

Role of platelets in blood–biomaterial interactions

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Abstract. Over 2 million cardiovascular procedures are performed annually in the United States. Every one of these procedures requires some period of contact with blood with several different biomaterials used in the manufacture of assist devices or implant devices. In view of the increasing importance of the biomaterials in clinical practice, it would be timely to review briefly physicochemical characterization as well as biological evaluations. Blood compatibility encompasses a variety of events associated with blood interaction with the biomaterials used in various procedures. Two separate coagulation mechanisms are involved (arterial and venous) depending upon the flow characteristics. At least three interacting factors modulate normal hemostasis and the pathogenesis of thromboembolic events. They are the state of activation of coagulation cascade, circulating levels of thrombin and fibrinogen and relative activity of platelets. In this overview we discuss the current concepts on the role of platelets in blood–biomaterial interactions.

When blood contacts a biomaterial surface a variety of blood components interact with the surface. Some of the key players in platelet activation on biomaterial surface include fibrinogen and von Willebrand factor. Currently available antiplatelet drugs effectively block aggregation and secretion induced by physiological agonists such as epinephrine, adenosine diphosphate and thromboxane in suspension. However, they do not prevent platelet interaction on biomaterial surfaces. Mechanisms involved in platelet activation in suspension and on surfaces as well as the pharmacology of newer antiplatelet drugs will be discussed.

Keywords. Platelet adhesion; protein adsorption; biomaterials; surface induced platelet activation; fibrinogen; platelet-surface receptors; antiplatelet drugs.

1. Introduction

The adhesion of circulating platelets at sites of injury on the vessel wall where subendothelium, in particular collagen, is exposed to the flowing blood, is known to be an important step in a sequence of events leading to the formation of a hemostatic plug (Mustard and Packham 1975). With the development of prosthetic devices and artificial organs, the study of platelet adhesion and thrombus formation on synthetic polymer surfaces has become very important in assessing the compatibility of biomaterials to blood. A clear understanding of the blood interactions with artificial surfaces would promote a better utilization of existing materials and the development of new materials with improved properties.

1.1 Contribution of platelets to thrombus formation

1.1a Platelet morphology, physiology and function: Platelets are the disc-shaped fragments of bone marrow megakaryocytes circulating in blood. They are about $250,000 \pm 80,000$ per μl . They have a life span of 8–10 days and play a critical role in the recognition of vascular injury, formation of effective hemostatic plugs, retraction of clots and wound healing. However, when hyperactive,

they can initiate events leading to clinical complications associated with cardiovascular and cerebrovascular diseases. Although completely nonsticky in the resting state, they become sticky with the slightest stimulation. The degree of activation depends on the strength of the stimulus and the type of signal generated by ligand–receptor interaction. Four well developed stages of activation are recognized: (i) development of stickiness, (ii) changes in cell shape, (iii) contraction and release of granule contents and (iv) irreversible aggregation.

Platelet plasma membranes contain transmembrane proteins as well as glycoproteins. Glycoproteins serve as the receptors for agonist/surface-mediated stimuli initiating platelet activation. Platelets contain integrin and nonintegrin domains in their plasma membranes. Integrins are transmembrane glycoproteins with α and β units coupled noncovalently (GPIIb–IIIa, GPIa–IIa, GPIc–IIa). They participate in both cell–cell and cell–matrix interactions. In addition, there are nonintegrin glycoprotein domains on platelets capable of interacting with acromolecules such as vWF and collagen (GPIV, GPIb).

1.1b Role of platelets in thrombosis: Circulating platelets rapidly adhere to the subendothelial matrix, become activated, adhere, spread, release the contents of various storage organelles and become cohesive, leading to

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