# 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)

2.5 μm

7.5 μm

Top view
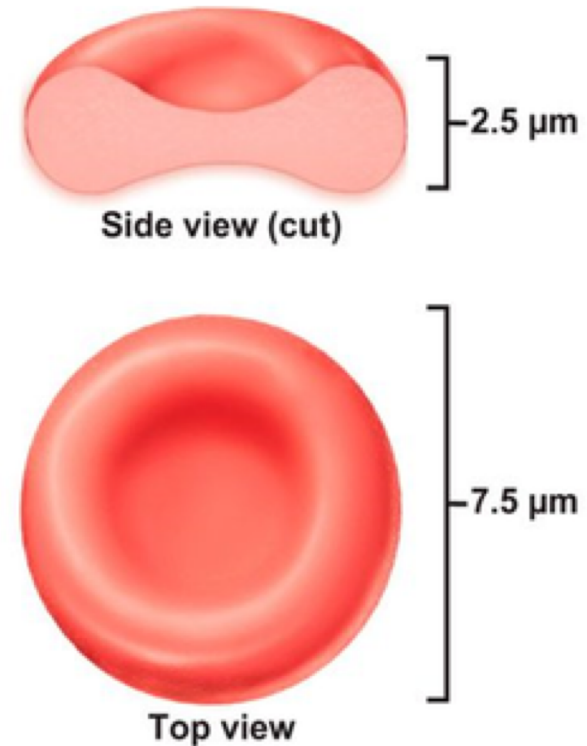
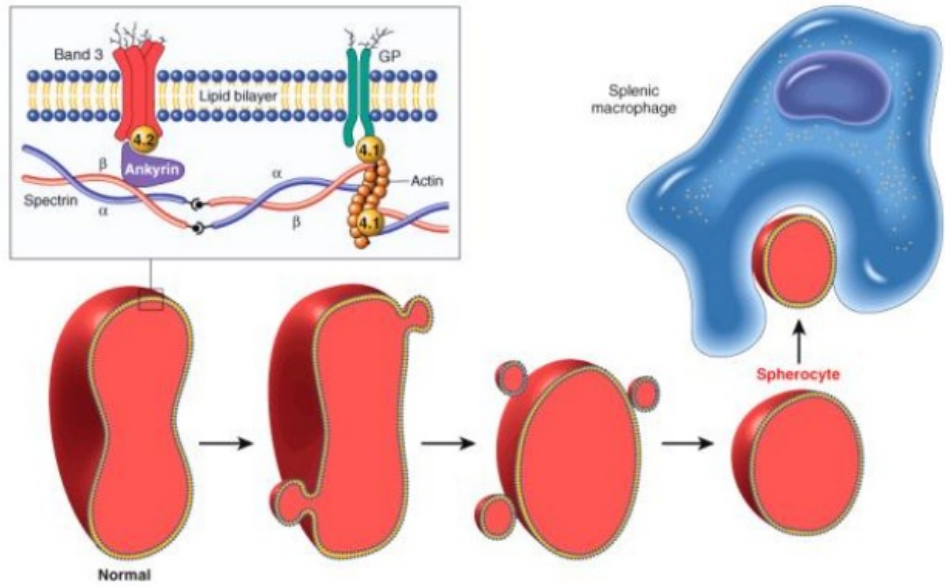# What keep them biconcave?
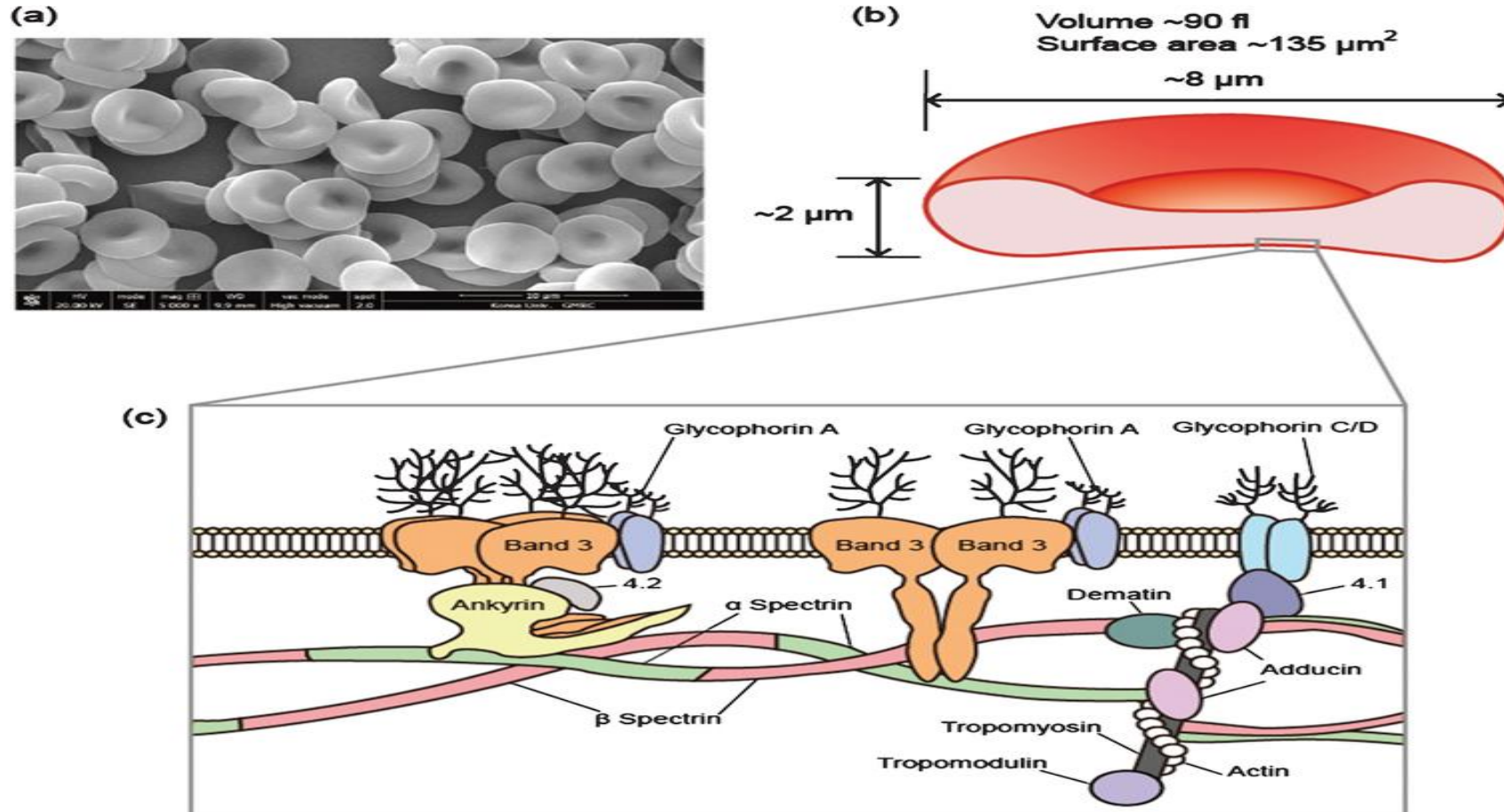
Terminology: spherocytosis

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

Loss of central pallor
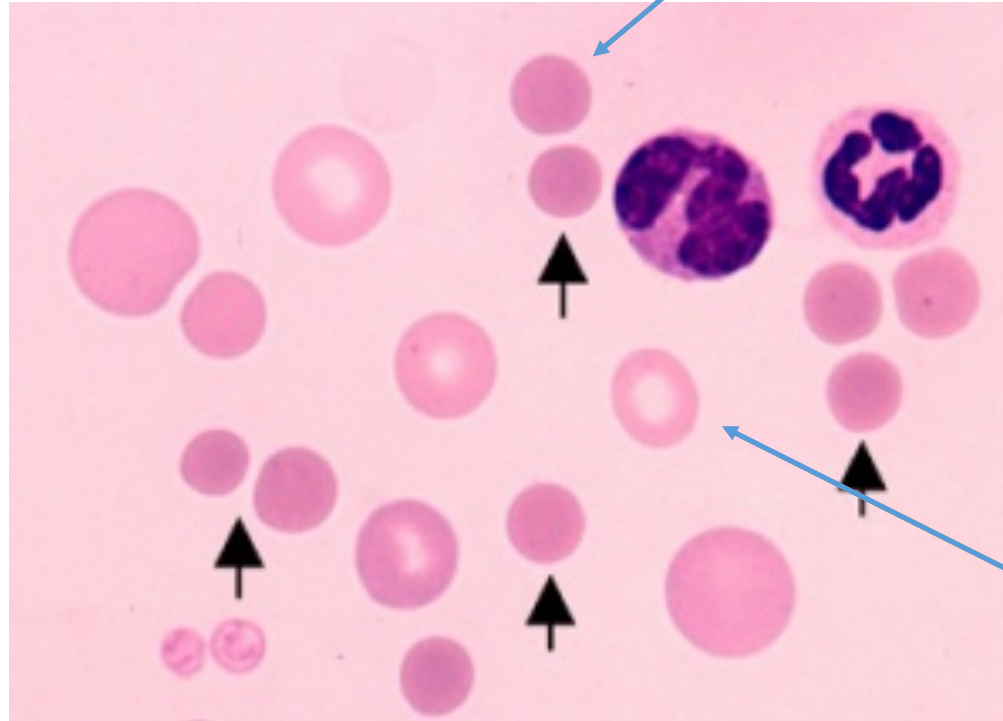
Central pallor 1/3rd

elliptocytosis
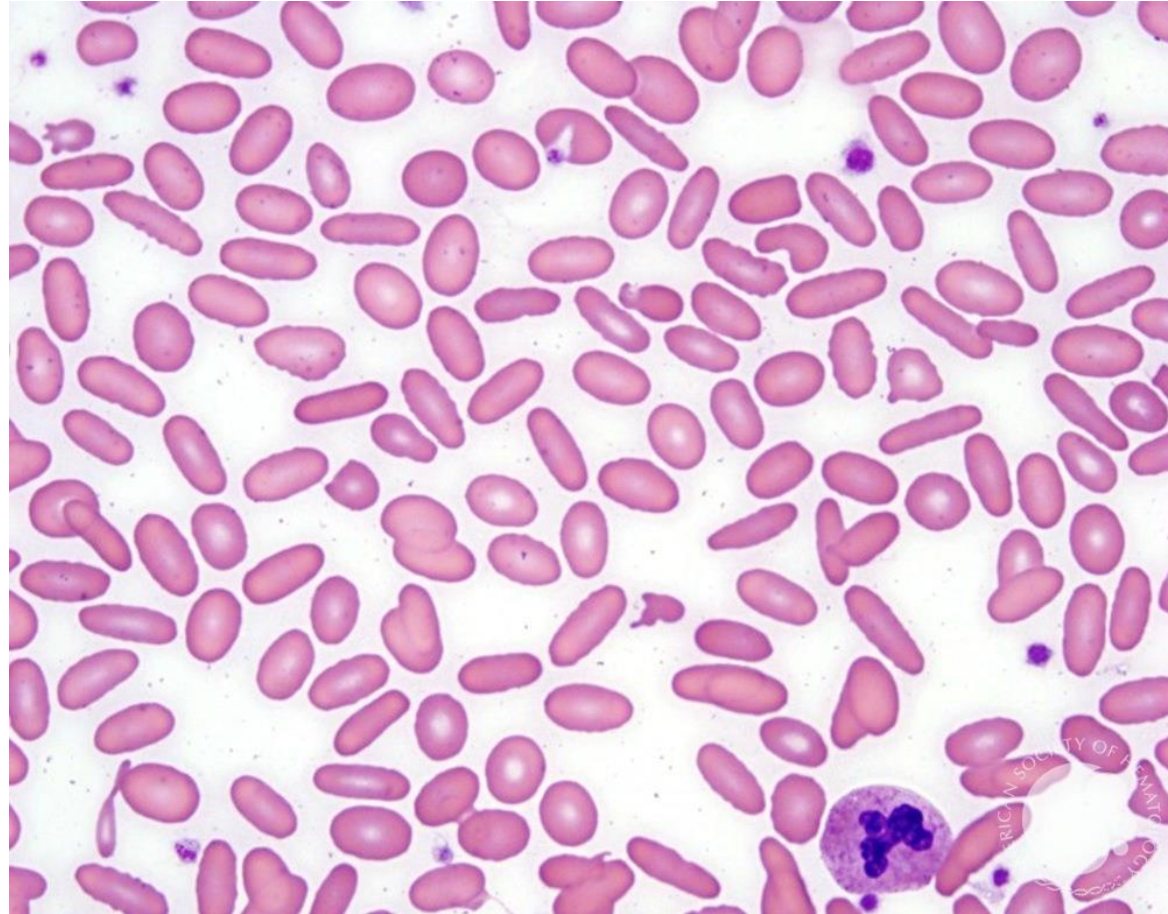
Schistocytes (Helmet cells)
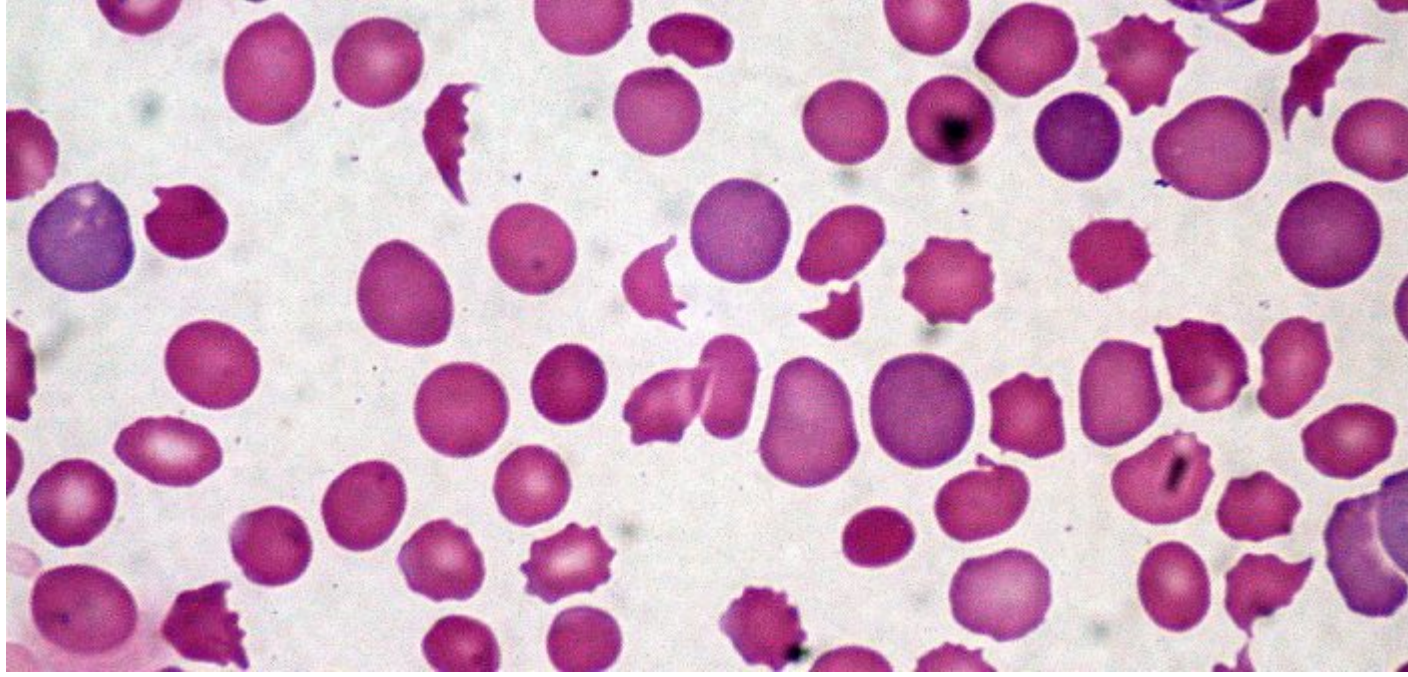
Spur and Burr cells

Acanthocytes (Spur Cells)
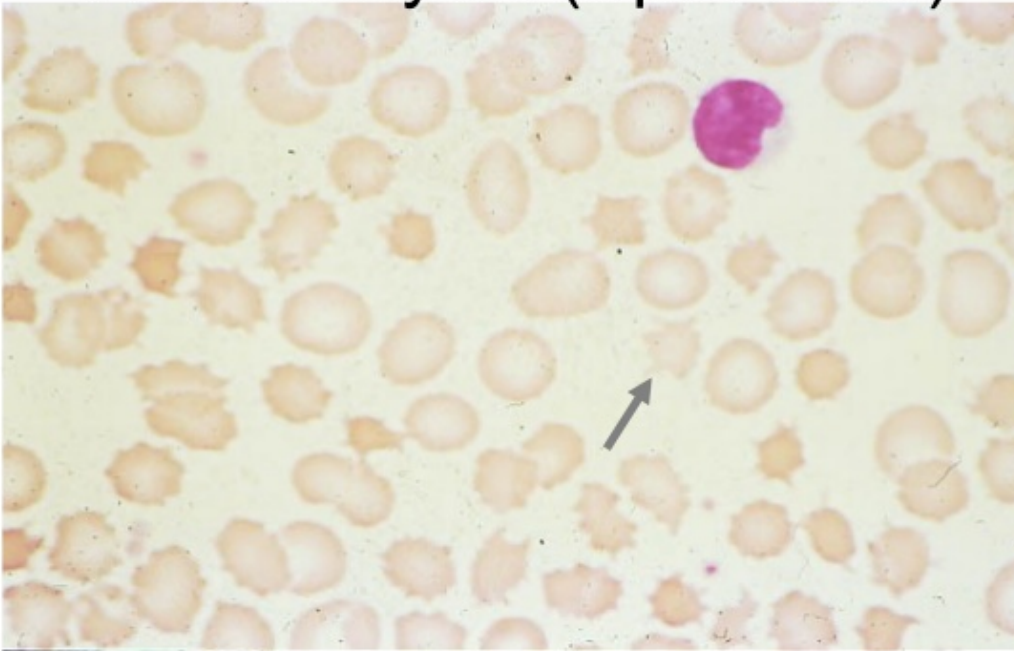
Liver disease

Echinocytes (Burr Cells)
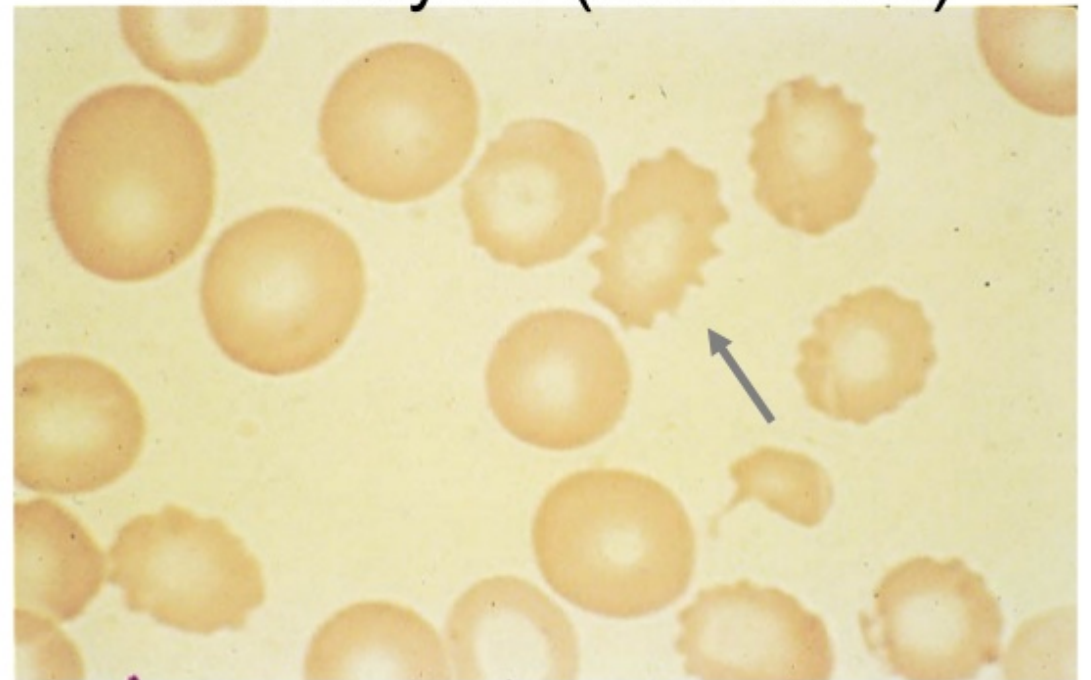
Renal disease

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 (10-15 L) × red blood cells (1012/L) × 100.

Plasma

White cells

Red cells

Normal   Anemia   Polycythemia
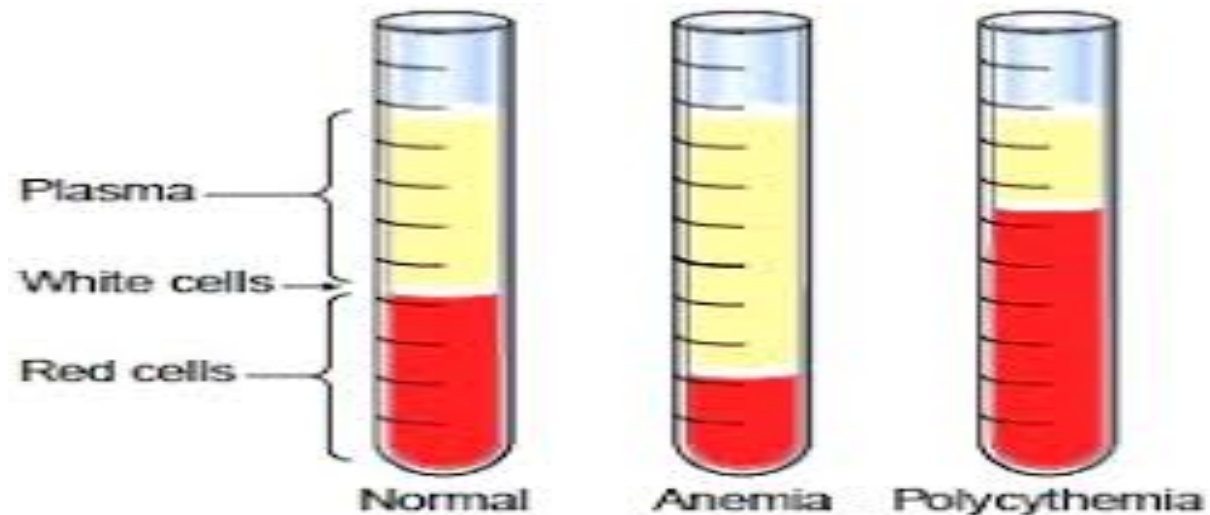
MCH

- The mean corpuscular hemoglobin (MCH)
- Is expressed in picograms (10-12 g).
- The MCH is calculated by dividing hemoglobin (g/L) by red blood cell count (1012/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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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

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	Value	Standard Range	Units
WBC COUNT		4.5 - 11.0	UL
RBC COUNT		3.50 - 5.50	MIL/UL
HEMOGLOBIN	14.1	12.0 - 15.0	G/DL
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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

Risk of infection not increased no need to investigate

Risk of infection not increased. But need to investigate

Risk of infection is increased. Must investigate

Complete Blood Count

CBC

Component Results

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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
PLATELET COUNT	221 ✓	150 - 420	K/UL
MPV	9.8	7 - 10	FL

Measures the absolute RBC count:
1- Low
2- Normal
3- High

Complete Blood Count

CBC

Component Results

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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

Low ➜ anemia
High ➜ polycythemia

PLATELET COUNT	221	150 - 420	K/UL
MPV	9.8	7 - 10	FL

Complete Blood Count

CBC

Component Results

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WBC COUNT	6.7	4.5 - 11.0	K/UL
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Low ➔ anemia
High ➔ polycythemia

Complete Blood Count

CBC

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MCV	93.7	79.0 - 101.0	FL
PLATELET COUNT	221	150 - 420	K/UL
MPV	9.8	7 - 10	FL

Low ➔ microcytic
Normal ➔ normocytic
High ➔ macrocytic

Complete Blood Count

CBC

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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
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
HEMATOCRIT			
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
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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

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
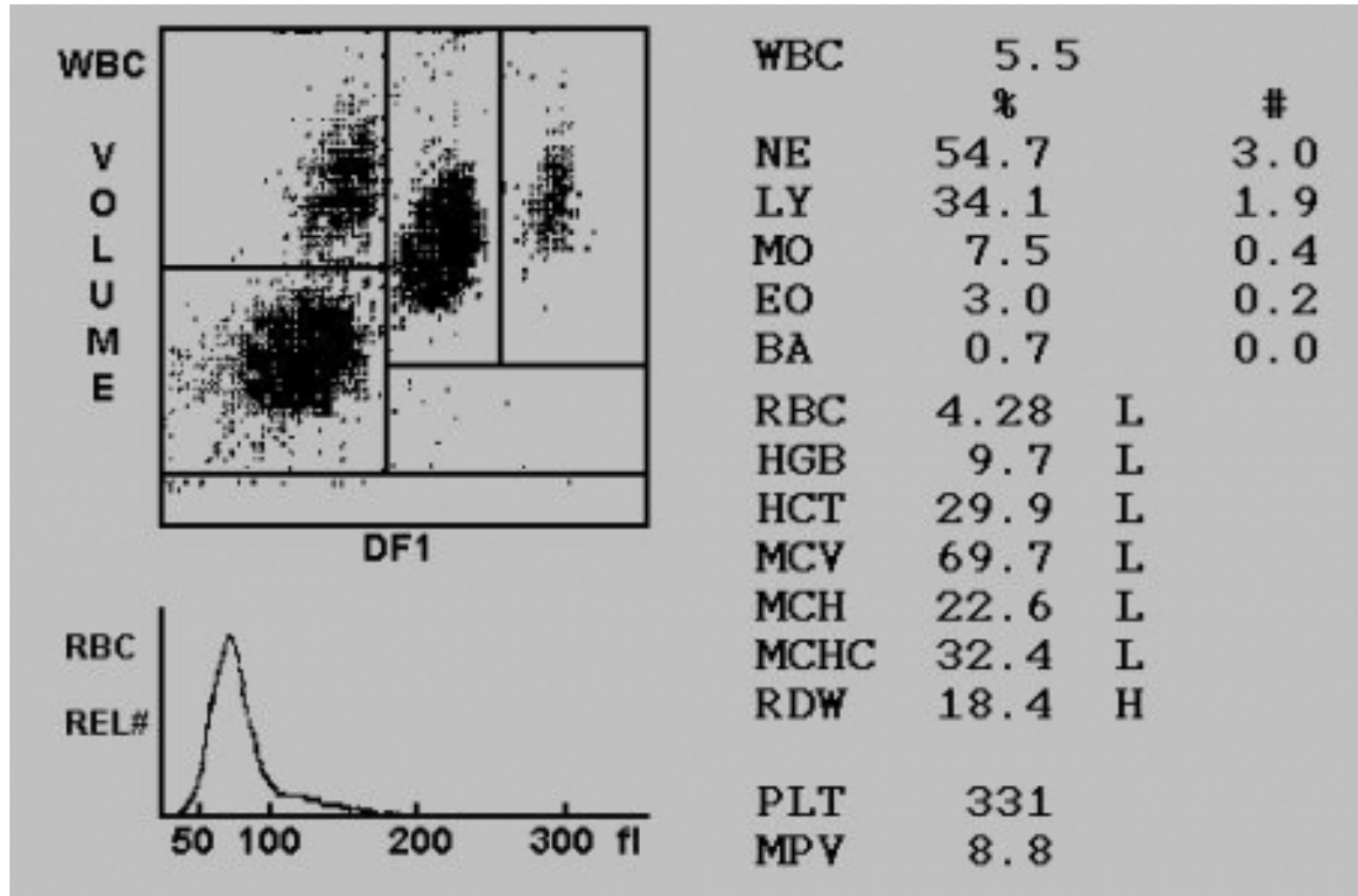
Case 2


```
-----------------------------------------------------------------------------------
Test                                   Lo Hi   Result     Test Information
-----------------------------------------------------------------------------------
```

CBC measurements   The patient's values

```
***********************************************************************************
*    SIGNED OFF by User Id:                   on  15Apr09 at 8:47        Normal Values        *
***********************************************************************************
FERRITIN                               "A"      42          UG/L 13-145                      FE
TSH                                    indicates 1.07       MU/L 0.30-4.70                   FE
VITAMIN B12                            abnormal  300        PMOL/L >131                      FE
HGB (GIVES CBC + DIFF)                                                                      (FE
   HEMOGLOBIN                               A    111        G/L 115-165                      FE
   HEMATOCRIT                               A    0.348      L/L 0.37-0.47                    FE
   WBC COUNT                                     9.3        X10 9/L 4.0-11.0                 FE
   RBC COUNT                                     5.35       X10 12/L 3.80-5.80              FE
   MCV                                      A    65.0       FL 80-97                         FE
   MCH                                      A    20.8       PG 27.0-32.0                     FE
   MCHC                                          320        G/L 320-360                      FE
   RDW                                      A    16.0       % 11.0-14.5                      FE
   PLATELET COUNT                                301        X10 9/L 150-400                 FE
   ABSOLUTE:  NEUTROS                            5.7        X10 9/L 2.0-7.5                 FE
   (A)    LYMPH                                  2.7        X10 9/L 1.1-3.3                 FE
   (A)    MONO                                   0.7        X10 9/L 0.0-0.8                 FE
      (A)    EOS                                 0.1        X10 9/L 0.0-0.5                 FE
   (A)    BASO                                   0.0        X10 9/L 0.0-0.2                 FE
   HYPOCHROMIA                              A    1+                                          FE
   MICROCYTOSIS                             A    2+                                          FE
   POLYCHROMASIA                            A                                                FE
{ SL INCREASED                                                                              }
   TARGET CELLS                             A    1+                                          FE
                                                                                            FE
E                                                                                           FE
                                                                                            }
   {                                                                                        }
   { RECOMMEND:   SERUM FERRITIN                                                            }
   {              HEMOGLOBIN ELECTROPHORESIS                                                }
   {                                                                                        }
GLUCOSE RANDOM                           .       5.1        MMOL/L 3.3-7.8                  FE
```
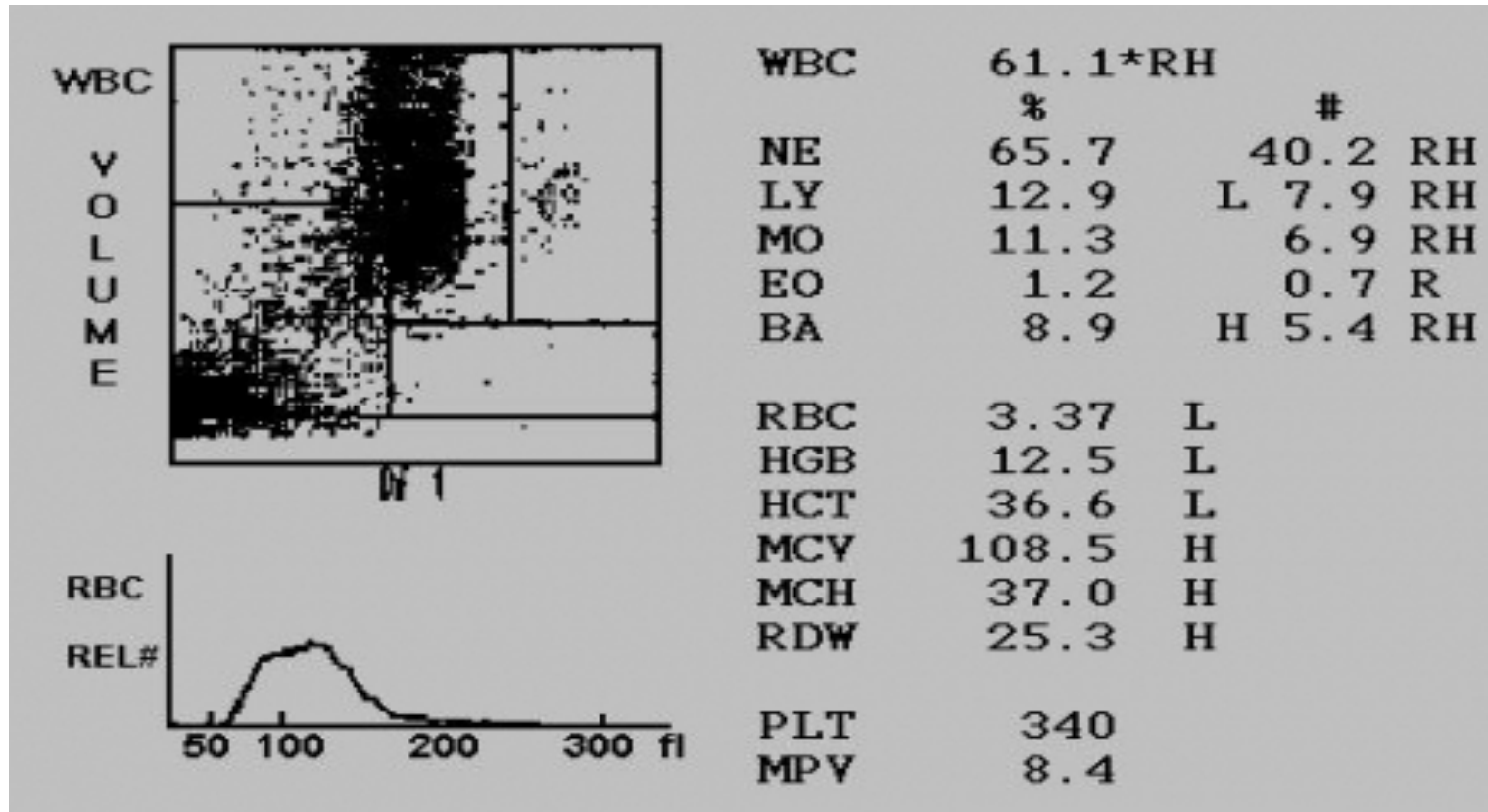
Case 3

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

Tests Ordered

CBC With Differential/Platelet

General Comments

PID: ▓▓▓▓▓

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

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.
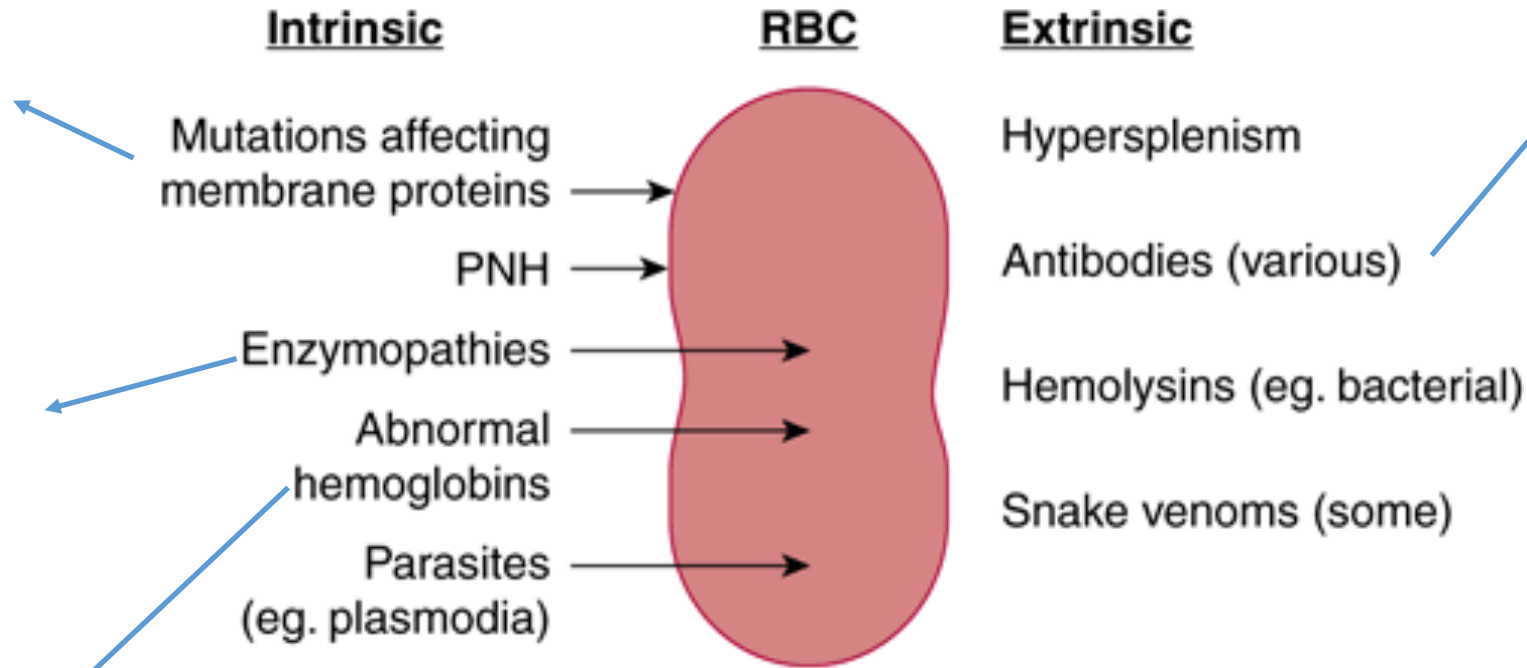- How to tell the difference?

	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

Autoimmune hemolytic anemia

Hereditary spherocytosis or elleptocytosis

G6PD or pyruvate kinase deficiency

Sickle cell anemia Thalassemia

Intrinsic   **RBC**   **Extrinsic**

Mutations affecting membrane proteins

PNH

Enzymopathies

Abnormal hemoglobins

Parasites (eg. plasmodia)

Hypersplenism

Antibodies (various)

Hemolysins (eg. bacterial)

Snake venoms (some)

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

Iron deficiency anemia

Smooth tongue

Angular stomatitis

ANGULAR CHEILITIS AND SMOOTH TONGUE IN IRON DEFICIENCY

Signs of iron deficiency anemia

- Pallor

- Glossitis

Koilonychia
(Spoon nails...the opposite of clubbing)

Iron-deficiency anemia (Hypochromic)

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

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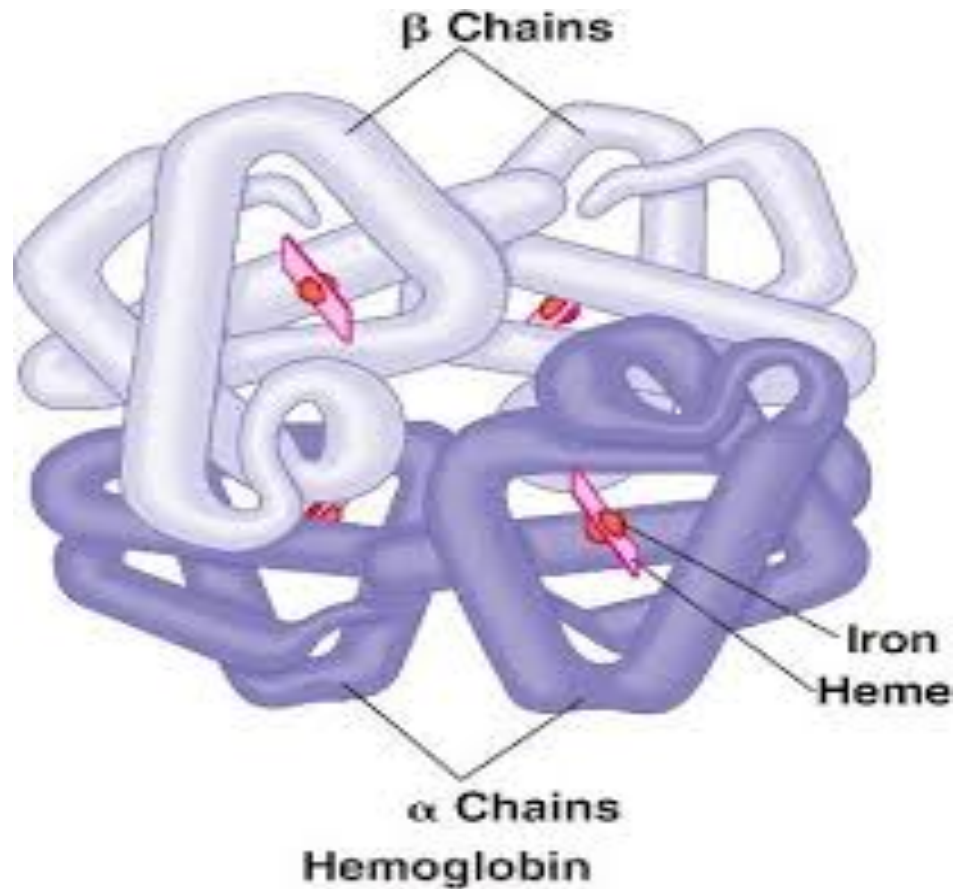
- Prominent malar eminences and mal-alignment of the teeth
- Secondary to bone marrow hyperplasia

HEMOLYTIC FACIES- CHIPMUNK FACIES

Alpha vs beta

β Chains

Iron
Heme

α Chains
Hemoglobin

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	$\beta 4$
Bart's Hgb	$\gamma 4$
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

Macrocytic anemia (megaloblastic)
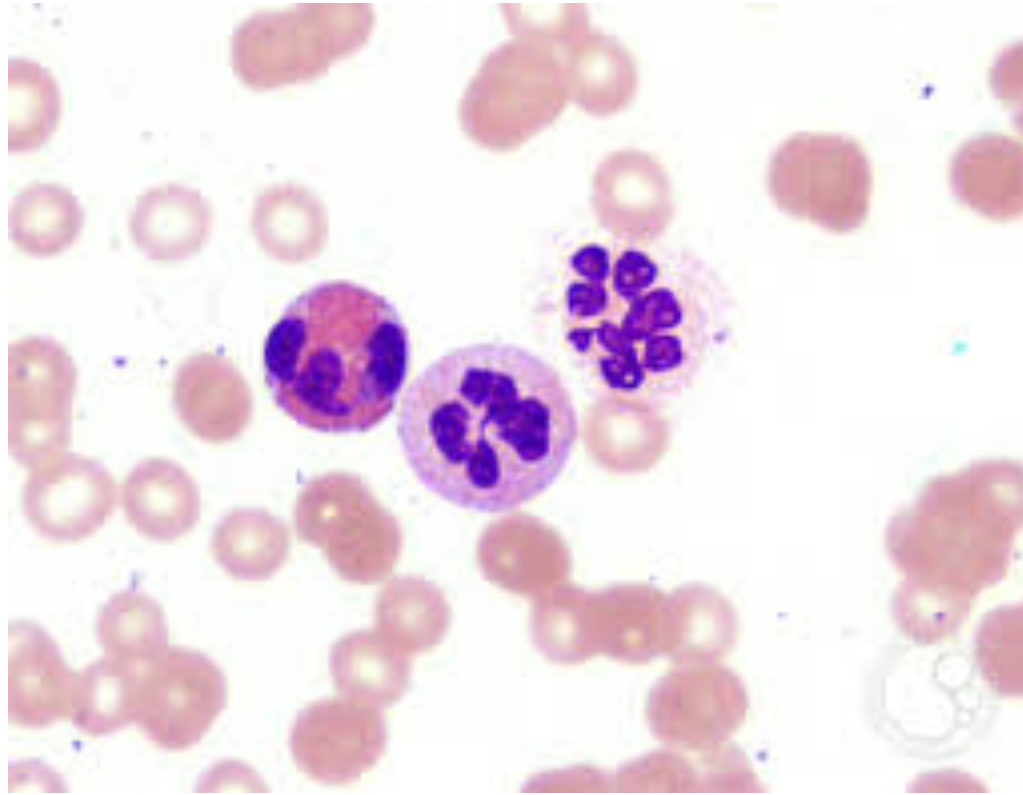
Macrocytic anemia (non-megaloblastic)

- Liver disease
- Alcohol
- Myelodysplasia
- Thyroid disease

Thanks

- Questions?