

Thrombotic Thrombocytopenic Purpura

Thrombotic Thrombocytopenic Purpura, or TTP, is a very rare disorder, which affects around three people in one million. The name describes the effects caused in a person and TTP is life threatening without treatment but it can be controlled, and in the majority of cases can be curable.

What is TTP?

The name describes the effects – so what are they?

Thrombotic – Small clumps (thrombi) of platelets that block or partially block small blood vessels (capillaries).

Thrombocytopenic – The clinical term for a low platelet count of less than 100 billion cells per litre of blood.

A normal platelet count is between 150 and 400 billion cells per litre.

Purpura – Little pin prick spots due to bruising caused by a low platelet count, which can occur spontaneously.

What causes these effects?

The exact cause of TTP has not been fully worked out. What is known is that the formation of platelet clumps is linked with a shortage of a protein called von Willebrand Factor cleaving protease.

Von Willebrand Factor (vWF) is necessary for blood clotting and is made up of lots of small units that are linked to form a long string. The vWF cleaving protease breaks up this long string into smaller, usable pieces. In TTP vWF cleaving protease is missing, leading to the long strings of vWF remaining. These bind to platelets causing them to clump.

When this happens they can become 'stuck' to blood vessel walls leading to blocking or partial blocking of the blood flow. The main blood vessels affected are in the brain but it can also occur in the kidney, heart, lungs and the gut.

The blockages then cause two things to happen:

- Firstly, the blockage prevents blood getting to the affected areas – so blockages in the brain lead to symptoms such as headaches, blurred vision, confusion, weakness seizures, and in extreme cases can cause unconsciousness.
- Secondly, as the red blood cells try to pass the blockage some are broken up (haemolyse) and so the numbers of red cells fall leading to anaemia. Because red blood cells carry oxygen in your body, a lack of them leads to feeling tired, light-headed or short of breath.

What triggers the TTP process?

Your immune system normally protects your body from bacteria and viruses, which it identifies as foreign or harmful. Certain white blood cells called lymphocytes release proteins called antibodies, which attach to the foreign substances and direct other cells to destroy them. In TTP this process malfunctions and the antibodies target vWF cleaving protease.

There are two types of TTP – inherited and acquired. In *Inherited TTP*, people are born with a shortage of vWF cleaving protease and tend to have TTP episodes from childhood – it isn't clear what sparks these episodes off.

Acquired TTP is triggered by an unwanted antibody in the body. Your immune system normally protects your body from bacteria and viruses, which it identifies as foreign or harmful. Certain white blood cells called lymphocytes release proteins called antibodies, which attach to the foreign substances and direct other cells to destroy them. In TTP this process malfunctions and the antibodies target vWF cleaving protease.

Some people describe recent flu-like episodes prior to the symptoms becoming apparent, suggesting the precipitating factor may be an infection. Very occasionally TTP is secondary to a known condition such as cancer or a serious viral infection. It is unusual to develop TTP and not be aware of an underlying condition.

How can acquired TTP be treated?

Treatment of TTP must achieve two things:

- Firstly, further platelet clump formation must be prevented. In order to remove the strands of vWF cleaving protease plasma exchange is performed by connecting the person affected to a machine called a blood cell separator. This process constantly takes off a small amount of blood and removes the plasma (clear fluid part of blood) and puts back the cells. The removed plasma is replaced with donated plasma. The donated plasma comes from the National Blood Service. Each unit has been tested to make sure it is not carrying HIV or hepatitis B and C and other transfusion transmitted diseases.
- Secondly, the antibody formation many need to be suppressed; so various immunosuppressive drugs are used such as prednisolone and ritoximab.

Each day, the clinical team looking after a person with TTP will assess a large number of blood results. These results, together with the person's clinical condition, will indicate how well treatment is going. Each person will react to the treatment at a different rate and that the blood results may be affected by other factors.

The main blood results are monitored for:

- *Platelet count* – to assess whether the platelets are still clumping.
- *Haemoglobin level* – whether red blood cells are being broken up (however plasma exchanging will decrease haemoglobin in the short-term).
- *Lactate Dehydrogenase (LDH)* – a measure of red cell damage.
- *Reticulocytes* – these are young red cells and their level indicates the state of blood cell production in your bone marrow.

Can it happen over and over again?

In 70% of cases TTP is a transient “one off” event. However it often is not clear which people belong to the other group of 30%, those who are affected by a second episode, which is why there are regular follow-ups. The risk of a person having another bout of TTP diminishes as time progresses from the previous episode.



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