offending drug usually results in an equally rapid rise in the platelet count. For some patients with prolonged thrombocytopenia after drug removal, immunosuppression with agents such as IVIG (2 g/kg in two to three divided doses) or steroids may restore baseline platelet counts.

Although confirmation of drug-induced thrombocytopenia can often be made by testing for antibodies with drug specificities, these tests are usually routinely performed only by specialty reference laboratories. When drug-induced thrombocytopenia is suspected, clinicians should not wait for specific antibody testing results before discontinuing potential offending agents.

Fetal and Neonatal Alloimmune Thrombocytopenia

Fetal and neonatal alloimmune thrombocytopenia (FNAIT) occurs when a mother is homozygous for an uncommon platelet alloantigen, most often human platelet antigen 1b (HPA-1b) on the platelet GPIIIa receptor, and a child expresses the HPA-1a haplotype inherited from the father. The pathogenesis of alloimmune thrombocytopenia is analogous to the mechanism by which Rh(D) sensitization induces hemolytic disease of the newborn. The mother is exposed to the HPA-1a antigen during a first pregnancy, and during that or subsequent pregnancies, she produces high-titer IgG antibody against HPA-1a. These antibodies cross the placenta, react with HPA-1a–positive fetal platelets, and cause peripheral-platelet destruction through the RES.

A diagnosis of FNAIT is frequently suspected when in utero fetal bleeding is observed by imaging studies or when an otherwise healthy newborn has unexpected bleeding associated with thrombocytopenia (typically with platelet counts of 50,000 to 75,000/μL or lower). A maternal history of FNAIT is a strong predictor of its occurrence during future pregnancies.

After a diagnosis of FNAIT is suspected, it may be confirmed by examining maternal sera for anti-HPA alloantibodies. Although bleeding may be severe in cases of FNAIT, the antibody does not necessarily predict whether bleeding will occur in utero, at delivery, or in the first days of life, and it is used primarily for confirmatory purposes.

Transfusion of washed maternal platelets (or random platelets lacking the HPA-1a antigen) and IVIG are useful for treating bleeding and restoring the platelet count. For newborns who recover from bleeding, there are few long-lasting deficits from FNAIT after circulating maternal antibodies are cleared from the circulation.

Post-transfusion Purpura

Alloimmune thrombocytopenia can occur in adults after transfusion (i.e., post-transfusion purpura [PTP]). As in neonates, this condition is based on exposure to a common platelet alloantigen that is not present on the patient's native platelets. For instance, PTP can occur after transfusion of a blood product in an individual who lacks HPA-1a and who has been previously alloimmunized to this antigen during a prior pregnancy or transfusion. Because more than 95% of blood donors express HPA-1a and the antigen is shed by platelets, any blood product can contain HPA-1a. Although not clearly understood, some investigators have speculated that soluble HPA antigens are deposited onto endogenous platelets, resulting in their rapid clearance by anti-HPA alloantibodies.

The diagnosis of PTP can be confirmed by demonstrating anti-HPA antibodies in the serum of an affected individual. Patients are typically treated with IVIG, and additional transfusions must be derived from donors lacking the implicated HPA. Although HPA-1a is the most common cause of alloimmune thrombocytopenia, other platelet alloantigens can cause this clinical syndrome (Table 51-3).

TABLE 51-2 COMMONLY USED DRUGS ASSOCIATED WITH IMMUNE THROMBOCYTOPENIA

DRUG CLASS	EXAMPLES
Antibiotics	Penicillins
	Cephalosporins (cephalothin, ceftazidime)
	Vancomycin
	Sulfonamides (sulfisoxazole)
	Rifampin
	Linezolid
	Quinine
Antiepileptics, antipsychotics, and sedative-hypnotics	Benzodiazepines (diazepam)
	Haloperidol
	Carbamazepine
	Lithium
	Phenytoin
Antihypertensives	Diuretics (chlorothiazide)
	Angiotensin-converting enzyme inhibitors (ramipril)
	Methyldopa
Analgesics and anti-inflammatories	Acetaminophen
	Ibuprofen
	Naproxen
Antiplatelet agents	Abciximab
	Tirofiban
Anticoagulants	Heparin
	Low-molecular-weight heparin

TABLE 51-3 MOLECULAR BASIS FOR ALLOIMMUNE THROMBOCYTOPENIA

GLYCOPROTEIN	ALLELES (ALLOANTIGENS)	PHENOTYPE/ FREQUENCY	AMINO ACID AND LOCATION
IIIa	HPA-1a/1b	0.98/0.25	Leucine/proline; 33
Ib	HPA-2a/2b	0.99/0.14	Threonine/methionine; 145
IIb	HPA-3a/3b	0.91/0.70	Isoleucine/serine; 843
IIIa	HPA-4a/4b	0.99/0.01	Arginine/glutamine; 143
Ia	HPA-5a/5b	0.99/0.21	Glutamic acid/lysine; 505
IIIa	HPA-6a/6b	NA	Proline/glutamic acid; 407
IIIa	HPA-7a/7b	NA	Proline/glutamic acid; 407
IIIa	HPA-8a/8b	NA	Arginine/cystine; 636

HPA, Human platelet antigen; NA, data not available.