9.1 INTRODUCTION

Diseases of the cardiovascular system contribute to about 20% of the fatality in older people. Arteriosclerosis, a process affecting the large and medium sized diameter arteries, specially the aorta, coronary arteries and cerebral arteries is a major cause of death. Diseased blood vessels and inefficient heart valves are routinely replaced with natural tissues or synthetic materials including natural or synthetic polymers. It is not surprising, therefore, that the market of blood-contacting polymers is relatively large and increases annually at a rate of 10-20%. Total world market for this range of devices was estimated to be 109 million U.S. dollars in 1982 (Jozefonvicz and Jozefowicz, 1994).

The materials used in vascular surgery can be grouped into two parts. The first group consists of biological tissues including autologous and homologous grafts, chemically processed human umbilical vein, and the bovine heterografts. Among these grafts autologous venous grafts still remain the gold standard and other materials are used when these grafts are not available. Their biodurability is, however, questionable. The second group of vascular prostheses involves the synthetic grafts made of Dacron® and Teflon®. Their current popularity attests to the fact that these grafts are most effective in the replacement and bypass of medium and large caliber vessels. These materials are also used for heart valve prostheses. Their lifetime depends on their porosity, texture, surface properties etc. Other blood contacting polymeric devices include extracorporeal blood circulating devices (ECCs) consisting of catheters, blood bags and tubing used for blood transfusion, membranes, hollow fibers and tubing used for dialysis, plasmapheresis, plasma detoxification, blood oxygenation devices and plasma expanders.

Polyvinyl chloride (PVC) is the most extensively used polymer for all short-term devices such as ECCs, (catheters and blood bags) however silicone rubber and polyethylene have also been employed for the same purpose. On the other hand, cellulose and cellulose derivatives, polyamides, polypropylene, polyacrylonitrile, polysulfone, and polyesters are basic materials for membranes and hollow fibers in dialysis. More recently, polyurethanes have been developed for these applications. Substituted dextrans are promising candidates for plasma expanders.

9.2 BLOOD CLOTTING

A clot that has formed inside a blood vessel is referred as a thrombus or an embolus depending on whether the clot is fixed or floating, respectively.

The control of blood coagulation process is essential to prevent continuous clot formation and vascular occlusion. A natural defense against clotting is the flow of blood, which sweeps away
activated procoagulants and dilutes them in larger volume. Liver and reticuloendothelial system also help removing activated factors from circulation. Finally, several inhibitors of serine proteases are present in plasma, most notably antithrombin III, α₁-antitrypsin and α₂-macroglobulin.

Immediately after an injury, the blood vessels constrict to minimize the flow of blood; platelets adhere to the vessel walls by coming into contact with the exposed collagen. The aggregation of platelets is achieved through release of adenosine diphosphate (ADP) from damaged red blood cells, vessel walls, and adherent platelets. Simultaneously blood clotting is initiated to control blood loss.

Two separate routes for activation of the cofactors leading to blood clotting are known as the extrinsic and intrinsic pathways (Fig. 9.1). The extrinsic pathway is so named because it requires a substance not normally present in the blood for activation. Tissue factor is a lipoprotein found in the endothelial cells that line the vascular system and other organs. Damage to tissues or vessels releases tissue factor, which activates factor VII to VIIa in the presence of calcium. Factor VIIa is a protease that converts factor X to Xa.

![Diagram of blood clot formation](Note the cascading sequence)

All the factors in the intrinsic pathway are available in circulation. Factor XII undergoes a conformational change when exposed to collagen, basement membrane or a variety of other foreign surfaces. Once activated XIIa initiates a series of reactions; each step is dependent on previous step as shown in Fig. 9.1.

The central event in clotting is the cleavage of fibrinogen in the presence of the proteolytic enzyme thrombin to a fibrin monomer, and its polymerization to form a fibrin polymer. A fibrin clot is cross-