Hematology

Thrombocytopenia — Symptoms and Treatment

See online here

Thrombocytes are responsible for the initial wound closure in the course of primary hemostasis. If there is a deficiency in thrombocytes the system bleeding time is significantly prolonged after an injury. The causes of the condition are many and have a wide spectrum. Regarding differential diagnosis, one has to consider different (malignant) underlying diseases. It is important to memorize the classification scheme for the sake of future medical occupation!

Definition, Etiology and Pathophysiology of Thrombocytopenia

Thrombocytopenia describes a deficiency in thrombocytes in peripheral blood. Thrombocytes are functionally integrated into the hemostasis system. Thus, thrombocyte function disorders cause

Image: “A film from a thrombocytopenic patient. Almost devoid of platelets.” by Prof. Erhabor Osaro. License: CC BY-SA 4.0
pathological bleeding. In the spectrum of hemorrhagic diatheses, this group of\ncoagulopathy is the main cause of pathological bleeding.

How does a disorder in thrombocyte cell count develop? Like almost all bleeding\ndisorders, the causes can be divided into disturbed synthesis or increased peripheral\nturnover.

Thrombocytopenia due to synthesis disorders

**Decreased thrombocytopoiesis** can occur in the context of an** aplastic disorder.** For\nevery example, [Fanconi anemia](https://en.wikipedia.org/wiki/Fanconi_anemia) is a congenital variation. Acquired blood cell (and, thus,\nthrombocyte) synthesis disorders concern bone marrow lesions via radiation, chemicals,\nmedicaments, infections ([HIV](https://en.wikipedia.org/wiki/Human IMMUNODEFICIENCY_VIRUS)) or antibodies. In addition, **bone marrow lesions** are\npossible in the context of malignant infiltration in [leukemia](https://en.wikipedia.org/wiki/Leukemia), [carcinomas](https://en.wikipedia.org/wiki/Carcinoma) or\nlymphomas. **Myeloproliferative diseases** can likewise replace the bone marrow in the\ncourse of the respective disease.

![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-4.0)

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

**Thrombocytopenia due to increased peripheral turnover**

The bone marrow can compensate peripheral thrombocyte consumption well and for long\nperiods of time. If this consumption exceeds the synthesis performance of the bone\nmarrow, thrombocytopenia develops. The already relatively short lifespan of the\nthrombocytes amounts to roughly one week. In the event of increased consumption, the\nthrombocytes are partially consumed after a couple of hours. The turnover experiences a\nfive fold increase. These numbers illustrate the high capability of the bone marrow.

For the sake of a better overview (and for internalization), the **peripheral consumption**\ncan be **further divided**:

**Immune thrombocytopenia**

Many mechanisms cause the occurrence of autoantibodies against thrombocytes. If\nthrombocytopenia is observed after a previous infection, an **acute post-infectious**\nimmune thrombocytopenia (ITP) is probably present. It often affects children after\ngastrointestinal 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.

Besides the acute form, there is also a chronic variation: the **chronic immune thrombocytopenic purpura (= Werlhof’s disease)**. Hereby, autoantibodies are produced in the spleen. The disease is often associated with a **Helicobacter pylori-gastritis**. Therapeutically, **immune suppressive therapy** is initiated (**glucocorticoids, immune globulins** or **rituximab**) besides the H. pylori eradication and temporizing behavior. The last-resort measure is the indication for **splenectomy**.

Also, it should be noted that medicaments can provoke antibody production. If thrombocytopenia manifests after the intake of medicaments, all medicaments should primarily be discontinued. A special and remarkable variation is **heparin-induced thrombocytopenia (HIT)**, during which **antibodies are produced against** the **heparin/platelet factor-4-complex** due to heparins. This syndrome is potentially life threatening. Therapy has to be stopped and changed immediately.

Autoantibodies can also be produced in the context of several underlying diseases, e.g. **systemic Lupus erythematoses**, **rheumatoid arthritis**, **HIV-infection**, **malignant lymphoma** and **HELLP syndrome**. 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. Also, **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**. On one hand, the **spleen** makes for 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 the **hemolytic-uremic syndrome** also leads to thrombocytopenia via development of thrombi rich in thrombocytes with...
Pseudothrombocytopenia

**Blood testing techniques** can lead to false conclusions and make you suspect thrombocytopenia. Due to **EDTA-agglutinins** or **cold agglutinins**, very low thrombocyte counts can be written on the laboratory printout, without the patient showing clinical symptoms. Before you inform the chief resident or even take your patient for a therapy session, you should at first take another, sovereign blood sample and send it to the laboratory for testing; this time, preferably in **citrate-blood**.

**Signs and Symptoms of Thrombocytopenia**

**Clinical presentation of thrombocytopenia**

Clinically, thrombocytopenia becomes relevant at **values of under 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, further symptoms can manifold and are heterogeneous in nature. You have to seek the exact cause of the clinical manifestation of a suspected underlying disease in the event of detected microangiopathy.
Diagnosis of Thrombocytopenia

Thrombocytopenia needs extensive anamnesis

The diagnosis of thrombocytopenia is made if less than 140,000 thrombocytes per µl blood are present. Diagnostically, you have to perform extensive and targeted anamnesis, which narrows your differential diagnostics down. Additionally, you should proceed to conduct the diagnostics concerning a possibly existing underlying disease progressively. In case of blood diseases, all cell lines have to be critically determined and evaluated!

Bone marrow analysis in thrombocytopenia

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. Of course, bone marrow analysis makes direct conclusions to primary or secondary bone marrow malignomas possible.

Therapy of Thrombocytopenia

How do I treat thrombocytopenia?

Therapy measures to be taken depend on the extent and kind of thrombocytopenia that the patient suffers from. A pre-existing disease should be treated where possible. Medicament intake that exacerbate the disease should immediately be discontinued.

Symptomatically, thrombocytopenia is balanced with transfusions of thrombocyte concentrations. In advance 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, you can memorize a target thrombocyte count of > 50,000/µl. Thrombocyte concentrations 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 concentrations, you should clarify the reason for this. The following causes
should be considered:

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

More Information about Thrombocytopenias

Thrombocytic bleeding behavior 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 receptor of metabolic diseases or simply due to therapy with antiplatelet drugs.

Review Questions

The correct answers can be found below the references.

1. For a long time, your patient has suffered from Werlhof’s disease (chronic immune thrombocytopenic purpura), which you can only ineffectively treat with glucocorticoids. You decide to carry out splenectomy. Which of the following statements is true concerning this procedure?

   A. Previous to splenectomy, you should perform immunizing therapy against sexually transmitted diseases on the patient.
   B. Due to the patient’s young age and healthy constitution, there is no increased propensity for infections after splenectomy.
   C. Signs of extramedullary hematopoiesis can be found in the surgical preparation.
   D. The spleen should be removed since it is probably the production location of the autoantibodies. Splenectomy is not an appropriate form of therapy for Werlhof’s disease.

2. You work in your own pediatric practice. For several weeks, you attend to an elementary school child, who has multiple petechiae in the context of an infection. You diagnose acute post-infectious autoimmune thrombocytopenia. Which of the following is correct?

   A. There is an immediate call for action to avoid the risk of bleeding.
   B. Your only option is to wait.
   C. The intravenous application of immune globulins is the first-resort therapy.
   D. The application of thrombocyte concentrations is the first-resort therapy.
   E. The application of glucocorticoids is the first-resort therapy.

3. You work a night shift. The laboratory calls and confirms a distinct case of thrombocytopenia in your recently admitted patient. You reconsider the physical examination you did on the patient and cannot recall to have seen petechiae or hematomas. Which condition are you most likely to exclude?

   A. Asplenia
   B. Stage B HIV infection
   C. Werlhof’s disease
   D. Systemic Lupus erythematoses
   E. Acute leukemia
References


Dickerhoff und Eberl, Leitlinie *Immunthrombozytopenie im Kindes- und Jugendalter*, 2010

MAztorff, A et al., *Diagnostik und Therapie der Immunthrombozytopenie*, Onkologie, 2010

**Correct answers:** 1D, 2E, 3A

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