Platelets are anucleate, cellular elements present in circulating blood that are critical for the achievement of hemostasis following tissue injury and, probably, for general maintenance of vascular integrity. The human circulation normally contains \( \approx 2.5 \times 10^9 \) platelets per ml, each \( \approx 5 \mu m^3 \) in volume. Over the past 3 decades, much has been learned about the biochemical mechanisms and structural changes that underlie platelet function. Simply stated, platelet membranes contain a group of receptors that can be activated by substances such as ADP and epinephrine as well as by vessel wall constituents such as collagen and von Willebrand factor. These receptors are linked to biochemical pathways that transmit signals leading to structural and conformational changes in platelet membranes and membrane-associated glycoproteins. The "activated" platelets adhere to damaged vascular surfaces and to one another to form hemostatic plugs and to promote blood coagulation.

When the importance of platelets in hemostasis was recognized >80 years ago, it was natural to consider whether these cells could be transfused with therapeutic effect to patients with low platelet levels (thrombocytopenia) and hemorrhagic symptoms. This was achieved in a small number of studies (1), but the lack of effective anticoagulants and systems for collection, isolation, and storage of platelets made routine platelet transfusion therapy impractical. This situation changed in the 1950s and 1960s when the development of plastic containers and improved anticoagulants together with the recognition that platelets, in contrast to red cells, are adversely affected by refrigeration and tolerate storage best at room temperature made it possible to maintain the hemostatic effectiveness of platelets for up to 5 days prior to transfusion (2, 3).

Ready availability of stored platelets led to a remarkable increase in the utilization of this blood component for the prevention and treatment of bleeding in patients with thrombocytopenia or qualitative (functional) platelet defects. The favorable impact of platelet transfusions on medical and surgical practice is exemplified by a dramatic reduction in mortality due to hemorrhage in patients with acute leukemia since 1970 (4). In 1989, the total volume of platelets transfused to patients in the United States approximated the amount that could be derived from \( \approx 7.5 \times 10^8 \) units of donated blood (5). This has been due to the collection, isolation, and storage of platelets, which can be achieved in a number of units for 1-7 days or indefinitely, under conditions that preserve function and viability while reducing the likelihood of bacterial growth.

More than 30 years ago, attempts were made to store platelets for long periods of time in gelatin (10) and in lyophilized form (11) with unsatisfactory or marginal results (12, 13). Subsequently, it was learned that human platelets frozen in dimethyl sulfoxide could survive and function after transfusion (14), but this method has proved impractical for large-scale application. More recently, several groups have examined whether liposomes containing platelet membranes (15) or microparticles derived from normal platelets (16, 17), preparations that could probably be stored indefinitely, are capable of producing hemostasis when transfused to thrombocytopenic patients. At this time, it is uncertain whether either of these approaches will lead to a product that can be transfused with benefit to thrombocytopenic patients.

Lyophilization (freeze-drying) is another approach to long-term preservation of blood cells for transfusion that was applied recently to red blood cells with reasonable preservation of metabolic activity following reconstitution (18). In a recent issue of this journal, Read and coworkers (19) described the application of this technique to platelets. Washed platelets isolated from human blood were fixed with paraformaldehyde, frozen in cryoprotective buffer containing 5% albumin, freeze-dried, and stored at -80°C. They were then rehydrated and their in vitro and in vivo properties were studied. Ultrastructural integrity of the reconstituted platelets was remarkably well preserved, and they were shown to be capable of adhering to subendothelium and of spreading on an inert surface almost as well as fresh platelets. Human platelets preserved in this way, when transfused to thrombocytopenic rats, increased circulating platelet levels to a hemostatic range and shortened the bleeding times of the animals from >15 min to the normal range of 0.5–1.5 min. The reconstituted lyophilized (RL) platelets, when labeled with a fluorescent probe and transfused to three normal dogs, became incorporated into wounds inflicted on these animals by a small incision in the ear and into thrombi formed in the carotid artery following a crush injury. The stored platelets were unable, however, to aggregate normally in vitro after stimulation with the agonist ADP.

These studies are remarkable in that they demonstrate convincingly that lyophilized platelets can be reconstituted with some degree of preservation of function by in vitro and in vivo criteria and suggest a possible approach to large-scale platelet preservation that might overcome some of the shortcomings of existing methods. However, additional studies are needed to determine whether this technique is practical for platelet transfusion therapy. Preparation of platelets for storage by the method described is likely to be quite labor intensive and costly. Conceivably, the process could be automated, but this might require pooling of platelets from many donors to achieve a scale large enough to realize cost efficiencies. Large-scale pooling of platelets is likely to be unacceptable because of the increased risk of transfusion-transmitted viral infection when a product derived from many donors is transfused to a single recipient. Reconstitution of platelets after storage might also be time consuming and expensive. It is unknown whether paraformal-
dehydrate (PFA) treatment, which appears to be important for the preservation of structure and function of the freeze-dried platelets, will affect their immunogenicity. This is more than a theoretical concern in view of the existence of naturally occurring human antibodies that recognize platelets treated with PFA (20). Finally, in vivo studies with RL platelets have been carried out to date only in a small number of rats and dogs. Larger numbers of animal studies and, eventually, investigations in humans will be necessary to evaluate the effectiveness of this preparation. Nonetheless, these observations are important because they suggest the possibility that platelets (and perhaps other blood cells) can be lyophilized, stored for long periods of time, reconstituted, and transfused with therapeutic benefit. Future developments in the laboratories of these investigators will be awaited with great interest by the transfusion medicine community.