001\) was performed as compared with the unincubated surfaces.

**Figure 6.** Line plot of fibrin deposition and fibrinopeptide A (FPA) generation during perfusions over mesothelial cells (○) or mesothelial cellular matrix (●). Perfusions were performed for various periods with low-molecular-weight heparin–anticoagulated whole blood at 200 sec\(^{-1}\). Values were quantified as described in "Methods." Fibrin deposition (—) is expressed in nanograms per milliliter and FPA generation (—) in micrograms per square centimeter. Values are mean±SEM based on three separate experiments performed in quadruplicate.
inhibitor of platelet aggregation that is synthesized by mesothelial cells. Prostacyclin, an inhibitor of platelet activation,\(^9\) is synthesized by mesothelial cells.\(^{12-14}\) However, blockade of prostacyclin production by acetylsalicylic acid did not increase the number of adherent or aggregated platelets on the fibrin network or the mesothelial cellular surface. Endothelial cells have been reported to synthesize another platelet aggregation inhibitor, nitric oxide.\(^{40-41}\) Possibly, nitric oxide plays a role at the mesothelial cellular surface. Further studies need to be done on this interesting observation.

Our experiments demonstrated that coagulation was initiated by cultured mesothelial cells or their matrixes but not by HUVECs. The procoagulant activity of the mesothelial cells and their matrixes was reduced when either antibodies against tissue factor or factor VII-deficient serum was used. These results strongly suggest that the extrinsic pathway of coagulation is activated by monolayers of cultured mesothelial cells as well as by their extracellular matrix. As the procoagulant activity of cultured cells is at least at the same level as that of the mesothelial cellular matrix (Table 1), one would suggest that the procoagulant activity is located on the cellular surface as well as on the cellular matrix. Therefore, one would assume that the initiating factor of the extrinsic pathway, i.e., tissue factor,\(^{42}\) is synthesized by cultured mesothelial cells. Mesothelial cells lining pieces of the abdominal wall, however, expressed significantly less procoagulant activity compared with monolayers of cultured cells (Table 1). Thus, mesothelial cells may change their phenotypic expression during culture. At present, unknown activators that are present under the conditions of artificial culture may stimulate the mesothelial cell to express tissue factor into its cell matrix or cell surface. On the other hand, we observed no in vitro expression of tissue factor by HUVECs under similar culture conditions. HUVECs have been described to synthesize tissue factor on activation by tumor necrosis factor,\(^{43}\) endotoxin,\(^{44-46}\) interleukin-1,\(^{47}\) thrombin,\(^{48}\) and 4β-phorbol 12-myristate 13-acetate.\(^{44}\) Adult arterial endothelial cells have also been reported to synthesize tissue factor during culture.\(^{49}\) Thus, there may be a difference in susceptibility to extrinsic factors between adult cells and neonatal endothelial cells. The addition of polymyxin B to our growth medium had no effect on the procoagulant activity of cultured mesothelial cells. By that observation we ruled out the possible contribution of low levels of endotoxin in the growth medium to the procoagulant activity.

Initiation of coagulation is an undesired effect in cell seeding. Oral anticoagulation therapy with coumarin derivatives has been described to reduce fibrin deposition on reactive surfaces in vitro.\(^{29}\) We do not know whether tissue factor is also expressed on mesothelial cells that are seeded on a graft. When tissue factor expression by seeded mesothelial cells on vascular grafts is temporary (and a quite fully grown monolayer has no tissue factor expression), the procoagulant period can be overcome by treating the patient with oral anticoagulants.

Tissue factor expression by mesothelial cells can also be explained as a defense mechanism of the peritoneal cavity. Peritoneal bleeding or plasma exudation caused by trauma or infection may result in an increased expression of tissue factor by the mesothelium. Finally, fibrin deposition followed by intra-abdominal adhesions may help to stop bleeding or the spread of infection.

Interestingly, we found evidence for phagocytosis of fibrin fibers by the mesothelial cells. Fibrinolytic adhesions are responsible for a major fraction of intestinal obstructions.\(^{50}\) Mesothelial cells are well known for their active fibrinolytic system,\(^{15}\) but phagocytosis of fibrin as another defense mechanism against adhesion formation has not yet been described for mesothelial cells. In addition, this phagocytic and fibrinolytic activity may be beneficial if mesothelial cells are used for cell seeding procedures on vascular grafts.

We conclude that mesothelial cells have a nonthrombogenic apical surface that can withstand blood flow at high shear rates in vitro. Relatively high tissue factor expression by cultured cells compared with mesothelial cells ex vivo suggests that the cells may become activated during culture. Experiments must now be performed to solve the question of which factor is responsible for the induction of tissue factor expression. When tissue factor expression can be controlled or fibrin deposition prevented, mesothelial cells may become very useful for cell seeding of grafts.

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References


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