Approach to Thrombocytopenia

HEMATOLOGY

99.8% — KEY DECISION RULE
4Ts score 0–3 (low probability)[1,2]
NPV for HIT (13 studies, 3068 patients): no PF4 test, keep heparin

Platelets <150 ×10⁹/L, or a fall from baseline → Bleeding history and exam; heparin and drug review; prior counts; smear, citrate tube if clumps[8] → CBC, creatinine, LFTs, PT/aPTT, fibrinogen, HIV, HCV, β-hCG, type and screen[8] → **Bleed, HIT, TMA, DIC, blasts or HELLP?**

Yes →

Emergency: treat now; call hematology[8]

- Major bleed; headache: CT head
- Heparin and fall >50%: suspect HIT
- Schistocytes: TTP until excluded
- Long PT/aPTT, low fibrinogen: DIC
- Blasts or pancytopenia on smear
- Pregnant: HELLP or preeclampsia

→ 4Ts ≥4: non-heparin AC; high PLASMIC: PLEX; major bleed: plt[1,3,8]

If not: which mechanism?

	Low production	Immune destruction	Consumption	Sequestration, dilution
CAUSES	• **Leukemia, MDS, marrow infiltration** • Sepsis; viral: HIV, HCV, EBV, CMV • Alcohol, B12 or folate lack, chemo	• **HIT: any heparin, even flushes** • Drugs: quinine, antibiotics, ASMs • ITP (exclusion); SLE, APS, lymphoma	• **TTP; HUS (Shiga toxin, complement)** • **DIC: sepsis, cancer, trauma, obstetric** • HELLP; ECMO, balloon pump, valves	• Hypersplenism: cirrhosis, portal HTN • Massive transfusion; hypothermia • Gestational thrombocytopenia
CLUES	• Other cytopenias; blasts on smear[8] • Alcohol use, poor diet; macrocytosis • Fever, bone pain, B symptoms	• Heparin d5–10; <24 h if ≤100 d prior[1,8] • New drug; sudden, deep fall[8] • Well; isolated; large platelets[8]	• Schistocytes, high LDH, low haptoglobin[8] • TTP: plt <30 ×10⁹/L, neuro signs, fever[8] • Bloody diarrhea, then AKI: ST-HUS[8]	• Splenomegaly; stigmata of liver disease • Pregnant, well, normal BP; plt ≥100[10]
WORKUP	• B12, folate, HIV, HCV[8] • Marrow biopsy if other lines low[8]	• 4Ts; anti-PF4 only if ≥4[1,2] • ANA, aPL if SLE or APS suspected[8]	• PLASMIC; ADAMTS13 before PLEX[3,4] • DAT, D-dimer; stool Shiga toxin if diarrhea[8]	• Ultrasound: spleen, liver • Pregnant: BP, urine protein, LFTs
MANAGE	• Treat cause; stop marrow toxins • No bleed, chemo: platelets if <10 ×10⁹/L[7] • Marrow disease: urgent hematology[8]	• Stop drug; HIT: argatroban/fonda/DOAC[1,8] • ITP <30: steroids + ritux or TPO-RA[6] • ITP critical bleed: plt, IVIG, steroid, TXA[9]	• TTP: PLEX, steroid, ritux, caplacizumab[5,11] • DIC: fix cause; plt <10, <50 if bleeding[7,12] • TTP: no platelets unless major bleed[8]	• Treat cause; usually observe • Major surgery: platelets if <50 ×10⁹/L[7]

Stethopedia
stethopedia.ca/approach/thrombocytopenia

Evidence [1] Cuker 2018, Blood Adv [2] Cuker 2012, Blood [3] Bendapudi 2017, Lancet Haematol [4] Zheng 2020, J Thromb Haemost (Dx) [5] Zheng 2020, J Thromb Haemost (Tx) [6] Cuker 2026, Blood Adv [7] Metcalf 2025, JAMA [8] Manual 2024–25, pp. 136, 138, 144 [9] Chowdhury 2026, Blood Adv [10] Reese 2018, N Engl J Med [11] Zheng 2025, J Thromb Haemost [12] Levi 2009, Br J Haematol