TABLE 51-6 DRUGS AFFECTING PLATELET FUNCTION

STRONG INHIBITORS	
Abciximab (and other anti-GPIIb/IIIa or anti-RGD compounds)	Dextran
Aspirin (often contained in over-the-counter medications)	Fibrinolytics
Clopidogrel, ticlopidine (ADP-receptor blockers)	Heparin
Nonsteroidal anti-inflammatory drugs	Hetastarch
MODERATE INHIBITORS	**WEAK INHIBITORS**
Antibiotics (penicillins, cephalosporins, nitrofurantoin)	Alcohol
	Nitroglycerin
	Nitroprusside

ADP, Adenosine diphosphate; GP, glycoprotein; RGD, arginine-glycine-aspartate.

Nonetheless, the uremic state does put an individual at risk for platelet dysfunction–related bleeding. Because no formal tests are available, the diagnosis should be suspected in individuals with acute or chronic renal failure who demonstrate platelet-like bleeding disorders.

Short-term treatment of uremic platelet dysfunction includes administration of DDAVP and cryoprecipitate. Both increase circulating von Willebrand antigens, which can help to overcome some of the uremia-associated platelet deficits. Conjugated estrogens are of some benefit for long-term treatment. Platelet transfusions may be marginally useful in patients with life-threatening bleeding and acute renal failure, but the effect of this treatment is short lived because the transfused platelets rapidly acquire the uremic defect. Platelet transfusion should not be considered as a first-line therapy for most forms of uremic bleeding.

Congenital Causes of Platelet Dysfunction

Platelet Glycoprotein Defects

Inherited qualitative platelet defects include abnormalities of platelet receptors and granules. Two rare but well-characterized platelet receptor disorders are Bernard-Soulier syndrome and Glanzmann's thrombasthenia.

Bernard-Soulier syndrome is caused by decreased surface expression of platelet GPIb (i.e., primary von Willebrand factor [vWF] receptor) and less commonly by diminished GPIb function. The syndrome is characterized by mild thrombocytopenia, increased bleeding time, large platelets, and mild to moderate bleeding symptoms. The diagnosis is usually made in children, but some may not show symptoms until adulthood. Laboratory testing for Bernard-Soulier syndrome shows an absent platelet aggregation response to ristocetin (see Table 51-5 and Fig. 51-5) despite adequate vWF levels and function, such as normal ristocetin cofactor (Rcof) activity.

Glanzmann's thrombasthenia is characterized by an increased bleeding time and abnormally low levels of expression of platelet GPIIb/IIIa (i.e., receptor for vWF and fibrinogen) or, less commonly, normal expression but absent GPIIb/IIIa function. Patients usually exhibit bleeding in childhood. In cases of Glanzmann's thrombasthenia, platelet aggregation testing confirms an absent or diminished response to all agonists except ristocetin (see Table 51-5 and Fig. 51-5).

Platelet transfusions correct the bleeding in Bernard-Soulier syndrome and Glanzmann's thrombasthenia. However, because of the high risk for alloimmunization with frequent platelet transfusions (i.e., patients lack GPIb or GPIIb/IIIa), this therapy should be used sparingly and only as clinically needed.

Platelet Granule or Secretory Defects

Inherited platelet granule disorders are defined by the type of granule that is absent or defective. Storage pool disease is characterized by a relative decrease or absence of dense granules and correspondingly moderate to severe mucosal bleeding. Release of dense granule constituents that recruit and activate platelets is impaired. Storage pool disease has a diminished or absent secondary wave of aggregation in response to most agonists (see Table 51-5 and Fig. 51-5).

Hermansky-Pudlak syndrome is a dense granule deficiency associated with oculocutaneous albinism and mild thrombocytopenia. Patients have significant bleeding, which may occur spontaneously but more often occurs with surgical procedures.

Chédiak-Higashi syndrome is a rare granule disorder characterized by mild bleeding, partial albinism, and recurrent pyogenic infections. Large, irregular, gray-blue inclusions are seen in neutrophils and monocytes.

Gray platelet syndrome is characterized by colorless or gray platelets that lack normal staining on the peripheral smear, and electron microscopy confirms the loss of α-granules or their contents. Patients with gray platelet syndrome have a history of mild bleeding, and aggregation testing detects diminished responses to epinephrine, ADP, and collagen.

All the platelet granule disorders are successfully treated by avoiding aspirin and other antiplatelet drugs and by hormonal control of menses in women. Platelet transfusions are used when bleeding occurs.

Platelet Transfusion Therapy

Standard Platelet Therapy

Platelet transfusions derived from the whole blood of healthy donors can be used to stop or prevent bleeding. The two broad categories of platelet transfusion support are based on the conditions previously discussed: prophylactic platelet transfusions for thrombocytopenia in nonbleeding patients and platelet transfusion for acute bleeding.

For the nonbleeding thrombocytopenic patient, several triggers can prompt platelet transfusion in the absence of frank hemorrhage. Patients receiving chemotherapy may be severely thrombocytopenic and should be transfused when their platelet counts are less than 10,000/μL to prevent spontaneous bleeding. This is a safe and appropriate threshold for patients with relatively uncomplicated clinical pictures without fever, sepsis, or GI bleeding. The threshold of 10,000/μL, which was rigorously established through several prospective, randomized, controlled trials, significantly decreases the frequency of platelet transfusion and thereby reduces risks associated with multiple blood product exposures. If the patient has complicating circumstances or is being treated on an outpatient basis, prophylactic transfusions