

# Approach to Peripheral Smear Review

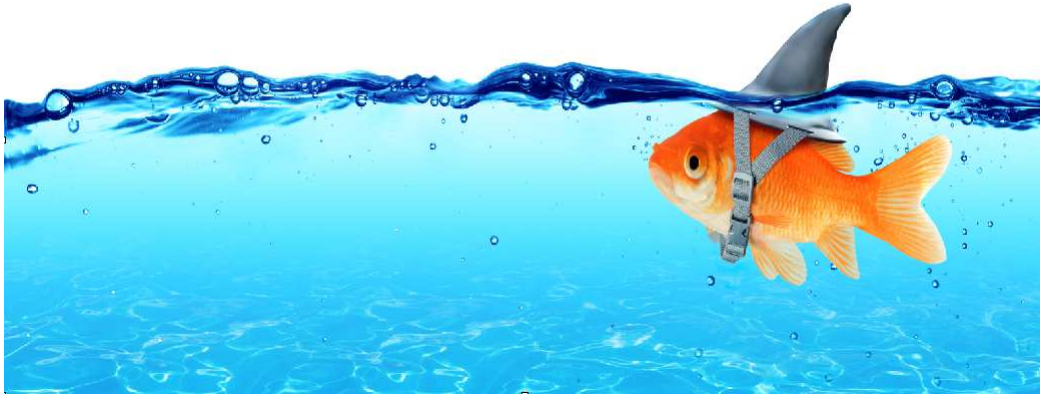
Current Concepts in Hematopathology 2022

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## Disclosures

- None

## Learning objective

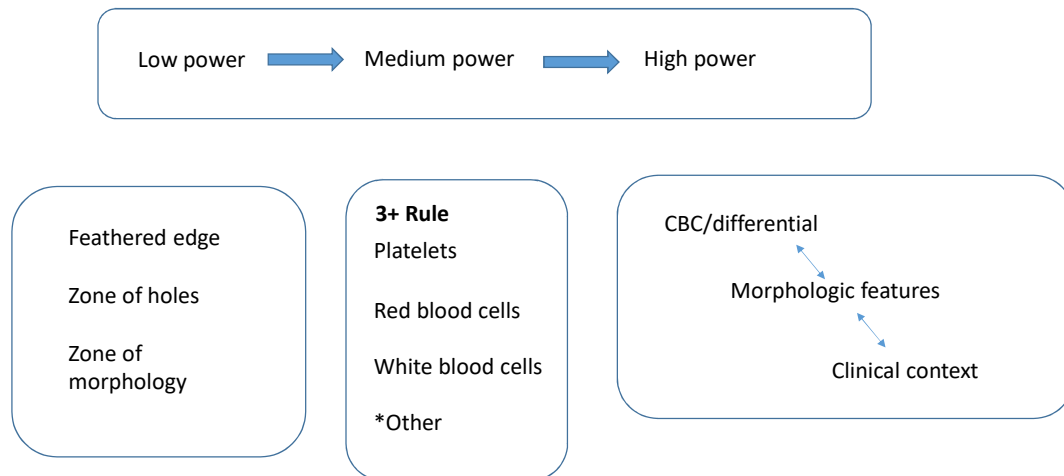


## Learning Objectives

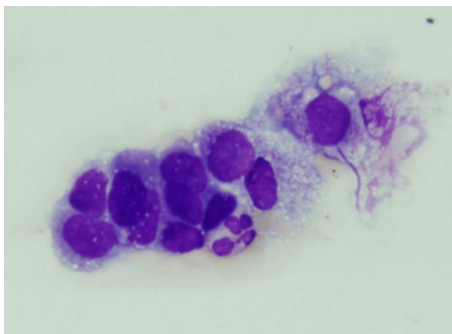
- Apply a systematic approach to peripheral blood smear evaluation
- Recognize the commonly identified platelet abnormalities
- Know terminology for red blood cell poikilocytosis, and be able to generate differentials based on the poikilocytes seen
- Recognize abnormal white blood cell cytomorphology
- Describe appropriate next steps for abnormal peripheral blood findings



## My approach to peripheral blood smear evaluation



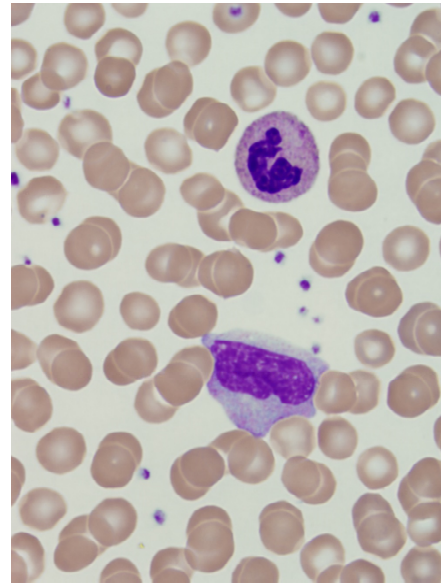
### Feathered edge



- Endothelial cells
- Squamous cells
- Circulating megakaryocyte
- Accumulation of white blood cells (high white count of >20,000/uL)
- Uneven distribution of white blood cells types between feathered edge/lateral edges and zone of morphology

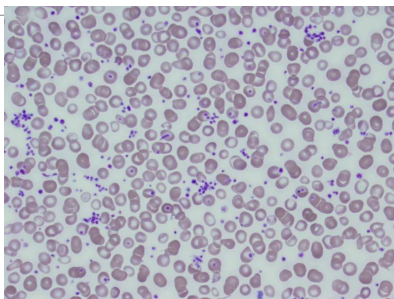
## Platelets

- Number
  - $150-400 \times 10^9/L$ , corresponding to 7-20 platelets per field at 1000x magnification.
- Size
  - 2-4  $\mu m$
- Granularity
  - fine purple granules
  - Three major storage granules:  $\alpha$  granules, dense ( $\delta$ ) granules, and lysosomes



## Thrombocytosis

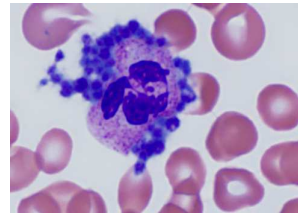
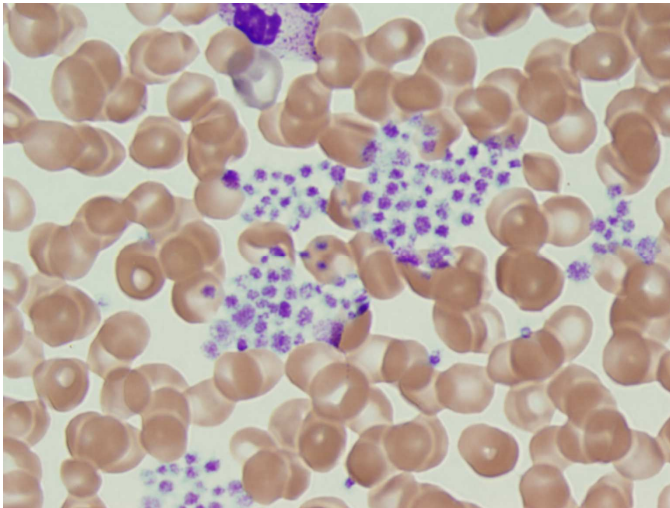
- Asplenia
- Iron deficiency
- Infectious processes
- Inflammatory processes
- Myeloid neoplasm



## Thrombocytopenia

- Spurious thrombocytopenia
- Microangiopathic hemolytic anemia
- Myeloid neoplasm
- Splenomegaly
- Liver disease
- Clotting
- Medication effect
- Idiopathic thrombocytopenic purpura

## Spurious Thrombocytopenia



### Next steps...

- Vortex
- Sodium citrate as anticoagulant (need to multiply certain CBC parameters by dilution factor)

Platelet clumping may be due to inadequate mixing of the blood tube prior to analysis, activation of platelets due to traumatic venipuncture or EDTA-dependent antibodies that react with platelet glycoprotein IIb/IIIa.

## Hypogranular platelets (grey platelets)

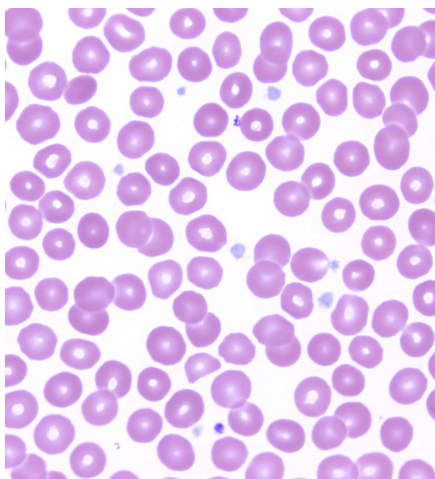
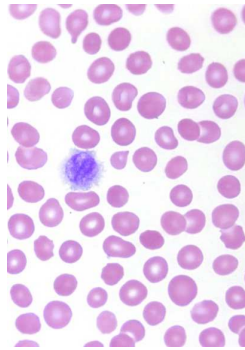
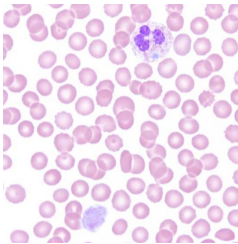


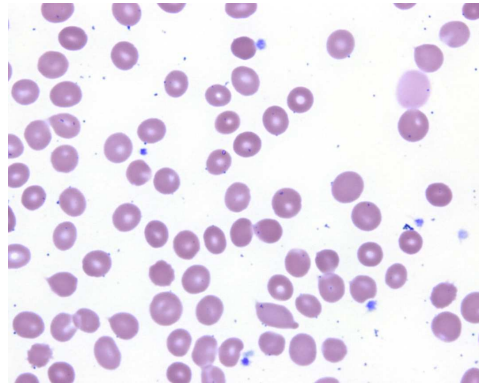
Image courtesy: Laura Brown, MD (UCSF)

- Artifact
  - Not all the platelets
  - Platelets activated by contact with foreign material (tube or slide)
- Myeloid neoplasm
  - Not all the platelets
  - Large /giant in size
  - Look for other clues
- Grey-platelet syndrome (rare platelet storage pool disorder)
  - All the platelets
  - Large in size
  - Autosomal recessive disease caused by germline homozygous mutations in *NBEAL2* gene
  - Mild to moderate bleeding diathesis
  - Moderate thrombocytopenia, splenomegaly, increased marrow fibrosis
  - Markedly reduced or absent  $\alpha$ -granules by EM

## Big platelets, little platelets



- Normal  $\leq$  Large  $\leq$  Giant  $\geq$  normal RBC
- Large/giant: younger platelets, can be seen rarely in normal PB, increased numbers in variety of conditions (nonspecific)



Thrombocytopenia and small platelets are seen in Wiskott-Aldrich syndrome and X-linked thrombocytopenia.

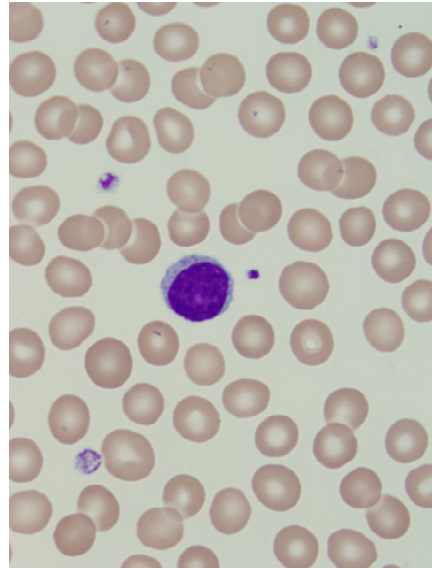
Images courtesy: Laura Brown, MD (UCSF)

## Practical points on platelet evaluation

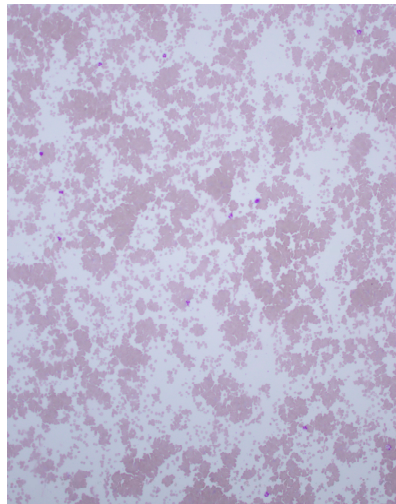
- ✓ Platelet clumping or satellitosis - vortex or recommend redraw
- ✓ Large, hypogranular platelets –clue to look carefully for other evidence of myeloid neoplasm
- ✓ Large/giant normal granulation –clue to look for inclusions of May-Hegglin
- ✓ Very small platelets – consideration of uncommon entities
- ✓ Low platelet count – look for clumping/satellitosis, red blood cell fragments, macrocytic RBCs with codocytes, dysplastic neutrophils/circulating blasts

## Red blood cells

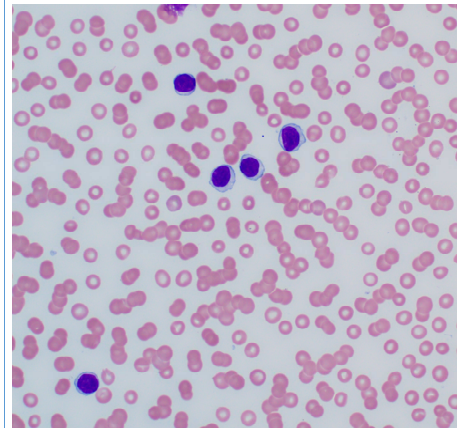
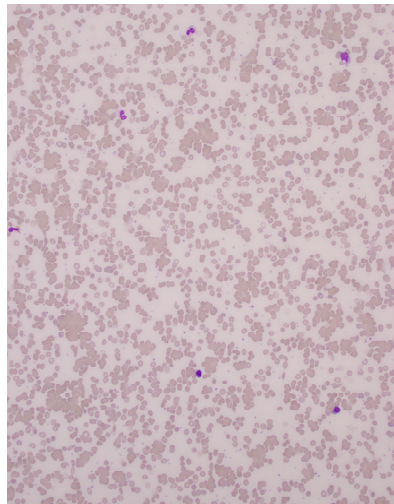
- Size
  - 6-8  $\mu\text{m}$
  - Anisocytosis = variation in size
- Color
  - Central zone of pallor normally comprises 1/3 of the area
- Shape(s)
  - Normally circular disks with smooth contours
  - Poikilocytosis = variation in shape



## Low power evaluation

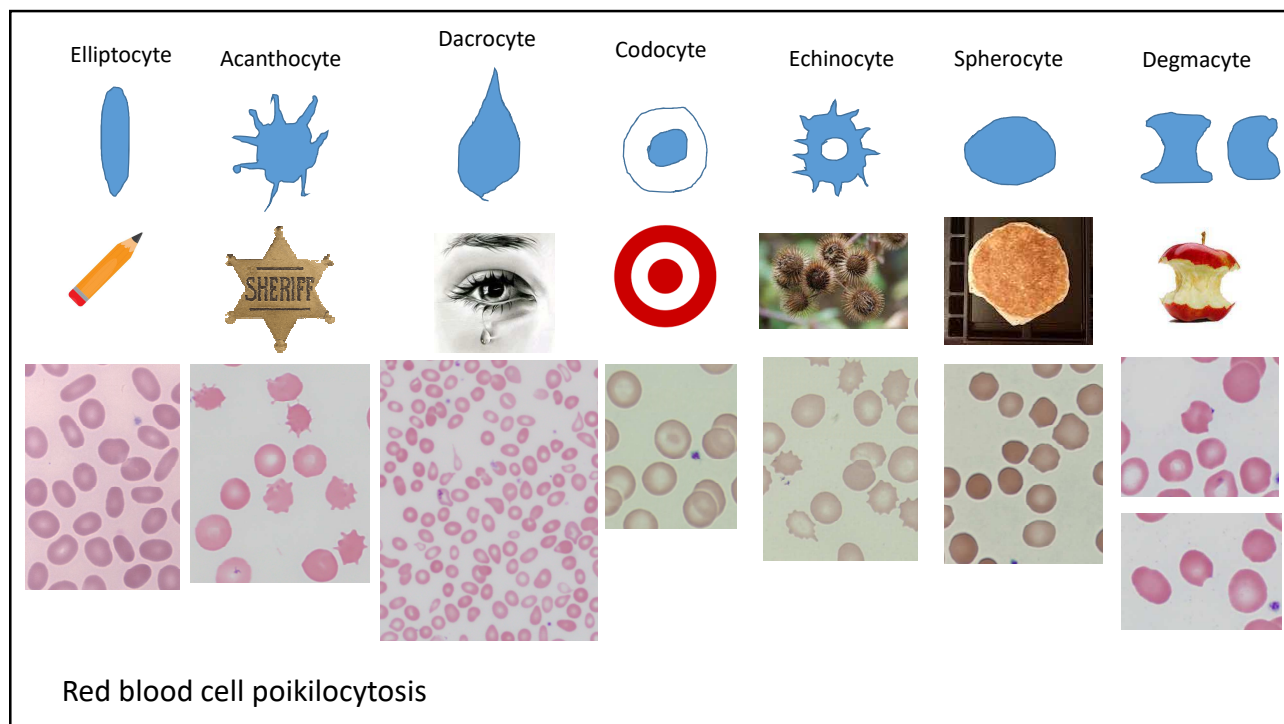









**Red blood cell agglutination** – may be due to infection (mycoplasma pneumonia), lymphoproliferative disorders or plasma cell disorders, or be idiopathic.



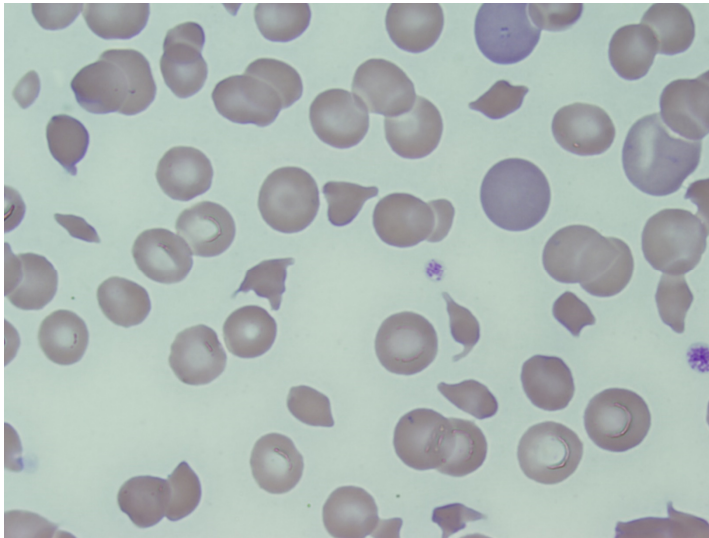
**Rouleaux** – associated with multiple myeloma, Waldenstrom macroglobulinemia, and infectious and inflammatory conditions (hyperproteinemia)





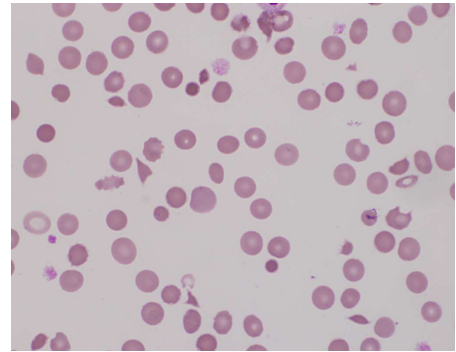
<b>Elliptocyte</b>  <ul style="list-style-type: none"> <li>• Hereditary elliptocytosis</li> <li>• Iron deficiency anemia</li> <li>• Thalassemia, burns, myelodysplasia, etc.</li> </ul>	<b>Codocyte</b>  <ul style="list-style-type: none"> <li>• Thalassemia</li> <li>• Hemoglobinopathies</li> <li>• Liver disease</li> </ul>	<b>Degmacyte</b>  <ul style="list-style-type: none"> <li>• Acute oxidation stress in G6PD deficiency</li> <li>• Hereditary Heinz body hemolytic anemia</li> <li>• Strong oxidant drugs (e.g. dapsone, phenylhydrazine)</li> </ul>
<b>Acanthocyte</b>  <ul style="list-style-type: none"> <li>• Advanced liver disease</li> <li>• Abetalipoproteinemia</li> <li>• McLeod blood group phenotype</li> <li>• MAHA, autoimmune hemolysis, thalassemia major, etc</li> </ul>	<b>Echinocyte</b>  <ul style="list-style-type: none"> <li>• Artifact</li> <li>• Uremia</li> <li>• Chronic renal disease</li> <li>• Liver disease</li> </ul>	
<b>Dacocyte</b>  <ul style="list-style-type: none"> <li>• Primary myelofibrosis</li> <li>• Bone marrow involvement by malignancy</li> <li>• Hemolytic anemia, iron deficiency, thalassemias, pernicious anemia</li> </ul>	<b>Spherocyte</b>  <ul style="list-style-type: none"> <li>• Hereditary spherocytosis</li> <li>• Immune hemolytic anemia</li> <li>• Burns, MAHA</li> </ul>	

### Microangiopathic hemolytic anemia (thrombotic microangiopathy)



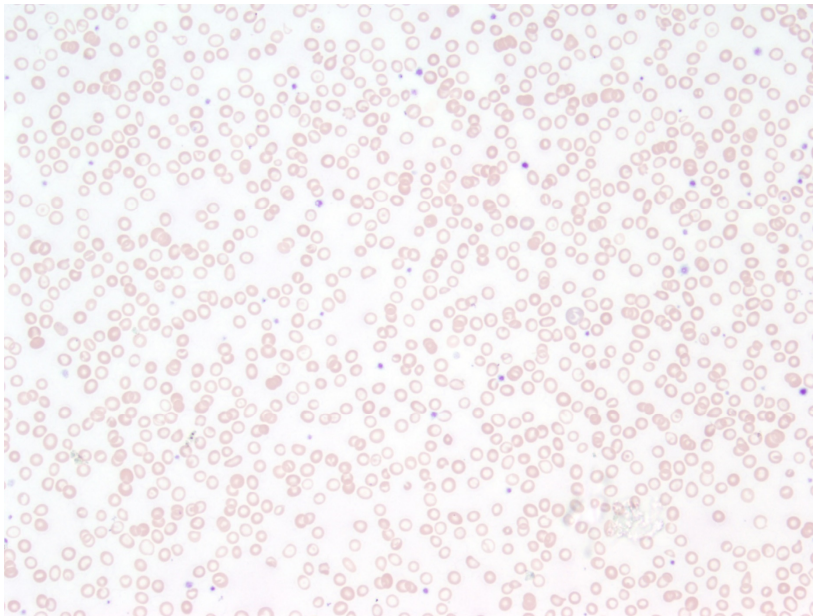
↑ lactate dehydrogenase (LDH)  
↑ indirect bilirubin  
↓ haptoglobin

Contact clinical team.

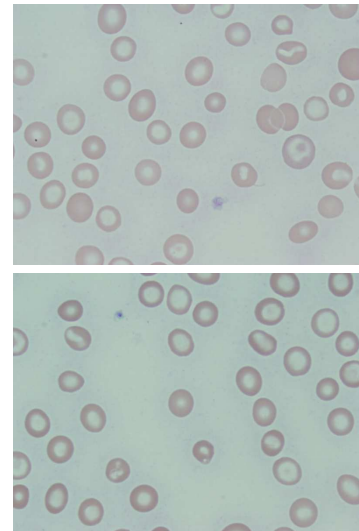


- Red blood cell fragments
  - Schistocytes, helmet cells, horn cells
  - Irregular cell shape; lack of central pallor
  - 1%, >2 per 50X hpf, >1 per 100X hpf
- Spherocytes
- Polychromasia/fine basophilic stippling
- Anemia and thrombocytopenia

### Iron deficiency anemia



Clara Camaschella; Iron deficiency: new insights into diagnosis and treatment. Hematology Am Soc Hematol Educ Program 2015; 2015 (1): 8–13. doi: <https://doi.org/10.1182/asheducation-2015.1.8>



Iron studies

# Iron deficiency anemia

Table 2. Laboratory tests to evaluate the iron status

	Iron deficiency	Functional iron deficiency	Iron deficiency anemia	IRIDA	Anemia of chronic disease	Iron deficiency and anemia of chronic disease	Normal values (adult subjects)
<b>Currently used tests</b>							
Serum iron	↓	N/↓	↓	↓	↓	↓	10-30 μMol/L
TSAT, %	≥16	N/↓	<16	<10	N/↓	N/↓	>16<45
Serum ferritin, μg/L	<30	N	<12	Variable	>100	<100	20-200 (F) 40-300 (M)
Hb g/dL	N	N	↓	↓	↓	↓	>12 (F) >13 (M)
MCV, fl	N	N	<80	↓↓	N/↓	↓	80-95
MCH, pg	N	N	<27	↓↓	N/↓	↓	27-34
<b>Other tests</b>							
sTFR	↑	↑	↑	↑	N/↑	Variable	†
sTFR/log ferritin	NA	NA	>2*	NA	<1*	>2*	
ZPP	N	↑	↑	↑	↑	↑	†
Serum hepcidin	↓	↓	↓	N/↑	↑	N/↑	†
CHR pg	<25	<29	↓	↓	↓	↓	31.2±1.6
BM iron staining	+	±	-	+	+++	+	±

N indicates normal; TSAT, transferrin saturation; F, females; M, males; Hb, hemoglobin; ZPP, Zn Protoporphyrin; CHR, reticulocyte Hb content; BM, bone marrow; MCV, mean corpuscular volume; MCH, mean corpuscular hemoglobin; and sTFR, soluble transferrin receptor.

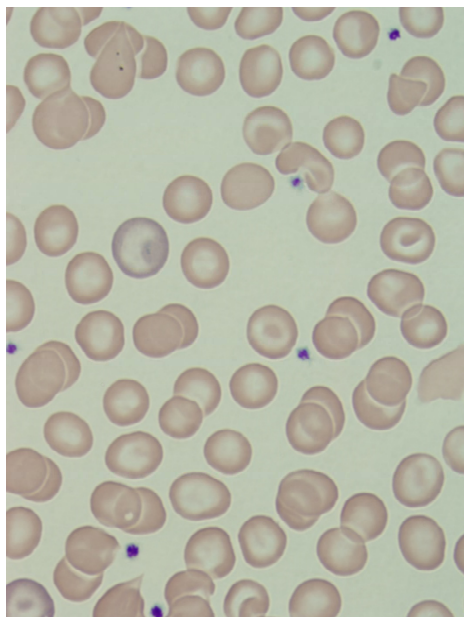
\* According to Weiss and Goodnough.<sup>28</sup>

† Normal values are according to the method used.

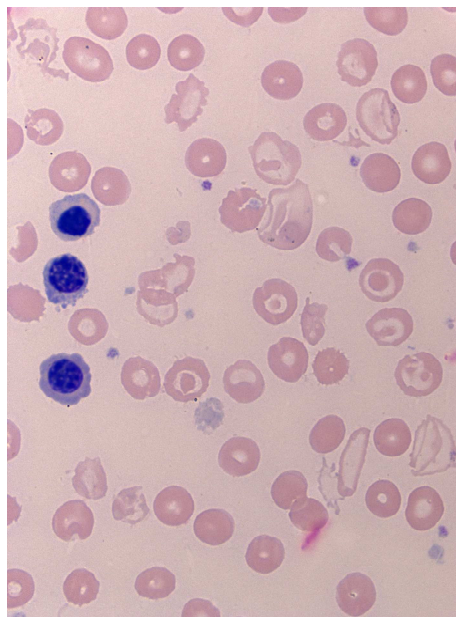
Adapted from Camaschella.<sup>14</sup>

Camaschella C. Iron deficiency: new insights into diagnosis and treatment. Hematology Am Soc Hematol Educ Program. 2015;2015:8-13. doi: 10.1182/asheducation-2015.1.8. PMID: 26637694.

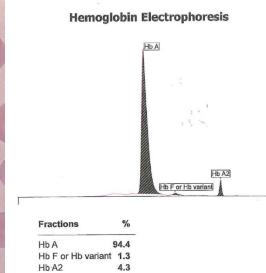
## Thalassemia



Beta thal minor



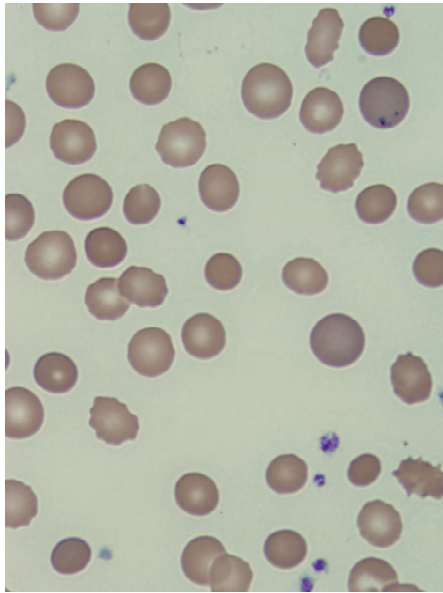
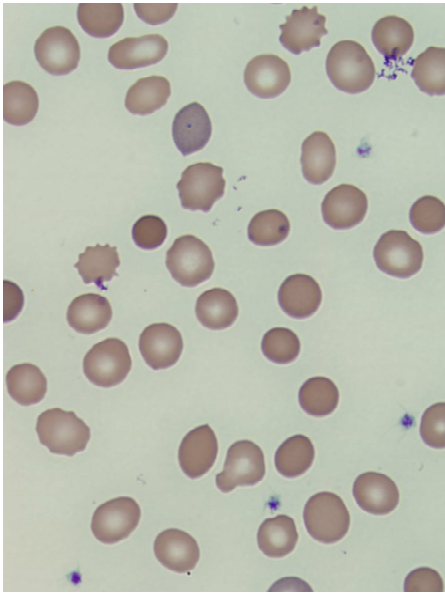
Beta thal intermedia



Iron studies and hemoglobin electrophoresis



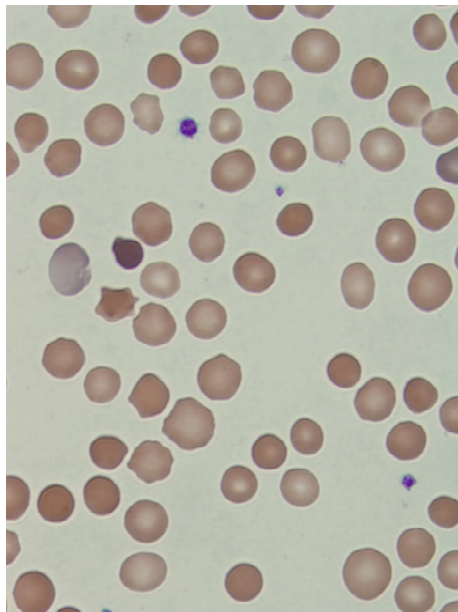
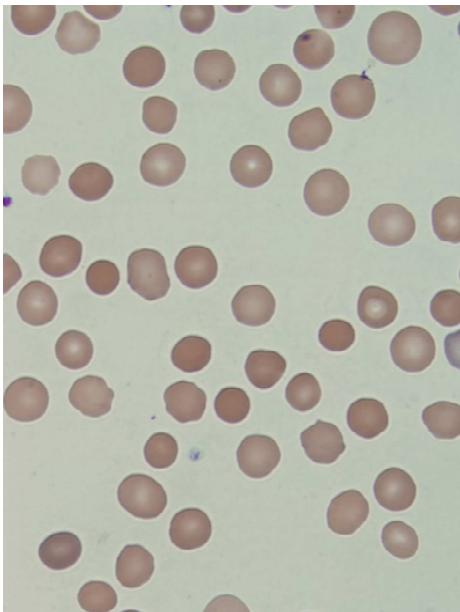
### Immune-mediated hemolysis



- RBC destruction due to antibodies and/or complement proteins bound to the RBC surface
- Autoimmune-hemolytic anemia, drug-induced hemolysis, hemolytic transfusion reaction, paroxysmal nocturnal hemoglobinuria (PNH), cold agglutinin disease
- Direct antiglobulin (Coombs) testing

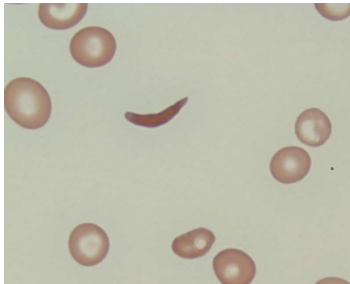
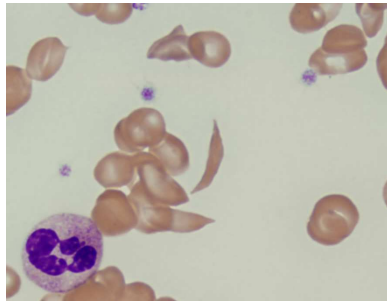
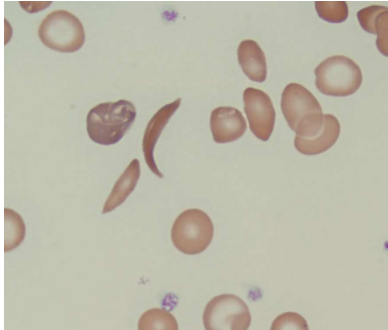
Evaluate for immune-mediated hemolysis

### Hereditary spherocytosis

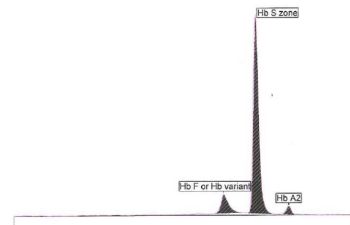


Rule out immune-mediated hemolysis; genetic testing

## Sickle cell disease



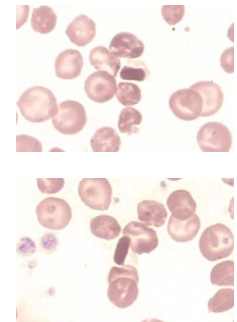
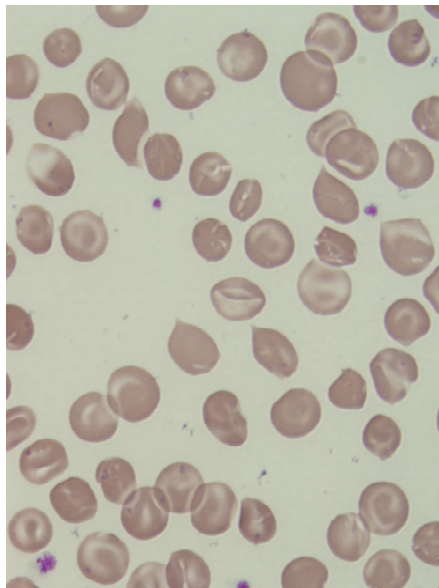
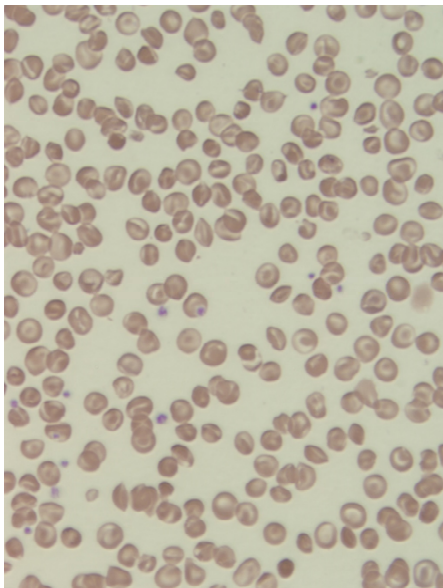
### Hemoglobin Electrophoresis



Fractions	%
Hb F or Hb variant	11.7
Hb S zone	85.1
Hb A2	3.2

Hemoglobin  
electrophoresis

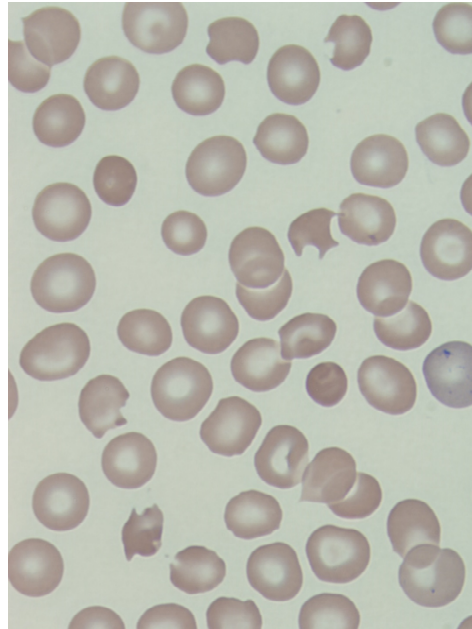
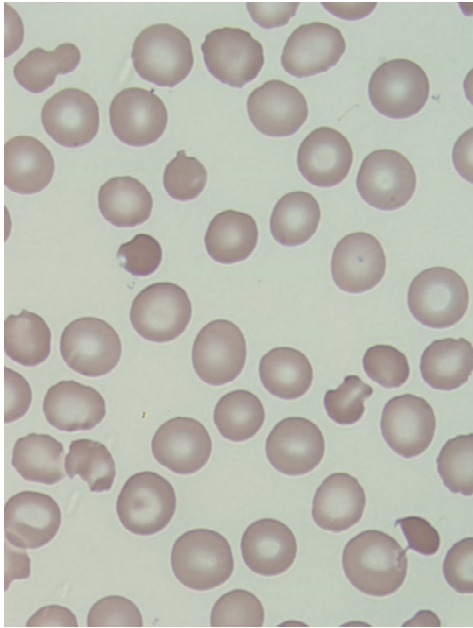
## Hemoglobin C



Hgb C crystals

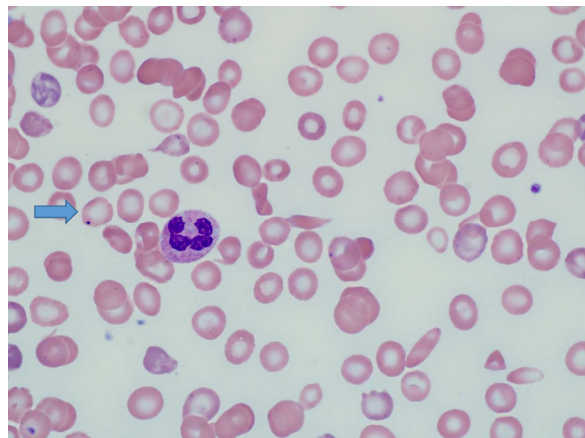
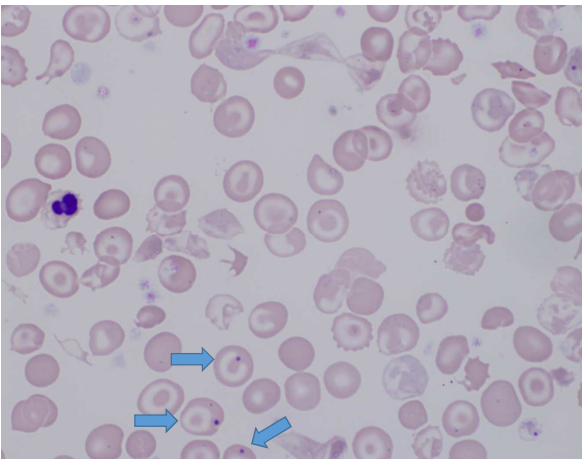
Hemoglobin  
electrophoresis

Oxidative hemolysis (dapsone)



Medication  
history

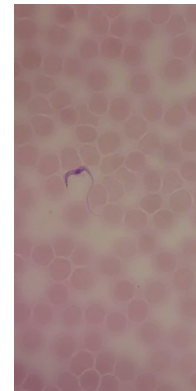
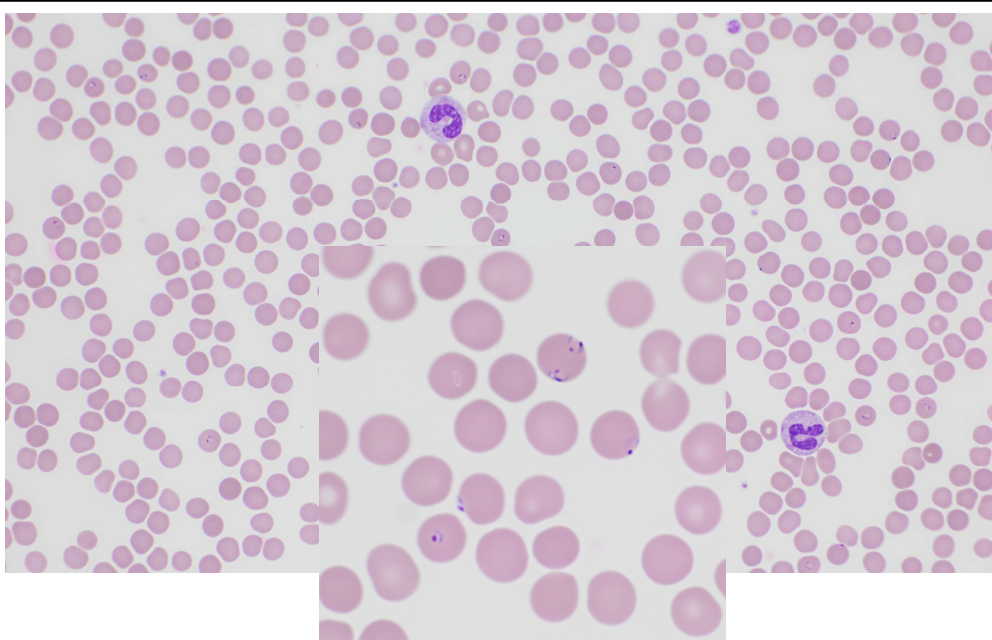
Asplenia



Don't over-interpret poikilocytosis

# Red blood cell inclusions

- **Howell-Jolly bodies**
  - Nuclear fragments normally removed by spleen
  - Asplenia or hypofunctioning spleen, severe hemolytic anemia, megaloblastic anemia
- **Pappenheimer bodies**
  - Lysosomes containing iron-protein complexes
  - Similar conditions as above
- **Basophilic stippling**
  - Coarse – aggregated ribosomes and polyribosomes; incomplete or impaired RNA degradation
  - Lead poisoning, thalassemias, hemoglobinopathies, sideroblastic anemia, MDS
- **Cabot rings**
  - Rare, ?remnants of microtubules of the mitotic spindle
  - Severe anemia
- **Parasites**



Images courtesy: Laura Brown, MD (UCSF)

Notify clinical team

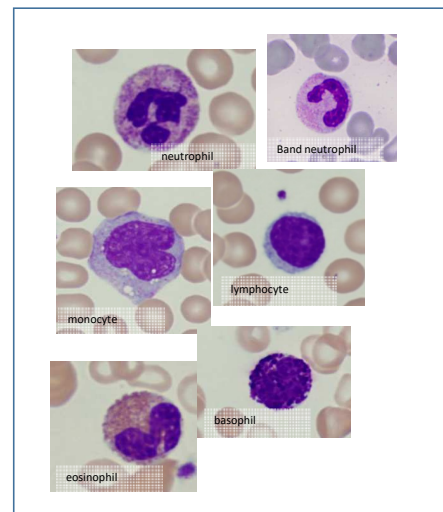


## Red blood cell reminders

- ✓ Contact the clinical team if see red blood cell fragments or parasites
- ✓ Evaluation of peripheral smear findings and CBC indices can help guide toward iron deficiency versus thalassemia
- ✓ Remember to look for Howell-Jolly bodies (indicating asplenia; functional hyposplenia) if marked poikilocytosis
- ✓ Remember to look for rouleaux/red cell agglutination on low power

## White blood cells

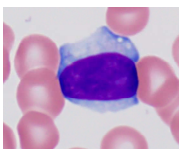
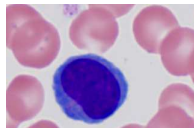
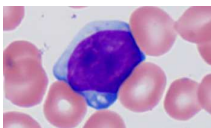
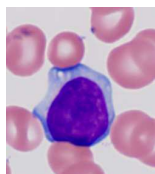
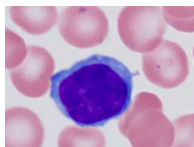
- Number
  - 4,000-11,000 per  $\mu\text{L}$  in adult
- Differential Count
  - Dependent on age of patient
  - In adults, neutrophils are the predominant WBC type.
- Normal vs abnormal cytology



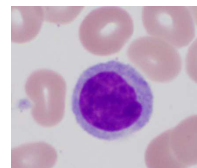
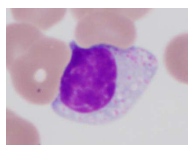
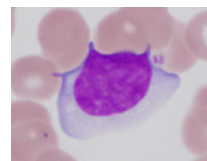
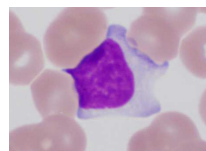
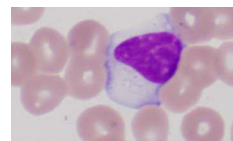
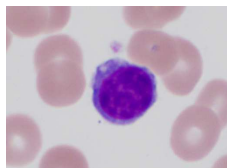
## Differential counts

- Manual differential count versus automated analyzer
- Manual – cellavision versus slide
- You are the expert
- Sometimes it is okay to be non-committal

## Lymphocytes

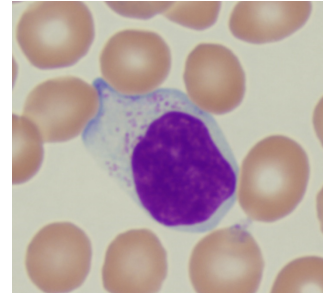
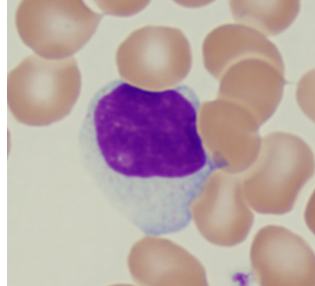
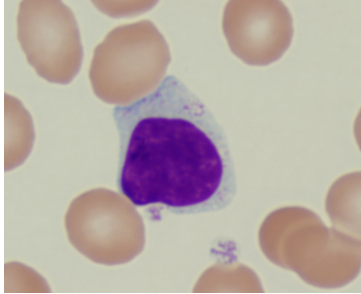


Representative lymphocytes from one patient



Representative lymphocytes from a different patient

## Large granular lymphocytes



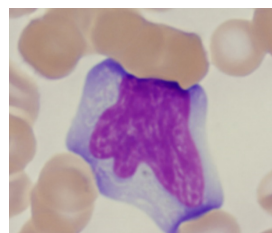
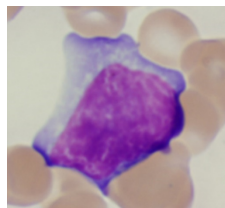
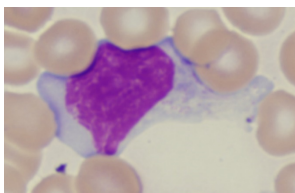
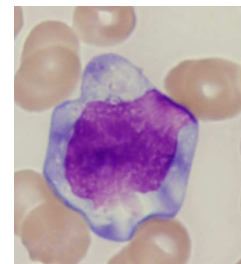
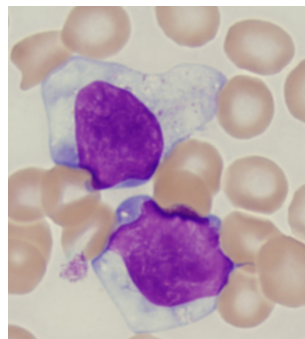
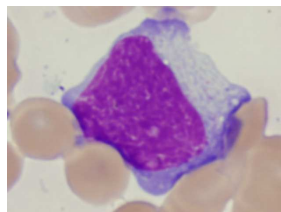
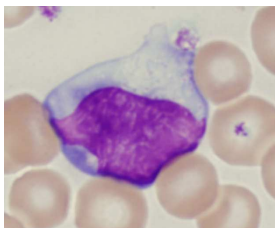
Expansions of T-large granular lymphocytes (T-LGLs) may occur:

- Following autologous and allogeneic stem cell transplants
- Following solid organ transplants
- In setting of dasatinib therapy for Ph+ B-ALL or CML
- With infection (viral)
- In the setting of B-cell clones

+/- flow cytometry

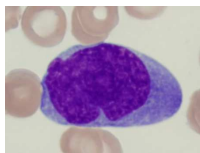
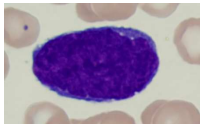
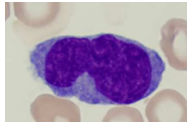
PMID: 17626255, 23355208, 26071471, 21617700

## Infectious mononucleosis

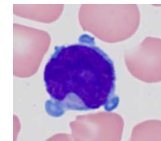
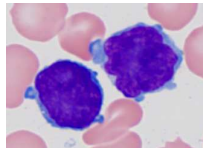


Monospot test; EBV titers

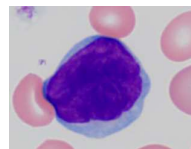
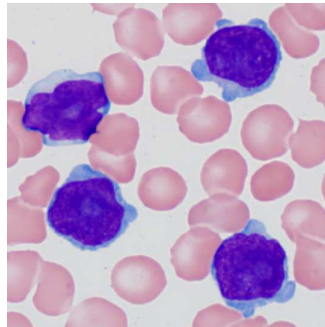
## Circulating lymphoma cells



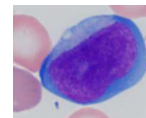
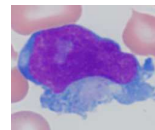
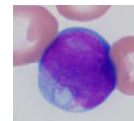
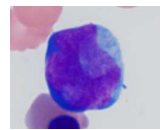
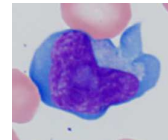
Mature T cell lymphoma



T-PLL



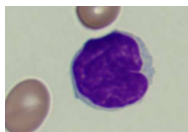
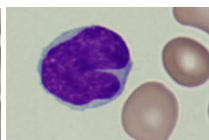
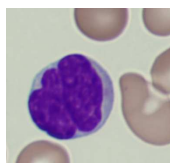
sezary



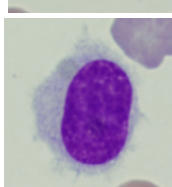
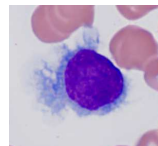
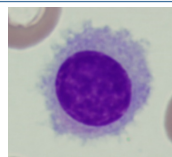
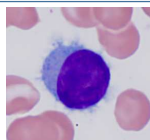
Hepatosplenic T cell lymphoma

Flow cytometry and clinical correlation

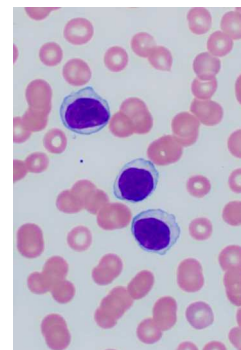
## Circulating lymphoma cells



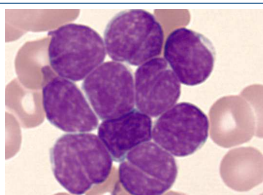
Mantle cell lymphoma



Hairy cell leukemia



Lymphoplasmacytic lymphoma

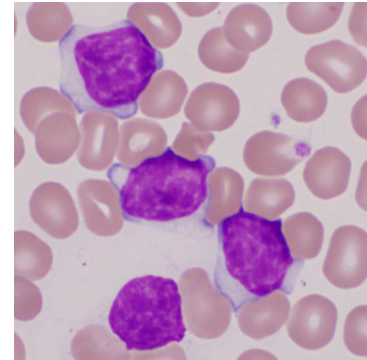
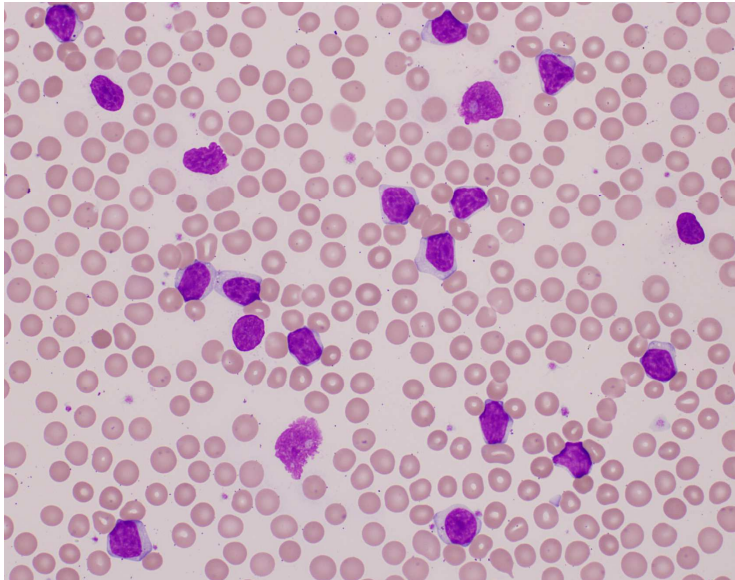


Follicular lymphoma

Flow cytometry and clinical correlation



## Chronic lymphocytic leukemia

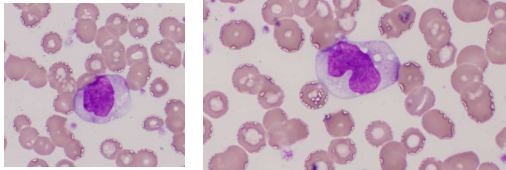
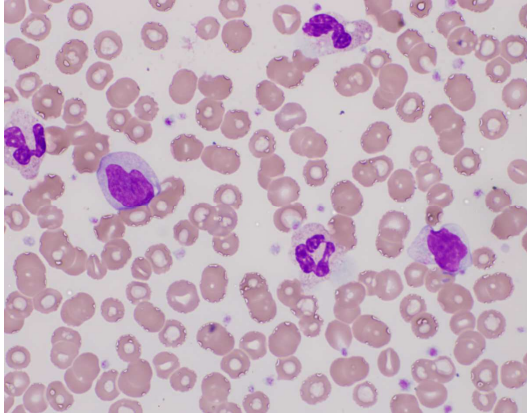


Flow cytometry and  
clinical correlation

## Flow cytometry for lymphocytosis

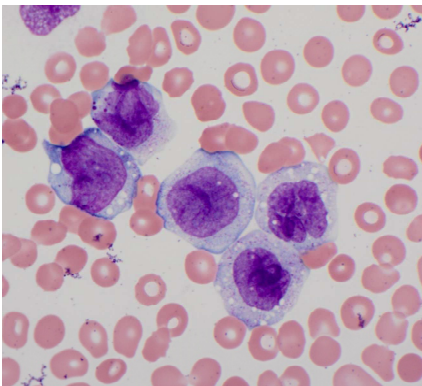
- ✓ Recommend flow cytometry for worrisome cytomorphology
- ✓ Exact approach to lymphocytosis likely to be institution/practice dependent
- ✓ Proposed cut-off for further review
  - ✓  $4.4 \times 10^9/\text{L}$  ALC for pts  $<75$  yo;  $4.0 \times 10^9/\text{L}$  ALC for pts  $>75$  yo.
  - ✓  $5 \times 10^9/\text{L}$  ALC for pts  $>35$  yo
- ✓ Transient stress lymphocytosis: abrupt increase in lymphocytes, recent hospitalization for trauma or medical event

## Monocytosis – reassuring features



- In the context of
  - Chronic infection
  - Recovery from acute infection
  - Postsplenectomy
  - CHL/NHL
  - Carcinoma
- No neutrophil dysplasia
- No circulating blasts
- No cytopenias
- Monocytes lack atypia

## Monocytosis – worrisome features



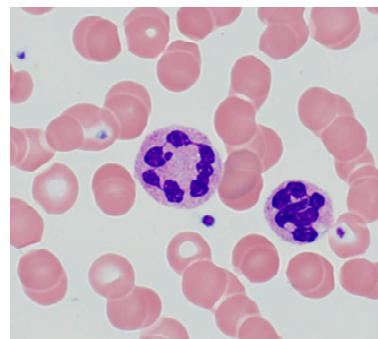
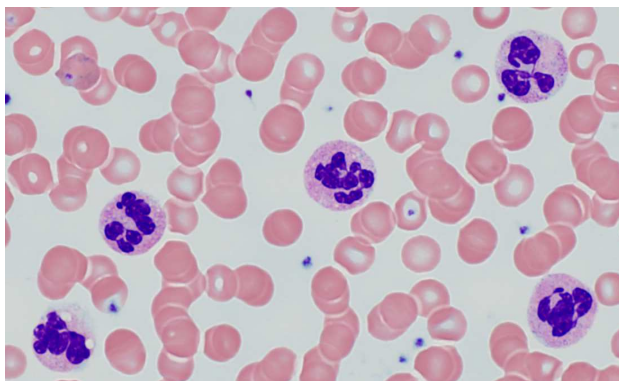
- Monocyte atypia
- Immature monocytes
- Circulating blasts
- Accompanying cytopenias
- Neutrophil dysplasia

## Flow cytometry of PB for monocytosis

- ✓ Utility depends on the flow cytometry panels available to your laboratory
  - ✓ Aberrant expression of CD56, decreased expression of HLA-DR, decreased expression of CD14
  - ✓ Increase in fraction of classical CD14+/CD16- monocytes
- ✓ Bone marrow biopsy may be the more appropriate next step
  - ✓ blasts/promonocytes present
  - ✓ monocytes appear atypical
  - ✓ dysplastic neutrophils are present
- ✓ Follow-up of counts may be the more appropriate next step
  - ✓ Reassuring clinical context
  - ✓ Monocytes are mature and typical in appearance

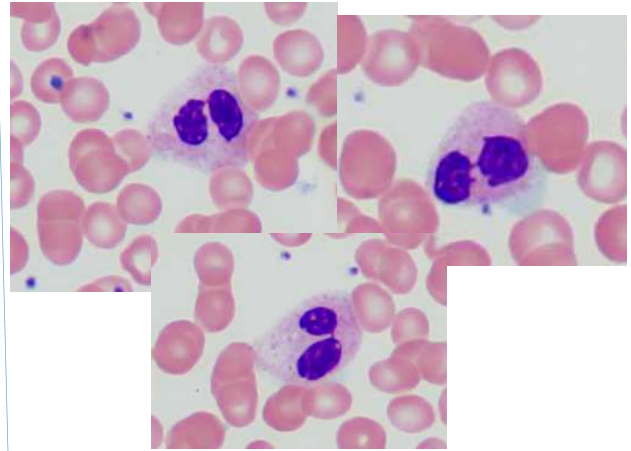
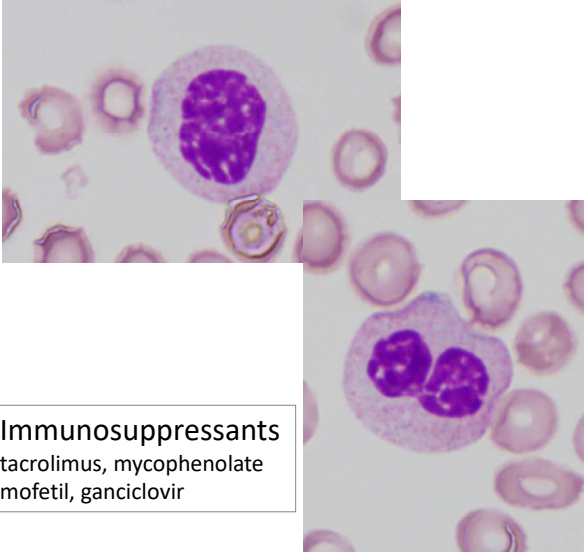
Selimoglu-Buet D, Wagner-Ballon O, Saada V, Bardet V, Itzykson R, Bencheikh L, Morabito M, Met E, Debord C, Benayoun E, Nloga AM, Fenaux P, Braun T, Willekens C, Quesnel B, Adès L, Fontenay M, Rameau P, Droin N, Koscielny S, Solary E; Francophone Myelodysplasia Group. Characteristic repartition of monocyte subsets as a diagnostic signature of chronic myelomonocytic leukemia. *Blood*. 2015 Jun 4;125(23):3618-26. doi: 10.1182/blood-2015-01-620781. Epub 2015 Apr 7. PMID: 25852055; PMCID: PMC4497970.

## Hypersegmented neutrophils



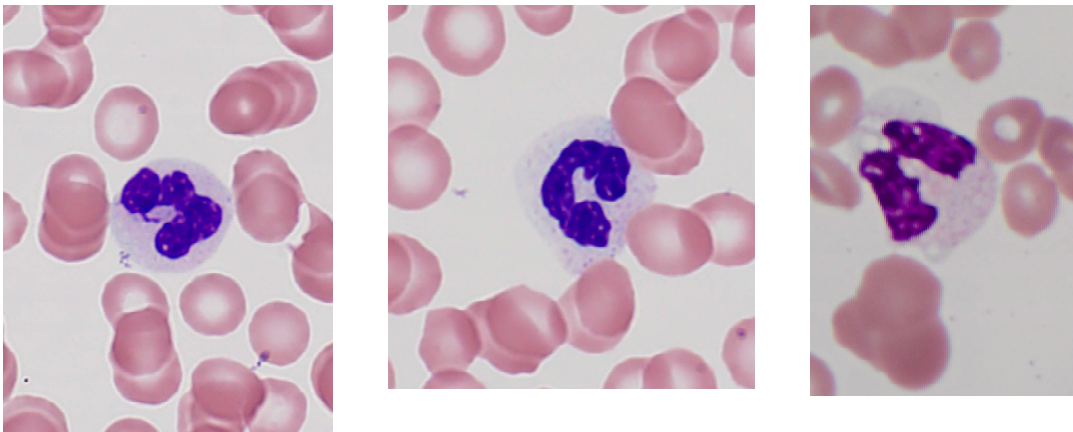
- Vitamin B12/folate deficiency
- Dysplasia
- Hydroxyurea therapy
- Normal variation (rare)

## Monolobate or bilobed neutrophils



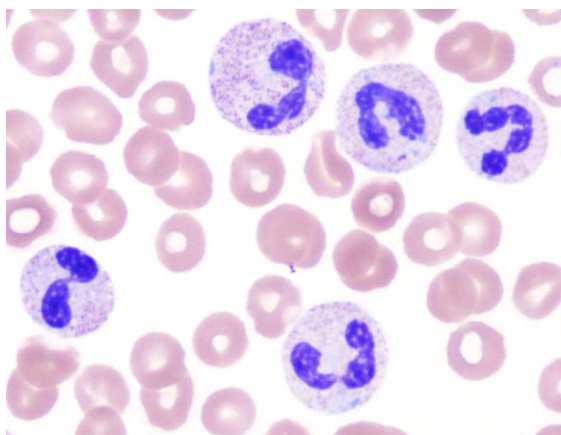
Pelger-Huet Anomaly  
benign congenital anomaly

## Hypogranular neutrophils

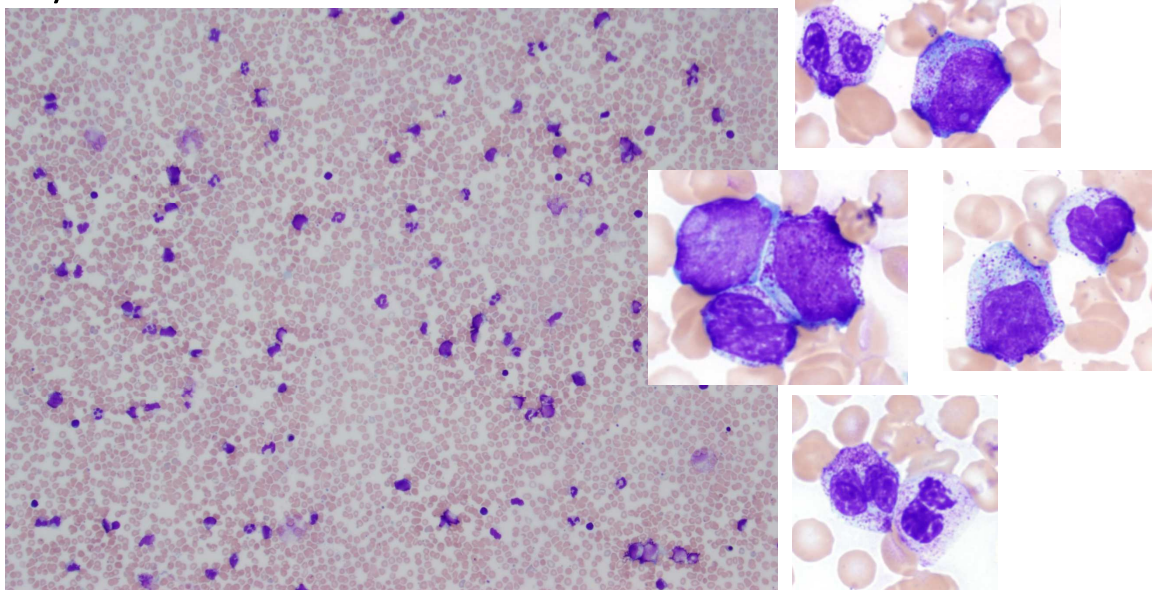




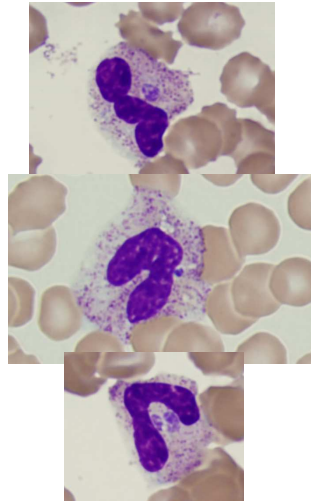
‘Toxic’ or reactive neutrophil changes



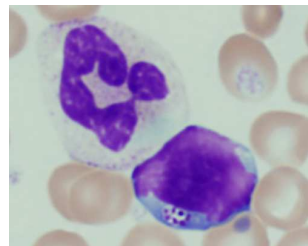
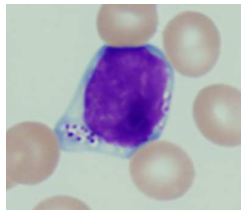
Myeloid left-shift



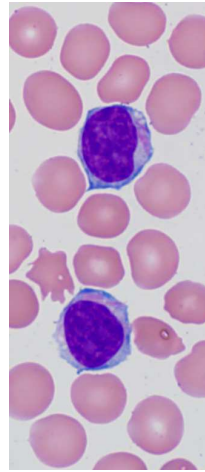
## White blood cell inclusions



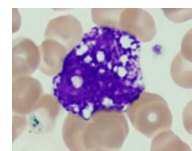
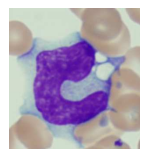
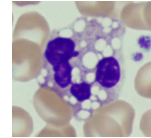
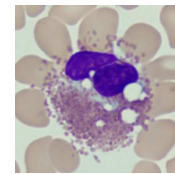
Anaplasmosis –bacterial disease transmitted to humans by deer tick



Mucopolysaccharidosis (inherited metabolic disorder with improper breakdown of mucopolysaccharides)

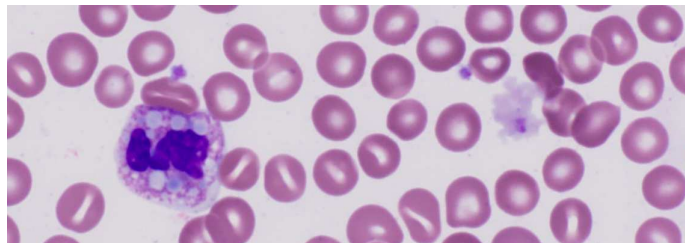
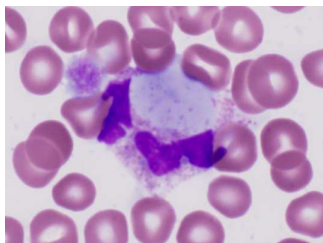


Marginal zone lymphoma with immunoglobulin inclusions

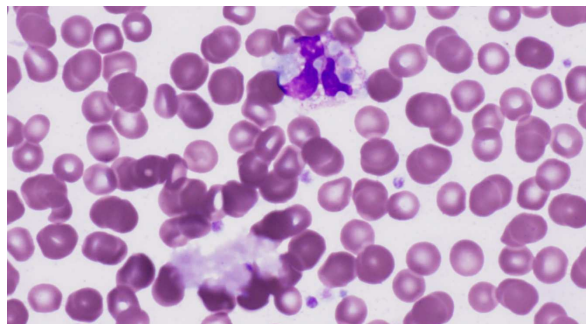


Jordans anomaly (finding in neutral-lipid storage disease)

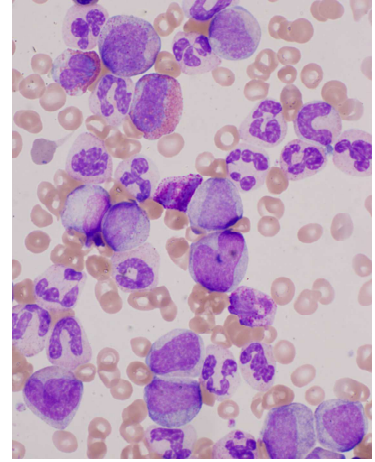
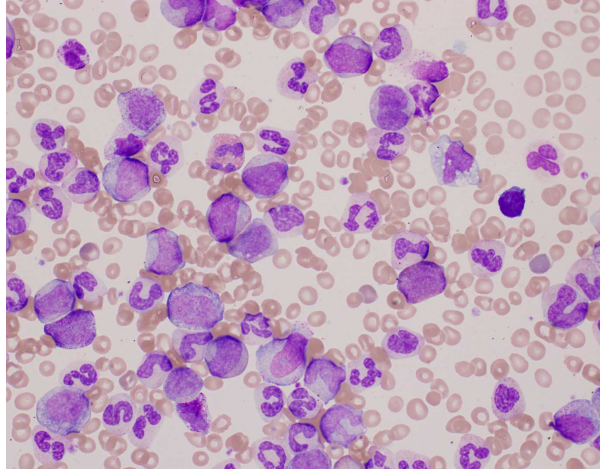
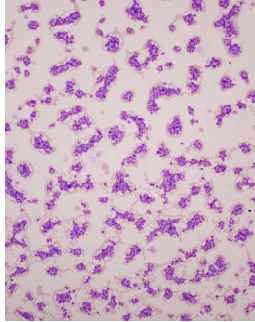
## Cryoglobulinemia



Cryoglobulinemia in patient with plasma cell neoplasm

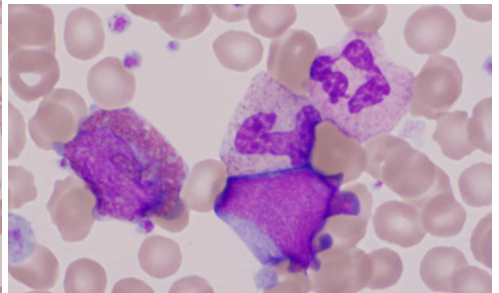
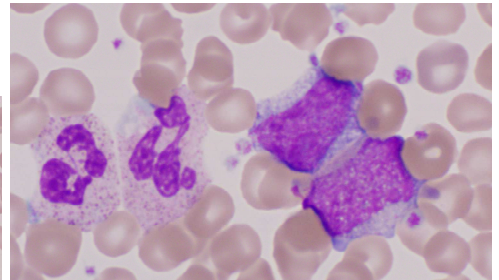
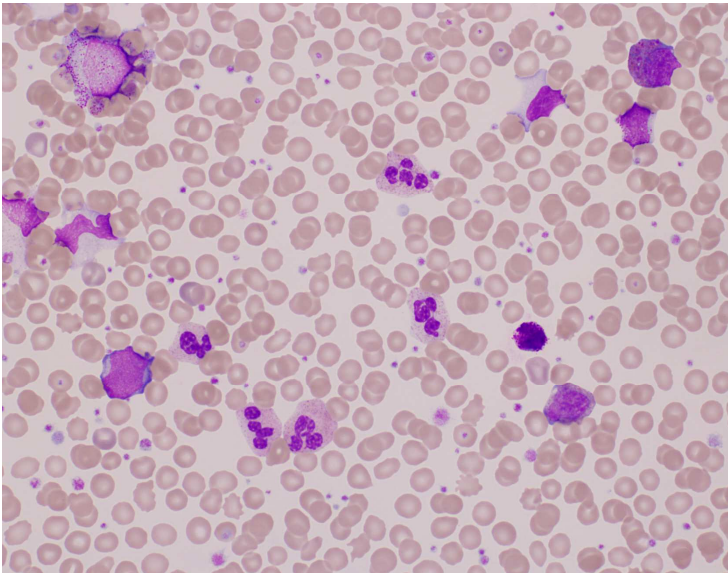


## Chronic myeloid leukemia



Documentation of *BCR-ABL1* fusion;  
accurate blast %, basophil %

## Chronic myeloid leukemia



Documentation of *BCR-ABL1* fusion;  
accurate blast %, basophil %



## Concern for CML

- CML shows variability in presentation with overlap with non-neoplastic etiologies
- Neutrophilia can be due to leukemoid reaction, infection, inflammation, steroids
- Variable CBC parameters have been evaluated as screening criteria:
  - Basophilia ( $>0.43 \times 10^9/L$ ); circulating immature granulocytes ( $>0.46 \times 10^9/L$ ) in pts with leukocytosis
  - $WBC \geq 20 \times 10^9/L$ ; Basophilia ( $>0.2 \times 10^9/L$ )

Fenu E, O'Neill SS, Insuasti-Beltran G. BCR-ABL1 p210 screening for chronic myeloid leukemia in patients with peripheral blood cytos. Int J Lab Hematol. 2021 Dec;43(6):1458-1464. doi: 10.1111/ijlh.13635. Epub 2021 Jun 29. PMID: 34185393.

Ogasawara A, Matsushita H, Tanaka Y, Shirasugi Y, Ando K, Asai S, Miyachi H. A simple screening method for the diagnosis of chronic myeloid leukemia using the parameters of a complete blood count and differentials. Clin Chim Acta. 2019 Feb;489:249-253. doi: 10.1016/j.cca.2018.08.038. Epub 2018 Aug 27. PMID: 30165034.



### American Society for Clinical Pathology

Thirty Five Things Physicians and Patients Should Question

Released February 21, 2014 (1–5), February 3, 2015 (6–10), September 14, 2016 (11–15), September 19, 2017 (16–20), September 25, 2018 (21–25), September 4, 2019 (26–30) and September 1, 2020 (31–35); Updated July 2021 (3)

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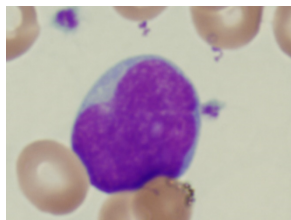
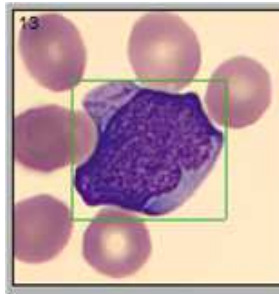
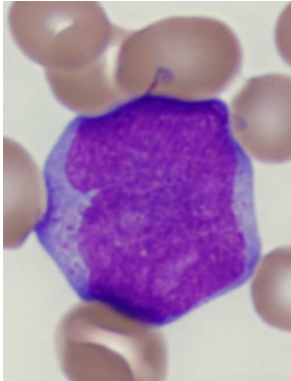
**Do not perform peripheral blood flow cytometry to screen for hematological malignancy in the settings of mature neutrophilia, basophilia, erythrocytosis, thrombocytosis, isolated anemia, or isolated thrombocytopenia.**

The role of peripheral blood flow cytometry for hematologic neoplasia is limited to settings in which either there are morphologically abnormal cells identified on a peripheral blood smear review (blasts, lymphoma cells) or there are clinical and/or laboratory findings that suggest a high pre-test probability for the presence of a disorder amenable to the immunophenotypic detection of neoplastic cells in the blood. The latter includes patients with neutropenia, absolute lymphocytosis, lymphadenopathy, or splenomegaly. The likelihood of flow cytometry of blood producing diagnostic results in the settings enumerated in the recommendation above is extremely low; bone marrow sampling with morphologic analysis (and appropriate ancillary diagnostic testing) may be indicated in those scenarios.

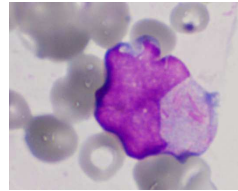
<https://www.choosingwisely.org/societies/american-society-for-clinical-pathology/>



## Lions and Tigers and Blasts, oh my!

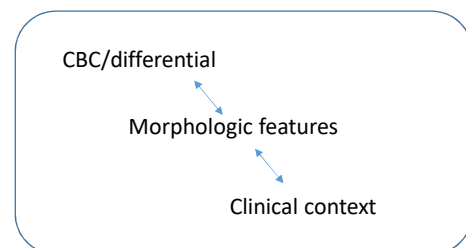


1. Take a breath
2. Are they really blasts?
3. What is the blast percentage?
4. What do the blasts look like?
5. What other cells are present?

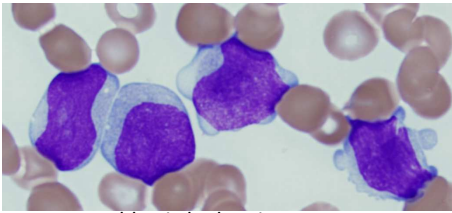


## Circulating blasts may be present in....

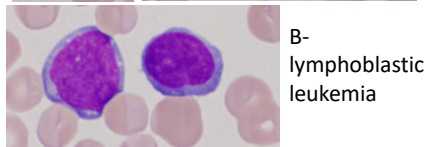
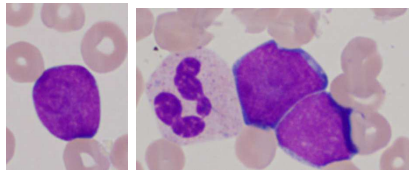
- Reactive myeloid left shift
  - Leukoerythroblastic blood picture (circulating nRBCs also)
  - Marrow regeneration
  - Recent chemotherapy
  - G-CSF
- Myelodysplastic syndrome
- Myeloproliferative neoplasm
- Acute myeloid leukemia
- Acute promyelocytic leukemia
- Acute lymphoblastic leukemia
- Circulating lymphoma cells (“blasts”)



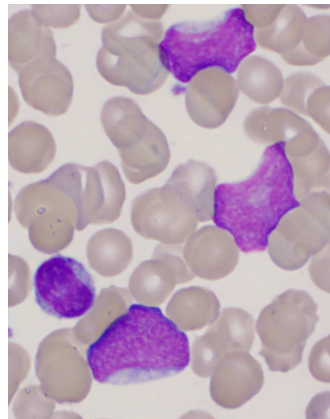
# Acute leukemia



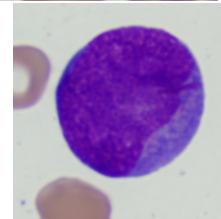
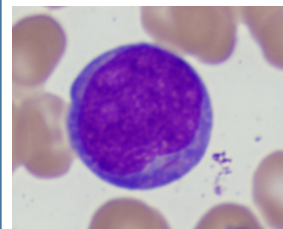
Acute monoblastic leukemia



B-lymphoblastic leukemia



B-lymphoblastic leukemia

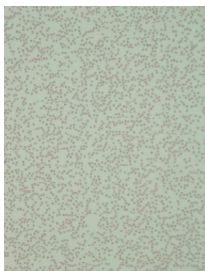


Acute myeloid leukemia t(8;21)

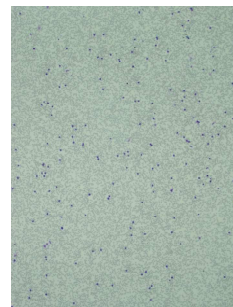
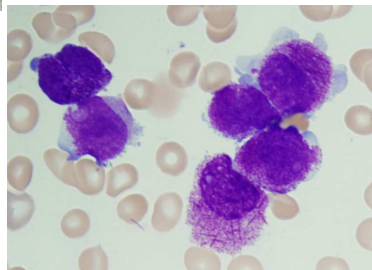
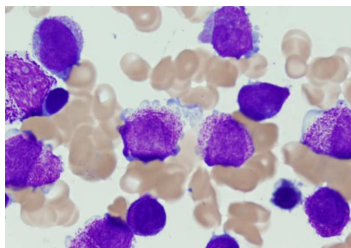
Additional work-up peripheral blood (flow cytometry/cytogenetics/molecular); bone marrow work-up

Contact clinical team.

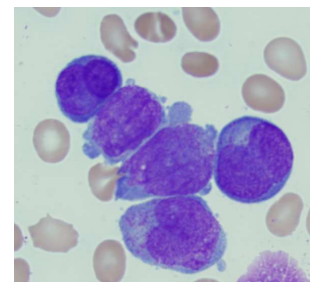
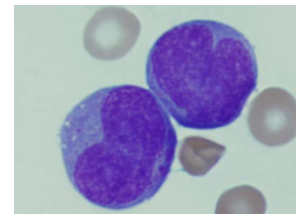
## APL- typical vs hypogranular



**Typical/Hypergranular**  
(60-70% of cases): low WBC, abundant cytoplasmic granules and bundles of Auer rods, weak or absent HLA-DR and absent CD34

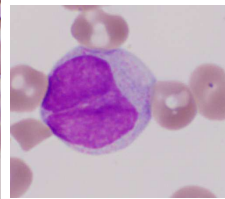
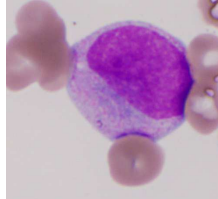
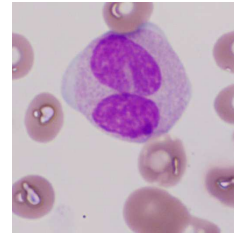
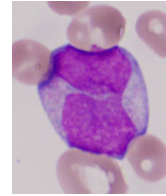
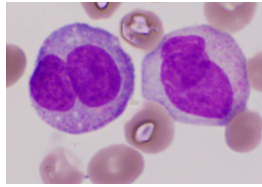
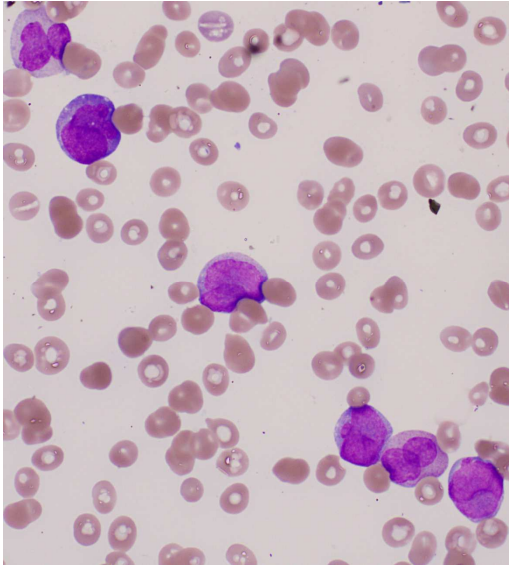


**Hypogranular/microgranular:**  
leukocytosis, indistinct granules and folded nuclei  
Some cases of microgranular APL can show dim CD34 and/or HLA-DR expression

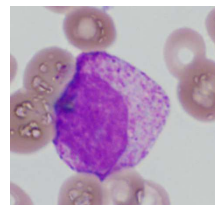
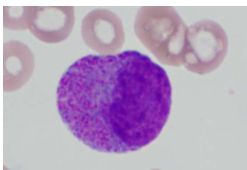
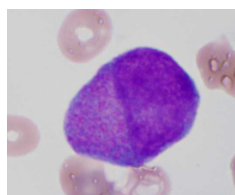
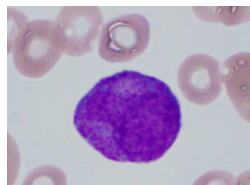
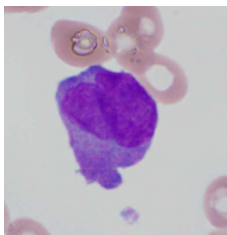


Contact clinical team. Rapid evaluation for PML/RARA

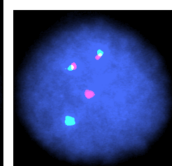
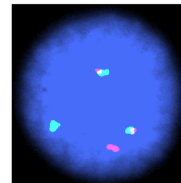
## Acute promyelocytic leukemia



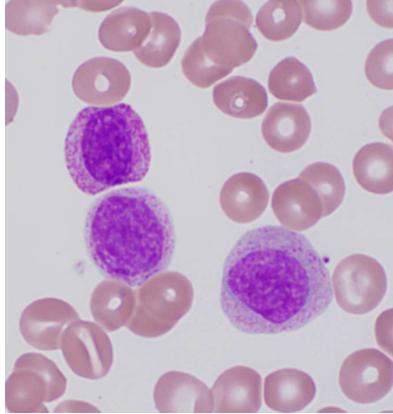
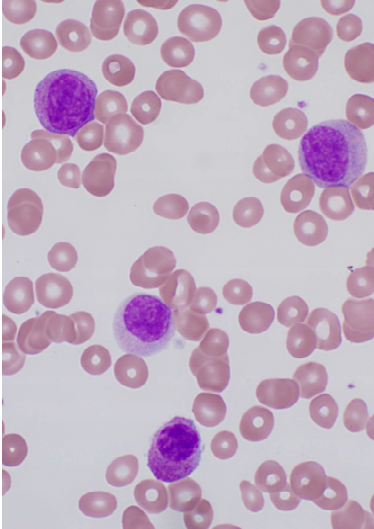
## Acute promyelocytic leukemia



PML/RARA t(15;17)



## Variant APL



- <5% of APL lack t(15;17)
- Non-*PML* translocations involving the *RARA* gene
- Described variant fusion partners include *ZBTB16* (previously termed *PLZF*), *NPM1*, *NUMA1*, and *STAT5b*, among others, with *ZBTB16/RARα* being the most common.
- *ZBTB16/RARα* APL blasts are distinct from classic APL, with more regular nuclei with condensed chromatin and abundant cytoplasm with coarse granules and fewer Auer rods.
- Most AML FISH analyses employ standard t(15;17) probe sets, which reveal an additional signal for *RARα* in variant APLs

Elizabeth L Courville, MD, Lindsey Shantzer, MD, Hans Christoph Vitzthum von Eckstaedt, V, BS, Holly Mellot, BSN, Michael Keng, MD, Jeremy Sen, PharmD, Amy Morris, PharmD, Eli Williams, PhD, Firas El Chaer, MD, Variant Acute Promyelocytic Leukemia Presenting Without Auer Rods Highlights the Need for Correlation with Cytogenetic Data in Leukemia Diagnosis, Laboratory Medicine, Volume 53, Issue 1, January 2022, Pages 95–99, <https://doi.org/10.1093/labmed/lmab051>

## Leukocyte Lessons

- ✓ Flow cytometry is very helpful in the workup of lymphocytes with abnormal cytology
- ✓ Yield of flow cytometry for absolute lymphocytosis is variable
- ✓ Neutrophils with abnormal nuclear segmentation or granulation can raise the differential of myelodysplasia
  - ✓ There are important caveats/mimics
- ✓ A systematic approach to the presence of circulating blasts is helpful
- ✓ Have a low threshold to raise possibility of acute promyelocytic leukemia



Low power → Medium power → High power

CBC/differential

Morphologic features

Clinical context

### 3+ Rule

Platelets

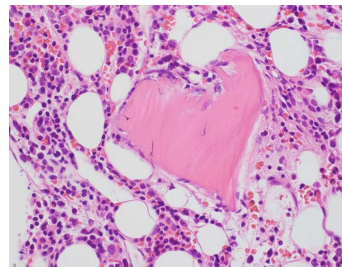
Red blood cells

White blood cells

\*Other

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- Julie Qualtieri, Laura Brown, Laura Wake, Sonam Prakash, Rose Beck, Alexa Siddon (Society for Hematopathology Education committee)
- Residents for asking hard questions.





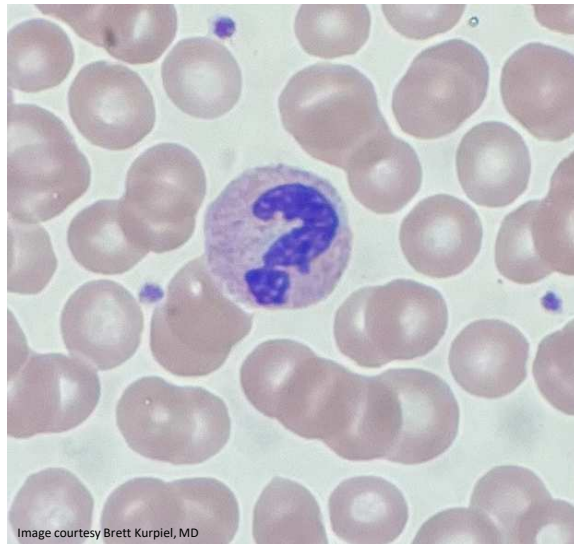


Image courtesy Brett Kurpiel, MD