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Understanding TTP

Alexis L. Koester
Parkland College

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Alexis Koester
Bio 141 Sect. 001
Dave Wilson

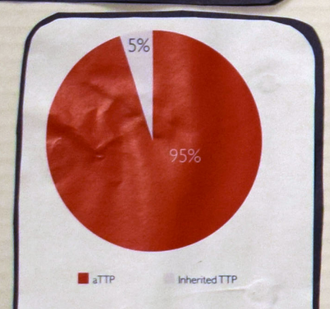
1 What is TTP?

Thrombotic thrombocytopenic purpura is an ultra-rare blood disorder that is potentially life-threatening.

- Between 1.2 and 11 new cases occur every year per million of population[1,2]
- More common in women
- Lifelong condition: after initial diagnosis, many patients will experience further episodes of TTP (called relapses)[3]

2 Two Main Types

- Inherited TTP
  - Occurs where the gene that produces ADAMTS13 is faulty[4]
  - People are born with the condition
  - Either have too little ADAMTS13 in their body or the ADAMTS13 that their body produce does not work properly[4]
- Acquired TTP
  - The body's immune system starts producing antibodies that stop ADAMTS13 from working[4]
  - No clear reason why patients are affected



https://www.understandingttp.com/patient/about-ttp/
It is clearly more common to have Acquired TTP than Inherited TTP.

3 Symptoms Caused by Bleeding Include: [3,4]

- Bleeding of the gums or nose, which may be caused by thrombocytopenia
- Purple bruises on the skin, called purpura
- Red or purple dots on the skin, called petechiae, which are caused by bleeding under the skin

4 Symptoms Caused by Formation of Blood Clots Include: [3,4]

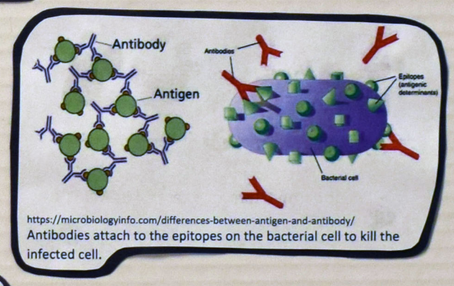
- Headaches, confusion, and disturbed vision
- Chest pain
- Fatigue, jaundice (yellowing of skin & eyes)
- Dark urine
- Kidney problems

5 Autoimmune Disease

- Immune system attacks healthy cells by mistake
- Basically, your body is harming itself
- Can affect many parts of the body

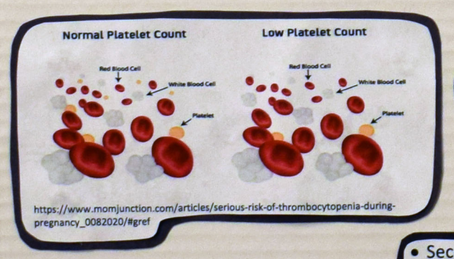
6 Antibodies vs. Antigens

- Antibodies are Y-shaped proteins produced by white blood cells called B cells of the immune system in response to exposure to antigens[5]
- The antibody marks the pathogen (antigen) by killing it or preventing it from entering a healthy cell[8]
- Antigens are molecules capable of stimulating an immune response (infected cell)[5]



https://microbiologyinfo.com/differences-between-antigen-and-antibody/
Antibodies attach to the epitopes on the bacterial cell to kill the infected cell.

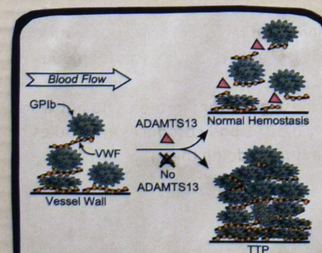
7 ADAMTS13 & Platelet Count



https://www.momjunction.com/articles/serious-risk-of-thrombocytopenia-during-pregnancy_0082020/#gref

- When diagnosed with TTP, platelet count is an important marker[6]
  - Normal count: 150-450 billion platelets per liter of blood[6]
  - During TTP: 20-50 billion platelets[6]

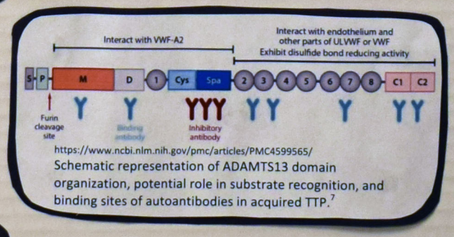
- Second important marker is ADAMTS13 enzyme levels
- ADAMTS13 gene provides instructions for making an enzyme that is involved in blood clotting[6]



http://www.bloodjournal.org/content/112/1/11?sso-checked=true
If ADAMTS13 is absent, the von Willebrand factor continues and causes thrombotic thrombocytopenic purpura.

- The ADAMTS13 enzyme processes a large protein called von Willebrand factor, which also plays a role clot formation[6]
- Von Willebrand factor helps platelets stick together and adhere to the walls of blood vessels[6]

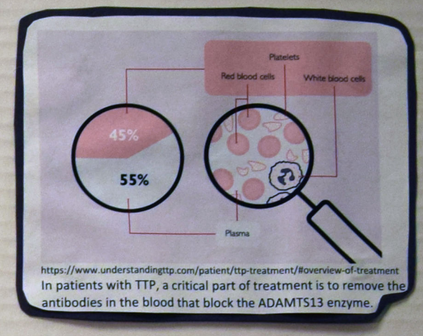
- In TTP, these genes and proteins do not work correctly b/c the body produces antibodies that stop them from doing their job[6]



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4599565/
Schematic representation of ADAMTS13 domain organization, potential role in substrate recognition, and binding sites of autoantibodies in acquired TTP.[7]

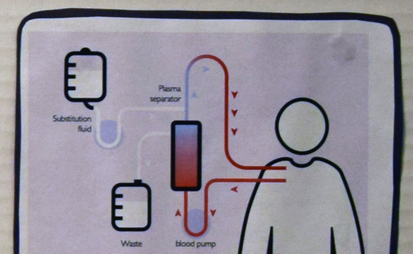
8 Treatment Options

- Plasma Exchange Therapy
  - The goal is to remove the antibodies that block the ADAMTS13 enzyme and replace the ADAMTS13 enzymes in the blood[1]



https://www.understandingttp.com/patient/ttp-treatment/#overview-of-treatment
In patients with TTP, a critical part of treatment is to remove the antibodies in the blood that block the ADAMTS13 enzyme.

- Immunosuppressant
  - Aims to stop the immune system from producing new antibodies against ADAMTS13[1,2]



https://www.understandingttp.com/patient/ttp-treatment/#overview-of-treatment
Immunosuppressants is medicine that will stop the produce of new antibodies.

9 Follow-Up

- Patients are monitored on an ongoing basis in an attempt to prevent relapses
- Regular blood tests to check platelet count
- There are new and emerging treatments nearing clinical practice that target the root cause of TTP
- Possibly in the future, a more direct and rapidly acting treatment approach would be to inhibit the binding of von Willebrand factor to platelets[9]

1 Terrell et al. J Thromb Haemost, 2005;3:1432-1436
2 Miller et al. Epidemiology, 2004;15: pp 208-215
3 Scully et al. Br J Haematol, 2012;158: pp 323-335
4 https://www.nhlbi.nih.gov/health-topics, National Institute of Health, *"What is Thrombotic Thrombocytopenic Purpura?"*, copyright 2014.
5 https://www.technologynetworks.com/immunology/articles/antigen-vs-antibody-what-are-the-differences-293550, Technology Networks, *"Antigen vs Antibody- What Are the Differences?"*, copyright 2017.
6 https://ghr.nlm.nih.gov/gene/ADAMTS13, Genetics Home Reference, *"ADAMTS13 gene"*, copyright 2018.
7 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4599565/, National Institute of Health, *"ADAMTS13 and von Willebrand Factor in Thrombotic Thrombocytopenic Purpura"*, copyright 2016.
8 https://www.verywellhealth.com/antibody-antigen-definition-48898, Very Well Health, *"What Are Antibodies and Antigens?"*, copyright 2018.
9 https://www.nejm.org/doi/10.1056/NEJMe1515876, The New England Journal of Medicine, *"Von Willebrand Factor—A New Target for TTP Treatment?"*, copyright 2016.