Consumption and Dilutional Thrombocytopenia

In addition to sequestration, hypoproductive, and destructive causes of thrombocytopenia, low platelet counts occasionally result from consumption and hemodilution. The pathophysiology of thrombocytopenia in these cases is directly attributable to the underlying cause of the bleeding, frequently large-scale trauma.

Overwhelming hemorrhage causes the consumption of endogenous platelets in an attempt to curb bleeding, and platelets are consumed faster than they can be released by the spleen or generated in the bone marrow. Resuscitative efforts after trauma, including infusion of massive volumes of intravenous solutions, red blood cells, and FFP, result in the dilution of circulating platelet numbers. The combination of platelet consumption and dilution during trauma can have catastrophic consequences and historically has been a leading cause of death in this setting. In addition to identifying the source of a large bleed, aggressive platelet transfusions in the setting of trauma may provide the greatest benefit in overcoming the effects of consumption and dilution (discussed later).

BLEEDING CAUSED BY PLATELET FUNCTION DEFECTS

The ability of platelets to adhere to damaged vasculature and to recruit additional platelets into the clot is essential for primary hemostasis, especially when patients are challenged by trauma or surgery. Unlike bleeding caused by thrombocytopenia, individuals with platelet function defects bleed because their platelets cannot adhere or aggregate appropriately in response to in vivo stimuli.

These qualitative platelet disorders are most frequently encountered in individuals with normal or near-normal platelet counts. Evaluation often relies on tests that assess the function (rather than the number) of circulating platelets. From an epidemiologic standpoint, acquired qualitative platelet defects are much more frequently encountered than their congenital counterparts.

Acquired Causes of Platelet Dysfunction

Aspirin and Antiplatelet Therapy

The patient's history and preoperative screening should assess whether patients are taking medications that interfere with platelet function, such as aspirin. Aspirin irreversibly blocks normal arachidonic acid metabolism, and all exposed platelets are irreversibly affected and do not respond to stimulation even after aspirin is discontinued. The characteristic aspirin-induced platelet aggregation pattern is shown in Table 51-5 and Figure 51-5.

Nonsteroidal anti-inflammatory drugs (NSAIDs) (e.g., indomethacin) reversibly inhibit COX, and platelet function is restored within 24 to 48 hours after discontinuing the drug. Bleeding after most surgical procedures that is associated with aspirin or NSAIDs is usually mild, and aspirin may not need to be discontinued before surgery, especially because aspirin-induced platelet dysfunction is desirable in patients at risk for stroke or myocardial infarction.

The aspirin effect is restricted to COX1, and various NSAIDs have different relative affinities for COX1 and COX2. COX2 is an inducible enzyme that is synthesized in endothelial cells in response to inflammatory cytokines. Suppression of COX2 reduces synthesis of endothelial cell prostaglandin I_2 (i.e., prostacyclin), a molecule that exhibits antithrombotic effects through inhibition of platelet aggregation. The net effect of nonselective NSAIDs on the prothrombotic or antithrombotic balance favors bleeding because NSAID-induced COX1 inhibition means that thromboxane A_2 production in platelets is blocked. In contrast, the increased cardiovascular risk with administration of more selective COX2 inhibitors is probably attributable to the COX2-induced lack of endothelial cell prostacyclin production, coupled with intact platelet function (i.e., no inhibition of thromboxane A_2 by COX2 blockade). Recent data show that NSAIDs given before aspirin compete for COX1 binding sites and diminish aspirin's antiplatelet effect, another possible factor in the coagulant balance of concomitant use of NSAIDs and aspirin.

Another category of antiplatelet agents acts independently of the COX1/2 pathways. These drugs are P2Y12 receptor antagonists (e.g., clopidogrel; prasugrel). They disrupt function by irreversibly binding to the surface receptor for the platelet agonist, ADP. P2Y12 receptor antagonists are primarily used as adjunctive anticoagulant therapy for individuals at risk for thrombosis associated with coronary artery disease and stroke. If an individual taking a P2Y12 receptor antagonist experiences bleeding, these drugs can inhibit platelet activation at the site of injury, not unlike the effect in an individual taking aspirin.

Regardless of the type of agent used, discontinuing an antiplatelet drug is a reasonable first step for a patient who has moderate to severe bleeding while on the therapy. Discontinuation of the drug has no effect on anticoagulated platelets given for

TABLE 51-5 DISORDERS CAUSING ABNORMAL PLATELET AGGREGATION

	RESPONSE TO AGONIST				
DISORDER	***Epinephrine***	***ADP***	***Collagen***	***Arachidonic Acid***	***Ristocetin***
Aspirin and NSAIDs	PW	PW	NL, ↓*	↓	NL
Glanzmann disease	Absent	Absent	Absent	Absent	PW
Bernard-Soulier syndrome	NL	NL	NL	NL	Absent
Storage pool disease	↓	PW	↓	NL, ↓	PW
Hermansky-Pudlak syndrome	↓	PW	↓	NL	PW
Gray platelet syndrome	↓	↓	↓	NL	NL
von Willebrand disease	NL	NL	NL	NL	↓, NL†

ADP, Adenosine diphosphate; NL, normal; NSAIDs, nonsteroidal anti-inflammatory drugs; PW, primary wave aggregation only; ↓, decreased.

*Aspirin results in decreased aggregation with most collagen doses.

†In von Willebrand disease type 2B, patients have increased aggregation with low-dose ristocetin and decreased or normal aggregation with standard doses of ristocetin.