Anemia

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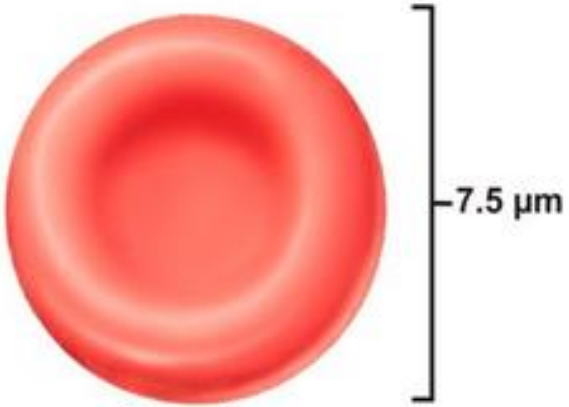
Objectives

- Know how to read a CBC (complete blood count)
- Approach to common causes of anemia
- Understand the common terminologies
- Brief overview of investigations and management

RBCs

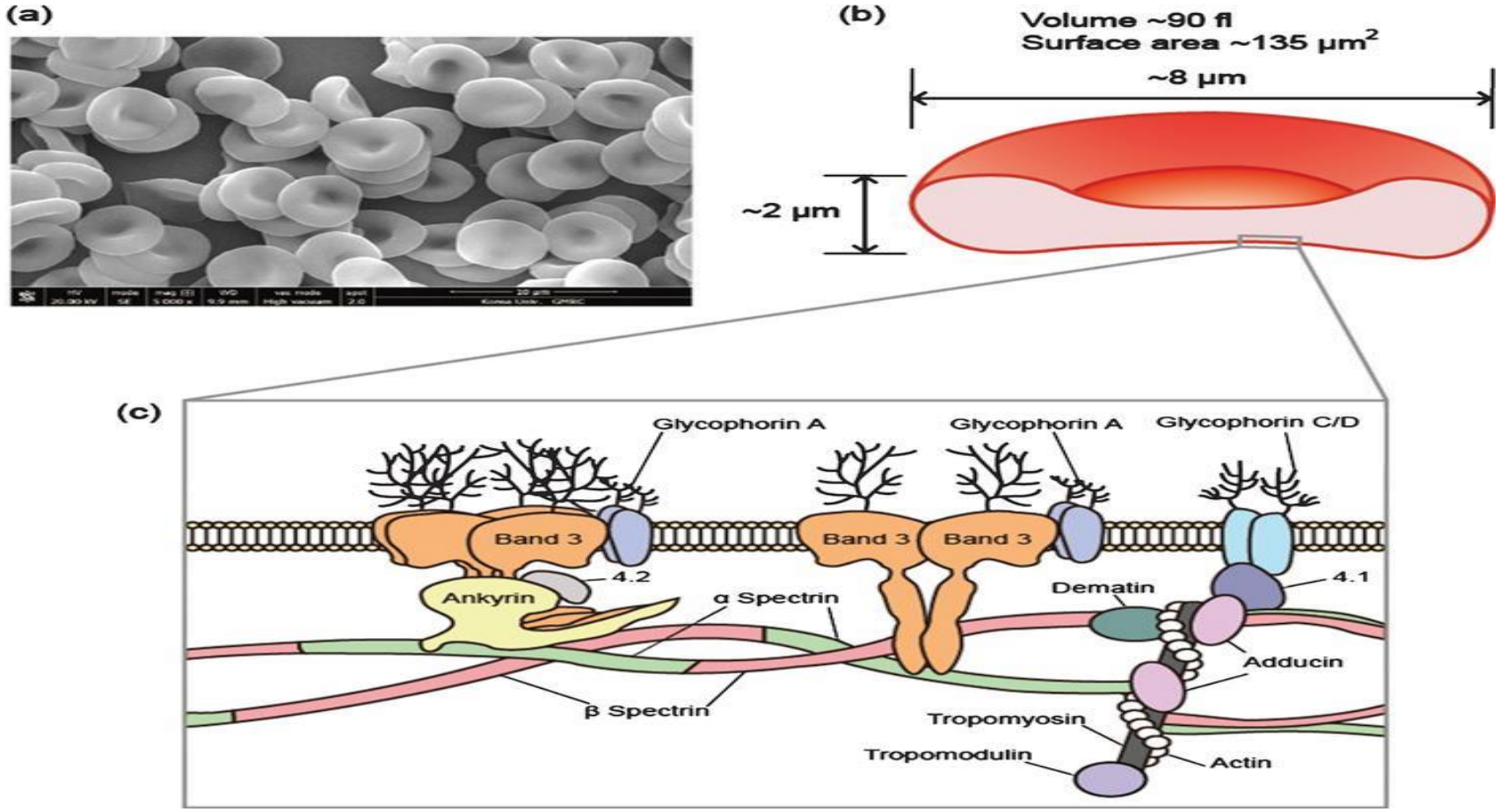
- Main function is to carry oxygen
- Biconcave disks
- Essentially bags of hemoglobin; few organelles
- Anucleate (no nucleus)
- Outnumber white blood cells 1000:1
- Contain the plasma membrane protein spectrin and other proteins
- Major factor contributing to blood viscosity

Side view (cut)

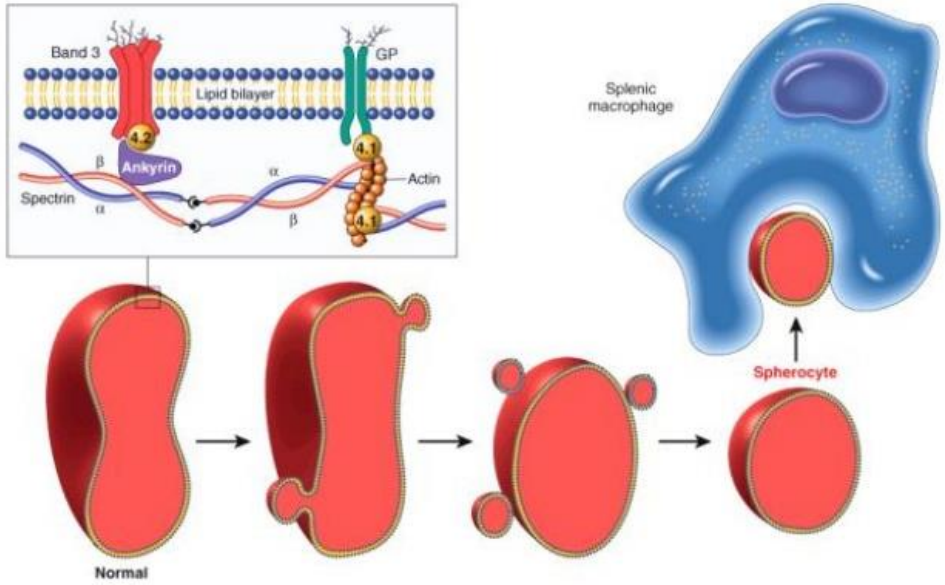


Top view

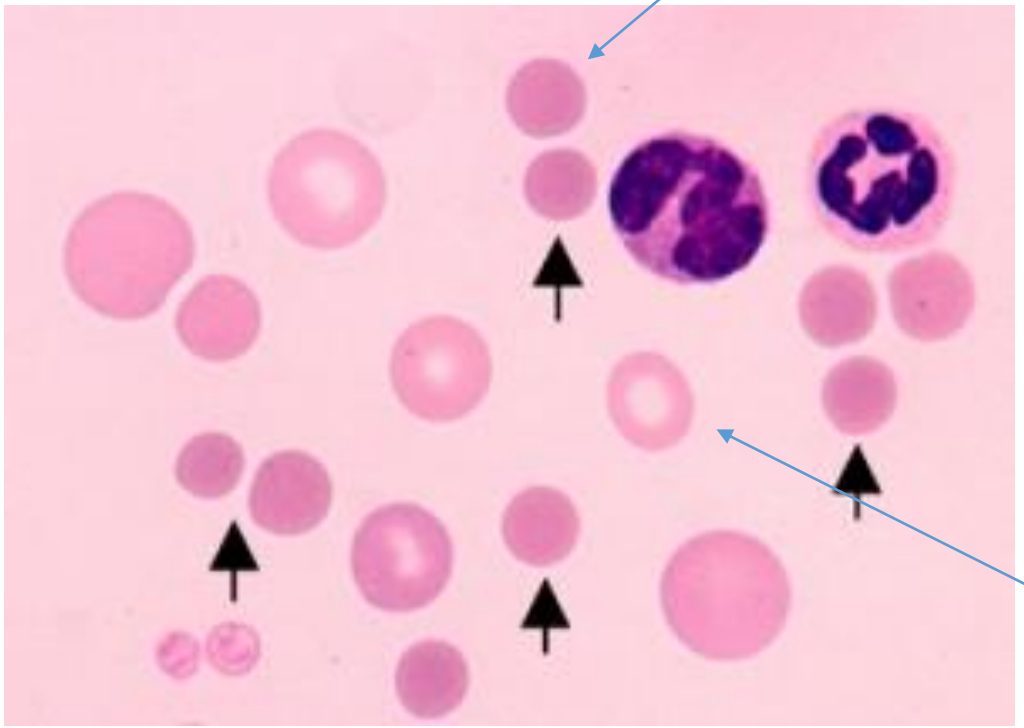
What keep them biconcave?



Terminology: spherocytosis



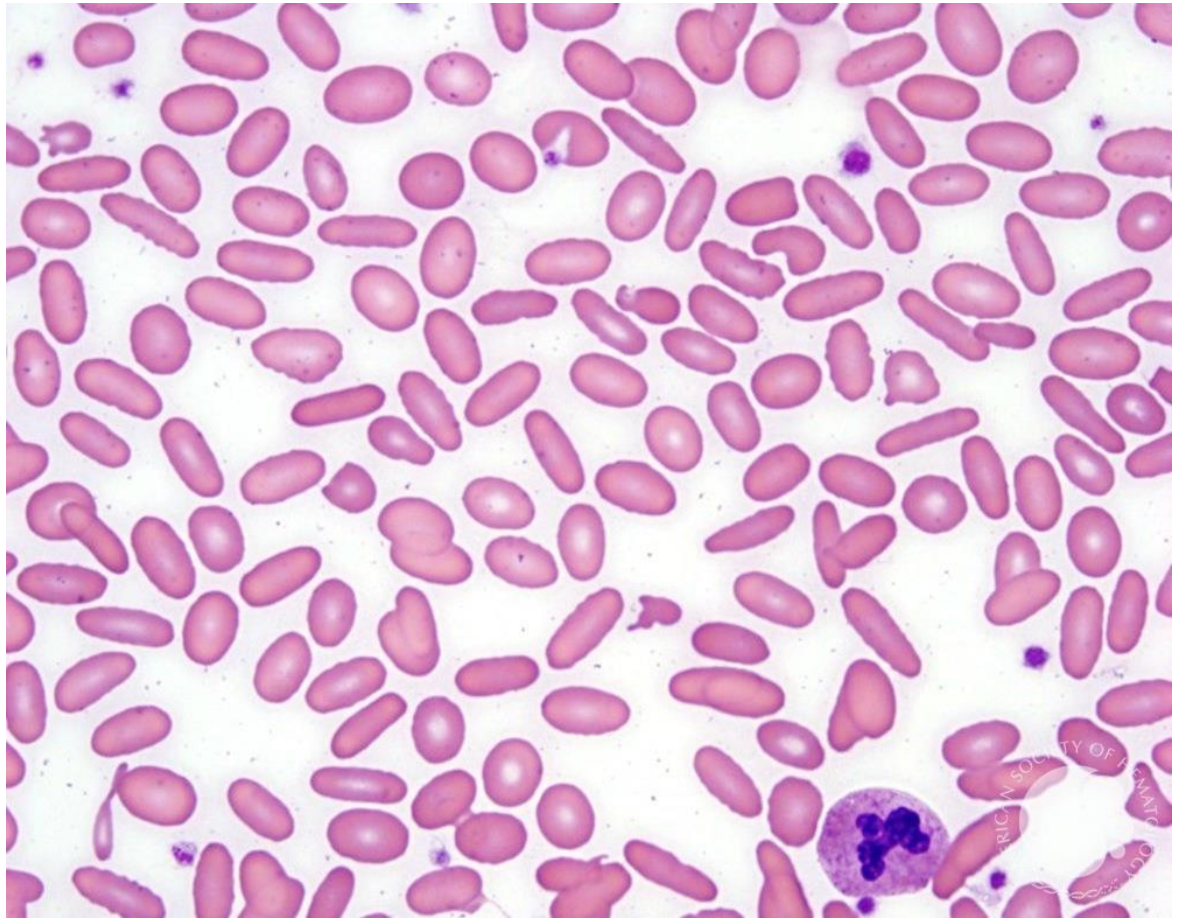
Schematic representation of the red cell membrane cytoskeleton and alterations leading to spherocytosis and hemolysis



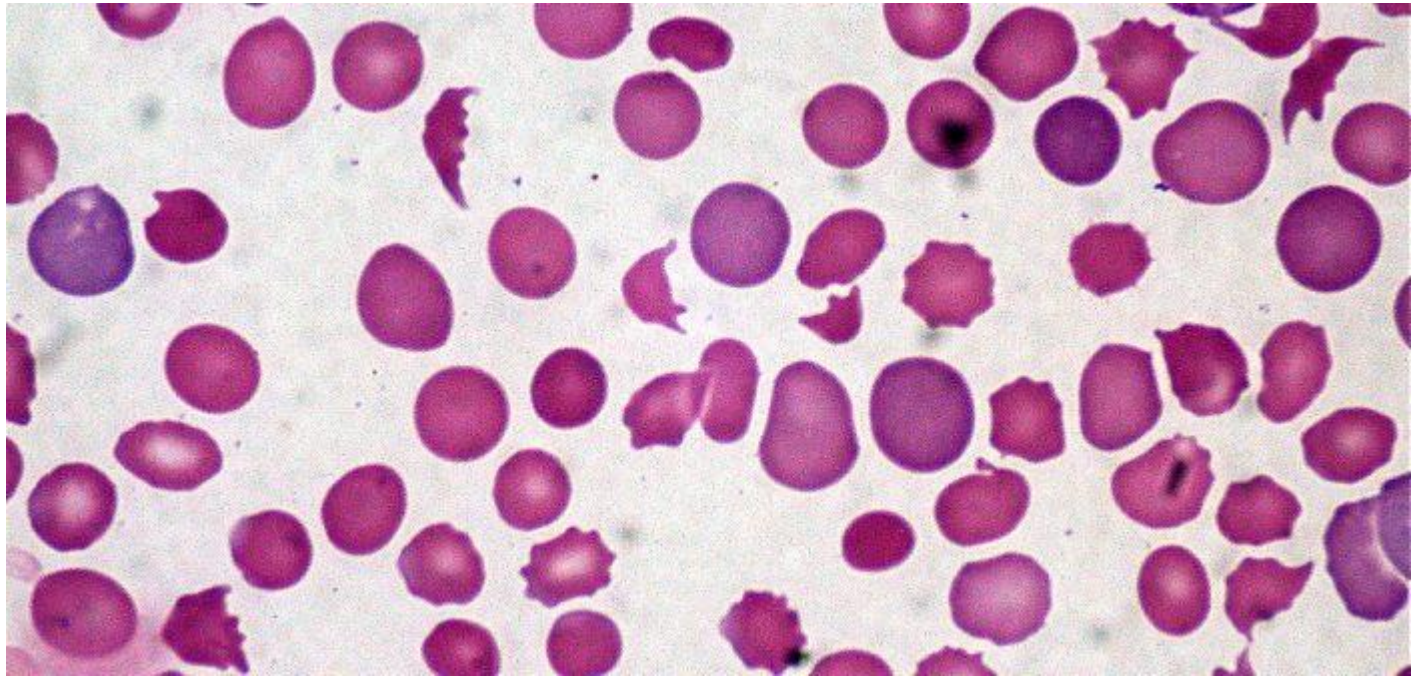
Loss of central pallor

Central pallor 1/3rd

elliptocytosis



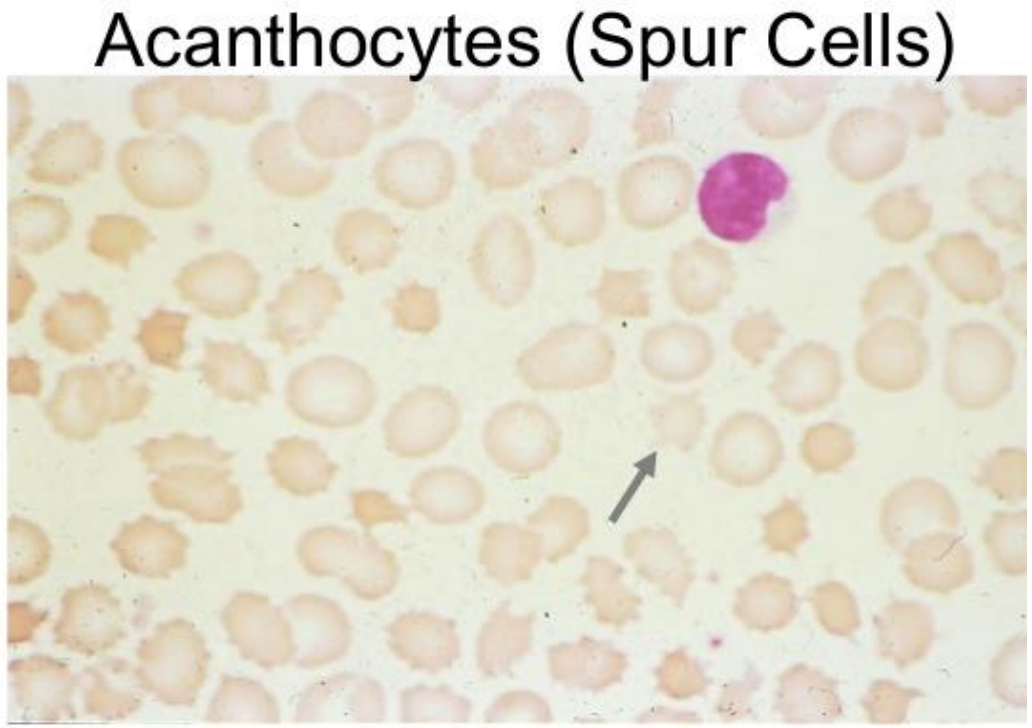
Schistocytes (Helmet cells)



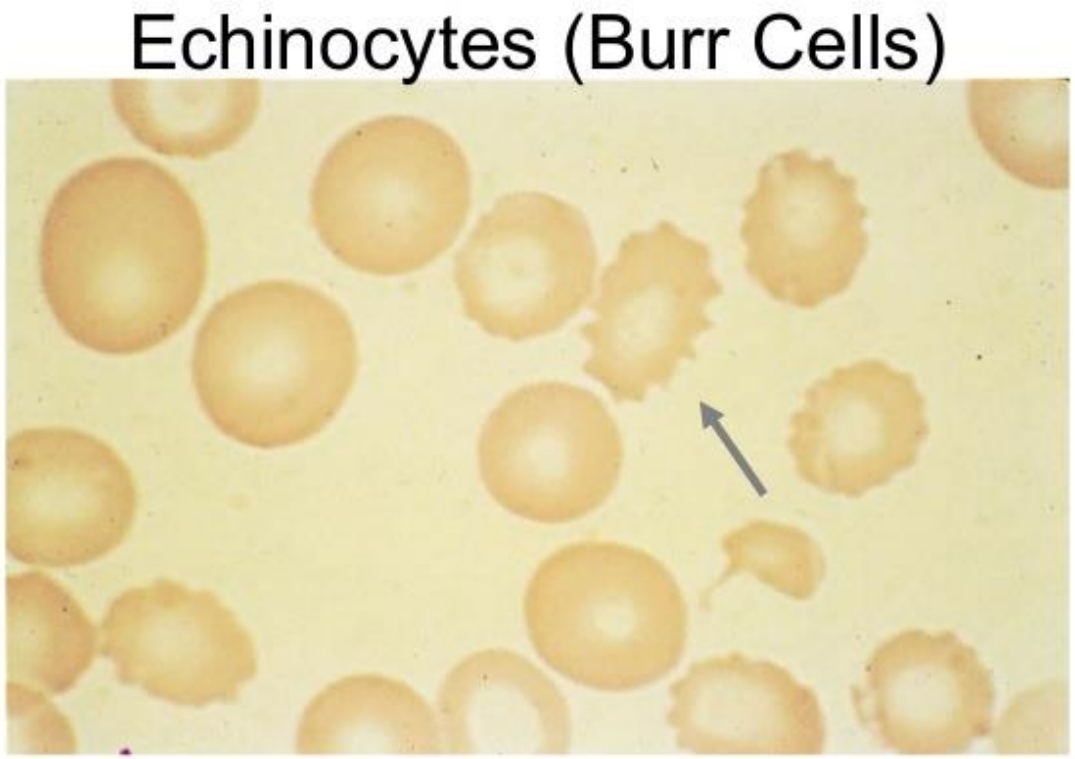
Thrombotic thrombocytopenic purpura (TTP)

- A fatal disorder with mortality >90% if left untreated
  - Triad: Low plt, anemia, schistocytes
  - Pentad: (+/- neurological signs or symptoms, +/- renal failure, +/- fever)
- Treatment is urgent PLasma EXchange (PLEX) and survival >85% if treated.
- TTP is a true medical emergency!

Spur and Burr cells



Liver disease



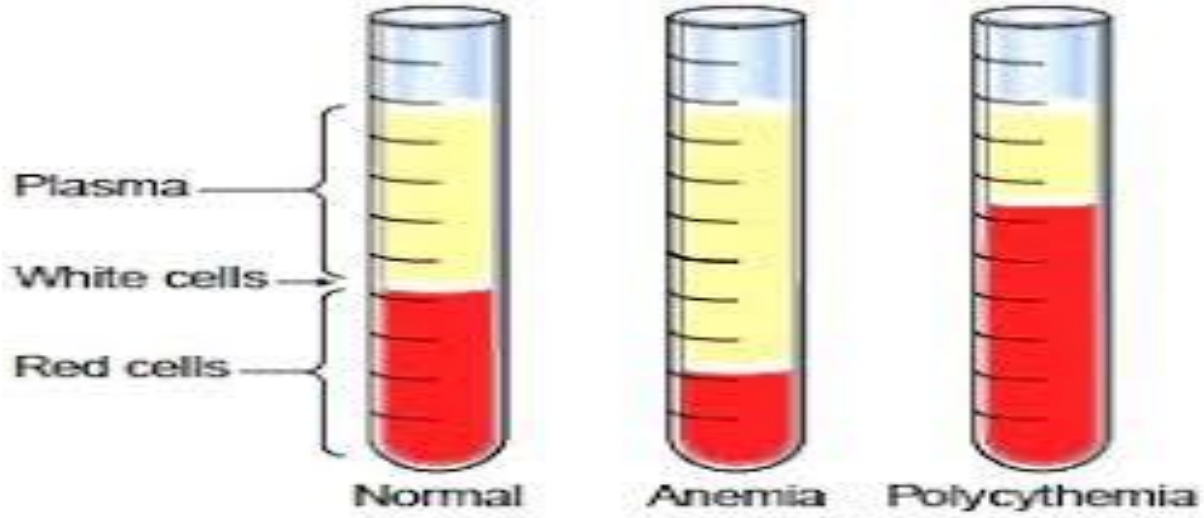
Renal disease

MCV

- The **mean corpuscular volume**, or **mean cell volume** (**MCV**)
- Is a measure of the average volume of a red blood corpuscle (or RBC).
- MCV is calculated from the distribution of individual RBC volumes.

Hematocrit

- Automated hematocrit (%) is calculated by multiplying the MCV by the RBC number
- Hematocrit = MCV × red blood cells × 100.



MCH

- The mean corpuscular hemoglobin (MCH)
- Is expressed in picograms.
- The MCH is calculated by dividing hemoglobin (g/L) by red blood cell count (10’12/L).

MCHC

- The MCH concentration (MCHC)
- Is expressed in grams of hemoglobin per deciliter of packed RBCs.
- The MCHC is calculated by dividing the hemoglobin concentration (g/dL) by the hematocrit (%) × 100.

Red blood cell distribution width (RDW)

- The RDW is the coefficient of **variation** of RBC size (anisocytosis).
- The RDW is used in the evaluation of anemia.
- The RDW is:
  - more frequently elevated with microcytic anemias due to iron deficiency anemia than to thalassemia or anemia of chronic disease
  - more frequently with macrocytic anemias due to vitamin B12 or folate deficiency than to liver disease, hypothyroidism.
- Myelodysplastic syndromes, or RBC transfusions to pts with low/high MCV can produce a dimorphic RBC pattern with a very wide RDW.

Complete Blood Count

CBC

Component Results

Component	Your Value	Standard Range	Units
WBC COUNT	6.7	4.5 - 11.0	K/UL
RBC COUNT	4.51	3.50 - 5.50	MIL/UL
HEMOGLOBIN	14.1	12.0 - 15.0	G/DL
HEMATOCRIT	42.3	36.0 - 48.0	%
MCV	93.7	79.0 - 101.0	FL
MCH	31.2	25.0 - 35.0	PG
MCHC	33.3	31.0 - 37.0	%
RDW-CV	12.4	11.0 - 16.0	FL
PLATELET COUNT	221	150 - 420	K/UL
MPV	9.8	7 - 10	FL

Complete Blood Count

Total WBC not the differential count.
Neutrophils, lymphocytes, Monocytes,
Eosinophils and basophils

CBC

Component Results

Component	Your Value	Standard Range	Units
WBC COUNT	6.7	4.5 - 11.0	K/UL
RBC COUNT	4.51	3.50 - 5.50	MIL/UL
HEMOGLOBIN	14.1	12.0 - 15.0	G/DL
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MPV	9.8	7 - 10	FL

CBC with differential count

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
CBC With Differential/Platelet					
WBC	5.7		x10E3/uL	4.0-10.5	01
RBC	5.27		x10E6/uL	4.10-5.60	01
Hemoglobin	15.4		g/dL	12.5-17.0	01
Hematocrit	44.1		%	36.0-50.0	01
MCV	84		fL	80-98	01
MCH	29.2		pg	27.0-34.0	01
MCHC	34.9		g/dL	32.0-36.0	01
RDW	13.7		%	11.7-15.0	01
Platelets	268		x10E3/uL	140-415	01
Neutrophils	47		%	40-74	01
Lymphs	46		%	14-46	01
Monocytes	6		%	4-13	01
Eos	1		%	0-7	01
Basos	0		%	0-3	01
Neutrophils (Absolute)	2.6		x10E3/uL	1.8-7.8	01
Lymphs (Absolute)	2.6		x10E3/uL	0.7-4.5	01
Monocytes(Absolute)	0.4		x10E3/uL	0.1-1.0	01
Eos (Absolute)	0.1		x10E3/uL	0.0-0.4	01
Baso (Absolute)	0.0		x10E3/uL	0.0-0.2	01
Immature Granulocytes	0		%	0-1	01
Immature Grans (Abs)	0.0		x10E3/uL	0.0-0.1	01

Complete Blood Count

CBC

Component Results

Component	Y	Standard Ra	Units
WBC COUNT		4.5 - 11.0	UL
RBC COUNT	4.	3.50 - 5.50	MIL/UL
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< leukopenia

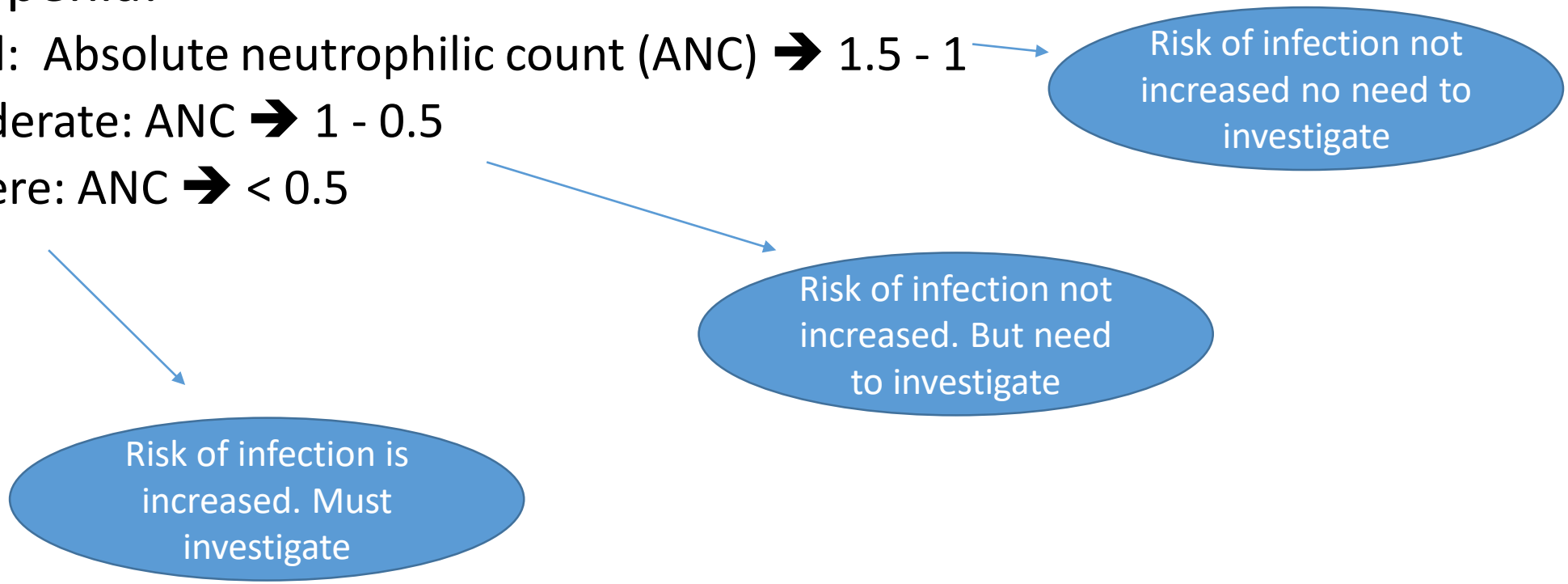
> Leukocytosis

Leukocytosis? Which cell line?

- Neutrophilia ➔
  - Acute: bacterial infection, steroids.
  - Chronic: Chronic myeloid leukemia (CML)
- Lymphocytosis ➔
  - Acute: viral infections
  - Chronic: chronic lymphocytic leukemia
- Monocytosis ➔ fungal infection, TB
- Eosinophilia ➔ allergic conditions, parasite, autoimmune diseases and eosinophilic leukemia
- Basophilia ➔ very rare, CML

Leukopenia? Which cell line? What degree?

- Neutropenia:
  - Mild: Absolute neutrophilic count (ANC) ➔ 1.5 - 1
  - Moderate: ANC ➔ 1 - 0.5
  - Severe: ANC ➔ < 0.5



Complete Blood Count

CBC

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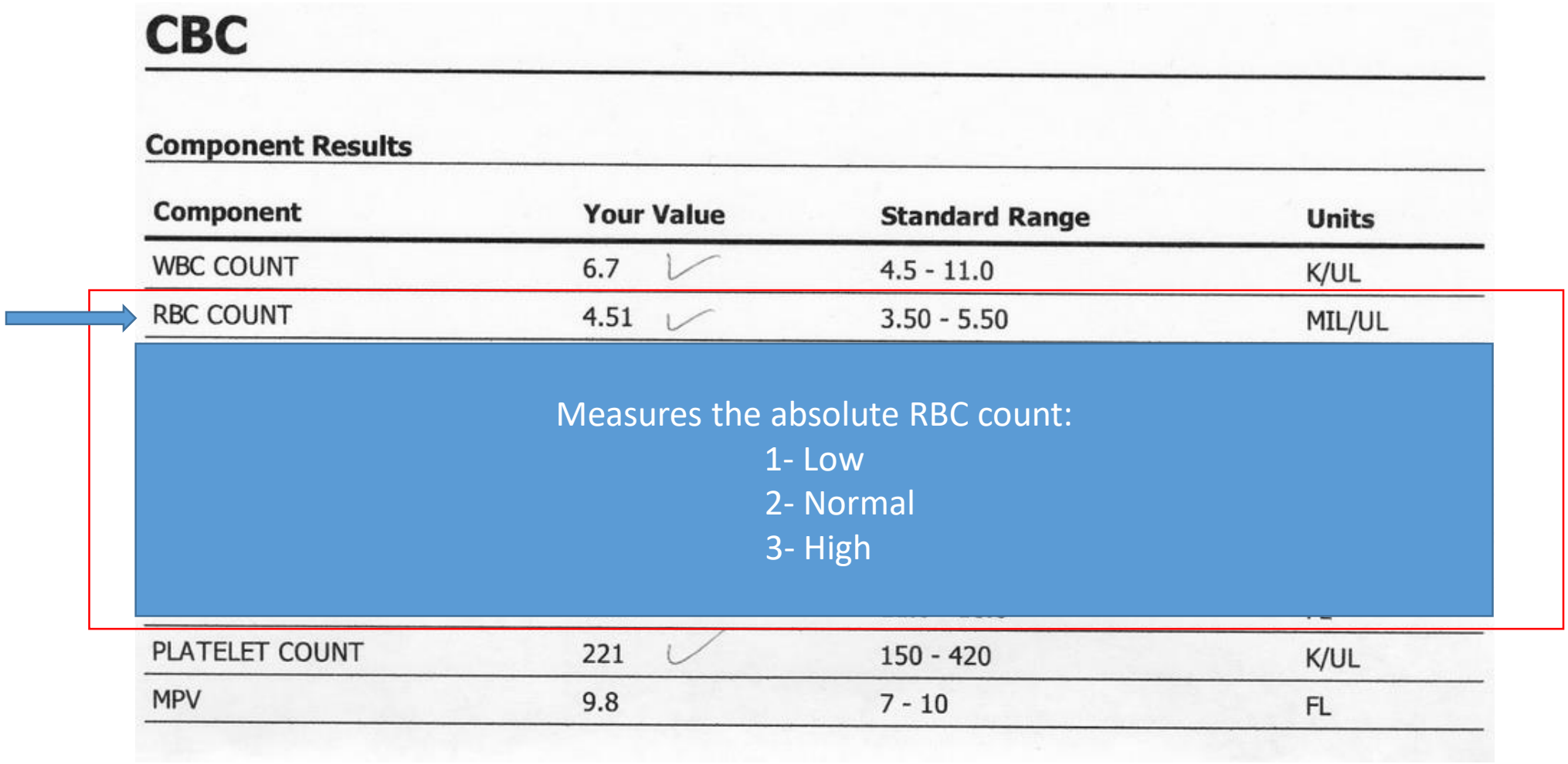
Complete Blood Count



CBC

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Measures the absolute RBC count:

1- Low

2- Normal

3- High

Complete Blood Count

CBC

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Low → anemia
High → polycythemia

Complete Blood Count

CBC

Component Results

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Low → anemia
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Complete Blood Count

CBC

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Low → microcytic
Normal → normocytic
High → macrocytic

Complete Blood Count

CBC

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WBC COUNT	6.7	4.5 - 11.0	K/UL
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HEMOGLOBIN	14.1	12.0 - 15.0	G/DL
HEMATOCRIT	42.3	36.0 - 48.0	%
MCV	93.7	79.0 - 101.0	FL
MCH	31.2	25.0 - 35.0	PG
MPV	9.8	7 - 10	FL

Low → hypochromic
Normal → normochromic

Complete Blood Count

CBC

Component Results

Component	Your Value	Standard Range	Units
WBC COUNT	6.7	4.5 - 11.0	K/UL
RBC COUNT	4.51	3.50 - 5.50	MIL/UL
HEMOGLOBIN	14.1	12.0 - 15.0	G/DL
[illegible]			
MCHC	33.3	31.0 - 37.0	%
RDW-CV	12.4	11.0 - 16.0	FL
PLATELET COUNT	221	150 - 420	K/UL
MPV	9.8	7 - 10	FL

High → hereditary spherocytosis

Complete Blood Count

CBC

Component Results

Component	Your Value	Standard Range	Units
WBC COUNT	6.7	4.5 - 11.0	K/UL
RBC COUNT	4.51	3.50 - 5.50	MIL/UL
HEMOGLOBIN	14.1	12.0 - 15.0	G/DL
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High ➔ high variation in RBC sizes (anisocytosis)
Normal/Low ➔ low or no variation in sizes

Approach to anemia

- To start your approach with any case of anemia you need to look at three CBC parameters and one additional test.
- The 3 CBC parameters are:
  - The hemoglobin (Hb)
  - MCV and
  - Reticulocyte count (retic count).
- And the additional required test is the peripheral blood smear.

Approach to anemia

- With the use of these 3 parameters your approach will be divided into 4 categories.
  - Low MCV (MCV < 80 fL), also called microcytic anemia.
  - Normal MCV (MCV 80-100 fL) with low retic count, also called normocytic anemia with inappropriately low bone marrow response.
  - Normal MCV (MCV80-100 fL) with high retic count, also called normocytic anemia with appropriate marrow response.
  - High MCV (MVC >100 fL), also called macrocytic anemia.

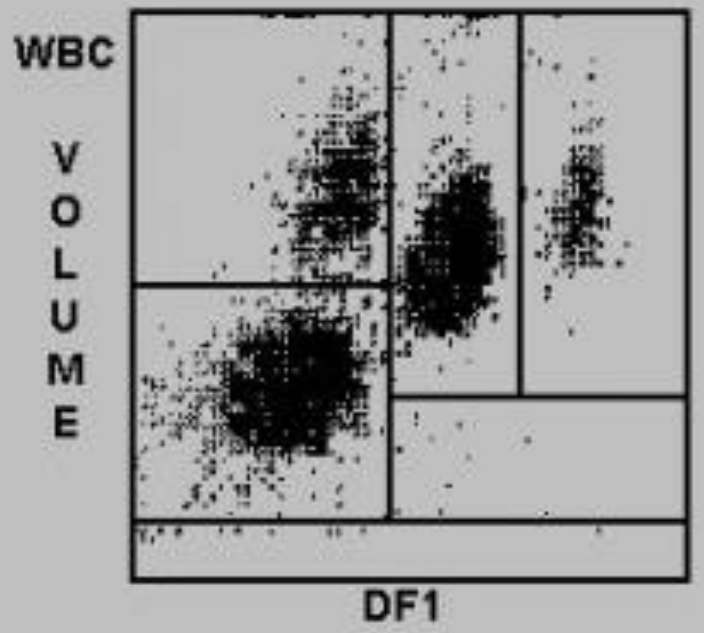
MCV < 80 fL (TAILS)	MCV N, low retic count	MCV N, high retic count	MCV > 100 fL
1) **T**halassemia 2) **A**nemia of inflammation 3) **I**ron deficiency 4) **L**ead poisoning 5) **S**ideroblastic anemia **Iron deficiency or thalsemia**	**1) Bone marrow failure:** - Aplastic anemia 2) **BM suppression**: - Toxins, sepsis. - Organ failure: renal failure, liver failure, adrenal insufficiency - Chronic inflammation - chronic diseases 3) **BM infiltration:** - Lymphoma, leukemia - metastatic solid tumour - granulomatous disease (e.g. TB)	**1) bleeding** **2) hemolysis** **3) treated nutritional deficiency**	1) **Megaloblastic:** (impaired nucleic acid metabolism): - B12 deficiency - folate deficiency - drugs: such as methotrexate 2) **Non megaloblastic**: - liver disease - alcohol - Myelodysplasia - thyroid disease - myeloma - Congenital bone marrow failure syndromes

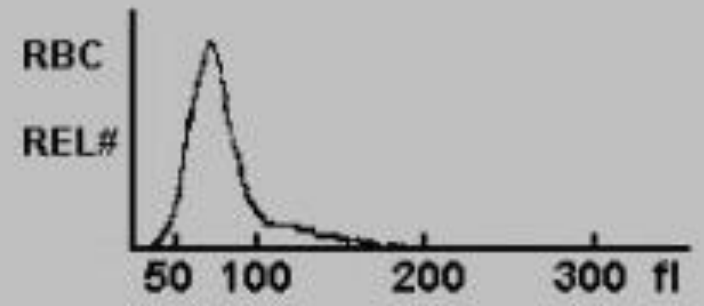
Microcytic anemia

- Iron deficiency anemia vs thalassemia.
- Both will have low Hb and low MCV. How to differentiate?

	Iron deficiency anemia	Thalassemia
MCV	Low (80-70s)	Very low (70-60s)
RBC	Low	High or normal
RDW	High	normal
Ferritin/iron level	Low	High or normal

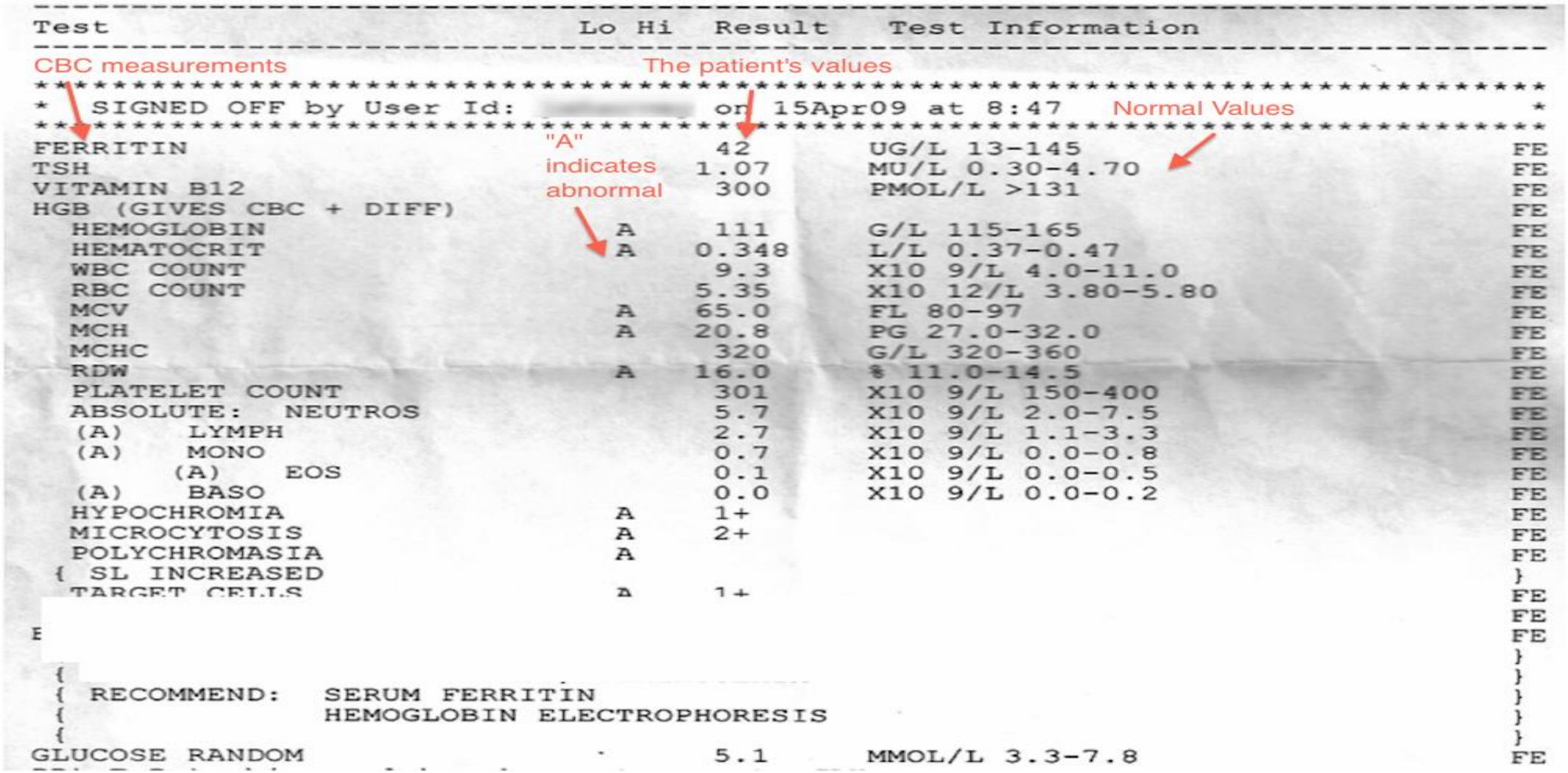
Read this CBC: case 1





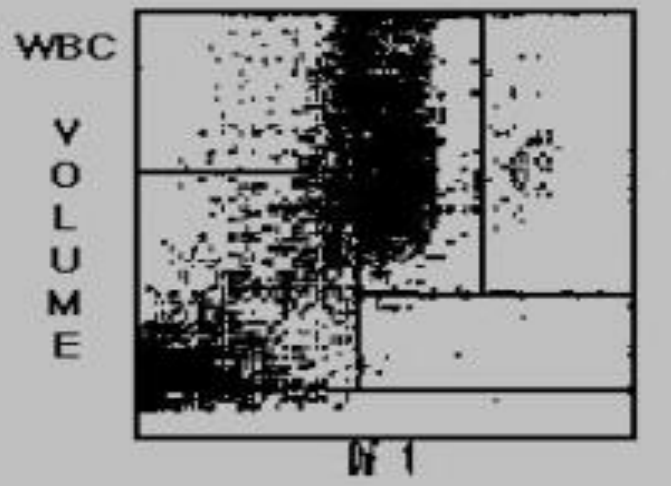
WBC	5.5		
	%		#
NE	54.7		3.0
LY	34.1		1.9
MO	7.5		0.4
EO	3.0		0.2
BA	0.7		0.0
RBC	4.28	L	
HGB	9.7	L	
HCT	29.9	L	
MCV	69.7	L	
MCH	22.6	L	
MCHC	32.4	L	
RDW	18.4	H	
PLT	331		
MPV	8.8		

Case 2



Test	Lo	Hi	Result	Test Information
SIGNED OFF by User Id: [redacted] on 15Apr09 at 8:47				
FERRITIN		A	42	UG/L 13-145
TSH			1.07	MU/L 0.30-4.70
VITAMIN B12			300	PMOL/L >131
HGB (GIVES CBC + DIFF)				
HEMOGLOBIN		A	111	G/L 115-165
HEMATOCRIT		A	0.348	L/L 0.37-0.47
WBC COUNT			9.3	X10 9/L 4.0-11.0
RBC COUNT			5.35	X10 12/L 3.80-5.80
MCV		A	65.0	FL 80-97
MCH		A	20.8	PG 27.0-32.0
MCHC			320	G/L 320-360
RDW		A	16.0	% 11.0-14.5
PLATELET COUNT			301	X10 9/L 150-400
ABSOLUTE: NEUTROS			5.7	X10 9/L 2.0-7.5
(A) LYMPH			2.7	X10 9/L 1.1-3.3
(A) MONO			0.7	X10 9/L 0.0-0.8
(A) EOS			0.1	X10 9/L 0.0-0.5
(A) BASO			0.0	X10 9/L 0.0-0.2
HYPOCHROMIA		A	1+	
MICROCYTOSIS		A	2+	
POLYCHROMASIA		A		
{ SL INCREASED				
TARGET CELLS		A	1+	
{ RECOMMEND: SERUM FERRITIN				
{ HEMOGLOBIN ELECTROPHORESIS				
GLUCOSE RANDOM			5.1	MMOL/L 3.3-7.8

Case 3



WBC	61.1*RH		
	%		#
NE	65.7		40.2 RH
LY	12.9	L	7.9 RH
MO	11.3		6.9 RH
EO	1.2		0.7 R
BA	8.9	H	5.4 RH
RBC	3.37	L	
HGB	12.5	L	
HCT	36.6	L	
MCV	108.5	H	
MCH	37.0	H	
RDW	25.3	H	
PLT	340		
MPV	8.4		

Case 4

Date and Time Collected	Date Entered	Date and Time Reported	Physician Name	NPI	Physician ID
03/09/12 14:51	03/09/12	03/09/12 16:15ET	KLIX, MARY	[redacted]	1669447595

Tests Ordered

CBC With Differential/Platelet

General Comments

PID: [redacted]

TESTS	RESULT	FLAG	UNITS	REFERENCE INTERVAL	LAB
CBC With Differential/Platelet					
WBC	4.5		x10E3/uL	4.0-10.5	01
RBC	4.13		x10E6/uL	4.10-5.60	01
Hemoglobin	14.2		g/dL	12.5-17.0	01
Hematocrit	42.5		%	36.0-50.0	01
MCV	**103**	**High**	fL	80-98	01
MCH	**34.4**	**High**	pg	27.0-34.0	01
MCHC	33.4		g/dL	32.0-36.0	01
RDW	12.7		%	11.7-15.0	01
Platelets	***86***	***Alert***	x10E3/uL	140-415	01
Results verified by repeat testing					
Neutrophils	60		%	40-74	01
Lymphs	31		%	14-46	01
Monocytes	7		%	4-13	01
Eos	1		%	0-7	01
Basos	1		%	0-3	01
Neutrophils (Absolute)	2.7		x10E3/uL	1.8-7.8	01
Lymphs (Absolute)	1.4		x10E3/uL	0.7-4.5	01
Monocytes(Absolute)	0.3		x10E3/uL	0.1-1.0	01
Eos (Absolute)	0.1		x10E3/uL	0.0-0.4	01
Baso (Absolute)	0.0		x10E3/uL	0.0-0.2	01

01 STLOU LabCorp St Louis
12855 N 40 Drive Ste 200, St Louis, MO
Dir: Meyers, James MD

For inquiries, the physician may contact: **Branch: 314-453-9648** **Lab: 314-453-9648**

Case 5

- Hb 5, MCV 85 (normal)? What's next?

Retic count

- Retic count can be reported as an absolute number or as a percentage.
- A normal retic count/ percentage in the absence of anemia is 100 or 1%, respectively.
- When someone with a healthy bone marrow (BM) develops anemia, the BM will automatically compensate for the anemia with production of more young red blood cells (reticulocytes)
- Thus the retic count will increase and can go up to 1000 or 10% in some severe cases.
- Therefore, a patient with anemia and a healthy bone marrow should have an appropriately elevated retic count.

Case 5

- Hb 5, MCV 85 (normal)? What's next?
- Retic count was 300 (3%)

MCV < 80 fL (TAILS)	MCV N, low retic count	MCV N, high retic count	MCV > 100 fL
1) **T**halassemia 2) **A**nemia of inflammation 3) **I**ron deficiency 4) **L**ead poisoning 5) **S**ideroblastic anemia	**1) Bone marrow failure:** - Aplastic anemia 2) **BM suppression**: - Toxins, sepsis. - Organ failure: renal failure, liver failure, adrenal insufficiency - Chronic inflammation - chronic diseases 3) **BM infiltration:** - Lymphoma, leukemia - metastatic solid tumour - granulomatous disease (e.g. TB)	**1) bleeding** **2) hemolysis** **3) treated nutritional deficiency**	1) **Megaloblastic:** (impaired nucleic acid metabolism): - B12 deficiency - folate deficiency - drugs: such as methotrexate 2) **Non megaloblastic**: - liver disease - alcohol - Myelodysplasia - thyroid disease - myeloma - Congenital bone marrow failure syndromes

Acute or chronic drop in Hb?

- Acute drop is either hemolysis or bleeding.
- How to tell the difference?

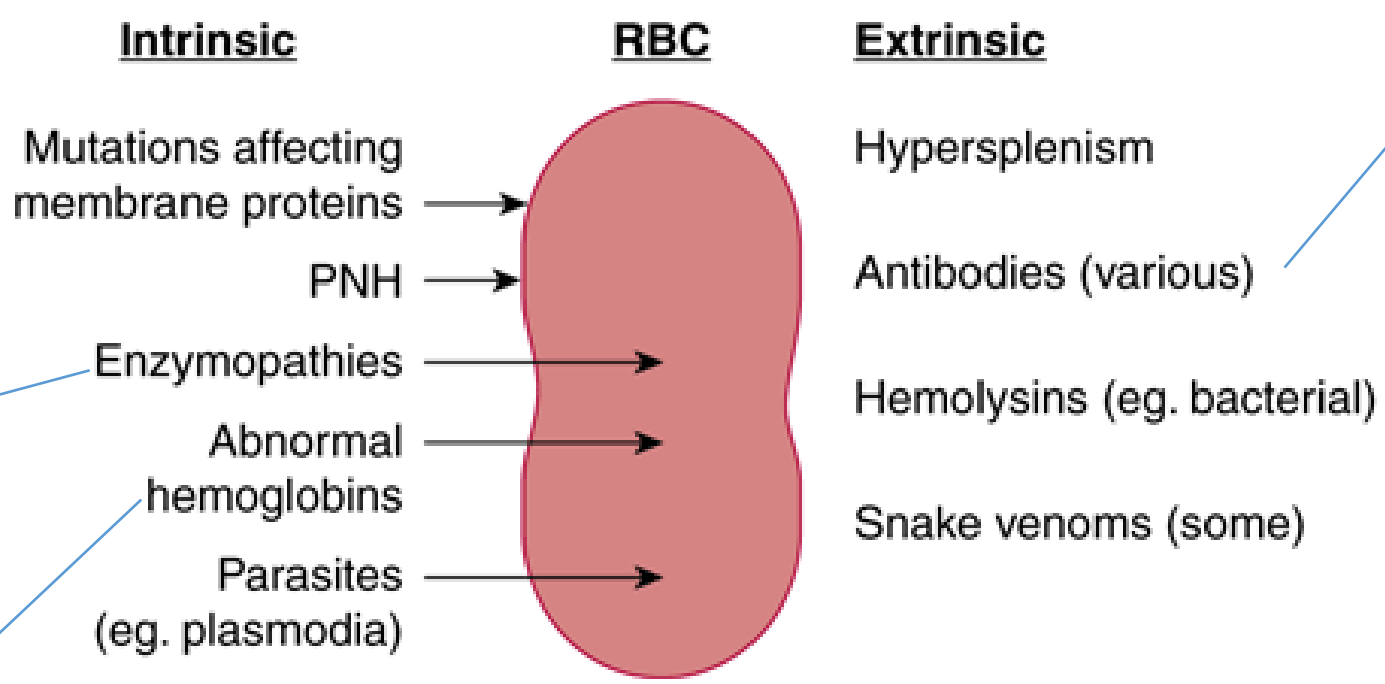
	Hemolysis	Bleeding
MCV	Normal or high	Normal or high
Retics	High	Normal or high
Bleeding	No	Yes, not always apparent
LDH	High	Normal
Haptoglobin	Low	Normal
Indirect bilirubin	High	Normal

Hemolytic anemia

Hereditary spherocytosis or elleptocytosis

G6PD or pyruvate kinase deficiency

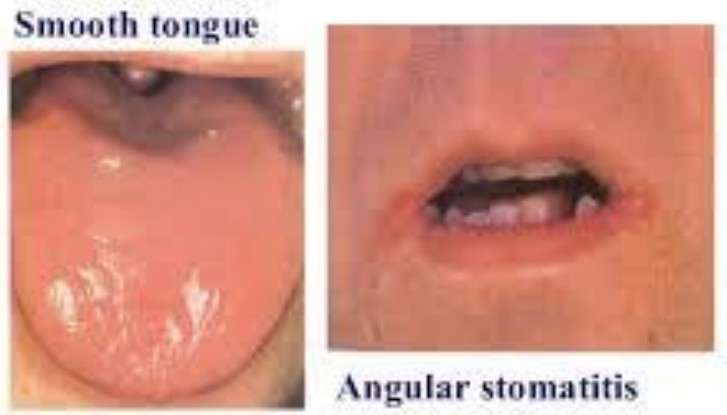
Sickle cell anemia Thalassemia



Source: Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, Weil PA: *Harper's Illustrated Biochemistry, 29th Edition*: www.accessmedicine.com

Autoimmune hemolytic anemia

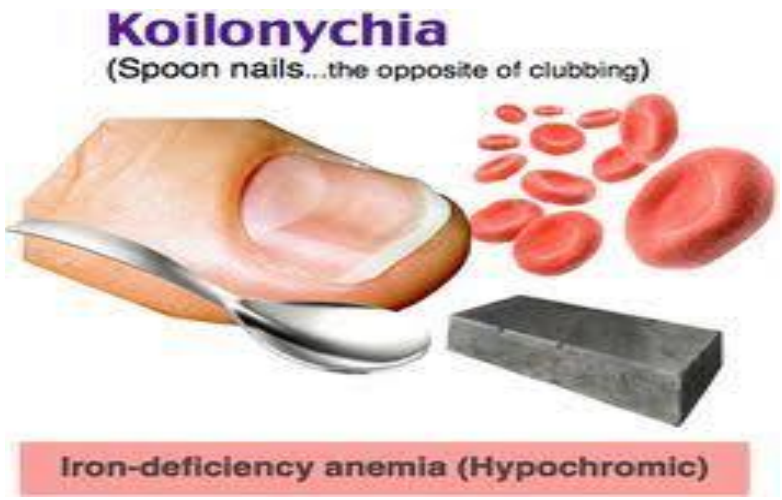
Iron deficiency anemia

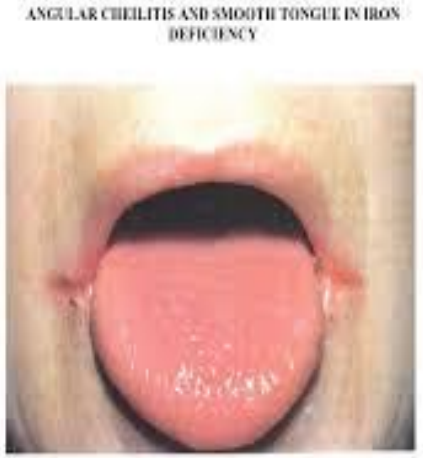


Signs of iron deficiency anemia

- Pallor

- Glossitis





Iron deficiency anemia

- More common in female: heavy menses
- In males: always investigate for GI causes: occult bleeding, colon cancer, malabsorption, celiac disease etc
- Diet: a rare cause

Iron deficiency diagnosis

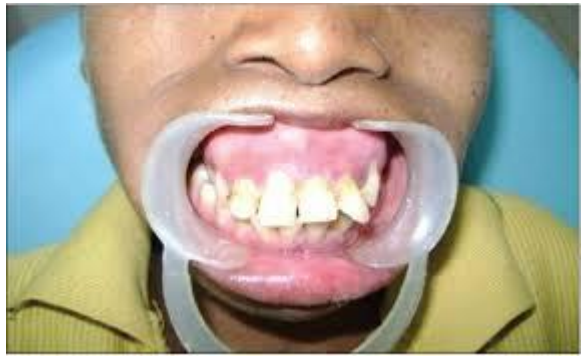
- Diagnosis: iron studies:
- Serum iron (Fe): measures the concentration of iron in the blood
- Transferrin: is the main transport protein for iron
  - The body produces transferrin in relationship to the need for iron.
  - When iron stores are low, transferrin levels increase and vice versa.
- TIBC:
  - is a measure of all the proteins in the blood that are available to bind with iron (including transferrin).
  - The TIBC test is a good indirect measurement of transferrin, as transferrin is the primary iron-binding protein
- Transferrin saturation:
  - TSAT is a good marker of iron status.
  - TSAT < 20% indicates iron deficiency, a TSAT > 50% may indicate iron overload.
  - TSAT: is calculated with:
  - TSAT = (Fe/TIBC) × 100].
- Ferritin level

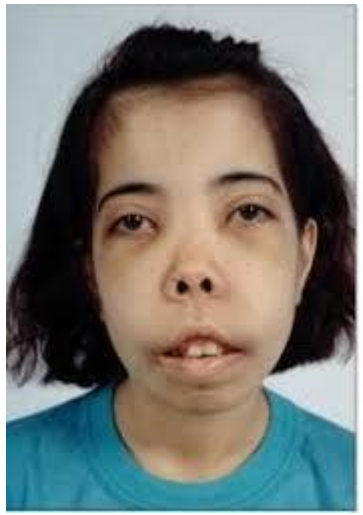
FSG

- Ferrous **F**umarate: 325mg tablet contains 106mg elemental iron
- Ferrous **S**ulfate: 325mg tablet contains 65mg elemental iron
- Ferrous **G**luconate: 325mg tablet contains 36mg elemental iron
- More elemental = more effective = more GI side effects.
- The recommended daily dose is between 150-200mg elemental iron per day.
- IV iron (several formulations):
  - If not tolerant to oral iron
  - If blood loss exceeds the capacity of oral iron to meet the needs

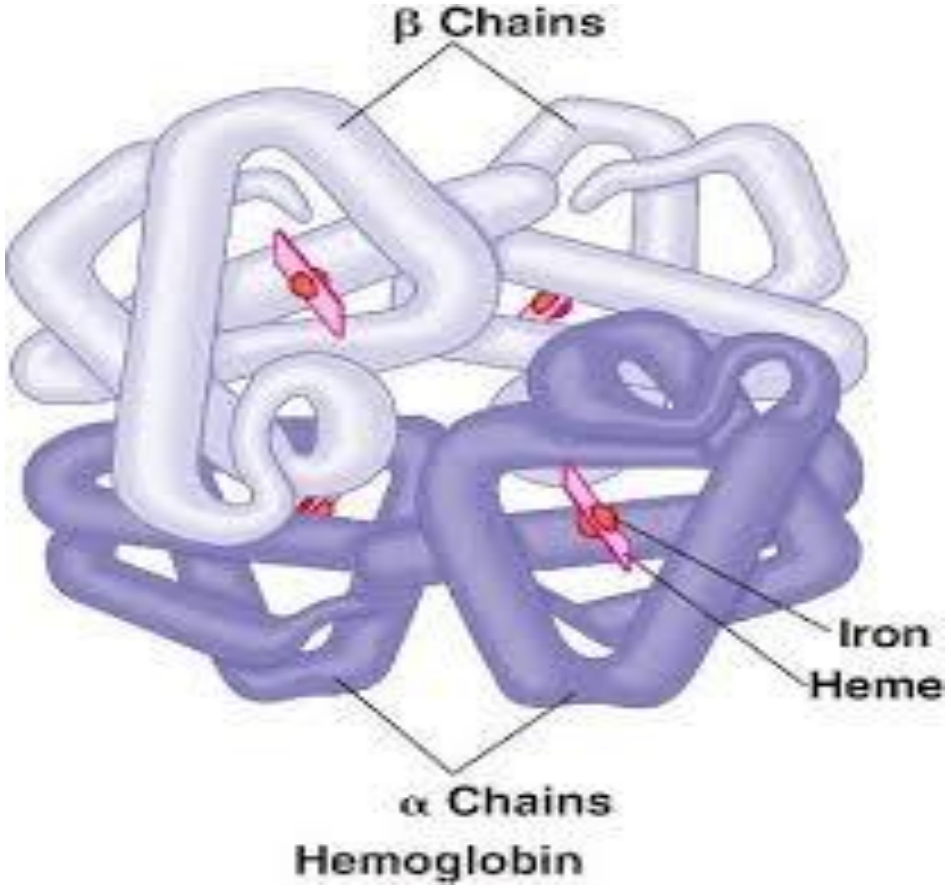
Thalassemia

- Prominent malar eminences and mal-alignment of the teeth
- Secondary to bone marrow hyperplasia





Alpha vs beta



Hemoglobin types

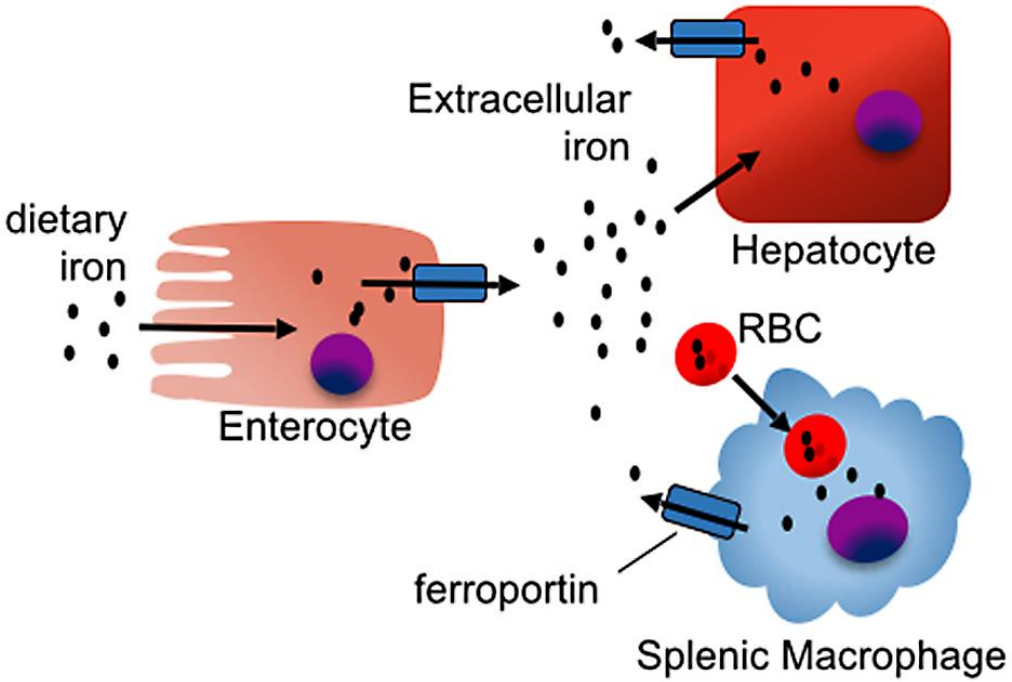
Hemoglobin Type	Globin Chains
Hb A1—92%	$\alpha_2\beta_2$
Hb A2—2.5%	$\alpha_2\delta_2$
Hb F — <1%	$\alpha_2\gamma_2$
Hb H	β_4
Bart's Hgb	γ_4
Hb S	$\alpha_2\beta_{26}^{glu\rightarrow val}$
Hb C	$\alpha_2\beta_{26}^{glu\rightarrow lys}$

Thalassemia

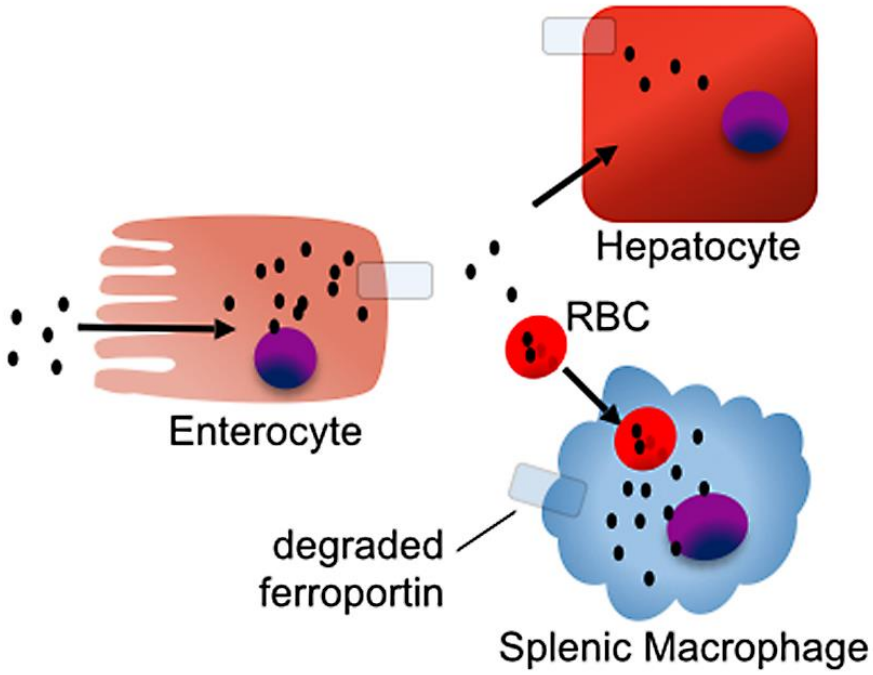
- Hereditary disorders
- Reduction in the synthesis of globin chains
- Alpha thalassemia has reduced alpha globin chains
- Beta thalassemia has reduced beta thalassemia chains

Anemia of chronic diseases

Low hepcidin conditions:
Iron exported via ferroportin into extracellular space



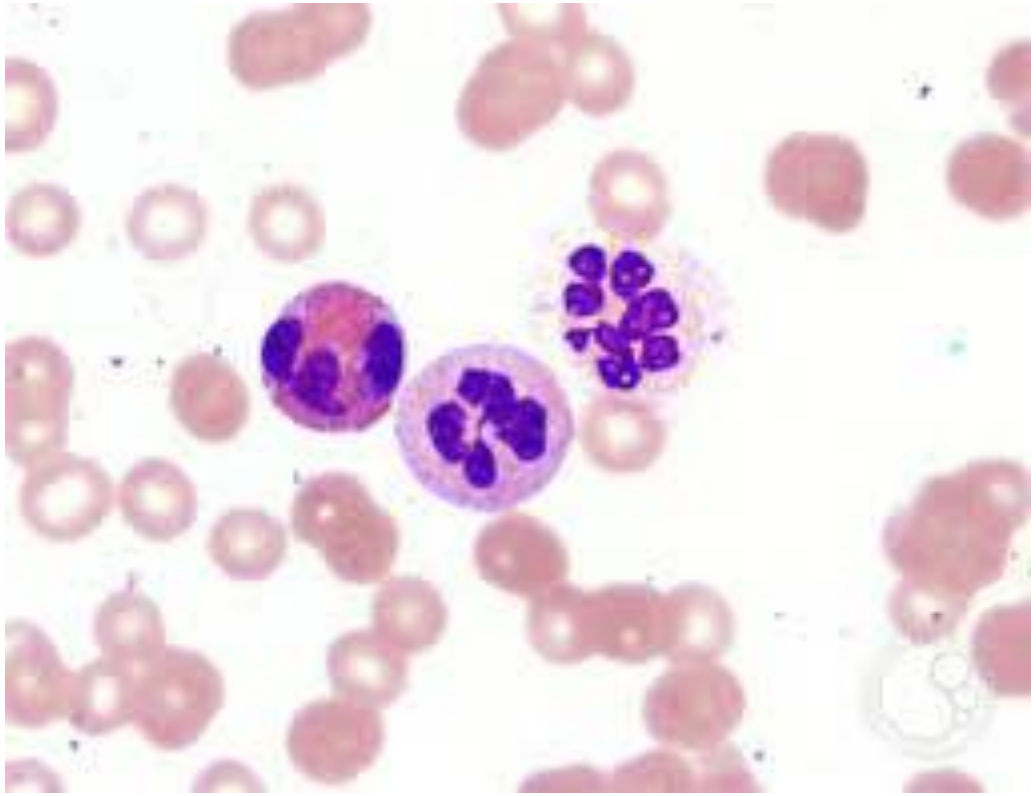
High hepcidin conditions:
Ferroportin degraded, iron accumulates intracellularly



Anemia of chronic diseases

- Serum iron is low.
- TIBC is low.
- Transferrin saturation is normal or low normal.

Macrocytic anemia (megaloblastic)



Macrocytic anemia (non-megaloblastic)

- Liver disease
- Alcohol
- Myelodysplasia
- Thyroid disease

Myelodysplastic syndromes (MDS)

- A heterogeneous group of malignant hematopoietic stem cell disorders
- Characterized by:
  - Dysplasia (abnormal morphology)
  - Varying degree of cytopenia
  - Variable risk of transformation to AML
- A disease of the elderly (median age >65)
- Treatment:
  - Supportive (transfusion, GCSF, antibiotics, EPO)
  - Hypomethylating agents (azacitidine)
  - Stem cell transplant (younger patients without comorbidities)

Thanks

- Questions?