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CBC APPROACH TO ANEMIA

Medical Editor: **Mina Ragy**

I. RED BLOOD CELLS (RBCS)

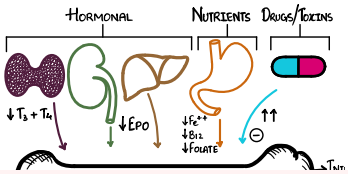
- Red blood cells are also known as **erythrocytes and Red Blood Corpuscles**
- Red blood cell production occurs in the **red bone marrow**
- They start as **Myeloid Stem Cell**
  - Progenitor for red blood cells, platelets, and granulocytes (e.g. neutrophil, basophil, eosinophil)
  - Receives **stimuli** which direct it to form red blood cells

What are those Stimuli?

A. STIMULI FOR CREATING RBCS

01:54

- **Erythropoiesis** refers to the process of red blood cell production
- There are different factors which influence production:
  - **Hormones** – stimulates production
  - **Nutrients** – stimulates production
  - **Drug/Toxins** – inhibits production
  - **Intrinsic Bone Marrow Function**



1. Hormones

a) Thyroid Hormones (T3 and T4)

b) Erythropoietin

- Produced by the liver and kidney
- Stimulates the bone marrow to produce RBCs

2. Nutrients

- We need a ton of nutrients to make RBCs
- Some of the essentials are:

a) Iron

b) Vitamin B12 / Cobalamin

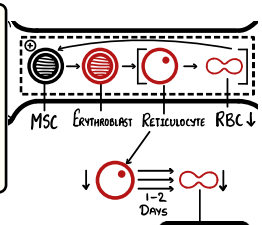
c) Vitamin B9 / Folate

3. Drugs/Toxins

- Suppress RBC production in the bone marrow
- Example: Alcohol

Remember

Erythropoiesis (RBC Development)
- Myeloid Stem Cell
  - → Erythroblast
    - → Reticulocyte
      - → Red Blood Cell / Erythrocyte



B. RETICULOCYTE INDEX INTRODUCTION

05:07

- Reticulocytes are immature/developing red blood cells
- It takes 1-2 days for a reticulocyte to develop into an RBC
  - **If we have low Erythropoiesis**
    - → We will have a few reticulocytes
    - → ↑ Reticulocyte Index
  - **If Loss or destruction of RBCs** and Erythropoiesis is compensating
    - → We will have many reticulocytes
    - → ↓ Reticulocyte Index

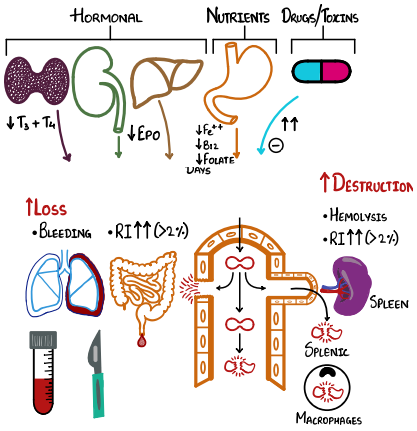


FIGURE 1 RETICULOCYTE INDEX IN EXAMPLE CASES OF ANEMIA

11:05

II. Anemia

- **Anemia** refers to a <u>decreased red blood cell mass</u>, manifested as:
  - Decrease in Hemoglobin (Hgb)
  - Decrease in Hematocrit (Hct)
  - Decrease in RBCs
- Anemia can be due to either:
  - External stimuli
  - Poor bone marrow function
  - Bleeding / Increased blood loss
  - Increased destruction of RBCs

01:54

A. Causes of Anemia

- To determine the cause of anemia, a **comprehensive history** and **laboratory tests** (e.g., complete blood count, iron studies, peripheral blood smear, etc.) are needed.

1. External Stimuli

- There are different stimuli/factors which influence red blood cell mass
  - **Hormones**
  - **Nutrients**
  - **Drugs/Toxins**

Reticulocyte index is low (less than 2%)

2. Bone marrow function is affected when:

- Exposure to **chemoradiation** destroys the structure of the bone marrow
- There is a **neoplasm/cancer** of the bone marrow

Reticulocyte index is low (less than 2%)

3. Poor Bone Marrow Function

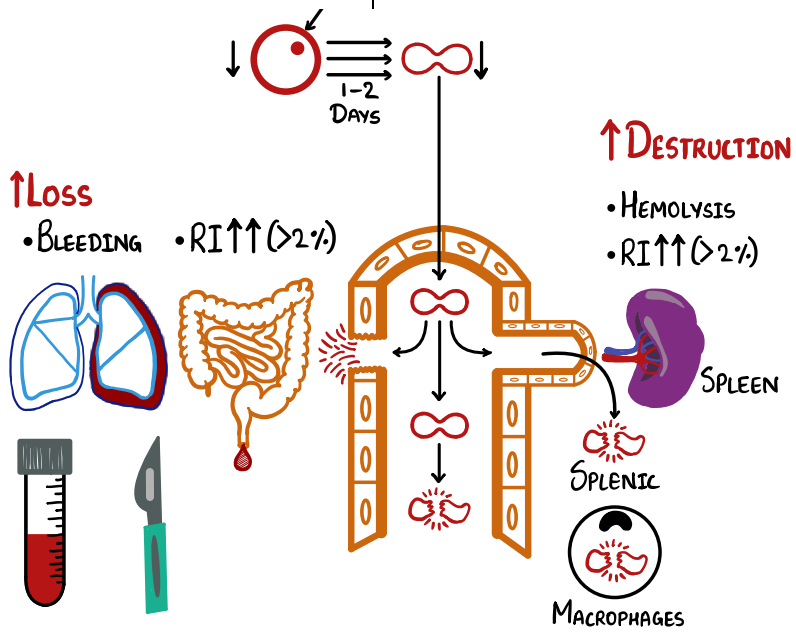
- When there is active bleeding or increased blood loss, the RBC count may decrease
- Since bone marrow function is normal, the decreased RBC count triggers a compensatory mechanism which <u>increases erythropoiesis and subsequently increases the reticulocyte index</u>
- Examples:
  - GI bleed
  - Frequent blood withdrawals (e.g. in the ICU)
  - Surgery

Reticulocyte index will increase as a compensatory mechanism

4. Poor Bone Marrow Function

- RBCs may be destroyed or lysed within the vasculature or the spleen
  - **Intravascular Hemolysis** – destroyed within the vasculature
  - **Extravascular Hemolysis** – destroyed within the splenic macrophages of the spleen

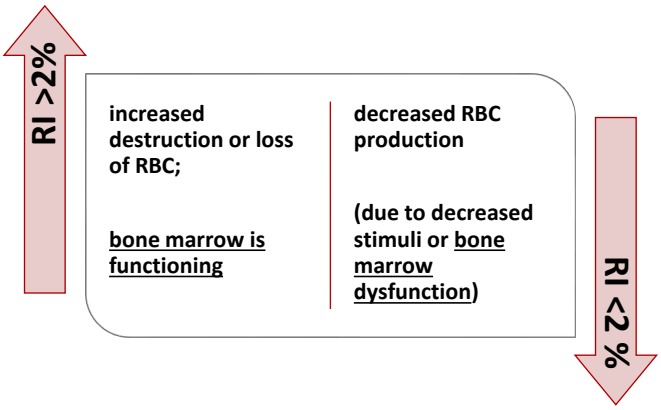
Reticulocyte index will increase as a compensatory mechanism

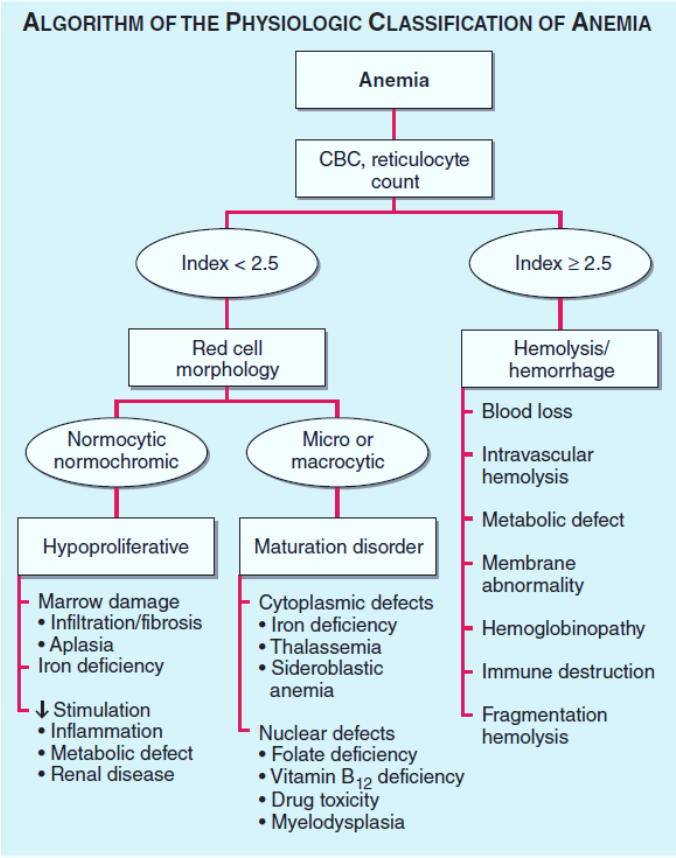


B. Classification of Anemia

01:54

- Anemia may be classified based on the **reticulocyte index**
- The reticulocyte index (RI) is a good indicator of bone marrow function
  - RI <2 % - decreased RBC production (due to decreased stimuli or bone marrow dysfunction)
  - RI >2% - increased destruction or loss of RBC; bone marrow is functioning
- **This diagnostic parameter is ordered separately from the complete blood count (CBC)**
  - The reticulocyte count shown in the diagnostic results is NOT the reticulocyte index, This value should be inputted in a reticulocyte index calculator





C. Classification of Anemia

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- Diagnostic tests are often necessary – on top of a comprehensive history and physical examination – to determine the cause of anemia
- The following are the most common diagnostic tests ordered for anemia:

1. RDW

- measures the variation in size of RBCs

2. RBC count

3. Menser's Index (MI)

- Computed as MVC / RBC

4. Iron Studies

- **Fe^{++}**
- **Ferritin**
  protein which binds to irons inside the cells; reflects iron reserves
- **Total Iron Binding Capacity (TIBC)**
- **Transferrin Saturation %**
- Computed as Fe/TIBC

5. Peripheral Blood Smear (PBS)

	Initial consult	3 Months later	Normal range
WBC	7.6	4.8	4.0–10.0 thousand/mm^3
RBC	4.57	4.26	4.0–5.2 million/mm^3
Hemoglobin	10.9	9.1	12.0–16.0 g/dL
Hematocrit	33.9	28.0	35.0–45.0%
MCV	74.2	67.4	78.0–100.0 μm^3
MCH	24.0	21.9	26–34 pg
RDW	14.1%	15.6%	11.0–14.0%
Reticulocyte count	1.2%	–	–
Platelets	286	194	150–450 thousand/mm^3
Total iron	22 mcg/dL	–	40–190 mcg/dL
TIBC	431 mcg/dL	–	250–450 mcg/dL
Iron saturation	5%	–	11–50%
Ferritin	3 ng/mL	–	10–154 ng/mL
Transferrin	323 mg/dL	–	188–341 mg/dL

MCH mean corpuscular hemoglobin, *MCV* mean corpuscular volume *RBC* red blood cells, *RDW* random distribution of red cell width, *TIBC* total iron-binding capacity, *WBC* white blood cells

FIGURE 2 HEMATOLOGY TESTS AND IRON PROFILE EXAMPLE

11:05

III. ↓ Production of RBC's (RI < 2%)

- Disorders with a reticulocyte index < 2% may be further classified based on the RBC morphology
- **The mean corpuscular volume (MCV) determines the size of the red blood cells**
  - Normal Value: 80 – 100 femtoliters (fl)
- **The types of anemia based on MCV value are:**
  - Microcytic Anemia: < 80 fl
  - Normocytic Anemia: 80 – 100 fl
  - Macrocytic Anemia: > 100

Microcytic Anemias

- **MCV: < 80 fl**
- **Differentials**
  - Iron Deficiency Anemia
  - Anemia of Chronic Disease
  - Thalassemia
  - Sideroblastic Anemia
- **Diagnostic Tests**
  - RDW
  - RBC
  - MI
  - Iron Studies
  - Peripheral Blood Smear (PBS)

1. Iron Deficiency Anemia

- ↑ RDW
- ↓ RBC
- MI > 13%
- ↓ Ferritin
- ↓ Transferrin Sat %
- PBS is not helpful

2. Anemia of Chronic Disease

- History is the most important factor; look for symptoms and signs of chronic disease
- ↔ RDW
- ↓ RBC
- MI is not helpful
- ↑↑ Ferritin
  - Ferritin is an acute phase reactant; it may be elevated when there is an active inflammatory process such as in chronic diseases
- Transferrin Sat % is variable

3. Thalassemia

- ↔ or ↑ RDW
- ↔ RBC
- MI < 13%
  - ↓↓↓ MCV / RBC
- Iron studies are not helpful
- PBS: may show **basophilic stippling**
  - Correlate with history findings (e.g. family history of thalassemia, Mediterranean ancestry)
- Hemoglobin Electrophoresis
  - Will clinch the diagnosis of thalassemia

4. Sideroblastic Anemia

- History: Look for exposure to lead, alcohol use, medication use
- Causes: lead poisoning, toxins
- ↑ RDW
- ↓ RBCs
- Iron studies are not helpful
- PBS
  - Shows **basophilic stippling**
    - Check lead (Pb) levels
  - Shows **sideroblasts**
    - Get a bone marrow biopsy to confirm

∞ Microcytic Anemias (↓MCV)

↓↓↓↓MCV/RBC - MI — RDW/RBC's/MI/Iron Studies/PBS + Hx

IDA
- ↑RDW
- ↓RBC's
- MI > 13%
- ↓Ferritin
- ↓Trans. Sat%

ACD
- ↔RDW
- ↓ RBC's
- ×
- ↑↑Ferritin
- History

Thalassemia
- ↔/↑RDW
- ↔ RBC's
- ↓↓↓MCV/RBC<13% (RAI)
- PBS- Basophillic Stipplings
- Hx ⊕
- Hb Electrophoresis ⊕

Sideroblastic Anemia
- ↑RDW
- ↓RBC's
- PBS → Basophillic Stipplings → pb Levels; Sideroblasts ⊕ → BM Bx To Confirm
- Hx ⊕

Iron Studies
- $-Fe^{++}$
- -Ferritin
- -TIBC
- -Trans Sat%
- ↓Fe^{++}/TIBC↑
- <↓ %

26:47

Normocytic Anemias

- **MCV: 80-100 fl**
- **Differentials**
  - Early Iron Deficiency Anemia
  - Early B12 deficiency
  - Early Folate deficiency
  - Thyroid Disease
  - Liver Disease
  - Kidney Disease
  - Hemolysis
- **Diagnostics**
  - Iron Studies
  - B12 Levels
  - Folate Levels
  - Thyroid Function Tests
  - Liver Function Tests
  - BMP (kidney function)
  - Hemolytic Labs
  - Bone Marrow Biopsy

1. Early Iron Deficiency Anemia

- ↓ Ferritin /
- ↓ Transferrin Sat %

2. Anemia of Chronic Disease

- ↑↑ Ferritin

3. B12 and Folate Deficiency

- ↓ B_{12} levels
- ↓ Folate levels
- If the levels are borderline, measure the **methylmalonic acid (MMA)** and **homocysteine** (HC) levels
  - **B_{12} Deficiency** = ↑ MMA, ↑ HC
  - **Folate Deficiency** = ↔ MMA, ↑ HC

4. Hypothyroidism

- ↓ T_3, T_4

5. Liver Failure

- ↑ AST, ALT (liver enzymes)
- ↓ Albumin
- ↑ INR

6. Chronic Kidney Disease

- ↑ BUN
- ↑ Creatinine
- ↓ Erythropoietin (EPO)
  - The kidney fails to produce EPO

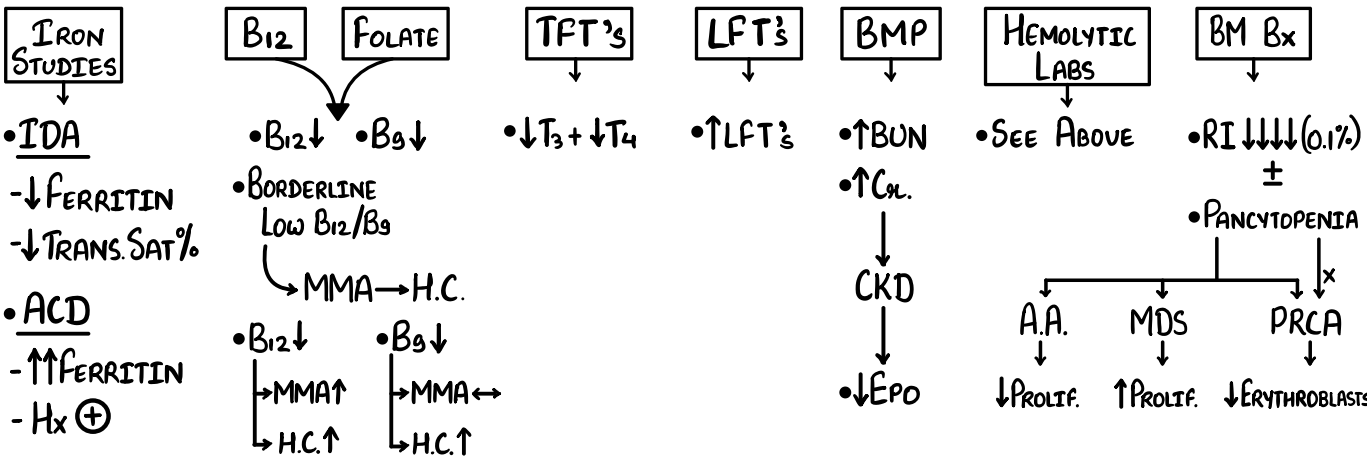
7. Intrinsic Bone Marrow Problem

- ↓↓↓ Reticulocyte Index (0.1%)
- Pancytopenia
  - ↓ RBC
  - ↓ WBC
  - ↓ Platelets

Bone Marrow Biopsy

- **Aplastic Anemia**
  - low proliferative bone marrow biopsy
- **Myelodysplastic Syndrome (MDS)**
  - hyperproliferative bone marrow due to overproduction of blast cells
- **Pure Red Cell Aplasia (PRCA)**
  - low erythroblasts
  - no pancytopenia because only the red blood cell line is affected

∞ Normocytic Anemias (↔MCV)



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Macrocytic Anemias

- **MCV: > 100 fl**
- **Differentials**
  - B12 Deficiency
  - Folate Deficiency
  - Hypothyroidism
  - Drug-induced
  - Alcohol Abuse
  - Myelodysplastic Disorder (MDS)
- **Diagnostics**
  - B_{12} / Folate levels
  - Thyroid Function Tests
  - Liver Function Tests
  - Look at medication use
  - Blood Alcohol Concentration
  - Peripheral Blood Smear
  - Bone Marrow Biopsy

1. B12 and Folate Deficiency

- ↓ B_{12} levels
- ↓ Folate levels
- If the levels are borderline, measure the **methylmalonic acid (MMA)** and **homocysteine** (HC) levels
  - B_{12} Deficiency = ↑ MMA, ↑ HC
  - Folate Deficiency = ↔ MMA, ↑ HC
- **Peripheral Blood Smear**: megaloblastic anemia
  - Shows **megaloblasts** (neutrophils with >5 lobes/segments)

2. Hypothyroidism

- History: hypothyroid symptoms
- ↓ T_3, T_4

3. Liver Failure

- History: cirrhosis, alcohol abuse
- ↑ AST, ALT (liver enzymes)
- ↓ Albumin
- ↑ INR

4. Drug-induced

- Drugs which can cause macrocytic anemia include:
  - **Chemotherapeutic agents**
    - Methotrexate
    - Fluorouracil (5FU)
    - Hydroxyurea
  - **HIV Medications**
    - Zidovudine
  - **Antibiotics**
    - Trimethoprim Sulfamethoxazole (TMP-SMX)
  - **Anti-seizure Medications**
    - Phenytoin
    - Valproic Acid
- **Peripheral Blood Smear**: megaloblastic anemia
  - Shows **megaloblasts** (neutrophils with >5 lobes/segments)

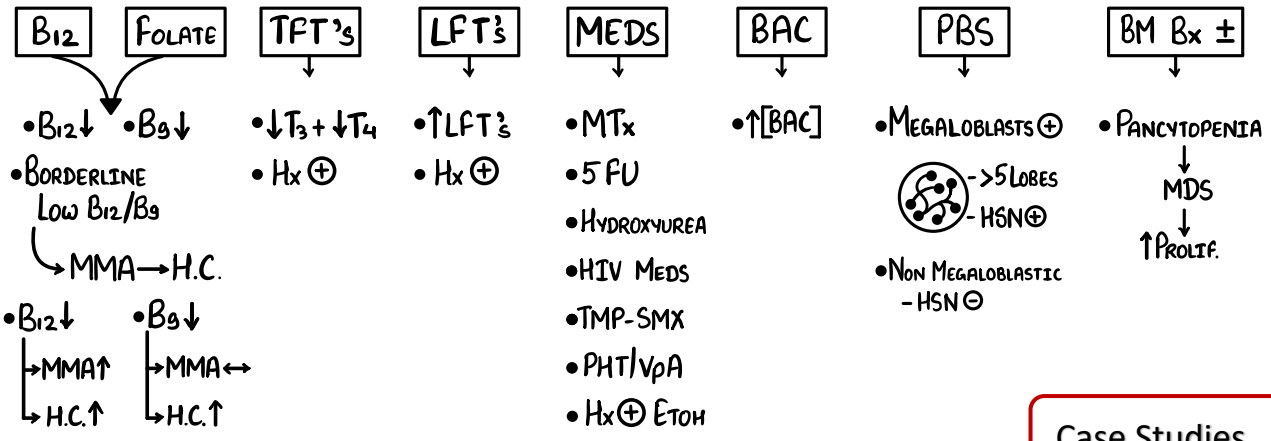
5. Alcohol

- History: heavy alcohol use
- ↑ Blood alcohol concentration
- **Peripheral Blood Smear**: megaloblastic anemia
  - Shows **megaloblasts** (neutrophils with >5 lobes/segments)

6. Myelodysplastic Disorder

- Peripheral Blood Smear: non-megaloblastic anemia
  - No megaloblasts / hyper-segmented neutrophils
  - Suggestive of a thyroid, liver, or bone marrow issue
- Bone Marrow Biopsy
  - Consider in patients with pancytopenia
  - Shows hyperproliferative bone marrow

Macrocytic Anemias (↑MCV)



Case Studies 45:40

59:47

IV. ↑ Destruction / Loss of RBC's (RI > 2%)

- We have somebody who has increased destruction or loss of their red blood cells
  - We think that they have anemia
    - Low hemoglobin
    - Low hematocrit
    - Potential low number of red blood cell
- **In a perfect world**, the reticulocyte index > 2%
  - Assuming that the red bone marrow is producing red blood cells to compensate for the drop in red blood cells caused by destruction or loss
  - We need an actual functioning bone marrow to see an elevated RI

1:01:18

Hemolytic Anemia (Destruction of RBCs)

1. Classification

- We can break them down
  - Inside the vasculature (**intravascular**)
  - Inside splenic macrophages inside spleen (**extravascular**)

2. Hemolytic labs

- When we break down red blood cells There are **different molecules that leak out from red blood cells** we must check these Part of hemolytic labs

a) Lactate dehydrogenase (LDH)

- Usually, the first one that is released into bloodstream

b) Bilirubin

Remember

- Hemoglobin is composed of Heme and a protein (-globin)
- **Heme breaks down into bilirubin**
- there are 2 types of bilirubin
  1) **Indirect/unconjugated bilirubin**
     - More increased in hemolytic anemia
     - So, they may have some jaundice-like appearance
  2) **Direct/conjugated bilirubin**

c) Hemoglobin

- Whenever hemoglobin gets released into the bloodstream
  - Liver makes a particular protein → **haptoglobin**
    → Haptoglobin and hemoglobin will bind to one another → making complexes
    → **Free haptoglobin level drops**
  - Some hemoglobin gets into kidneys
    - Pee out hemoglobin into the urine
      → increased hemoglobin in urine (**hemoglobinuria**)

Important labs to remember in clinical vignette

- **Hemolytic lab**
  - **LDH**
  - **Haptoglobin**
- If it comes back positive, We can say with some relative confidence → **there is hemolysis**
  - **Intravascular** → **the elevation is really high**
  - **Extravascular** (inside splenic macrophage)
    → the elevation is high but not significant

3. Splenic ultrasound

- Consider getting splenic ultrasound looking at the spleen
  - Especially in extravascular hemolysis
- Look for any splenomegaly to rule out hypersplenism
  - Look to see if they have any splenic disease or liver disease
- Splenic ultrasound may show splenomegaly
  - Sometimes we might have **hypersplenism**
    - Entraps red blood cells from bloodstream way faster
    - Usually old and defective red blood cells gets destroyed
    - **But the spleen can just go hyperfunction and destroys the normal red blood cells**

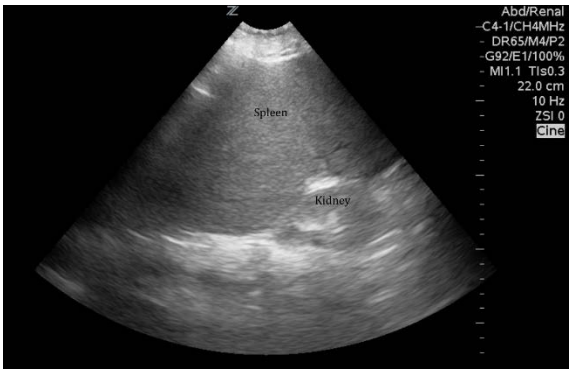
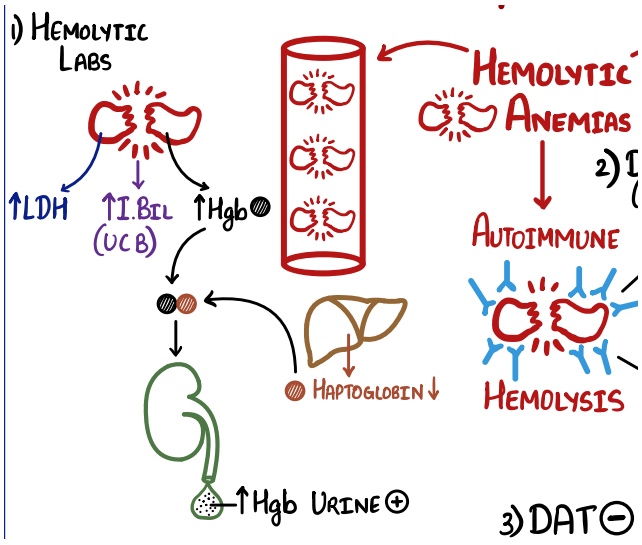


Figure 3 US Showing Splenomegaly



1:07:29 Autoimmune Hemolysis

1. Direct antibody test/DAT (Coombs test)

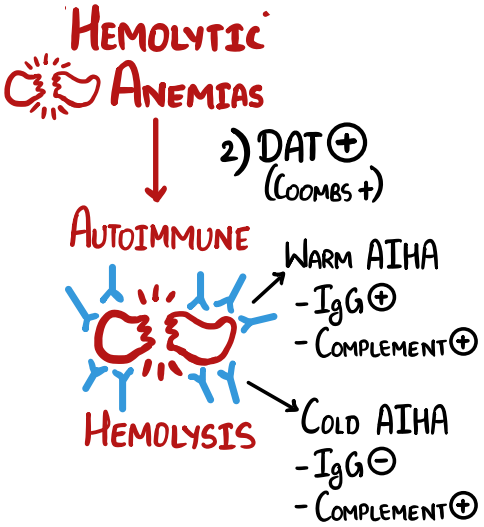
- **Positive result → autoimmune hemolytic anemia**
  - Warm AIHA
    - **Positive IgG**
    - Positive complement
  - Cold AIHA
    - **Negative IgG**
    - Positive complement

2. Simplest point

- Check for hemolytic lab → positive
- Check for direct antibody test → positive
  - Hence, we have autoimmune hemolytic anemia
- Figure out warm or cold AIHA
  - **Look at the pattern of IgG and complement**

Negative result

- Looking for another cause of hemolysis
- They're hemolyzing due to something else that's not autoimmune
  - **Something wrong against red blood cell intrinsically or extrinsically** (outside red blood cell)
    - E.g., trauma, infection



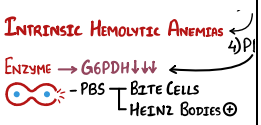
3) DAT⊖

Intrinsic Hemolytic Anemias ← → Extrinsic Hemolytic Anemias

1:09:33 Intrinsic Hemolytic Anemia

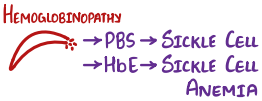
1. Enzyme Defect

- **G6PDH deficiency**
  - Can be seen in younger **African American children**
  - Clinical workup
    - **Low G6PDH enzyme level**
      - We only want to check it when they're not in hemolytic crisis
    - **Peripheral blood smear**
      - Bite cells
      - Heinz body
    - **History**
      - Usually, they've had infection
      - Exposed to some kind of fava beans



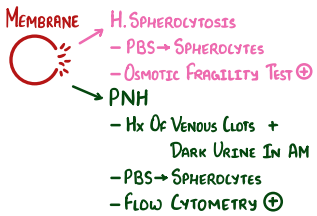
2. Hemoglobinopathy

- **Sickle cell anemia**
  - Clinical workup
    - They have **history of sickle cell anemia**
    - Family history of sickle cell anemia
    - History of **vaso-occlusive crisis**
    - Peripheral blood smear
      - We'll see sickle cells
  - If this is potentially their first vaso-occlusive event and with peripheral blood smear we see sickle cells
    - We can **confirm with hemoglobin electrophoresis** to show sickle cell anemia
      - The result will show HbF



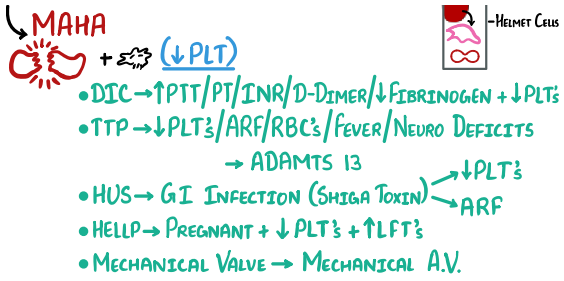
3. Membrane defect

- **Hereditary spherocytosis**
  - Won't have a lot of symptoms or clinical features
  - Clinical workup
    - Peripheral blood smear
      - Spherocytes
    - **Osmotic fragility test**
      - Positive → very high degree of suspicion for hereditary spherocytosis
- **Paroxysmal nocturnal hemoglobinuria**
  - At night they go through these hemolytic events
  - Mutation in very specific proteins in their red blood cell membrane
  - Clinical workup
    - History of venous clots
      - Deep venous thrombosis (DVT)
      - Pulmonary embolism (PE)
      - Budd-Chiari syndrome
    - Peripheral blood smear
      - Spherocytes
  - Key thing
    - History of **venous clots**
    - Wake up in the morning, they **have dark urine in the a.m.**
  - High degree of suspicion with this history and spherocytes → consider flow cytometry
    - Positive → suggestive of paroxysmal nocturnal hemoglobinuria



Microangiopathic Hemolytic Anemia (MAHA)

- Red blood cells problem and also look for **low platelet count**
  - Low platelets count due to thrombotic microangiopathies



Basic concept behind this

- There are small clots in the vessels
- As the red blood cells and platelets are trying to squeeze through
  - They get ripped apart as they're bumping against these microthrombi
- Sometimes people that have mechanical heart valve
  - The red blood cells can just get sheared apart
  - **Look for low platelet**

1. Disseminated intravascular coagulation (DIC)

- Cue features
  - Septic or critically ill
  - Elevated coagulation problem
    - Increased PT
    - Increased aPTT
    - Increased INR
    - Increased D-dimer
      - Low fibrinogen
      - Low platelet

2. Thrombotic Thrombocytopenic Purpura (TTP)

- Cue features
  - Low platelet
  - Acute renal failure
  - Drop in red blood cells
  - Fever potentially
  - Neuro deficits
- High degree suspicion of TTP
  - **Confirm with ADAMTS13 testing**

- More common in younger children
- Prior GI infection
  - Usually by sugar toxin
- Low platelets
- Acute renal failure
- Evidence of anemia
  - Probably some type of underlying history of GI issues

4. HELLP syndrome

- **Pregnant woman**
- **HELLP syndrome include**
  - Hemolysis
  - Low platelet
  - Elevated LFT

5. Mechanical valve

- Mechanical aortic valve
  - Chew up their red blood cells

6. Peripheral blood smear

- **Schistocytes**
  - Torn up red blood cells
  - Think about MAHA
    - And look do they have low platelets that also suggests MAHA
    - And think which one it is based upon their history
- **Helmet cells**

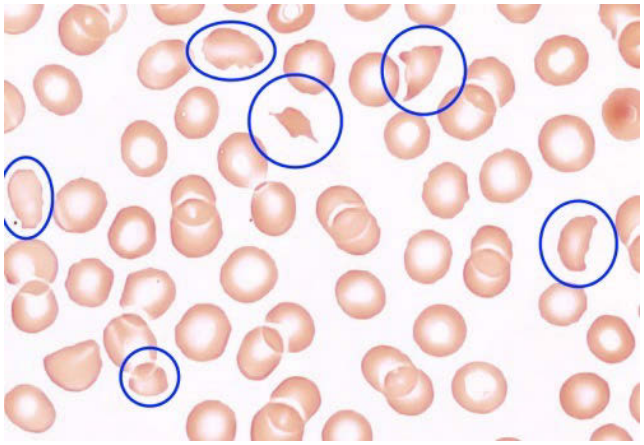


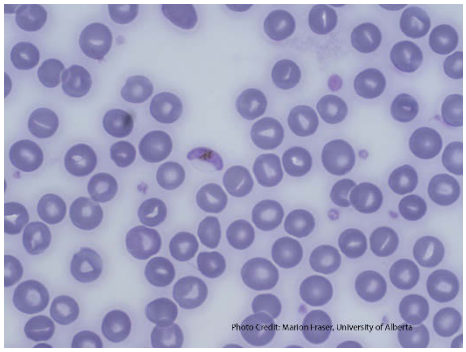
Figure 4 Peripheral blood smear in patient with thrombotic thrombocytopenic purpura. Typical schistocytes are annotated (fragmented and helmet cells).

1:15:40 Infectious

- Super obvious → think about a patient who is having a super **high fever**
  - **Maybe there's kind of rash**
  - Also, some kind of recent travel into areas where there's high exposure

1. Malaria

- History of recent travel to Africa or some kind of area where there's high possibility of it's being exposed to malaria
  - And come back with myalgia
- Peripheral blood smear
  - Inclusion of malaria inside red blood cells



2. Babesiosis

- **History of tick bite**
  - They have rash, high fever
  - They were in area like Wisconsin or some kind of area where there's high possibility of getting babesiosis
- Peripheral blood smear
  - **Pathognomic → Maltese cross**

3. Disseminated C. diff

- Really nasty *Clostridium difficile* infection
- **Clinical workup**
  - Physical examination
    - They look septic
    - High fever
  - Lots of diarrhea
  - Check for C. diff
  - Peripheral blood smear
    - Ghost cells
  - Also, some kind of recent travel into areas where there's high exposure of C. diff

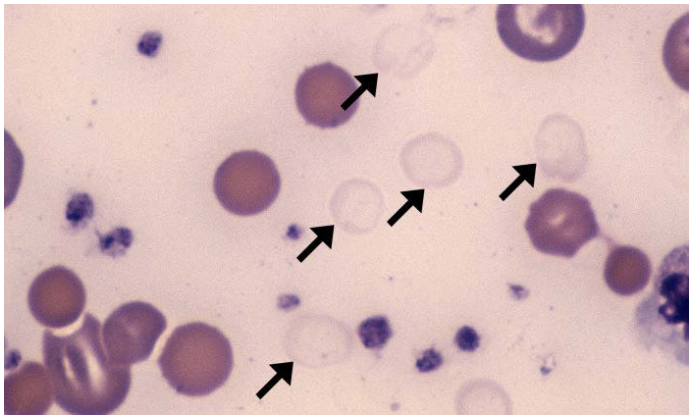
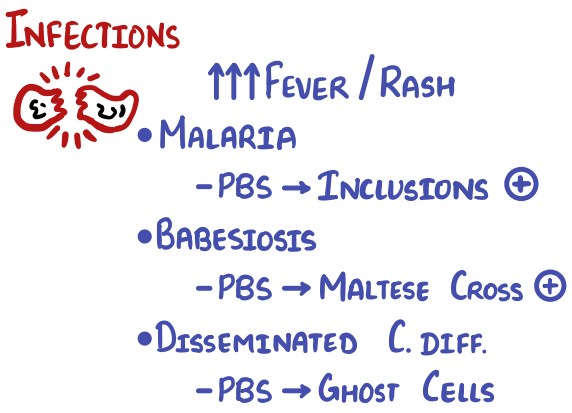


FIGURE 5 GHOST CELLS



1:24:18

V. BLOOD LOSS

Remember the first thing we do

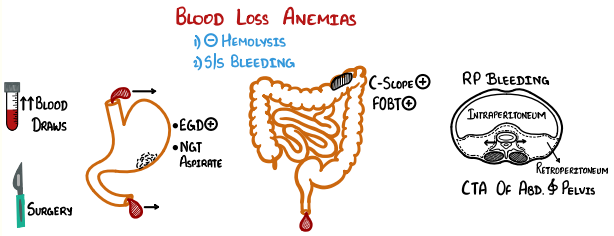
- **Anemia**
  - Low hemoglobin
  - Low hematocrit
  - Low red blood cells
- **Check reticulocyte index > 2%**
  - Increased destruction or loss problem
- **How do we know it's not actually a destruction problem?**
  - No evidence of hemolysis
    - Normal LDH
    - Normal haptoglobin
    - Doesn't need to check for direct antibody test (DAT)
      - Because we know it's not hemolysis

1:15:40

CAUSES

Be intelligent!

- If someone is losing blood, **look at their actual physical exams**
  - **Do they have signs or symptoms of bleeding?**
    - Do they look pale?
    - Do they have power?
    - Do they have dry mucous membrane?
    - Decreased capillary refill?
    - Are they having hypotension, tachycardia?



1. Anticoagulants

2. Recent surgery procedure done

3. Frequent blood draws every single day

- Probably will be experience a lot in the clinical world especially in the ICU
- Especially if they don't have no obvious other source

4. Recent surgery procedure

5. GI bleeds

6. Hemoptysis

- Vomiting up the bloods

7. Retroperitoneal bleed

- Remember retroperitoneum is a little space behind peritoneum
- Due to
  - Aortic bleed
  - Small vessel bleed within the lag
  - On anticoagulants
- Do CTA of the abdomen and pelvis area
  - Look for any kind of bleed in the area

8. Blood accumulation within the leg

- Due to
  - Hit artery in the leg
  - Fracture a bone
  - Undergo some type of procedure
- Look for swollen legs or hematomas

9. Look out for bright red blood per rectum or dark stools

Upper GI bleed

- We can do EGD
- Also, we can do nasogastric tube
  - Aspirate out some areas from gastric tube and see if there's any blood in there after we lavage it and then aspirate some stuff back

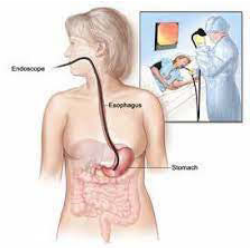


FIGURE 6 UPPER GI ENDOSCOPY (EGD)

Lower GI bleed

- C scope (colonoscopy)
- Fecal occult blood test
  - Positive → test their stool
  - Do a digital rectal
    - Positive for blood → potential problem

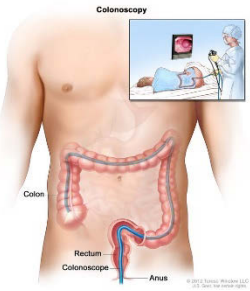


FIGURE 7 COLONOSCOPY

Case Studies 1:29:14

VI. Appendex

	Differential Diagnosis	RI	MCV	RDW	RBC	Mentzer's Index	Iron Studies	Peripheral Blood Smear	Additional Information
Microcytic	**Iron deficiency anemia**		< 80 fl	↑	↓	**> 13%**	**↓ Ferritin** **↓ Transferrin Sat %**		
	Anemia of chronic disease			↔	↓		**↑↑ Ferritin**		● Ferritin is an acute phase reactant; it may be elevated when there is an active inflammatory process such as in chronic diseases
	Thalassemia			↔ / ↑	↔	**< 13%**		**Basophilic stippling**	● Correlate with history findings (e.g., family history of thalassemia, Mediterranean ancestry) ● Hemoglobin Electrophoresis
	Sideroblastic anemia			↑	↓			**Basophilic stippling** **Sideroblasts**	● History: Look for exposure to lead, alcohol use, medication use ● Causes: lead poisoning, toxins ● Check lead (Pb) levels ● Get bone marrow biopsy to confirm
Normocytic	**Early iron deficiency anemia**		< 80 fl				**↓ Ferritin** **↓ Transferrin Sat %**		
	chronic disease						**↑↑ Ferritin**		
	B_{12} and folate deficiency			● ↓ B_{12} levels ● ↓ Folate levels ● If the levels are borderline, measure the **methylmalonic acid (MMA)** and **homocysteine** (HC) levels ○ **B_{12}** Deficiency = ↑ MMA, ↑ HC ○ Folate Deficiency = ↔ MMA, ↑ HC				
	Hypothyroidism			● ↓ T3, T4					
	Liver failure			● ↑ AST, ALT (liver enzymes) ● ↓ Albumin ● ↑ INR					
	Chronic kidney disease			● ↑ BUN ● ↑ Creatinine ● ↓ Erythropoietin (EPO) ● The kidney fails to produce EPO					
Macrocytic	**B_{12} and folate deficiency**		> 100 fL	● ↓ B_{12} levels ● ↓ Folate levels ● If the levels are borderline, measure the **methylmalonic acid (MMA)** and **homocysteine** (HC) levels ○ **B_{12}** Deficiency = ↑ MMA, ↑ HC Folate Deficiency = ↔ MMA, ↑ HC				
	Hypothyroidism			↓ T3, T4					
	Liver failure			● ↑ AST, ALT (liver enzymes) ● ↓ Albumin ↑ INR					
	Drug-induced							Peripheral Blood Smear: **megaloblastic anemia** **Shows megaloblasts (neutrophils with >5 lobes/segments)**	
	Alcohol								
	Myelodysplastic disorder							● Peripheral Blood Smear: **non-megaloblastic anemia** ○ No megaloblasts / hyper-segmented neutrophils ○ Suggestive of a thyroid, liver, or bone marrow issue ● Bone Marrow Biopsy ○ Consider in patients with pancytopenia ○ Shows hyperproliferative bone marrow	

VII. Review Questions

1) Which of the following parameters reflects bone marrow function?

a) Mean Corpuscular Volume
b) Reticulocyte Index
c) Total Iron Binding Capacity
d) INR

2) If the reticulocyte index is 0.9%, which of the following is the LEAST LIKELY differential?

a) B_{12} Deficiency
b) Myelodysplastic Syndrome
c) G6PD Deficiency
d) Hypothyroidism

3) A 31-year-old female patient's CBC results showed the following:

Hgb 10.3 g/dL
Hct 30.3 %
MCV 121

a) Iron Deficiency
b) Folate Deficiency
c) Gastrointestinal bleeding
d) Thalassemia

4) Which of the following is CORRECTLY paired?

a) MCV < 80 : Normocytic Anemia
b) MI < 13% : Iron Deficiency Anemia
c) ↔ MMA, ↑ HC : Folate Deficiency Anemia
d) RI < 0.8% : Hemolytic Anemia

5) Reticulocyte index > 2% in anemia cases indicates

a) Functional bone marrow → compensates for blood loss
b) Aplastic anemia → unable to compensate for blood loss
c) Anemia caused by nutrient deficiencies
d) Anemia induced by drugs with bone marrow suppression effect

6) What clinical result that is always present and unique to microangiopathic hemolytic anemia?

a) High platelet count
b) Low platelet count
c) Warm AIHA
d) Cold AIHA

7) Osmotic fragility test is commonly used to diagnose which type of anemia?

a) Hereditary spherocytosis
b) Paroxysmal nocturnal hemoglobinuria
c) Thalassemia
d) G6PDH deficiency

VIII. Refrences

● Harrison, T. R., & Kasper, D. L. (2015). Harrison's principles of Internal Medicine. McGraw-Hill Medical Publ. Division.