Compatibility with blood means, in broadest terms, no adverse effect on blood or any of its components. The complex nature of blood with its formed elements, coagulation system, and multitude of proteins puts not only a variety of restrictions, largely undefined, on the blood-contacting surface, but also makes the determination of blood compatibility an added significant problem. Further complicating the matter is the reverse requirement—no adverse effects by the blood on the polymer. Of the possible adverse effects of a foreign surface on blood, thrombogenesis—promotion of clotting—being most obvious and of immediate consequence, has received, the most attention. Fortunately, this very serious and disabling aspect of incompatibility can be overcome sufficiently by the administration of systemic anticoagulants such as heparin or coumadin to permit the use of the lifesaving devices such as heart-lung and kidney machines and artificial heart valves. Early postulates as to factors increasing thromboresistance included increased hydrophobicity, increased negative surface charge, and increased surface smoothness. The first real indication that thromboresistance was within grasp was the finding by a group at the University of Wisconsin (1) that heparin, ionically bonded to a surface, did provide a very significant degree of thromboresistance.

Very shortly after this finding, a concerted effort was begun in 1964 to find or develop thromboresistant polymers. This effort was the biomaterial portion of the Artificial Heart Program of the National Heart Institute. Descriptions of the approaches taken and progress made have been published in some detail. The early work on individual polymers is not described or referenced here because of space limitation. Consult references (2) and (3) for more specific information. These early efforts were in directions such as:
(1) **Anionic polymers** - as by the inclusion of acid groups to form surfaces having negative charges as does the blood vessel intima. An extension of this was the use of electrets.

(2) **Low surface energy polymers** - in accord with the early finding that paraffined surfaces delayed the clotting of blood compared to glass surfaces.

(3) **Hydrogels** - both because there were early indications that polyhydroxyethylmethacrylate (HEMA) possessed some degree of thromboresistance and because of the hypothesis that a water gel surface would be less recognizable as a foreign surface to the blood. Polymers and copolymers of this type, sometimes including anionic and/or cationic groups, have been extensively investigated.

(4) **Polyurethanes** - have received most attention because of the wide variety of compositions made possible by variations in the choice of components -- diisocyanate, polyether or polyester, and chain extender. In addition, a commercial span-dex-type polyurethane, Lycra®, was found to have appreciable thromboresistance, as was a polyurethane-polydimethyl siloxane block copolymer, Avcothane 51®. (Trade names--Lycra, Dupont; and Avcothane 51, Avco-Everett Research Lab., Inc.)

(5) **Biologically modified surfaces** - were a different approach in that if surface treatments could be found that were compatible, or at least thromboresistant, substrates could be chosen on the basis of suitability for the application. Because of the promise shown by the ionically-bonded heparinized surfaces, considerable study was devoted to methods of heparinization, by both ionic and covalent bonding.

Parallel to the development of thromboresistant and hopefully completely compatible polymers or surface treatments, research proceeded on (a) the development of methods to evaluate blood compatibility, and (b) the understanding of blood-material interactions that define compatibility. The latter would not only contribute to the development of badly needed improved evaluation methods but also form the basis for the development of truly blood-compatible surfaces. The most recent comprehensive review of blood-materials interactions is found in Reference No. 4.

It was known early that the first reaction when blood contacted a foreign surface was the adsorption of proteins (5) and it was recognized that it was the nature of this protein adsorbate that governed the further reactions that, in toto, governed the compat-