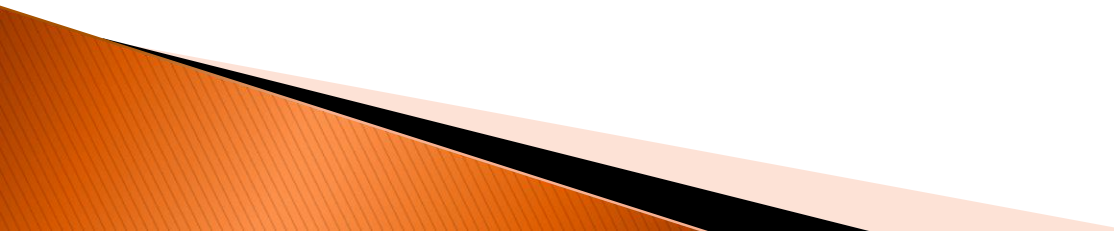


Idiopathic Thrombocytopenic Purpura (ITP)

Heather Ipema, PharmD
PGY2 Drug Information Resident
November 12, 2009

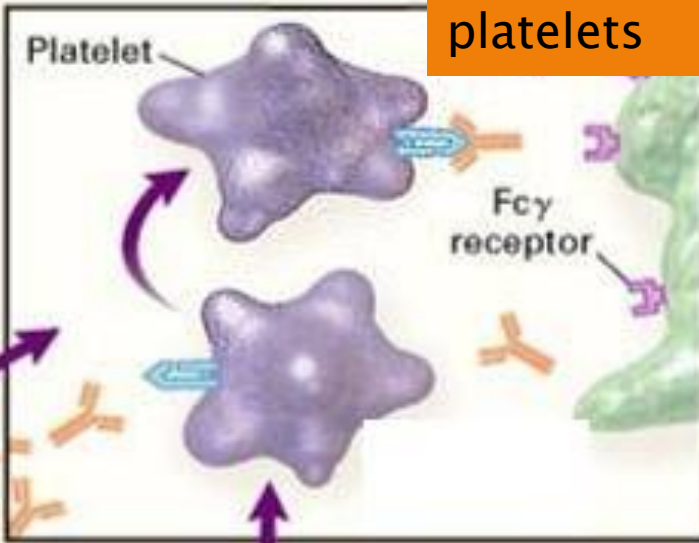
Outline

- ▶ Definition
 - ▶ Pathophysiology
 - ▶ Epidemiology
 - ▶ Etiology
 - ▶ Treatment options
- 

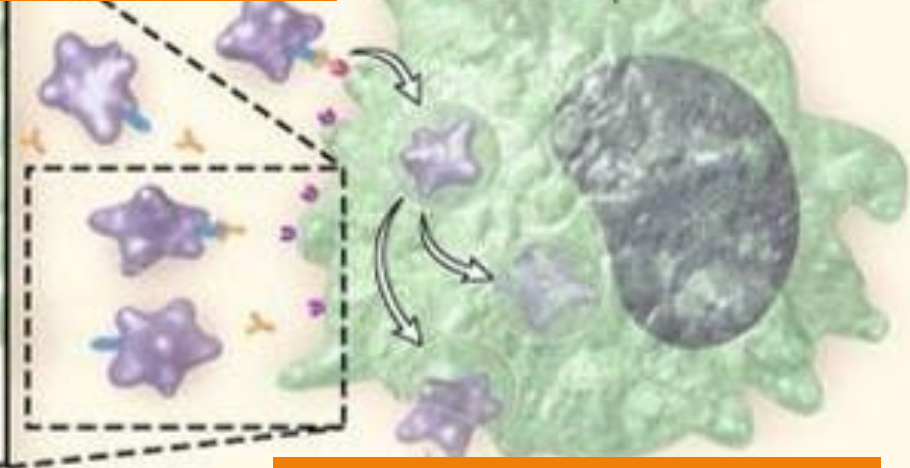
What is ITP?

- ▶ Autoimmune disorder
 - Inability to distinguish self from non-self
 - Immune system produces antibodies against platelets
 - Platelets coated with antibodies are destroyed in spleen

Autoantibodies bind to platelets



Platelets destroyed by macrophages in spleen



Autoantibodies produced by B-cells



B cell

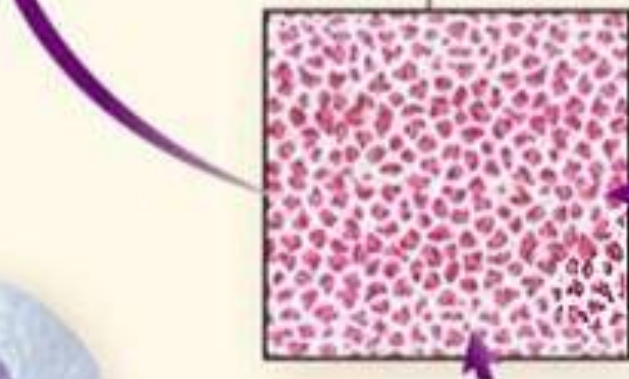
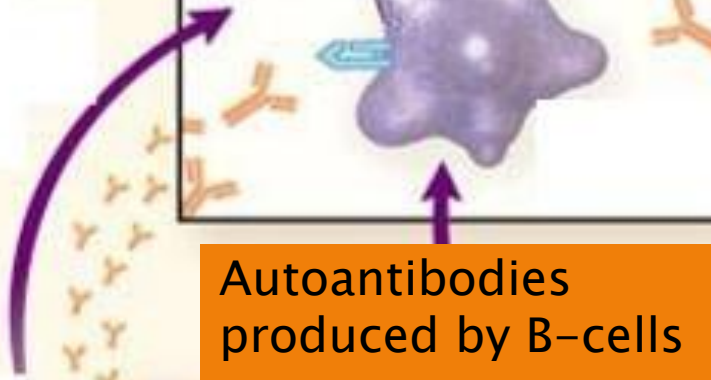


T cell

Bone marrow



Platelet production continues in bone marrow



Effects on Platelets

Normal platelet levels	ITP platelet levels
150 to 400 x cells/mm ³	100 to <10 cells/mm ³

Thrombocytopenia = low platelets

Note: platelet values are 10³

Epidemiology

- ▶ Estimated incidence
 - 100 cases per million people per year
 - 1 to 13 cases per 100,000 people
- ▶ Half of ITP cases occur in children

Etiology

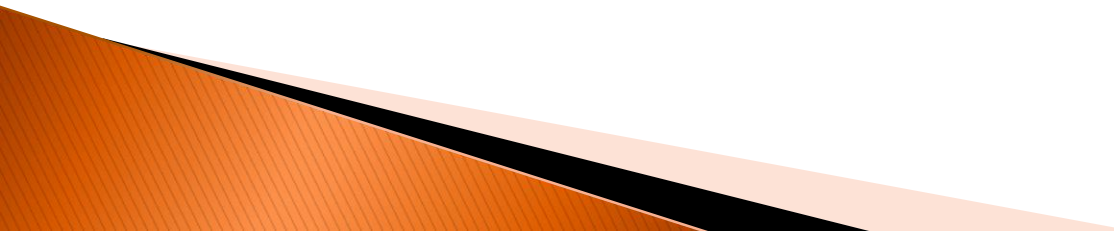
Primary ITP

- ▶ Does not occur secondary to another disease state

Secondary ITP

- ▶ Secondary to another disease state
 - HIV
 - Systemic lupus
 - Certain leukemias/lymphomas

Medications Causing Thrombocytopenia

- ▶ Heparin
 - ▶ Excessive alcohol
 - ▶ Amiodarone
 - ▶ Chemotherapy
 - ▶ Valproic acid
 - ▶ Quinidine
 - ▶ Interferon alpha
- 

Bleeding Risk

▶ 30–50 cells/mm³

◦ Minor

- Nosebleeds
- Bruising
- Purpura, petechiae
- Mucosal bleeding
- Heavy menstrual bleeding
- Conjunctival hemorrhage
- Hematuria

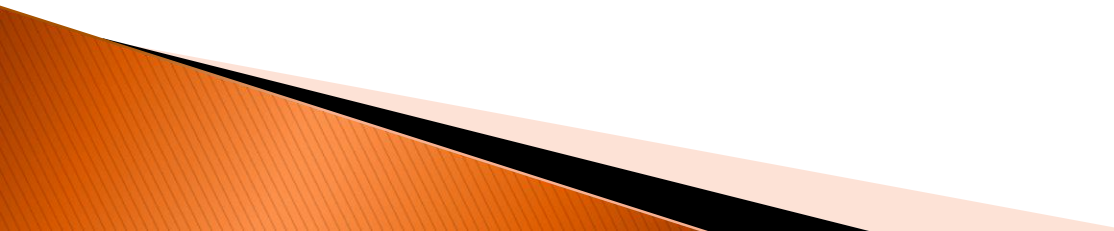
▶ <10 cells/mm³

◦ Major

- Intracranial hemorrhage (ICH)
- GI bleeding
- #1 cause of mortality with ITP (up to 50%)
- Occurs in <1% of ITP cases



Morbidity of ITP

- ▶ Bleeding complications
 - ▶ Bruising, purpura, fatigue
 - ▶ Adverse effects of surgery, medications
 - ▶ Social/lifestyle
 - Activity restrictions (pediatrics)
 - Hospital admissions
 - Blood tests, medications
- 

Diagnosis

- ▶ **Diagnosis of exclusion**
 - Need to rule out other diseases/medications
- ▶ **Physical exam**
 - Usually only petechiae or purpura
- ▶ **Labs**
 - Low platelets, normal WBC and RBC
 - Antiplatelet antibody test positive (rarely done)
- ▶ **Bone marrow biopsy**
 - Increased number of immature platelets
 - Usually only done in select adults

ITP Classifications

▶ Acute

- <6 month duration
- More common in children
- Peak age 2–6 y.o.
- May be associated with viral infections
- 85–90% will recover completely within 6–12 months (often spontaneously)
- 15–20% will develop chronic ITP

▶ Chronic

- >6 month duration
- More common in adults
- Peak age 18–40 y.o.
- 2–3X more common in females
- 10–20% recover completely
- Relapse common

Treatment of ITP

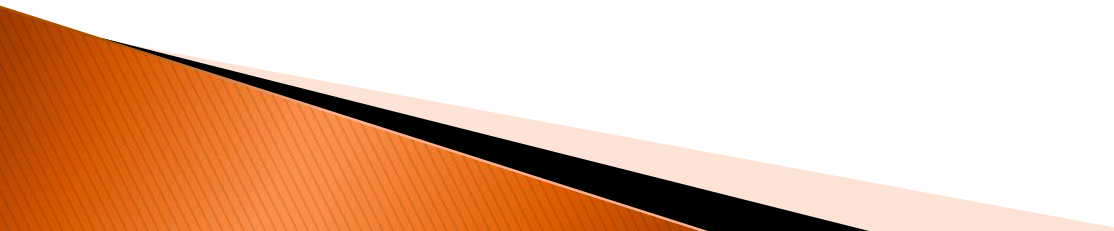
▶ Acute

- Goal to stop/prevent bleeding
- Hospitalization if severe bleeding, mucus membrane bleeding, history of bleeding, or <20 cells/mm³

▶ Chronic

- Goal to maintain hemostasis and prevent bleeding (not remission)

Treatment Options

- ▶ Corticosteroids
 - ▶ IVIG
 - ▶ Anti-D
 - ▶ Vinca alkaloids
 - ▶ Donazol
 - ▶ Splenectomy
 - ▶ Thrombopoetin receptor agonists
- 

Treatment Algorithm

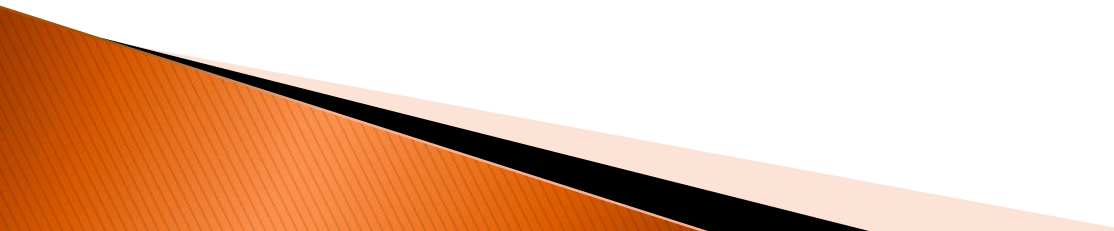
▶ American Society of Hematology Guidelines (1996)

- First-line
 - Corticosteroids (PO or IV), IVIG
- Second-line
 - Anti-D, vinca alkaloids, donazol
- Refractory
 - Splenectomy

▶ British Society of Hematology Guidelines (2003)

- First-line
 - Corticosteroids (PO), IVIG
- Second-line
 - Splenectomy
- Refractory
 - High dose corticosteroids, high dose IVIG, anti-D, vinca alkaloids, immunosuppressants

Factors to Consider

- ▶ Likelihood of response
 - ▶ Bleeding risk
 - ▶ Quality of life
 - ▶ Adverse events
 - ▶ Cost
- 

Corticosteroids

- ▶ MOA: reduces platelet destruction by suppressing immune response
 - Fewer antiplatelet antibodies
- ▶ Used to acutely raise platelets >30 cells/mm³
- ▶ Response rates 50–90%
- ▶ Relapse can occur after discontinuation
- ▶ Avoided when possible due to ADE
 - Diabetes, osteoporosis, risk of infection, moon facies, stunted growth, fluid retention, HTN

Intravenous Immune Globulin (IVIG)

- ▶ MOA (proposed): binds macrophages in spleen and prevents uptake of platelets
 - Decreased destruction of platelets
- ▶ Most effective for acute therapy
- ▶ Response rate ~80%
- ▶ Effects may last for 3–4 weeks
- ▶ Many ADE
 - Infusion reactions, thromboembolism, aseptic meningitis, renal failure
- ▶ Blood product = expensive

Anti-D

- ▶ Rh0(D) Immune Globulin
- ▶ MOA: binds to Rh0 antigen on RBC
 - RBC taken up into macrophages preventing uptake of platelets
 - Decreased platelet destruction
- ▶ Response rate 80–90%
- ▶ Only effective for Rh(+), non-splenectomized patients
- ▶ Hemolysis and decreased Hgb (average 2 mg/dL)
- ▶ Can have serious ADE (renal failure, DIC)

Splenectomy

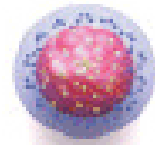
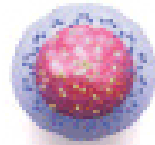
- ▶ Surgical procedure to remove spleen
 - Removes site of platelet destruction
- ▶ Risk of bleeding
 - Mortality 1%, complications 13%
- ▶ Considered second-line treatment option for chronic ITP
- ▶ Response rate 66%
- ▶ Decreased response to vaccines

Thrombopoietin receptor agonists

- ▶ Romiplostim
- ▶ Eltrombopag

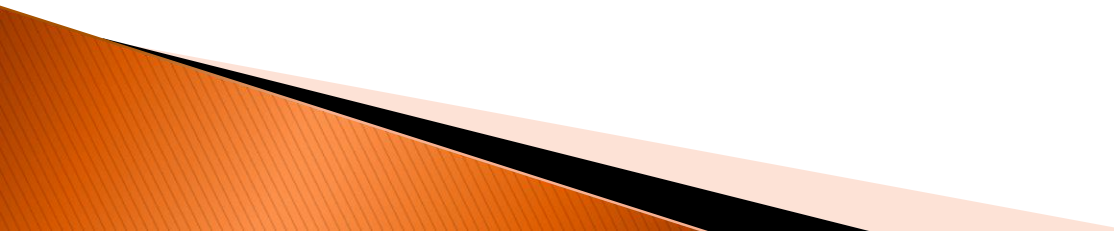
- ▶ MOA: agonist at TPO receptor of stem cells
 - Increases production of platelets

TPO
receptor



Other options

- ▶ Platelet transfusion?
 - ▶ Plasmapheresis not recommended

 - ▶ Vinca alkaloids
 - Vincristine, vinblastine
 - ▶ Immunosuppressants
 - Azathioprine, cyclosporine, mycophenolate
 - ▶ Rituximab
 - ▶ Danazol
- 

For More Information

1. Cines DB, Blanchette VS. Immune thrombocytopenic purpura. *N Engl J Med*. 2002;346:995–1008.
2. Chu YW, Korb J, Sakamoto KM. Idiopathic thrombocytopenic purpura. *Pediatrics Rev*. 2000;21:95–104.
3. George JN, Woolf SH, Raskob GE, et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. *Blood*. 1996;88:3–40.
4. Godeau B, Provan D, Bussel J. Immune thrombocytopenic purpura in adults. *Curr Opin Hematol*. 2007;14:535–556.
5. Cines DB, McMillan R. Pathogenesis of chronic immune thrombocytopenic purpura. *Curr Opin Hematol*. 2007;14:511–514.
6. British Committee for Standards in Haematology General Haematology Task Force. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children, and in pregnancy. *Br J Haematol*. 2003;120:574–596.
7. Newland A. Emerging strategies to treat chronic immune thrombocytopenic purpura. *Eur J Haematol*. 2008;80:27–33.
8. Kuter DJ. New thrombopoietic growth factors. *Blood*. 2007;109:4607–4616.

