HUTCHINSON
REGIONAL MEDICAL CENTER

Thrombocytopenia

What is Thrombocytopenia?

Thrombocytopenia means a low level of platelets in the blood. Platelets are blood cells that stop bleeding and help the blood to clot. If your platelet count becomes too low, you may be at risk of uncontrolled bleeding or bruising. When your platelets are very low, you may have spontaneous bleeding even without injury. Chemotherapy, radiation therapy, certain types of cancer and some drugs can cause thrombocytopenia.

What are Platelets?

Platelets are tiny cells that circulate in the blood and whose function is to take part in the clotting process.

Inside each platelet are many granules, containing compounds that enhance the ability of platelets to stick to each other and also to the surface of a damaged blood vessel wall.

The platelet count in the circulating blood is normally between 150 and 400 million per milliliter of blood. Newborn babies have a slightly lower level, but are normally within the adult range by three months of age.

Many factors can influence an individual's platelet count including exercise and racial origin. The average life span of a platelet in the blood is 10 days.

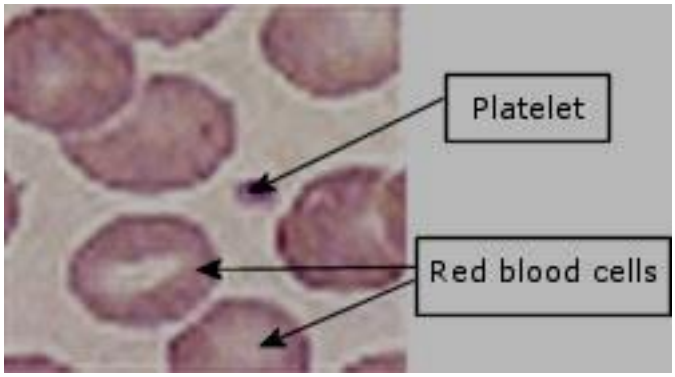

Figure 1: Normal blood film

What do platelets do?

Platelets are essential in the formation of blood clots to prevent hemorrhage - bleeding from a ruptured blood vessel.

An adequate number of normally functioning platelets is also needed to prevent leakage of red blood cells from apparently uninjured vessels.

In the event of bleeding, muscles in the vessel wall contract and reduce blood flow. The platelets then stick to each other (aggregation) and hold on to the vessel wall (primary hemostasis). The coagulation factors are then activated, resulting in normally liquid blood becoming an insoluble clot or glue.

What are the risks of a low platelet count?

The main effect of a reduced platelet count is an increased risk of bleeding, but this rarely occurs until there are less than 80-100 million platelets per ml.

There is not a close relationship between the number of platelets and the severity of bleeding, but there is an increasing risk of hemorrhage if platelet numbers fall or if platelet function is impaired (for example by aspirin, which reduces the 'stickiness' of the platelets).

There is a particularly high risk of spontaneous bleeding once the platelet count drops below 10 million per ml. The bleeding is usually seen on the skin in the form of tiny pin-prick hemorrhages (purpura), or bruises (ecchymoses) following minor trauma.

Bleeding from the nose and the gums is also quite common. More serious hemorrhage can occur at the back of the eye (retina), sometimes threatening sight.

The most serious complication, which is potentially fatal, is spontaneous bleeding inside the head (intracranial) or from the lining of the gut (gastrointestinal).

What causes a low platelet count?

The many different causes of thrombocytopenia are detailed below. These causes are not mutually exclusive and more than one may be responsible for an abnormal platelet count.

Artefactual (false) thrombocytopenia

Some people have platelets that stick together due to the presence of proteins in the blood (antibodies) that bind to the platelets.

These antibodies also bind to a chemical in blood that is tested in the lab, giving a falsely low platelet count. For this reason, it is helpful to repeat the sample in different tubes with different chemicals.

Causes summary

- ☐ Clot in the sample.
- ☐ Platelets clumped.

Congenital thrombocytopenia

Several rare inherited diseases cause low platelet counts. The severity of the thrombocytopenia varies with the condition and also the individual patient.

Causes summary

- ☐ Rare inherited disorders (eg May Hegglin anomaly, Bernard Soulier syndrome).

Defective platelet production

Platelets are produced within the bone marrow from cells called megakaryocytes.

If there is a problem in the bone marrow, for example due to abnormal cells, then the number of megakaryocytes will drop, lowering the number of

platelets that can be produced.

Examples of abnormal cells accumulating in the bone marrow include:

- acute leukemia where leukemic cells, or 'blasts', are seen
- other abnormal cancer cells such as lymphoma
- more rarely, when cancers develop in another part of the body and have spread (metastasized) to the bone marrow.

Alternatively, there may be something wrong with the platelet production process itself so not enough platelets are formed.

Impaired platelet production can also be due to:

- the side-effects of drugs such as chemotherapy (anti-cancer) agents
- viral infections such as HIV
- metabolic disorders such as shortage of vitamin B12 or folic acid, kidney failure, alcohol.
- an abnormality of the bone marrow called myelodysplasia.

Sometimes platelet production is defective because of an abnormality in the cells that make up the structural parts of the bone marrow, called the stroma. Examples include:

- marble bone disease (osteopetrosis). This hereditary condition causes dense, brittle bones at the expense of bone marrow.
- myelofibrosis. This causes a massive increase in the amount of fibrous tissue, which impairs platelet production as well as the production of other blood cells.

Causes summary

☐ Bone marrow aplasia (failure).
☐ Metabolic disorders, eg kidney failure, alcohol.
☐ Abnormal platelet precursors: viral infections, inherited abnormalities.
☐ Bone marrow infiltration, eg leukemia, lymphoma.

Diminished platelet survival

Platelet numbers fall if they are removed from the circulation more rapidly than they are produced.

Antibodies that cause platelet removal can be due to:

- infections such as HIV
- medicines such as the anti-malaria drug quinine
- a specific disease in which abnormal production of other antibodies may occur, eg rheumatoid arthritis, the skin disease systemic lupus erythematosis or the blood disease chronic lymphocytic leukemia.

These antibodies can also occur in someone who is otherwise completely well. This is called idiopathic thrombocytopenia (ITP) - literally, a low

platelet count of unknown cause.

Alternatively, the platelets may be used up if the blood clotting process is inappropriately 'switched on'. This condition is known as disseminated intravascular coagulation (DIC).

DIC can result from the following:

- in severe infections such as meningitis.
- as a complication of pregnancy or labor, eg high blood pressure and pre-eclampsia
- in some cancers, specifically types of acute myeloid leukemia and prostate cancer
- in some rare blood disorders such as thrombotic thrombocytopenic purpura or hemolytic uremic syndrome (sometimes due to food poisoning outbreaks).

Causes summary

- ☐ Antibodies in response to drugs, blood transfusion or another disease, eg glandular fever, malaria.
- ☐ Unknown cause (ITP).
- ☐ Clotting disorder (DIC).
- ☐ Blood disorder (TTP).

Loss of platelets from the circulation

- **Abnormal distribution of platelets**: a low platelet count may be due to a build up of platelets outside the normal blood pool, for example in a patient with a very large spleen.
- **Dilution of platelets**: the platelet count can fall when a patient is transfused with a large volume of red blood cells that do not contain platelets, because of dilution of normal blood factors.

Causes summary

- ☐ Massive blood transfusion or exchange.
- ☐ Enlarged spleen.

How is a low platelet count diagnosed?

Investigation usually starts with a history of symptoms, signs of bleeding or bruising, other medical problems, recent infections and medications. A blood test is then taken.

In the hematology lab the doctor:

- performs a full blood count
- examines the blood film under a microscope (see Figure 1)
- examines the blood sample in the test tube.

Usually, another full blood count sample is requested to confirm the result and see if it is a persisting abnormality.

Depending upon the severity of the platelet lack and the likely cause, the person is likely to be referred to a hematologist at the hospital.

If the platelet count is very low, the person may need to be seen on the same day, and have a bone marrow test performed.

A bone marrow test is done under local anesthetic, with samples usually taken from the back of the pelvis.

This test helps the hematologist to decide if platelets are being produced normally and whether the rest of the bone marrow appears normal.

Further tests such as genetic tests can also be done on a bone marrow sample.

What treatment is available?

The choice of treatment depends upon the severity of the platelet count, its cause and whether or not there is any bleeding.

If life-threatening bleeding occurs, eg to the head or bowel, urgent treatment is needed with platelet concentrates via blood transfusion.

The effect of the concentrates is then monitored by measuring the platelet count and assessing any continuing bleeding.

The management of acute bleeding also involves treatment of the underlying cause of the low platelets.

If there is no major bleeding, treatment is aimed at the cause of the low platelet count.

- If a drug is thought to be the cause, it should be stopped, providing this is safe, and the platelet count monitored.
- If an infection is suspected, treatment of it with antibiotics could be started.
- For some infections, especially viral ones such as glandular fever, there is no specific treatment and close observation may be necessary.
- When an infection results in a low platelet count by causing DIC, treatment tackles the underlying infection and the DIC. Blood components are used to replace the clotting factors and platelets.
- If platelet production fails due to the presence of abnormal or malignant cells, treatment is directed at those abnormal cells - for example, chemotherapy or radiotherapy would be used in leukemia. This can temporarily damage the bone marrow and worsen the thrombocytopenia. Transfusions would then be given if the platelet count becomes very low until it reaches a safer level or the bone marrow recovers.

Figure 2: A bag of platelets for transfusion