***INTRODUCTION TO MACROCYTIC ANEMIA***

**Normal adult red cell values:**

|  |  |  |
| --- | --- | --- |
|  | **Male** | **Female** |
| **Hb(g/dl)** | **13.5-17.5** | **11.5-15.5** |
| **PCV (%)** | **40-52** | **36-48** |
| **Red cell cont** | **4.5-6.5** | **3.9-5.6** |
| **MCH (pg)** | **27-34** |  |
| **MCV (fl)** | **80-95** |  |
| **MCHC (g/dl)** | **30-35** |  |
| **Reticulocyte count** | **25-125** |  |

**Note:**

* Hb , PCV and Red cell count are the only three values that differ in male with female.
* MCV "size of RBCs" : If less than 80, microcytic anemia occur

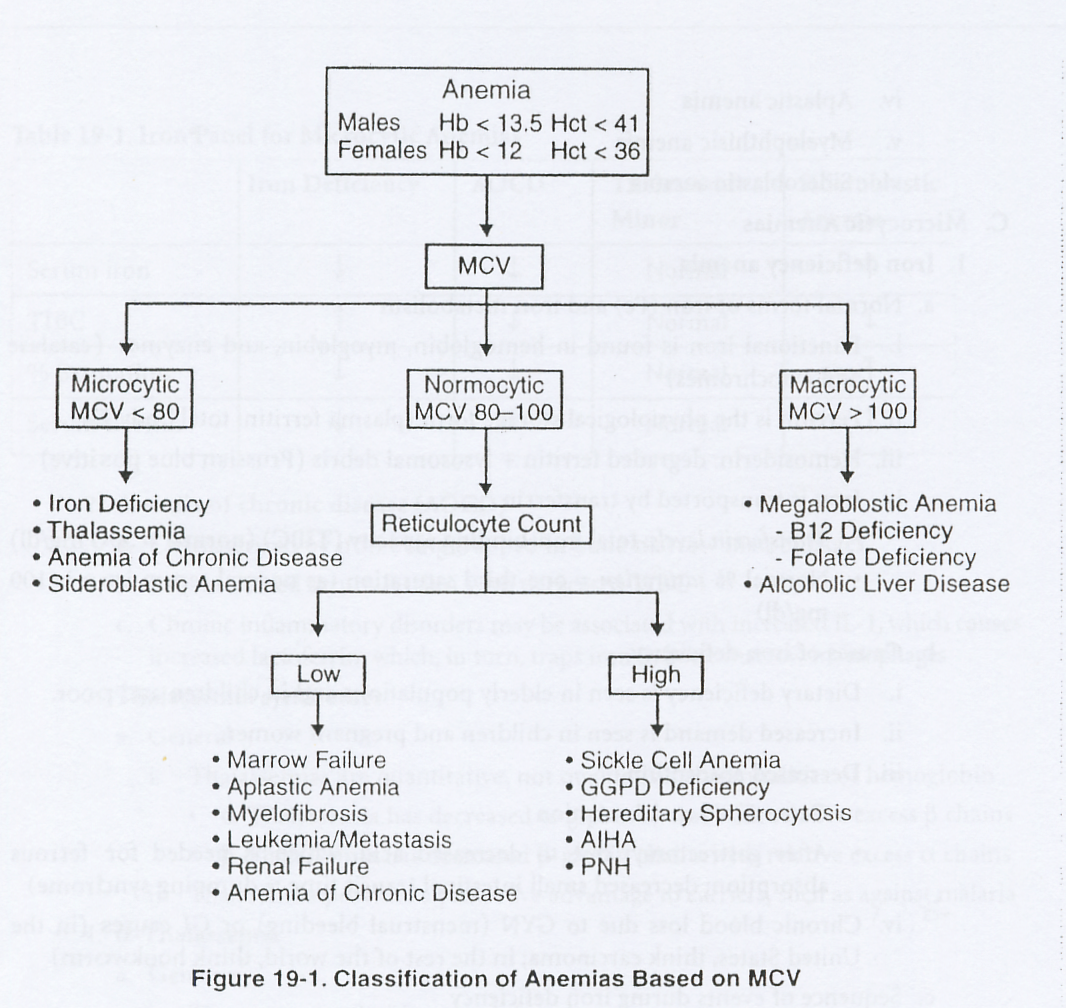
If more than 95 , macrocytic anemia occur

Between 80-95 normocytic normocronic aneamia

* MCH "concentration of Hb" : If less than 26, hypochromic anemia occur.

**No hyperchromic condition.**

* In children Hb is 15-21 because of the low O2
* After birth phy jaundice happens



***MACROCYTIC ANEMIA***

* Large RBCs.
* Based on appearance of developing erythroblast ( with delayed nucleus maturation ) macroctic anemia is divided into :

|  |  |
| --- | --- |
| ***Megaloblastic*** | ***Non – Megaloblastic*** |
| * **Delay of nucleus maturation in bone marrow erythroblast** * **Defect DNA synthesis due to Vit. B12 or Folate deficiency** | **alcoholism, liver disease, aplastic anemia, reticlocytosis, hypothyroidism myeloma , pregnancy and newborn** |

## -MEGALOBLASTIC ANEMIA:

* Not only RBCs and bone marrow becomes larger but all body cells because of the deficiency in Vit. B12 or Folate those are required in DNA synthesis.
* Anemia's characterized by delayed maturation of the nucleus compared to the cytoplasm.
* It s usually associated with neurological symptoms because of Vit. B12 role in the maintenance of myelin .

## Laboratory findings:

* Anemia, macrocytic.
* Peripheral blood: macrocytosis, ovalocytosis. Imp. in this test to differentiate between small fragmented WBCs and platelets "don't miss up".
* Decrease WBC: with hypersegmented neutrophils "more than 5 lobes".
* Decrease platelets.
* Bone marrow: hyper cellular, Megaloblastic erythropoiesis – immature nuclei with normal hemoglobinization "hemoglobinization = cytoplasm".
* Increase bilirubin; increase Lactate dehydrogenase "LDH" due to marrow cell breakdown.
* Decrease serum B12 serum Folate and RBC Folate.

***Vitamin B12:***

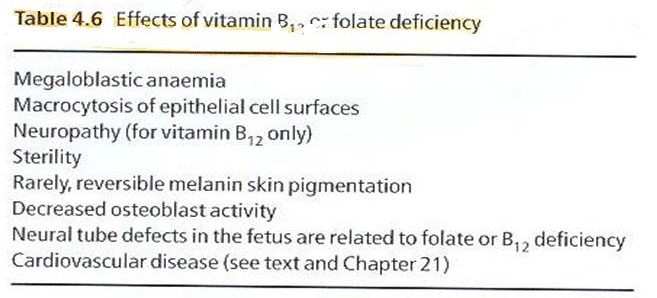
* Source: food of animal origin.
* Absorption after combination with intrinsic factor (synthesized by gastric parietal cells), the complex is absorbed in the distal ileum.
* Transport: the absorbed Vit. B12 is attached to transcobalamin II which transports Vit. B12 to the bone marrow.
* Deficiency:
* Causes:
  + - Dietary 🡪strict vegetarians.
    - Pernicious anemia: Gastric mucosa ( chief and parietal cells) destruction due to autoimmune disease lead to
* No intrinsic factor 🡪 no B12 absorption
* No HCL (achlorohydria) 🡪 decrease iron absorption
  + - Gastrectomy.
    - Intestinal disorders: e.g. chron's disease, ileac resection, parasites " fish tapeworm"
* Notes:
  + Deficiency takes 2 years at least to develop
  + It is not destroyed by heat " cooking"
  + Treatment: IM Vit B12

***Folate:***

* Source: not synthesized in the body and thus obtained in diet only.
* Absorbed in the upper small intestine.
* Deficiency:
* Dietary.
* Mal-absorption.
* Increased requirements: e.g. pregnancy, hemolytic anemia.
* Drugs: e.g. anticonvulsant.
* Notes:
  + Deficiency takes only months to develop
  + Easly destroyed by heat
  + The requirement is increased in Pregnant and infant
  + The main defference between the Vit B12 and Folate deficncy is that Folate don't have neurological symptoms

***Clinical features:*** *"MCQ"*

* **general:** Pallor, lethargy, etc …. .
* Specific:
  + Jaundice.
  + Glossitis: painful.
  + Angular stomatitis.
  + Purpusa: due to thrombocytopenia.
  + Neuropathy: sensory and motor, especially in the lower limbs.
  + Neural tube defect.
  + Psychological impairment.
  + Ulceration of the tongue

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***MEGALOBLASTIC ANEMIA***

**What is the cause?**

Deficiency of vitamin B12 or Folate

**How do these deficiencies lead to anemia?**

Both vitamin 12 and Folate are necessary for DNA synthesis. Decreased DNA synthesis subsequently leads to decreased RBC production.

**What is a Megaloblastic?**

An erythroid precursor cell found in the bone marrow

**What are typical lab findings?**

Pancytopenia, decreased vitamin B12, decreased Folate

**What is seen on histology?**

Oval macrocytosis, hypersegmented neutrophils (> 5 lobes), and megaloblastic hyperplasia of bone marrow

FOLATE DEFICIENCY

**What are some causes of Folate deficiency?**

Poor diet, pregnancy, spme, drug effects, and Giardia lamblia infection

**In which populations is diet-related Folate deficiency often found?**

Chronic alcoholics and fad dieters

**What drugs are associated with decreased Folate?**

Phenytoin, oral contraceptives, and methotrexate

**How does hemolytic anemia cause a relative deficiency of Folate?**

The compensatory accelerated eythropoiesis uses up the body stores of Folate.

***VITAMIN B12 DEFICIENCY***

**What is the most common cause?**

Pernicious anemia

Define pernicious anemia.

An autoimmune disorder with failure of production of intrinsic factor (IF) due to

Anti-IF antibodies

**How is IF related to vitamin B12?**

IF is essential for the absorption of vitamin B12 in the distal ileum.

**What are the 4 clinical findings of pernicious anemia?**

1. Yellow skin .2 Stomatitis .3 Clossitis .

4Subacute combined degeneration of the spinal cord

**How does subacute combined degeneration of the spinal cord manifest?**

Ataxic gait, hyperrefiexia, and impaired vibratory and positional sensation

**What abnormal antibodies are found?**

**Anti-IF and autiparietal cell antibodies**

**What are the results of a Schilling test**?

Decreased vitamin B12 absorption corrected by adding IF

**What type of gastritis is present?**

Chronic fundal gastritis (Type A)

**What feared entity may Type A gastritis progress to?**

Gastric cancer

**What are some other causes of vitamin B12 deficiency?**

Intestinal bacterial overgrowth, gastric resection, vegetarian diet, intestinal malabsorption, *D. latum* infestation

**What are 2 causes of excess bacteria in the intestine?**

Broad-spectrum antibiotics and blind- loop syndrome