

ENDOTHELIAL CELL-LINED VASCULAR PROSTHESES. W. Burke.
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While considerable effort has been expended to develop blood compatible artificial devices, the only truly non-thrombogenic surface known is that of vascular endothelium. Early prosthetic studies emphasized graft material from the surgical viewpoint. Later the emphasis changed to the physical configuration of the graft (woven, knitted, velour, porous, nonporous grafts, etc.) which gave the best tissue ingrowth, stable flow surface and hopefully an endothelial lining. Since vascular grafts seldom become lined with endothelium in man as a natural consequence of the healing process, methods to enhance the development of an endothelial surface would be of considerable value in reducing thrombosis, infection and the destruction of blood elements. To accomplish this objective, a wide variety of cells and tissue fragments have been added to grafts in order to produce pseudointimas.

In our experiments endothelial cells have been isolated from the external jugular veins of 20-30kg foxhounds using trypsin and collagenase. The harvested cells were either cultivated *in vitro* for 14 days and then seeded into Dacron and PTFE vascular grafts during preclotting, or seeded into grafts immediately after derivation. Grafts were implanted as thoracoabdominal bypasses (25-30 cm in length) and incorporation of the graft and the formation of an endothelial lining followed from 1 day to 1 year. Grafts treated in an identical manner, but preclotted without endothelial cells served as controls.

Endothelial cells are first visible in seeded grafts at 4 days, approach 70% coverage of the graft surface by 2 weeks and 90% at 1 month. Four month seeded grafts are completely lined with endothelium, while unseeded grafts still have 20-30% of their surface covered with a fibrin coagulum at 6 months. Preliminary results indicate that blood parameters are greatly perturbed initially, but return to normal levels with the evolution of an endothelial lining in seeded grafts.

CLINICAL APPLICATION OF BLOOD SURFACE INTERACTIONS
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Blood contact with non-endothelial cell surfaces activates Factor XII and platelets. Clinical applications of temporary or permanent devices placed within or in series with the circulation are limited by this fact. Depending upon whether or not coagulation is inhibited, thrombosis or blood injury occur.

In recent years improvements have been made in vascular prostheses, heart valves and assist devices. PTFE (Gortex) prostheses as small as 4 mm in diameter have been successfully used in selected high-flow applications such as aorto-pulmonary shunts. Improved mechanical heart valves have reduced the tendency of valve thrombosis and possibly late emboli, but long-term anticoagulation is still required for patients with aortic bioprostheses and some patients with mitral xenografts. Development of durable relatively thromboresistant materials has led to wide and successful application of the intra-aortic balloon with few thromboembolic complications. Improved designs and development of durable, relatively thromboresistant materials have advanced experimental left ventricular assist devices to the stage of limited clinical application.

When coagulation is inhibited by heparin, extracorporeal perfusion systems injure formed and unformed blood elements. Platelets particularly are activated with the result that platelet function is depressed and postoperative bleeding times are prolonged after perfusion with either membrane or bubble oxygenator systems. Currently clinical trials using prostacyclin to protect platelets during the period of bypass are underway. Bleeding consequences of platelet dysfunction and heparin continue to limit clinical application of long-term extracorporeal perfusion applications for cardiac and respiratory assistance.