Friday, July 17, 1981

Symposium XIV

Blood Contacting Prosthetic Devices

15:30–17:30 h

Grand Ballroom West

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NEW DEVELOPMENTS IN INTERACTIONS OF BLOOD WITH ARTIFICIAL SURFACES. E.W. Salzman. Harvard Medical School and Beth Israel Hospital, Boston, MA, USA.

There are major new developments concerning interactions of blood with artificial surfaces. There is new understanding of mechanisms: the nature of the plasma protein film adsorbed on artificial surfaces, the interaction of HMW kininogen with adsorbed fibrinogen, the significance of adsorbed antithrombin to the behavior of heparinized surfaces, and the lack of prostacyclin production and ADPase activity. There are new in vivo diagnostic methods: measurement of labelled platelet and fibrinogen survival, assay of plasma levels of products of activated coagulation or platelets (FPA, thrombin/antithrombin complexes, β-thromboglobulin, platelet factor 4, thromboxane B_2), and in vivo detection of thrombi with ^{125}I-fibrinogen or ^{111}In-platelets. New methods also exist for characterization of surfaces: ESCA, SEM, TIRIS, TIRFS. New materials are available with different modes of thromboresistance: bland polymers such as polyurethanes and siloxanes, modified collagens, heparinized surfaces, porous materials, and aldehyde treated materials of animal origin. There are new drugs for protection of hemostatic elements during extracorporeal circulation: PGI_2, PGE_1, ibuprofen. New applications for prosthetic devices have become practical: peritoneo-jugular shunts for treatment of ascites, left ventricular assist devices, intra-aortic balloon pumps, total artificial hearts.

Such developments raise important new questions: the relation of short-term tests of thromboresistance to long-term behavior of devices in vivo, the problem of thrombi at the junction of prosthetic device with the host, calcification in long-term applications, and new approaches to management of traditional clinical problems (e.g., continuous treatment with portable miniaturized hemodialysers, small vessel prostheses, extracorporeal cardiopulmonary support without anticoagulation).

Subsequent speakers will consider these topics more fully.

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NON-THROMBOGENIC POLYMER SURFACES.
E.W. Merrill, E.W. Salzman, V. Sa da Costa, D. Brier-Russell. Dept. of Chem. Eng., MIT, Cambridge; Dept. of Surgery, Harvard Medical School and Beth Israel Hospital, Boston.

Activation of the intrinsic clotting system, and platelet adsorption and activation by a foreign surface are preceeded by adsorption of plasma proteins, often accompanied by change of conformation (denaturing). Protein molecules are modelled as particles having heterogeneous surface characteristics, i.e., separate "patches" of lipophilic (hydrophobic) groups, of H-bonding groups, of fixed aniomic groups, and of fixed cationic groups. Any of these "patches" can anchor the protein to the "foreign" surface if it finds a receptive "patch" on the surface of sufficient area. When thus stabilized on the surface, and in sufficiently close proximity, proteins like fibrinogen can then bind platelets which can become activated. We postulate that protein adsorption is minimized, if the molecular segments of polymer molecules which create the synthetic surface (1) are disordered (amorphous) rather than ordered (crystalline) (2) undergo Brownian fluctuations rather than being fixed in the glassy state (3) are mixed in chemical composition rather than being all of the same type (4) are such as to minimize the bonding energy per segment to any of the receptive sites on the protein (anionic, cationic, H-bonding, hydrophobic) (5) are "diluted" by swelling in water, to reduce the surface density. Using the above model and postulates, we review currently used polymers (vinyls, silicones, polyurethanes etc). Surfaces containing polyethers such as polyethylene oxide (PEO) that are water absorbing and non-crystalline, rank highest in the list of non-thrombogenic polymers. We suggest that this arises from the alternation of hydrophobic CH_2-segments with hydrophilic ether oxygen, and the total absence of ionic groups and bonding hydrogens. Our observations on the blandness of hydrophilic cross-linked polyethers is supported by evidence from the literature concerning nearly total phase exclusion of protein from homogeneous PEO solutions, and the non-adsorption of proteins on surfaces coated by PEO.

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THE HEPARIN-GLUTAR SURFACE; MODE OF ACTION AND PRACTICAL APPLICATION. P. Olsson, R. Larsson, L.-E. Lins and E. Nilsson. Department of Experimental Surgery, Karolinska Institute, IRD Biomaterial AB, Stockholm, Sweden.

A heparinized surface with non-thrombogenic characteristics was prepared by stabilization of an ionic heparin-amine complex with glutardialdehyde. The process can be applied to a large variety of materials.

The coating makes the surface platelet compatible because no fibrinogen is adsorbed. The interaction of the surface with plasma coagulation system is based upon its ability to adsorb active coagulation enzymes (thrombin) and to promote inhibition of the adsorbed enzyme in the presence of circulating antithrombin III. The sequence involving enzyme adsorbation and subsequent inhibition is regenerative. Investigations on blood vessels have revealed that the intact endothelium exerts a similar mode of action with regard to inhibition of coagulation enzymes.

When the heparin in the surface coating is substituted for glucosaminoglycans with less anticoagulant activity than heparin, the created surfaces is still platelet compatible and maintains the ability to adsorb enzyme, but loses the ability to generate inhibition of the adsorbed enzymes. Such surfaces are highly thrombogenic.

The heparin surfaces have been tested experimentally for various applications. A heparin coated intravascular pO_2 sensor was used for accurate measurements without recalibrations for several days. A non-heparinized electrode deteriorated within hours. Hemodialysis was performed on non-heparinized dogs using surface-heparinized hemodialysis set.