The ABCs of the LABs:
CBCs and
WBC Abnormalities

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Physician Assistant Online Program

Disclosures

Physician Assistant Education Association
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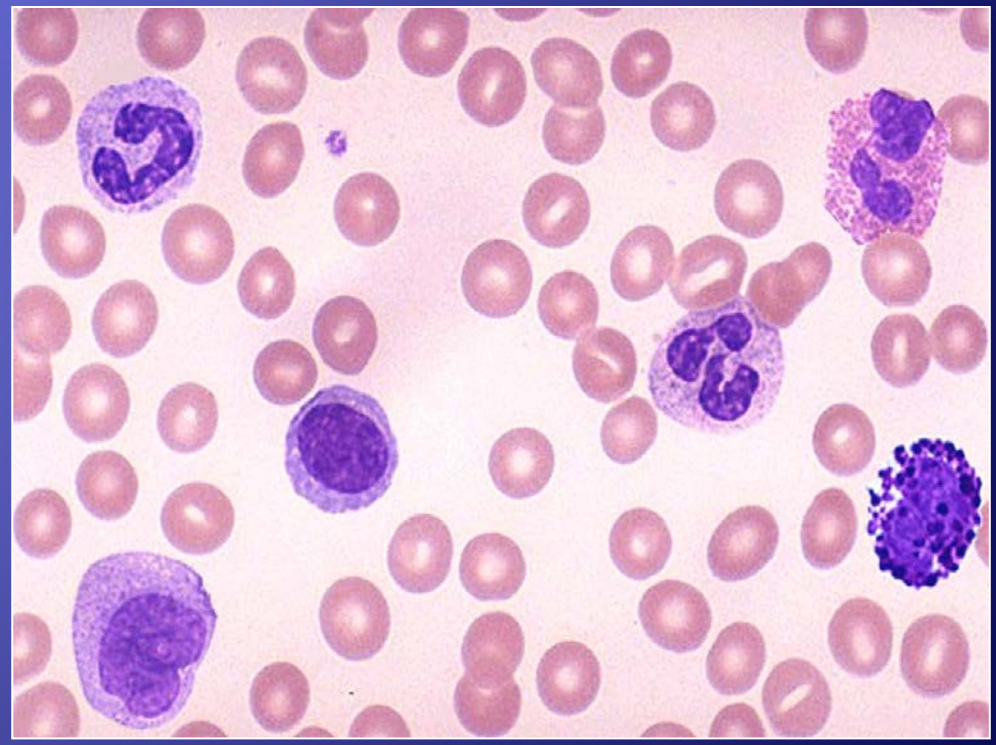
Learning Objectives

At the conclusion of this session, participants should be able to:

- Interpret complete blood counts and WBC differentials used in making a clinical diagnosis
- Identify correlating disease states indicated by common abnormal hematology laboratory results
- Establish clinical correlation of hematology laboratory values to specific patient presentations
- Differentiate unique laboratory specialty tests and when applicable to order for hematologic disease states

Complete Blood Count (CBC)

- CBC Includes:
  - Hemoglobin
  - Hematocrit
  - RBC count
  - WBC count
  - Platelet count
  - RBC Indices
  - WBC Differential

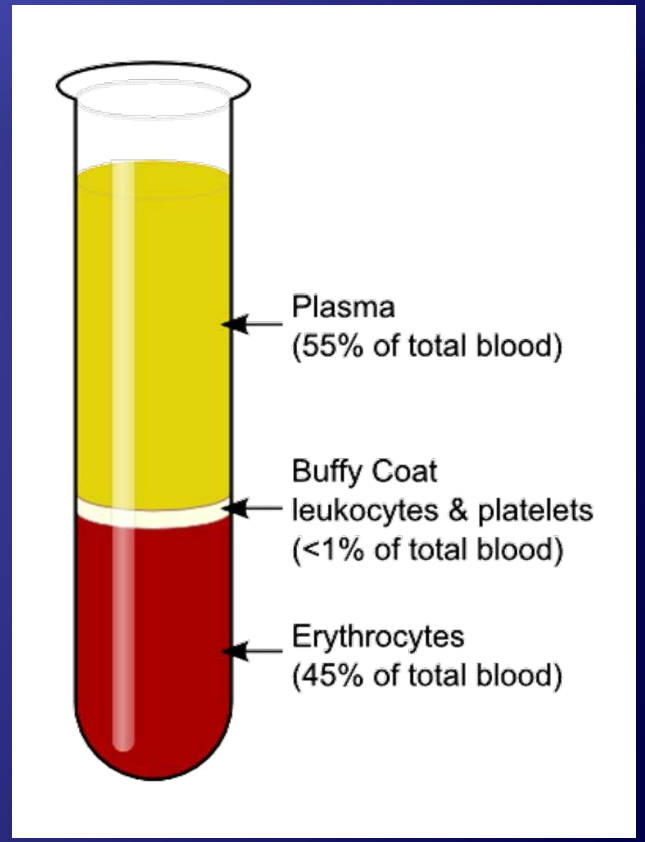


Why Order a CBC?

- Support presence of infectious agents
  - Viruses and bacteria
- Identify white blood cell disorders
  - Acute and chronic leukemia
- Determine presence of anemia
  - Hemolytic, macrocytic, microcytic
- Assess platelets in bleeding disorders

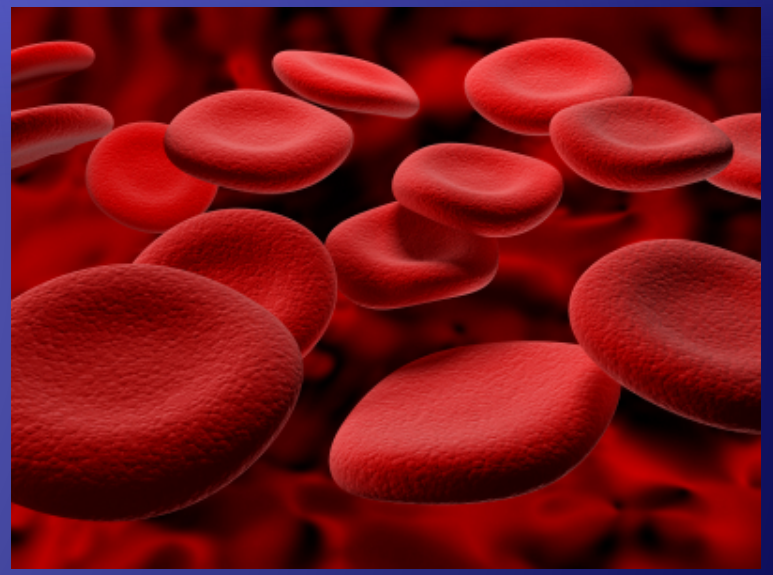
Hemoglobin and Hematocrit

- Hemoglobin
  - 4-globin complex containing heme
  - Normals:
    - 14-18 mg/dL (males)
    - 12-16 mg/dL (females)
- Hematocrit
  - Proportion of RBCs to whole blood
  - Normals:
    - 45-52% (males)
    - 37-47% (females)



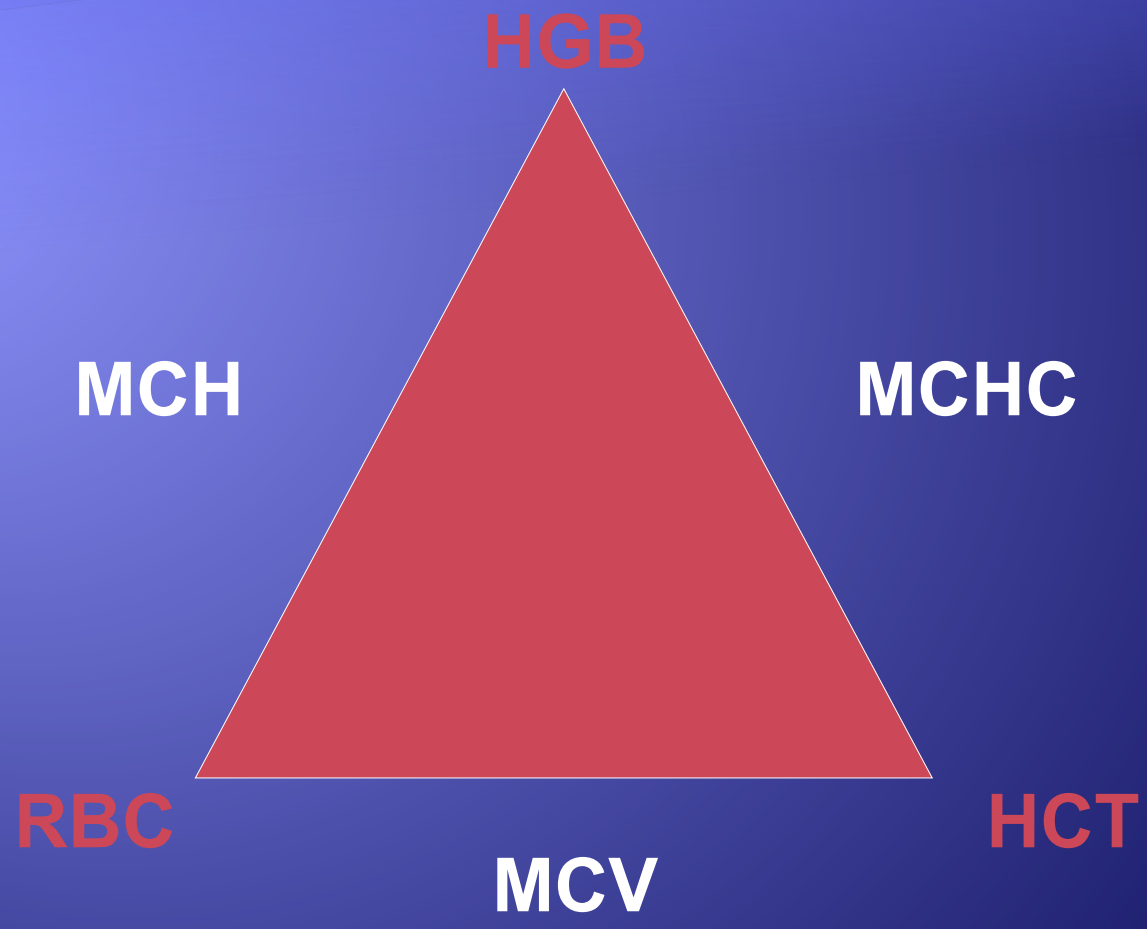
RBCs and RBC Indices

- Red Blood Cell (RBC) Count
  - Normals:
    - 4.7-6.1 x 10^6/uL (males)
    - 4.2-5.4 x 10^6/uL (females)



- MCV – mean cell volume
- MCH – mean cell hemoglobin
- MCHC – mean cell hemoglobin concentration
- RDW – red cell distribution width

Triangular Relationship

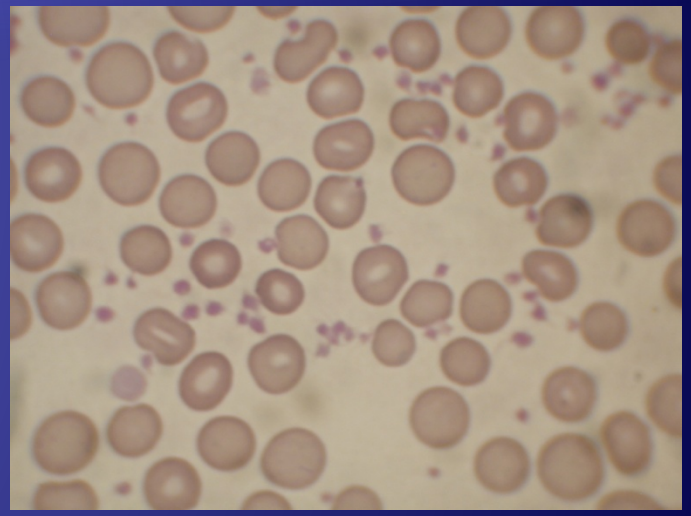


RBC Indices

- MCV = 80-100 fL
  - size of the cells (microcytic, macrocytic)
- MCH = 28-32 pg
  - amount of Hgb present in each RBC
- MCHC = 32-36%
  - proportion of each RBC occupied by Hgb
- RDW = 11.5 – 14.5 %
  - standard deviation of the size of the RBC

Platelets

- Platelet Count
  - Normal = 150 – 450 x 10^3/uL
- MPV = mean platelet volume
  - Normal = 7.4 – 10.4 fL
  - Inverse, non-linear relationship to count



Question #1

Which of the following WBC types are the most prevalent in a normal patient?

A. Basophils
B. Eosinophils
C. Lymphocytes
D. Monocytes
E. Neutrophils

White Blood Cell Differential

White Blood Cell (WBC) Count

Normal: 4.5 – 11.0 x 10^3/uL

Cell type	Relative Normal (%)	Absolute Normal (% x Total WBC)
Neutrophils	54-62%	2000-8000
Lymphocytes	25-33%	1000-4000
Monocytes	3-7%	200-800
Eosinophils	1-3%	100-400
Basophils	0-1%	0-400
Comments included on abnormal WBC Morphology		

WBC Function

- Neutrophils – respond to bacterial infections
- Lymphocytes – respond to viral infections
- Monocytes – recovery phase of bacterial infections or chronic infections
- Eosinophils – respond to parasitic infections and allergic reactions
- Basophils – related to mast cells in the tissue

Case 1

- 21 year-old student presents with fever and fatigue.
  - He also notes headache and sore throat.
- His past medical history is unremarkable.
- He denies sexual activity but does state he started dating a new girlfriend a few weeks ago.

Case 1

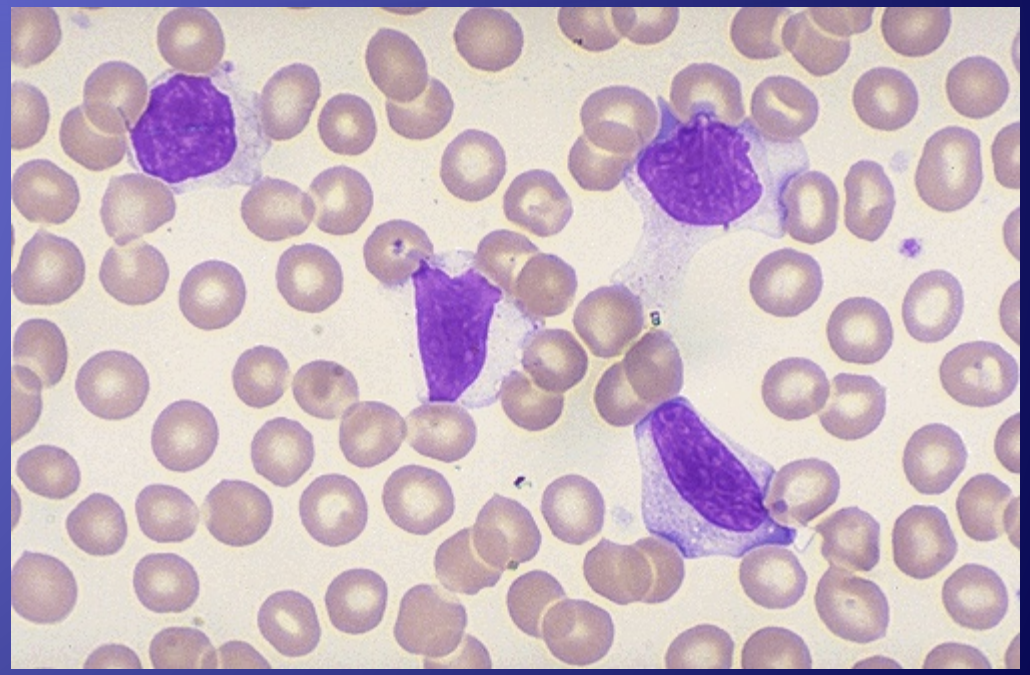
- T 39.3°C; P 104/min; RR 14/min;
  BP 124/72 mmHg
- Posterior cervical adenopathy is noted
- No hepatosplenomegaly is noted
- No rash is noted
- Pharynx is erythematous with bilaterally enlarged tonsils without exudates

Case 1

Laboratory Data

- WBC 12,000/µL
- Hgb 12.5 g/dl
- Hct 38%
- MCV 86 fL
- PLT 90,000/µL

- Liver function tests are mildly elevated

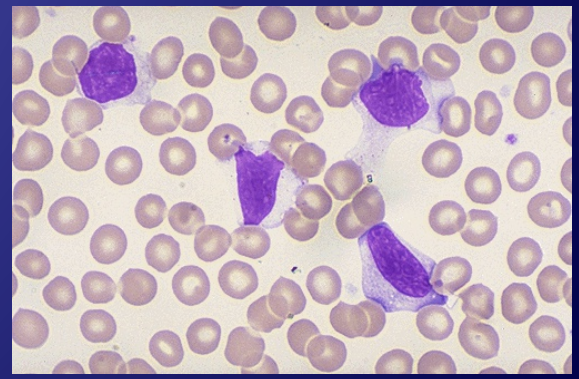


Question #2

What is the most important concern noted in this CBC report and accompanying blood smear?

A. White blood cell count
B. White blood cell morphology
C. Hemoglobin and hematocrit
D. Mean cell volume of red cells
E. Platelet count

WBC 12,000/µL
Hgb 12.5 g/dl
Hct 38%
MCV 86 fL
PLT 90,000/µL



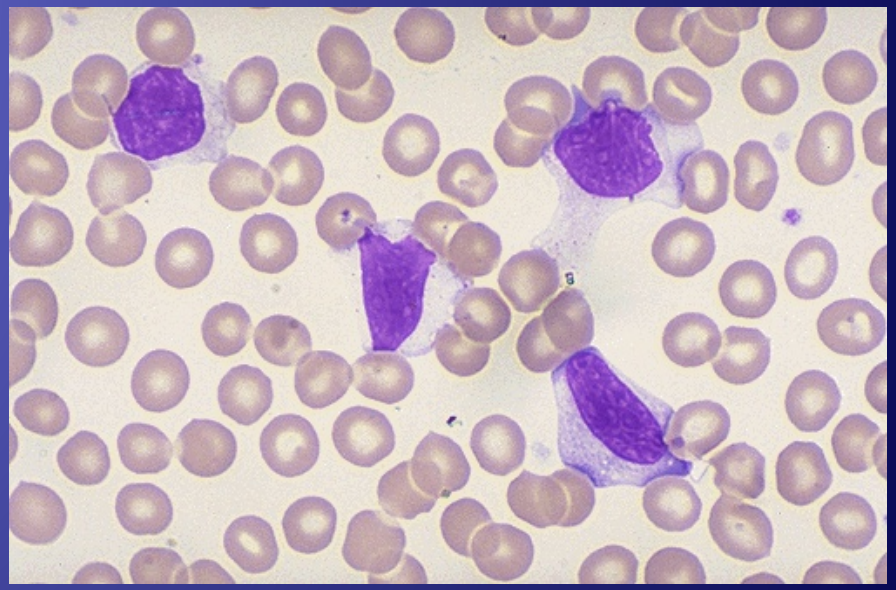
White Blood Cell Count (WBC)

- Total WBC Count
  - Normal = 4.5 – 11.0 x 10^3/uL
- Leukocytosis = > 11.0 x 10^3/uL
  - Bacterial Infection
  - Myeloproliferative Disorders
- Leukopenia = < 4.5 x 10^3/uL
  - Viral infection
  - Autoimmune disorders, drugs, aplastic anemia

Question #3

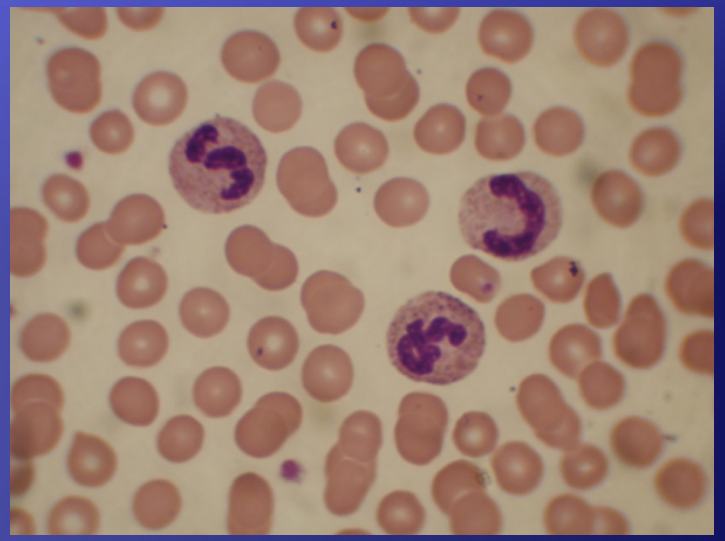
What white blood cell morphology is seen in this blood smear?

A. Atypical lymphocytes
B. Immature WBCs (blasts)
C. Neutrophilia
D. Normal monocytes
E. Toxic granulation of neutrophils

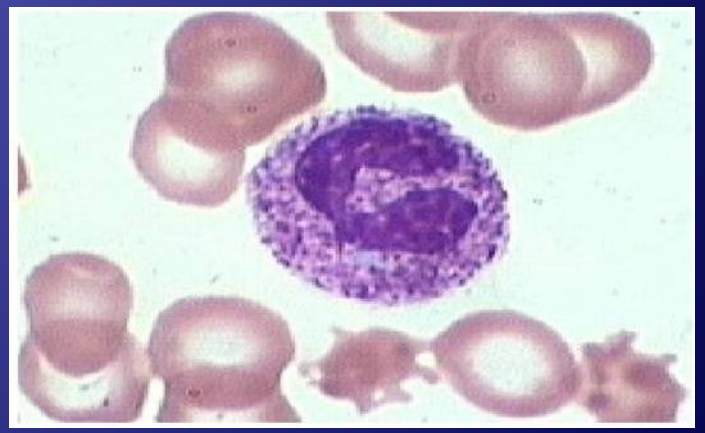


Abnormal WBCs & Counts

- Neutrophilia
  - Shift to the left - increase in immature neutrophils (bands, metamyelocytes, myelocytes)

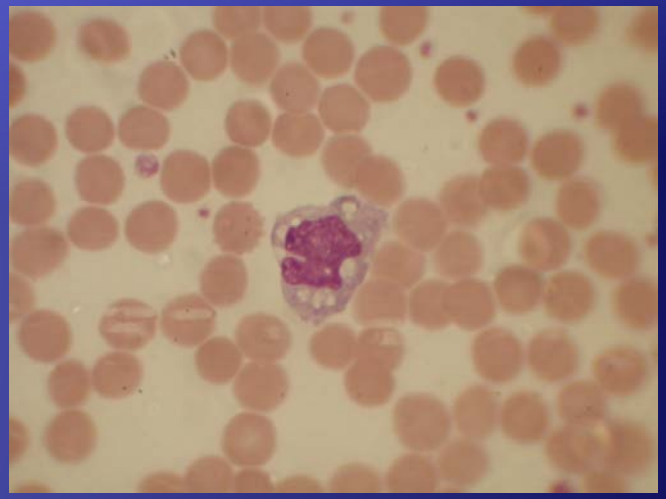


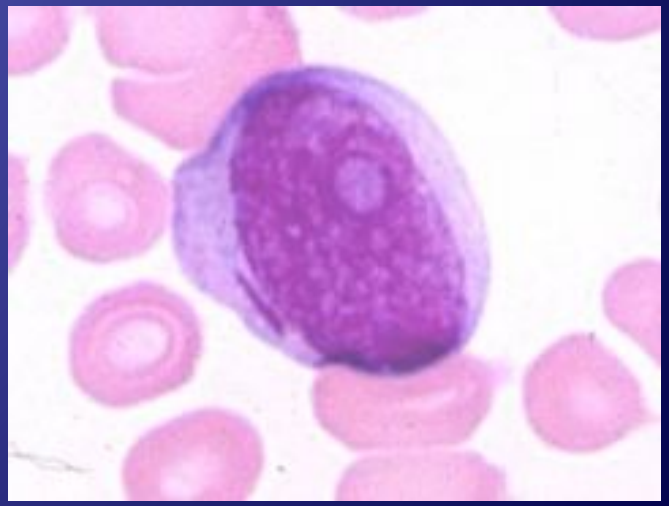
- Toxic Granulation of Neutrophils
  - Not inclusion granules, but abnormally activated enzyme-containing granules
  - Dohle bodies may be present



Abnormal WBCs & Counts

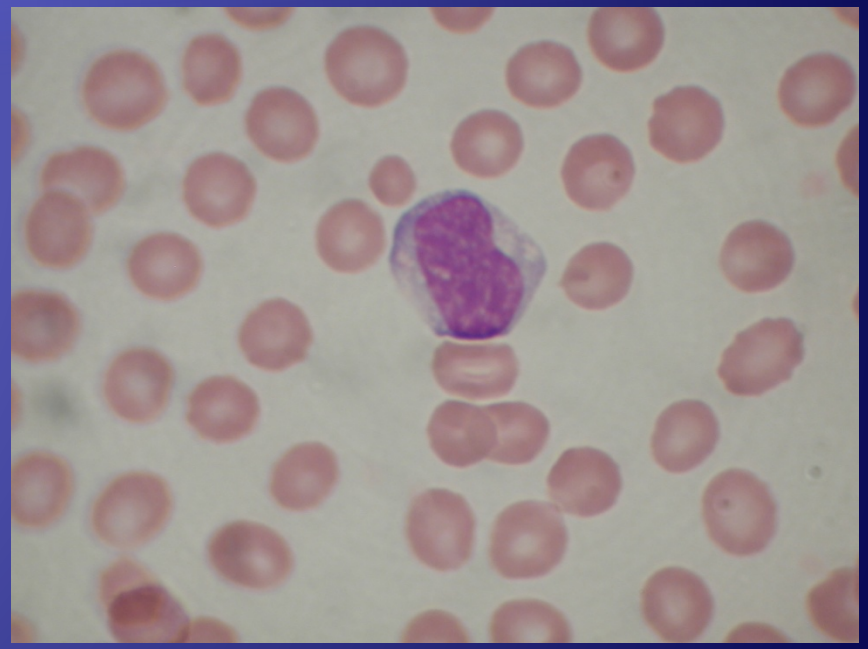
- Monocytes
  - large irregular cells with fine nucleus, gray/blue cytoplasm, and vacuoles
  - increased in newborns, recovery phase of bacterial infections, TB
- Immature WBCs (blasts)
  - Large, fine chromatin, blue cytoplasm, nucleoli
  - Normally in bone marrow
  - Seen in peripheral blood in acute leukemias





Abnormal WBCs & Counts

- Atypical Lymphocytes
  - Atypical lymphs (Downey cells)
    - Larger, bluer cytoplasm
    - Radial basophilia
    - Plasmacytoid, nucleoli
  - Absolute and relative lymphocytosis with atypical lymphs



Question #4

In which of the following conditions would a patient present with atypical lymphocytes on a peripheral blood smear?

A. Leukemoid reaction
B. Bacterial pneumonia
C. Infectious mononucleosis
D. Acute lymphocytic leukemia
E. Chronic lymphocytic leukemia

Abnormal WBC Morphology

- Neutrophilia (left shift) and toxic granulation of neutrophils – Bacterial Infection
- Atypical lymphocytes – Mononucleosis and other viral infections
- Acute Leukemia – proliferation of blast cells in the peripheral blood
- Chronic Leukemia - occasional blast cells with proliferation of mature cells in peripheral blood

Case 1

- Final diagnosis
  - Infectious mononucleosis (EBV)
- Monospot was positive
- Why the anemia and thrombocytopenia?

Ebell MH. *Epstein-Barr Virus Infectious Mononucleosis.*
Am Fam Physician 2004;70(7):1279-1287.

Case 2

- A 67 year-old female presents with acute onset of chills and fever.
  - Also noting pleuritic right-sided chest pain and a productive cough
- The patient is a smoker and has a history of type 2 diabetes.

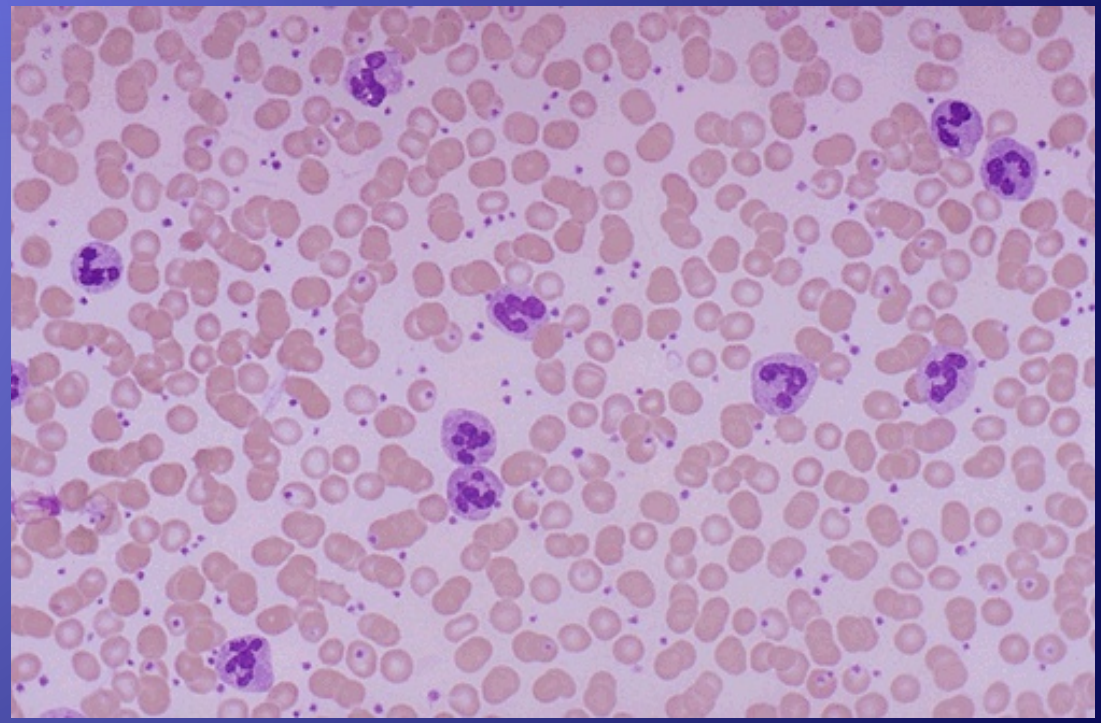
Case 2

- T 39.6°C; P 130/min; RR 32/min;
  BP 159/77 mmHg
- Patient is ill-appearing, confused, and in moderate distress
- Pulmonary exam reveals bronchial breath sounds and crackles over the right upper lobe. Dullness to percussion and increased fremitus also noted in this area

Case 2

Laboratory Data

- WBC 22,400/µL
- Hgb 13 g/dl
- Hct 39%
- MCV 86 fL
- PLT 190,000/µL
- Differential
  - 65% Neutrophils
  - 24% bands
  - 8% lymphocytes
  - 3% monocytes



Question #5

What is the most important concern noted in this CBC report and accompanying blood smear?

A. Hemoglobin and hematocrit
B. Mean cell volume of red cells
C. Platelet count
D. White blood cell count/differential

- WBC 22,400/µL
- Hgb 13 g/dl
- Hct 39%
- MCV 86 fL
- PLT 190,000/µL
- Differential
  - 65% Neutrophils
  - 24% bands
  - 8% lymphocytes
  - 3% monocytes

CBC Interpretation

- Hgb/Hct = 13 gm/dL; 39%
  - Normal = 12-16 gm/dL; 36-49%
- MCV = 86 fL
  - Normal = 80-100 fL
- Platelet Count = 190,000/uL
  - Normal = 150,000 – 450,000/uL
- WBC Count = 22,400/uL plus shift to the left (increased % of immature neutrophils)
  - Normal = 5,000 – 10, 000/uL

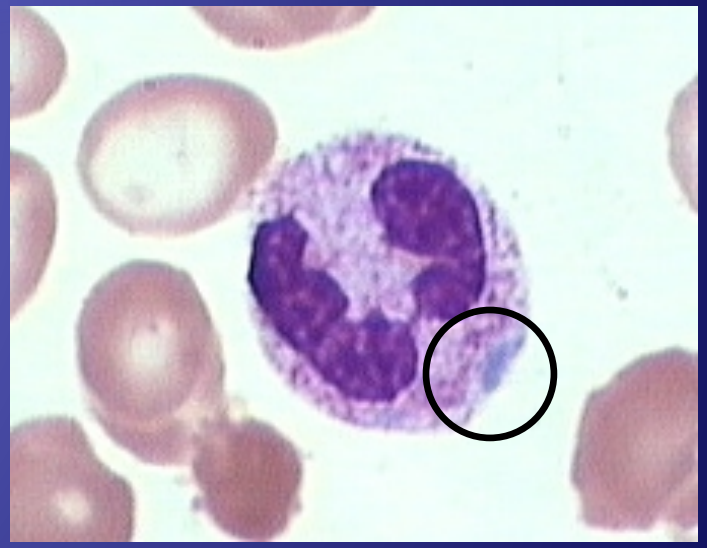
Question #6

What white blood cell morphology is seen in the outlined area on this blood smear?

A. Band neutrophil
B. Dohle body
C. Nucleoli
D. Radial basophilia
E. Toxic granulation

White Blood Cell Morphology

- Segmented neutrophil (not a band)
- Nucleoli seen on immature blast cells
- Radial basophilia seen on atypical lymphocytes
- Neutrophil does have toxic granulation with Dohle body in cytoplasm
- Dohle bodies thought to be remnants of endoplasmic reticulum



Question #7

What is the final diagnosis for this patient?

A. Tuberculosis
B. Histoplamosis
C. Bacterial pneumonia
D. Mycoplasma pneumonia

Lab Findings in Lung Diseases

- Tuberculosis – typically more monocytes present
- Histoplasmosis – fungal infection; chronic so more monocytes
- Mycoplasma pneumonia – atypical pneumonia; WBC count can be normal
- Bacterial pneumonia – presents with elevated WBC count, shift to the left, toxic granulation and Dohle bodies

Case 2

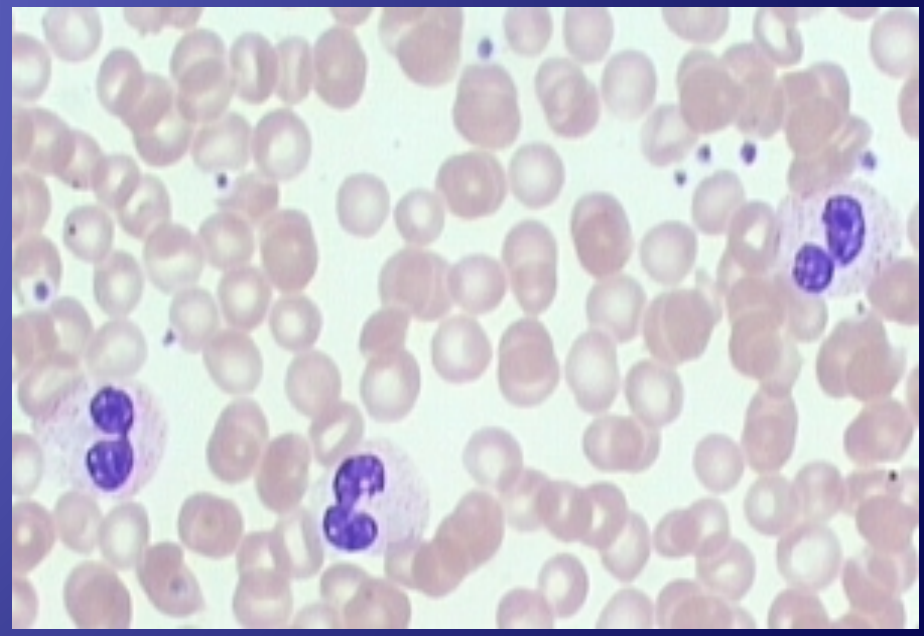
- Final diagnosis
  - Bacterial Pneumonia
- Chest x-ray revealed a RUL consolidation
- CBC differential revealed a left shift with toxic granulation and Dohle bodies present.

Mizgerd JP. *Acute Lower Respiratory Tract Infection.* N Engl J Med 2008;358:716-27.

Question #8

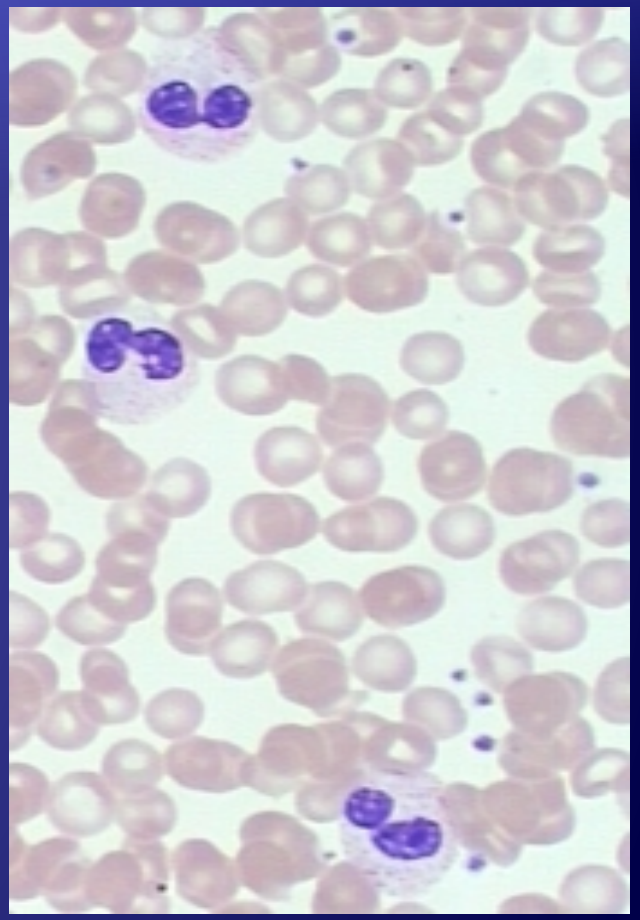
What disorder is indicated by this white blood cell morphology?

A. Bacterial infection
B. Chronic myelocytic leukemia
C. Parasitic infection
D. Pelger-Huet anomaly



Pelger-Huet Anomaly

- Congenital autosomal dominant disorder
- Granulocyte nuclei fail to segment normally
- Homozygote state - nucleus is round
- Heterozygotes - most granulocytes have bilobed nuclei ("pince-nez" cells) resembling band neutrophils
- Trait is benign and occurs in 1 in 6,000 people
- Cell function is normal.



Case 3

- 47-year-old presents with low back pain.
  - Has noted a 12-pound weight loss and increasing fatigue
  - No history of fever, chills, or sweats
  - No cough, shortness of breath, or chest pain
- History significant for hypertension

Case 3

- T 36.1°C; P 80/min; RR 20/min;
  BP 152/88 mmHg
- Patient is in no acute distress
- Pulmonary and cardiac exam are normal
- No hepatosplenomegaly
- Skin reveals bruises in various stages of healing on the arms, left foot, and LUQ

Question #9

Case 3

Laboratory Data

- WBC 10,700/µL
- Hgb 15.9 g/dl
- Hct 45.5%
- MCV 88 fL
- PLT 17,000/µL

What is the most important concern noted in this CBC report?

A. **White blood cell count**
B. **Hemoglobin**
C. **Hematocrit**
D. **Mean cell volume of the red cells**
E. **Platelet count**

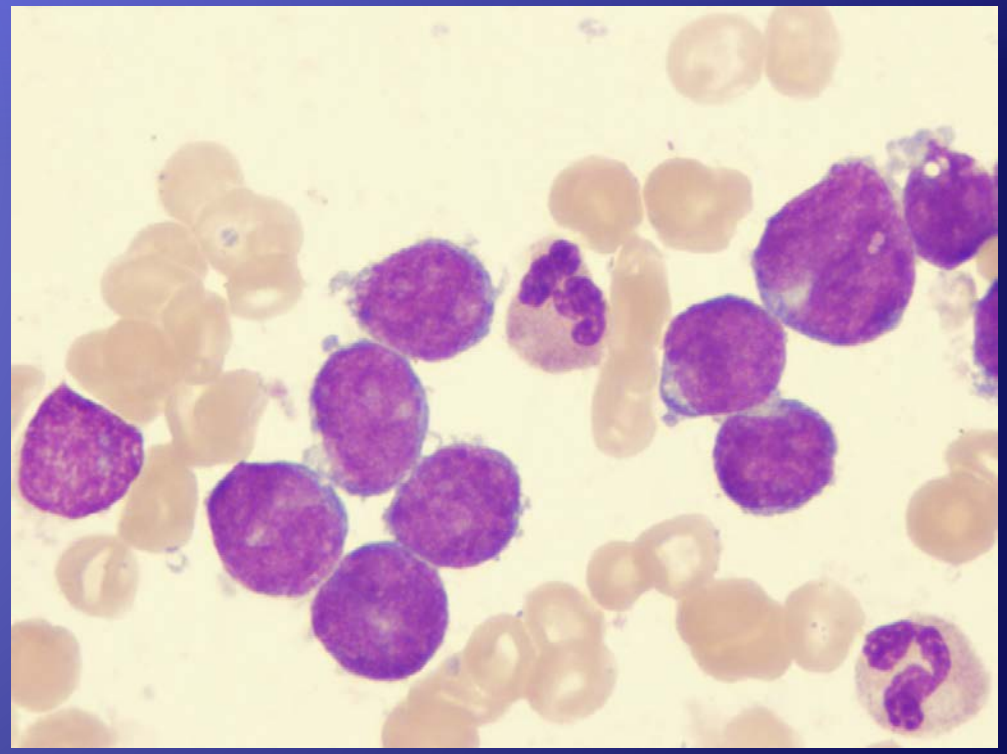
CBC Interpretation

- WBC Count = 10,700/uL
  - Normal = 5,000 – 10, 000/uL
- Hgb/Hct = 15.9 gm/dL; 44.5%
  - Normal = 14 – 18 gm/dL; 44-53%
- MCV = 88 fL
  - Normal = 80-100 fL
- Platelet Count = 17,000/uL
  - Normal = 150,000 – 450,000/uL

Case 3

Laboratory Data

- Differential
  - 40% Neutrophils
  - 22% lymphocytes
  - 2% monocytes
  - 2% eosinophils
  - 2% metamyelocytes
  - 5% myelocytes
  - 10% blasts



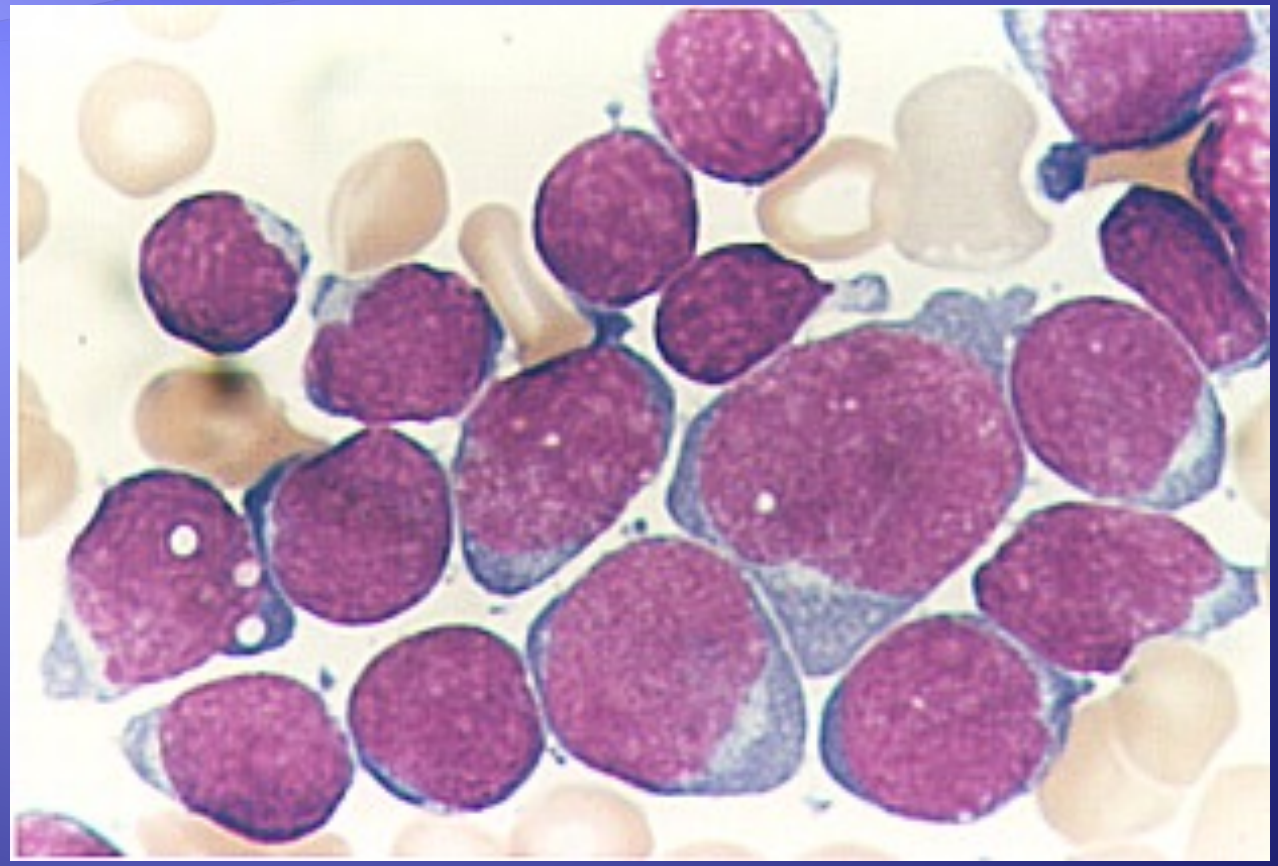
Question #10

What is the most important concern noted in this WBC differential and accompanying peripheral blood smear?

A. Percentage of neutrophils
B. Presence of myelocytes and metamyelocytes
C. Presence of blast cells
D. Red blood cell morphology
E. Absence of platelets

- Differential
  - 40% Neutrophils
  - 22% lymphocytes
  - 2% monocytes
  - 2% eosinophils
  - 2% metamyelocytes
  - 5% myelocytes
  - 10% blasts

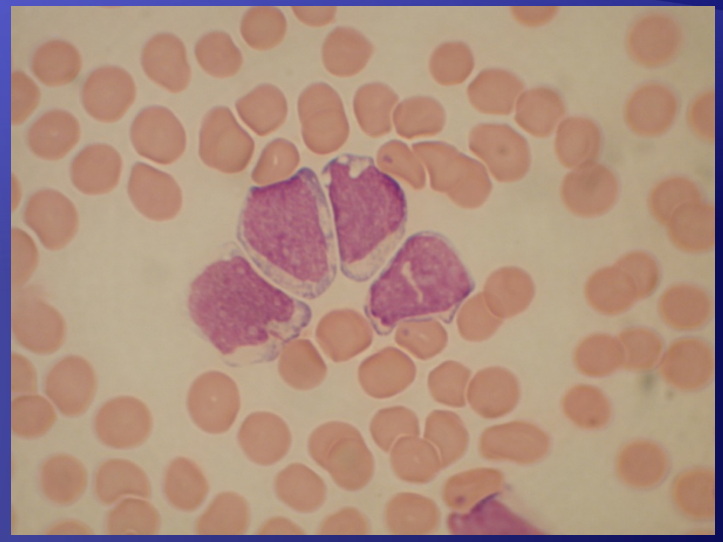
Case 3



Bone Marrow

Acute Leukemia

- Acute onset, patient symptomatic
- Proliferation of blast cells in bone marrow and peripheral blood
  - Auer rods – in Acute Myelocytic Leukemia
- Variable WBC
- Anemia, thrombocytopenia
- All ages
- Typically > 30% blasts

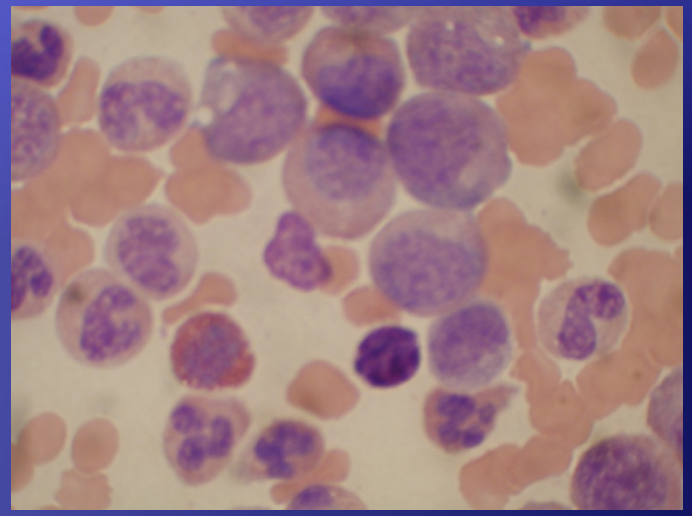


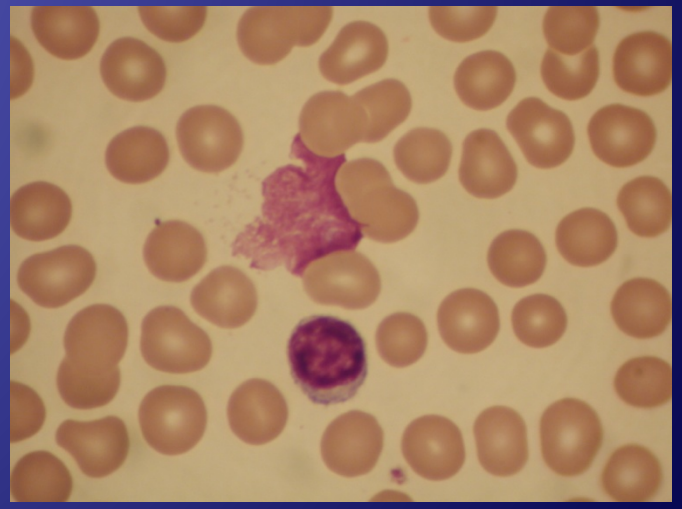
Chronic Leukemia

- Slow onset
- Many asymptomatic or mild symptoms
- More mature cells
  - Leukocytosis
  - Anemia and thrombocytopenia as disease progresses
- Middle age or elderly

Chronic Leukemia

- Proliferation of mature cells in the peripheral blood with occasional (< 10%) blast cells
  - Chronic Myelocytic Leukemia – mature granulocytes
  - Chronic Lymphocytic Leukemia – mature lymphocytes; presence of smudge cells





Case 3

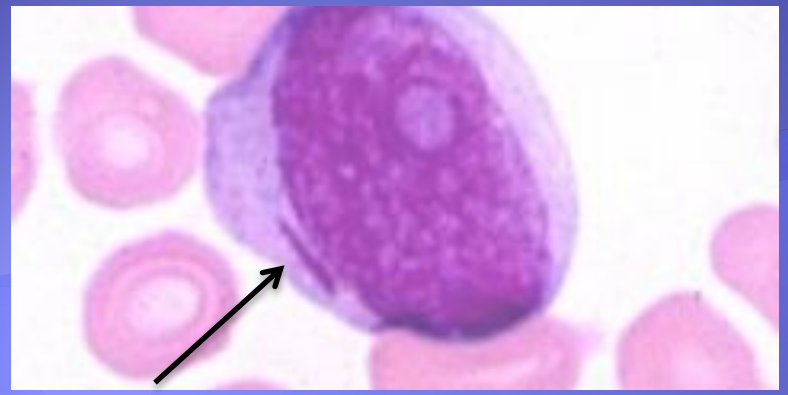
- Final diagnosis
  - Acute lymphocytic leukemia
- Patient symptomatic with acute onset
- CBC differential revealed blast cells in peripheral blood; thrombocytopenia; could be either ALL or AML

Inaba H, Greaves M, Mullighan CG. *Acute lymphoblastic leukaemia.* Lancet 2013;381;1943-55.

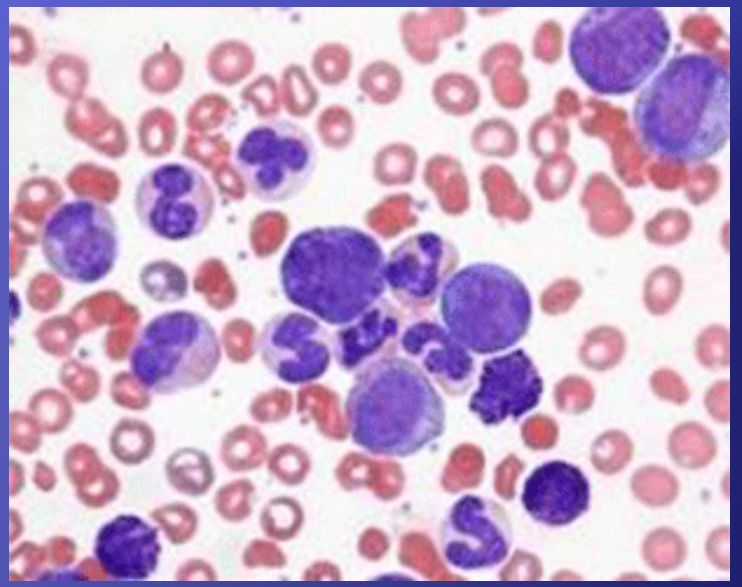
Question #11

If this patient had acute myelocytic leukemia, the presence of which of the following distinguishing features could be seen in the peripheral blood and/or the bone marrow?

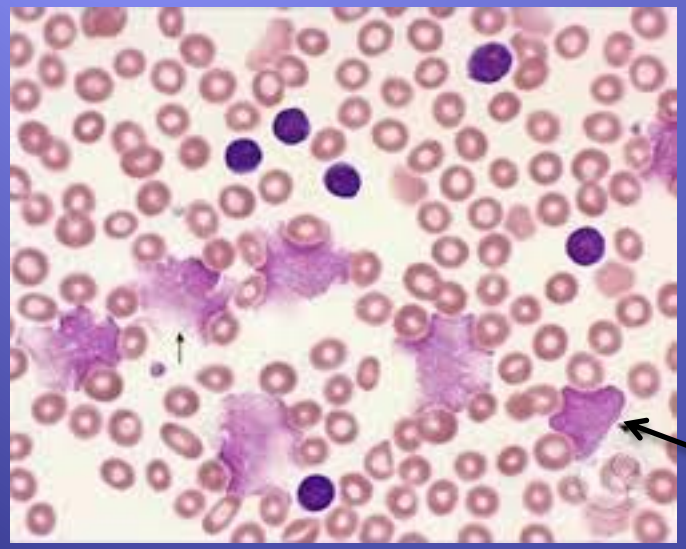
A. Auer rods in the blast cells
B. Proliferation of mature granulocytes
C. Proliferation of mature lymphocytes
D. Smudge cells



Auer rods in blast cells



Proliferation of mature granulocytes



Smudge cells

Proliferation of mature lymphocytes

Case 4

- 52 yo male comes into the ER with c/o fever, chills, and a very swollen right hand.
  - PMHx: HTN
  - PSHx: none
  - FHx: non-contributory
  - SHx: non-smoker, occasional beer, no illicit drugs
  - Meds: Lisinopril 5 mg daily
  - Allergies: none

Case 4

- PE:
  - WDWN male, appears acutely ill
  - P 110, R 22, BP 72/40, T 104.0
  - LUE – puncture wound noted on the dorsum of right hand with significant erythema and edema to shoulder
  - BLE: multiple non-blanchable purpura noted

Case 4

- Patient states he was bitten by his dog 3 days ago.

Question # 12

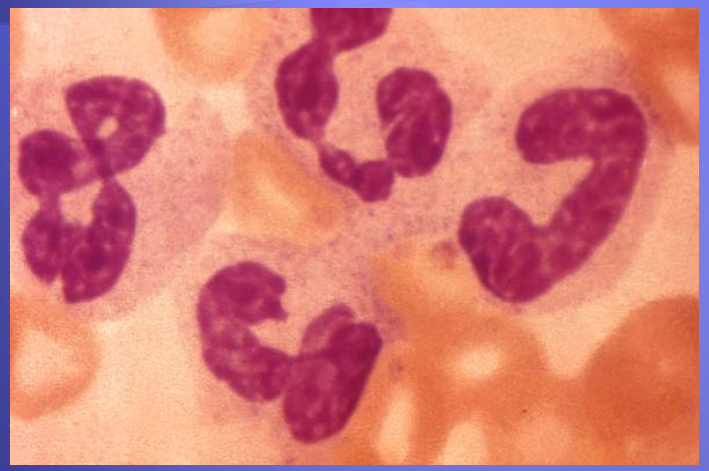
What is the most important concern noted in this laboratory report?

A. Hemoglobin and hematocrit
B. RBC Indices
C. White blood cell count
D. WBC Differential

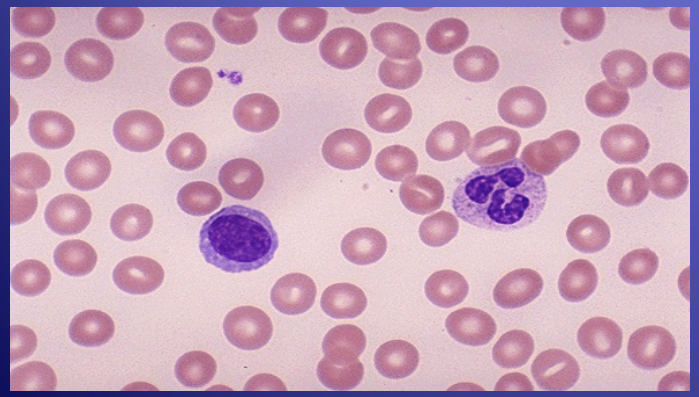
Test	Patient Value	Test	Patient Value
CBC		**WBC Diff and Smear Eval**	
WBC	22.2	PMNs	34%
RBC	4.29	Bands	51%
Hgb	13.8	Lymphocytes	6%
Hct	40.7	Monocytes	1%
MCV	94.9	Eosinophils	0
MCH	32.2	Basophils	0
MCHC	33.9	Meta	6%
RDW	15.5	Myelo	2%
PLT	19	Toxic Gran	+2
		Vac PMNs	+2
		Schistocytes	+1

Case 4 – CBC Results

Patient

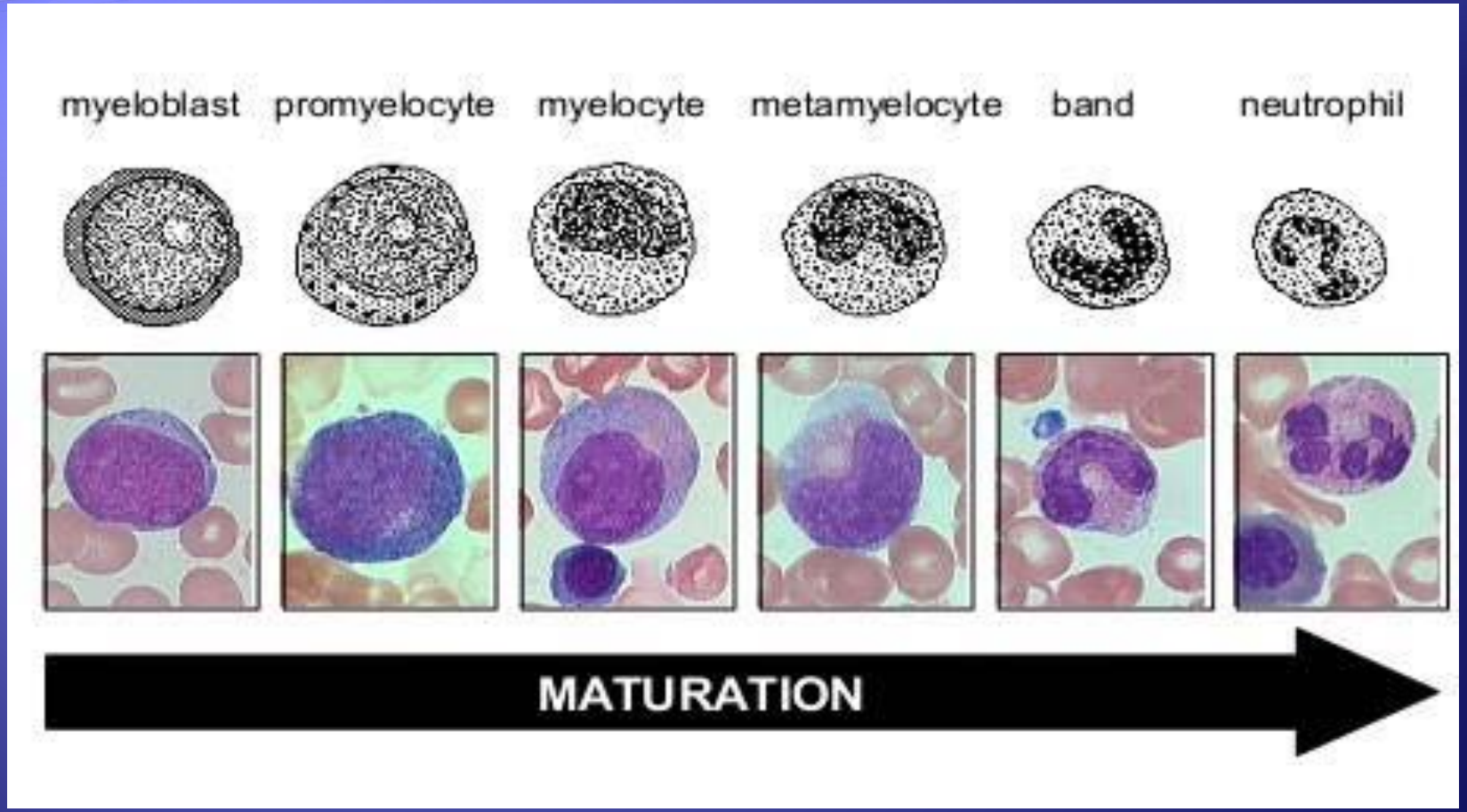


Normal



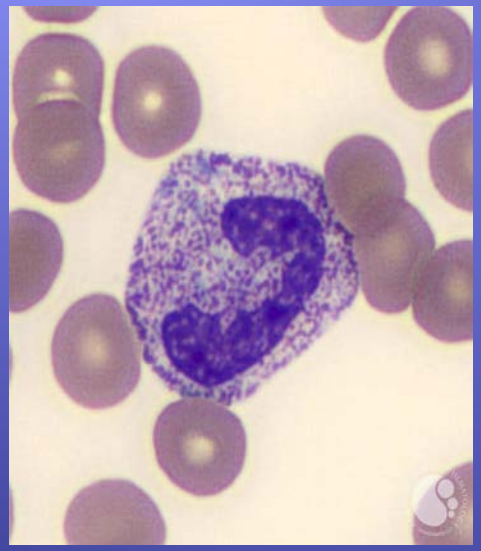
Test	Patient Value	Test	Patient Value
CBC		**WBC Diff and Smear Eval**	
WBC	22.2	PMNs	34%
RBC	4.29	Bands	51%
Hgb	13.8	Lymphocytes	6%
Hct	40.7	Monocytes	1%
MCV	94.9	Eosinophils	0
MCH	32.2	Basophils	0
MCHC	33.9	Meta	6%
RDW	15.5	Myelo	2%
PLT	19	Toxic Gran	+2
		Vac PMNs	+2
		Schistocytes	+1

“Left Shift"

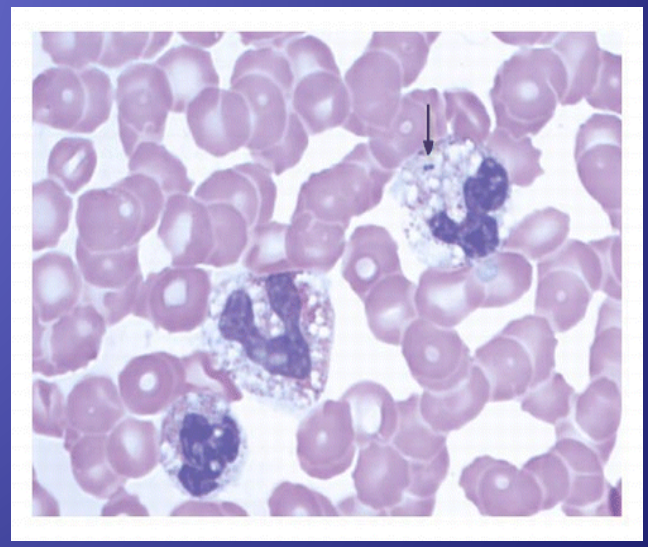

myeloblast
promyelocyte
myelocyte
metamyelocyte
band
neutrophil
MATURATION

WBC Morphology?

- What does toxic granulation and vacuolated PMNs indicate?
  - Severe bacterial infection



Toxic granulation



Vacuolated PMNs (Segs)

Additional Lab Results

- Additional tests:
  - Lactate 6.9 (normal < 1.5)
  - CRP 23.6(normal for this pt < 1)
  - ESR 82 (normal for this pt < 20)

Question #13

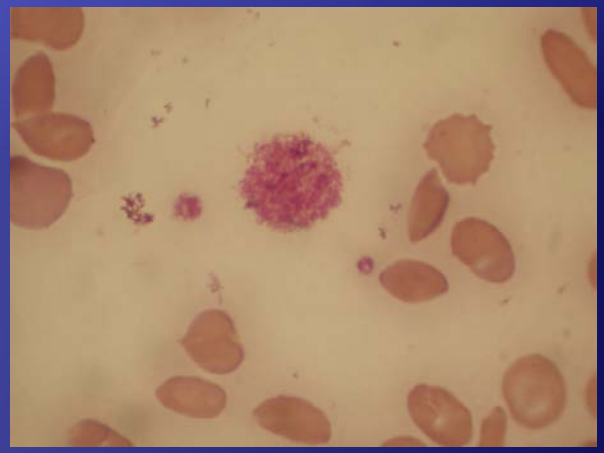
What is the second most important concern noted in this laboratory report?

A. White blood cell count
B. Hemoglobin and hematocrit
C. Platelet count
D. Presence of schistocytes

- WBC 22,200/µL
- Hgb 13.8 g/dl
- Hct 40.7%
- MCV 94.9 fL
- PLT 19,000/µL
- Schistocytes 1+

Platelets & RBC Morphology?

- Platelets = 19 x 10^3/uL
- RBC morphology shows schistocytes



- What else is going on with this patient?
  - Coagulation disorder???

Why Order Coagulation Studies?

Question #14

Which of these options applies to this patient?

A. To determine if a low hemoglobin is due to a bleeding disorder
B. To determine if a bleeding disorder is present, and to help distinguish the etiology of the bleeding disorder
C. In order to establish a baseline before beginning anti-coagulation therapies

Coagulation Studies

- PTT or aPTT = Partial Thromboplastin Time
  - Measures intrinsic and common pathway
  - Normal = 25-35 sec
  - Heparin proper dosage = PTT 1.5-2.5 times normal

- PT = Prothrombin Time
  - Measures extrinsic and common pathway
  - Normal = 10-13 sec
  - Coumadin (warfarin) proper dosage = 2-3 times pre-therapy level
    - INR = International Normalized Ratio = 2.0 – 3.0

Coagulation Testing

- ↑PT, ↔PTT = extrinsic pathway
  - Factor VII deficiency, liver disease, vitamin K deficiency,
  - Coumadin therapy
- ↑PT, ↑PTT = common pathway
  - Factors I, II, V, X or multiple factor deficiencies
  - Coumadin therapy
- ↔PT, ↑PTT = intrinsic pathway
  - Factors VIII, IX, XI, XII, or von Willebrand's disease
  - Heparin therapy
- ↔PT, ↔PTT
  - Platelet deficiency, vascular defect or factor XIII deficiency

Coagulation Studies

- Fibrinogen
  - Converted to fibrin by thrombin in common pathway
  - Diagnose fibrin disorders or inhibitors of thrombin
  - Normal = 150-350 mg/dL
- D-Dimer
  - Breakdown product of fibrin clots (fibrinolysis)
  - Elevated levels of Fibrin Degradation Products (FDP) and D-Dimer indicate increased fibrinolysis
  - Normal = < 200 ng/mL

Case 4: Additional Lab Results

- Additional tests:
  - PT/INR 2.4 (normal 0.9-1.1)
  - aPTT 76.8 (normal 28-40 seconds)
  - Fibrinogen 80 (normal 200-400 mg/dL)
  - D-dimer 13.5 (normal 0-0.4 ug/mL)

  - CMP: labs consistent with liver and kidney failure

ITP vs. TTP vs. DIC

	ITP	TTP	DIC
Pathogenesis	Antiplatelet antibodies	Endothelial defect	Thrombin excess
Clinical	Not sick	Sick	Sick
RBCs	Normal	Schistocytes	Schistocytes +/-
PT	Normal	Normal/Slight increase	Increased
PTT	Normal	Normal/Slight increase	Increased
Fibrinogen	Normal	Normal	Decreased
FDP	Normal	Slight increase	Increased
D-Dimer	Normal	Slight increase	Increased

Case 4

Final diagnosis: Severe Sepsis with DIC

In disseminated intravascular coagulation (DIC), the patient is in a hypercoagulable state. As fibrin clots are formed, platelets are decreased due to platelet aggregation, coagulation factors are decreased due to their use in the coagulation cascade, fibrinogen is decreased due to the conversion of fibrinogen to fibrin, and D-dimer is increased due to the excessive breakdown of fibrin.

Iba, T., Connors, J.M., Nagaoka, I. *et al.* Recent advances in the research and management of sepsis-associated DIC. *Int J Hematol* **113,** 24–33 (2021).

Take Home Points

- Appropriate interpretation of laboratory test results can eliminate unnecessary follow-up testing.
- Consider all laboratory test result abnormalities when establishing a diagnosis.
- Some laboratory test result abnormalities can alter other laboratory test results.
- Don’t rule out the possibility of multiple hematologic abnormalities in a given disease process.

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