

**Thursday, July 16, 1981**

## Symposium X

# Platelets and the Vessel Wall

15:30-17:30 h

**Grand Ballroom West**

OVERVIEW: REACTION TO TWO TYPES OF THROMBUS DEPOSITION. S. Moore\*, L.W. Belbeck, M. Richardson, Department of Pathology, McMaster University, Hamilton, Ontario, Canada.

Damage to the luminal surface of an artery is associated with the development of platelet-fibrin thrombus or a monolayer of platelets. The first type of reaction (Type 1) follows damage caused by an indwelling catheter or by repeated exposure of the endothelial surface to antibody. The second (Type 2) follows removal of the endothelium by a Fogarty balloon catheter. The reaction of the vessel wall to these two types of injury, while having many similar features, differs in a number of important respects. Both are dependant on the interaction of platelets with the vessel wall and can be suppressed or inhibited by inducing a severe thrombocytopenia using anti-platelet serum. In both, the thickness of lesions is related to repetitiveness of injury. Both are characterized by smooth muscle cell proliferation and lipid accumulation in normolipemic rabbits. The type 1 lesion regresses rapidly, losing size and lipid content, when the injury stimulus is removed. The Type 2 lesion persists and continues to accumulate lipid over time.

In the Type 1 lesion, induced by an indwelling aortic catheter, platelet consumption is increased for eight days and fresh platelet-fibrin thrombus may be found on the surface of the lesion months after placement of the catheter. Platelet survival is shortened. In the Type 2 lesion the initial interaction of platelets with the vessel wall is short lived, and the surface covering of platelets is rapidly lost. Platelet survival is not shortened in rabbits. While both lesions exhibit abundant accumulation of extracellular and intracellular lipid, this occurs earlier in the Type 1 lesion and disappears fairly rapidly when the injury stimulus is removed. Lipid appears later in the Type 2 lesion, persists and increases in amount, even following a single injury. Fatty streaks, though observed in both types of injury, are more likely to be seen as a stage of regression of Type 1 lesions. The Type 1 lesion closely resembles the raised (complicated) lesion of human atherosclerosis. The Type 2 lesion resembles the human fibrous plaque. Supported by Grants MT-2168, M.R.C., 15-7 O.H.F.

## 0777

PLATELET AND SMOOTH MUSCLE CELL RESPONSES AFTER ENDOTHELIAL DESQUAMATION. M.B. Stemerman. Thrombosis & Hemostasis Unit Charles A. Dana Research Inst., of Harvard Med. Sch., at Beth Israel Hospital, Boston, MA.

Although compromise of endothelial integrity occurs through many mechanisms, mechanical removal by balloon catheter is an excellent experimental method to study vascular responsiveness after injury. The interaction of platelets with the vessel wall, as well as proliferation of vascular smooth muscle cells can be assessed in this model. Following platelet attachment to the subendothelium, platelets release materials from their alpha granules. Using an antibody raised against platelet factor 4, a protein stored in alpha granules, we have demonstrated that material released from platelets do enter the vessel wall. A large amount of PF 4 antigen enters the wall shortly after endothelial removal, permeating the wall completely by 30 minutes, but little trace of the antigen can be found four hours after injury. Using infusions of PGI<sub>2</sub> to a level of 850 ng/kg/min in rabbits, in vivo platelet adhesion to the exposed subendothelium can be greatly reduced and release of PF4 antigen into the vessel wall markedly diminished. Growth of smooth muscle cells (SMC) after endothelial removal has also been measured by <sup>3</sup>H-Thymidine labeling of SMC DNA. As measured by this method as well as direct cell counts, SMC proliferation in the abdominal aorta is significantly greater than the thoracic. Reinjury of only the abdominal aorta by balloon catheter 4 days after the initial total aortic injury causes a proliferative spurt in the thoracic aortic SMC, thus demonstrating that a humoral signal can initiate SMC proliferation. In addition, the response of SMC from 21 month old rats when compared with 3 month old rats is much greater. These studies demonstrate in vivo methods for examining the response of platelets and SMC following endothelial injury. Further, these studies indicate that the response to injury hypothesis of atherosclerosis progression should now be broadened to the concept of a response to signal view of atherogenesis.

## 0778

PLATELET SURVIVAL IN RELATION TO VESSEL WALL INJURY. R.L. Kinlough-Rathbone, M.A. Packham and J.F. Mustard. McMaster University, Hamilton and University of Toronto, Toronto, Ontario, Canada.

Shortened platelet survival is associated with the thromboembolic complications of vascular disease. Shortened platelet survival occurs in animals with repeated mechanical injury to the vessel wall, hypercholesterolemia, or during infusion of homocysteine; in these circumstances endothelial cells are damaged and platelets interact with the injured vessels. In rabbits, de-endothelialization of aortae with a balloon catheter does not shorten platelet survival and the injured vessel wall rapidly loses its ability to attract significant numbers of circulating platelets. In contrast, repeated mechanical injury of rabbit aortae induced by indwelling aortic catheters shortens platelet survival and platelets continue to interact with the vessel wall. When short aortic catheters are used in rabbits, thrombi continue to form but platelet survival is unaffected, possibly because damage to the vessel wall is less extensive. Mechanical injury to rat aortae shortens platelet survival without macroscopic thrombi. Thus, shortened platelet survival may occur because of increased platelet consumption resulting from platelet interaction with repeatedly injured vessel walls, or because alterations of platelets that interact with injured vessels or participate in thrombosis lead to their clearance from the circulation. Of the stimuli known to be involved in thrombosis, only plasmin, which cleaves membrane glycoproteins, alters platelets sufficiently for platelet survival to be shortened. Agents that prolong platelet survival may exert their effects by modifying the extent of vessel wall injury, modifying or inhibiting changes in platelet glycoproteins or by inhibiting the clearance of altered platelets from the circulation.