* Individual platelet range relatively narrow; delta >100 bij <0.1%: 50% afname kan nog normaal zijn
* Risico bloeding, afhankelijk van
* – ziekte (minder bij ITP bij zelfde trombocytengetal)
* – hoogte trombocyten, spontane bloeding pas <20 en meestal pas <10
* – plaatjesfunctie (Bernard-Soulier, MDS)
* – plasmatische stollingsziekte (leverziekte, DIS)
* – invasieve ingreep, dan risico op bloeding indien <50 (hoog-risico als neuro-chirurgie, cardiale of orthopedische chirurgie)
* – redistributie bij splenomegalie (ernstige bloeding en TR >60 past hier niet bij)
* – natte purpura risico
* numerous herbal preparations [[25,26](https://www.uptodate.com/contents/approach-to-the-adult-with-unexplained-thrombocytopenia/abstract/25%2C26)], foods [[27,28](https://www.uptodate.com/contents/approach-to-the-adult-with-unexplained-thrombocytopenia/abstract/27%2C28)], and over-the-counter medicines
* vascular conditions associated with platelet destruction (eg, giant capillary hemangioma, large aortic aneurysms, cardiopulmonary bypass, intraaortic balloon pumps)
* Asymptomatic: ITP, leverziekte, HIV, MDS congenitaal
* • bloeding maar niet ziek: medicatie, ITP
* • neurologic findings – TMA, B12, koper
* veelvoorkomende bij zieke patienten
* wisselt per studie, gemiddeld 30%
* **IC**
* 35% sepsis/infectie/DIS
* 10% leverziekte / hypersplenisme
* 5% hematologische ziekte
* 5% medicatie
* 5% chemotherapie
* 2% massale transfusie
* 2% alcoholisme
* bloedkweken, stollingsonderzoek, leverwaarden
* gevaarlijk: HIT, TTP, PTP, ITP, acute leukemie
* ●Bleeding in the setting of severe thrombocytopenia (ie, platelet count <50,000/microL)
* ●Urgently needed invasive procedure with severe thrombocytopenia
* ●Pregnancy with severe thrombocytopenia
* ●Suspected heparin-induced thrombocytopenia (HIT) or post-transfusion purpura
* ●Suspected thrombotic thrombocytopenic purpura (TTP), hemolytic uremic syndrome (HUS), or drug-induced thrombotic microangiopathy (DITMA)
* ●Suspected acute leukemia, aplastic anemia, or other bone marrow failure syndrome
* HISTORY
* veganism, vegetarianism, zinc ingestion
* Patients with bleeding due to thrombocytopenia may have petechiae, purpura, or frank mucosal bleeding.
* ●
* Anemie en trombopenie: ijzergebrek, TMA, Evans, dd pancytopenie
* Leukocytose en trombopenie: infection, chronic inflammation, malignancy.
* Pancytopenie

ADDITIONAL EVALUATION

* ●Megaloblastic changes in the RBC and granulocytic series suggest a nutrient deficiency (eg, [vitamin B12](https://www.uptodate.com/contents/cyanocobalamin-vitamin-b12-drug-information?search=thrombopenia&topicRef=6680&source=see_link), folate, copper)
* High-impact sporten vermijden
* NSAID/gingko biloba vermijden
* Antistolling heroverwegen
* Overweeg invasieve procedures vermijden
* Oorzaak behandelen
* Transfusie
* SUMMARY AND RECOMMENDATIONS
* •In patients with other clinical findings, causes of thrombocytopenia include infection, sepsis, disseminated intravascular coagulation (DIC), drug-induced thrombocytopenia, HIT, liver disease, lymphoma, other malignancies, nutrient deficiencies ([vitamin B12](https://www.uptodate.com/contents/cyanocobalamin-vitamin-b12-drug-information?search=thrombopenia&topicRef=6680&source=see_link), folate, copper), TTP or HUS, antiphospholipid syndrome (APS), and paroxysmal nocturnal hemoglobinuria (PNH). (See ['Thrombocytopenia with bleeding or other symptoms'](https://www.uptodate.com/index.html%22%20%5Cl%20%22H1189684) above.)
* •In acutely ill patients, common causes of new-onset thrombocytopenia include sepsis, DIC, and drug-induced thrombocytopenia ([table 1](https://www.uptodate.com/contents/image?imageKey=HEME%2F58104&topicKey=HEME%2F6680&search=thrombopenia&rank=1~150&source=see_link)). Many patients in the intensive care unit with thrombocytopenia have more than one cause. (See ['Acutely ill/intensive care unit'](https://www.uptodate.com/index.html%22%20%5Cl%20%22H35177928) above.)
* ●The history should focus on prior platelet counts, family history, bleeding, medications ([table 3](https://www.uptodate.com/contents/image?imageKey=HEME%2F73618&topicKey=HEME%2F6680&search=thrombopenia&rank=1~150&source=see_link)), over-the-counter remedies ([table 4](https://www.uptodate.com/contents/image?imageKey=HEME%2F60296&topicKey=HEME%2F6680&search=thrombopenia&rank=1~150&source=see_link)), infectious exposures, dietary practices, and other medical conditions (eg, hematologic disorders, rheumatologic conditions, surgery, transfusion).
* GRAPHICS
* Major causes of disseminated intravascular coagulation

|  |
| --- |
| * Events that initiate DIC
 |
| * Septicemia - Gram negative and Gram positive
 |
| * Crush injury or complicated surgery
 |
| * Severe head injury
 |
| * Cancer procoagulant (Trousseau's syndrome)
 |
| * Acute leukemia, especially promyelocytic
 |
| * Complications of pregnancy
 |
| * Amniotic fluid embolism
 |
| * Abruptio placentae
 |
| * HELLP syndrome
 |
| * Eclampsia and severe preeclampsia
 |
| * Septic abortion
 |
| * Amphetamine overdose
 |
| * Giant hemangioma (Kasabach-Merritt syndrome)
 |
| * Abdominal aortic aneurysm
 |
| * Peritoneovenous shunt
 |
| * Acute hemolytic transfusion reaction (ABO incompatibility)
 |
| * Paroxysmal nocturnal hemoglobinuria
 |
| * Snake and viper venoms
 |
| * Liver disease
 |
| * Fulminant hepatic failure
 |
| * Reperfusion after liver transplantation
 |
| * Heat stroke
 |
| * Burns
 |
| * Purpura fulminans
 |
| * Events that complicate and propagate DIC
 |
| * Shock
 |
| * Complement pathway activation
 |

* Graphic 58104 Version 3.0
* Causes of thrombocytopenia in adults

|  |
| --- |
| * Falsely low platelet counts (pseudothrombocytopenia)
 |
| * In vitro platelet clumping caused by ethylenediaminetetraacetic acid (EDTA)-dependent agglutinins (naturally occurring antibodies)
 |
| * In vitro platelet clumping caused by an insufficiently anticoagulated specimen
 |
| * In vitro platelet clumping caused by glycoprotein IIb/IIIa inhibitors (eg, abciximab) (NOTE: these can also cause true thrombocytopenia)
 |
| * Giant platelets counted by automated counter as white blood cells rather than platelets
 |
| * Common causes of thrombocytopenia
 |
| * Primary immune thrombocytopenia (ITP)
 |
| * Drug-induced immune thrombocytopenia (DITP)
 |
| * Heparin (NOTE: special case, also can cause thrombosis)
 |
| * Quinine (as in over-the-counter tablets for leg cramps; also in beverages)
 |
| * Sulfonamides (eg, trimethoprim-sulfamethoxazole [Bactrim; Septra])
 |
| * Acetaminophen (Tylenol, Panadol)
 |
| * Cimetidine (Tagamet)
 |
| * Ibuprofen (Advil, Motrin)
 |
| * Naproxen (Aleve, Midol)
 |
| * Ampicillin (Omnipen, Apo-Ampi)
 |
| * Piperacillin (Pipracil, Zosyn)
 |
| * Vancomycin (Vancocin)
 |
| * Glycoprotein IIb/IIIa inhibitors (abciximab [ReoPro], tirofiban [Aggrastat], eptifibatide [Integrilin])
 |
| * Food and beverages
 |
| * Quinine-containing beverages (tonic water, Schweppes bitter lemon)
 |
| * Walnuts
 |
| * Certain herbal teas
 |
| * Infections
 |
| * HIV
 |
| * Hepatitis C
 |
| * Epstein-Barr virus (EBV; can be associated with infectious mononucleosis)
 |
| * Helicobacter pylori (suspected in patients with symptoms of dyspepsia or peptic ulcer disease)
 |
| * Sepsis with disseminated intravascular coagulation (DIC)
 |
| * Intracellular parasites (eg, malaria, babesia)
 |
| * Hypersplenism due to chronic liver disease
 |
| * Alcohol
 |
| * Nutrient deficiencies (eg, vitamin B12, folate, copper)
 |
| * Rheumatologic/autoimmune disorders (eg, systemic lupus erythematosus, rheumatoid arthritis)
 |
| * Pregnancy
 |
| * Gestational thrombocytopenia
 |
| * Preeclampsia
 |
| * HELLP syndrome (hemolysis, elevated liver function tests, low platelets)
 |
| * Other causes of thrombocytopenia
 |
| * Myelodysplasia
 |
| * Suspected in older patients, in whom a bone marrow biopsy may be appropriate
 |
| * Cancer with disseminated intravascular coagulation
 |
| * Cancer with bone marrow infiltration or suppression (eg, lymphoma, leukemia, some solid tumors)
 |
| * Paroxysmal nocturnal hemoglobinuria (PNH)
 |
| * Thrombotic microangiopathy (TMA)
 |
| * Thrombotic thrombocytopenic purpura (TTP) is manifested by thrombocytopenia and microangiopathic hemolytic anemia; fever, renal failure, and/or neurologic symptoms may or may not be present
 |
| * Hemolytic uremic syndrome (HUS) is typically seen in children following infection with a Shiga-toxin producing organism (Escherichia coli or Shigella)
 |
| * Drug-induced TMA may occur with quinine, certain cancer therapies, calcineurin inhibitors, and others
 |
| * Antiphospholipid syndrome (APS)
 |
| * Aplastic anemia
 |
| * Hereditary thrombocytopenias
 |
| * An important consideration, especially in young patients who do not respond to treatment. Some specific syndromes are listed. However, many patients appear to have autosomal dominant thrombocytopenia with no other clinical features.
 |
| * Von Willebrand disease type 2B
 |
| * Wiskott-Aldrich syndrome
 |
| * Alport syndrome
 |
| * May-Hegglin anomaly
 |
| * Fanconi syndrome
 |
| * Bernard-Soulier syndrome
 |
| * Thrombocytopenia absent radius syndrome
 |

* Δ In addition to parenteral formulations, vancomycin may be present in orthopedic cement used for joint replacement.
* Commercially available sources of quinine

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|

|  |
| --- |
| * Available forms of quinine:
 |
| * Quinine sulfate capsules/tablets (as anti-malarial therapy or for leg cramps)
 |
| * Quinine-containing beverages (eg, quinine water, tonic water, bitter lemon, gin and tonic)
 |
| * Quinine is also added to other popular beverages because of its fluorescent properties (eg, "jello shots," "shocktails")
 |
| * Herbal preparations containing quinine or bark from the Cinchona tree\*
 |

 |

* In the United States, quinine tablets are available only by prescription for the treatment of malaria (as Qualaquin). In other countries, quinine may be available for leg cramps by prescription or over-the-counter. We believe all of the products listed above have the potential for causing drug-induced immune thrombocytopenia (DITP) and/or immune-mediated drug-induced thrombotic microangiopathy (DITMA).
* Adapted from: Liles NW, Page EE, Liles AL, et al. Diversity and severity of adverse reactions to quinine: a systematic review. Am J Hematol 2016; 91:461.
* Common presentations of patients with thrombocytopenia

|  |
| --- |
| * Office presentation
 |
| * Asymptomatic, ISOLATED, incidentally-discovered thrombocytopenia
 |
| * Common
 |
| * Immune thrombocytopenia (ITP)
 |
| * Gestational thrombocytopenia during pregnancy
 |
| * Less common
 |
| * Occult liver disease
 |
| * Myelodysplastic syndrome
 |
| * Congenital thrombocytopenia
 |
| * HIV infection
 |
| * Symptomatic, severe thrombocytopenia
 |
| * Common
 |
| * Drug-induced thrombocytopenia
 |
| * Immune thrombocytopenia (ITP)
 |
| * Hospital presentation
 |
| * Thrombocytopenia as part of a multisystem illness
 |
| * Common
 |
| * Drug-induced thrombocytopenia
 |
| * Heparin-induced thrombocytopenia
 |
| * Liver disease
 |
| * Sepsis with disseminated intravascular coagulation (DIC)
 |
| * Cancer with DIC
 |
| * Pregnancy
 |
| * Preeclampsia
 |
| * HELLP syndrome (hemolysis, elevated liver enzymes, and low platelets)
 |
| * Abruptio placentae with DIC
 |
| * Multi-organ failure syndromes
 |
| * Less common
 |
| * Thrombotic thrombocytopenic purpura (TTP, acquired or hereditary)
 |
| * Drug-induced thrombotic microangiopathy (DITMA)
 |
| * Hemolytic uremic syndrome (HUS)
 |
| * Lymphoma
 |
| * Acute leukemia
 |
| * Antiphospholipid syndrome
 |
| * Paroxysmal nocturnal hemoglobinuria (PNH)
 |
| * Nutrient deficiency (vitamin B12, folate, copper)
 |

* Refer to UpToDate topics on thrombocytopenia for further details.
* Graphic 50310 Version 4.0
* Clinical features of bleeding disorders

|  |  |
| --- | --- |
| * Bleeding characteristics
 | * Type of bleeding disorder
 |
| * Thrombocytopenia or platelet function defects
 | * Clotting factor deficiencies or inhibitors
 |
| * Major sites of bleeding
 | * Mucocutaneous (eg, mouth, nose, gastrointestinal tract, urinary tract, menorrhagia)
 | * Deep tissue (eg, joints, muscles) or soft tissue hematomas
 |
| * Petechiae
 | * Common
 | * Uncommon
 |
| * Ecchymoses
 | * Generally small and superficial; may be significant, depending upon the degree of thrombocytopenia
 | * May develop large ecchymoses
 |
| * Excessive bleeding after minor cuts
 | * Yes
 | * Not usually
 |
| * Excessive bleeding with surgery or invasive procedures
 | * Often immediate; degree varies with severity of the defect (eg, no excess bleeding with mild thrombocytopenia, severe bleeding with certain platelet function defects such as GT)
 | * Often during the procedure. Some individuals may experience delayed bleeding (eg, those with factor XIII deficiency).
 |

* Individuals with mild disorders may not report significant bleeding. Refer to UpToDate for details of the evaluation of a suspected bleeding disorder.
* GT: Glanzmann thrombasthenia.
* 