



# Hematology

# **Problem Based Learning**



]Slide

]Handout

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#### **Clinical Problems in Hematology:**

- Hematological diseases may be benign or malignant, and may affect RBCs, WBCs or platelets. Also plasma proteins may be associated with some abnormalities.
- Notes:

1- Normal MCV (80-96). > 96  $\rightarrow$  Macrocytosis < 80  $\rightarrow$  Microcytosis **ex:** If the MCV is 69.7, what is the status of RBCs? Microcytic.

2- RDW: Red Cell Distribution Width Normally, it's between 12-15 %.

#### The significance of RDW:

When there is low hemoglobin and low MCV, the patient either has:

a- Iron deficiency anemia

or b- Thalassemia trait (thalassemia minor).

So, how can we distinguish between them? We look at the RDW.

Normal RDW  $\rightarrow$  Thalassemia trait High RDW  $\rightarrow$  Iron deficiency anemia.

Note: MCV in thalassemia is much lower

Always remember this!!!

	Men	Women
Hemoglobin (g/dL)	14-17.4	12.3-15.3
Hematocrit (%)	42-50%	36-44%
RBC Count (10 <sup>6</sup> /mm <sup>3</sup> )	4.5-5.9	4.1-5.1
Reticulocytes	1.6 ± 0.5%	1.4 ± 0.5%
WBC (cells/mm <sup>3</sup> )	~4,00	00-11,000
MCV (fL)	8	30-96
MCH (pg/RBC)	30.	.4 ± 2.8
MCHC (g/dL of RBC)	34.	4 ± 1.1
RDW (%)	12	2-15%

Figure 1:

These are the normal ranges in men and women. You have to be familiar with them as they are important for diagnosis.

#### Reminder!

High RDW indicates that RBCs are of unequal size which is called "Anisocytosis"



Figure 2: MCV = 69.7 and RDW = 18.4. This indicates iron deficiency anemia.

#### Case 1: Elderly with low back pain.

#### 68 years old,

- Back pain for several months,
- Fractured his leg 2 days ago, In the X ray there is also a pathological fracture (Bone Related symptoms!)

#### Lab results:

- Hemoglobin 7.3 g/dL,
- WBC count is normal, platelet count is normal,
- <u>ESR</u> is 120 mm/hr very high.
- Blood urea nitrogen is 115 mg/dL very high, Creatinine 3.2 "normal is 1" which means acute renal failure.
   Total protein is high, serum albumin is low, calcium level is high 13 mg/dL (normal 5-10).

#### Clinical note:

In an elderly patient "above 50" with low back pain, we have to rule out metastatic disease to the bone, breast, prostate or multiple myeloma first then we can say it may be a spinal disc problems.



Figure 3: Blood film shows multiple erythrocytes lining up together in a form called **Rouleaux formation**, which is characteristic of plasma cell disorders "due to high protein level".



Figure 4: X-ray showing a pathological fracture.



Figure 5: Plasma cells in the bone marrow.

#### Serum Protein Electrophoresis SPEP:



#### Figure 6:

a- This is the normal levels of plasma proteins on SPEP.

b- There is a spike in the gamma globulins. This indicates *plasma cell disorders*.

c- If it's a clear <mark>spike</mark>, then its origin is from one type of cell "monoclonal". If there's a wide base, this means that its origin is from many types of cells "polyclonal".

SPEP results of the patient shows M spike (Elevated Gamma globulins)

- To know which type of antibodies is produced by plasma cells in this case, we do something called immunofixation
- Immunofixation results shows that it is IgG kappa myeloma!

Note: Gamma globulins (IgM, IgD, IgG, IgE, IgA) are produced by Plasma cells which are derived from B-cells

In each antibody, the two light chains are of the same type, either the two are **kappa**  $\kappa$  or the two are **lambda**  $\lambda$  (i.e. never a mixture in the same antibody).



Multiple myeloma diagnostic criteria:

- 1. Elevated serum or urinary monoclonal protein.
- 2. Presence of clonal plasma cells in BM or elsewhere called (Plasmacytoma)
- 3. End Organ damage (due to plasma cell dyscrasia) : (CRAB)
- C= high Calcium, R= Renal Failure, A= Anemia, B= Bone lesions.
  - Always remember that all these three criteria has to be met in order to diagnose multiple myeloma.

Why did the patient had.....?

- 1- Low Back pain, Fractured leg, pathological fracture -> due to bone lesions
- 2- High ESR, Rouleaux formation in the Blood film -> due to high serum protein (IgG gamma globulin)
- 3- High Creatinine and blood urea nitrogen -> due to Acute renal failure
- 4- High Calcium Level -> breakdown of bone(resorption)

#### Caution!

You can't diagnose MM to a patient below 40 years of age! (Disease of elderly people)



Figure 8: Lytic bone lesions.



#### **Plasma Cell Disorders:**



## SMM



#### Monoclonal Gammopathy of Unknown Significance (MGUS):

- Elevated serum proteins only! (M proteins) A monoclonal paraprotein band (M band) < 3 g/dL.
- 2. No increase in plasma cells (<10%) on BM examination.
- 3. No <u>CRAB</u>
- 4. No evidence of another B-cell proliferative disorder
- MGUS transformed into multiple myeloma or similar lymphoproliferative disorder at the rate of about 1-2% a year
  - At 10 years: 17%
  - At 20 years: 34%
  - At 25 years: 39%

These patients can transform into Multiple Myeloma at a rate of 1-2% per year

Note: (MGUS can develop into MM, but not every MM patient have to go through MUGS phase first, MM can occur directly! Also, not every MGUS will develop into MM"1-2%".)

#### **Smoldering Multiple Myeloma (SMM):**

Anything between MGUS and MM is called Smoldering Multiple Myeloma

(SMM), or Asymptomatic Myeloma. (Slightly higher M protein levels than MGUS but no sign and symptoms of MM, like bone disease and Anemia)

SMM must meet first two criteria:

- Serum monoclonal protein  $\geq 3 \text{ g/dL}$  and/or  $\geq 10 \%$  to < 60% bone marrow clonal plasma cells
- No end organ damage related to plasma cell dyscrasia
- See the meaning of dyscrasia on Wikipedia. It's really interesting.

#### Case 2: Elderly with Loss of Balance:

Elderly 68 years old male, Presented with **loss of balance** and **paresthesia** in the hand and feet for 8 months.

Patient is type 2 diabetic and **alcoholic**.

Physical examination showed a short-termed **memory loss** and an absence of **vibration** sensation and proprioception in the toes and ankles, he was positive for **Romberg** test when he closes his eyes. Lab Results:

Hemoglobin is 9.7 g/dL, MCV 105 fl/cell, white and platelet counts are normal he is "<u>Macrocytic</u>"

Blood film has a **Hypersegmented** neutrophil which is a characteristic for *Vit B12 deficiency* 



\*When you see anemia with low MCV and hypersegmented neutrophils, then it's vitamin B12 deficiency anemia.!! Figure 9: Hypersegmented Neutrophils.

But what are the other causes of macrocytosis that should by suspected from the high MCV?

Other causes of macrocytosis:

Macrocytosis Possibilities:	Drugs that cause
<ul> <li>a- Alcoholism</li> <li>b- Liver disease</li> <li>c- hypothyrodism</li> <li>d- Megaloblastic anemia (B12 or folate deficiency)</li> <li>e- MDS(Myelodisplastic syndrome)</li> <li>f- Reticulocytosis</li> <li>g- Exposure to antimetabolites</li> </ul>	<ul> <li><u>Hydroxyurea (Sickle</u> <u>Cell)</u></li> <li><u>Zidovudine (HIV)</u></li> <li>Cytosine arabinoside</li> <li><u>Methotrexate</u></li> <li>Azathioprine or 6- mercaptopurine</li> <li>Cladribine</li> <li>Capecitabine</li> <li><u>Imatinib</u>, sunitinib</li> </ul>

- There are a lot of causes of vitamin B12 deficiency and folate deficiency, but here we will focus on things that are common in Jordan.
- Metformin:

- <u>Metformin</u> reduces intestinal absorption of <u>vitamin B12</u> in up to 30% of patients, and lowers serum vitamin B12 concentrations in 5-10%, but only rarely causes megaloblastic anemia.

- The dose and duration of use of metformin correlates with the risk of vitamin B12 deficiency .
- Reduction appears to be due to absorption in the ileum and can be corrected by administration of oral calcium .
- Proton-pump Inhibitors: Prolonged use of proton pump inhibitors (eg, omeprazole) can result in Cbl (cobolamin) deficiency as a consequence of impaired release of Cbl from food in the absence of gastric acid secretion.
- Metformin and PPIs are frequently used drugs in Jordan due to the high prevalence of type 2 diabetes and peptic ulcer, which are treated primarily by these two drugs.



Vitamin B12 deficiency causes:	Pancreatitis
Gastric abnormalities	- Pancreatic insufficiency
- Pernicious anemia	Diet
<ul> <li>Gastrectomy/bariatric surgery</li> </ul>	- Strict <u>vegans</u>
- <u>Gastritis</u>	- Vegetarian diet in pregnancy
<ul> <li>Autoimmune metaplastic atrophic gastritis</li> </ul>	CAgents that block absorption
	- Neomycin
Small bowel disease	- Biguanides (eg, metformin) <i>"reduces</i>
<ul> <li>Malabsorption syndrome</li> </ul>	intestinal absorption of <u>vitamin B12</u> in up to
<ul> <li>Ileal <u>resection</u> or bypass</li> </ul>	30% of patients"
- Crohn's disease	<ul> <li>Proton pump inhibitors (eg, omeprazole)</li> </ul>
- Blind loops	<ul> <li>N2O anesthesia inhibits methionine</li> </ul>
- Diphyllobothrium latum (fish	synthase
tapeworm) infestation	<ul> <li>Inherited transcobalamin II deficiency</li> </ul>
Folate deficiency causes:	Drugs (various mechanisms)
Nutritional deficiency	- <u>Methotrexate</u>
- Substance abuse	- Trimethoprim
- Alcoholism	- <u>Ethanol</u>
<ul> <li>Poor dietary intake</li> </ul>	- <u>Phenytoin</u>
<ul> <li>Overcooked foods</li> </ul>	Increased requirements
<ul> <li>Depressed patients</li> </ul>	
<ul> <li>Nursing homes</li> </ul>	- <u>Pregnancy, lactation</u>
Malabsorption	<ul> <li>Chronic hemolysis</li> <li>Exfoliative dermatitis</li> </ul>
- <u>Celiac disease (sprue)</u>	Note: preanant ladies are advised to take a
- Inflammatory bowel disease	supplement drug called FFFOI "fe for iron
- Infiltrative bowel disease	and fol for folate" to avoid their deficiency

Other causes of vitamin B12 deficiency (taken from the slides):

Short bowel syndrome -

#### Case 3: 62-year-old Man with Anemia

62 years old male patient,

Presented with fatigue, pallor, progressive shortness of breath and generalized weakness "symptoms of anemia".



Figure 11: Angular Cheilitis

	Total (mg/day)
Adult male	0.5-1
Postmenopausal female	0.5-1
Menstruating female	1-2
Pregnant female	1.5-3
Children (average)	1.1
Female (age 12-15)	1.6-2.6

Figure 12: Daily iron requirement. This shows that pregnant females need iron the most, hence they are most likely to develop IDA during pregnancy.

#### Lab Results:

- Hemoglobin is 9.7 g/dL  $\rightarrow$  Anemia.

- MCV 69 fl/cell "normal 80-96" → Microcytosis
- RDW is 18% (Normal 12-15%)  $\rightarrow$  Anisocytosis.

Patient have abnormal nails, pale conjunctiva and Angular Cheilitis\* which are a characteristic of **Iron deficiency Anemia** 

\*Iron is needed for healthy mucosa



Figure 10: Pallor (pale skin and conjuctivae) due to anemia.



Figure 13: Koilonvchia (spoon nails).

- Blood film shows increased central pallor (a characteristic of hypochromia associated with IDA).
- To confirm the diagnosis of IDA, we have to do iron studies:

Serum Fe:  $10 \,\mu g/dL$ 

- Serum Ferritin: 2 ng/ml
- TIBC: 450 μg/dL
- → Low serum iron and high TIBC (this is consistent with IDA).

#### Treatment:

- Oral iron supplement, but patient may not respond due to continuous hemorrhage, wrong diagnosis, mixed deficiency, malabsorption or the poor compliance to the oral supplement.
- In the case of malabsorption, we give **<u>IV iron</u>** infusion to avoid this problem.



#### Remember!

\*When there is low hemoglobin and low MCV then the patient have <u>Iron</u> <u>deficiency</u> anemia or <u>Thalassemia</u> <u>trait</u> (thalassemia minor), if the RDW is normal then it is Thalassemia trait if it's high then it's Iron deficiency anemia.

Also, notice that MCV in thalassemia is much lower than in IDA *"below 60"* 

The doctor stated a point that in a case like this the elderly people are not supposed to be iron deficient so when we see a patient with these symptoms we have to rule out malignancy first, this patient could be bleeding from gastric cancer, or bleeding from colonic cancer

So to complete your work up, any patient above the <u>age of 50</u> with iron deficiency anemia should have an upper and lower <u>Endoscopy</u> to detect any tumor there

#### Case 4: Young woman with fever, confusion and low platelets.

40 year old lady with one week history of	Laboratory studies showed:
<mark>fever</mark> and <mark>confusion</mark> .	- BUN: 52 mg/Dl, Creatinine 5.3 mg/dL
Physical examination shows the patient is febrile, temperature is 38.2 C	<ul> <li>→ Renal Impairment</li> <li>Hb:12.2 g/dL, MCV: 93 Fl → Normal</li> <li>Platelets: 19,000/microliter → Very low</li> </ul>
Have a lot of what's called "Petechial rash"	(Thrombocytopenia). - WBC: 8180/microliter → Normal



Figure 16: Petechial Rash

- Blood film:

When schistocytes are present on blood film, this is called MAHA (Microangiopathic Hemolytic Anemia).

- When we see schistocytes on blood film, there are four possible diagnoses:

1- Disseminated Intravascular Coagulation (DIC)

2- Thrombotic Thrombocytopenic Purpura (TTP)

- 3- Heart Valve Hemolysis
- 4- Hemolytic-Uremic Syndrome

So we have 1. Fever and confusion, 2. Low platelet, 3.renal impairment, 4. Schistocytes.

### ITP vs. TTP vs. DIC

Figure 15: Blood film showing schistocytes.

•Parameter	ITP	TTP	DIC
Pathogenesis	Antiplatelet antibodies	Endothelial defect	Thrombin excess
<ul> <li>Clinical Condition</li> </ul>	Not sick	Sick	Sick
•Red Cells	NL	Schistocytes	Schitocytes +/-
•PT (INR)	NL	NL/Slightly Incr.	Incr.
•PTT	NL	NL/Slightly Incr.	Incr.
<ul> <li>Fibrinogen</li> </ul>	NL	NL	Decr.
•Fibrin Monomers	NL	Slight Incr.	Incr.
•Fibrin Degradation	NL	Slight Incr.	Incr.
•D-dimers	NL	Slight Incr.	Incr.
•Therapy	Steroids IVIG Splenectomy	Plasma Xchange Vincristine	Rx cause Plasma/Plts ATIII (?)

- Which of the following is the most likely diagnosis?
- a. Disseminated intravascular coagulopathy
- b. Idiopathic thrombocytopenic purpura
- c. Thrombotic thrombocytopenic purpura

- Thrombotic Thrombocytopenic Purpura (TTP)
- Microangiopathic hemolytic anemia (MAHA)
- Thrombocytopenia, often with purpura but not usually severe bleeding
- Renal function may be normal, but acute renal insufficiency may be present
- Neurologic abnormalities, usually fluctuating, are common
- Fever is rare; high fever with chills suggests sepsis rather than TTP-HUS
- Reduced ADAMTS13 activity

- d. Trousseau syndrome
- e. Warm autoimmune hemolytic anemia
- Fever, low platelets, confusion and renal impairment all suggest TTP. However, to confirm the diagnosis, we have to do an ADAMTS13 test,

if it's less than 10% then it is TTP

\*in our case it's less than 10% so the diagnosis is definitely TTP!

Note: it's important to confirm the diagnosis because the treatment is specific!!

TTP can be congenital (due to ADAMTS13 deficiency) or drug-induced.

ADAMTS13:
It's von Willebrand factor cleaving protease.

ITP: Only low platelet. No fever and confusion, no Schistocytes, no renal impairment.

- ADAMTS13 activity measurement should not influence the decision to initiate plasma exchange.
- Plasma or serum for measuring ADAMTS13 activity must be obtained before the initiation of plasma infusion or plasma exchange.
- If ADAMTS13 is below 10 %, then it's TTP.
- The treatment in this case is plasma exchange or fresh-frozen plasma.

Drug-induced TTP: there are 6 drugs that can cause TTP and you should memorize them

#### Immune mediated

**Quinine** is most common cause. Among drugs suspected to be the cause of acute TTP-HUS, drug-dependent antibodies have only been documented for quinine. Other drugs may cause immune-mediated TTP-HUS but are rare.

Dose-dependent toxicity

Cancer chemotherapy (mitomycin C, gemcitabine, possibly others) Immunosuppressive agents (cyclosporine, tacrolimus, sirolimus)

#### Case 5: 64-year-old Male with Asymptomatic Leukocytosis

- 64-year-old male patient.
- CBC shows elevated WBC count while being worked up for hernia repair.
- Physical examination shows lymphadenopathy, spleen is not palpable.
- No fever, night sweats, fatigue, or shortness of breath!

Lab Results:

- Hemoglobin is 14 g/dL, WBC count is 22000 which is high and most of the cells are lymphocytes "75%".
- Blood film shows mature lymphocyte and "<u>Smudge cells</u>".
- When we see smudge cells, we should think of Chronic Lymphocytic Leukemia! "<u>CLL</u>".
- To diagnose a patient with CLL, he should be above the <u>age of 50</u>, lymphocyte count is elevated, with normal looking lymphocytes in the blood film.





Smudge cells are fragile lymphocytes which get damaged during preparation of the blood film

- To <u>confirm</u> the diagnosis, we do a <u>Flow</u> Cytometry
- Flow Cytometry is used to know what type of lymphocyte clusters are present based on the type of cell membrane protein on its surface like CD5, CD22, CD23 etc...
  - And in this case we can make our diagnosis based on the flow Cytometry results which showed a monoclonal, mature B-cell population that is positive for CD5 and CD23.
  - If it was positive for CD5 only then the diagnoses is Mantle cell lymphoma.
  - So if the result is CD5 +ve, then it's either CLL or Mantle cell lymphoma, so we check for CD23 to distinguish between them. See Figure 16.

	CD 5	CD 43	CD 22	CD 23	CD 25	CD 103	Cytogenetics
CLL/SLL	+	+	-/+	+	+/-	-	
Mantle	+	+	_/+	-	-	-	T (11,14 )
PLL	-/+	+	+	-/+	-	-	
HCL	-	+	+	-	+	+	
MZL	-	-/+	+/-	+/-	-	-	
Follicular	-/+	-	-/+	-/+	-	_	T (14,18)
Figure 1	7		*		•	•	•

- Hairy cell leukemia (HCL): it's the only type that expresses CD103, and flow cytometry is used to confirm its diagnosis by checking CD103 on cell surface.



- Mantle Cell Lymphoma

1- Older male 2- Cyclin D overexpression, poor prognosis

- Follicular Lymphoma
  - 1- bcl-2 overexpression (inhibit apoptosis) 2- Difficult to cure
  - 3- Indolent (recurring/remitting course)
- Burkitt's Lymphoma

C-myc to Heavy Chain IG gene



Which of the following factor deficiency can explain her situation?

- a. Factor VIII deficiency
- b. Factor IX deficiency
- c. Factor X deficiency
- d. Factor XI deficiency
- e. Factor XII deficiency

Pay attention to the Coagulation cascade diagram, you should now each pathway's factors and what test is used for it, "PT for extrinsic, PTT for intrinsic"

Elevated PTT means problem in the intrinsic pathway. "factor XII, XI, IX & VIII"

Elevated PT means problem in the extrinsic pathway. "factor VII"

When both PT & PTT are elevated this means a problem in the common pathway. "factor X, V, II & I"

TEST	NORMAL VALUE
Platelet count	150,000-300,000/uL
Bleeding time (BT)	3-7min
Prothrombin time (PT)	10-12 sec
Partial thromboplastin time (aPTT)	25-38 sec
Inrombin time (11)	9-35 Sec
Fibrinogen assay	200-400mb/dL
Fibrin Degradation products and D dimer	0-11 and <500 ng/mL



# **Coagulation Cascade**

PT is normal  $\rightarrow$  we rule out the extrinsic pathway factors and common pathway too!

So, we think of factors XII, XI, IX, and VIII

So, factor XII is deficient in this case because the patient <u>have no history</u> <u>of bleeding</u>! ANS: "e"

→ She can do the surgery without any problem!

\*Any patient with a problem in contact factors (HMWK, prekallikrein & factor XII), his PTT becomes very high, yet bleeding will be normal because the body can compensate with other methods of coagulation...

Why not factor XI, IX or VIII deficiency?

- Deficiency of these factors increases PTT, but also it would cause bleeding because it's essential in the coagulation cascade!

Why not X? Because PT is normal





#### Case 7: Young Male with Leukocytosis

30 years old male patient

Presented with worsening productive cough for one month,

- Physical examination:

1- Small non-tender lymph nodes are palpable in the axillae

2- Tip of the spleen is palpable

Peripheral blood smear is shown.

This shows myeloblasts with **Auer** rods.

Which of the following is the most likely diagnosis?

- a. Leukemoid reaction
- b. Acute myelogenous leukemia
- c. Chronic lymphocytic leukemia
- d. Acute lymphoblastic leukemia
- e. Leukoerythroblastosis

Lab result:

Hb: 8.2 g/dl, MCV 90 fL  $\rightarrow$  Anemia and normocytic

WBC: 67,000/microliter → Leukocytosis

Platelets: 36,000/microliter  $\rightarrow$  Thrombocytopenia



Auer rods are diagnostic for AML!, whenever you see Auer rods you diagnose with Acute Myelogenous Leukemia. "b"

\*Most patients with leukemia present with infections or cytopenia

#### Case 8: Young male with leukocytosis, thrombocytosis and splenomegaly

<ul> <li>one month of increasing generalized weakness and easy fatigability</li> <li>"Anemia"</li> <li>epigastric pain but without vomiting.</li> <li>Physical exam was significant for splenomegaly but with no lymphadenopathy.</li> <li>Hemoglobin is 10.2, WBC count is 78,000!, and platelet count is 890,000!, both are very very high → Leukocytosis, and thrombocytosis.</li> <li>Blood film shows all stages of WBC maturation Myeloblast, promyelocyte, band cells</li> </ul>

Which one of the following is the most likely diagnosis?

- A. Chronic granulocytic leukemia
- B. Acute granulocytic leukemia
- C. Acute lymphocytic, T-cell type leukemia
- D. Acute lymphocytic, B-cell type leukemia
- E. Chronic Lymphocytic Lymphoma
  - Whenever you see all types of WBC maturation the diagnoses is CML!





CML is cause by translocation at (9,22) called Philadelphia Chromosome

Treatment by new drug called <u>tyrosine kinase inhibitor</u> "Imatinib &

dasatinib"





#### Case 9: 57-year-old Male with progressive weakness and anemia

#### 57 years old male patient

Evaluated for 3 month history of progressive fatigability, shortness of breath and weakness (anemia)

Physical examination shows splenomegaly,

Hemoglobin is 9 g/dL, his stool was negative for occult bleeding,

Blood film shows a significant **NUCLEATED** red blood cells

Which of the following should be included in the patient's differential diagnosis?

- A) Myelofibrosis
- B) Vitamin B 12 deficiency
- C) Anemia of chronic disease
- D) Iron deficiency anemia

Ans: Myelofibrosis "because of the nucleated RBCs..."



## Pathological possibilities of Nucleated RBCs

- Hemoglobinopathies
  - Sickle cell diseases
  - Thalassemia
- Marrow-infiltrative diseases
  - Myelofibrosis
  - Metastatic Cancers
- Non-Hematological diseases
  - Sepsis
  - Sever trauma

Myelofibrosis is associated with BM fibrosis and massive splenomegaly.



Massive Splenomegaly due to Myelofibrosis



**Fibrotic BM** 

#### The doctor told us to solve the rest of the cases by our own!

#### so here they are Enjoy!

#### Case 10:

63 years old patient diagnosed with CLL

Evaluated because of increasing dyspnea on exertion (which is a manifestation of anemia),

Currently taking no medication,

On physical examination the patient is afebrile, pale conjunctivae, with scattered axillary and inguinal lymphadenopathy that are unchanged since his last examination 1 year ago,

Hemoglobin is 6.2 g/dL (one year ago was 14.2),

platelet and WBC counts are normal "12,000/µL (25% polymorphonuclear, 75% lymphocytes)", but <u>reticulocyte</u> count is high 10% "when reticulocyte count is high this means that the patient is <u>hemolytic</u>"

In the blood film we see Spherocytes "sphere shaped RBC", when we see spherocytes there are only <u>two possibilities</u>, either **Hereditary Spherocytosis** or **Autoimmune Hemolytic Anemia** 

Most likely Autoimmune Hemolytic Anemia "due to high reticulocyte percentage"

#### Case 11:

26 years old male with hemoglobin of 4.0!

Evaluated for two weeks history of:

Progressive fatigue, dyspnea on exertion, vague and non exertional chest discomfort, mild cough,

Takes no medication, was a carpenter and does a lot of exercise but not anymore

Hemoglobin is 4.8 g/dL, hematocrit is 13% very low, reticulocyte count is zero! "No blood formation, BM failure".

X ray shows anterior mediastinal mass,



\*When a patient have an anterior mediastinal mass and low hemoglobin this could only mean one diagnosis,

Which of the following is the most likely cause of

the mediastinal mass?

- a. Hodgkin's disease
- b. Non-Hodgkin's lymphoma
- c. Thyroid carcinoma
- d. Thymoma
- e. Germ cell carcinoma

ans: Non-Hodgkin lymphoma



We're a little concerned about your potassium levels.

#### Case 12:

33 years old female with low grade fever, night sweats, generalized malaise, and weight loss for the past 2 months.

The last three are called "B symptoms", which are indicators of hodgkin's and non-hodgkin's lymphoma.

Physical examination shows non tender cervical and supraclavicular lymphadenopathy, Lymph node biopsy shows a very characteristic pathological finding. (Reed Sternberg)

Which of the following is the most likely diagnosis?

- a. Burkitt lymphoma
- b. Hodgkin lymphoma
- c. Cat scratch disease
- d. Mycosis fungoides
- e. Multiple myeloma
- ans: Hodgkin's lymphoma

#### Case 13:

8 years old kid

Presented with unexplained large bruises over the skin,

Physical examination shows no sign of anemia

Hemoglobin is 14 g/dL, WBC count is normal, platelet is low "thrombocytopenic", PT,PTT are normal, but bleeding time is 19 minutes "normal time is 3-10 minutes".

Blood film shows very huge size of platelet! We will know what that means later.

Diagnosis is Giant platelet disorder,





Giant platelet disorder occurs for inherited diseases like Bernard-Soulier syndrome, gray platelet syndrome and May-Hegglin anomaly.

Most likely Bernard-Soulier syndrome

#### Case 14:

69 years old lady with hip replacement 10 days ago, presented with swollen right leg,

Doppler ultrasound was done to check blood flow, artery flow was normal but the vein was blocked "DVT" so an anticoagulant drug is needed.



- a. Enoxaparin
- b. Rivaroxaban
- c. Warfarin
- d. Dabigatran
- e. Fondaparinux

ans: Warfarin





#### Case 15:

77 years old

with history of coronary artery disease "CAD" diagnosed with diffuse large cell lymphoma "DLBCL" with bulky lymphadenopathy,

Started with chemotherapy and after three days the patient presented in the ER with symptoms of severe fatigue, nausea, vomiting, abdominal pain,

High potassium 5.3 mEq/L, low calcium 8.1 mg/dL, high phosphates, LDH very high 28000, uric acid is high.

These symptoms are called "tumor lysis syndrome".

Which of the following is helpful to avoid this

problem:

- a. IV Hydration
- b. Allopurinol "lowers uric acid"
- c. Rasburicase "clears blood from uric acid"
- d. All of the above
- ans: All of the above



No matter how ímpossíble, unattaínable, or unimaginable something may seem...

If it's meant to be, it'll be.

