Platelet disorders

All platelet disorders have ↑ bleeding time (BT), mucous membrane bleeding, and microhemorrhages (eg, petechiae, epistaxis). Platelet count (PC) is usually low, but may be normal in qualitative disorders.

DISORDER	PC	BT	NOTES
Bernard-Soulier syndrome	–/↓	↑	Defect in adhesion. ↓ GpIb → ↓ platelet-to-vWF adhesion. Labs: abnormal ristocetin test, large platelets.
Glanzmann thrombasthenia	–	↑	Defect in aggregation. ↓ GpIIb/IIIa (↓ integrin $\alpha_{IIb}\beta_3$) → ↓ platelet-to-platelet aggregation and defective platelet plug formation. Labs: blood smear shows no platelet clumping.
Immune thrombocytopenia	↓	↑	Destruction of platelets in spleen. Anti-GpIIb/IIIa antibodies → splenic macrophages phagocytose platelets. May be idiopathic or 2° to autoimmune disorders (eg, SLE), viral illness (eg, HIV, HCV), malignancy (eg, CLL), or drug reactions. Labs: ↑ megakaryocytes on bone marrow biopsy, ↓ platelet count. Treatment: steroids, IVIG, rituximab, TPO receptor agonists (eg, eltrombopag, romiplostim), or splenectomy for refractory ITP.
Thrombotic thrombocytopenic purpura and hemolytic-uremic syndrome	↓	↑	Disorders overlap significantly in symptomatology. Pathophysiology: ▪ TTP: inhibition or deficiency of ADAMTS13 (a vWF metalloprotease) → ↓ degradation of vWF multimers → ↑ large vWF multimers → ↑ platelet adhesion and aggregation (microthrombi formation). ▪ HUS: commonly caused by shiga-like toxin from EHEC (serotype O157:H7) infection. Atypical form (aHUS) is caused by complement gene mutations or autoimmune response. Presentation: triad of thrombocytopenia, microangiopathic hemolytic anemia, acute kidney injury. Also: ▪ TTP: pentad (triad + fever + neurologic symptoms). ▪ HUS: history of bloody diarrhea. Epidemiology: ▪ TTP, typically in females. ▪ HUS, typically in children. Labs: ↓ platelet count, hemolytic anemia (eg, schistocytes, ↑ LDH). Normal PT/PTT helps distinguish HUS and TTP (coagulation pathway is not activated) from DIC (coagulation pathway is activated). Treatment: plasmapheresis, steroids, rituximab.