* Multipotent stem cell → Erythroid stem cell —(3-4 days, Maturation, (Reticulocytes))→ Mature RBC (no nucleus)

* Erythropoiesis is influenced by EPO (secreted by Kidneys), stimulated by hypoxia.

• Anemia » Reduction in one or more of major RBC mesurments (Hb conc. / Hct / RBC count)

[value at −2 SD from the mean]

Threshold: women not pregnant = 12 g/dL / women pregnant = 11 / Men = 13

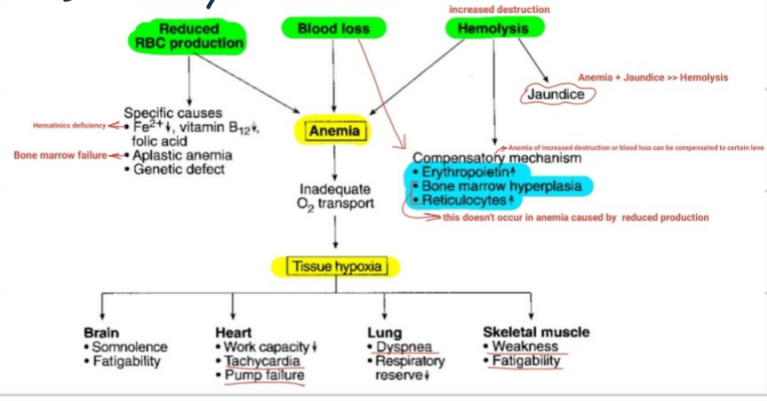
Severe: ↓ <8 / ↓ <7 / ↓ <8

∴ Anemia → Disease to be treated on its own merits

OR

2nd Condition of another disease

▶ Signs & symptoms :



↓ production

↓ Hemolysis — Causes — ↑ Blood Loss

* Hemolysis + Blood loss » Compensatory (↑ Reticulocyte)

* ↓ production » normal or less reticulocyte.

▶ History :

✓ history of bleeding / systemic illness

✓ Dietary / Past history / family

✓ Drug / Travel

▶ Physical examination

✓ pallor : skin, mucous membrane / Resting tachy

postural hypotension

✓ splenomegaly / hepatomegaly

✓ systemic disease.

Anemia Syndrome due to tissue hypoxia :

① Dizziness ② fatigue ③ SOB ④ headache ⑤ chest pain

▶ labs → CBC (Hb, RBC, WBC, MCV, RDW)
→ Reticulocyte count [using methylene blue to stain rRNA particles]
→ Peripheral smear

Anemia classifications : ① Biological or clinical approach by reticulocytes.

~ Acute vs Chronic

② Morphology by MCV

Normo	Micro	Macro
- Blood loss - Hemolysis - BM failure	- IDA - Thalasemia - chronic disease - sideroblastic	- Folate ↓ - B12 ↓

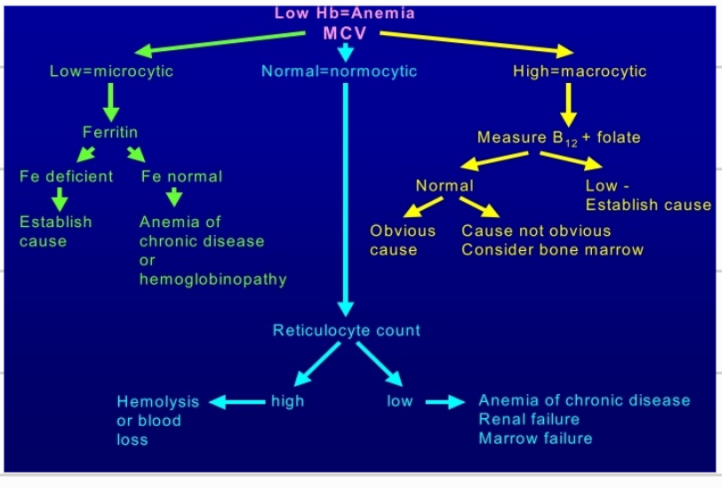
▶ Reticulocyte count

- Normal absolute = 60,000 - 100,000

- Production index = 2.5

> 2.5 : Hemolysis or hemorrhage

< 2.5 : decrease production



** Corrected retic. = Patients retic. (%) x (Pt Hct / 45)

** Retics index = corrected retic / Maturation time
- 1 for Hct 45%
- 1.5 for 35%
- 2 for 25%
- 2.5 for 15%

** Absolute Retic count = corrected retic x RBC no.

★ Microcytic hypochromic anemia

1. Iron def. anemia → Mild (MCV > 70)
   → Sever (MCV < 70)

* Ferritin ⇒ Best markers

↓Fe ↓Hb = IDA

▶ Causes: Nutritional / Blood loss / Malabsorption / Repeated pregnancies

↓ ↓ ↓ ↓

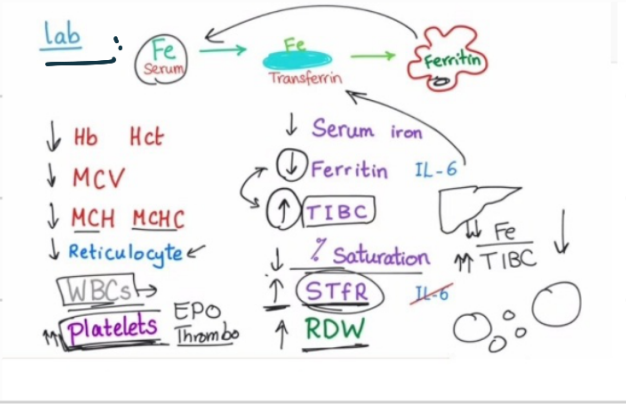
↓ Red meat | GI / GU | gluten enteropathy | ↑ demand

▶ Symptoms:

✓ Anemia syndrome ✓ Frontal blading ✓ Koilonychia

✓ Angular cheilitis ✓ Glossitis ✓ Pica

▶ lab:



#Most accurate test :-

BM Biopsy, BUT harmful!

▶ Blood film: Microcytosis + severe hypochromia (central pallor) + Anisocytosis (↑RDW) + Poikylocytosis

* Target cell can be seen in IDA, but must associated with Anisocytosis.

↓

Thalassemia Trait

** Transport protein for Fe⁺⁺ DMT 1 (lumen → enterocyte), Ferroportin 1 (enterocyte → circulation)

Hepicidin: Key regulator of iron / peptide protein produced by liver.

↓ iron absorption in intestine - ↓ iron releasing from hepatocyte & macrophages ⇒ Serum Fe ↓

Mechanism → Regulation of transmembrane iron transport.

Bind to ferroprotein ⇒ hepcidine - ferroportein complex ⇒ degraded in lysosomes

& iron is locked inside enterocyte / hepatocyte / macrophages

- Affecting level of hepcidin ⇒ ① hypoxemia / anemia ⇒ ↓

② inflammation ⇒ ↑ (like hemochromatosis)

Normal values

- ✓ Normal MCV >> 80-100 FL
- ✓ Normal RDW >> 11.5-15%
- ✓ Normal MCH >> 29±2 picograms
- ✓ Normal Ferritin >> 12-150 in females
  12-300 in males

▶ Treatment: oral iron < Fe gluconate / sulphate | IV iron < Fe sucrose / carboxymaltose / Fe Dextran

expected Hb +1g / 10 days.

∴ IDA not a diagnosis, find the cause < intake ↓ / upper GI bleeding, gastric cancer

★ Macrocytic anemia

[1] V. B12 def. < hypoxia symptoms
neurologic symptoms

▶ ↓Hb / ↑MCV / [↓retics ↓WBC ↓platelets] underproduction / ↑LDH / ↓B12

Other test >> - Intrinsic factor Ab + parietal cell ab

- Endoscopy of upper GI + Biopsy

Normal values
- platelets = (150 - 400K)
- B12 = > 200
- folate = 3-4 ng/ml
- blasts ≤ 5%

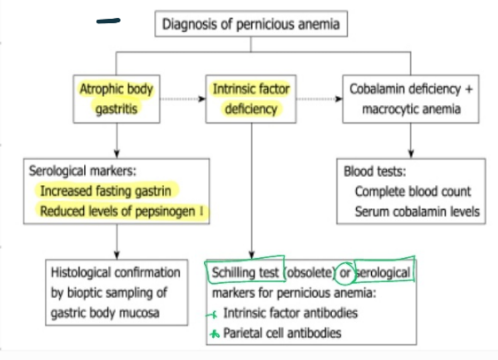
▶ Physical >> Red beefy tongue / vitiligo (Autoimmune)

▶ Blood film >> hypersegmented neutrophils >5

BM : Megaloblastic

#Pernicious anemia: End stage of Atrophic Body Gastritis => Achlorhydria

-Autoimmune disease



characteristic of V.B12 def. ↴

#Subacute combined degeneration of spinal cord => post. & lateral column

-other causes of cobalamin def. ← gastric sleeve
H. pylori
PPI therapy long term
ileal disease
fish tapeworm
severe pancreatic insufficiency
vegetarianism

▶ Treatment : -V.B12 [IM] daily 7-10 days, then monthly.

- Monitoring

[2] Folic acid def.

- Inadequate intake ← ↓ fish, Chronic alcoholism, uncooked food, total parenteral nutrition
- Malabsorption
- Increase requirement ← pregnancy & lactation, infancy, Malignancy ⇒ ↑ demand needs ⇒ ↑ biopsy, hemolysis, hemodialysis
- Defective utilisation (Drugs) ← Methotrexate, purine analogs, hydroxyurea, phenytoin, N_2

▶ ↓HB | ↑MCV | normal (WBC, platelet, B12) | ↓retics | ↑LDH | ↓ folate .. hypersegmented neutrophil

▶ Treatment ⇒ oral folic 5mg x 2 daily for 3 months, maintenance if necessary.

#Role in neural tube closure

[3] Mylodysplastic Syndrom [RARS / RAEB type 1 with ring sidroblasts]

▶ Hb↓ / MCV↑ / Low (WBC, platelet, retics) / normal LDH / ↑↑ blasts

▶ Splenomegaly ▶ BM: Ringed sideroblasts ▶ FISH 11 q del

Pancytopenia + blasts (hypercellular) - dysplastic + cytogentics

▶ ↑risk of AML >20%.

▶ Primary MDS-b / secondary or treatment-related MDS ← chemo radiation neoplasm

▶ Elderly - ♂ - 50% cytogenetics abnormalities.

▶ Clinical feature:

- Anemia → ↑risk of HF
- Granulocytopenia → ↑ infection
- Thrompocytopenia → ↑ Bleeding

#only 5 genes are mutated in >10% of patients.

#WPSS (0-6)

▶ Therapeutic

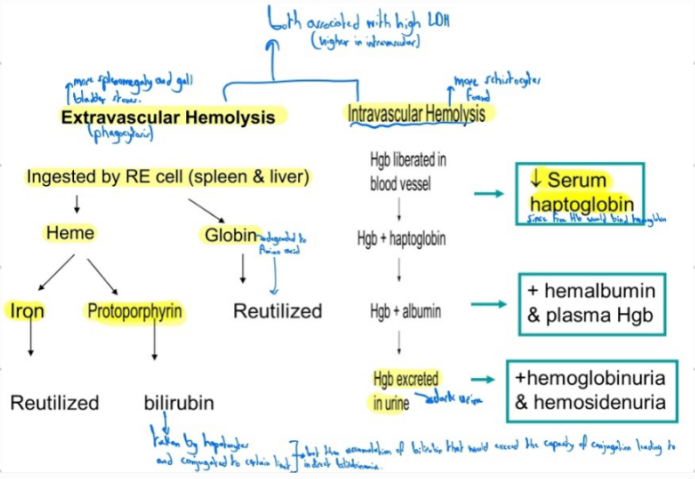
* Iron Chelation
* SCT if sever

★ Normocytic anemia

[1] Autoimmune hemolytic anemia ← anemia syndrom, jaundice

- ↓Hb / ↑LDH / DAT ⊕
  ↑bilirubin
- Blood film: spherocytosis, polychromasia
- BM: erythroid hyperplasia
- Treated with steriods + folic acid

- Hemolysis { internal, external
  - congenital
  - Acquired { immune, non-immune



Evidence for increase RBC production:-

Blood (↑retics) - BM (erythroid hypoplasia) - Bone (frontal bossing)

- Clinical features: ① Anemia syndrome ② gallstones ③ spleenomegaly
  ④ Dark urine ⑤ chronic ankle ulcer ⑥ Aplastic crises with B19 parovirus.
  ↑folate demand
  → cause 7-10days cessation of erythropoiesis

▶ AIHA (warm ab) { primary = 45%, secondary = 40% → CT diseases / Infectious / chronic lymphocytic leukemia, Drugs = 15%

∴ Coombs Test → DAT → Anti-C3d / Anti-IgG ⇒ pt. RBC
→ Indirect Antiglobin Testing → RBC + IgG ⇒ Pt. serum (RBC not from pt.)

∴ Treatment ›› Treat cause → prednisone → splectomy / others → Immunosuppresiv, IV-IG

▶ Hemolytic anemia with intravascular hemolysis

- Mechanical damage → [Microangiopathic hemolytic anemia = Schitocyte]
- chemical damage
- Infection
- Transfusion reaction

② Aplastic anemia

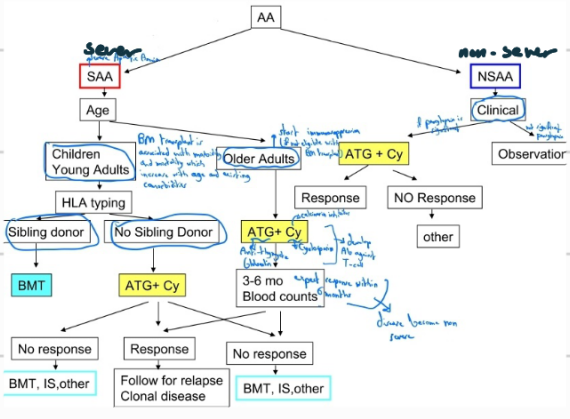
- ⊗ production of erythrocyte, WBC, platelets » peripheral pancytopenia & hypocellular BM
- occur in all ages & both genders
- causes of BM failure
  - Aquired → PNH / drugs / radiation / viruses
  - Inherited → Fanconi anemia / Diamond-Blackfan anemia
- clinical manifestations
  - Anemia syndrom
  - Neutropenia
  - Thrombocytopenia

  } => Bleeding / Anemia / Infection

- classification →

Classification	Criteria
Severe	BM cellularity < 25% (or < 50% if < 30% of BM is hematopoietic cells) AND ≥ 2 of the following: • Peripheral blood neutrophil count < 0.5×10^9/L • Peripheral blood platelet count < 20×10^9/L • Peripheral blood reticulocyte count < 20×10^9/L
Very severe	As above, but peripheral blood neutrophil count must be < 0.2×10^9/L
Nonsevere	Hypocellular BM with peripheral blood values not meeting criteria for severe aplastic anemia

- Treatment →



=>
① supportive
- RBC transfusions
- Treat infection
- Treat bleeding

② BM transplant

③ Immune suppression
- CSA
- ATG

* HLA matching siblings better than unrelated donor.
* Age effect => Best outcome with very young pt.

- Related disorders »
  ① Pancytopenia + hyper-normocellular BM → Myelophthesic anemia
  ② Myelodysplastic anemia
  ③ Pure red cell aplasia.