# Abnormal CBCs

National Pediatric Nighttime Curriculum

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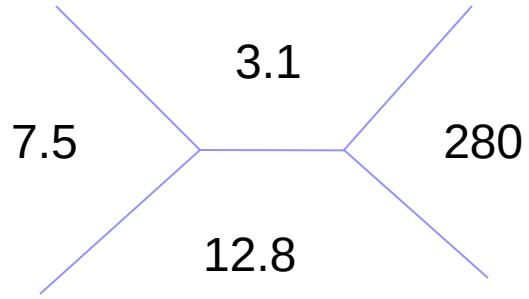
# LEARNING OBJECTIVES

- Identify common abnormalities of complete blood counts and interpret them using the available indices
- Formulate a complete differential diagnosis for anemia and thrombocytopenia
- Recognize when additional studies might be needed to further clarify the diagnosis when the CBC is abnormal

# CASE 1

- You have just admitted a 2 year-old boy with a history of intermittent blood streaked stools. On exam he has pallor, tachycardia, and a 2/6 systolic ejection murmur at the upper left sternal border. His hemoglobin is 3.1 g/dL.
  - What additional historical information would you want to know?
  - What else would you like to know about his initial assessment?
  - How will this information change management?
  - What other lab values would you like and what additional testing would you consider?

# THE FULL CBC WITH INDICES




MCV 53.8 fL
RBC 2.38 M/microL
MCH 13 pg
MCHC 24.2 %
RDW 24.1 %
MPV 8 fL

Neut 40 Bands 0 Lymphs 48 Mono 10 Eos 2 Baso 0 ANC 3

Peripheral Smear: slight polychromasia, marked hypochromasia and microcytosis

Reticulocyte 0.9%

Without additional testing, is there a way to predict the type of anemia using the CBC and indices?

# A FEW FACTS ABOUT RED BLOOD CELLS

- Fetal hematopoiesis initially occurs in the yolk sac, then transitions to the liver before ultimately residing in the bone marrow.
- Red cell production is under the control of Erythropoietin (EPO) which is produced in the kidneys in response to both hypoxia and anemia.
- Hemoglobin is a protein that consists of iron-containing heme groups and a protein globin chains.
- Hemoglobin has the vital role of reversibly transporting oxygen.
- The average RBC life span is 60-90 days in neonates and 120 days in children and adults.
- Anemia is defined as reduction of RBC volume or Hemoglobin concentration below the lower limit of normal for age and sex.
  - In general, 6 months old-puberty Hgb < 11 g/dL is abnormal.

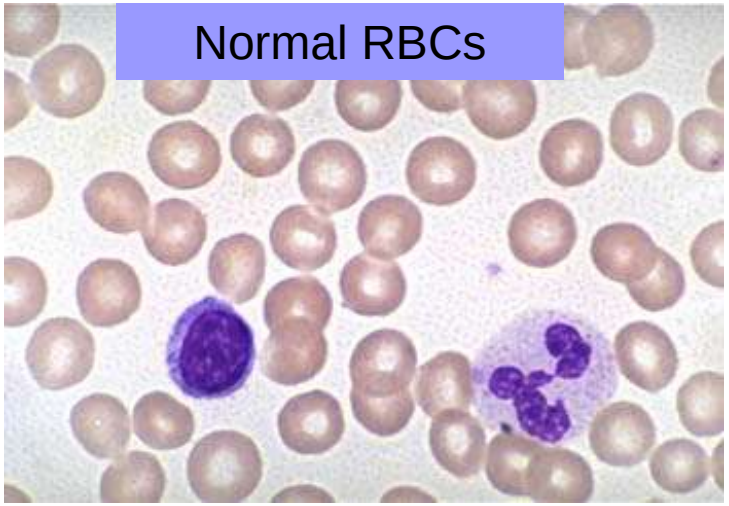
# APPROACH TO ANEMIA

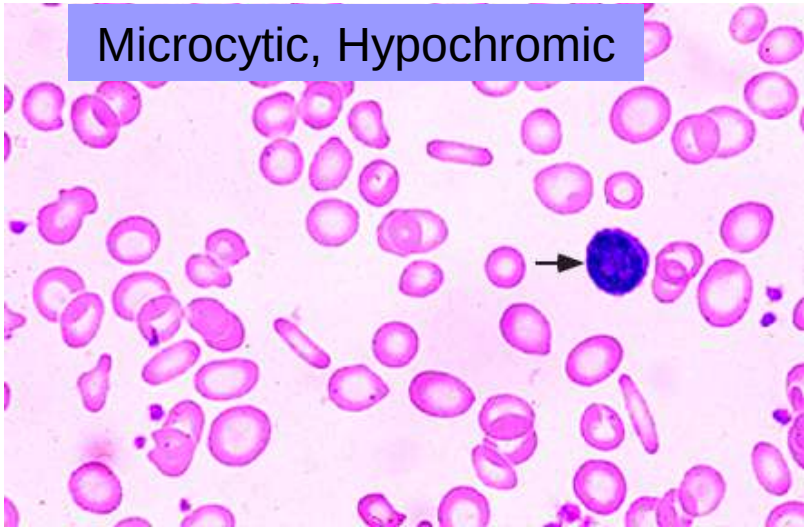
| Microcytic | Normocytic | Macrocytic |
|---|---|---|
| •Iron Deficiency Anemia<br>•Acute/Chronic Inflammation*<br>•Thalassemias<br>•Sideroblastic<br>▪ Lead poisoning<br>▪ Pyridoxine deficiency/ dependency | ➢Low Retic (Inadequate production)<br>•Diamond-Blackfan**<br>•Transient Erythroblastopenia of Childhood (TEC)<br>•Infection/Infiltration<br>•Medication<br>•Aplastic | ➢Megaloblastic<br>•Folate Deficiency<br>•Vitamin B12 Deficiency<br>•Methylcobalamin defects<br>•Hereditary Orotic Aciduria<br>•Medications |
| | ➢Nl/High Retic (Increased destruction)<br>○Coombs Negative<br>•Acute blood loss<br>•Microangiopathic hemolytic anemia<br>•Membrane Defects<br>•Hemoglobinopathies***<br>•Enzyme defects<br><br>○Coombs Positive<br>•Iso-immune<br>•Auto-immune | ➢Non-megaloblastic<br>•Fanconi's anemia<br>•Liver disease<br>•Hypothyroidism<br>•Myelodysplasia<br>•Dyserythropoetic anemia<br>•Down Syndrome |

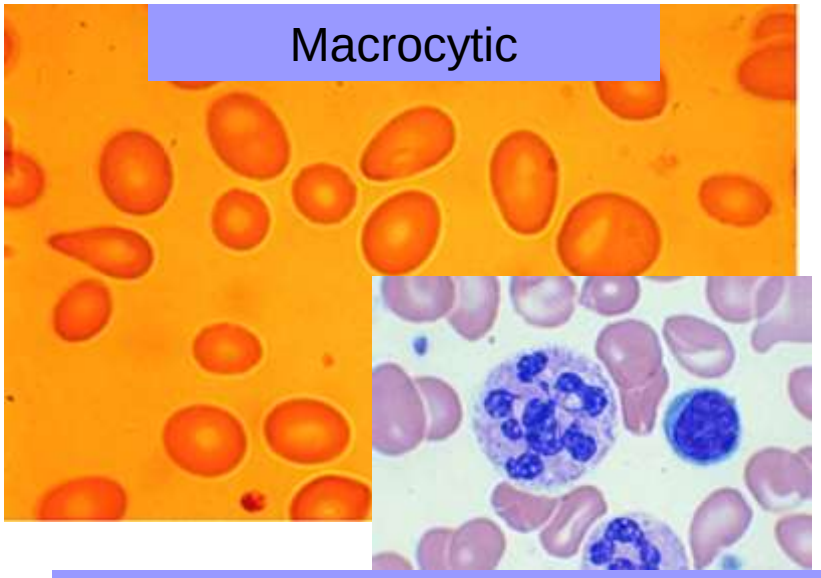
**Can also be normocytic*
*** Can also be macrocytic*
****Can also be microcytic*

Ref:3

# PERIPHERAL BLOOD SMEAR




Megaloblastic Anemia with Hypersegmented Neutrophils

Ref: 9, 10

# HOW DOES THE RETICULOCYTE COUNT HELP YOU?

- Calculate the “corrected reticulocyte count” or Reticulocyte Index (RI)
  - (Measured Hct/Expected Hct) * Retic % /Maturation Factor
  - Maturation Factors vary with Hct

| Hct≥36 % | 1 |
|---|---|
| 35-26% | 1.5 |
| 25-16% | 2 |
| ≤15% | 2.5 |

  - RI should be >2, indicating adequate response
- For our patient, RI= (12.8/36)*0.9=0.32/2.5=0.13
  - Inappropriately low response in the face of anemia

# WHAT TYPE OF ANEMIA DOES YOUR PATIENT HAVE AND WHAT IS YOUR DIAGNOSIS?

- Microcytic, hypochromic anemia
- Inappropriately low reticulocyte count
- Probably due to a mix of blood loss and dietary related iron deficiency anemia (IDA)

# WHAT OTHER TESTING WOULD YOU CONSIDER FOR THIS PATIENT?

- Iron Studies

| Test | Change in IDA | Notes |
|---|---|---|
| Ferritin | Low | •Accurate indicator of iron stores<br>•Can be falsely elevated if inflammation present |
| Total Iron Binding Capacity | High | |
| Iron level | Low | •Can be affected by many factors (iron absorption, iron available after RBC destruction, iron stores) |
| Iron saturation | Low | • serum iron/TIBC |
| Free erythrocyte protoporphyrin | High | •Accumulates when the patient is unable to complete heme production<br>•Can also be increased in lead toxicity and chronic disease |

- Lead Level
- Fecal Occult Blood

Ref. 2,3

# HOW WOULD YOU MANAGE THIS PATIENT?

- Packed red blood cell transfusion

| Guidelines for Pediatric RBC Transfusions | |
|---|---|
| Children & Adolescents<br>▪ Acute loss >25% circulating blood volume<br>▪Hemoglobin <8 g/dL in perioperative period<br>▪Hemoglobin <13g/dL in severe cardiopulmonary disease<br>▪***Hemoglobin < 8g/dL and symptomatic***<br>▪Hemoglobin <8g/dL and marrow failure | Infants ≤ 4 months old<br>▪Hemoglobin <13 g/dL in severe pulmonary disease<br>▪Hemoglobin <10g/dL in moderate pulmonary disease<br>▪Hemoglobin < 13g/dL and severe cardiac disease<br>▪Hemoglobin <10g/dL and major surgery<br>▪Hemoglobin <8g/dL and symptomatic |

- Symptomatic Anemia: tachycardia, mental status change, shortness of breath, congestive heart failure

Ref. 4

# TREATMENT OF IRON DEFICIENCY ANEMIA- FOR PATIENTS WITHOUT SYMPTOMS OF SEVERE ANEMIA

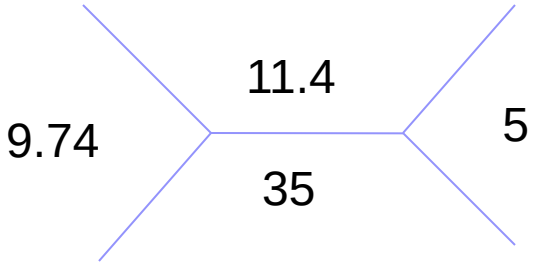
- Iron supplementation
  - Treatment for severe anemia 6mg/kg/day of oral ferrous sulfate (dosing based on elemental iron)
  - Should be administered with vitamin C containing food or beverage to enhance absorption
  - Treatment length ~2-3 months to replace stores
- Follow-up
  - For severe anemia, reticulocyte count should be re-checked to ensure response and should respond in 7-10 days
  - For mild-moderate anemia, repeat Hgb in 1 month should increase by at least 1g/dL
  - Most likely cause of treatment failure is due to non-compliance with iron supplementation
  - If patient compliant, but not responding then need to consider other diagnoses, like Thalassemia or ongoing blood loss

Ref. 2,3

# CASE 2

- You have just admitted a 12 year-old girl with new onset bruising and petechiae. She also reported easy bleeding from the gums while brushing her teeth. She has had one prolonged episode of epistaxis, still ongoing, which is what brought her to the Emergency Department. She thinks she remembers having a cold a few weeks ago. She is otherwise well appearing with normal vital signs.
  - What additional historical information would you want to know?
  - What else would you like to know about her initial assessment?
  - How will this information change management?
  - What diagnoses are you suspecting?
  - What initial labs would you like and what additional testing would you consider?

# INITIAL WORK UP




MCV 91.5 fL
RBC 4.1 M/microL
MCH 28.3 pg
MCHC 28.3%
RDW 13%
MPV 12 fL

Neut 66 Bands 0 Lymphs 28.3 Mono 5.2 Eos 0.4 Baso 0.1 ANC 6.42

Peripheral Smear: normocytic, normochromic RBCs, few large platelets, no schistocytes

# A FEW FACTS ABOUT PLATELETS

- Platelets are released from megakaryocytes in the bone marrow
- They are anucleate cellular fragments that effect primary hemostasis
- Normal Mean Platelet Volume (MPV) is 7-11fL
- The average platelet lives for 9-14 days
- Platelet production is controlled by Thrombopoiten (TPO), which is produced by the liver and regulated by presence of TPO receptors in circulation

Ref. 4,5

# HOW DO YOU DEFINE THROMBOCYTOPENIA?

- Platelet count <150,000 per microL
- Can present with symptoms of primary hemostasis, including:
  - Mucocutaneous bleeding, bruising and petechiae
- The risk of intra-cranial hemorrhage is low with platelet counts above 20,000
  - Risk increases with head trauma and with use of anti-platelet medications.
- Thrombocytopenia can result from multiple causes:
  - Decreased platelet production
  - Sequestration of platelets
  - Increased platelet destruction

Ref. 4, 7

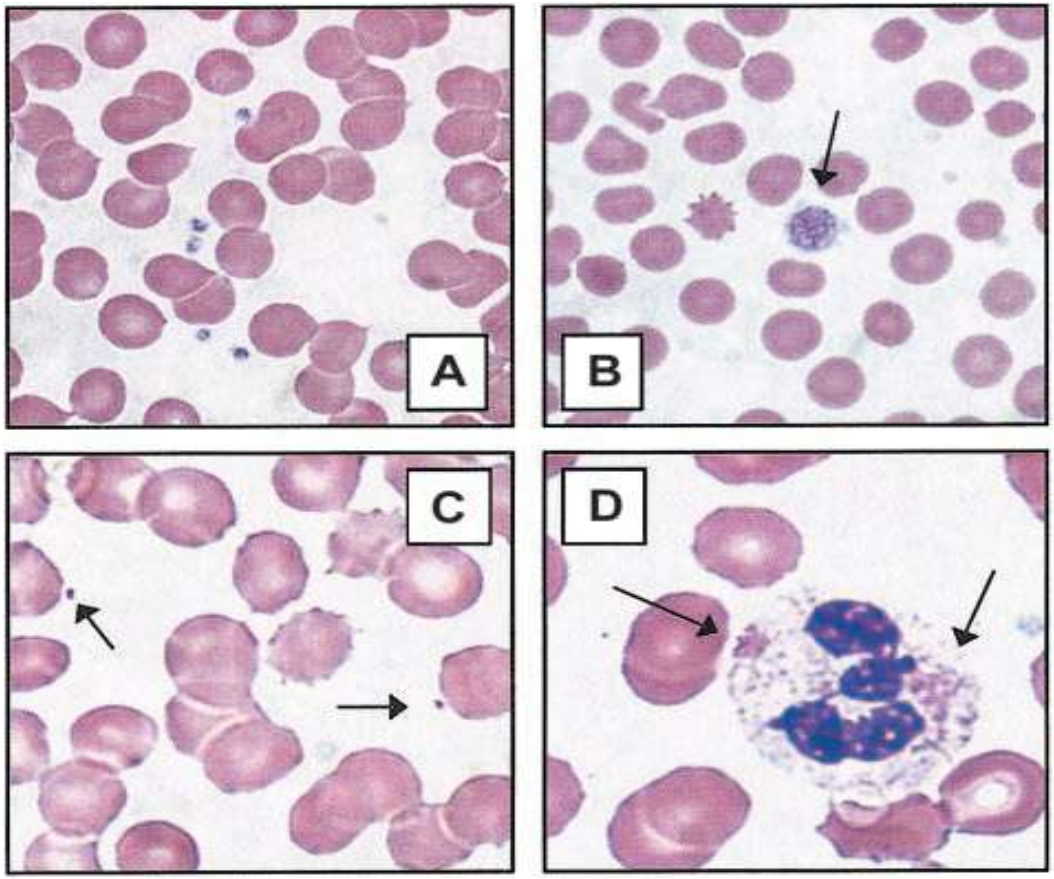
# THROMBOCYTOPENIA-WHAT'S YOUR DIFFERENTIAL?

| Decreased platelet production | Increased platelet destruction | |
|---|---|---|
| •Infiltrative Bone Marrow Diseases<br>•Inherited/Acquired bone marrow failure syndromes<br>•Congenital thrombocytopenias<br>•TAR Syndrome<br>•Wiskott-Aldrich Syndrome<br>•Amegakaryocytic thrombocytopenia<br>•MYH9-related (i.e.May-Hegglin)<br>•Bernard-Soulier (also abnormal platelet function)<br>•Cyanotic heart disease | **Immune Mediated**<br>•Idiopathic Thrombocytopenic Purpura (ITP)<br>•Evan's Syndrome (anemia and thrombocytopenia)<br>•Drug induced thrombocytopenia<br>•Infection<br>•Neonatal alloimmune thrombocytopenia<br>•Autoimmune disorders<br>•Post-transplant thrombocytopenia | **Non-Immune Mediated**<br>•Hemolytic Uremic Syndrome<br>•Thrombotic thrombocytopenic purpura<br>•Disseminated intravascular coagulation<br>•Kasabach-Merritt Syndrome<br>•Hypersplenism<br>•Hypothermia<br>•Mechanical destruction (prosthetic valve/indwelling device/HD/ECMO) |

Ref. 4, 5, 6

# HOW CAN THE PERIPHERAL SMEAR HELP YOU IN THROMBOCYTOPENIA?

Box A: Normal Blood Smear




Box B: Macrothrombocyte, platelet depicted by arrow is larger than the erythrocytes

Box C: Microthrombocyte, typical for Wiskott-Aldrich (or X linked thrombocytopenia)

Box D: Dohle-like bodies in the neutrophilic cytoplasm, as seen with May-Hegglin Anomaly

Ref. 5

# LET'S REVIEW YOUR PATIENT'S PROBLEMS

- Acute onset thrombocytopenia
- Normal exam other than signs of mucocutaneous bleeding
- Lack of other cell line involvement
- Normal smear, except for large platelets
- Possible preceding viral infection

# WHAT'S YOUR DIAGNOSIS?

- Immune Thrombocytopenic Purpura
  - Remains a diagnosis of exclusion
  - Affects both children and adults, but with very different disease course in each age group
    - In childhood, only chronic in 10-20%, peak age of onset ~5 years, and equally affects boys and girls
    - In adulthood, tends to be more chronic and more commonly affects females
  - Associated with other autoimmune disorders, like Systemic Lupus Erythematosus (SLE). Especially when onset insidious, and age >11y/o
  - Platelet count can be very low (<20), but should have a normal Hgb, WBC, and differential
  - If physical exam reveals lymphadenopathy or hepatosplenomegaly, need to consider infiltrative processes
  - Bone marrow biopsy may be indicated to rule out other causes if unexplained anemia or wbc abnormalities present

Ref. 4,7

# MANAGEMENT OF ITP

- Treatment remains controversial!
- In general, most children can be observed and recover within a few weeks without treatment.
  - 70-80% have spontaneous resolution by 6 weeks
- There is not yet evidence that treatment prevents intracranial hemorrhage.
- Possible treatment options to consider:
  - Observation alone
  - Steroids (Prednisone vs. Methylpredisolone)
  - Anti-D Immune globulin
  - Intravenous Immune globulin
  - Platelet transfusion (only for acute hemorrhage)

Ref. 4,7

# TAKE HOME POINTS

- Routinely utilize the indices of the CBC to help guide your differential diagnosis.
- Occasionally, additional calculations or testing may be required to support the diagnosis (i.e. reticulocyte index, mentzer index, iron studies).
- Iron deficiency remains a common problem and IDA is the most common cause of microcytic anemia.
- Thrombocytopenia can be categorized by mechanism (destruction vs. decreased production vs. sequestration).

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