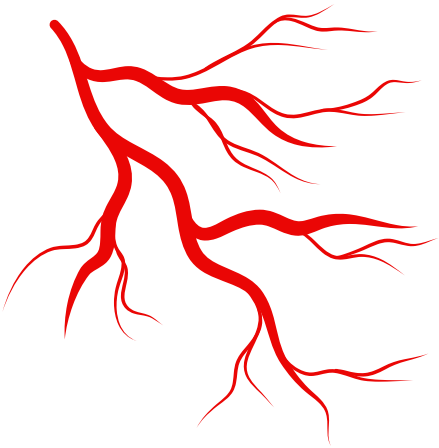
The Blood Project

Patient Information



Immune Thrombotic Thrombocytopenia Purpura (TTP)

A Pocket Resource for Patients

William C. Aird, MD

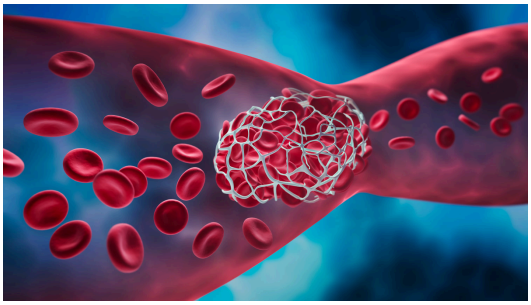
What does TTP Stand For?

T T P

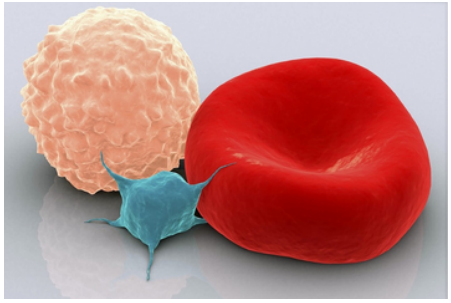
Thrombotic

Thrombocytopenia

Purpura



Thrombosis
(blood clot)

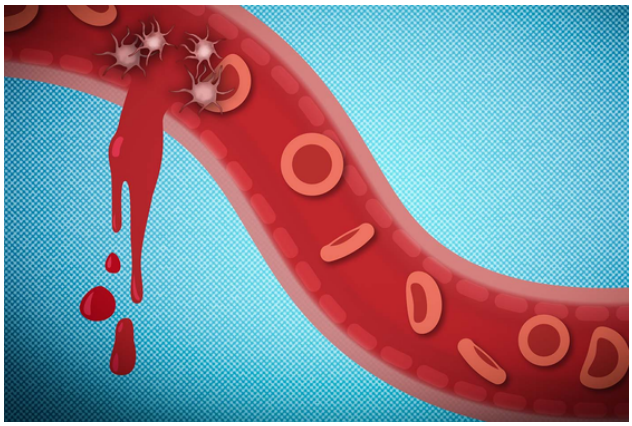


Thrombocytopenia
(low platelet count)

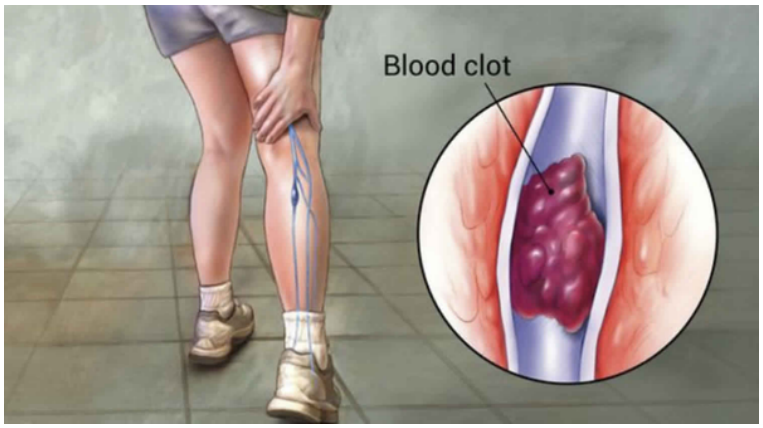
Purpura
(bleeding into skin)

What is Thrombosis?

Formation of a blood clot (thrombus) inside a blood vessel, obstructing normal blood flow



Normal clotting
(plugs the hole in vessel wall)



Thrombosis
(plugs the lumen of the blood vessel)

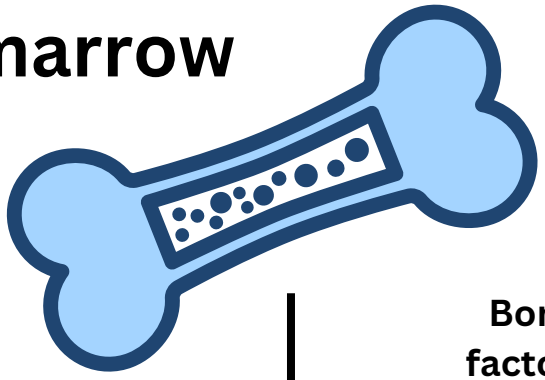
- **Our *heart* pumps blood around the body**
- **This pumping function generates *blood pressure***
- **Blood is normally contained within blood vessels**
- **Blood vessels can leak from normal wear and tear**
- **The *clotting system* evolved to patch defects in the blood vessel wall**
- **It consists of platelets which rush to the site of injury, and the formation of a glue called fibrin (think of the platelets as the bricks and fibrin as the mortar)**
- **In some diseases, the clotting system is overactive and leads to spontaneous brick-and-mortar formation inside otherwise healthy blood vessels**
- **Instead of patching holes, these "clots" or "thrombi" can obstruct the lumen (the tube) of the blood vessel and impede blood flow to body parts**

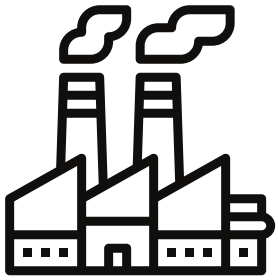
What is Thrombocytopenia?

Thrombocyte = platelet *Penia = low*

Low platelet count (low numbers in blood)

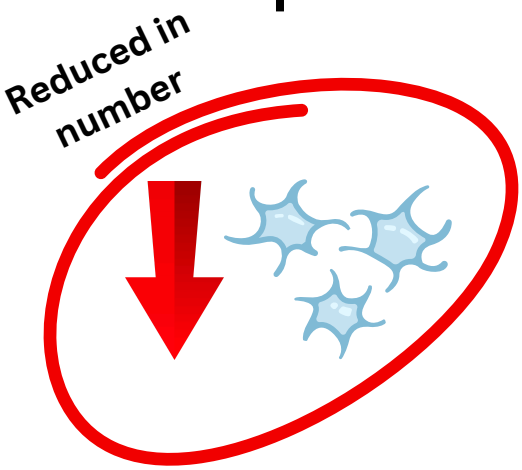
Bone marrow

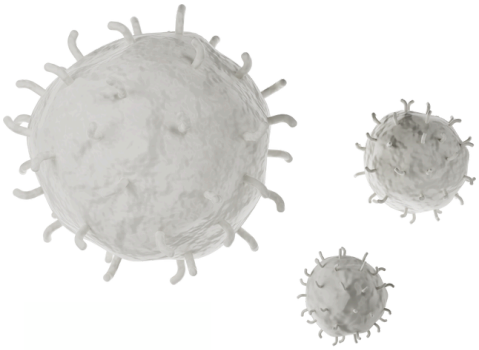




There are 3 types of cells that circulate in our blood

Bone marrow is the factory that produces blood cells





Red blood cells

Deliver oxygen to body parts

Platelets

Prevent bleeding

White blood cells

Fight infection

What is purpura?

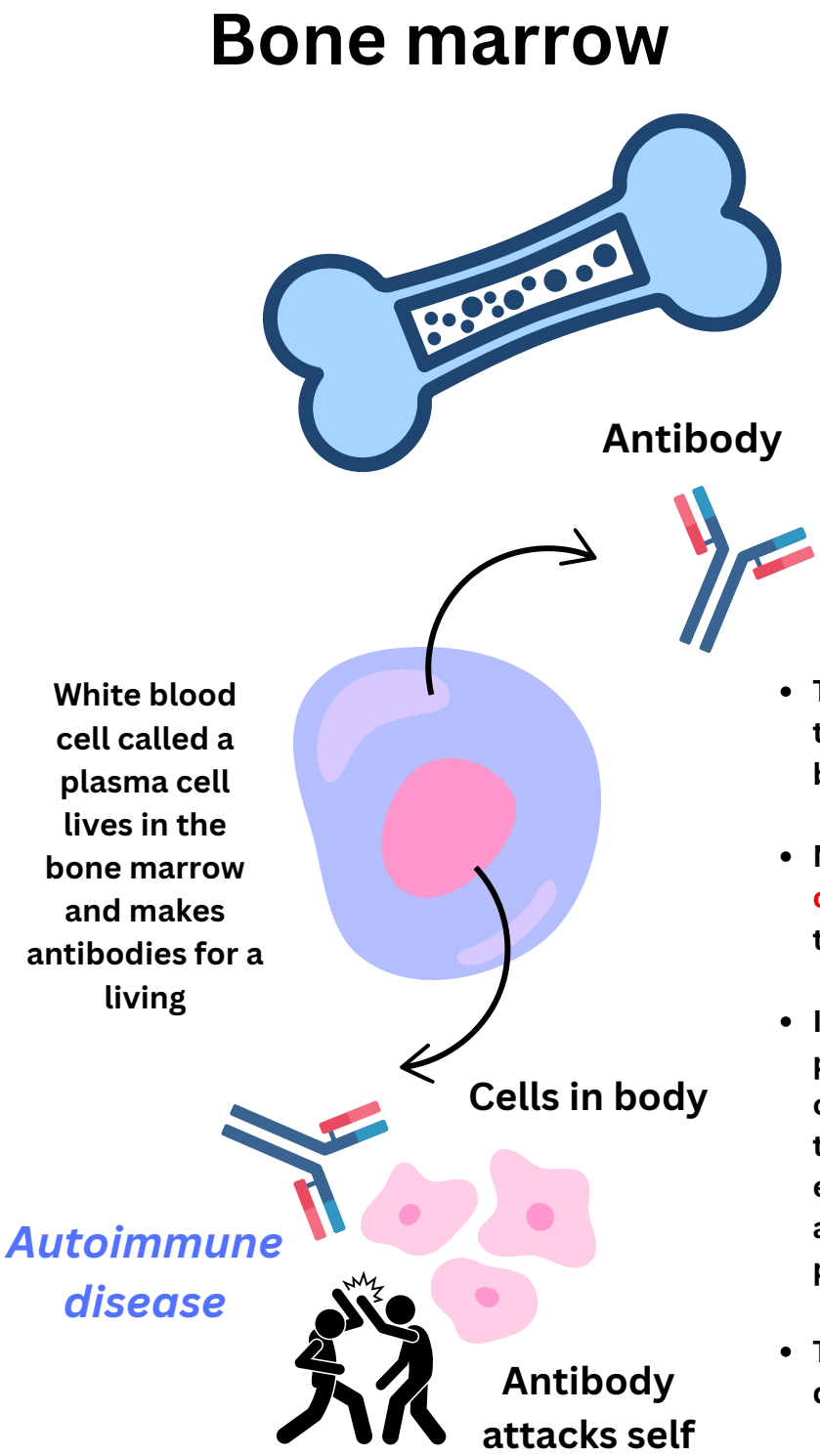
Bleeding in the skin

Purpura causes red, purple or brown blood spots on your skin. It happens when small blood vessels leak blood under the skin's surface.

Purpura and other types of bleeding occur in TTP because the platelet count is often very low and platelets normally function to prevent bleeding

What Causes TTP?

TTP is an autoimmune disease

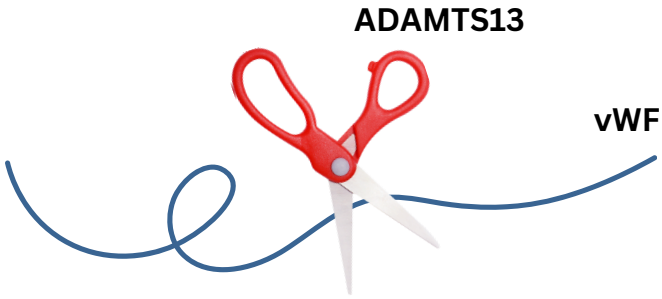


- The bone marrow contains white blood cells that make and release antibodies into the blood stream
- Normally, antibodies target infectious organisms like bacteria and viruses, leading to their clearance
- In certain diseases, antibodies target proteins +/- cells in the body. These are called autoimmune diseases (auto because the antibodies target "self"). Diabetes is an example of an autoimmune disease where antibodies target and destroy insulin-producing cells in the pancreas
- TTP is another example of an autoimmune disorder

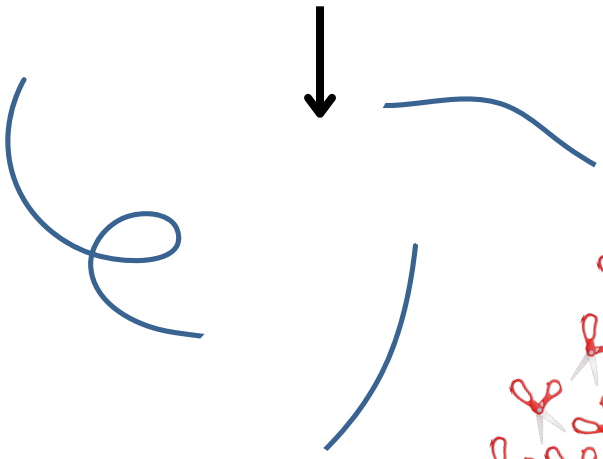
What Causes TTP?

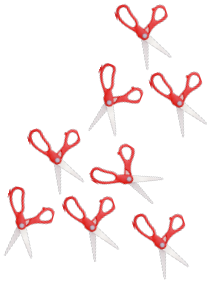
Antibody against a scissor-like protein

Healthy condition



Normally, a scissor-like protein called ADAMTS13 cleaves another protein in the blood called von Willebrand factor (vWF). vWF promotes clumping of platelets (the bricks in the brick-and-mortar analogy) in blood vessels. So, ADAMTS13 is a protective mechanism to prevent excessive platelet clots/plugs

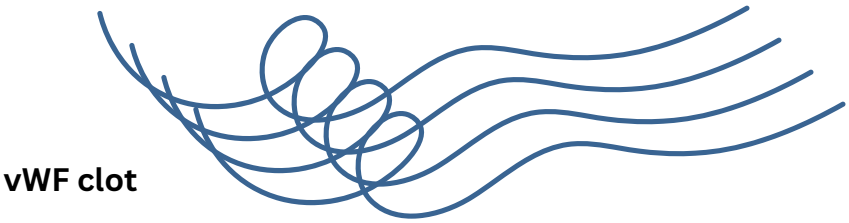




Normal levels of ADAMTS13 in blood

TTP

In TTP, antibodies bind to ADAMTS13, resulting in low levels of ADAMTS13 in the bloodstream. As a result, vWF cleavage is reduced with the result that platelets form clots in small blood vessels throughout the body

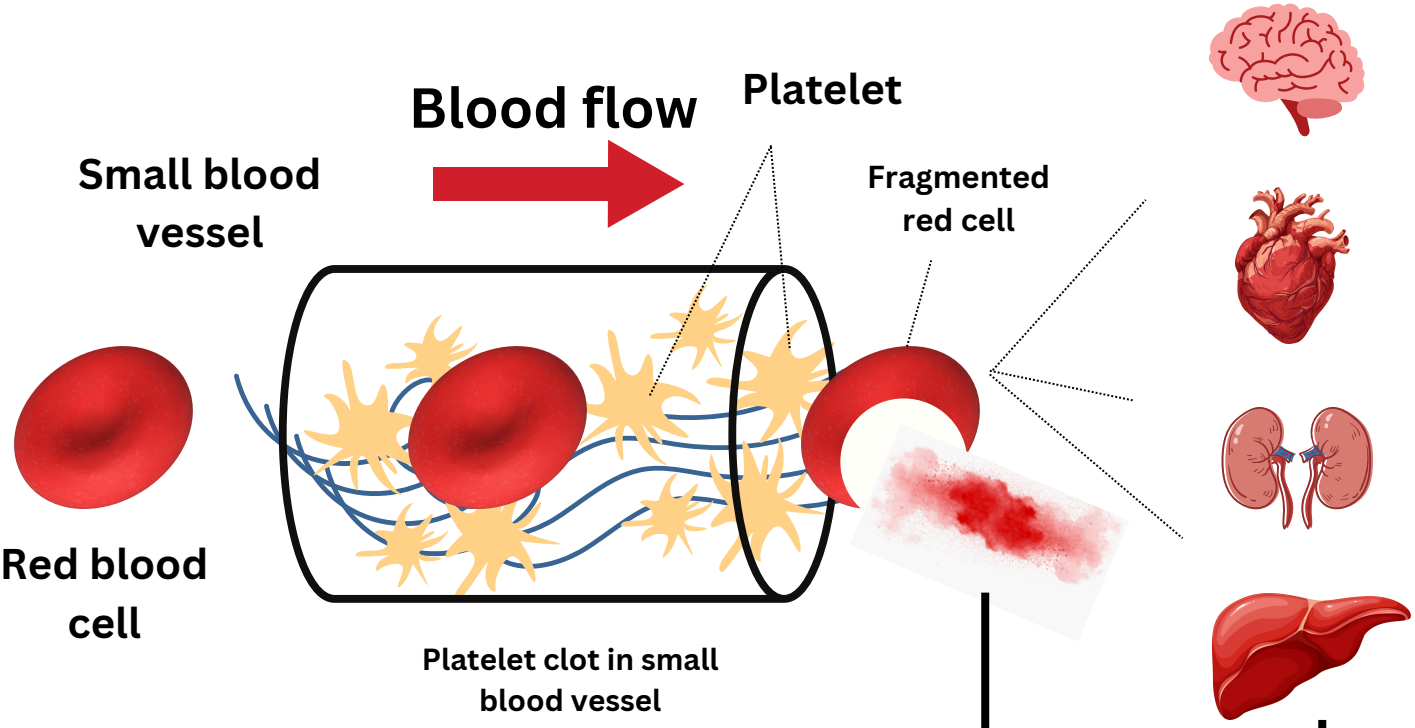


Reduced levels of ADAMTS13

What Causes TTP?

Consequence of low ADAMTS13 levels

Thrombocytopenia, anemia, organ changes



Consumption of platelets

Destruction and fragmentationof red blood cells as they navigate through the plugged blood vessel

Lower blood flow, fewer red cells leads to reduced oxygen delivery to organs

A common symptom of organ dysfunction is confusion and headache

Thrombocytopenia (low platelet count)

Anemia (low red cell count)

Organ dysfunction

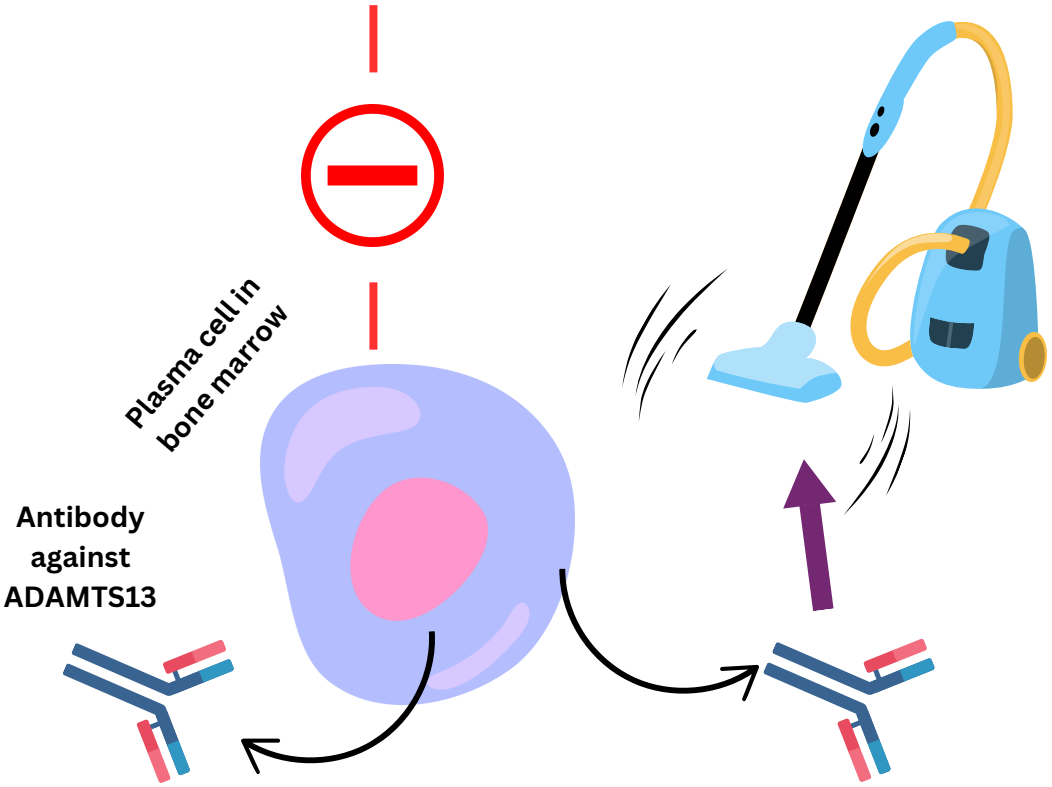
Doctors will order frequent blood draws to follow the platelet count, the hemoglobin (a marker of red cell count) and markers of red cell destruction. They will also test for signs of organ dysfunction

How is TTP Treated?

Three-Pronged Attack

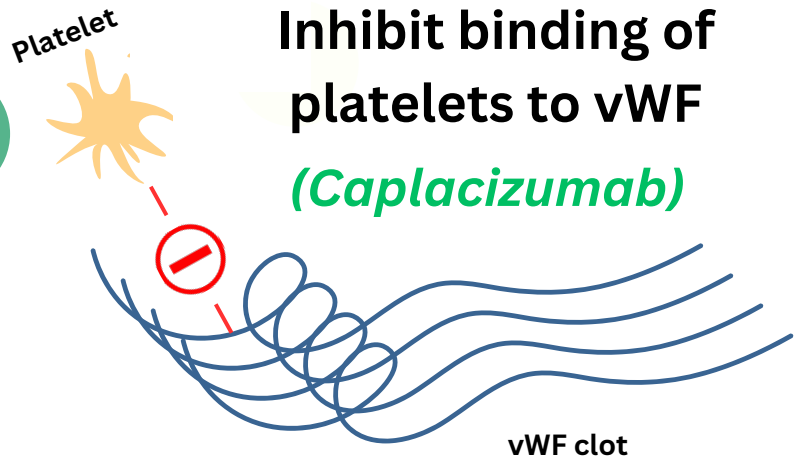
1 Suppress antibody production *(Corticosteroids)*

2 Remove antibodies from the body *(Plasmapheresis)*



Mainstay of treatment. All patients with a high suspicion of TTP should receive timely, daily plasmapheresis whereby plasma (the liquid part of blood) is removed and replaced with normal donor plasma; this not only removes antibodies against ADAMTS13 but it also provides ADAMTS13 from the donor plasma

All patients with a new episode of TTP should receive high doses of daily corticosteroids (for example prednisone)

... many patients will also receive another immunosuppressant called ***rituximab***, which is given as 4 weekly injections

3 Inhibit binding of platelets to vWF *(Caplacizumab)*