APPROACHES IN HEMATOLOGY

Hematology Made Easy

Microcytic hypochromic anemia

- Q: definition of anemia?

A: Anemia is a lab diagnosis, defined when HB is below 13 gm/dl in males and < 12 gm/dl in females, and < 11 gm/dl in pregnant females.

- Q: how to classify a case of anemia?

A: the most widely used practical classification is according to MCV {mean corpuscular volume}.

- Normal MCV values vary slightly among textbooks and lab references. Some report that MCV is normally 80 -100. Others report that MCV is normally 78- 98. So, the normal range of MCV lies between 78-100.

- According to MCV value, Anemia might be ⤵⤵ Either ⤵⤵
  - Microcytic hypochromic (MCV < 78)
  - normocytic normochromic (MCV: 78 - 100)
  - Macrocytic anemia (MCV > 100)

- Anemia is:
  - Isolated
  - Or a part of bicytopenia (anemia with leucopenia or anemia with thrombocytopenia)
  - Or pancytopenia (anemia + leukopenia + thrombocytopenia)
  - Or associated with leukocytosis and/ or thrombocytosis.

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- Q: what is the DD of Microcytic hypochromic anemia?!

1. Iron deficiency anemia (IDA)
2. Thalassemias (Major, intermedia and minor).
3. Anemia of chronic disease (late in the disease).
4. Sideroblastic anemia.
5. Lead Poisoning.

- Q: What is the next the step in lab approach of Microcytic hypochromic anemia in order to reach the definite DX?!

  - Iron profile is the main next lab step.
  - RDW (red cell distribution width) may recognize IDA as a cause (high RDW). RDW is normally 11.5-14.5.
  - Blood film may help, but it is of low value in practice in such cases!!

- Q: What might be found in each possibility as regards IRON PROFILE?!

	IDA	Thalassemia	Anemia of Chronic disease	Sideroblastic anemia*
Iron	Low	Normal or increased	low or normal (failure of iron utilization)	normal or increased
Ferritin	Low < 15	increased (iron overload state)	normal or increased (ferritin is an acute phase reactant)	normal or increased
TIBC	High	Normal	slightly decreased	normal
TSAT	Low	Normal to increased	normal or slightly decreased	normal or increased

Note (1): Sideroblastic anemia: BM is unable to produce enough mature RBCs, instead it produces immature ring sideroblasts which contain iron inside them!!

Note (2): Lead poisoning: Nonspecific iron profile.

Focused history & focused exam in a case of Microcytic hypochromic anemia

IDA

Focused history

- Ask about previous OVERT BLEEDING from orifices particularly GIT bleeding.

  - So, ask about, previous hematemesis, Melena, Hematochezia, Chronic bloody diarrhea, Recurrent hematuria, Recurrent epistaxis, and to less extent recurrent hemoptysis ➞in males and females.
  - In females, ask specifically about menses: Vaginal bleeding (amount, duration, regular or not).

- Ask indirectly about GIT symptoms which might be clues for certain underlying GIT diseases that lead to OCCULT BLEEDING.
  - Upper GIT symptoms:
    - Ask about Heartburn & regurgitation (GERD❓)
    - Ask about Dysphagia and WEIGHT LOSS (Esophageal carcinoma❓)
    - Ask about dysphagia (If upper GIT endoscopy or EGD, shows webs or rings (Plummer Vinson Syndrome❓)
    - Epigastric pain & dyspepsia (chronic gastritis PUD & H pylori ❓)
    - Ask about chronic use of NSAID (NSAID-induced gastritis❓)
    - Ask specifically about alarm symptoms in cases of epigastric pain & dyspepsia for example WEIGHT LOSS, abdominal lump/mass, and overt bleeding, particularly in patients more than 55 years.
    - Ask about Pica & craving for ice.
    - Ask about abnormal leg movements & sensations at night (restless leg syndrome)
  - Lower GIT symptoms
    - Ask specifically about chronic diarrhea.
    - Chronic inflammatory diarrhea dysentery (mucus ±blood + tenesmus) (IBD❓)
    - Chronic malabsorptive diarrhea (steatorrhea) {bulky, pale, offensive greasy stools which are difficult to flush away (malabsorption syndrome, with all underlying causes especially Celiac disease❓)
    - -Ask about Constipation with Wight loss in old people (CRC: Colo-rectal carcinoma❓)
    - -Ask about abdominal masses (GIT cancers❓)
    - -Ask about abdominal enlargement (Ascites) (Liver cirrhosis & Malignancy❓)
    - Ask about history of liver disease, and previous endoscopies!! (Bleeding Varices❓)
- In females, ask about pregnancy.
- Ask about nutritional status, especially in elderly.
- Ask about parasitic infestation currently or in the past (Ancylostomiasis❓)
- Ask about vesicular rash on the extensor surfaces, IBS-like features, unexplained IDA, unexplained peripheral neuropathy, history of Vitiligo, pernicious anemia, Type 1 DM, and Addison & Hashimoto's thyroiditis (Celiac disease❓)

Focused exam

- General
  - Nails: pallor
    Koilonychia {Spoon shaped nails} ➞ (pathognomonic)
    Leukonychia in CLD.
  - Hand: palmar erythema in CLD.
  - Eyes: pallor& jaundice in CLD.

- Built: cachexia in cancers.
- Other stigmata of CLD: spider naevi, gynecomastia, ascites.

❖ Local (abdomen is the target exam)
- Examine specifically for abdominal masses (gastric carcinoma & CRC)
- Examine Liver & spleen.

Thalassemia

Focused history & focused exam:

❖ Ask if there is a history of thalassemia & repeated blood transfusions since childhood.
❖ Then do a focused exam as discussed before
- Mongloid features.
- Jaundice
- Palpable hepatomegaly
- Palpable marked splenomegaly (or scar in cases that underwent Splenectomy)
- Features of iron overload (dark skin due to secondary hemochromatosis)

Note: Thalassemia trait& minor. There are no certain clues, but ask if there is a previous failure of response to iron therapy (oral or IV)

Anemia of chronic disease

Focused history

❖ Ask about if there is a history of one or more of the following:
1. Chronic disease: most common are chronic renal failure (ESKD), Heart failure, COPD, DM.
2. Chronic inflammatory diseases.
3. Rheumatoid arthritis, SLE, and all collagen rheumatological diseases.
4. Chronic infections.
5. TB, recurrent abscesses, Osteomyelitis, recurrent septic arthritis, recurrent cellulitis.
6. Anemia of malignancy
7. Solid cancers like Cancers in lungs, etc.
8. Chronic endocrine disease e.g., thyroid disease.

Sideroblastic Anemia

Focused history

❖ Ask about:
- Alcohol abuse
- Drugs (INH, linezolid, chloramphenicol)
- Refractory anemia to iron & recurrence after blood transfusion
- History of onset since childhood

Lead poisoing

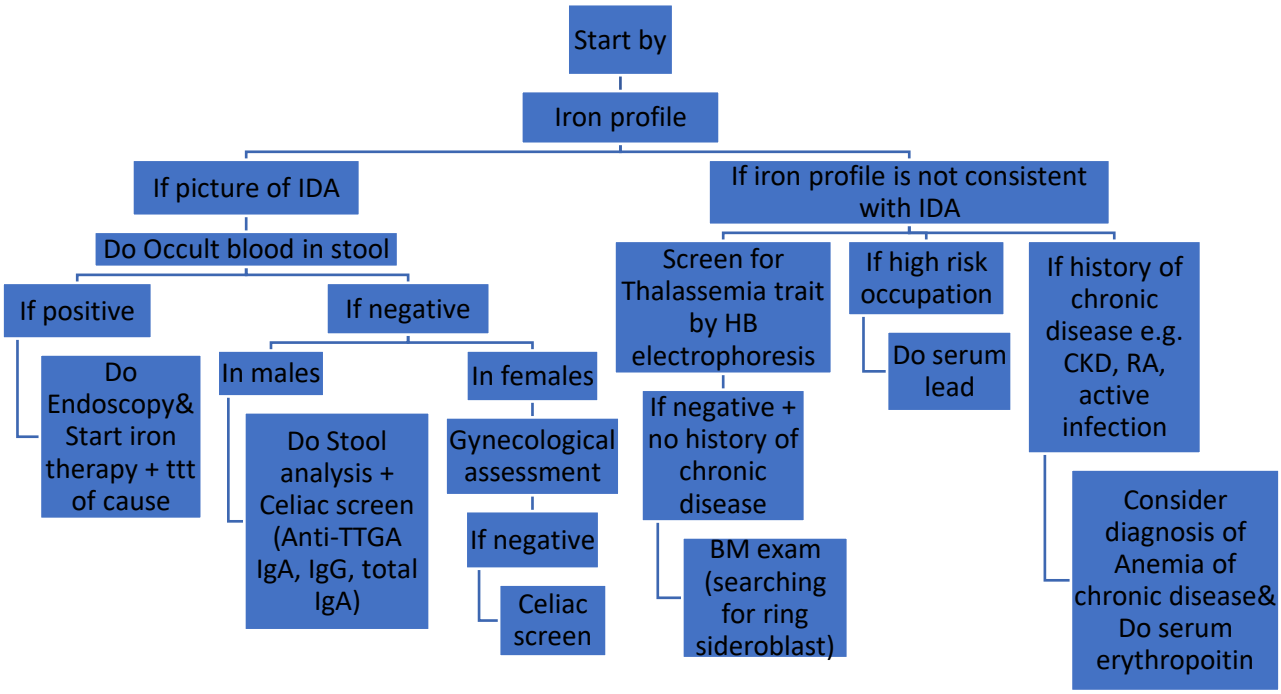
Focused history

- Ask about the occupation (discussed previously in detail)
  - Ask about leg weakness.
  - abdominal pain
  - anorexia
  - constipation

Focused exam

- Look for blue lines in the tooth-gum line.
- neurological exam for LL& UL.

Diagnostic workup in isolated microcytic anemia (stepwise)



- Q: If you found the iron profile is consistent with IDA !! What are your next lab steps?!
  A: IDA per se is not an endpoint of diagnosis, you should search for the underlying cause.

Causes of IDA:

- Chronic blood loss (The most common cause)

- In males: Chronic GIT loss
  - either obvious bleeding, recurrent hematemesis, melena, hematuria, piles (external and internal) are common causes and are easily overlooked.
  - Or Occult bleeding from GIT source (which is very common).It is demonstrated by doing a test for occult blood in stool

Name of tests:

- Guaiac fecal occult blood test (gFOBT).
- conventional test (hemoccult II or R) has low specificity with multiple disadvantages. It might be repeated 3 times with the restriction of meat.
- Recent Hemoccult SENSA is more sensitive than ordinary tests and is recommended as an initial screening test by guidelines.
- RECENT fecal immunochemical test {FIT} is more specific than the guaiac test.

➢ If the test for occult blood is positive, then ask about upper GIT symptoms, like epigastric pain, heartburn, and dysphagia.
If present, then do an Upper GIT endoscopy, then treat accordingly.
If negative, do Colonoscopy.
If negative, do capsule endoscopy ± MR enterography.

➢ If upper GIT symptoms are absent or there are lower GIT symptoms, do Colonoscopy first and treat accordingly.
If negative, do Capsule endoscopy ± MR enterography.

- In females:
  - In the Childbearing period, Menstrual blood loss is more considered if GIT manifestations are absent irrespective of the definitive cause of abnormal menses.
  - Overt and occult bleeding are also common causes in females.
  - you should do a Stool analysis to exclude parasitic ancylostomiasis infection, particularly in young adults.
  - In cases of failure to reach the underlying cause of IDA, Consider the possibility of Celiac disease.

So, do anti-TTGA IgA & IgG ± EGD with duodenal biopsies.

➢ Q: How would you treat a case of established iron deficiency anemia?!

1. Treatment of the cause such as bleeding from the GIT (either overt or occult) and its underlying cause.

2. mild to moderate IDA: Oral iron therapy is the treatment of choice.
   ℛ Ferrous sulfate 325 mg tab, TDS 3 times daily.
   - Each tab of 325 mg gives 65 mg of elemental iron.

-Trade name: Ferro Sanol duodenal cap 2- 3 times daily

℞ Ferrous fumarate 325 mg tds
-325 mg gives 106 mg of elemental iron.
-Trade name: Theragran H cap (iron + multivitamins)
-Dose: 1 × 2

Duration of treatment: 3-6 months

Side effects: Abdominal pain, constipation, dark black stools

3. severe IDA (<8- 9)
4. And if the patient is intolerable to oral iron in moderate cases.

℞ Use IV iron therapy.
-Iron sucrose (ferrosac or sacrofer or fermed amp) 100 mg
-The total required IV iron is calculated using GANZONI formula

Total required iron = body weight (kg) × (target HB: 14 - actual HB) × 2.4 + storage iron (500)

then, the total dose is divided by 100 to calculate the number of ampoules.

then, the dose will be 3 amp + 100 cc saline every other day until total number of iron amp are given.

- Precautions: First IV iron should be tested for anaphylaxis by monitoring of signs of anaphylaxis (flushing, angioedema, suffocation, shock) for 15 minutes only in the first dose.

- Q: What makes you suspect Thalassemia as a cause for microcytic anemia?!
  A: Clinically, Thalassemia major and intermedia have certain pathognomonic striking clinical features:
  - Jaundice& pallor
  - Features of extra-medullary hematopoiesis
  - Mongloid features: Frontal bossing, prominent maxilla, and depressed nasal bridge.
  - stunted growth
  - history of diagnosis since childhood and blood transfusions ± Splenectomy
  - features of iron overload (if present) like dark skin, etc.
  - marked hepatomegaly.
  - If the spleen is not removed, it is moderate to huge splenomegaly.

Such features are more obvious in Thalassemia major than intermedia while, Thalassemia trait has no features at all, so it is easily overlooked and missed. So, you should suspect it at the following situations:

- extremely low MCV
- Mentzer's index = MCV ÷ RBCS count without million < 13
- iron profile is as described before.
- history of failure to respond to iron especially IV iron.

Clinical tip

-It is more evident in pregnant females as they often receive IV iron.

-HB value is often around 9 - 10.

-The definitive test to diagnose All types of Thalassemia is HB electrophoresis (test the percentages of HbF & HB A2 which are different in their percentages among types of Thalassemias.