Thrombocytopenia — Symptoms and Treatment

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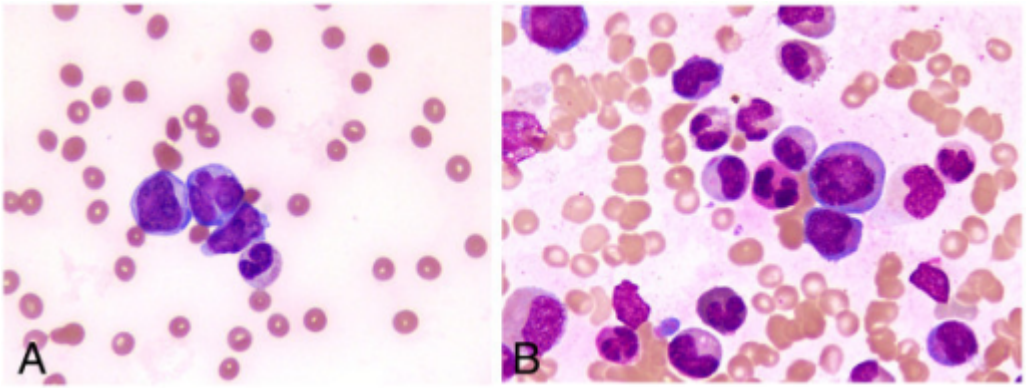
Thrombocytes are responsible for the initial wound closure in the course of primary hemostasis. If there is a deficiency in thrombocytes, the bleeding time is significantly prolonged after an injury. There are several causes of this condition so it is important to consider different (malignant) underlying diseases. This article also discusses the classification scheme for thrombocytopenia.



Definition, Etiology, and Pathophysiology

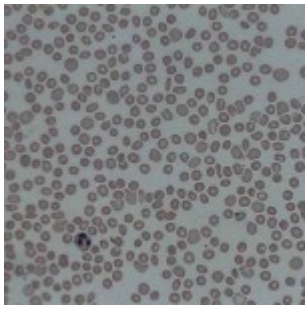


Image: 'A film from a thrombocytopenic patient. Almost devoid of platelets.' by Prof. Erhabor Osaro. License: CC BY-SA 4.0

Thrombocytopenia is a **deficiency of thrombocytes in peripheral blood**. Thrombocytes are functionally integrated into the hemostasis system. Thus, **disorders** of **thrombocyte function** cause **pathological bleeding**. In the spectrum of hemorrhagic diatheses, this type of coagulopathy is the main cause of pathological bleeding.

Like almost all bleeding disorders, the causes of thrombocytopenia can be divided into

disturbed synthesis or increased peripheral turnover.

Thrombocytopenia due to synthesis disorders

Decreased thrombocytopoiesis can occur in the context of an **aplastic disorder**. For example, **Fanconi anemia** is a congenital variation. Acquired blood cell (and thus, thrombocyte) synthesis disorders include bone marrow lesions via radiation, chemicals, medications, infections (e.g., HIV), or antibodies. In addition, **bone marrow lesions** are possible in the context of malignant infiltration in **leukemia, carcinomas,** or **lymphomas**. Similarly, the **myeloproliferative disease** can likewise replace the bone marrow in the course of the respective disease.

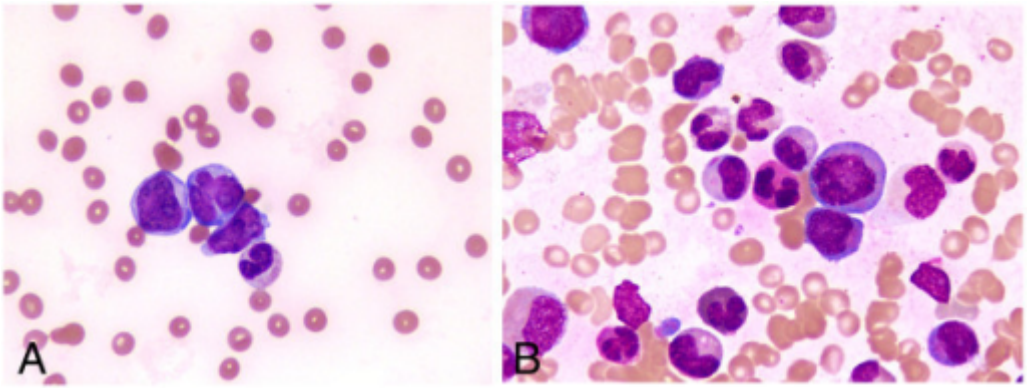


Image: 'Peripheral blood smear and bone marrow aspirate. (A) Peripheral blood smear showing blast cells. (B) Bone marrow smear revealing a blast cell exhibiting an Auer rod' by Openi. License: CC BY 2.0

Synthesis disorders can, however, also develop if the bone marrow is functioning properly. For example, maturation of the cells can be impaired, which occurs in cases of vitamin deficiency. In this context, vitamin B12 or folic acid deficiencies are especially important.

Thrombocytopenia due to increased peripheral turnover

The bone marrow can adequately compensate peripheral thrombocyte consumption and for long periods of time. If this consumption exceeds the synthesis ability of the bone marrow, thrombocytopenia develops. The lifespan of thrombocytes is short (about 1 week), and in the event of increased consumption, the thrombocytes are partially consumed after some hours, and the turnover experiences a fivefold increase. These numbers illustrate the high capability of the bone marrow.

Peripheral consumption can be **further divided** into:

Immune thrombocytopenia

Many mechanisms lead to the production of autoantibodies against thrombocytes. If thrombocytopenia is observed after a previous infection, an **acute post-infectious immune thrombocytopenia** is probably present. It often affects children after gastrointestinal or respiratory viral infections. In most cases, the disease is self-limiting. In such cases, aspirin must not be given! If spontaneous healing does not occur, glucocorticoids can be administered. Thrombocyte concentrations only become necessary in the event of life-threatening bleeding.

Apart from the acute form, there is also a chronic variation: **chronic immune thrombocytopenic purpura (Werlhof's disease)**. Here, autoantibodies are produced in the spleen. The disease is often associated with ***Helicobacter pylori-gastritis***.

Therapeutically, **immunosuppressive therapy** is initiated (**glucocorticoids, immunoglobulins,** or **rituximab**) besides the *H. pylori* eradication and careful observation. The last resort is **splenectomy**.

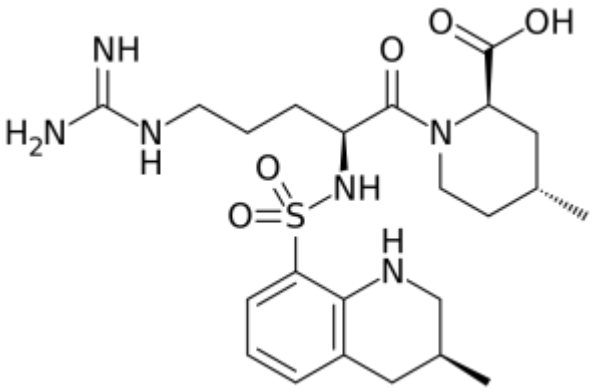


Image: 'Skeletal formula of argatroban, a direct thrombin inhibitor as an alternative to heparin in HIT' by Fvasconcellos. License: Public Domain

Further, it should be noted that drugs can provoke antibody production. However, a notable variation is **heparin-induced thrombocytopenia (HIT)**, during which **antibodies are produced against** the **heparin/platelet factor-4-complex** due to heparin therapy. This syndrome is potentially life-threatening. Therapy has to be stopped or changed immediately.

Autoantibodies can also be produced in the context of several underlying diseases, e.g., **systemic lupus erythematosus, rheumatoid arthritis**, **HIV infection**, **malignant lymphoma,** and **HELLP syndrome** (**h**emolysis, **e**levated **l**iver enzymes, and a **l**ow **p**latelet count). It is also important to consider **allo-antibody-induced thrombocytopenia** after blood transfusions.

Thrombocytopenia due to enhanced thrombin activity

Enhanced thrombin activity can be observed in **disseminated intravascular coagulation (DIC)** and in malignant and infectious processes.

Thrombocytopenia of mechanical genesis

Implanted artificial cardiac valves can mechanically damage the thrombocytes and, thus, alter the blood count. Further, **extracorporeal exchange measures** like dialysis or heart-lung-machines show a similar effect.

Thrombocytopenia due to other causes

Thrombocytopenia often occurs in the context of **splenomegaly**. However, the **spleen** allows the pooling of thrombocytes and simultaneously causes increased degradation. Compared to synthesis disorders in the bone marrow, all cell lines are mostly affected. **Thrombotic microangiopathy** or **hemolytic-uremic syndrome** also leads to thrombocytopenia via the development of thrombi rich in thrombocytes with microangiopathy.

Pseudo-thrombocytopenia

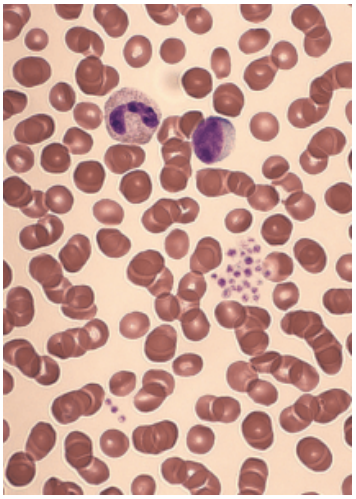


Image: ‘Blood smear of an EDTA sample showing activated lymphocytes and platelet aggregates’ by Openi. License: CC BY 2.0

Blood testing techniques can lead to false conclusions and a wrong suspicion of thrombocytopenia. Due to **EDTA-agglutinins** or **cold agglutinins**, very low thrombocyte counts can be reported, without the patient showing clinical symptoms. Thus, another blood sample should be taken and sent to the laboratory for testing; this time, preferably in a **citrate tube**.

Signs and Symptoms

Clinical presentation of thrombocytopenia

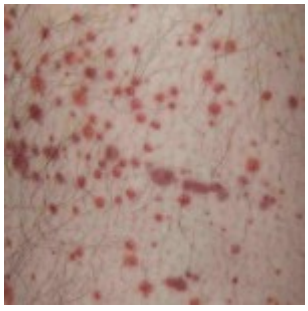


Image: ‘Purpura spots’ by Hektor. License: CC BY-SA 3.0

Clinically, thrombocytopenia becomes relevant at **values of < 80,000/µL** since increased bleeding tendency has to be assumed at this level, as long as no functional disorder of the thrombocytes (thrombocytopathy) is present. The classic characteristic of thrombocytic bleedings are **petechiae**, which develop **at thrombocyte counts of under < 50,000/µL**. Depending on the underlying disease, additional symptoms can manifest and are heterogeneous in nature. It is important to identify the exact cause of the clinical manifestation of a suspected underlying disease in the event of detected thrombocytopenia.

Diagnosis

Thrombocytopenia needs extensive anamnesis

The diagnosis of thrombocytopenia is made if **< 140,000 thrombocytes per µL of blood** are present. Diagnostically, it is important to conduct an extensive and targeted review, which narrows down the differential diagnoses. Additionally, the physician should consider the existence of an underlying disease. In the case of blood diseases, all cell lines have to be critically determined and evaluated!

Bone marrow analysis in thrombocytopenia

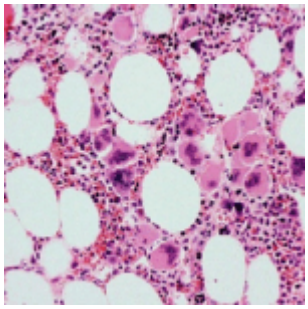


Image: 'Bone marrow biopsy in essential thrombocytosis showing increased megakaryocytes.' by Openi. License: CC BY 2.0

Diagnostics can include **bone marrow analysis**. If the **megakaryocyte count is decreased**, a **synthesis disorder** is present. In the event of an **increased megakaryocyte count**, a **maturation or turnover disorder** exists. Further, bone marrow analysis allows direct conclusions regarding primary or secondary bone marrow malignancies.

Therapy

Therapy depends on the extent and kind of thrombocytopenia. A pre-existing disease should be treated where possible. Drugs that exacerbate the disease should be immediately discontinued.

Symptomatically, thrombocytopenia is treated with **transfusions of thrombocyte concentrates**. In addition to different interventional or surgical measures, the thrombocyte count should be raised to certain values to minimize the risk of severe blood loss. As a benchmark, a **target thrombocyte count of > 50,000/µL** is reasonable. Thrombocyte concentrates are either acquired from freshly taken whole-blood units or via mechanical thrombocyte apheresis.

If no significant increase in thrombocyte count occurs after the administration of thrombocyte concentrates, the cause should be identified. The following causes should be considered:

- Splenomegaly, fever, sepsis, DIC, infections, or bleedings: The new thrombocytes are directly consumed.
- Immunological factors: Antibodies are eliminating the new thrombocytes.

More Information about Thrombocytopathies

Thrombocytic bleeding can also occur at normal thrombocyte values. In such a case, one should consider **thrombocyte function disorders**, which can occur in the context of different inherited diseases of metabolism or antiplatelet drug therapy.

Notes