Deconstructing the Complete Blood Count (CBC)

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UMKC School of Medicine

BEST CHILDREN'S HOSPITALS U.S.News & WORLD REPORT RANKED IN 10 SPECIALTIES 2018-19

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Outline

- Introduction
- Defining components of the CBC with differential
- Interpreting the CBC with differential
- Cases
- References

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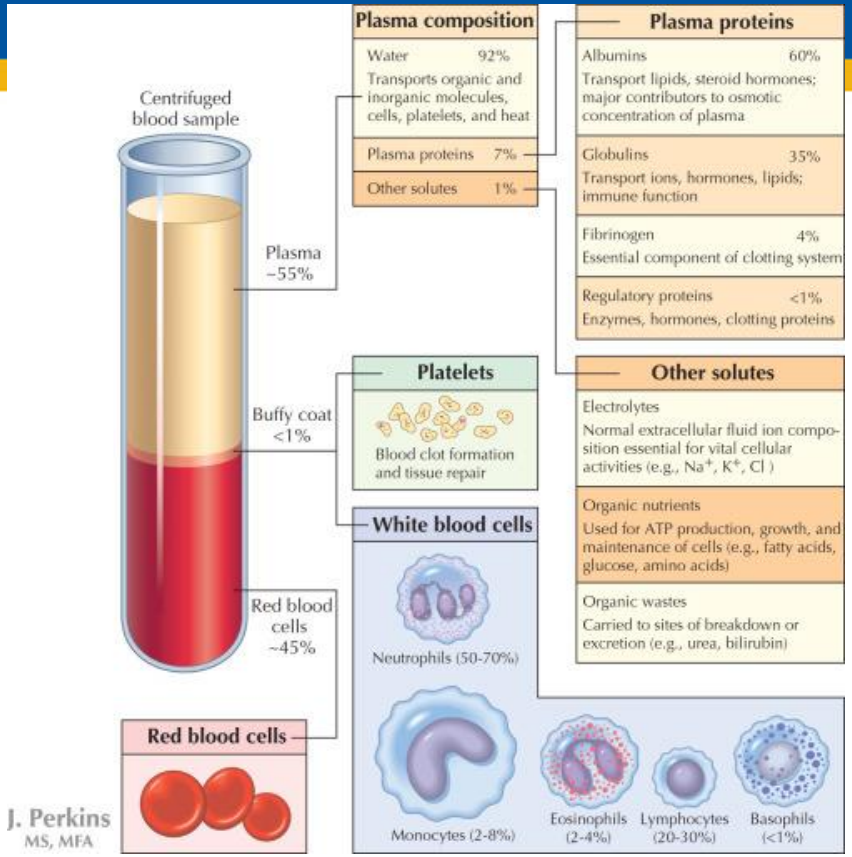
Blood



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Hansen JT. Netter's Clinical Anatomy

Why check?

- Monitor overall health
- Screen for some diseases
- Confirm or make a diagnosis based on a patient's symptoms
- Monitor an existing condition
- Monitor body's response to medical treatment
- Most informative *single* test
- Relatively inexpensive

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What's "normal?"

- Normal ranges from lab to lab (reference ranges should be included)
- Normal depends on age, sex, pregnancy status, altitude

Defining the Components of CBC

White blood cells (WBC)

- Also known as leukocytes
- Protect body against infection and fight foreign material
- Use WBC to:
  - help identify if an infection is present
  - differentiate between different types of infection
  - See how body is responding to medical treatment (leukemia)

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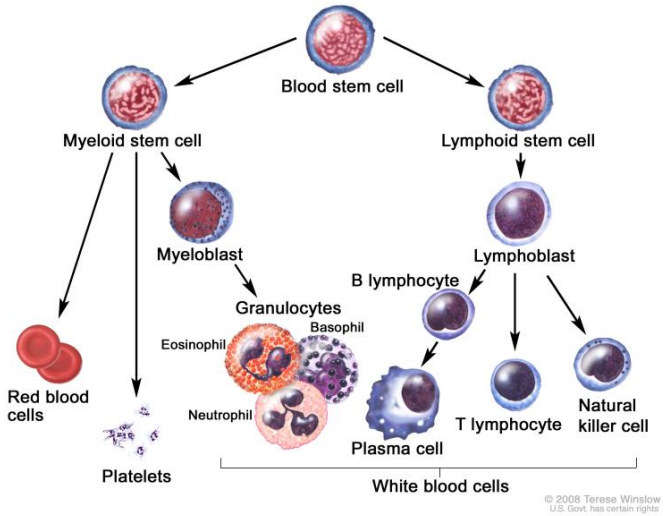
WBC Differential

- Breaks down WBC into their types
  - Neutrophils
    - Bands (immature) and segs (mature)
  - Monocytes
  - Lymphocytes
  - Eosinophils
  - Basophils



Blood cell development. A blood stem cell goes through several steps to become a red blood cell, platelet, or white blood cell.

The web site of the National Cancer Institute (http://www.cancer.gov)

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Types of WBC	Function	Increased in…	Decreased in…
Neutrophil (31-68%)	•1st line of defense •Phagocytosis of bacteria and cell debris	•Infection •Stress/Inflammation •Tissue damage •Malignancies of bone marrow •Steroid therapy	•Some viral conditions •Cancer treatment •Newborns with sepsis •Some hereditary disorders •Medications
Lymphocytes (31-61%)	•B cells: make antibodies •T- and NK cells: fight viral infection	•Viral infection	• Steroid therapy •Adrenocortical hyperfunction •Stress / Shock
Eosinophils (2-4%)	Granules have a toxic protein receptor that binds to IgE to help kill parasites	•Parasitic infection •Asthma •Allergic reaction •Hay Fever •Drug reaction	•Steroid therapy •Adrenocortical hyperfunction •Stress/ shock
Monocytes Aka macrophage (once out of blood stream) (4-9%)	•Phagocytosis •Present pieces of pathogens to T cells to mount an Ab response	•Viral infection •TB •Parasitic disease •Monocytic leukemia	•Bone marrow failure or suppression •Steroid therapy •Adrenocortical hyperfunction •Stress/ shock
Basophils (0-1%)	Release histamine and prostaglandins	•Chronic inflammatory and hypersensitivity reactions	•Steroid therapy •Adrenocortical hyperfunction •Stress/ shock

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Table 1. **Normal Blood Leukocyte Counts***

	Total Leukocytes		Neutrophils			Lymphocytes			Monocytes		Eosinophils	
Age	Mean	(Range)	Mean	(Range)	%	Mean	(Range)	%	Mean	%	Mean	%
Birth	18.1	(9.0 to 30.0)	11.0	(6.0 to 26.0)	61	5.5	(2.0 to 11.0)	31	1.1	6	0.4	2
12 h	22.8	(13.0 to 38.0)	15.5	(6.0 to 28.0)	68	5.5	(2.0 to 11.0)	24	1.2	5	0.5	2
24 h	18.9	(9.4 to 34.0)	11.5	(5.0 to 21.0)	61	5.8	(2.0 to 11.5)	31	1.1	6	0.5	2
1 wk	12.2	(5.0 to 21.0)	5.5	(1.5 to 10.0)	45	5.0	(2.0 to 17.0)	41	1.1	9	0.5	4
2 wk	11.4	(5.0 to 20.0)	4.5	(1.0 to 9.5)	40	5.5	(2.0 to 17.0)	48	1.0	9	0.4	3
1 mo	10.8	(5.0 to 19.5)	3.8	(1.0 to 9.0)	35	6.0	(2.5 to 16.5)	56	0.7	7	0.3	3
6 mo	11.9	(6.0 to 17.5)	3.8	(1.0 to 8.5)	32	7.3	(4.0 to 13.5)	61	0.6	5	0.3	3
1 y	11.4	(6.0 to 17.5)	3.5	(1.5 to 8.5)	31	7.0	(4.0 to 10.5)	61	0.6	5	0.3	3
2 y	10.6	(6.0 to 17.0)	3.5	(1.5 to 8.5)	33	6.3	(3.0 to 9.5)	59	0.5	5	0.3	3
4 y	9.1	(5.5 to 15.5)	3.8	(1.5 to 8.5)	42	4.5	(2.0 to 8.0)	50	0.5	5	0.3	3
6 y	8.5	(5.0 to 14.5)	4.3	(1.5 to 8.0)	51	3.5	(1.5 to 7.0)	42	0.4	5	0.2	3
8 y	8.3	(4.5 to 13.5)	4.4	(1.5 to 8.0)	53	3.3	(1.5 to 6.8)	39	0.4	4	0.2	2
10 y	8.1	(4.5 to 13.5)	4.4	(1.8 to 8.0)	54	3.1	(1.5 to 6.5)	38	0.4	4	0.2	2
16 y	7.8	(4.5 to 13.0)	4.4	(1.8 to 8.0)	57	2.8	(1.2 to 5.2)	35	0.4	5	0.2	3
21 y	7.4	(4.5 to 11.0)	4.4	(1.8 to 7.7)	59	2.5	(1.0 to 4.8)	34	0.3	4	0.2	3

*Numbers of leukocytes are in thousands/mcL ($\times 10^9$/L), ranges are estimates of 95% confidence limits, and percentages refer to differential counts. Neutrophils include band cells at all ages and a small number of metamyelocytes and myelocytes in the first few postnatal days.
From Dallman PR. Blood and blood-forming tissues. In: Rudolph AM, ed. *Rudolph's Pediatrics.* 16th ed. New York, NY: Appleton-Century-Crofts; 1977:1178, with permission.

Segel,G. *AA* 2008 29(12):1-12

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RBC (aka Erythrocyte)

- RBCs carry oxygen (O2) from lungs to the body, and also carbon dioxide (CO2) back to lungs to exhalation

- # of RBCs: Reported as an absolute number per liter of blood

Hemoglobin (Hgb)

- Hgb is the protein in RBCs that binds O2 and carries it to tissues of the body
- Hgb gives blood its red color
- Good measure of the blood's ability to carry O2
- Too few (anemia) may indicate the body is not getting enough O2
- With too many (polycythemia), RBCs may clump and block capillaries

Hematocrit (Hct)

- Aka packed cell volume (PCV)
- Measures the amount of space RBCs take up in the blood
- Value is given as a % of RBCs in a volume of blood
  - Hematocrit of 36% = 36% of blood's volume is made up of RBCs
  - Aka percentage of volume of whole blood that is made up of RBCs
- Measurement depends on the # and size of RBCs

Normal Values

- RBC x 3 = Hemoglobin
- Hgb x 3 = Hematocrit

Normal Values

Normal blood count values from birth to 18 years

Age	Hb g/dl	RBC $\times 10^{12}$/l	HCT	MCV fl
Birth (term infants)	14.9–23.7	3.7–6.5	0.47–0.75	100–125
2 weeks	13.4–19.8	3.9–5.9	0.41–0.65	88–110
2 months	9.4–13.0	3.1–4.3	0.28–0.42	84– 98
6 months	10.0–13.0	3.8–4.9	0.30–0.38	73– 84
1 year	10.1–13.0	3.9–5.1	0.30–0.38	70– 82
2–6 years	11.0–13.8	3.9–5.0	0.32–0.40	72– 87
6–12 years	11.1–14.7	3.9–5.2	0.32–0.43	76– 90
12–18 years				
Female	12.1–15.1	4.1–5.1	0.35–0.44	77– 94
Male	12.1–16.6	4.2–5.6	0.35–0.49	77– 92

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Compiled from various sources. Red cell values at birth derived from skin puncture blood; most other data from venous blood.
Reproduced with permission from Elsevier Science, from *Hinchliffe RF:* Reference values; in *Lilleyman J, Hann I, Blanchette V (eds):* Pediatric Hematology, ed 2. London, Churchill Livingstone, 1999, p 2.

Indices	Meaning	Definition	Normal Values	Use
MCV	Mean corpuscular volume	Average size (volume) of RBCs	75-108 (fL)	Help differentiate between types of anemia
MCH	Mean corpuscular hemoglobin	Average weight of Hgb per RBC	25-44 picograms	Clinical implications are the same as for MCV
MCHC	Mean corpuscular hemoglobin concentration	Average concentration of Hgb per RBC	33-36 (g/dL RBC) (normochromic)	Hyperchromic vs hypochromic
RDW	Red cell distribution width	Measures uniformity of RBC size	11.5-14.5	> 14.5 indicates greater cell size variability
Reticulocytes		# of immature RBCs	0.5-1.5%	Indicates active RBC production from BM

Platelet Count

- Measures how many platelets you have in your blood
- Platelets are smallest type of cell
- Important in clotting
- Too few → uncontrolled bleeding
- Too many → risk of clot
- Normal value: 150,000-350,000 / mL

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Mean Platelet Volume (MPV)

- Measures average size of platelets
- Even if platelet count is normal, MPV can be too high or too low
- Normal range: 7.5-11.5 fL

Interpreting the CBC

Anemia

- Low RBC, Hgb, Hct (less than 5th percentile for age) → blood has low O2 carrying capacity
- Can be due to:
  - Blood loss
  - Nutritional deficiency
  - Destruction of RBCs (hemolysis)
  - Decreased production (defects in bone marrow, low EPO)
- Most children with mild anemia have no signs or symptoms

Screening

ORG	RECOMMENDATIONS	High-Risk Groups
AAP	•Screen at 9-12 months •Again 6 months later in high risk groups	•Premature infants •LBW infants •Infants fed with low-iron formula •Breastfed infants > 6 months who are not receiving iron supplement
CDC	•Screen kids from low-income families or newly immigrated families between 9-12 months, then 6 months later, then annually from 2-5 years •Consider screening for pre-term and LBW infants < 6 months of age if not fed with iron-fortified formula •Infants with RF should be assessed at 9-12 months and again 6 months later •Non-pregnant adolescents should be screened q 5-10 years	•Infants fed non-iron-fortified formula / cows milk before 12 months •Breastfed infants > 6 months without supplementation •Children who consume > 24 oz of cow's milk /day •Children with special health care needs

https://www.aap.org/en-us/Documents/periodicity_schedule_oral_health.pdf

Anemia

1) Acute vs chronic
- hemodynamic stability
- Previous CBC
- Active bleeding?

2) History/Exam: pallor, glossitis, jaundice, lymphadenopathy, hepatosplenomegaly, tachycardia, acute bleeding, pica, tachypnea

3) MCV
- microcytic (<80 μm^3)
- normocytic (80-100 μm^3)
- macrocytic (>100 μm^3)

4) Reticulocyte count

>2%: hemolytic process

<2%: hypoproliferative

5) Smear: look for size/shape of RBCs, color, inclusions

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Differential based on age

Neonatal	Infancy to Toddlerhood	Late Childhood and Adolescence
•Blood loss •**Isoimmunization** •Congenital hemolytic anemia (spherocytosis, G6PD def) •**Congenital Infection** (parvo, HIV, TORCH) •Diamond Blackfan Syndrome •Fanconi Anemia	•**Iron deficiency** •Concurrent infection •Blood loss •Disorder of Hgb structure of synthesis (thalassemia, SCD) •RBC enzyme defects (G6PD def, PK def) •RBC membrane defects (spherocytosis, elliptocytosis) •Acquired hemolytic anemias (antibody-mediated, drug, HUS, DIC) •**Transient Erythroblastopenia of childhood** •Leukemia •Lead poisoning	•**Iron deficiency** •Chronic disease •Blood loss •Rest same as infancy to toddlerhood

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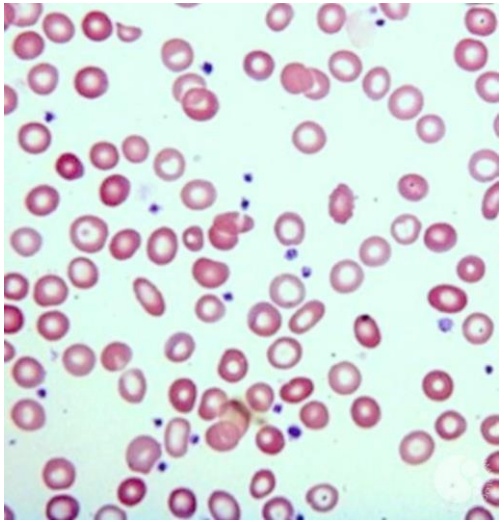
Lanzkowsky P, Lipton JM, Fish JD. *Lanzkowsky's Manual of Pediatric Hematology and Oncology, Sixth Edition.* Amsterdam: Academic Press, 2016.

Microcytic Anemia

- Most common causes in children:
  - Iron deficiency
  - Thalassemias
  - Lead poisoning
  - Anemia of chronic disease
- Check **ferritin**, zinc protoporphyrin, CRP
- Look at peripheral smear



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Iron Deficiency

- Microcytosis with elevated RDW
- Toddlers and Adolescents
  - Milk consumption, diet, blood loss
- Treat with 4-6 mg/kg/day of elemental iron divided BID or TID
  - Avoid dairy products when administering
  - Better absorbed with citrus juice
- Reticulocyte count should increase within 1 week
- Hemoglobin should normalized in 1 month
- Treat for at least 3 months to replenish iron stores

Iron Deficiency

- Most likely reason for failure of anemia to correct is non-adherence
- Trial a different oral formulation which is better tasting
  - NovaFerrum
- If adherence not in question and still refractory, refer to Hematology

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Differentiate IDA and Thalassemia

- Mentzer Index (MCV / RBC count)
- Example:

Patient	MCV (fl)	RBC ($x10^6$ per mm^3)	Mentzer Index
5 y/o AA child	64	5.3	12
2 y/o child who drinks 30 oz of cow's milk daily	72	4.8	15

- < 13 suggests thalassemia; > 13 suggests iron deficiency
- Can request newborn screen if born in United States or get hemoglobin electrophoresis

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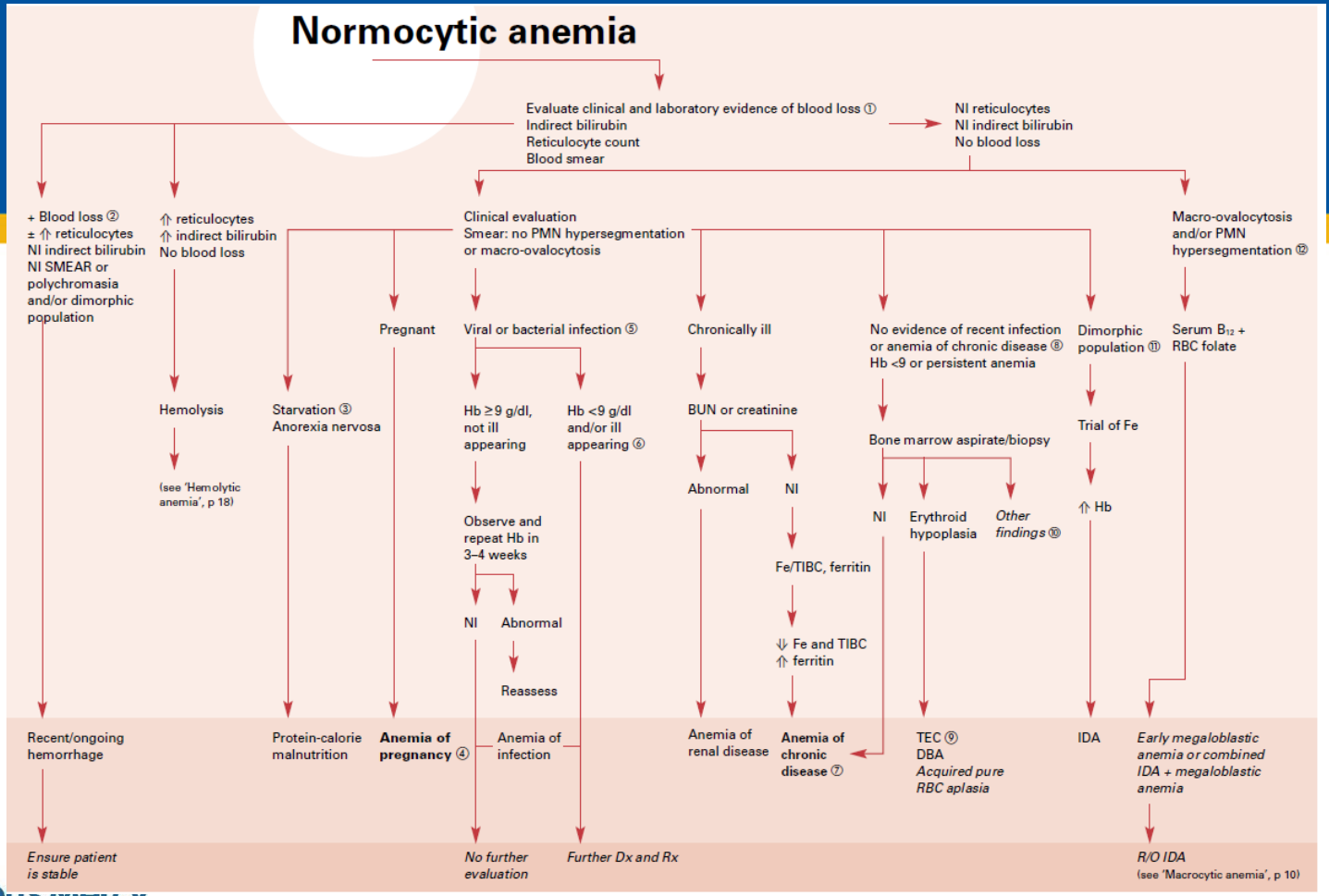
Normocytic Anemia

- Work-up is based on bone marrow function as determined by the reticulocyte count
  - If elevated, evaluate for blood loss or hemolysis
    - Check a DAT and evaluate the peripheral smear for spherocytes
  - If low, consider aplasia or bone marrow disorder



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Sills RH. *Practical Algorithms in Pediatric Hematology and Oncology.* Albany: Karger, 2003.

Macrocytic Anemia

- Rare in children
- Initial work up is a peripheral smear
  - Presence of hypersegmented neutrophils indicates a megaloblastic anemia (B12 or folate deficiency)
  - Nonmegaloblastic causes of macrocytosis include
    - Alcoholism
    - Hemolysis
    - Hemorrhage
    - Hepatic disease
    - Bone marrow disorders (aplastic anemia, myelodysplasia, sideroblastic anemia)
    - Hypothyroidism

Macrocytic Anemia

- Check vitamin B12, folate
- Check medication list
- Check MMA and homocysteine
  - B12 deficiency: elevated homocysteine and MMA
    - Vegan diet
  - Folate deficiency: increased homocysteine, NORMAL MMA
    - Goat's milk

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Special Considerations

- Volume Depletion
  - Severely dehydrated patients may not show anemia until after rehydration
- Acute blood loss
  - Although patient may be hypotensive, lab values may not reflect anemia until 36-48 hours after acute bleed

Leukocytosis

- Causes
  - Infection
  - Chronic inflammation
  - Medications (steroids, WBC growth factors)
  - Malignancy (leukemia)
    - Will likely have blasts on the differential

Leukopenia

- May indicate:
  - Infection, bacterial or viral
  - Effect of chemotherapy
  - Medications (AEDs, antibiotics, immunosuppressants)
  - Malignancy
  - Aplastic anemia
  - Hypersplenism
  - Autoimmune disorders
- African Americans can have lower WBC at baseline

Neutropenia

- Normal ANC varies by age, particularly during infancy
  - Lower limit of normal:
    - First 24 hours of life: 6,000/mcL
    - First week of life: 5,000/mcL
    - Second week of life 1,500/mcL
    - Week 2- 1 year of life: 1,000/mcL
    - Age 1 year and on: 1,500/mcL
      - 1,200/mcL for African Americans

Neutropenia

- Beyond 1 year of life
  - Mild: ANC 1,000-1,500
  - Moderate: 500-1,000
  - Severe: < 500

Initial Evaluation of Neutopenia

- History:
  - Underlying disease, congenital anomalies, medication exposure
  - Infection (systemic bacterial such as sepsis, meningitis; serious respiratory such as pneumonia; multiple bacterial such as cellulitis, otitis media, lymphadenitis; unusual such as liver or brain abscesses; unusual pathogens)
  - Viral symptoms
- Physical Examination
  - Short stature, poor growth, congenital anomalies such as skeletal
  - Eczema, abnormal skin pigmentation, adenopathy, organomegaly
  - Recurrent gingivitis or oral ulcers

Table 3. Acquired Causes of Neutropenia

Cause	Etiologic Factors/Agents	Associated Findings
Infection	Viruses, bacteria, protozoa, rickettsia, fungi	Redistribution from circulating to marginating pools, impaired production, accelerated destruction
Drug-induced	Phenothiazines, sulfonamides, anticonvulsants, penicillins, aminopyrine	Hypersensitivity reaction (fever, lymphadenopathy, rash, hepatitis, nephritis, pneumonitis, aplastic anemia), antineutrophil antibodies
Immune neutropenia	Alloimmune, autoimmune	Variable arrest from metamyelocyte to segmented neutrophils in bone marrow
Reticuloendothelial sequestration	Hypersplenism	Anemia, thrombocytopenia, neutropenia
Bone marrow replacement	Malignancy (eg, lymphoma, metastatic solid tumor)	Presence of immature myeloid and erythroid precursors in peripheral blood
Cancer chemotherapy or radiation therapy to bone marrow	Suppression of myeloid cell production	Bone marrow hypoplasia, anemia, thrombocytosis
Aplastic anemia	Stem cell destruction and depletion	Pancytopenia
Vitamin B_{12} or folate deficiency	Malnutrition; congenital deficiency of vitamin B_{12} absorption, transport, and storage; vitamin avoidance	Megaloblastic anemia, hypersegmented neutrophils
Acute leukemia, chronic myelogenous leukemia	Bone marrow replacement with malignant cells	Pancytopenia, leukocytosis
Myelodysplasia	Dysplastic maturation of stem cells	Bone marrow hypoplasia with megaloblastoid red cell precursors, thrombocytopenia
Prematurity with birthweight <2 kg	Impaired regulation of myeloid proliferation and reduced size of postmitotic pool	Maternal preeclampsia
Chronic idiopathic neutropenia	Impaired myeloid proliferation and/or maturation	None
Paroxysmal nocturnal hemoglobinuria	Acquired stem cell defect to secondary to mutation of *PIG-A* gene	Pancytopenia, thrombosis

Reprinted with permission from Newburger PE, Boxer LA. Leukopenia. In: Kliegman RM, Stanton BF, St Gene IW III, Schor NF, Behrman RE, eds. *Nelson Textbook of Pediatrics*. 19th ed. Philadelphia, PA: Elsevier Saunders; 2011:748.

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Walkovich K, Boxer LA. How to Approach Neutropenia in Childhood. *Pediatrics in Review* 2013; 34: 173-84.

Thrombocytosis

- Mild (450-700,000/mm^3)
- Moderate (700-900,000/mm^3)
- Severe (900,000-1 million/mm^3)
- Extreme (>1 million/mm^3)

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Thrombocytosis in Children

- Relatively common in young children
- Usually transient, benign finding secondary to infection/inflammation
  - Repeat in 1-2 months and will likely resolve
- Platelets are acute phase reactants
- Reactive thrombocytosis
  - Iron deficiency
  - Major trauma
  - Surgery
  - Postsplenectomy

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Thrombocytopenia

- Defined as platelet count <150,000/mm^3
- Clinical features:
  - Petechiae, purpura, gingival bleeding, epistaxis, menorrhagia, hematuria
- History and exam will guide your differential!

Table 3. Relationship Between Platelet Count and Bleeding

Platelet Count ($\times 10^3$/mcL [$\times 10^9$/L])	Signs and Symptoms
>100	None
50 to 100	Minimal (after major trauma and surgery)
20 to 50	Mild (cutaneous)
5 to 20	Moderate (cutaneous and mucosal)
<5	Severe (mucosal and central nervous system)
Other variables: function of platelets, anatomic defect, associated coagulopathy	

Buchanan GR, Pediatrics in Review. 2005

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Thrombocytopenia

Can watch and repeat platelet count

- Infection
  - EBV, CMV, HIV, Hantavirus, Parvovirus, Dengue Hemorrhagic Fever, Malaria
  - Evaluate for infection, repeat platelet count 4-6 weeks after resolution of symptoms
- Medications
  - Discontinue medication and repeat platelet count in 4-6 weeks

Refer to Hematology

- Malignancy: leukemia, lymphoma, neuroblastoma
- Bone marrow failure
  - Aplastic anemia, Fanconi Anemia, Amegakaryocytic thrombocytopenia
- ITP
- Inherited thrombocytopenia
- DIC

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Case #1

- 15 month old male presents for well child check. Mom reports he appears pale and drinks 40 ounces of milk per day. On your exam, you note pallor. Which lab values would be most consistent with iron deficiency anemia?
  - A. Hgb 8 gm/dL, MCV 60 fL, RDW 17% (11.5-14.5), rbc 4.5x10(6)mcL (3.9-5.3)
  - B. Hgb 8 gm/dL, MCV 80 fL, RDW 14%, rbc 5x10(6)mcL
  - C. Hgb 8 gm/dL, MCV 60 fL, RDW 14%, rbc 6x10(6)mcL
  - D. Hgb 11 gm/dL, MCV 70 fL, RDW 12%, rbc 5x10(6)mcL

Case #2

- A 6 year old male with past medical history of asthma develops shortness of breath, cough, and wheezing consistent with an acute asthma exacerbation. He is afebrile without rhinorrhea or congestion. His exam is notable for diffuse end-expiratory wheezing. He is started on schedule albuterol and a prednisone burst. Five days later, he returns to your clinic for follow-up. He remains afebrile and symptoms have greatly improved. You order a cbc with differential. His white blood cell count is elevated at 25x10(3)mcL. What is the most likely cause for his leukocytosis?
  - A. Leukemia
  - B. Bacterial pneumonia
  - C. Prednisone
  - D. Lymphoma

Case #3

- A previously healthy 14 year old male presents to your clinic for evaluation of fever, pharyngitis, and fatigue. His exam is significant for bilateral cervical adenopathy and splenomegaly. You decide to obtain labs. His cbc with differential is significant for a platelet count of 20,000/mm^3 and atypical lymphocytes. What is the most likely etiology for his thrombocytopenia?
  - A. Alcohol abuse
  - B. EBV infection
  - C. Leukemia
  - D. ITP

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