MEGALOBLASTIC ANEMIA

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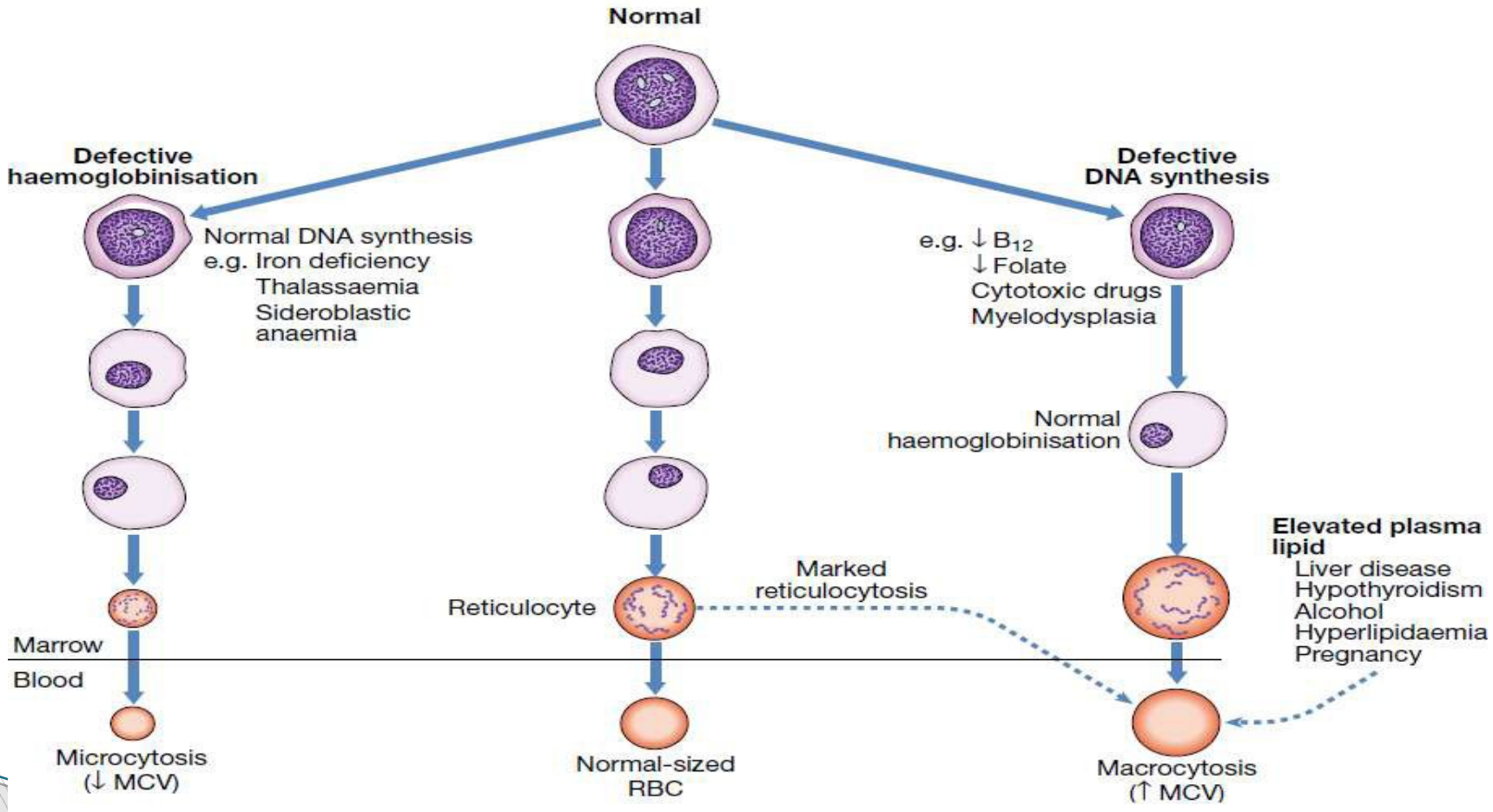
Definition

- ***Megaloblastic anaemia is a red blood cell disorder due to the inhibition of DNA synthesis during erythropioesis.***
- Mitotically, the inhibition of the DNA synthesis impaires the progression of the cell cycle development from G2 to (M) stage.

erythropoises



Etiology of megaloblastic anemias

a. Vitamin B12 or Cobalamin deficiency.

b. Folic acid deficiency

c. a and b deficiency.

- Etiology
- □ Cobalamin: Deficiency / abnormal
- metabolism.
- □ Folate: Deficiency / abnormal metabolism
- / antifolate drugs.
- □ Drugs interfering with synthesis of DNA.
- □ Rarely- orotic aciduria, AML,
- myelodysplasia.
- □ Arsenic poisoning
- □ Nitrous oxide inhalation.

Cobalamin (vitamin B12)

- *It is solely synthesized by microorganisms and the only source for humans is food of animal origin like meat, fish and dairy products.*
- *Adult daily losses (mainly in urine and feces) are 1-3 ug*
- *and so daily requirements are also 1-3 ug.*
- *Body stores are of the order of 2-3 mg, sufficient for 3-4*
- *years if supplies are completely cut off.*

VITAMIN B12 DEFICIENCY Etiology

Inadequate intake:

This is common among pure vegetarians**,** old and bed ridden patients

Inability to absorb vitamin B12:

- after gastric surgery,
- lack of hydrochloric acid in gastric juice,
- lack of intrinsic factor due to auto antibodies to parietal cells.

Competition for intestinal vit.B12 :

- Competitive absorption of the vitamin by fish tape worm (Diphyllobothrium latum) and bacteria overgrowth in blind-loop syndrome, intestinal stasis.

Drugs Inhibition:

- Metformin,
- Proton pump inhibitors

Folate

- Destroyed easily by cooking especially in
- large amounts of water.
- Storage in liver (sufficient for 3-4 months)
- Total body folate around 10mg.
- Daily requirements: 200-300µg.
- Pregnancy: 400µg.

Sources of Folic Acid

- Liver
- Yeast
- Nuts
- Dried beans
- Whole grains
- Spinach and other leafy greens
- Oranges
- Avacados

Source: The Nutrition Bible

FOLATE DEFICIENCY

- **Inadequate intake:**
- **a poor diet**
- **Old and bed ridden patients**
- **ICU patients.**
- **over cooked food especially vegetable**
- **Increased requirements**
- **pregnancy and lactating mothers.**
- **Growing infants**
- **Hemolytic anemic patients.**
- **Drugs**
- **Folic acid antagonists: Methotrexate**
- **Chronic alcoholism:**
- **It inhibits folic acid absorption.**
- **It increases folate excretion through the urine**
- **Inability to absorb folic acid:**
- **Following gastric surgery, chronic diarrhoea.**

Clinical features

• Older children present with pallor, easy fatigability, irritability, chronic diarrhea or poor weight gain.
• Hemorrhages from thrombocytopenia may occur in advanced cases.
• Congenital folate mal-absorption may be further a/w hypogammaglobulinemia, severe infections, Failure to thrive, neurological abnormalities and cognitive delays

- **Investigations**
- The goal is to confirm the diagnosis of
- megaloblastic anemia, distinguish between
- folate or cobalamin or combined deficiency,
- and to determine the underlying cause—
- dietary, sociocultural or disease related.

Lab. investigations

- 1. Peripheral Blood Examination
- a) Haemoglobin : Decreased
- b) Red cells : Characteristic macrocytosis is seen.
- Marked anisocytosis, poikilocytosis with presence of
- Macro ovalocytosis. Basophilic stippling may be seen.
- c) Retic count : Low to normal
- d) Indices : Elevated MCV (>120fl), elevated MCH (
- >50pg)
- e) Leucocytes : May be reduced. Presence of
- Hypersegmented Neutrophil is characteristic.
- f) Platelets : Moderately reduced

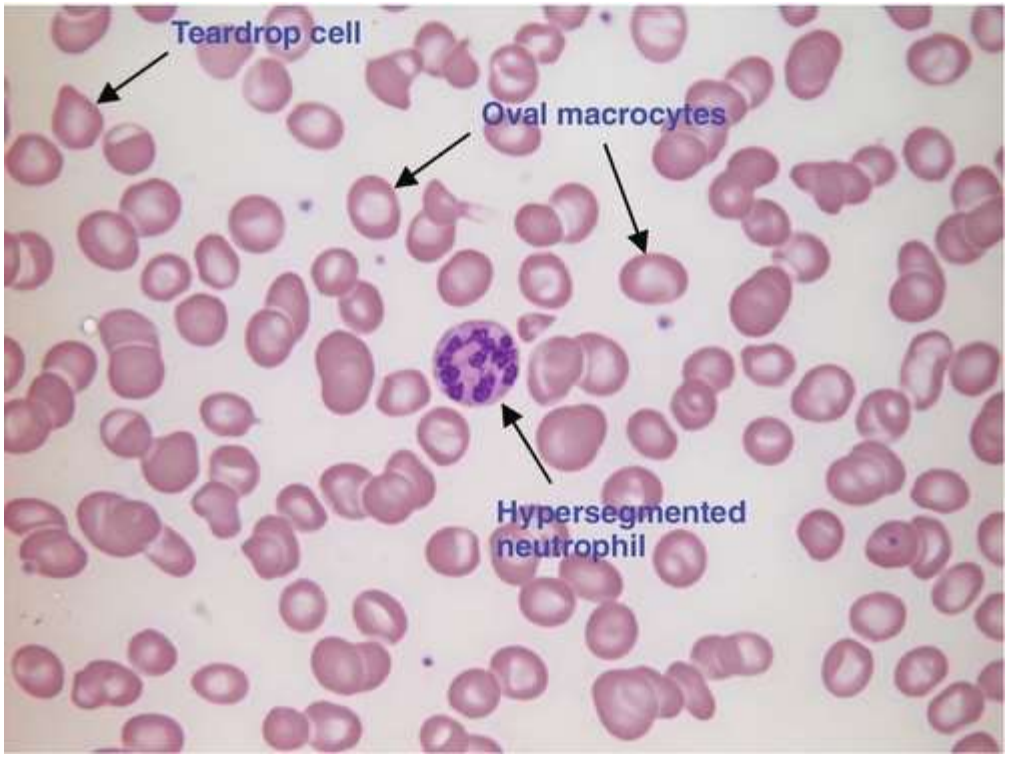
Megaloblastic anemia:

Characterized by abnormally large nucleated red cell precursors called megaloblasts in bone

Marrow Megaloblast because of unbalance between cytoplasm and nucleus due to improper and defective synthesis of nucleoproteins

95 % cases due to vit B12 or folic acid deficiency

leading to defective DNA synthesis


Teardrop cell
Oval macrocytes
Hypersegmented
neutrophil

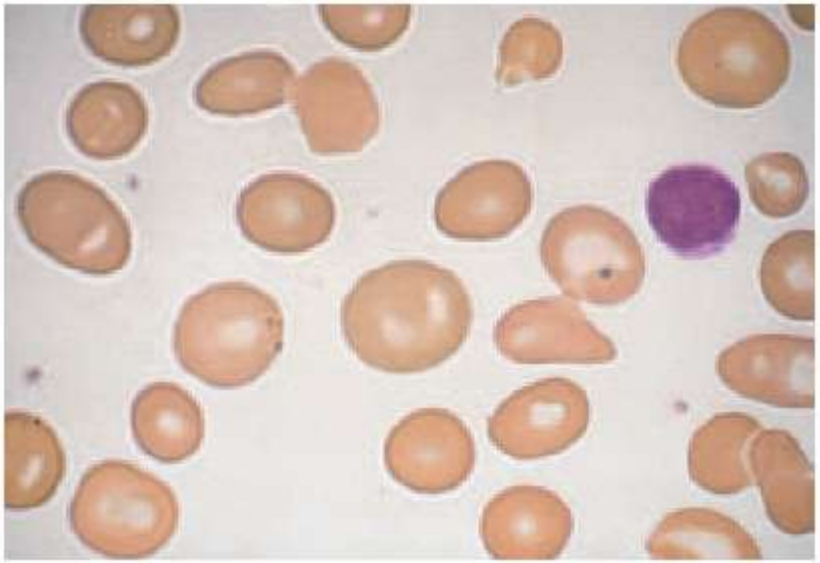
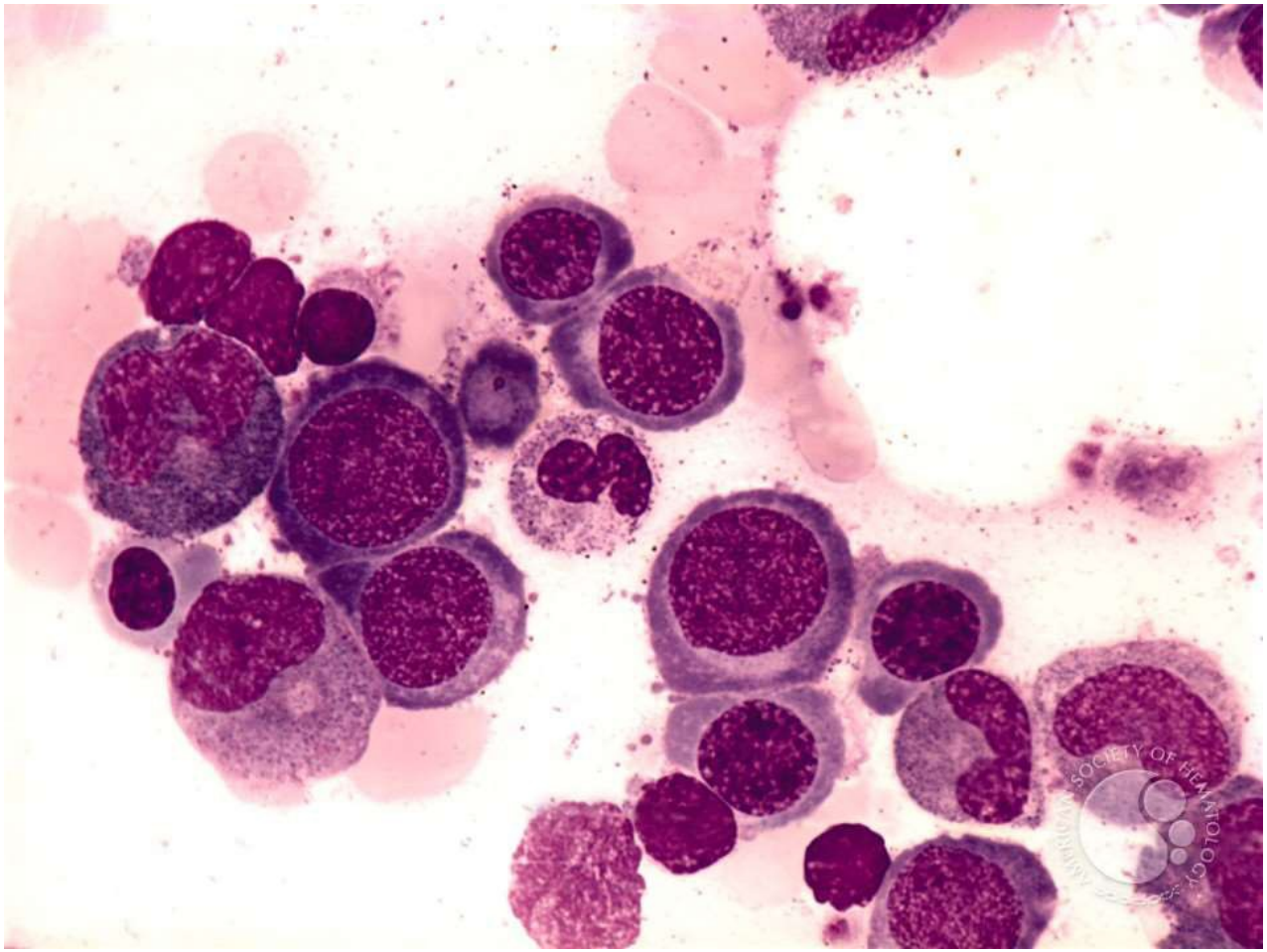


FIGURE 52-5 Macrocytosis. Red cells are larger than a small lymphocyte and well hemoglobinized. Often macrocytes are oval-shaped, so-called macroovalocytes.

Bone Marrow Examination

a) Marrow cellularity : Marrow is Hypercellular with a decreased myeloid : erythroid ratio (from 3:1 to 1:1)
b) Erythropoiesis : Erythroid Hyperplasia is due to characteristic megaloblastic erythropoeisis.
c) Orthochromatic features : sieve like nucleus and haemoglobinized cytoplasm and mitotic figures seen
d) Dyserythropoiesis : nuclear remnants, bi- and trinucleated cells and dying cells

Bone marrow



Vitamin B12 Assessment

- Serum Homocysteine and Serum Methylmalonic acid levels are raised.
- Both are sensitive indicators of vit b12 deficiency and corelate with clinical abnormalities and therapeutic response. Specificity is low.
- Excessive excretion of methylmalonic acid in urine (normal = 0 to 3.5mg/day) is a reliable and sensitive index of vitamin b12 deficiency
- Serum vit b12 levels : Normal value : 200-800 pg/ml Deficiency levels : less than 80 pg/ml

Folate Assessment

- Only Homocysteine is raised with normal methylmalonic acid levels.
- RBC folate assessment is the best measure of metabolically active folate and included 5-MTHF in the assay.
- Serum folate measures the circulating pool of folate but does not accurately reflect the amount of THF present in tissues
- Serum Folate Levels : Normal : 5-20ng/ml
- Deficiency levels : < 3 ng/ml
- RBC Folate Normal levels : 150-600ng/ml

Treatment

- Cobalamin Deficiency
- – Daily dose of 25-100mcg may be used to start the
- therapy.
- – Monthly IM injection in a dose of 200-1000mcg can
- be started as maintainance therapy.
- Conventional therapy :
- 1000 mcg of cyanoCbl or Hydroxy Cbl IM daily for 1 week.
- Followed by 100 mcg of cyanoCbl weekly for 1 month.
- Followed by 100 mcg of cyanoCbl monthly.

Thank you