# Idiopathic (Immune) Thrombocytopenic Purpura (ITP)

**Background**

1. Definition
   - Isolated thrombocytopenia with normal bone marrow and absence of other causes of thrombocytopenia
2. General info
   - One of the most common causes of symptomatic thrombocytopenia in children
   - 2 major forms of ITP:
     - Acute thrombocytopenic purpura
       - Most commonly seen in children 2-6 yrs of age
       - May follow viral illness
       - Usually very sudden onset
       - Symptoms disappear in <6 mos (often within few wks)
       - Spontaneous remission occurs in >80% of children w/acute ITP, usually without recurrence
       - Male to female ratio 1.2:1
     - Chronic thrombocytopenic purpura
       - Can occur at any age, usually between ages 20-30 yrs, not in children
       - Usually does not follow an infection
       - Subtle onset
       - Symptoms last a minimum of 6 mos to several yrs
       - Female to male ratio 2-3:1
       - Spontaneous remission rate is <20%

**Pathophysiology**

1. Incidence/ prevalence
   - Incidence of acute ITP
     - 3-8 cases per 100,000/yr
   - Incidence of ITP in adults
     - 6-7 cases per 100,000/yr
   - 40% of pts are <10 yrs
2. Pathogenesis
   - Autoantibodies (usually IgG) are directed against platelet membrane antigens, such as glycoprotein complex IIb/IIIa
   - Antibody-coated platelets have a shortened half-life because of accelerated clearance by tissue macrophages in spleen and other portions of reticuloendothelial system
   - Net effect is a decr in platelet count
3. Risk factors
   - Age: bimodal peak
     - 20-30 yrs old
     - 2-6 yrs old
   - Gender:
     - Females more likely to develop ITP during adulthood than males
   - Prior viral infection (measles, mumps and rubella) or MMR vaccine
     - 60% of acute ITP preceded by viral infection or MMR vaccination

4. Morbidity/ mortality
    - Hemorrhage
        - Most serious complication
            - Intracranial hemorrhage is most significant
        - Mortality rate:
            - 1% in children
            - 5% in adults
        - In pts w/severe thrombocytopenia (platelet count <20,000)
            - Predicted 5-yr mortality from bleeding significantly raised in pts >60 yrs versus pts <40 yrs, 47.8% versus 2.2% respectively
        - Previous Hx of hemorrhage incr risk of severe bleeding in adult ITP

**Diagnostics**

1. History
    - Focus on symptoms of bleeding
        - Type
        - Severity
        - Duration
        - That may exclude other causes of thrombocytopenia
    - Elicit risk factors for HIV and systemic symptoms linked to other illnesses or meds that can cause thrombocytopenia
        - Liver dz, thrombosis, and autoimmune dz
        - Heparin, alcohol, quinidine/quinine, sulfonamides
    - Address risk factors for incr bleeding, as these may determine aggressiveness of Tx or mgmt
        - GI dz
        - CNS dz
        - Urologic dz
        - Active lifestyle
    - Common Sx/S
        - Purpura
            - Tiny red dots (3-10 mm) under skin that are a result of very small bleeds
        - Menorrhagia/ metrorrhagia in women of child bearing age
        - Epistaxis
        - Gingival bleeding
        - Bruising tendency
2. Physical exam
    - Abdominal
        - Inspection, auscultation, palpation, percussion
        - Note tenderness, masses, organomegaly (liver and spleen)
    - Skin
        - Inspection, palpation
        - Note for nonpalpable petechiae, which mostly occur in dependent area, bruising
    - Oral and nasal cavity
        - Inspection, palpation
        - Look for gingival swelling and bleeding
        - S/S of nasal bleeding

- Menstrual
  - Cycle (freq, duration, quality)
- Eye
  - Look for retinal hemorrhages, papilledema for incr intracranial pressure from intracranial bleeding

3. Dx tests
   - Lab evaluation
     - CBC
       - Thrombocytopenia usually is only abnormality
       - Platelet count is usually <20,000/mL
       - WBC count and hemoglobin are generally normal
         - Although anemia can be seen in pts with significant bleeding
     - Peripheral blood smear
       - Examination of peripheral blood smear is mandatory and should detect no morphological abnormalities in WBC and RBC
       - Platelets are often large in size, particularly when Sx present several days or longer
     - Coagulation studies are normal and bleeding time is not useful
     - Antiplatelet antibody testing
       - Variety of tests are available for detecting platelet antibodies but are not routinely indicated due to lack of specificity
   - Imaging studies
     - CT scan of head is warranted if concern exists regarding intracranial hemorrhage

**Differential Diagnosis**

1. Active infection
   - Infectious mononucleosis
   - Hepatitis
   - HIV-1
2. Drug exposure
   - Heparin
   - Alcohol
   - Quinidine/ quinine
   - Sulfonamides
   - Furosemide
   - Gold salts
   - Cimetidine
3. Autoimmune dz
   - Systemic lupus erythematosus
   - Juvenile rheumatoid arthritis
4. Leukemia
   - CBC and bone marrow Dx
5. Acquired bone marrow failure syndrome
   - Aplastic anemia: anemia prominent, bone marrow Dx
6. Inherited disorders of thrombocytopenia
   - Inherited aplastic anemia
     - Prominent anemia, bone marrow dx

- Thrombocytopenia: absent radius syndrome
  - Bone marrow dx
  - Forearm imaging
  - Family hx
- Wiskott-Aldrich syndrome
  - Peripheral blood smear
  - Immunoglobulin levels

**Therapeutics**

1. Glucocorticoids
   - Helps bleeding by decr rate of platelet destruction
   - Usually results in an increase in platelet count within 2-3 wks
   - Side effects may include:
     - Hypertension
     - Irritability
     - Stomach ache
     - Wt gain
     - Acne
     - Growth delay in children
   - Most commonly used glucocorticoids
     - Prednisone
       - Adult dose for prednisone is 1-2 mg/kg/day
       - Children dose is 4-8 mg/kg/day by mouth
     - Methylprednisolone
       - Loading dose for adults 125-250 mg IV
         - Maintenance dose is 0.5 mg/kg/dose IV every 6 hrs for up to 5 days
       - Loading dose for children 2 mg/kg IV
         - Maintenance dose of 0.5 mg/kg IV every 6 hrs for up to 5 days
2. IV gamma globulin (IVGG)
   - Can be used alone or in addition to glucocorticoids
   - It is an antibody mixture
   - Slows destruction of platelets
   - Works more quickly than steroids (within 24-48 hrs)
   - Adult dose
     - 1-2 g/kg IV admin over 1-5 days
   - Children's dose
     - 1 g/kg IV admin x1
   - Side effects may include:
     - Urticaria, pruritis, incr risk of infection
3. Other Tx for ITP may include
   - Rh immune globulin
     - Temporarily stops spleen from destroying platelets
   - Medication changes
     - If drug is suspected as a cause, discontinuation or changing med may be necessary
   - Infection Tx

        - If a treatable infection is cause for ITP, then Tx of infection may result in higher platelet counts
    - Splenectomy
        - Spleen may need to be removed since this is site of platelet destruction
        - Considered more often in older children w/chronic ITP to decr rate of platelet destruction
        - Tx of last resort if other Tx's fail
    - Hormones
        - Teenage girls may need OCP / hormone Tx to decrease excessive menstrual bleeding

**Follow-Up**

1. Hematology consultation is often helpful
2. Pneumococcal infection prophylaxis if pt required splenectomy for Tx
3. Monitor for SE of meds

**Prognosis**

1. Children
    - 83% of children have spontaneous remission
    - 89% of children eventually recover
    - >50% of pts recover within 4-8 wks
    - 2% of pts die
2. Adults
    - Only 2% of adults have a spontaneous recovery
    - 64% of adults eventually recover
    - 30% of pts have chronic dz
    - 5% of pts die from hemorrhage

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