Thrombotic Thrombocytopenic Purpura

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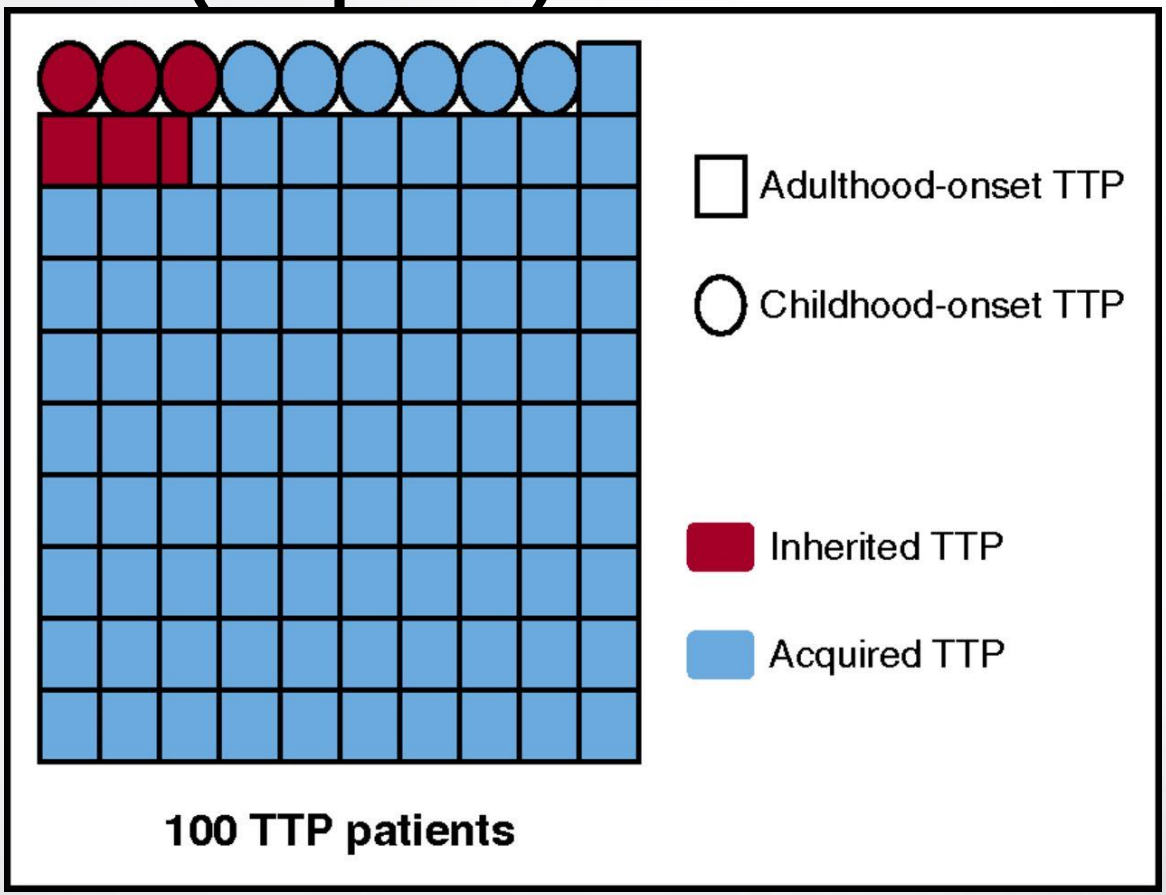
Types of TTP

- **Hereditary (Familial) TTP**
- **Idiopathic (Acquired) TTP**

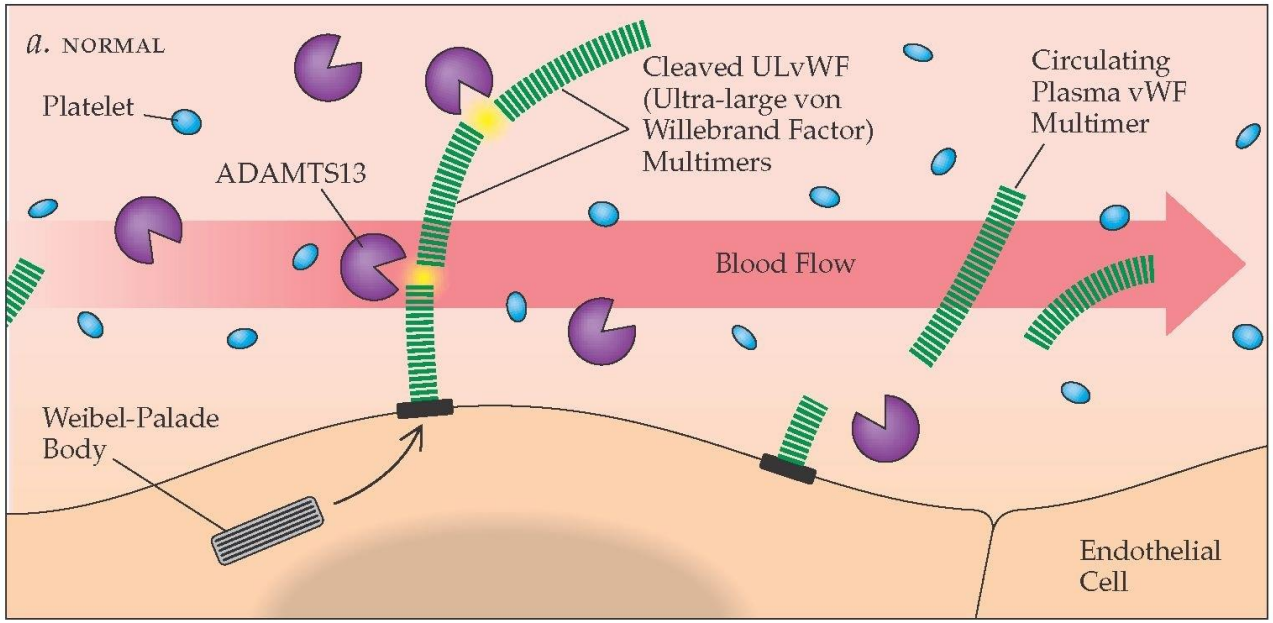


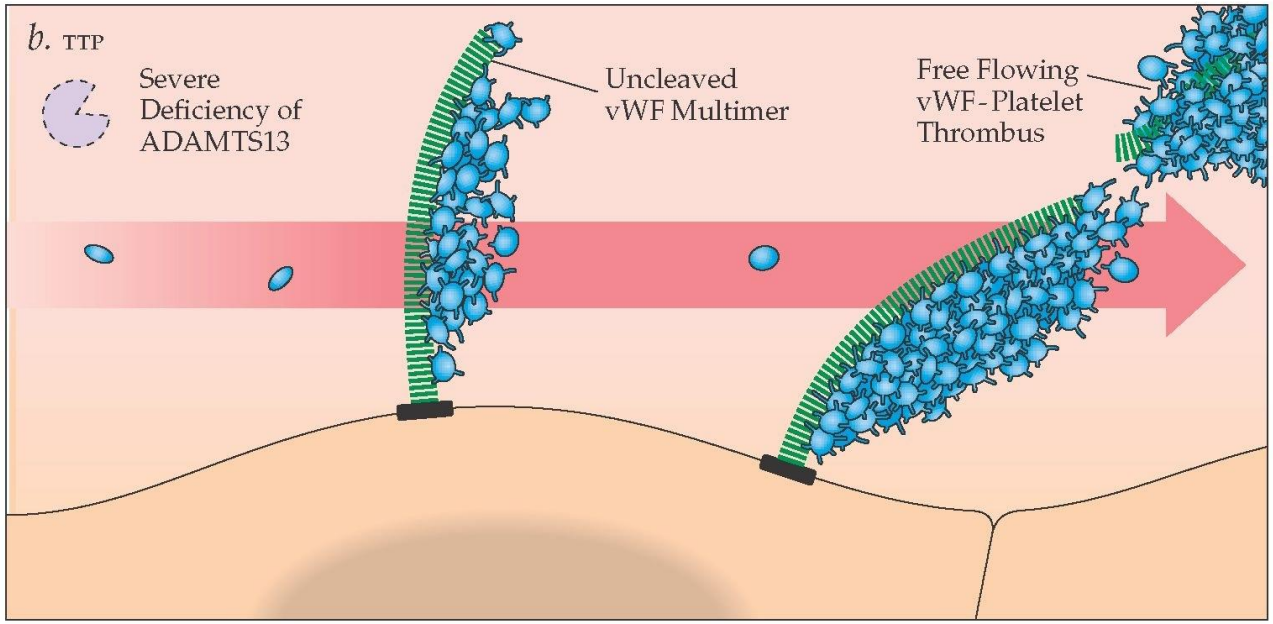
Berangere, Blood 2017

Hereditary (Familial) TTP

- <10% of cases
- Typically appears in infancy or early childhood
- Often recurs
- Caused by a mutation in the ADAMTS13 gene
  - Protein involved in blood clotting
    - Cleaves von Willebrand factor (vWF)
  - Disease caused by a decrease in activity so that clotting is abnormal:
    - As the platelets clump together in these clots, fewer platelets are available in the blood in other parts of the body to help with clotting.
    - This can lead to bleeding under the skin.
    - The blood clots prevent oxygen from reaching these parts of the body.

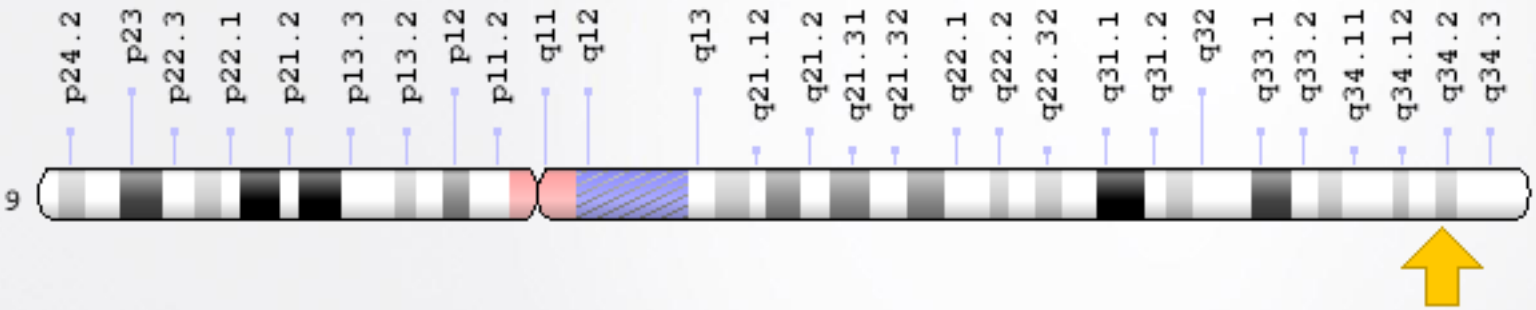
Pathophysiology of TTP





http://what-when-how.com/acp-medicine/platelet-and-vascular-disorders-part-2/

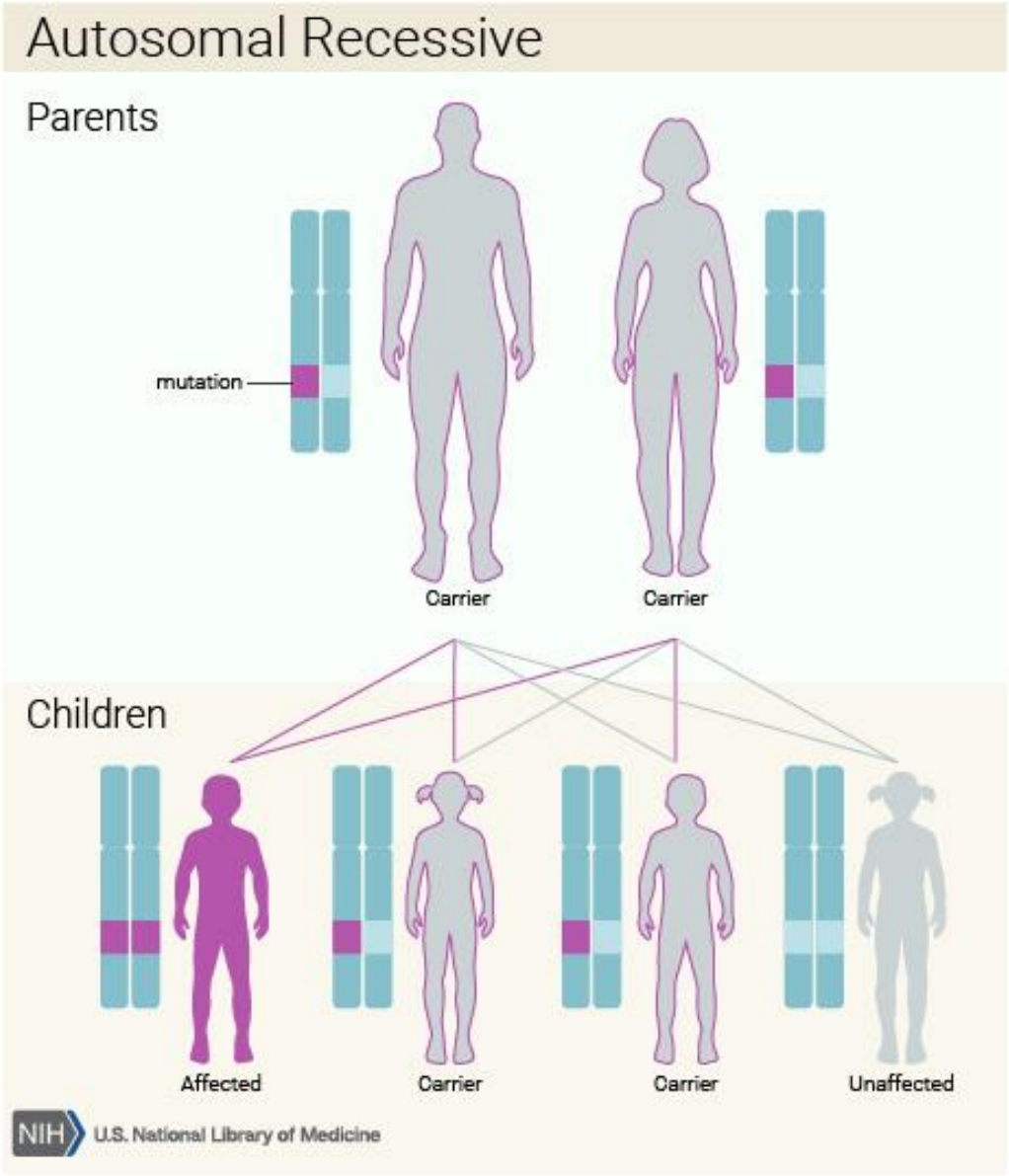
ADAMTS 13 gene is found on Chromosome 9 at position 34.2



https://ghr.nlm.nih.gov/gene/ADAMTS13#location

Hereditary (Familial) TTP

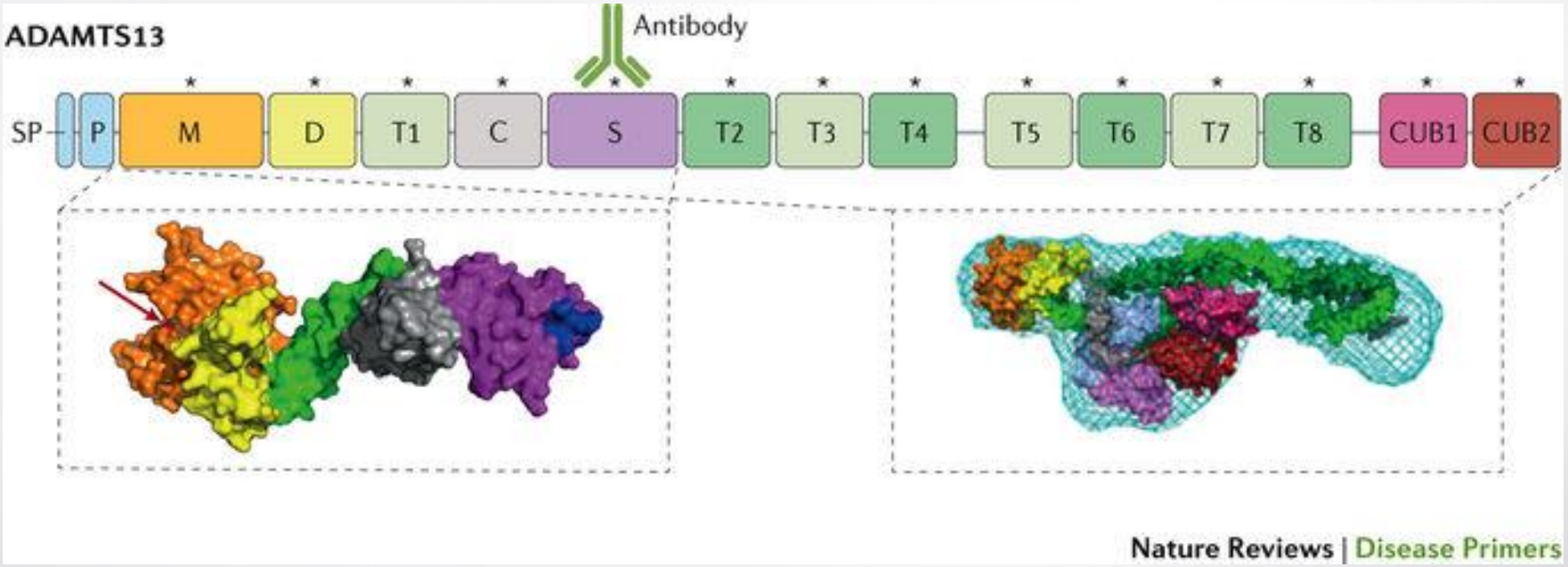
- <10% of cases
- Typically appears in infancy or early childhood
- Often recurs
- Caused by a mutation in the ADAMTS13 gene
  - Protein involved in blood clotting
  - Disease caused by a decrease in activity
- Inherited in an autosomal recessive pattern



Idiopathic (Acquired) TTP

- 45% of cases
- Idiopathic = no defined cause
- Usually appears in late childhood or adulthood
- May only have a single episode or may recur over time
- NOT inherited
- Decreased level of the ADAMTS 13 enzyme as a result of antibodies to the enzyme

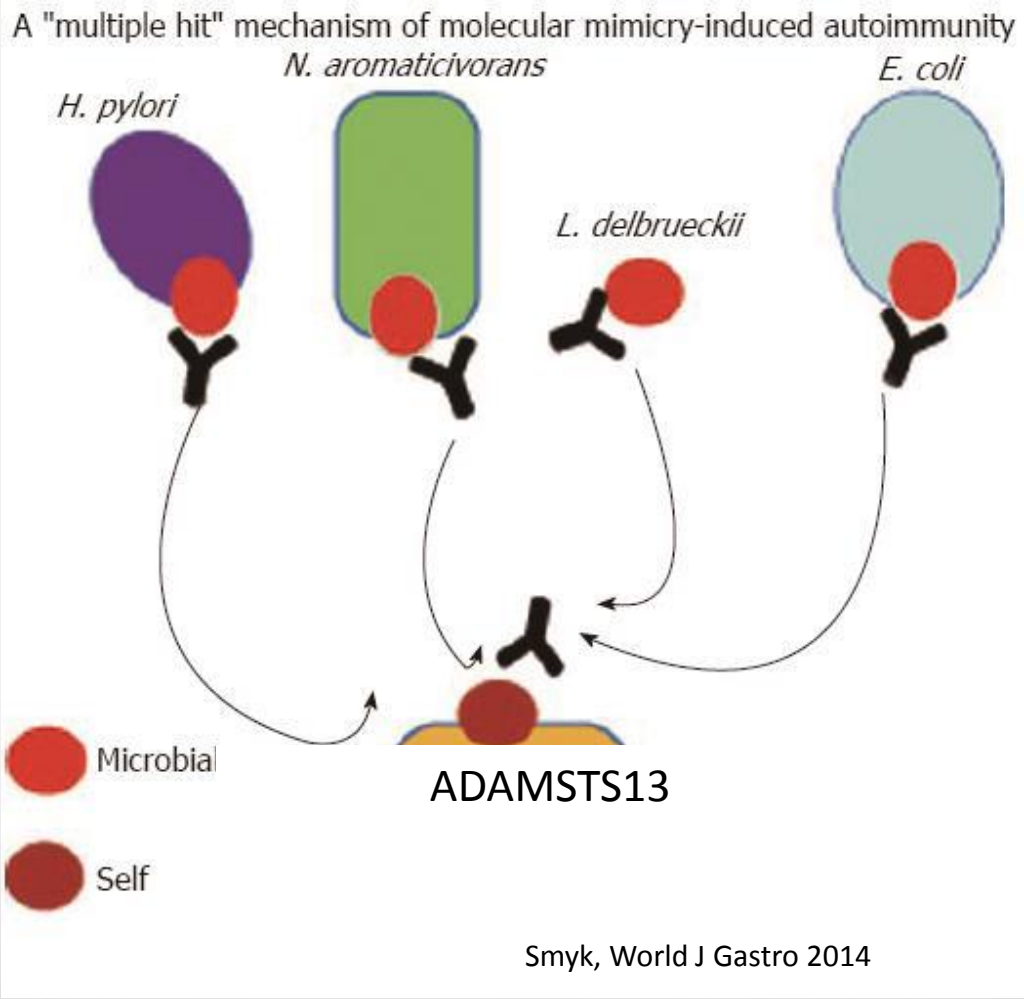
Antibody to ADAMTS13



What causes anti-ADAMTS13 antibodies to form?

- Unknown
- Molecular mimicry
  - Infection
  - Immune response against infectious agent
  - Antibodies against the infectious agent also recognize normal self (i.e. ADAMSTS13)
  - Triggers TTP

Molecular Mimicry



Smyk, World J Gastro 2014

What causes anti-ADAMTS13 antibodies to form?

- Bystander activation
  - Infection may activate antigen-presenting cells resulting in recognition of self-antigens
    - Influenza A
    - HIV
    - Parvovirus
    - Helicobacter pylori
    - Hepatitis C
  - Pregnancy
    - Increased levels of steroid hormomes

4) Bystander activation

- Infections of particular tissues may induce local innate immune responses
- Recruit leukocytes into the tissues
- Result in the expression of co-stimulators on tissue APCs
- The breakdown of T cell tolerance to self antigens
- Infection results in the activation of T cells that are not specific for the infectious pathogen