IMMUNE THROMBOCYTOPENIC PURPURA
INTRODUCTION

• Platelets are non nucleated cellular fragments
• Produced from megakaryocytes in the bone marrow
• Megakaryocytes are large polypoid cells
• Mature megakaryocyte – budding of cytoplasm occurs & large number of platelets are liberated into circulation
• Thrombopoeitin- primary growth factor controls platelet production
INTRODUCTION

• Normal platelet count
  Newborn  84,000 – 4,78,000 cells/ cu mm
  After 1 week – adults – 1,50,000- 4,00,000 cells/mm³

• Average life span of platelets- 7- 10 days

• Decrease in platelet count – Thrombocytopenia

• Increase in platelet count - Thrombocytosis
THROMBOCYTOPENIA

• Platelet count - < 1,50,000 cells/cu mm
• Causes
  • Increased platelet sequestration
    Hypersplenism, Hypothermia, Burns
  • Increased platelet destruction
  • Immune, Non immune
3. Decreased platelet production
CUT – OFF VALUES

• Neonates – 20,000 – 50,000 cells/mm³ [high risk for ICH]
• Children – 10,000- 20,000 cells/ mm³
• Spontaneous bleeding do not occur until counts are < 20,000 cells/mm³
IMMUNE THROMBOCYTOPENIC PURPURA

- Commonest bleeding disorder manifesting in children.
- Usual age of presentation – between 1-7 years.
- Acute ITP- lasts less than 6 months.
- Chronic ITP- lasts more than 6 months.
- The majority of children [60-75%] are likely to have acute ITP and that resolves within 2-4 months of diagnosis, regardless of therapy.
• Secondary to antibodies directed against the platelet glycoprotein II b/ III a complex
• These platelets are trapped in the spleen, where they are removed by macrophages
• Mechanism of production of antibodies is not known
• Hall mark is increased number of megakaryocytes in the bone marrow
• Th1 dominant pro-inflammatory cytokine state is also described recently
ACUTE ITP

- Benign, self limited
- Young children [<10 years ]
- Often Viral infection or Vaccination precedes
- Resolves within weeks or a few months of original presentation.
CHRONIC ITP

- Persistence of Thrombocytopenia [ <150000/mm³ ] for longer than 6 months after initial presentation
- > 10 years
- Insidious onset
- Female gender.
ITP –CLINICAL FEATURES

• Abrupt onset of bruising & bleeding in an otherwise healthy child
• H/O preceding viral illness or vaccination +/-
• Seasonal clustering of cases and more frequent during change of seasons
• Petechiae, purpura & ecchymosis
• Epistaxis & oral mucosal bleeds occur in < 1/3\textsuperscript{rd}
• Hematuria, hematochezia, melena in < 10%
• Menorrhagia
ITP – CLINICAL FEATURES (CONT..)

• Palpable spleen - < 10% cases
• Symptoms & signs depend on the platelet count
• Bleeding is mild unless the platelet count falls <20,000/cu mm
• Petechiae & ecchymosis can occur following mild trauma with a platelet count of 20000-50000/mm$^3$
• No dysmorphic features/bony anomalies/hyperpigmentation
• Suspect malignancy when there is malaise, bone pain, organomegaly or lymphadenopathy
CLASSIFICATION - BASED ON SYMPTOMS

1. No symptoms
2. Mild symptoms - bruising, petechiae, occasional minor epistaxis & very little interference with daily living
3. Moderate symptoms - more severe skin & mucosal bleeds, more troublesome epistaxis & menorrhagia
4. Severe symptoms - bleeding episodes – menorrhagia, epistaxis, melena - requiring transfusion or hospitalization, symptoms interfering seriously with the quality of life
INVESTIGATIONS

• Complete blood count:-
  • Low platelet count, Hb% and WBC counts are normal

• Peripheral smear evaluation
  • To see all cell lines, to estimate the platelet count & to exclude spurious thrombocytopenia, to examine for abnormal cells [ blasts] or malarial parasites
  • Circulatory platelets are larger in size, indicating increased production

• Liver function tests & Lactate dehydrogenase levels
  • To rule out Hepatitis, Malignancy & Hemolysis
INVESTIGATIONS

• Evaluate all cases with fever for infection
• Screening tests for disseminated intravascular coagulopathy when sepsis is suspected
• Bone marrow examination- Aspiration/Biopsy indicated in
• Abnormal WBC count or differential
• Unexplained anemia
• History & physical examination suggestive of bone marrow failure
• Failure of initial therapy
ADDITIONAL TESTS [CHRONIC CASES]

- Screening tests for Immunodeficiency
- Anti nuclear antibodies
- Direct Coomb’s test
- Anti phospholipid antibody assay
- Thyroid function tests
- Blood counts and peripheral smear for parents
- Serology testing for platelet antibody is seldom useful.
MANAGEMENT

- Child’s activity should be limited
- Aspirin containing medication should be avoided
- Detailed education & counseling of the family and patient
- Careful follow up
- Observation only
  - Platelet count >20,000/mm³ & only minor purpura
- Platelet transfusion in ITP is contra indicated unless life-threatening bleeding is present
FIRST LINE MEDICAL THERAPIES

- Corticosteroids
- Intra venous Immunoglobulin
- Anti D
CORTICOSTEROIDS

• Inhibition of both phagocytosis & Antibody production
• Improved platelet production and micro vascular endothelial stability
• Dose
  Prednisolone – 1-4 mg/kg/day x 2-3 weeks & tapered Dexamethasone – 20mg/mt² over 4 days every 3 weeks for 4-6 courses
  Alternate- mega pulse dose therapy
  Methyl Prednisolone 30mg/kg/day IV / oral x 3days
INTRA VENOUS IMMUNOGLOBULIN

• Clearance of antibody coated blood cells from the circulation by inhibiting the phagocytic activity of cells of reticulo-endothelial system
• Fc receptor blockade
• Dose - 2gm/kg divided over 2-5 days
• Expensive but cost effective
• Side effects: - flu like symptoms, aseptic meningitis, anaphylaxis, hemolytic anemia, HCV transmission
• Duration of response is brief [2-4 weeks]
ANTI - D

- Plasma derived Immunoglobulin prepared from donors selected for a high titer of anti Rh antibody
- Elicits an increase in platelet counts along with mild to moderate anemia
- Can only be used in Rh positive patients
- Dose – 50-75 micro gm./kg as IV infusion
- Therapeutic effect lasts for 1-5 weeks
- Side effects:- headache, nausea, chills, dizziness, fever, hemolysis
• Primary goal – prevent bleeding episodes & not to cure the disease
• 1/3 of these children will go into remission in months or years later
• Observation alone is an approach for many patients, especially those with minimal symptoms
Indications for Splenectomy

• Children with ITP for more than 1 year
• Symptoms of bleeding and counts
• < 10000/mm3 [3-12 yrs. of age]
• 10000-30000/mm3 [8-12 yrs. of age]
MANAGEMENT OF C/C ITP

• First line Medical therapy:-
  Intermittent Steroids, IV Ig, Anti D
• Second line therapy – for 10- 15% of children who fail to respond to first line drugs / splenectomy
• Danazole – 300- 400 mg/m²/day orally for 2 months
• Vinca Alkaloids – Vincristine 1.5 mg/m² IV weekly x 1 month
• Azathioprine – 50-200 mg/m²/day orally for 4- 6 months
• Cyclosporine – 5mg/kg/day in divided dose
• Cyclophosphamide & Interferon may be used
• Plasmapheresis may be done
LIFE THREATENING HEAMORRHAGE

• Intra venous Immunoglobulin- 1gm/kg
• Anti D – 50- 75 microgram/kg as IV Infusion
• High dose Corticosteroid – IV Methyl Prednisolone 30mg/kg
• Platelet Transfusion
• A combination of above can be tried
PROGNOSIS

• Excellent chance of recovery, irrespective of therapy
• Platelet count returns to normal in 4-8 weeks in ½ of the patients and in 2/3 of children by 3 months after diagnosis
• 5% have recurrent ITP, characterized by intermittent episodes of thrombocytopenia followed by lengthy periods of remission
THANK YOU