Team Medicine

Lecture # 1

Lecture Title: Anemia

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Slides · Doctors notes · Additional

what do we mean by type of hemoglobin? because some types are with high affinity to oxygen(بخيل) like Hb-F and other types with low

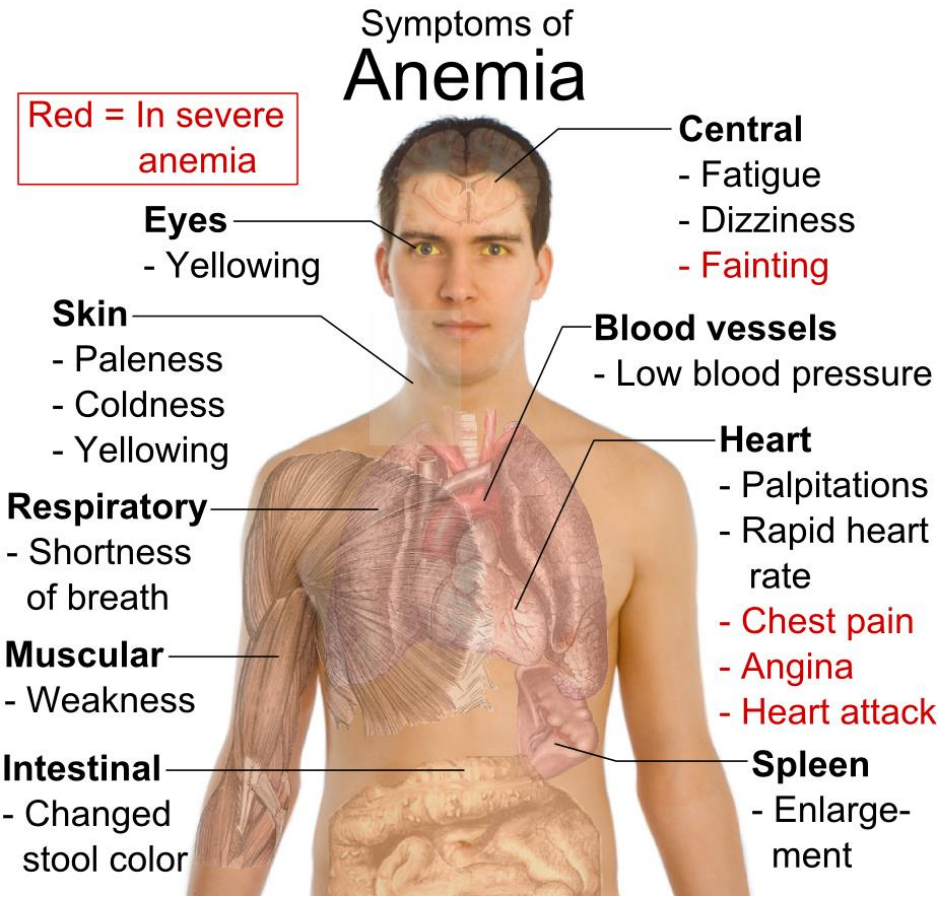
of tested healthy population at there own normal circumstances (Age,Gender,Type of Hb, Oxygen tension).

Average normal Hb/Hct (PCV) level in various populations

Population	Average Hb level g/l (Hct=(PCV %)	Comment
Fetus	200 (0.60)	
Newborn	180 (0.54)	
Child(1-10 y/o)male and female have lower Hb levels than other age groups	110 (0.33)	
Adult: Male & Female	160 (0.48) why more in males than females?? Because of the Androgen which increases the Erythropoyesis	
High altitude:	↑	
High affinity Hb	↑	
Low Affinity Hb	↓	

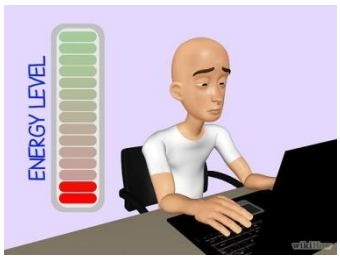
Symptoms of anemia:

(very non-specific, it depends on the onset and severity)e.g. acute is more severe than chronic cases.why?
because the body adapt the long term changes of Anemia
(compensate: 1-increase the stroke volume
2- increase 2,3-DPG(Which DECREASES THE AFFINITY)

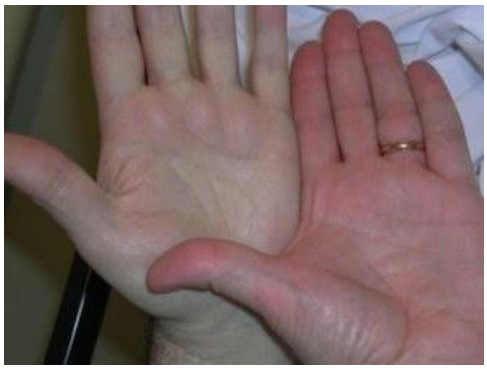


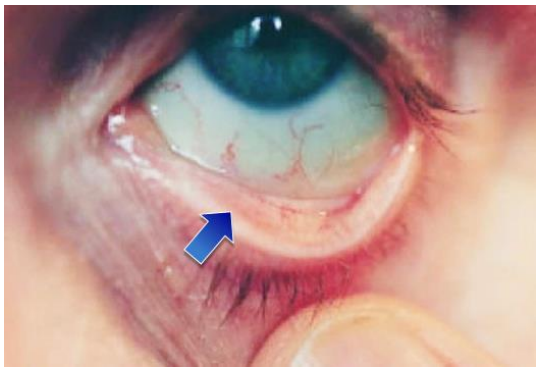
- Symptoms: (non-specific) fatigue, weakness, ↓ exercise tolerance, impaired memory, comprehension, appetite, *Pica (craving for non-food substances such as mud, sand, ice) *It's common in children, pregnant women, and people who have Iron deficiency anemia
- Signs: Depend on severity: pallor (↓ circulation to skin),
- Symptoms and signs vary greatly and correlate with severity (severe > mild) and onset/chronicity (acute > chronic)
- Adaptation to anemia:
- ↑ Heart rate,
- ↑ stroke volume,
- ↑ 2,3 DPG (→↓ affinity)

-Lack of energy:

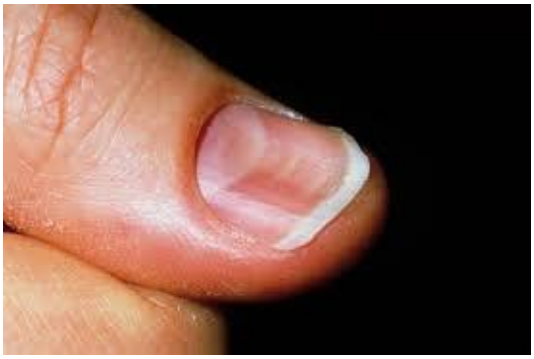


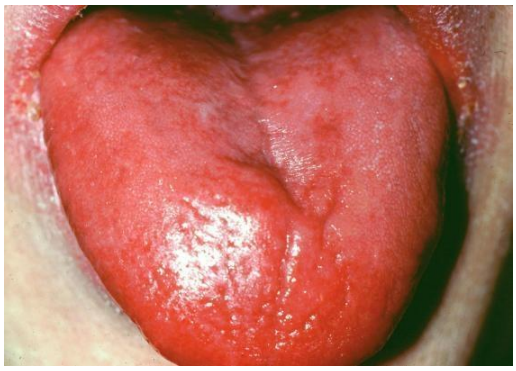
-Pallor.. can anemic patients present without paleness?? yes, because of the hyper-dynamic circulation they may have anemia and may be a severe case without pale conjunctiva and skin.





- Koilonychia(especially in Iron deficiency anemia), Papillary atrophy, erythema and angular stomatitis.





Classification:

Congenital/ hereditary Or Acquired

The most common type of Anemia classifications

Morphological:

MCV (Microcytic, normocytic, macrocytic) , RDW (↑)

Etiological: Blood loss, Nutritional deficiencies, Hemolysis (RBC Destruction), Erythropoietin deficiency, Chronic inflammation, (Infection, Malignancy, Connective tissue disease).

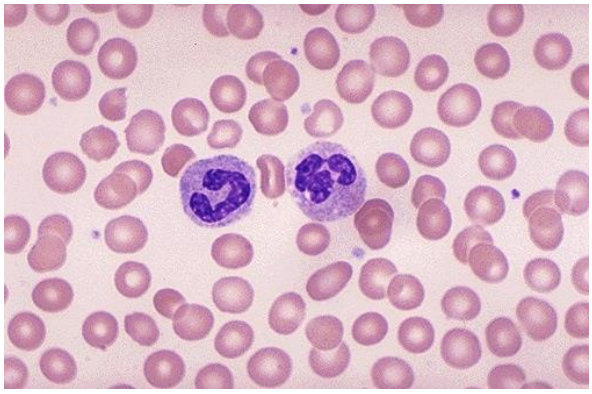
Morphological(the size of the cell) Classification of Anemia:

Low MCV (<84 fl)	High MCV (>96fl)	Normal MCV (84-94 fl)
• * IDA(Iron deficiency anemia), Thalassemia(beta and alpha) traits, some cases of chronic illnesses,lead poisoning(because it affects on some of the enzymes that build-up the RBCs)	Megaloblastic (Folate & B12 defeciency), Aplastic anemia, Myelodysplastic syndrome, Cytotoxic drugs (e.g. hydroxyurea)	Acute blood loss, Erythropoietin deficiency, some cases of chronic illnesses (malignancy, infection)

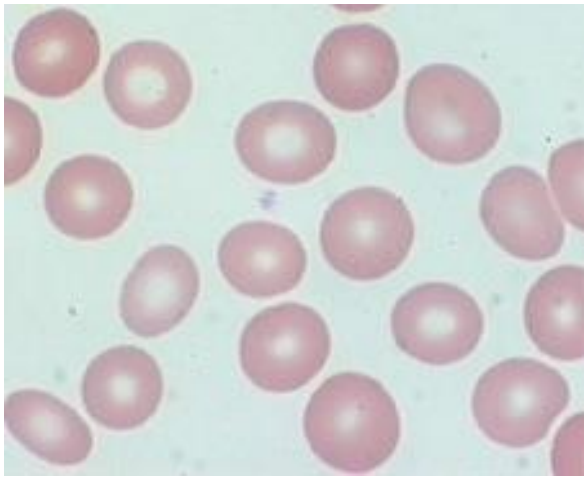
*The commonest cause of low MCV

some cases of anemia come with enzymes suppression and this may result in either low MCV (especially if it affects on the iron utilization,so Iron is there but you can't utilize it) or normal MCV anemia.

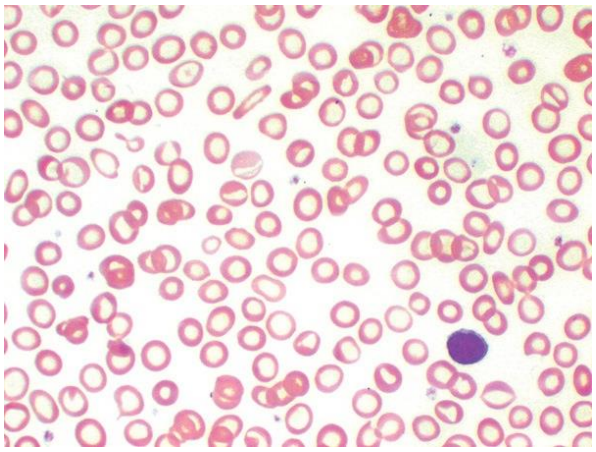
Normocytic anemia



(1/3 of the cell is pale so it's normo-chromic)

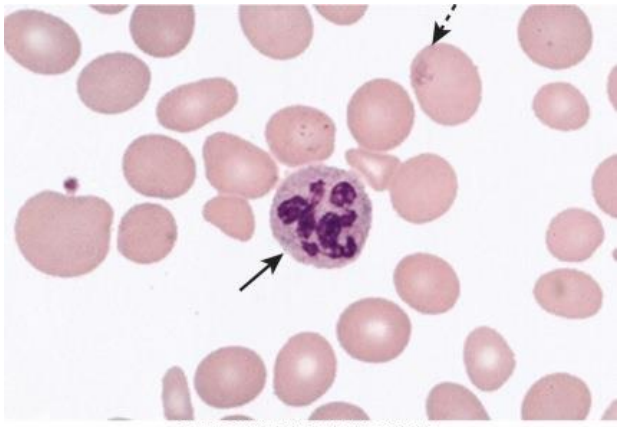


Normal red cell morphology
Microcytic anemia



(2/3 of the cell is pale so this is hypo-chromic)

Macrocytic Anemia



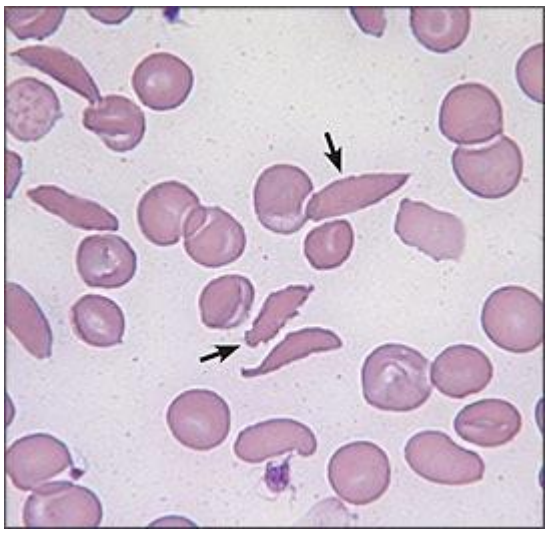
Hereditary Anemia

sickle cell anemia	Alpha-Thalassemia	Beta-Thalassemia	enzymopathies	membrane defects
1- Hemoglobinopathies: a- Sickle cell anemia (homozygous) due to replacement of glutamic acid at position 6 in the beta chain →change of Hb character when Oxygen tension is low →↓ solubility, crystallization, fiber formation, cell rigidity, Obstruction of microcirculation, hemolysis, painful crises, thrombosis.	Types: 1) - aaa = alpha thalassemia trait type 2 (silent), 2) - - aa = alpha thalassemia trait type 1(↓ MCV), 3) - - - A = Hb H disease 4)- - - - = Hydropes fetalis (incompatible with life)	Types: 1) -b = thalassemia trait (↓ MCV), 2) - - = (Homozygous) thalassemia major: severe anemia with severe intramedullary hemolysis, bone marrow expansion, hepato-splenomegally, growth and sexual retardation,	G6PD deficiency:(it affects mainly men because it's x-linked)(x-linked)→↓ production of the antioxidant glutathione, → Hemolysis due oxygen free radicals that can be produced by certain foods and drugs e.g. fava beans. Note: in SEVERE cases of G6PD deficiency patients may have hemolysis from any type of beans not just fava beans. Prevention: avoidance of oxidative foods & drugs patients with this disease may show normal G6PD enzyme levels in the blood but don't take the result in to consideration from the first time instead repeat the test after a month to make sure.	The most common type is Hereditary spherocytosis: → ↓ RBC survival, hemolysis, reticulocytosis, splenomegaly, jaundice, gall stones. -Treatment: Splenectomy

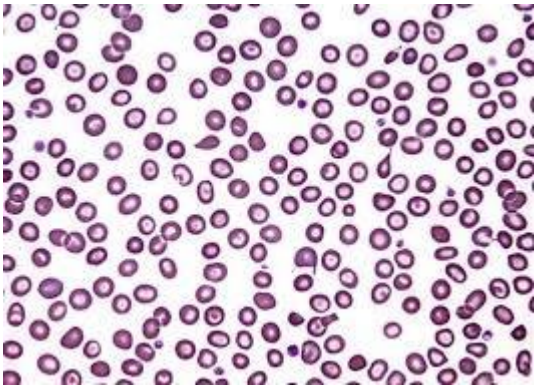
sickle cell anemia	Alpha-Thalassemia	Beta-Thalassemia	enzymopathies	membrane defects
sickle cell anemia: hematuria + sudden death because of that they can't join the military or any type of sports. Painful episodes are precipitated by ↓ Oxygen tension in circulation (high altitude, basements, use of charcoal in heating, pulmonary diseases, cardiac diseases). ↑ viscosity (↑ Hb(so, better for them to have low Hb), WBC, Platelets, dehydration, infection). Unknown causes.	Prevention: premarital screening, early abortion (in some countries). Treatment: regular blood transfusion (Q 2-4 weeks)*Doctor said every 3-6 weeks. Splenectomy (after vaccination) at 6 years of age (to reduce transfusion requirements), Iron chelation. Stem cell transplantation (in some cases)	Prevention: premarital screening, early abortion (in some countries). Treatment: regular blood transfusion (Q 2-4 weeks)*Doctor said every 3-6 weeks. Splenectomy (after vaccination) at 6 years of age (to reduce transfusion requirements), Iron chelation. Stem cell transplantation (in some cases)		

Prevention of disease: premarital testing, contraception, fetal selection (IVF) Prevention of painful episodes: daily hydroxyurea(it decrease the WBCs so decreases the viscosity + it enlarges the RBCs forming macrocytes.. but what is the benefit from having large RBCs?? it increases the amount of hemoglobin inside it occupied by more oxygen so prevent hypoxemia (and hypoxia) as a result decreases the pain), avoidance of hypoxia, dehydration, infection. Management of painful crises; Hydration, pain killers(e.g.morphine), (Rarely transfusion). Other complications of Sickle cell anemia; Hemolytic crises (severe episodes), Splenic sequestration(mostly in children) (medical emergency), aplastic crisis (parvovirus B19 infection), Priapism (continuous, painful erection), stroke (cerebral infarction) -Treat accordingly			

Sickle cell Anemia



Thalassemia



Nutritional Anemia

- a- Iron deficiency anemia (IDA;the commonest acquired anemia)
- Causes: Blood loss, impaired iron absorption (↓ pH), Increased requirement (growth, pregnancy, EPO therapy).
- Functional IDA (Suppression of erythropoiesis due to inflammation), Erythropoietin deficiency
- Iron salt must be taken on empty stomach..why? because the acidity will be high and this will convert the ferric in to ferrous .so, anything reduce acidity can reduce Iron absorption including:pup inhibitors and surgery.

a- Iron deficiency anemia

- Treatment: Ferrous sulphate/ gluconate/ fumerate, or iron polymaltose orally,
- Intravenous iron succharate or iron dextran (only when oral iron is intolerable, unabsorpable, or ineffective)
- DON'T GIVE Iron supplement IM(intramuscularly) because it's painful and may cause infection, abscess and rarely cancer like:Rhabdomyosarcoma.
- Liver (good for iron & B12 deficiency)

b-Megaloblastic anemia

1-Folate deficiency: MTHFR mutation>hyperhomocysteinemia due to defective folate metabolism, Eating only cooked food, lack of vegetables and fruits, Hemolytic anemia anti-folate drugs (e.g. methotrexate),

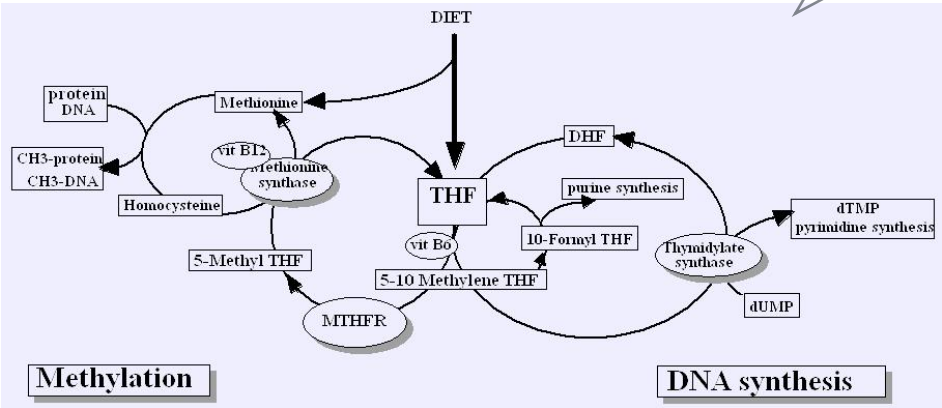
- Treatment: folate supplement

2-Vitamin B12/Cobalamin deficiency: vegetarian diet,

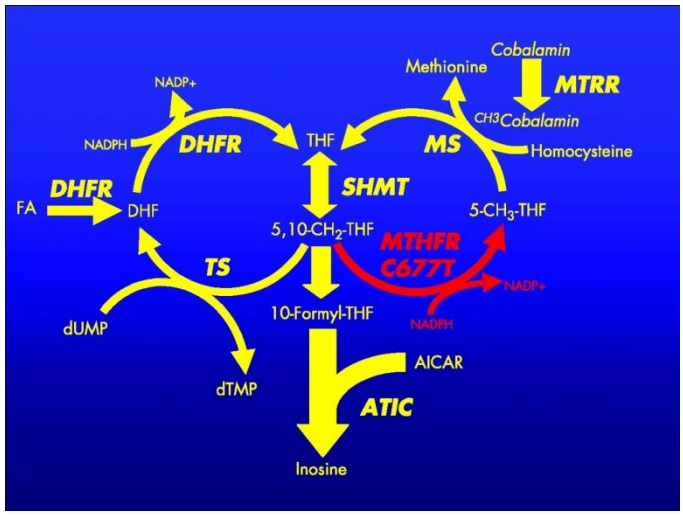
- Gastric, pancreatic or terminal elium resection, lack of gastric acidity, lack of intrinsic factor(like incase of pernicious anemia when the antibodies come and attack the parietal cells or the intrinsic factor), intestinal bacterial overgrowth,
- fish worm (Diphyllobothrium latum),Crohn's diseases, metformin (which inhibits the absorption of VB12 in the terminal ileum)

The doctor didn't explain it in details

Role of MTHFR

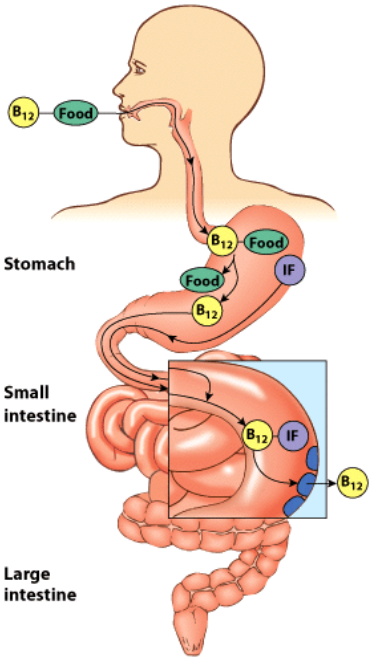


MTHFR mutation



Cobalamin/B12 absorption

Hemolytic Anemia



1-Autoimmune: IgG (Warmthe commonest) and cold)
*1ry*2ry: autoimmune diseases, lymphoid malignancies, drug-induced

2- Autoimmune: IgM (cold)

3-Non-immune: RBC abnormalities

(Sickle, thalassema, spherocytosis, enzyme deficiency,MAHA)

- Treatment:

- 1ry warm, autoimmune hemolytic anemia ; steroids, IgG, Rituximab (anti-CD 20), splenectomy
- 2ry: treatment of underlying disease.

Anemia of Chronic Illnesses:

- Functional iron deficiency+ Erythropoietic inhibitors.
- Infection.
- Connective tissue/autoimmune diseases.
- Malignancies.
- Treatment: Transfusion,Treat underlying illnesses,mega doses of erythropoietic stimulants.

Type of anemia	Definition	Etiology	Risk factors	Signs and symptoms	Diagnosis	Treatment
Iron deficiency anemia	Anemia due to decreased iron stores (iron is needed in hemoglobin synthesis); most common anemia	*Blood loss (chronic GI bleed or menorrhagia most common) *Malnutrition *Pregnancy		* Fatigue, exertional dyspnea *Glossitis *Angular cheilosis (cracking at the corners of mouth) *Pallor * Koilonychia (spoon nails) *Pica (ingestion of clay, ice)	*Low hemoglobin/hematocrit *Low MCV (microcytic) *Low TIBC, ferritin	Oral iron replacement and investigation into underlying cause.
Folate deficiency anemia	Decreased hemoglobin content of red blood cells due to impaired DNA synthesis. Treatment is oral folate.		*Alcoholism *Diet low in folic acid *Pregnancy	*Diarrhea *Cheilosis *Glossitis	Blood smear: Macrocytosis (high mean corpuscular volume [MCV]), basophilic stippling, hypersegmented neutrophils, low	

			*Malabsorption		reticulocyte count	
Vitamin B12 (COBALAMIN) deficiency	Anemia due to lack of available vitamin B12 (used in DNA synthesis)	*Pernicious anemia (no intrinsic factor) *Vegan diet (excludes meat, eggs, milk products) *Fish tapeworm (Diphyllobothriumlatum) *Malabsorption (ileal resection, bacterial overgrowth, sprue)		*Symptoms of anemia *Neurologic symptoms from subacute combined degeneration of the dor- sal columns causing paresthesias, positive Romberg, slowed reflexes, im- paired touch and temperature sensitivity, ataxia *Dementia *Atrophy of lingual papillae and glossitis	*Blood smear shows macrocytosis, basophilic stippling, hypersegmented neutrophils, low reticulocyte count *Decreased plasma cobalamin levels	B12 replacement (usually IM)

Aplastic anemia	Marrow failure resulting in severe pancytopenia. PATHOPHYSIOLOGY: Two mechanisms for are postulated: *Stem cell defect *Immune-mediated destruction	*Viral hepatitis *Chloramphenicol (idiosyncratic) *Parvovirus B19 with sickle cell anemia *Benzene (dose related), lindane, DDT		*Weakness, fatigue *Mucosal bleeding *Pallor	*Normochromic, normocytic pancytopenia *Low reticulocyte count	*Bone marrow transplant is treatment of choice, prior blood transfusions can impair success due to sensitization to minor HLA antigens. *Immunosuppression (steroids, cyclophosphamide)
Anemia of Chronic Disease	Anemia observed in patients with infectious, inflammatory, or neoplastic dis- eases PATHOPHYSIOLOGY: Iron deficiency in the presence of ample iron stores due to impaired iron mo- bilization	*Tuberculosis *Malignancies *Rheumatologic disorders that put body in a state of prolonged inflam- mation		Signs and symptoms of the underlying disorder	*Ferritin is normal to increased; serum iron, total iron-binding capacity (TIBC), and transferrin all decreased. *Erythropoietin appropriately elevated *Normocytic, normochromic anemia	Identification and treatment of underlying disease

*Summary: (from First Aid)

*Questions: (from Step-Up to Medicine)

1- **A 58-year-old male present to your office with weakness in his leg and a history of frequent falls over the past few months. He also compliant of fatigue at the end of the day.He does not drink alcohol or smoke, and his medical history is significant for gastric carcinoma for which he underwent gastrectomy 2 years ago. On physical examination, he is found to have increased deep tendon reflexes and mild weakness of his lower extremities, along with diminished vibratory sense in his toes. His examination is otherwise unremarkable. What is he likely diagnosed and what is the appropriate next step in managing this patient?**

This patient likely has vitamin B_{12} deficiency. After gastrectomy, lack of intrinsic factors leads to vitamin B_{12} deficiency. The patient's neurological deficits are consistent with vitamin B_{12} deficiency. Check routine laboratory values to document anemia and the patient's MCV (should be high). Check the serum vitamin B_{12} level. Serum homocysteine and methylmalonic acid may also be helpful.

2- **A 35-year-old male present with complaint of a 6-month history of fatigue and lethargy. His medical history is unremarkable. He denies melena and recent trauma or surgery. He reports that he does not drink alcohol, smoke, or take any medications. His family history is noncontributory. He appears well nourished. Vital signs are as follows: RR= 16, BP= 130/80, Pulse= 70. Laboratory test results are as follows: Hb= 7.6, Hct= 22.8%, and MCV= 68. The reminder of his laboratory test results are normal. What is the likely diagnosis? Describe the appropriate management of this patient.**

This patient has a microcytic anemia—Causes include iron deficiency, thalassemia, ring sideroblastic anemia, and anemia of chronic disease. Draw blood for iron studies (ferritin, TIBC, transferring, serum iron). If iron deficiency anemia is diagnosed, look for a source of bleeding (chronic blood loss is the most common cause of iron deficiency anemia in adults). If iron studies are within normal limits, consider the possibility of thalassemia and perform a hemoglobin electrophoresis.