CBC 101
"Cracking the Code"

Sherry L. Bayliff, MD, MPH
Assistant Professor of Pediatrics
Kentucky Children's Hospital

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Faculty Disclosure

- My spouse or I **have not** had any relevant financial relationships during the past 12 months.

Objectives

1) Clarify a systematic approach to the interpretation of pediatric CBCs that identifies abnormalities of concern.
2) Distinguish abnormalities on the CBC that indicate further evaluation is warranted and the appropriate timeline for initiation of that workup.
3) Identify those CBC abnormalities that warrant referral for further evaluation to establish an appropriate plan of care.

Educational Need/Practice Gap

- Interpreting the complete blood count report can often be the source of great confusion
- Misinterpretation of the reported results may lead to great anxiety for both the *provider* and the *patient/family*

Expected Outcome

- Our goal today is to "crack the code" of the CBC report and increase the ability to identify when to be concerned and how/where/when to act on that concern
- By empowering you to read beyond the "H"s and "L"s, you can return to your calm and cool demeanor (and so will your patients/families!)

Active Learning

- Please try and incorporate some activity participation into your presentation either through case study discussions or audience response questions.

What am I working with?

What is the CBC?

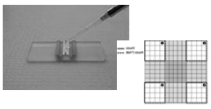
- a.k.a. Complete Blood Count
- 3 parts:
  - red blood cells
  - white blood cells
  - platelets
- 10 tests: RBC, Hgb, HCT, MCV, MCH, MCHC, RDW, WBC, Platelets, MPV
- the differential (just do it!)

Definitions x 10

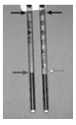
- **RBC** – number of **RBC**s per microL of blood (or number of RBCs x 10^{12}/L
- **HGB** – **Hemoglobin** is the concentration of hemoglobin in whole blood, in grams/deciliter (g/dL).
- **HCT-** The **Hematocrit** is the packed spun volume of blood made up of RBC, expressed as a percentage of total blood volume. It can be measured or calculated as Hct = (RBC x MCV)/10.
- **MCV** – **Mean corpuscular volume** is the average volume (size) of the patient's RBCs. It can be measured or calculated as above .
- **MCH** – **Mean corpuscular hemoglobin** is the average hemoglobin content in a RBC. It is calculated as MCH (pg/red cell) = Hgb (g/dL) x 10 ÷ RBC (millions/microL).
- **MCHC** – **Mean corpuscular hemoglobin concentration** is the average hemoglobin concentration per RBC, in grams/dL. It is calculated as MCHC (g/dL) = Hgb (g/dL) X 100 ÷ Hct (percent).
- **RDW** – **Red cell distribution width** is a measure of the variation in RBC size, which is reflected in the degree of anisocytosis on the peripheral blood smear.
- **WBC** – The **white blood cell** count is the number of WBC per microL of blood (or number of WBC x 10^9/L).
- **PLT** – The **platelet count** is the number of platelets per microL of blood (or number of platelets x 10^9/L).
- **MPV** – **Mean platelet volume** is the average volume (size) of the patient's platelets as measured in femtoliters (fL).

Abbreviation	Test Name	Definition	Associated Disorders
WBC	White blood cells	WBCs fight infection. The 5 different types of WBCs are listed to the left.	Infection, leukemia
WBC Diff	WBC differential Neutrophils Lymphocytes Monocytes Eosinophils Basophils		
RBC	Red blood cells	RBCs (with the help of hemoglobin) carry oxygen throughout the body	↓ Anemia, bleeding, malnutrition, kidney disease ↑ Polycythemia, heart and lung disease, dehydration
Hb or Hgb	Hemoglobin	Protein that carries oxygen	↓ Anemia, bleeding, malnutrition, cirrhosis, cancer ↑ Dehydration, polycythemia
Hct	Hematocrit	Amount of space in the blood that is occupied by RBCs	↓ Anemia, bleeding, malnutrition, cirrhosis, cancer ↑ Dehydration, polycythemia, hemochromatosis
MCV	Mean corpuscle volume	Average size of the RBCs	Anemia, thalassemia, malnutrition
MCH	Mean corpuscle hemoglobin	Average amount of Hb in each RBC	Anemia, thalassemia, malnutrition
MCHC	Mean corpuscle hemoglobin concentration	Average amount of Hb in the RBCs compared to the average size of the RBCs	Anemia, thalassemia, malnutrition
RDW	Red cell distribution width	Amount of variation in size of the RBCs	Anemia, thalassemia, malnutrition
Plt	Platelet count	Platelets are sticky cells that help to form blood clots	Bleeding and clotting disorders
MPV	Mean platelet volume	Average size of the platelets	Bleeding and clotting disorders

Where we were . . .

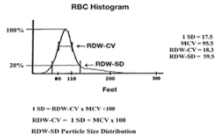


- Manual techniques
  - Hemocytometer
  - Cyanomethemoglobin method
  - Wintrobe tube
- Imprecise and laborious



Automated Coulter Counters

- electric impedance aperture
- multi-chamber coulters
- modern day "channelizers"
  - plot of frequency vs channel size=RBC distribution curve
- calculations

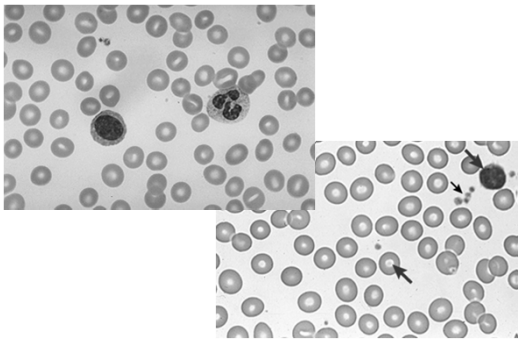


Getting the Test: When? Why?

- concerns aplenty:
  - Infections (qualified)
  - Anemia
  - Bruising/Bleeding
  - Just Cause
- med monitoring
- BEFORE corticosteroids

The Peripheral Blood Smear

NORMAL Peripheral Blood Smears



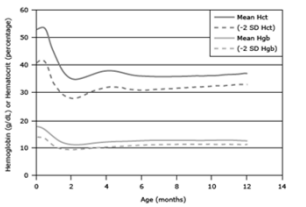
Courtesy of Carola von Kapff, SH (ASCP).

Complete Blood Count
Normal Pediatric Values

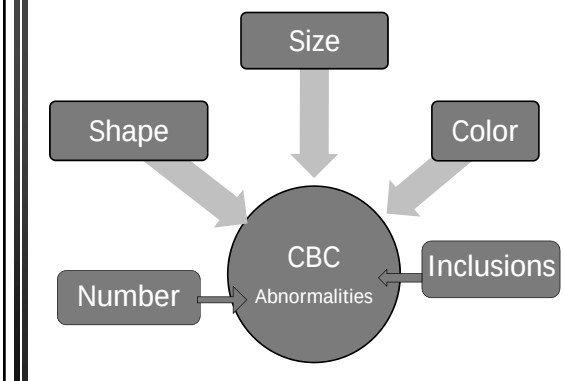
Age	Red Blood Cells ($x 10^6/\mu L$)	Hemoglobin (g/dL)	Hematocrit (%)	MCV (fL)	MCHC (%)	Reticulocyte Count (%)
Cord blood		14.0-18.8	42-68	96-125	30-34	3-7
Term newborn	5.00-6.30	18.0-21.5	51-68	95-125	30-35	3-7
1-3 days	4.10-6.10	14.0-24.0	43-68	95-125	30-38	1 day: 3-7 2 days: 2-5 3 days: 1-3
4-7 days	4.10-6.10	14.3-22.3	42-62	95-125	30-38	
7-14 days	4.10-6.10	12.9-20.5	39-59	88-115	30-36	
14-60 days	3.80-5.60	10.7-17.3	33-51	80-112	30-35	
2-5 months	3.80-5.20	10.1-14.5	30-40	70-98	32-36	
6 months-1 year	3.80-5.20	10.0-13.2	30-39	70-90	32-36	
1-2 years	3.80-5.20	10.0-13.5	30-40	70-90	30-35	
2-4 years	3.80-5.20	10.5-14.5	32-42	74-94	32-36	
5-7 years	3.80-5.20	10.9-14.9	33-44	76-96	32-36	
8-10 years	3.80-5.20	10.9-14.9	33-44	78-98	32-36	
10-15 years	3.80-5.20	11.4-15.4	34-45	78-98	32-36	

Mayo Clinic Laboratories

Normal values for hematocrit and hemoglobin during the first year of life in healthy term infants

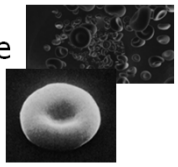


Data from:
1. Jopling J, Henry E, Wiedmeier SE, et al. Reference ranges for hematocrit and blood hemoglobin concentration during the neonatal period: data from a multihospital health care system. Pediatrics 2009; 123:e333.
2. Oski FA, Naiman JL. Hematologic problems in the newborn, 2nd ed, WB Saunders, Philadelphia 1972; p.13.
3. Saarinen UM, Siimes MA. Developmental changes in red blood cell counts and indices of infants after exclusion of iron deficiency by laboratory criteria and continuous iron supplementation. J Pediatr 1978; 92:412.

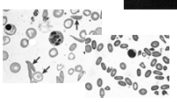


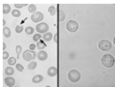
RBC "Inclusion"	*Etiology*	*Conditions*	*Special Staining?*
Reticulocytes	Polyribosomes	Increased RBC production	*supravital stains
Nucleated RBC	Nuclear Remnants	Severe hemolysis, Profound stress, MDS/MPS	*NOT NORMAL on peripheral smear
Howell Jolly Bodies	Nuclear remnants	Post-splenectomy Asplenism	
Heinz Body	Denatured Hgb aggregates	G6PD, oxidant exposure, unstable Hgb	*supravital stains
Basophilic Stippling	Cytoplasmic Ribosomes	Thalassemias, ETOH, lead/heavy metals, Pyrimidine 5' Nucleotidase deficiency	
Pappenheimer Bodies	Iron	Sideroblastic anemia	
Hgb crystals	Artifacts	Hgb C disease Hgb SC disease	*dehydrated sample
Red cell GHOSTS	Lysed Red Cells	Fulminant bacteremia	*NEVER NORMAL
RBC organisms	Parasites, Bacteria	Malaria, Trypansomes C. perfringens	

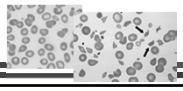
RBC Abnormalities: Shape



- Normal: biconcave disc
- Poikilocytosis
- MCH/MCHC
- Other:
  - sickle cells, target cell
  - fragmented red cells, bite cells, helmet cells
  - teardrop
  - Spiculated (echinocytes, acanthocytes)



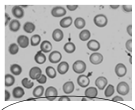




Pictures by Carola von Kapff, SH (ASCP)

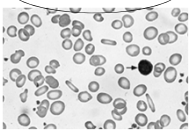
RBC Abnormalities: Size

- Normal: 7-8 microns/MCV 90 fL
- Anisocytosis
- MCV ⬇/⬆
- RDW



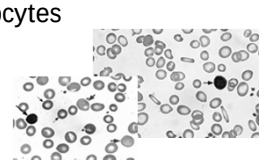
RDW is normal

RDW > 20%



RBC Abnormalities: Color

- Normal: central pallor 1/3 dm of width
- Hypochromia/Hyperchromia
- MCHC
- Absence of pallor: spherocytes
- Bluish tint: reticulocytes



Complete Blood Count:

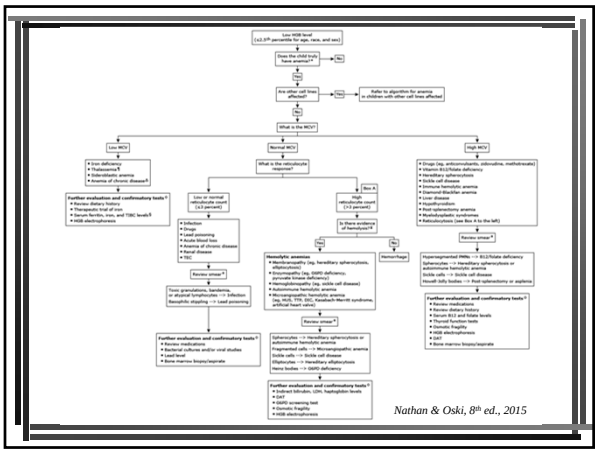
	Patient Value	Normal Range 2 years – 6 years
WBC	8.4 x 10^9 / L	(5.0 – 17.0)
RBC	2.77 x 10^{12} / L	(3.90 – 5.30)
Hgb	7.5 g/dl	(11.5 – 13.5)
Hct	21.8 %	(34.0 – 40.0)
MCV	78.6 fl	(75.0 – 87.0)
MCH	26.9 pg	(25.0 – 31.0)
MCHC	34.2 gm/dl	(31.0 – 36.0)
RDW	17.3 %	(11.5 – 15.0)
PLT	192 x 10^9 / L	(150 – 450)

Differential:

	Absolute	Normal Range Number	2 years – 6 years
Neutrophils	43 %	(3.61)	(1.50 – 8.50)
Bands	6 %	(0.50)	(0.00 – 1.00)
Lymphocytes	41 %	(3.44)	(3.00 – 9.50)
Monocytes	4 %	(0.34)	(0.00 – 0.80)
Eosinophils	3 %	(0.25)	(0.02 – 0.65)
Metamyelocytes	3 %	(0.25)	N/A
NRBC / 100 WBC	1		

Classification of Anemia

Blood Loss	Impaired Production (Hypoproliferative)	Increased Destruction (Hemolytic)
Acute/Chronic	Iron deficiency	Extrinsic:
Perinatal (placental/umbilical)	Megaloblastic (Vitamin B12 or Folate)	-auto-immune or iso-immune -infections -chemical or physical agents
Postnatal (gut, lung, nose, GU, trauma)	Myelophthistic (infiltrative or myelodysplastic)	-hypersplenism Intrinsic:
	Chronic Disease	-membrane defects -enzyme deficiencies
	Aplastic (congenital or acquired)	



Nathan & Oski, 8th ed., 2015

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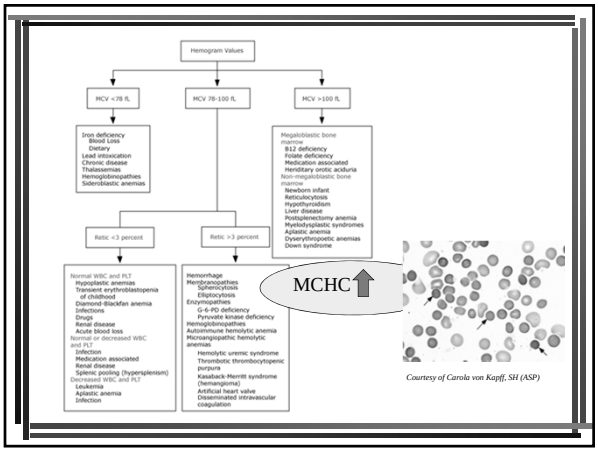


Courtesy of Carola von Kapff, SH (ASP)

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL
CBC With Differential and Platelets				
WBC	6.9		x10E3/uL	4.0 - 10.5
Lymphs	29		%	14 - 46
Neutrophils	62		%	40 - 74
Lymphocytes (Absolute) ALC	2.0		x10E3/uL	0.7 - 4.5
Neutrophils (Absolute) ANC	4.3		x10E3/uL	1.8 - 7.8
Monocytes	7		%	4 - 13
Eosinophils	2		%	0 - 7
Basophils	0		%	0 - 3
RBC	4.59		x10E3/uL	3.80 - 5.10
(Hemoglobin (Hg)	11.2	*	g/dL	11.5 - 15.0
Hematocrit (HCT)	37.6		%	34.0 - 44.0
MCV	80		fL	80 - 98
MCH	24.4	*	pg	27.0 - 34.0
MCHC	29.8	*	g/dL	32.0 - 36.0
RDW	13.7		%	11.7 - 15.0

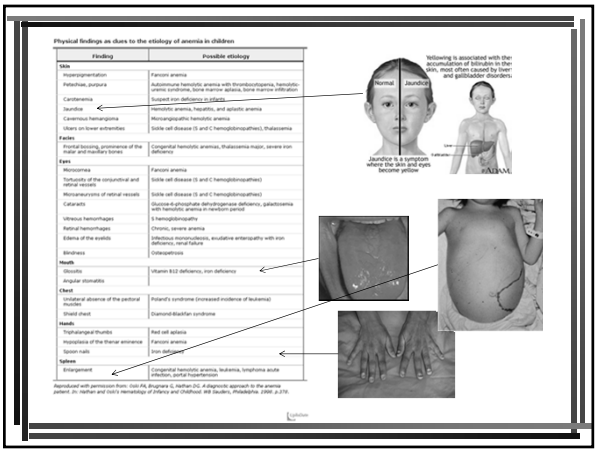
History & Physical

Targeted History

- Onset/Severity of symptoms
- Symptoms related to hemolysis
- Prior history of events
- Possible blood loss
- Underlying medical conditions
- Drug/toxin exposure
- Diet
- Birth/developmental history
- Family history

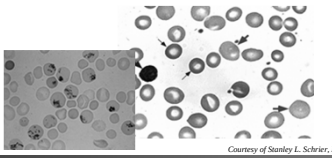
Physical Exam

- General Appearance
- Skin
- Eyes
- Mouth
- Cardiac
- Abdomen
- Musculoskeletal



Reticulocyte response

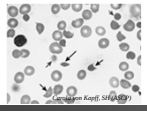
- Absolute reticulocyte count (ARC)
  - ARC= % reticulocytes x RBC/L
  - ↑ ARC: active erythropoiesis response
    - hemolysis, acute blood loss
  - ↓ ARC: suboptimal response
    - marrow aplasia, marrow infiltration, toxic insult



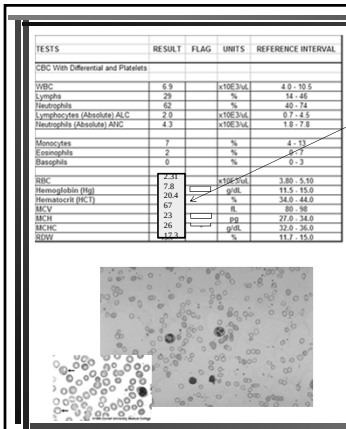
Courtesy of Stanley L. Schrier, MD

Physiologic classification

↑ Reticulocytosis
- Hemorrhage
- Membranopathies
- Enzymopathies
- Hemoglobinopathies
- AIHA
- Microangiopathic HA



↓ Reticulocytosis
- Hypoplastic anemias
  - Congenital
  - Acquired
- TEC
- Systemic disease
- Marrow infiltration
- Medications
- Infections



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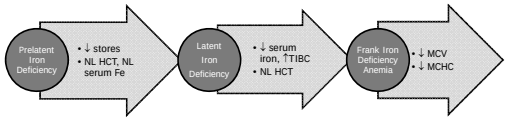
Monocytes	7		%	4 - 13
Eosinophils	2		%	0 - 7
Basophils	0		%	0 - 3
RBC	2.31		x10E6/uL	3.80 - 5.10
Hemoglobin (Hg)	7.8		g/dL	11.5 - 15.0
Hematocrit (HCT)	20.4		%	34.0 - 44.0
MCV	67		fL	80 - 98
MCH	23		pg	27.0 - 34.0
MCHC	26		g/dL	32.0 - 36.0
RDW	17.3		%	11.7 - 15.0

Poikilocytosis
Anisocytosis
Hypochromia
Microcytosis

Supportive Labs
↓ iron, ↑ TIBC
↓ transferrin sat
ferritin ↓
NORMAL retic
thrombocytosis
stool guaiac +/-

**Gold Standard Test:*
**RESPONSE to Iron*

Iron Deficiency Anemia



*most common nutritional deficiency worldwide

Dietary factors that increase risk . . .

- Insufficient Intake
  - Normal Infants: 1 mg/kg/day*
  - LBW Infants: double* (*max=15mg/kg/d)
  - 1 kg ↑ in body wt requires ↑ 35-45 mg body iron
- Poor Dietary Practices
  - early cow's milk, early solid food intake, tea, ↓ Vit C intake, ↓ meat intake
- Breast feeding > 6 mos w/o supplements
- Low socioeconomic status

> 1 quart/day of Cow's Milk

Management of IDA

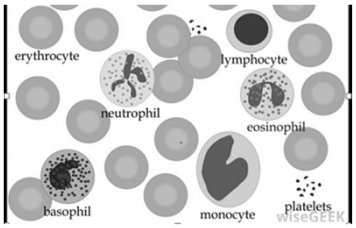
Dietary Counseling
- Review good choices:
  - liver, other meats, seafood
  - dried fruits, nuts, beans
  - green leafy vegetables
  - whole grains
- iron-fortified products

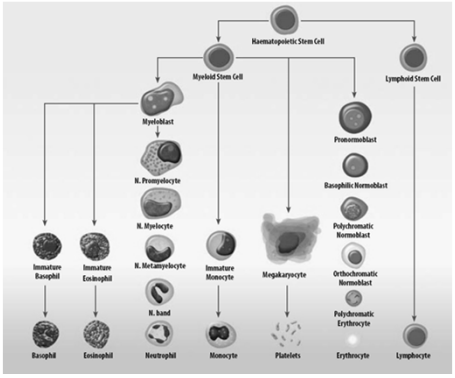
Implemented Changes
- Breast feed 6 mos minimum
- Iron-fortified formula
- < 1 pint/day whole milk
- WEAN!
- Iron-fortified cereals
- Supplemental iron
  - Facilitators: citrus juice, fruits, Vit C pills, tomatoes, potatoes, meat, fish, poultry
  - Inhibitors: coffee, tea, egg yolks, milk, fiber, soy protein, antacids, H2-blockers, PPIs

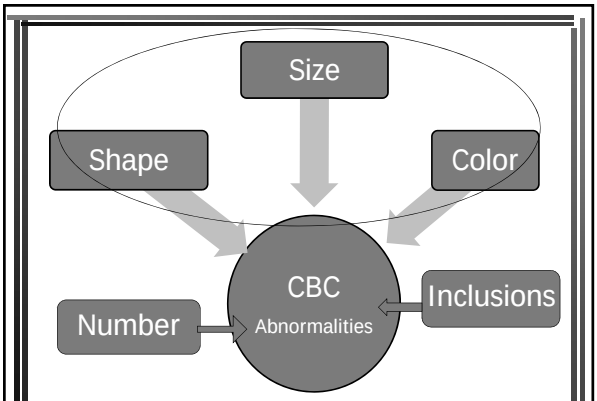
Supplemental Iron

- Oral
  - Ferrous iron
  - 3-6 mg Elemental iron/kg/day divided BID
  - between meals
  - continue for 2-3 months AFTER correction of the Hgb
  - side effects: GI*
- Parenteral
  - failure of oral tx
  - IV
  - Iron sucrose
  - reduced SE

White Blood Cells







ORDERED: CBC W/DIFF, MANUAL DIFF
COMMENTS: CONSERVATION
CBN: NO
Campus: MAIN

Test	Result	Flag	Reference
CBC W/DIFF			
WBC	18.4	H	3.9-11.0 K/ul
RBC	4.48		3.5-5.5 M/uL
HGB	13.6	L	14.0-16.5 gm/dl
HCT	39.7		40.0-55.0 %
MCV	88.6		80.0-100.0 fL
MCH	30.4		25.4-34.6 pg
MCHC	34.3		32.0-36.0 g/dL
RDW	13.9		11.5-14.5 %
PLT	215		140-440 K/uL
MPV	9.3		7.4-10.4 fL
MANUAL DIFF			
TOTAL CELLS	100		#CELLS
NEUTROPHIL	71		40-80 %
BAND NEUT	22	H	0-5 %
METAMYELOCYTE	1	H	0-0 %
LYMPHOCYTE	3	L	20-50 %
MONOCYTE	3		2-12 %
RBC MORPH			
RBC COMMENTS	NORM MORPH		
PLT ESTIMATE	ADEQ		

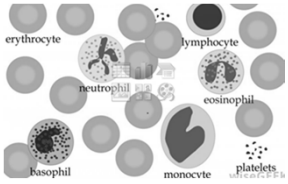
WBC Numbers

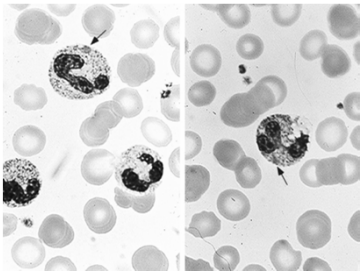
Leukocytosis

- *INFECTION*
  - viral
  - bacterial
- reactive
- malignant

Leukocytopenias

- *NEUTROPENIA*
- Lymphocytopenia

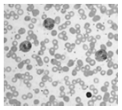




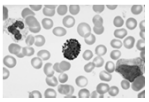
Toxic granulations and Döhle bodies

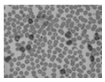
Courtesy of Carola von Kapff, SH (ASCP)

Neutrophilia

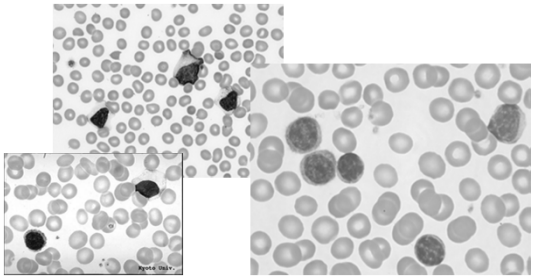


- Eosinophilia
  - allergic state, parasitic infections
- Basophilia
  - very unusual
- Monocytosis
  - EBV, reactive processes, post-chemotherapy





Lymphocyte—abnormal shape/size



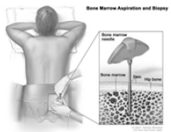
Causes of lymphocytopenia

Infection
Bacterial (eg, tuberculosis, typhoid fever, brucellosis)
Viral (eg, HIV, severe acute respiratory syndrome [SARS], measles, hepatitis)
Fungal (eg, histoplasmosis)
Parasitic (eg, malaria)
Congenital immunodeficiency disorders
Iatrogenic
Immunosuppressive agents (eg, glucocorticoids, antilymphocyte globulin, alemtuzumab, rituximab)
Chemotherapy (eg, fludarabine, cladribine), hematopoietic cell transplantation
Radiation therapy (eg, total body irradiation, radiation injury)
Systemic disease
Autoimmune disorders (eg, systemic lupus erythematosus, rheumatoid arthritis, Sjögren syndrome)
Lymphoma
Other malignancies
Sarcoidosis
Renal failure
Aplastic anemia, pancytopenia
Cushing's syndrome
Other causes
Alcohol abuse
Zinc deficiency
Malnutrition, stress, exercise, trauma
Thoracic duct leak, rupture, diversion
Protein-losing enteropathy
Idiopathic CD4+ lymphocytopenia

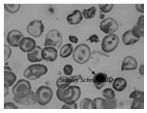
HIV: human immunodeficiency virus.

UpToDate®

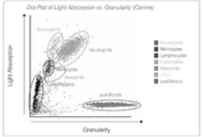
	Patient Value		Normal Reference Range Female
WBC	33.6 x10E+9/L	H	(3.8-10.6)
RBC	2.28 x10E+12/L	L	(3.73-4.89)
Hgb	8.3 g/dl	L	(11.6-14.6)
Hct	24.3 %	L	(34.1-43.3)
MCV	106.5 fL	H	(82.6-97.4)
MCH	36.5 pg	H	(27.8-33.4)
MCHC	34.3 gm/dL		(32.7-35.5)
RDW	23.7 %	H	(11.8-15.2)
PLT	11 x10E+9/L	L	(156-369)
Peripheral Blood Differential		**ABS. No.**	**Normal Range (ABS)**
POLYS	25.0 %	(8.40)	(2.24-7.68)
BANDS	7.0 %	(2.35)	(0.10-0.80)
LYMPHS	5.0 %	(1.68)	(0.80-3.65)
ATYP LYMPH	1.0 %	(0.34)	
MONOS	4.0 %	(1.34)	(0.30-0.90)
BLASTS	58.0 %	(19.45)	

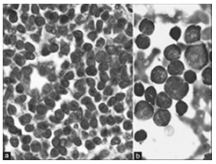


cancer.gov



Bone Marrow Examination





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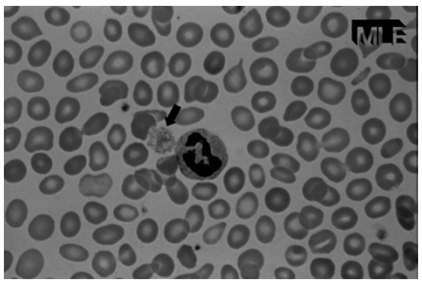
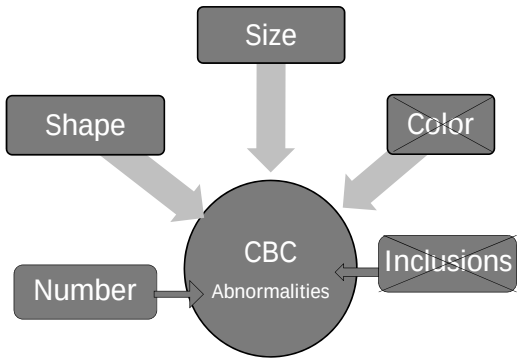
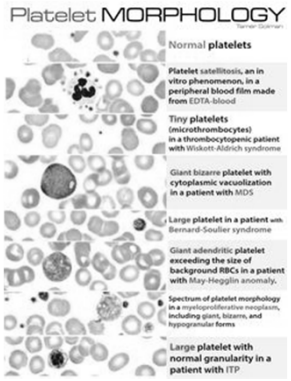
WBC Abnormality	Condition	Pictures
Auer rods (cytoplasmic granules)	Acute Myeloid Leukemia	
Dohle bodies (cytoplasmic granules)	Infection or Inflammation	
GIANT cytoplasmic granules	Chediak-Higashi	
Other: Small Cleaved Lymphocytes	Follicular Lymphoma	
Bipolar Villous Projections Ragged "Hairy" Cytoplasm	Splenic marginal zone lymphoma Hairy Cell Leukemia	
"Cloverleaf" Nuclei	Adult T Cell Leukemia	
Parasites		

Platelets







Platelet Numbers

Thrombocytopenia

- Pseudo-
- Confirmed
  - Destruction (↻ platelets)
    - ITP, DIC, TTP, HUS
  - Decreased Production
    - Viral
    - Congenital (TAR)
    - Replacement

Thrombocytosis (>450K)

- Reactive
  - cytokine driven
  - 3 primary qualities
    - *not* MPD/MDD
    - has a likely cause
    - expected normalization
- Autonomous
  - clonal overproduction
    - PV, PMF, CML, myelodysplasia
    - Essential Thrombocytosis

N=91 (plts>600K)
RT→70%
AT→22%
Combo→8%

31% infection
27% infection + post op
16% post surgical
9% malignancy
9% post splenectomy
8% acute blood loss or iron deficiency

Tefferi et al. Am J Med 1994;96: 247

Extreme Thrombocytopenia (>1,000,000/microL)

- N=280
- RT 82%
- AT 14%
- Unknown 4%

31% infection
19% post splenectomy/hyposplenism
14% malignancy
14% trauma
9% inflammation
6% blood loss
3% rebound thrombocytosis
4% uncertain

Buss DH, et al. Am J Med 1994; 96:247

Symptoms of Thrombocytosis

- Vasomotor
  - HA, visual, lightheadedness, atypical chest pain, acral dysesthesias, erythromelalgia
- Thrombotic
- Bleeding

ET 24% (each)
RT 1% thrombosis
3% bleeding

Buss DH, et al. Am J Med 1994; 96:247

Evaluation of Thrombocytosis

- Confirm
  - repeat testing
  - peripheral blood smear
- H & P
  - establish the duration of the thrombocytosis
- Labs
  - CBCd, smear, ferritin
  - CRP, ESR, fibrinogen, ferritin
  - Gene expression (platelet RNA)

Essential Thrombocytosis

- *rate of cytogenetic abnormalities < 5%
- JAK2 V617F in ~50%

Management of Thrombocytosis

Bleeding

- stop anti-platelet meds
- FFP/Platelets
  - Acquired Factor V
- Platelet apheresis
  - Acquired Factor II vWd
- treat the underlying dz
  - Iron therapy, direct endoscopy/imaging, myelosuppressive agent or plt-lowering agent

Thrombosis

- Platelet apheresis(>800K)
- Platelet lowering agent
- Anticoagulant therapy

Reviewing the basics. . .

- a CBC is meant to HELP . . . NOT hinder
- **always** get a DIFFERENTIAL
- a SMEAR gains you exponential info
- Phone-a-Friend
- BUT—if it feels *wrong*

REFER