1. INTRODUCTION

The importance of the RES in regulating blood platelet dynamics is well established. Upon review of the pertinent literature, however, much of the evidence supporting the interaction between platelets and the RES is found to be indirect. There are relatively few comprehensive studies of the physiological mechanisms underlying the removal of senescent, damaged, and altered platelets. The need to understand these mechanisms has been most apparent in the clinical management of thrombocytopenic and hypersplenic syndromes in which excess platelet destruction has been implicated. Thus, a large number of studies have been performed concerning the survival of platelets in these syndromes. Most of the current knowledge of platelet recognition and removal by the RES derives from such studies. This review will begin with a discussion of phagocytosis of platelets in the hypersplenic/thrombocytopenic, normal, and thrombotic states. The mechanisms of recognition of platelets by the RES will be considered particularly in the context of alterations which enhance platelet removal. Next, the literature indicating that platelets interact directly with circulating microparticulates will be reviewed. Evidence will be presented that platelets may be phagocytic in their own right and may augment RES phagocytosis by virtue of their ability to agglutinate foreign particulates. Following this will be a consideration of RES clearance of proaggregatory agents. Finally, the most recent advances in our understanding of potential platelet–macrophage interactions will be reviewed. Both platelets and macrophages participate in inflammation and tissue repair. Evidence now suggests that platelets are also involved in immune reactions. Since platelets and macrophages react with and release a number of common mediators, it seems quite reasonable that they might modulate one another’s function. Before proceeding, a brief discussion of platelet morphology and phys-
iology is in order. More extensive reviews of this aspect are available (Zucker, 1980; Holmsen et al., 1977; Day et al., 1978; de Gaetano and Garattini, 1978).

2. PHYSIOLOGY AND ANATOMY OF PLATELETS

The mammalian blood platelet is a nonnucleated cell fragment irregularly discoid in shape with a diameter of 1–6 μm. The human platelet is usually 1–2 μm in diameter. They originate in the bone marrow by budding from megakaryocytes. Though sparse in organelles, platelets contain two readily identifiable populations of granules. Dense granules contain small molecules including amines, adenine nucleotides, and calcium. The α granules contain proteins including molecules which modulate and participate in the hemostatic process and conventional lysosomal constituents. It has been suggested that these granules are functionally heterogeneous, some acting as storage reservoirs for such molecules, fibrinogen, and platelet factor 4 and others representing lysosomes and peroxisomes.

The major physiological function of platelets is generally believed to relate to the maintenance of integrity and continuity of the vascular lining. This is accomplished primarily through participation in hemostasis as well as in a poorly defined relationship to the support of vascular endothelial integrity. The role of platelets in hemostasis is accomplished via sequential adhesion, aggregation, secretion and contraction at a site of vascular injury. Briefly, circulating platelets adhere upon exposure of the collagenous subendothelium. Once adherent, secretion of ADP and elaboration of thromboxane A₂ (TXA₂) lead to platelet aggregation and the formation of a hemostatic plug. Adhesion and aggregation are both stimuli for secretion so a positive feedback cycle results. ADP released from injured tissue or thrombin elaborated through activation of coagulation may initiate these reactions via stimulation of aggregation. Concomitantly with these responses, contraction of platelet actinomycin initiates retraction and organization of the platelet plug. Release of serotonin and TXA₂ leads to local vasoconstriction in the area of the plug. Deposition of areas not requiring hemostatic intervention leads to thrombosis. Detachment of a hemostatic plug or aggregation initiated without adhesion may lead to thromboembolization. Because high flow velocities limit the role of coagulation in achieving hemostasis on the arterial side of the circulation, platelet events assume special significance in these areas. Platelets are the primary components of arterial thrombi and thromboemboli. Under most conditions these events are precluded by the uninterrupted continuity of the nonreactive luminal face of the vascular endothelium and by elaboration of the platelet-inhibiting prostaglandin, prostacyclin (PGI₂).

The reason for elaborating upon these processes is to emphasize that in the course of executing normal function, platelets undergo shape changes and membrane alterations. These transitions may thus characterize the activated platelet as "altered self" or "effete self," characteristics often associated with recognition and removal by the RES. In addition, since platelets are blood components