Case 1: 52 y/o female presents 4 years after a gastric bypass with fatigue and dyspnea on exertion:

**History:** her only medication is vit B12 IM 1000mcg monthly. She denies any GI bleeding and is postmenopausal.

**PE:** Pallor and pale conjunctivae. Stool is guaiac negative.

**Laboratory:** Hemoglobin 7.4 g/dl; MCV 74 fl; WBC 5,200, Platelets 502,000/uL; and reticulocyte count 1%

Smear shows microcytic hypochromic red cells, platelet and leukocyte morphology are normal.
Reticulocytic Indices

- RETICULOCYTE PERCENTAGE (0.5-1.5%)
- CORRECTED RETICULOCYTE PERCENTAGE
  \[ \text{RAW RETICULOCYTE} \times \frac{HCT}{45} \]
- RETICULOCYTE PRODUCTION INDEX
  \[ \text{RAW RETICULOCYTE} \times \frac{HCT}{45} \times \frac{1}{\text{RETICULOCYTE MATURATION TIME}} \]

Approach to Anemia

RETICULOCYTE COUNT / RPI

< 75,000 / <2  
> 75,000 / >3

Decreased production  
HYPOPROLIFERATIVE ANEMIA

Increased loss  
HYPERPROLIFERATIVE ANEMIA

Hypoproliferative Anemias

RETICULOCYTE COUNT < 75,000

MCV

< 80  
80 - 94  
> 94

MICROCYTIC  
NORMOCYTIC  
MACROCYTIC

Microcytic Anemias

- IRON DEFICIENCY ANEMIA
- ANEMIA of CHRONIC INFLAMMATION
- THALASSEMIA SYNDROMES
- SIDEROBLASTIC ANEMIAS

Microcytic Anemias

Erythrocytes are microcytic and hypochromic. Target cell are not seen in size and color with lighter-colored area in the center.

Red blood cells normally are the same Increased platelet number

Iron Deficiency Anemia

<table>
<thead>
<tr>
<th>Increased iron requirements</th>
<th>Inadequate iron supply</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood Loss</td>
<td>Intravasc. hemolysis + hemoglobinuria</td>
</tr>
<tr>
<td>GI disorders</td>
<td>PNH (paroxysmal nocturnal hemoglobinuria)</td>
</tr>
<tr>
<td>Menorrhagia</td>
<td>Cardiac valve prosthesis</td>
</tr>
<tr>
<td>Chronic donation</td>
<td>Pregnancy and lactation</td>
</tr>
<tr>
<td>Dialysis</td>
<td>Celiac sprue</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Measures of Iron Status

<table>
<thead>
<tr>
<th>Test</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum iron level</td>
<td>Reflection of iron stores</td>
</tr>
<tr>
<td>TIBC</td>
<td>Transferrin</td>
</tr>
<tr>
<td>Iron saturation</td>
<td>Ratio of serum iron to TIBC</td>
</tr>
<tr>
<td>Serum Ferritin</td>
<td>Iron stores (indirect) Acute phase reactant</td>
</tr>
<tr>
<td>Bone marrow and liver iron</td>
<td>Iron stores (direct)</td>
</tr>
</tbody>
</table>

Iron Deficiency Laboratory

- Anemia with a **Low Reticulocyte Count**
- **Decreased MCV** and **MCHC**
- **Decreased Serum Ferritin** Level
- **Low Serum Iron**, **Increased Transferrin**, and **decreased % Transferrin Saturation**
- No Sideroblasts or Reticuloendothelial Iron in Bone Marrow

Case 1: Evaluation

a) B12 and folic acid

b) Ferritin alone

c) Ferritin, iron, and transferrin

d) Direct anti-globulin test (Coombs)

e) Bone Marrow evaluation

Case 1: Treatment

Which of the following is the most appropriate treatment for this patient?

- Iron therapy
- Plasmapheresis
- Corticosteroids therapy
- Vitamin B12 supplementation

Case 2: 62 year old man is evaluated during a routine examination

**History:** colon cancer successfully treated with resection 12 years ago. No fatigue or other medical complaints.
**PE:** bilateral symmetric swelling and effusions in metacarpophalangeal and proximal interphalangeal joints.

**Laboratory:** Hemoglobin 10.1 g/dl; MCV 90 fl; WBC: 6.2; Platelets: 234,000. Retic count 0.1%, serum ferritin 250ng/mL (250mg/L), TIBC: 175 (31.22), serum iron 37 ug/L (6.62 umol/L). Peripheral smear normal

Anemia of Chronic Inflammation

Associated with chronic conditions:

- Chronic infections
- Neoplastic disease
- Inflammation: collagen vascular disease
- Trauma
- Post-surgery
- Critical ill patients

Activated monocytes and macrophages release IL6, IL1, and TNF
Stimulate 'hepcidin' production with sequestration of iron
Anemia of Chronic Inflammation

- Moderate anemia Hgb 7 to 11 g/dl
- Normochromic 70% Microcytic 30%
- Iron, transferrin, and saturation low
- Ferritin increased
- Bone marrow: Increased reticuloendothelial storage iron; reduced or absent sideroblasts

Thalassemia

**Most common** inherited abnormality of hemoglobin characterized by a quantitative **defect** in the synthesis of either the alpha or beta globin leading to **ineffective erythropoiesis** and hemolysis (the intracellular precipitation of excess globin chains with damage of red cell precursors and circulating red cells)

**Beta Thalassemia**

<table>
<thead>
<tr>
<th>BETA THALASSEMIA (chromosome 11)</th>
<th>Beta zero Thalassemia Minor</th>
<th>Beta Thalassemia Major</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterozygous carrier-type or beta thalassemia trait: one of the beta-globin genes is defective</td>
<td>Homozygous beta thalassemia</td>
<td>The production of beta-globin is severely impaired; ineffective erythropoiesis and severe microcytic hypochromic anemia</td>
</tr>
</tbody>
</table>

**Diagnosis of Thalassemia**

- Exclude Iron Deficiency
- RBC Count, Hb/MCV, Blood Smear: **Target cells**
- **Beta Thalassemia**: elevation of hemoglobin A2 and variable increase of hgb F
- **Alpha Thalassemia**: alpha thalassemia trait has normal hemoglobin electrophoresis with mild anemia and microcytosis
- **Homozygous alpha thalassemia** presents with hydrops fetalis and hemoglobin Bart (Y4)

Hemoglobin types

<table>
<thead>
<tr>
<th></th>
<th>Hgb A</th>
<th>α2β2</th>
<th>Hgb A2</th>
<th>α2γ2</th>
<th>Hgb H β4</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hgb A</strong></td>
<td>97%</td>
<td></td>
<td>3%</td>
<td>0%</td>
<td>0%</td>
</tr>
</tbody>
</table>

**Hemoglobin types**

<table>
<thead>
<tr>
<th>Alpha (0) Thalassemia</th>
<th>Alpha (+) Thalassemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha globin gene (α-/-)</td>
<td>Silent carrier (α/α)</td>
</tr>
<tr>
<td>Hydrops fetalis</td>
<td>Mild reduction MCV and MCH</td>
</tr>
<tr>
<td>Alpha thalassemia major Hemoglobin Bart’s</td>
<td>Increased</td>
</tr>
<tr>
<td>Alpha thalassemia Trait (αα/-) or (-/αα)</td>
<td>Abundant formation of Hgb H, excess of beta globin. High affinity for oxygen with ineffective supplier of oxygen to the tissue. Susceptible to hemolysis.</td>
</tr>
</tbody>
</table>

Case 2: Which of the following is the most appropriate next step in management?

1) Packed red blood cell transfusion
2) Oral ferrous sulfate
3) Erythropoietin
4) No treatment necessary
Hematological Indices of Iron deficiency anemia and thalassemia

<table>
<thead>
<tr>
<th>Test</th>
<th>Iron Deficiency</th>
<th>Beta Thalasemia</th>
<th>Alpha Thalasemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCV (&lt;80fL)</td>
<td>low</td>
<td>Low</td>
<td>low</td>
</tr>
<tr>
<td>RDW (RBC distribution width)</td>
<td>High</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Ferritin</td>
<td>Low</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Hgb electrophoresis</td>
<td>Normal (may have reduced A2)</td>
<td>Increase Hgb A2, reduced A, increased H</td>
<td>normal</td>
</tr>
</tbody>
</table>

Differential diagnosis of microcytosis

<table>
<thead>
<tr>
<th>Blood Smear</th>
<th>Iron Deficiency</th>
<th>Chronic Inflammation</th>
<th>Thalasemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total Iron TIBC Saturation</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Normal/Increased</td>
</tr>
<tr>
<td>Ferritin</td>
<td>Decreased</td>
<td>Normal/Increased</td>
<td>Normal/Increased</td>
</tr>
</tbody>
</table>

Bone Marrow Sideroblasts

- Absent
- Increased

Echinocytes: Renal Disease

- Erythrocyte destruction, loss and underproduction. EPO deficiency due to decrease in number of renal cortical cells. Normocytic normochromic anemia associated with iron deficiency or other vitamins. Retic count is low.

Normocytic Anemias

- Metabolic
  - Renal Failure
  - Pregnancy
- Endocrine Deficiency
  - Androgen deficiency
  - Hypothyroidism
  - Adrenal Failure
- Marrow Replacement (Myelophthistic)
- Marrow Failure
  - Aplastic anemia
  - Leukemia
- Anemia of Chronic Disease

Case 3: 64 year old man with severe fatigue and recurrent epistaxis

Myelophthisic Anemia

Characterized by teardrop-shaped erythrocytes, immature leukocytes, nucleated erythrocytes and large megakaryocytes fragments on peripheral smear.
**Myelophthisic Anemia**

**Secondary**
- response to infiltration of marrow by tumor, macrophages in lipid storage disease, fibrosis or granulomas
- Usually there is extramedullary hematopoiesis leading to organomegaly (spleen, liver)
- Occur as a result of cytokines release which stimulate fibroblastic proliferation and fibrosis in marrow
- Common in myelofibrosis

**Aplastic Anemia (AA)**

Normal hematopoietic tissue is replaced by fat result in hypocellular marrow and pancytopenia

**Treatment:**
- Immunosuppression (ATG and cyclosporine)
- Bone marrow transplant

---

**Etiologies and Differential Diagnosis**

<table>
<thead>
<tr>
<th>Acquired AA</th>
<th>Inherited AA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Idiopathic</td>
<td>Fanconi anemia; AR pancytopenia and urogenital anomalies</td>
</tr>
<tr>
<td>Medications and Toxins:</td>
<td>Shwachman-Diamond syndrome</td>
</tr>
<tr>
<td>Benzene, alcohol, diclofenac, indomethacin, ticlopidine</td>
<td></td>
</tr>
<tr>
<td>Infections:</td>
<td>Amegakaryocytic thrombocytopenia</td>
</tr>
<tr>
<td>EBV, Hepatitis, HIV, CMV</td>
<td></td>
</tr>
<tr>
<td>Pregnancy</td>
<td>Down syndrome</td>
</tr>
<tr>
<td>SLE</td>
<td>Dyskeratosis congenita</td>
</tr>
<tr>
<td>Thymoma / thymic carcinoma</td>
<td></td>
</tr>
<tr>
<td>GVHD</td>
<td></td>
</tr>
</tbody>
</table>

---

**Case 3: which of the following is the most appropriate treatment for this patient?**

a) Prednisone  
b) Antithymocyte globulin and cyclosporine  
c) Allogeneic stem cell transplantation  
d) Plasma exchange

---

**Macrocytic Anemias**

- Elevated MCV > 100fL
  - Megaloblastic anemias: impair DNA synthesis
  - Non-megaloblastic anemias:
    - increased membrane surface area
    - accelerated erythrocytosis
    - alcoholism
    - COPD (excess cell water secondary to carbon dioxide retention).
  - Deposition of cholesterol and phospholipids in the membrane of RBC
    - Liver disease/Obstructive jaundice
    - Splenectomies

**Megaloblastic Anemia**

- Three cell lines are affected
  - Hypersegmented neutrophils: 5 lobes
  - RBC are large, often oval cells Macroovalocytes
  - Cabot Ring: remnant of the mitotic spindle apparatus
  - Howell-Jolly bodies: nuclear remnant

---
Megaloblastic Anemia
DNA Synthesis Impaired

- Vitamin B12 Deficiency: Pernicious anemia, gastrectomy, atrophic gastritis, reduce dietary intake.
- Folic Acid Deficiency: dietary deficiency
- Chemotherapeutics
- Myelodysplastic Syndromes
- Hereditary Defects in DNA synthesis

Laboratory Findings of Cobalamin and Folate Deficiency

<table>
<thead>
<tr>
<th>Serum levels</th>
<th>Clinical cobalamin deficiency</th>
<th>Subclinical cobalamin deficiency</th>
<th>Folate Deficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cobalamin level</td>
<td>&lt; 200 ng/L</td>
<td>200-350 ng/L</td>
<td>&gt; 300 ng/L</td>
</tr>
<tr>
<td>Folate level</td>
<td>&gt; 4 ng/ml</td>
<td>&gt; 4 ng/ml</td>
<td>&lt;2 ng/ml</td>
</tr>
<tr>
<td>Homocysteine</td>
<td>++</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Methylmalonic acid</td>
<td>++</td>
<td>+</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Case 4: 32 year old female referred for evaluation of dark urine

**History:** Gradually noticed yellow eyes and dark urine, felt tired and short of breath when climbing stairs. No fever, itching, bleeding and is not taking drugs

**PE:** Pale and jaundiced. No palpable lymphadenopathy, hepatosplenomegaly, rash or joint deformities or pain

**Laboratory:** Hemoglobin of 5.4 g/dL, WBC: 40,000 (nucleated red cell elevated) Retic count 9% Total bil: 4.7, AST 90, LDH 572. Blood smear showed agglutination or RBC Coomb’s test was positive for IgG and C3, ANA and RA negative. Immunoglobulins were normal. Large amount of urinary hemosiderin.

Hyperproliferative Anemia

- Indirect hyperbilirubinemia
- Anemia
- Reticulocytosis

Overview and Evaluation of Hemolytic Anemia

**Acquired**

- **EXTRINSIC DEFECT**
  - Direct Antiglobulin Test
  - Positive IMMUNE
    - Autoimmune
    - Alloimmune
    - Drug induced
  - Negative NON-IMMUNE
    - Microangiopathic
    - Infection
    - Hypersplenism
    - Chemical agent

**Inherited**

- **INTRINSIC DEFECT**
  - Blood Smear
  - Enzymopathies: G6PD deficiency
  - Membranopathies: spherocytosis
  - Hemoglobinopathies: Thalassemia and sickle cell

Coombs’s Test or DAT: Direct Anti-Immunoglobulin test

Coombs is used to determine if RBC-binding Antibody (IgG) or complement (C3) is present on RBC membranes
**Indirect Anti-Immunoglobulin test**

Indirect antiglobulin test detects IgG Ab against RBC in patient’s serum.

**Autoimmune Hemolytic Anemia (AIHA)**

<table>
<thead>
<tr>
<th>Warm Antibodies</th>
<th>Cold Agglutinin</th>
<th>Paroxysmal cold hemoglobinuria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antibody</td>
<td>IgG or IgG + C3</td>
<td>IgM fixed C3 Landsteiner Ab</td>
</tr>
<tr>
<td>Antigen</td>
<td>Rh at 37°C</td>
<td>Ii at &lt; 37°C P &lt; 37°C</td>
</tr>
<tr>
<td>Clearance</td>
<td>Splenic Macrophages</td>
<td>Kupffer cell in the liver</td>
</tr>
<tr>
<td>Smear</td>
<td>Micro-spherocytes</td>
<td>Agglutination</td>
</tr>
<tr>
<td>Steroids</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Splenectomy</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

**Drug Induced Hemolysis**

<table>
<thead>
<tr>
<th>Mechanism</th>
<th>Drug absorption</th>
<th>Immune complex</th>
<th>Autoantibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAT</td>
<td>Positive anti-IgG</td>
<td>Positive anti-C3</td>
<td>Positive IgG</td>
</tr>
<tr>
<td>Site hemolysis</td>
<td>Extravascular</td>
<td>Intravascular</td>
<td>Extravascular</td>
</tr>
<tr>
<td>Medication</td>
<td>Penicillin</td>
<td>Quinidine</td>
<td>Alpha methyl Dopa</td>
</tr>
<tr>
<td></td>
<td>Ampicillin</td>
<td>Rifampin</td>
<td>L-Dopa</td>
</tr>
<tr>
<td></td>
<td>Methicillin</td>
<td>Sulfonamide</td>
<td>Procanamid</td>
</tr>
<tr>
<td></td>
<td>Cabenicillin</td>
<td>Isoniazid</td>
<td>Ibuprofen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insulin</td>
<td>Diclofenac</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Tetracyclin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Alpha methyl Dopa</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>L-Dopa</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Procanamid</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cephalothin</td>
<td>Melphalan</td>
<td>Interferon alpha</td>
</tr>
<tr>
<td></td>
<td>Cephaloridine</td>
<td>Fluoracil</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sulindac</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Acquired Hemolysis: immune mediated with Positive Coomb’s**

- Alloimmune hemolytic anemia: acute transfusion and delayed hemolytic transfusions
- Autoimmune hemolytic anemia
  - COLD Antibodies
  - WARM Antibodies
  - PCH Paroxysmal cold hemoglobinuria
- Drug induced Hemolytic anemia

**Drug Induced Hemolysis**

- Hypersplenism
- Fragmentation
- Physical agents
- Chemical agents
- Lipid abnormalities
- Hypophosphatemia
- Infectious agents

**Case 4: Which of the following is the most appropriate treatment?**

1) Red blood cell transfusion
2) Steroids
3) Splenectomy
4) Immunosuppression (Rituximab)
ACQUIRED HEMOLYSIS - NON-IMMUNE
FRAGMENTATION HEMOLYTIC ANEMIA

Hereditary Hemolytic Anemias

- Neonatal Jaundice
- Recurrent “Hepatitis”
- Personal or Familial FH of Premature Gallstones, Anemias, Splenectomy, or Specific Diagnosis
- Specific Chronic or Recurrent Symptoms

Fragmentation Hemolysis

- MAHA: microangiopathic hemolytic anemia: intravascular hemolysis = schistocytes
- Intravascular devices
- DIC disseminated intravascular coagulation
- Thrombotic thrombocytopenic purpura
- Hemolytic Uremic syndrome
- Eclampsia and preeclampsia
- Malignant hypertension
- Scleroderma renal crisis
- Pulmonary Hypertension
- Vasculitis
- Hemangiomas

Congenital Defective Erythrocytes

- Mature RBC → does not have nucleus, organelles or protein machinery
- Any defect in the remaining components lead to hemolysis
  Membranes: disorders in membranes skeleton proteins
    - Hereditary Spherocytosis AD, increase osmotic fragility
    - Hereditary Elliptocytosis
  Hemoglobin: disorders in hemoglobin synthesis
    - Sickle Cell Anemia
    - Unstable Hemoglobin
  Enzymopathies
    - Glucose-6-phosphate Dehydrogenase Deficiency: X-link disorder critical in glutathione production protecting cell to oxidation. Bite cells
    - Pyruvate Kinase Deficiency

Congenital defects of erythrocytes

Bite cells: removal of denature hgb by spleen in G6PD deficiency
Spherocytes

Sickle Cell Disease

Inherited disorder caused by a point mutation leading to a substitution of valine for glutamic acid in the sixth position of β chain with splenic sequestration and some degree of intravascular hemolysis
Sickle Syndromes

- **Sickle Cell Anemia** SS disease
  Homozygous substitution valine to glutamic acid in 6th position of β gene
- **Sickle-hemoglobin C SC disease**
  Compound heterozygote for above and substitution of lysine for glutamic acid
- **Sickle Beta Thalassemia**
  S beta⁻ thalassemia
  S beta+ thalassemia - Hb SA
- **Sickle Trait - Hb AS**

Sickle Cell Disease: Its Complications

- **Hemolytic anemia**
  Aplastic crisis Parvo virus B19
  Splenic and Hepatic sequestration
- **Increased severity of infection**
  Encapsulated organisms
- **Organ infarction**
  Stroke and retinopathy
  Acute Chest and pulmonary fibrosis
  Avascular necrosis of hips and shoulder
  Renal concentrating defect and renal failure
- **Pain Episodes**
  Vaso occlusive crisis

Treatment

- Hydration
- Blood transfusions → Iron overload
- Hydroxyurea: decrease number of painful crises and prevent stroke
- Exchange transfusions

Acquired Neutropenia

Drug and infections are the most common causes of leukopenia/neutropenia

Drug Induced Leukopenia

- Chemotherapy
- **Antimicrobials**
  - Penicillins,
  - Cephalosporins
  - Trimethoprim - sulfamethoxazole
- **Antihistamines**
  - Cimetidine
  - Ranitidine
- **Anticonvulsants**
  - Valproic acid
  - Phenytoin
  - Carbamazepine
- NSAIDs
- **Antipsychotics**
  - Phenothiazines
  - Clozapine
- Gold salts
- Antithyroid drugs
- **Cardiovascular**
  - Procainamide
  - Captopril
- **Miscellaneous**
  - Thiazides
  - Oral hypoglycemics

Infections Induced Leukopenia

- Hepatitis -B
- Cytomegalovirus
- Epstein-Barr virus
- HIV
- Gram negative sepsis
- Rickettsial infections
- Malaria
- *Ehrlichiosis*
Leukopenia

- Chronic benign neutropenia - African Americans (Duffy blood group protein) and Yemenite Jews
- Folate and B₁₂ deficiency
- Alcohol
- Myelodysplastic syndromes
- Autoimmune – Felty’s syndrome
- Hypersplenism
- Cyclic neutropenia
- Large granular lymphocytes

Case 5: 20 year old female referred for evaluation of thrombocytopenia

- History: She first learned of her low platelet count 5 years ago. Her count was 60,000. Denies any bleeding symptoms except for heavy menstrual periods and recent easy bruising. She is not taking medications. No exposed to blood transfusions
- PE: unremarkable
- Laboratory: Hemoglobin 7.8 g/dL, MCV 68 WBC 6,800/μL. Platelet count 12,000/μL. Normal renal function

Thrombocytopenia

- Pseudothrombocytopenia
  - EDTA induced platelet aggregation
  - Smear and count with citrate anticoagulation

Thrombocytopenia

- Increased Platelet Destruction
  - Disseminated intravascular coagulation
  - Vasculitis/vascular damage
  - Adhesion to artificial surfaces
  - Hemophagocytosis
  - Thrombotic microangiopathy
  - Splenic sequestration
  - Von Willebrand’s disease Type IIIb
  - Platelet-type von Willebrand disease

- Immune
  - Immune thrombocytopenic purpura
  - TTP with anti ADAMTS13 antibody
  - Infection and sepsis
  - Drug induced: Heparin HIT Sulfas
  - Quinine
  - Quinidine
  - Post-transfusion purpura
  - HIV

- Non-immune
  - Immune thrombocytopenic purpura
  - Thrombotic thrombocytopenic purpura
  - Drug induced: Heparin HIT Sulfas
  - Bone marrow infiltration
  - Other:
    - RITC
    - HEC
    - EOC
    - EPO
    - Fragile platelet factor

- Inherited disorders:
  - Congenital aplastic anemia
  - Congenital amegakaryocytic thrombocytopenia
  - Thrombocytopenia with absent radius syndrome
  - Bernard-Soulier syndrome
  - Microcytosis and X-linked thrombocytopenia
  - X-linked thrombocytopenia associated with Wiskott-Aldrich syndrome.

- MYH9-related disorders:
  - Bernard-Soulier syndrome
  - Fechtner’s syndrome
  - Alport’s syndrome

- Nutritional disorders: folate and B₁₂

- Aplastic anemia, PNH, MDS
Immune Thrombocytopenic Purpura:

- **Autoimmune destruction** caused by antibodies reactive to platelet glycoproteins: IIb-IIIa, Ib and fibrinogen receptor
- Primary disorder of platelet destruction
- **Removal** of the Ab coated platelet in the spleen but some Ab inhibit proliferation and/or differentiation of megakaryocytes
- Increased platelet associated IgG

**Diagnosis**

- Initial history and physical examination: identify bleeding and exclude other causes of thrombocytopenia
- If during the course of treatment or monitoring → atypical features developed → reassess Dx ITP

Anti-platelet antibodies are NOT recommended nor part of the diagnosis

Bone Marrow biopsy
- If over 60 years or other evidence of marrow pathology
- Prior to splenectomy or poor response to initial therapy

**Immune Thrombocytopenic Purpura: 1st line treatment**

<table>
<thead>
<tr>
<th>Agent and dose</th>
<th>Response</th>
<th>Toxicities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Corticosteroids</td>
<td>Initial rate: 70-80%</td>
<td>Hypertension, GI distress, Cataract, Hypoglycemia, Osteoporosis, Avascular necrosis, Infections, Adrenal insufficiency, Psychological distress</td>
</tr>
<tr>
<td>Adults: prednisone 1-2 mg/kg/d for 4 weeks</td>
<td>Time: 1 week</td>
<td>Duration: 10-30%</td>
</tr>
<tr>
<td>IV Ig 0.8-1 gm/kg given 1-2 days</td>
<td>Initial rate: 80%</td>
<td>Headache, aseptic meningitis, neutropenia, thrombosis, renal insufficiency, infusion reactions, anaphylaxis in IgA deficiency</td>
</tr>
<tr>
<td>Anti-D 50-70 ug/kg for one dose</td>
<td>Initial rate: 80%</td>
<td>Hemolytic anemia, DIC, intravascular hemolysis, renal failure</td>
</tr>
<tr>
<td></td>
<td>Time: 24-48 hours</td>
<td>Duration: 3-4 wk</td>
</tr>
</tbody>
</table>

**Thrombotic Thrombocytopenic Purpura**

- Incidence 4-11 cases per million in US
- Pentad
  - Fever
  - Microangiopathic hemolytic anemia
  - Thrombocytopenia
  - Renal symptoms
  - Neurological symptoms
- Overall mortality treated patients is 29%

**Case 5: Which of the following is NOT the next step?**

- a) Review blood smear
- b) Check HIV and Hepatitis panel
- c) Review in detail personal and family history of bleeding
- d) Start steroids
- e) Platelet transfusion
Case 1: Evaluation

THANK YOU

a) B12 and folic acid
b) Ferritin alone
c) Ferritin, iron, and transferrin
d) Direct anti-globulin test (Coombs)
e) Bone Marrow evaluation

Case 1: Treatment

Which of the following is the most appropriate treatment for this patient?

- Iron therapy
- Plasmapheresis
- Corticosteroids therapy
- Vitamin B12 supplementation

Case 2: Which of the following is the most appropriate next step in management?

1) Packed red blood cell transfusion
2) Oral ferrous sulfate
3) Erythropoietin
4) No treatment necessary

Case 3: Which of the following is the most appropriate treatment for this patient?

a) Prednisone
b) Antithymocyte globulin and cyclosporine
c) Allogeneic stem cell transplantation
d) Plasma exchange

Case 4: Which of the following is the most appropriate treatment?

1) Red blood cell transfusion
2) Steroids
3) Splenectomy
4) Immunosuppression (Rituximab)
Case 5: Which of the following is NOT the next step?

a) Review blood smear
b) Check HIV and Hepatitis panel
c) Review in detail personal and family history of bleeding
d) Start steroids
e) Platelet transfusion