

ANAEMIA 1

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Syllabus of „Anaemia 1“

- 1. What is anaemia?**
- 2. The anaemic syndrom.**
- 3. Anaemia_sign *versus* Anaemia_disaease**
- 4. Why and how anaemia develops?**
- 5. Classifications of anaemias**
- 6. Summary of the most important items of the lecture.**

Signs *versus* symptoms

Signs are commonly distinguished from symptoms as follows:

Both are something abnormal

- **a symptom** is experienced and reported by the patient,
while
- **a sign** is discovered by the physician during examination of the patient.

1. What is anaemia?

The anaemia is
pathological condition
characterized by
specific signs and **symptoms.**

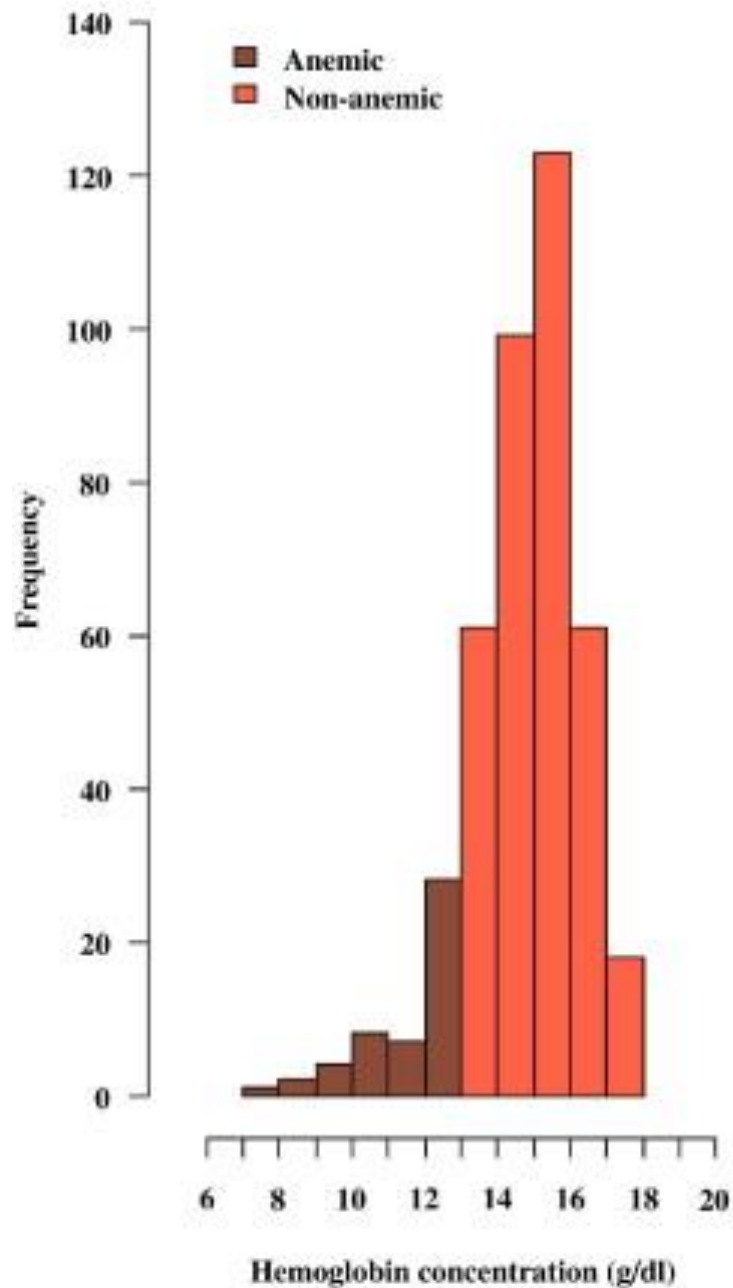
Symptoms of anaemia

- fatigue
- shortness of breath
- pale skin and mucosae
- palpitations

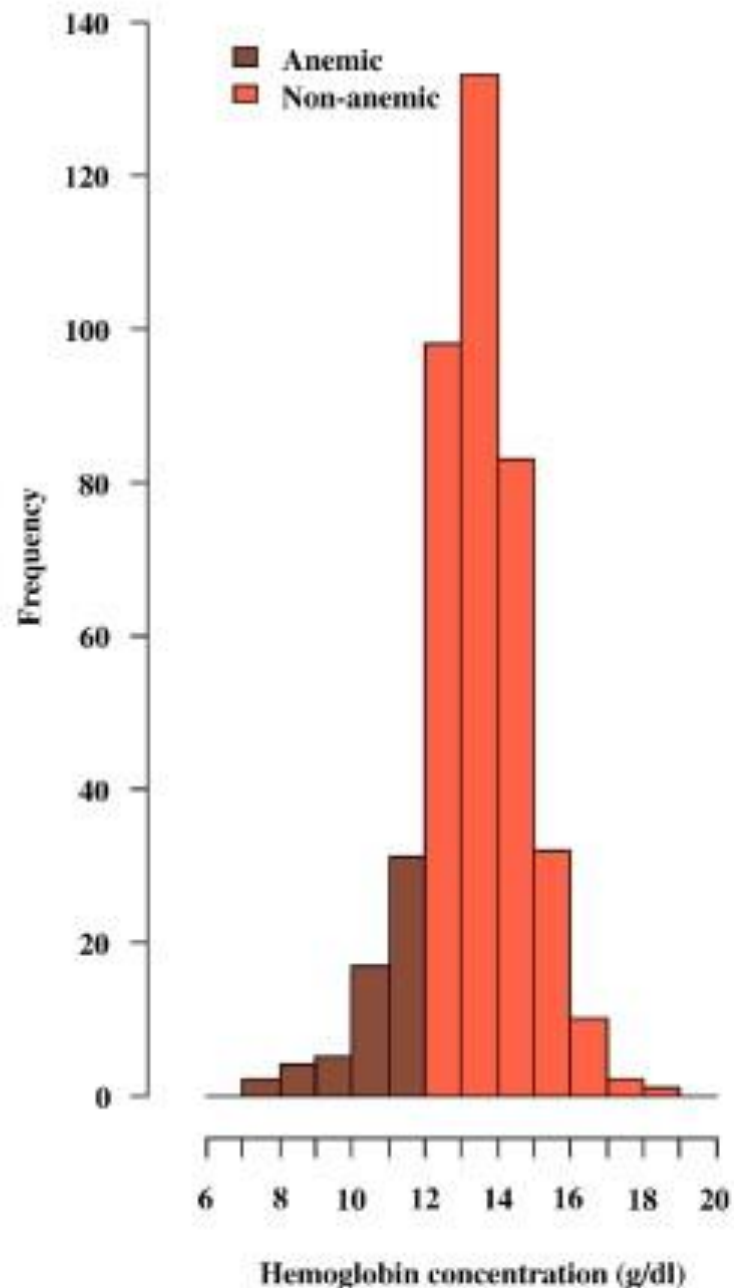
The major criteria (signs) for anaemia are results of laboratory examination

- decreased number of red blood cells in the blood
- decreased concentration of hemoglobin in the blood
- a low haematocrit

Male



Female



The haemoglobin concentration in blood should be below

- in men < 120 g Hb/L
- in women < 110 g Hb/L

A life threatening anaemia

haemoglobin concentration in blood

40 to 30 g Hb/L

(an acute onset anaemia
vs. chronic anaemia)

Adaptive, compensatory mechanisms
in acute and chronic anaemia.

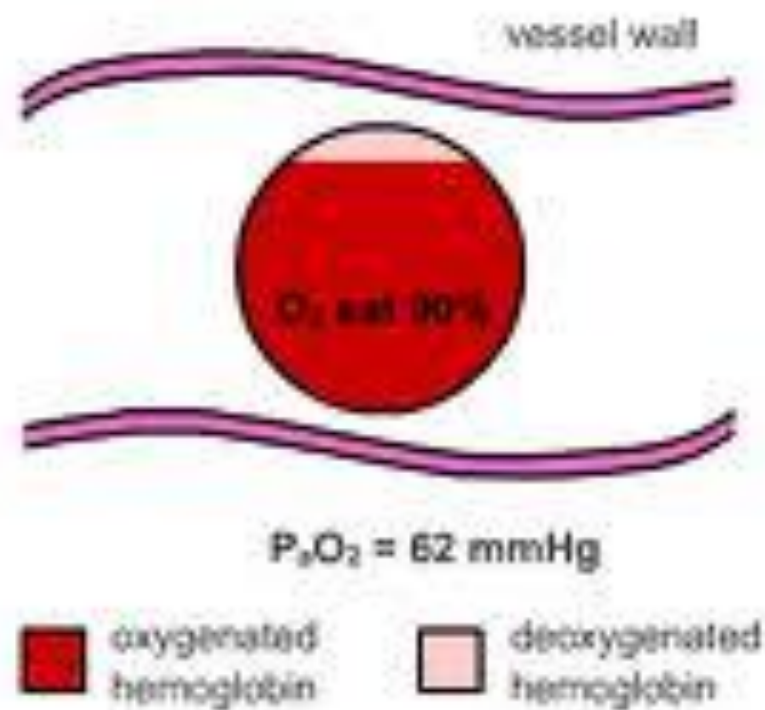
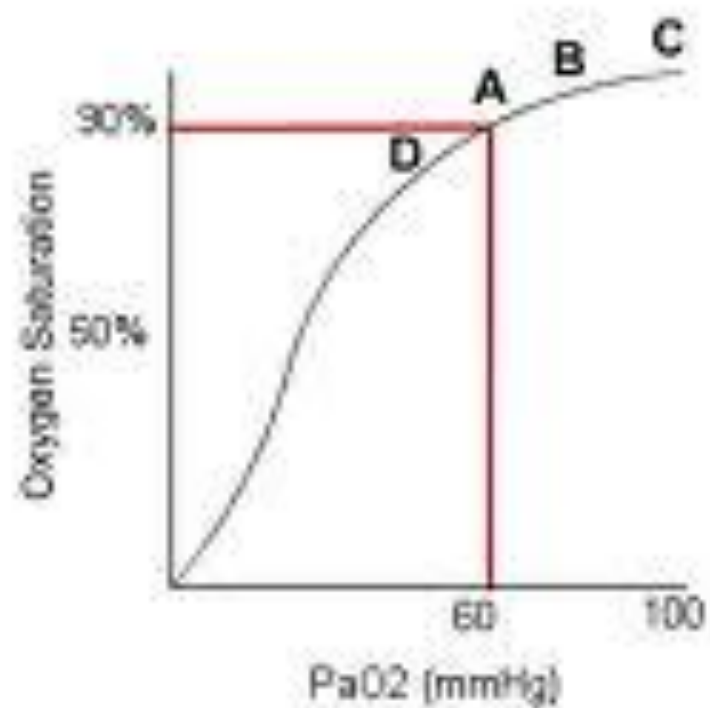
Adaptive, compensatory mechanisms in acute and chronic anaemia

Acute anaemia:

- increased cardiac output
- increased arterio-venous oxygen content difference

Chronic anaemia:

- increased arterio-venous oxygen content difference
- decreased affinity of blood to oxygen (2,3-DPG)



2. The anaemic syndrome.

A syndrome (generally) includes several symptoms occurring together - this is helpful in the diagnostic process.

The anaemic syndrome includes:

- mucosal ev. skin pallor
- exertional dyspnea (shortness of breath)
 - a rapid heart rate (tachycardia),
 - fatigue,
 - sleepiness

(all the symptoms depend on a degree of anaemia and a rate of its development)

3.

Anaemia_sign

versus

Anaemia_disease

Anaemia means that something is
wrong – it is
sign of a disease.

It can be a part of various diseases
(e.g. a tumour, a chronic inflammatory
disease) – „**secondary anaemia**“).

It can be caused by
**a primary disease of the blood
forming tissues or red blood cells.**

The symptomatic *versus* the causal treatment of anaemia

- **Symptomatic treatment** – transfusion of the red cell mass or the whole blood
- **Causal treatment** – after establishing cause of anaemia – e.g. vitamin B12 or iron supplementation, splenectomy, immunosuppressive therapy ...

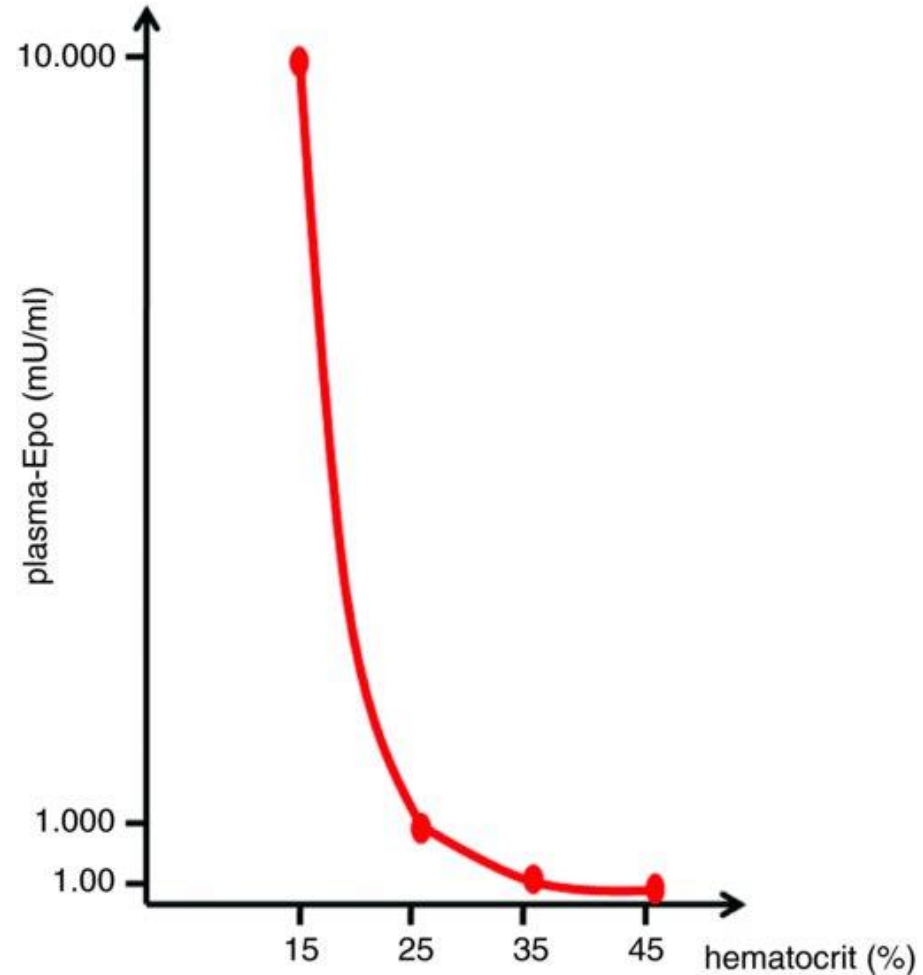
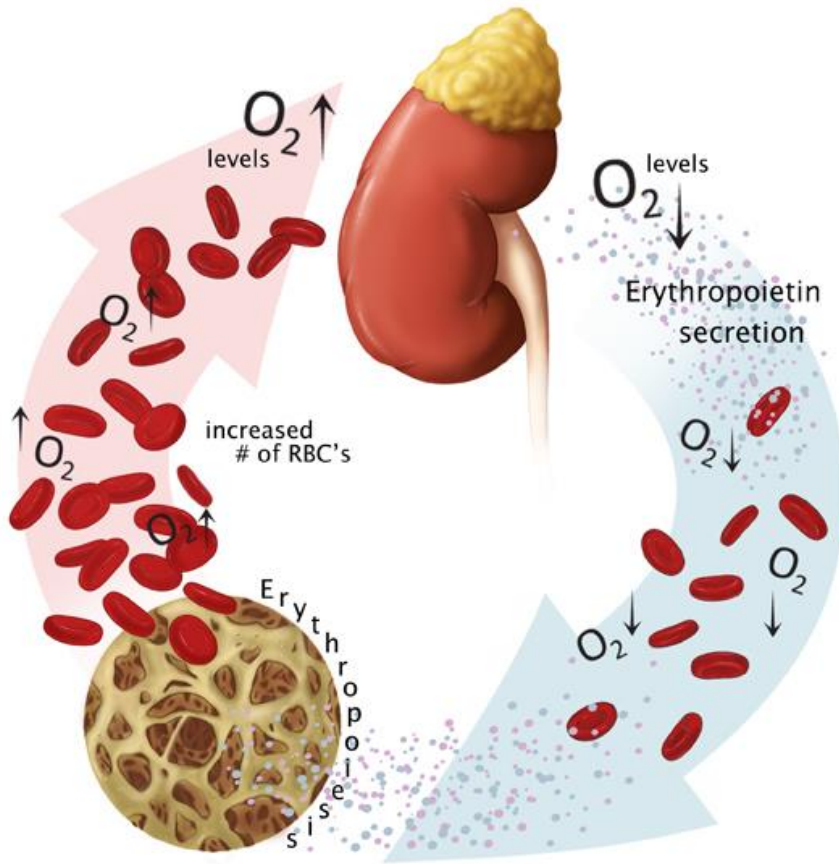
4. Why and how anaemia develops?

**Losses and production of red blood cells
are normally well balanced ...**

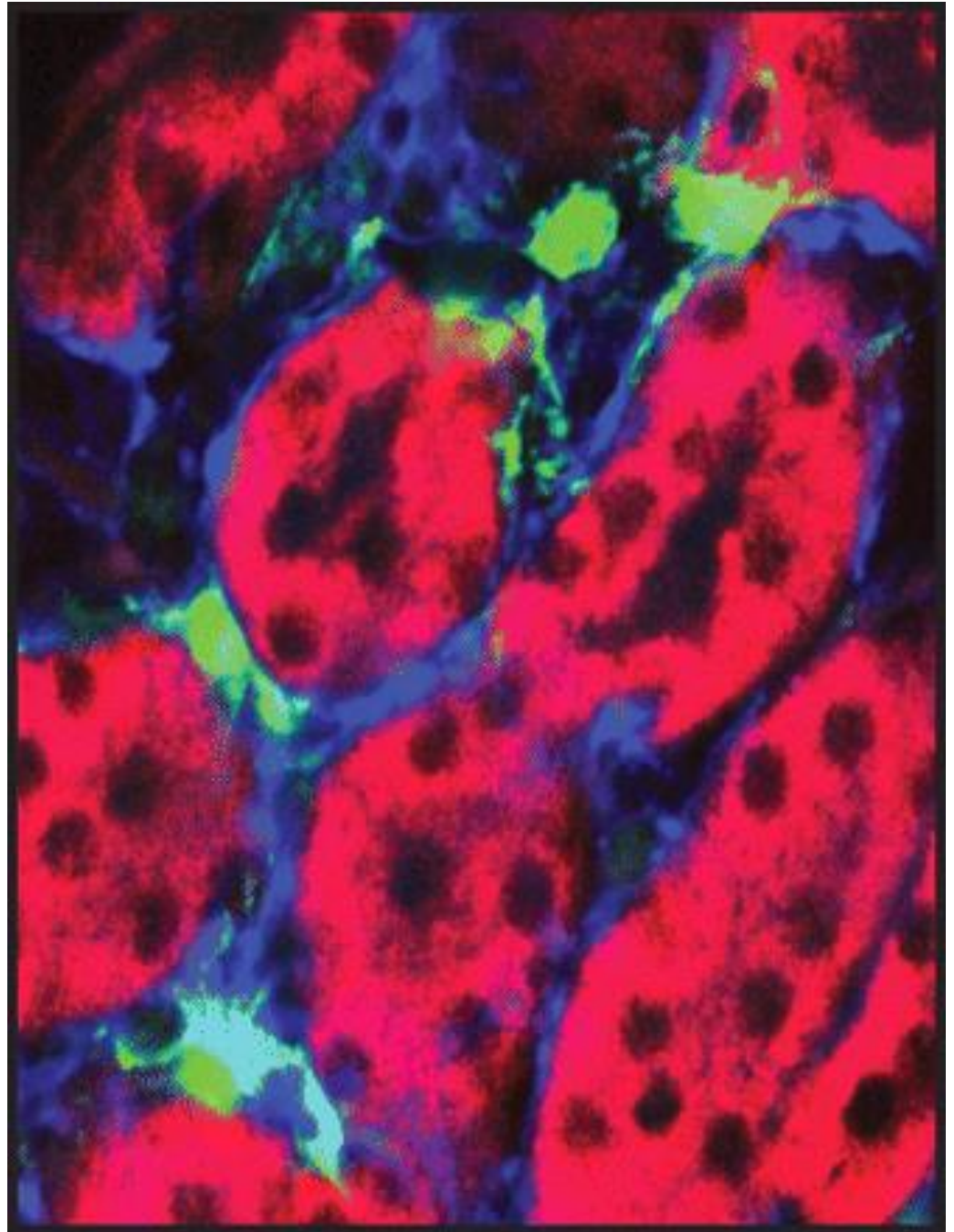
**Anaemia results from
the losses of red blood cells
outweighing
their production rate.**

Control of the Red Blood Cell Production

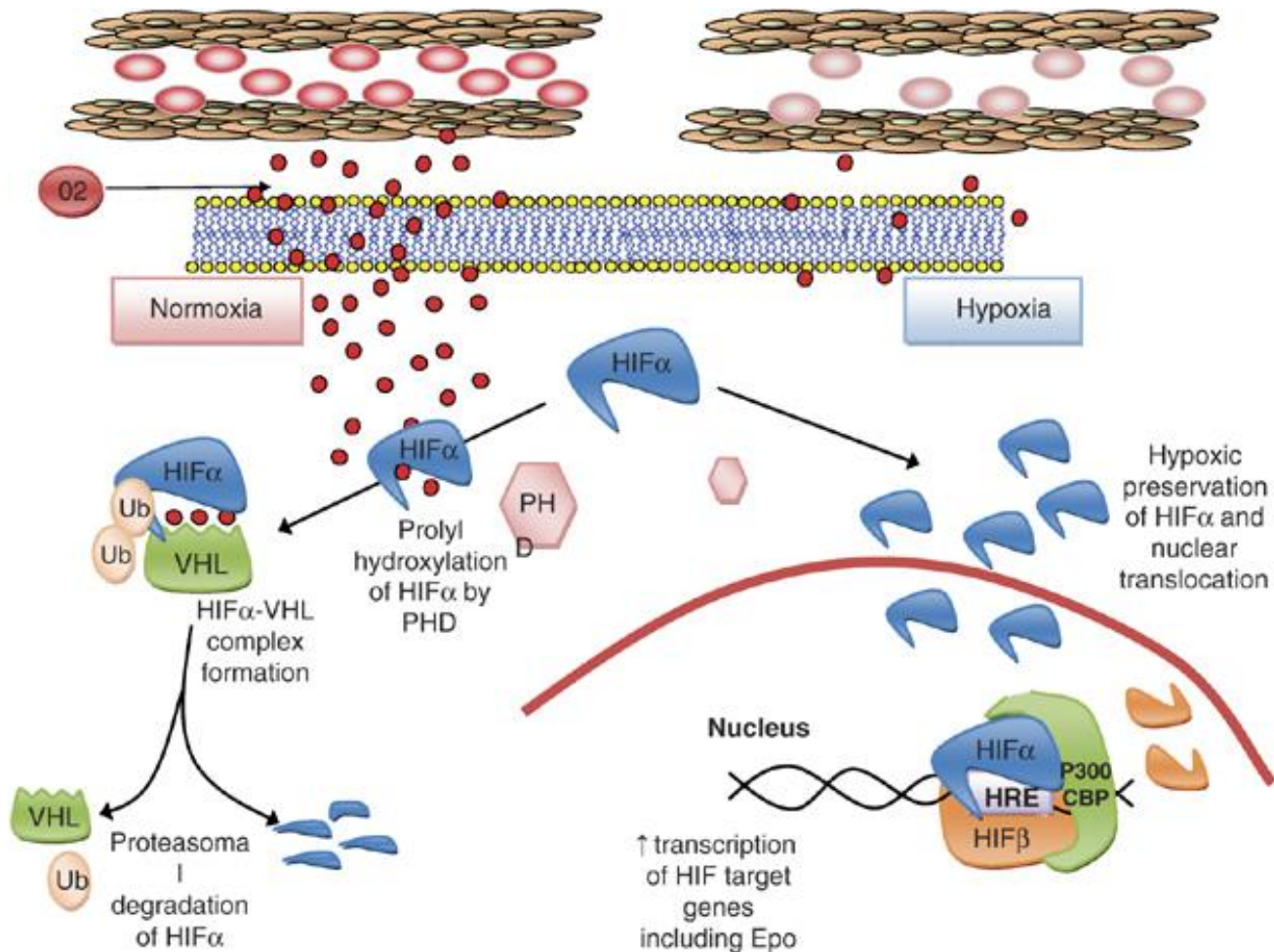
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Cells producing
erythropoietin in
the kidney
according to
oxygen availability



Oxygen sensing mechanism governing erythropoietin production



COMPUTER SIMULATION

Aneamia may improve, may worsen, may be stable.

- **A new equilibrium**, a new dynamic steady-state between red blood cell losses and production rates may result in **a chronic stable anaemia**.
 - A special case is **a compensated haemolytic syndrome** when both: the red blood cell losses and production are increased.

5.

Classifications of anaemias

Classification of anaemia

- **pathogenetic**
- **morphologic (laboratory)**
- **etiologic**

Morphological (laboratory) classification of anaemia

Morphological (laboratory) classification of anaemia

1. according to **red blood and bone marrow cell volume (size)**
2. according to **red blood cell hemoglobinization**
3. according to **red blood cell shape**

Morphological classification of anaemias - 1

Normocytic anaemia (MCV is 80–95 fL)

- after **acute blood loss**
- **aplastic anaemia**
- some haemolytic anaemias

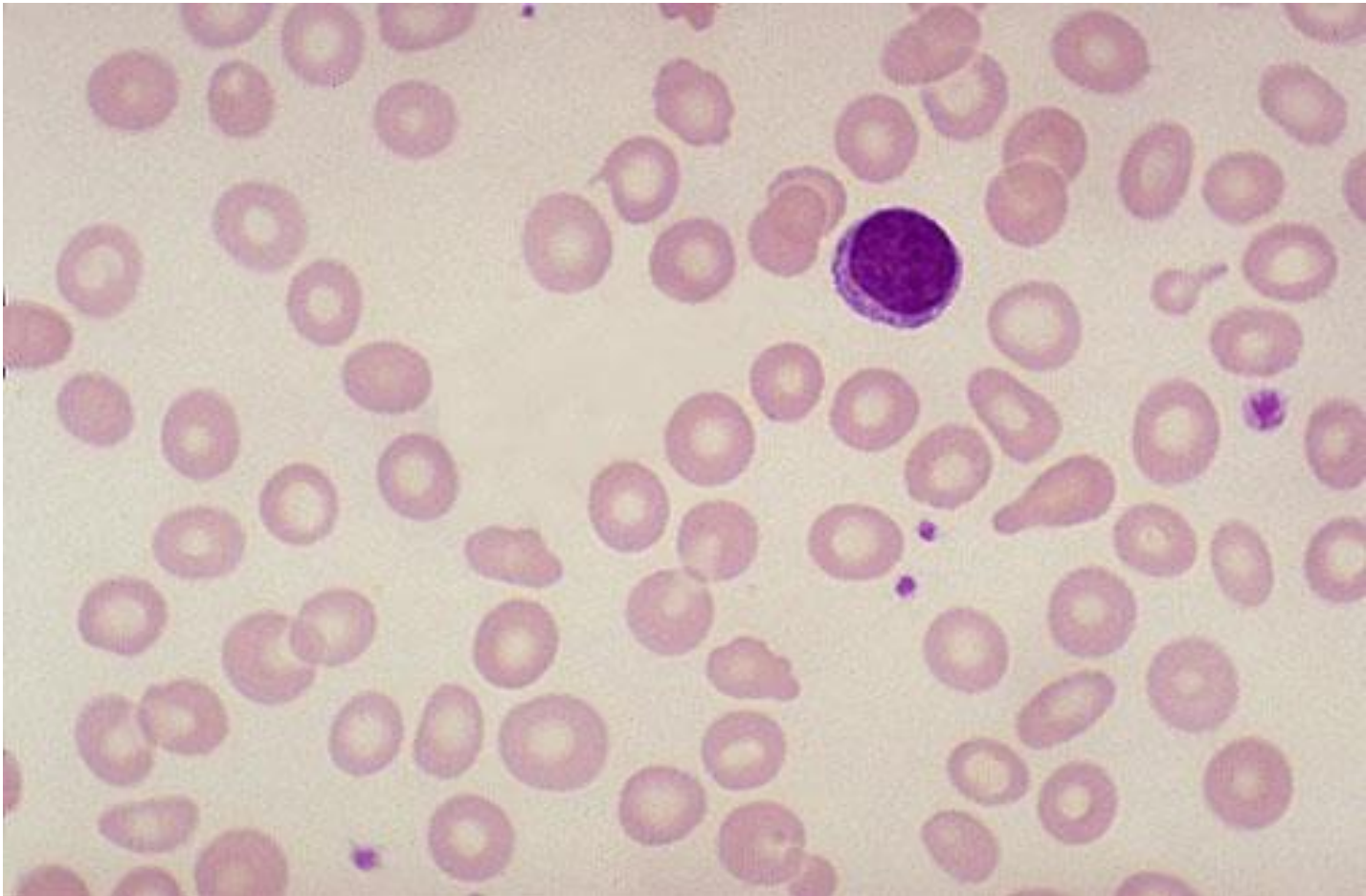
Makrocytic anaemia (MCV higher than 95 fL)

- **megaloblastic anaemia** (folic acid or vitamin B₁₂ deficit)
- anaemia accompanying **hypothyreosis**, high number of **reticulocytes** in the blood

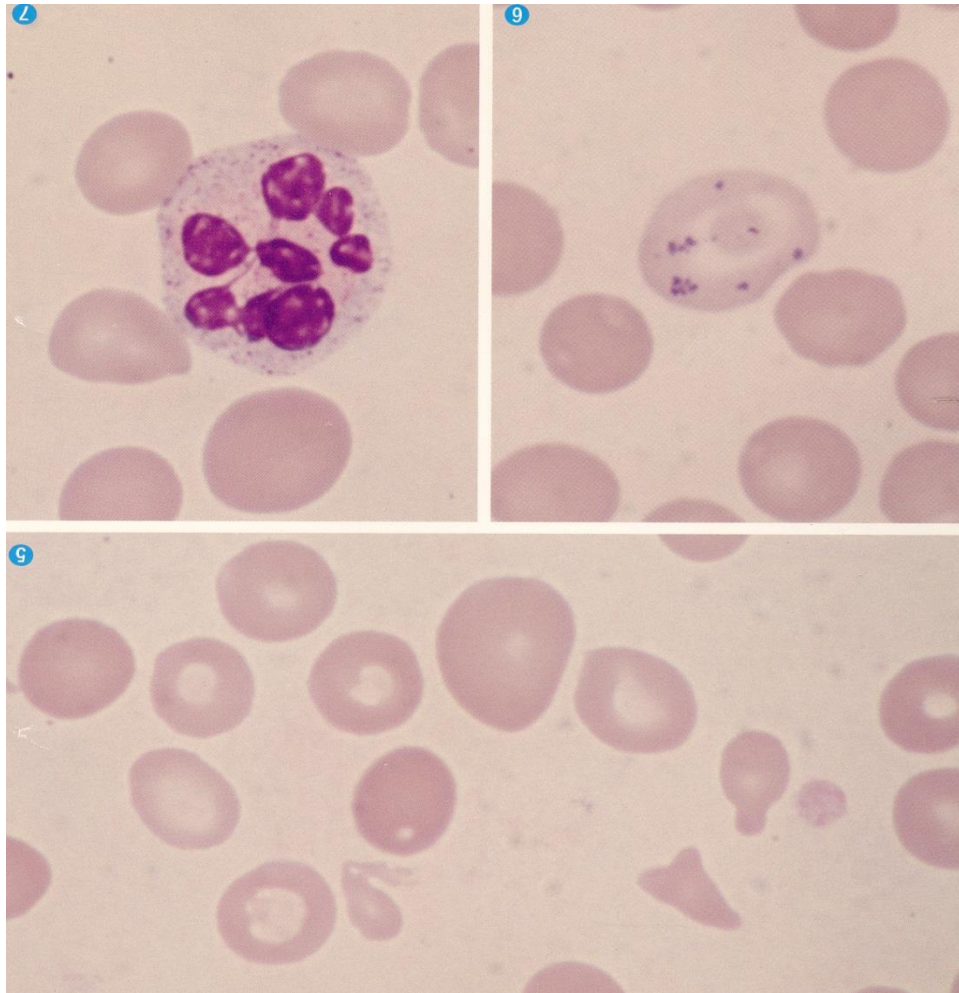
Mikrocytic anaemia (MCV less than 80 fL)

- **iron deficiency anaemia**
- **β-thalassaemia major**
- **hereditary spherocytosis**

**Mikrocytic (MCV < 80 fL)
hypochromic anaemia**

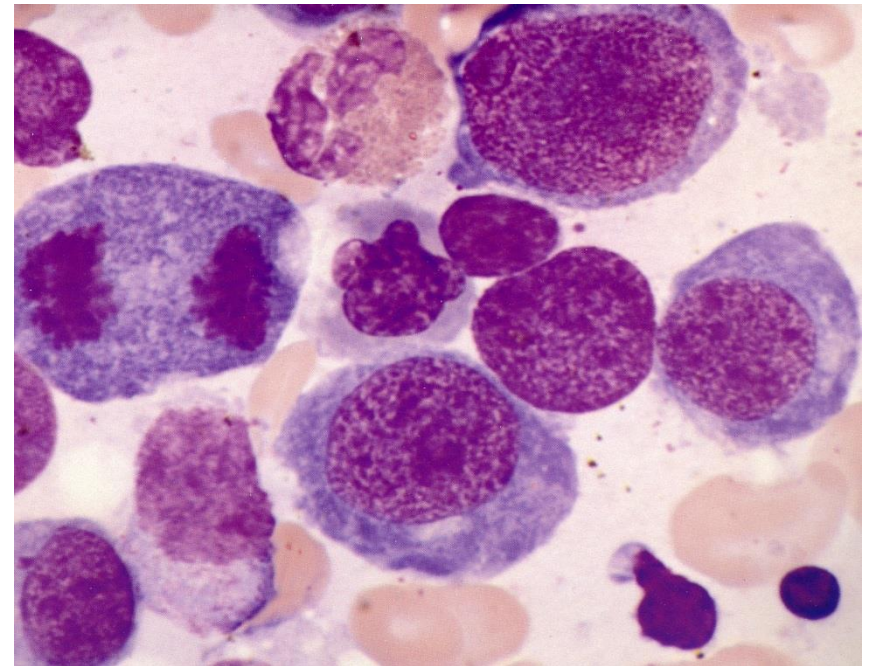
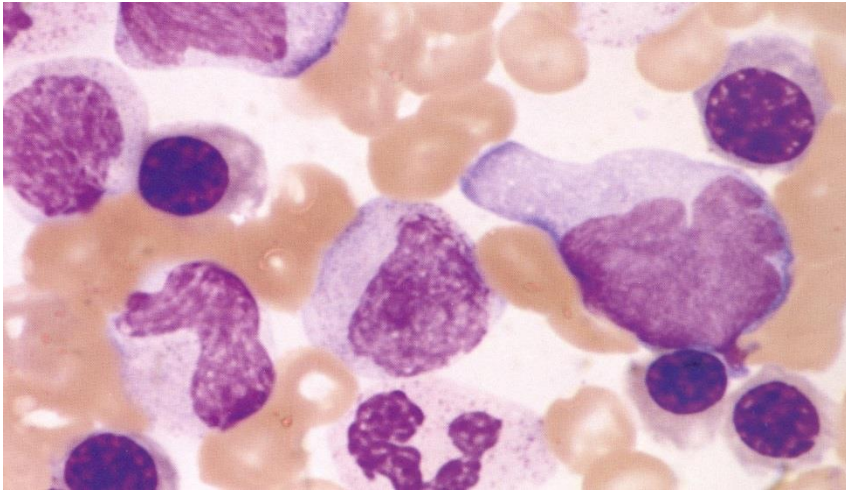


MACROCYTIC ANAEMIA (MCV > 95 fL) anisocytosis, poikilocytosis



Megaloblastic (and macrocytic) anaemia from vitamin B12 or folic acid deficiencies

*- bone marrow is not aplastic but there are few
reticulocytes in the blood*



Morphological classification of anaemias - 2

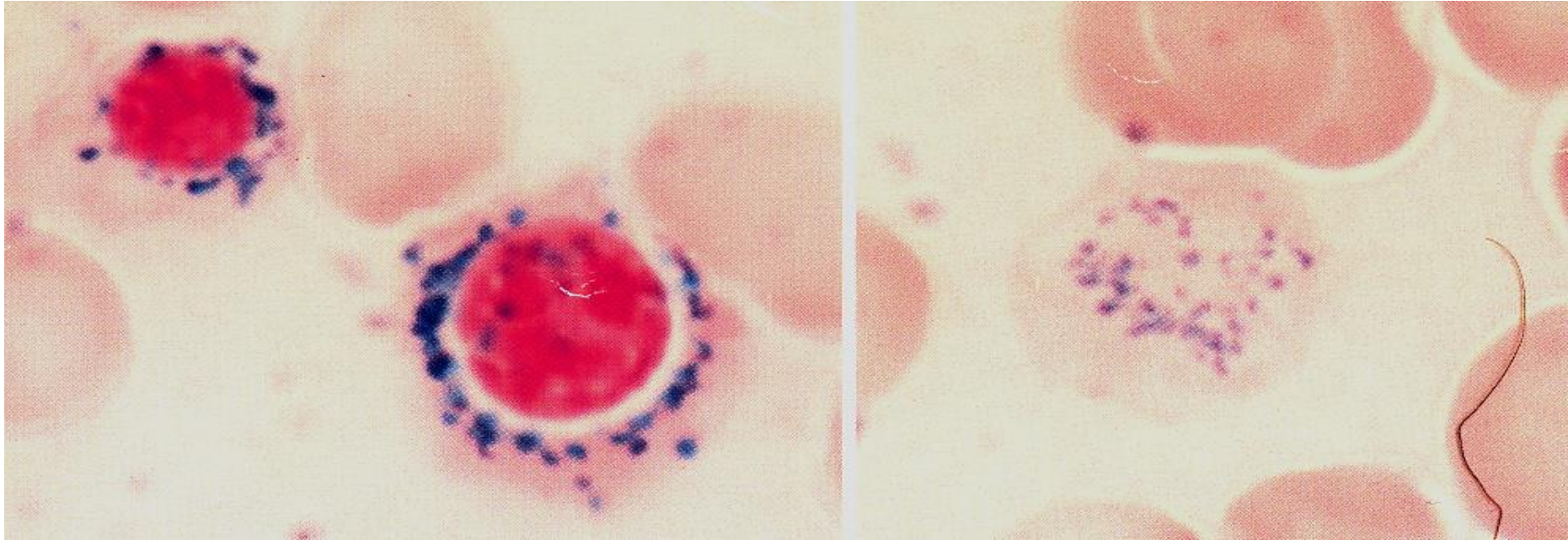
Normochromic anaemia (MCHC is 300–350 g/L of packed red blood cells)

- anaemias of various aetiologies

Hypochromic anaemia (MCHC below 300 g/L of packed red blood cells)

- iron deficiency anaemia
- β -thalassaemia major
- pyridoxin (vitamine B6) responsive anaemia
- anaemia due to plumb (Pb) intoxication

Sideroblastic anaemia



Pathogenetic classification of anaemia

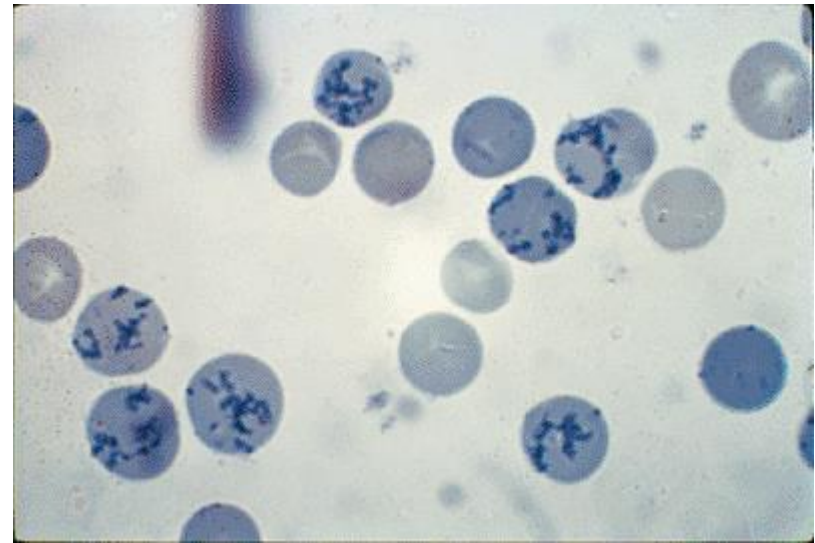
1. Anaemias caused by
**insufficient (low, decreased)
red blood cell production.**

2. Anaemias caused by
increased red blood cell losses
(bleeding or hemolysis).

Anaemias from decreased red blood cell production

- *reticulocytes* are very low in the blood

Reticulocytes grossly indicate activity of erythropoiesis



(1)

Anaemia
from

**decreased
red blood cell production**

Causes of decreased red blood cell production

1. BONE MARROW FAILURE

- aplastic anaemia
- myelodysplastic syndrome (MDS)
- leukaemia
- myelofibrosis
- tumour infiltration of the bone marrow

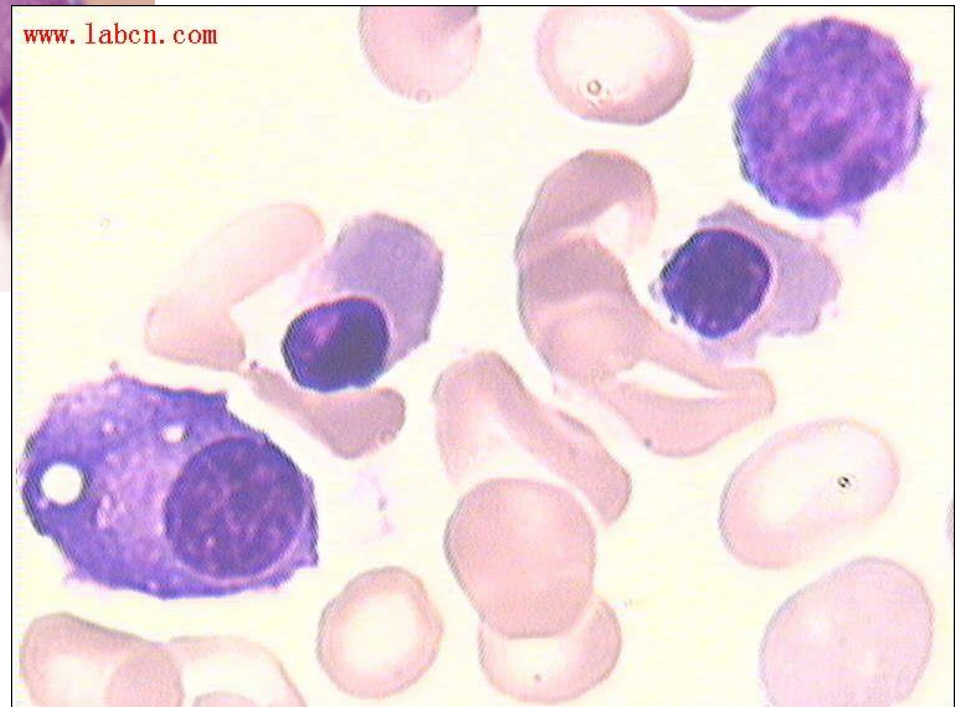
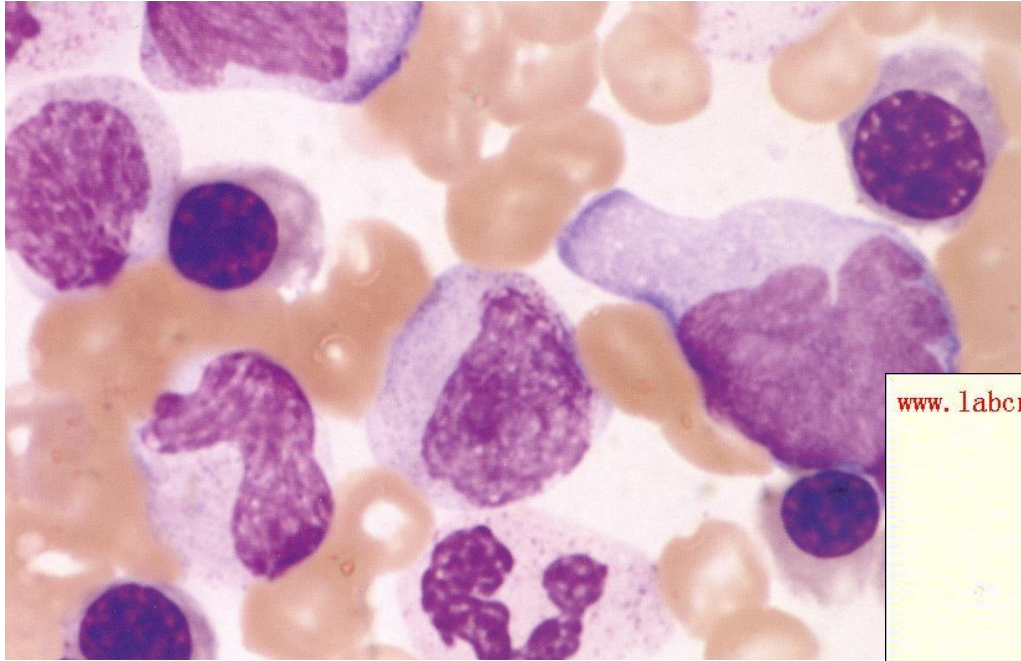
2. DEFICIENCY OF ESSENTIAL FACTORS

- iron deficiency
- folic acid or vitamin B12 deficiency
- severe protein malnutrition

3. LOW ERYTHROPOIETIN

- severe damage of both kidneys
- chronic inflammation
- severe protein malnutrition

NORMAL and APLASTIC BONE MARROW



Anaemia as a part of pancytopenia

- *pancytopenia* means low numbers of all blood cells
- „**myeloid**“ (red blood cells, granulocytes, monocytes, platelets)
eventually also
- „**lymphoid**“ (different types of lymphocytes)

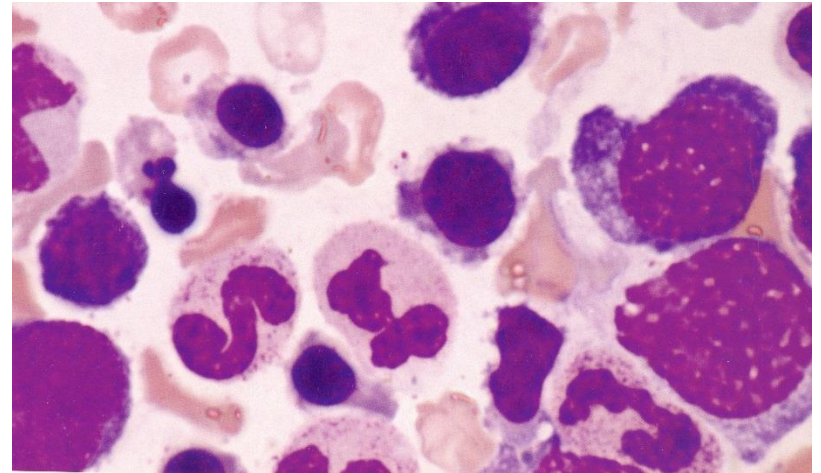
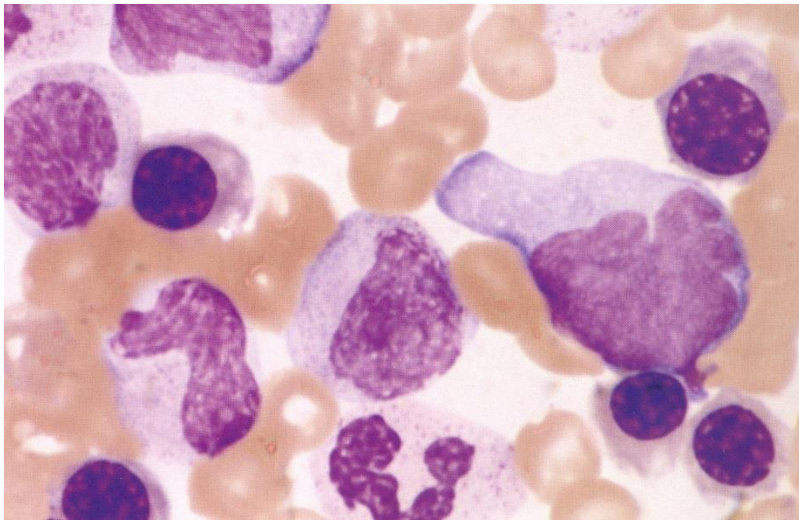
Anaemia from deficiency of essential factors (Fe, vitamin B12, folic acid ...)

- **blood:** mikrocytic or makrocytic anaemia, may be hypochromic
- **bone marrow:** contains enough hematopoietic cells (precursors of blood cells), they look abnormal (large – megaloblasts, changed nucleus-cytoplasmic ratio, little hemoglobin in the cytoplasm ...)

Iron deficiency anaemia (a microcytic hypochromic anaemia)

- Iron (Fe^{2+}) essential for heme synthesis
- erythropoiesis needs about 30 mg of iron every day (gain from food is only 1 to 2 mg a day). Iron is intensively recycled.

IRON DEFICIENCY - BONE MARROW



Vitamin B₁₂ and folic acid deficiency anaemia

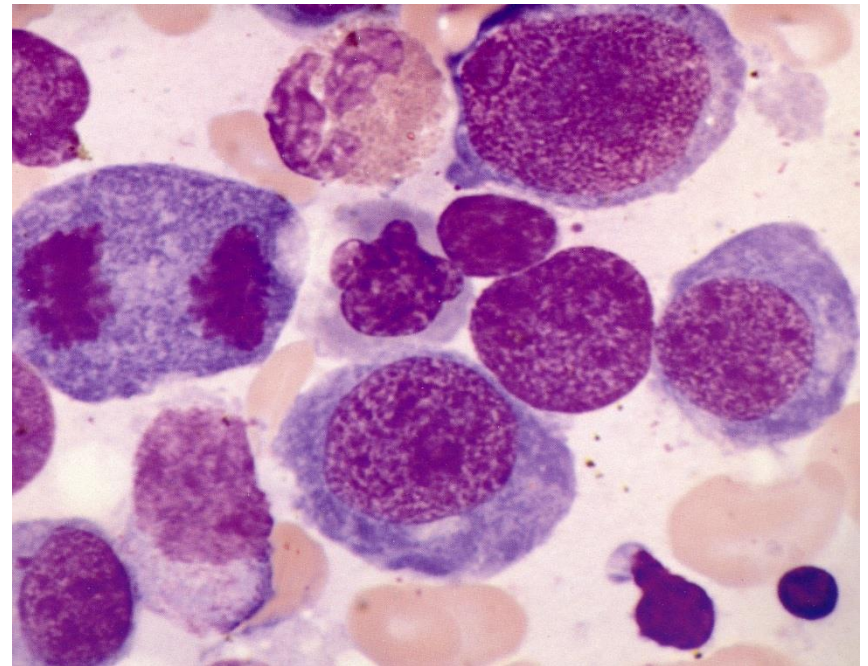
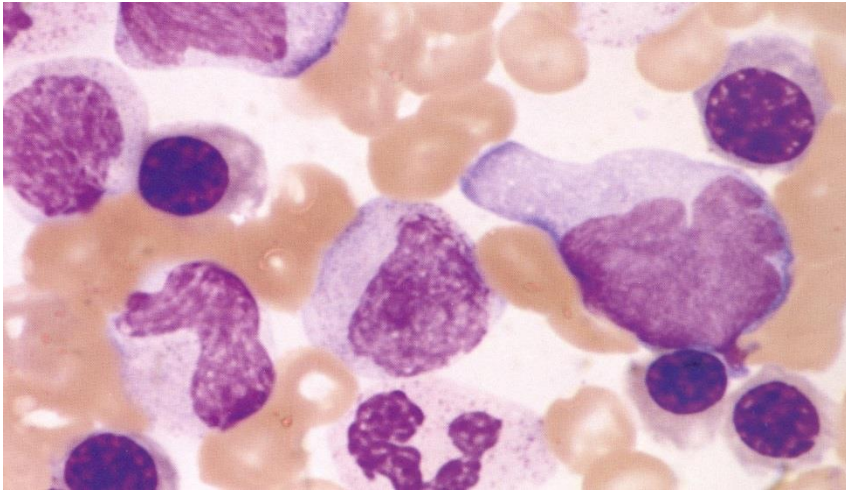
- folic acid and vitamin B12 are needed for synthesis desoxynucleotides
- cells in the bone marrow divide intensively and this is hampered by deficiency of the factors
- vitamin B12 deficiency, but not that of folic acid, may have also a neural symptoms manifested by senitivity and motoric disorders

Pernicious anaemia

- there is a deficit in vitamin B12 absorption due to lack of the intrinsic factor produced normally by gastric mucosa
- this used to be a deadly disease (anaemia)

Megaloblastic (and macrocytic) anaemia from vitamin B12 or folic acid deficiencies

*- bone marrow is not aplastic but there are few
reticulocytes in the blood*



(2)

Anaemia
from

increased red blood cell losses

- chronic or acute **bleeding** (Fe losses!)

- **haemolysis**

(red blood cells „live“ less than 120 days)

... **reticulocytes** counts are often elevated

- intravascular haemolysis
- extravascular haemolysis

Acute and chronic bleeding

- a normocytic anaemia
- bone marrow increases production of red blood cells (reticulocytes)
- 1 mL blood contains 0.6 mg iron (a daily gain of iron from food is 1 to 2 mg)
- chronic bleeding often leads to iron deficiency and this limits capacity of the bone marrow to replace lost red blood cells

Hemolytic anaemias

- **corpuscular** (mostly hereditary)
- **extracorpuscular** (mostly acquired)

CORPUSCULAR HAEMOLYTIC ANAEMIAS

inborn, hereditary mostly (gene defects)

DEFECTS OF THE RED BLOOD CELL MEMBRANE

- hereditary spherocytosis, elliptocytosis
- paroxysmal nocturnal haemoglobinuria (acquired)

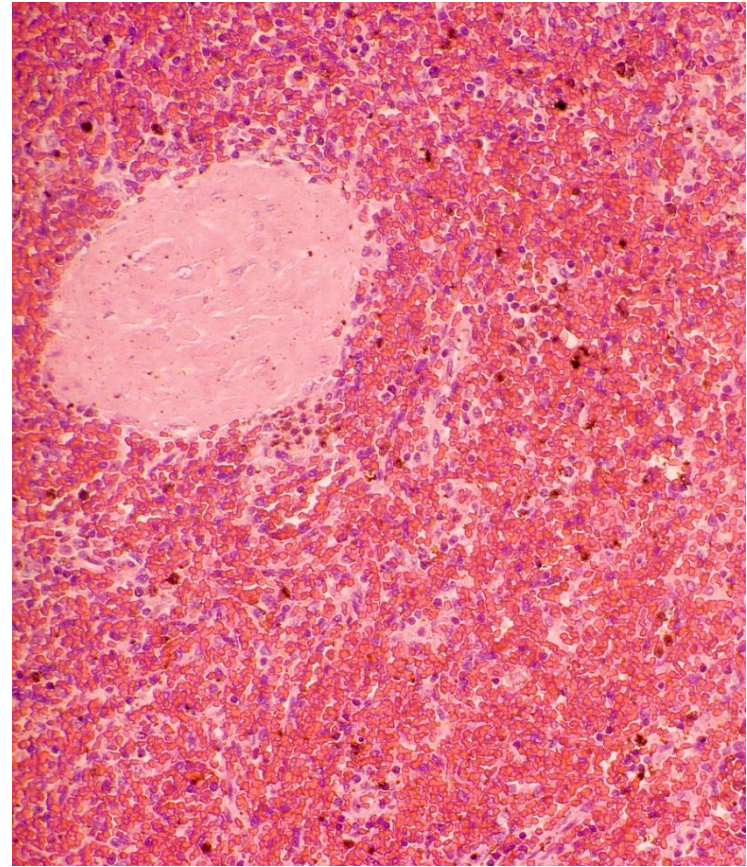
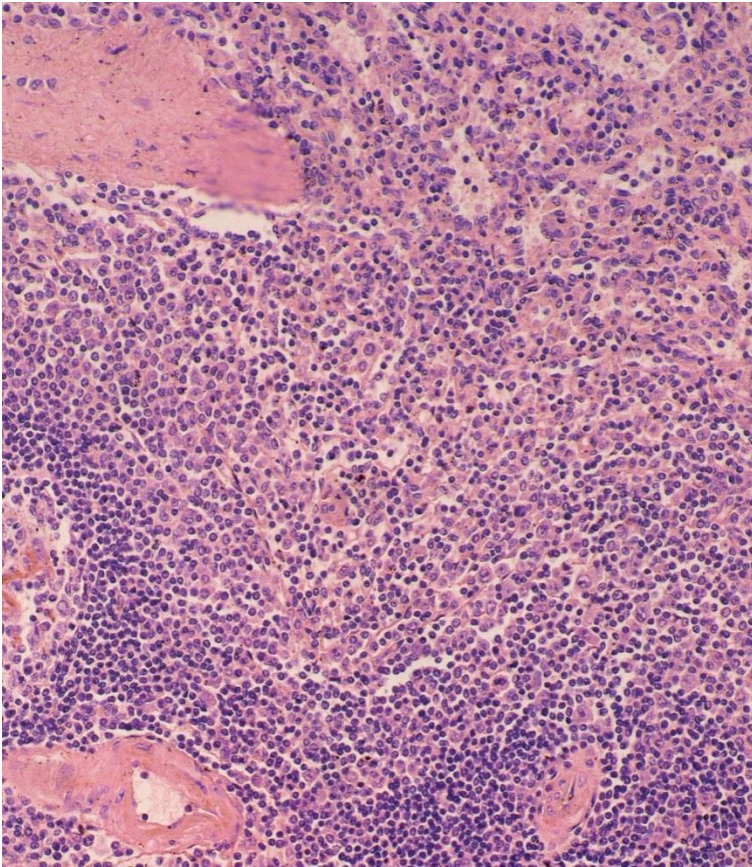
DEFECTS OF ENERGY METABOLISM

- defects of enzymes of the pentose cycle (glucose-6-phosphate-dehydrogenase, glutathion-reductase)
- defects of enzymes of the Embden-Mayerhof cycle (hexokinase, 2,3-difosfoglycerate-mutase, pyruvátkinase)

DEFECTS OF HAEMOGLOBIN SYNTHESIS OR HAEMOGLOBINOPATHIES

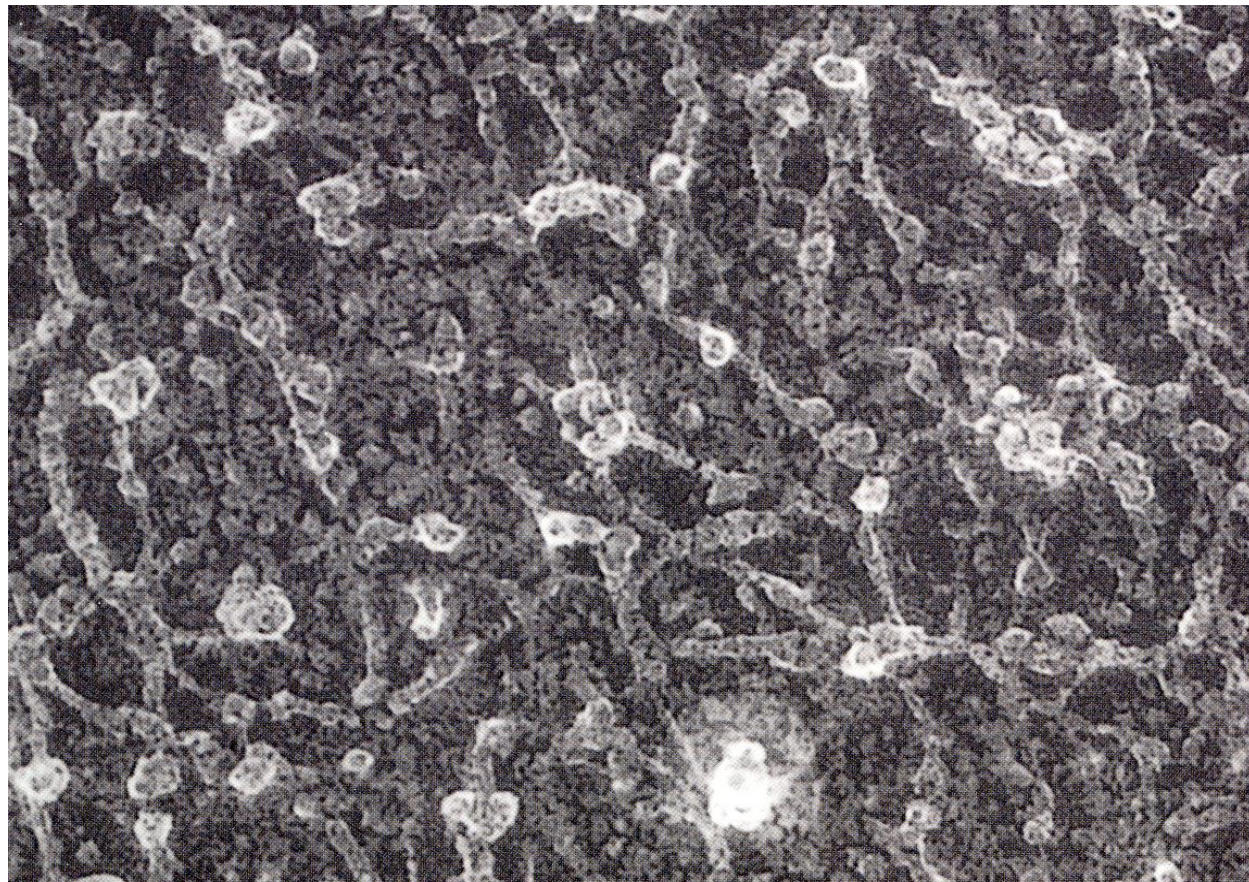
- thalasaemias
- some haemoglobinopathies (e.g. methaemoglobinaemia ...)

Hereditary spherocytosis, epiptocytosis – spleen histology (*splenomegaly*)



HEREDITARY ELIPTOCYTOSIS

A CELL MEMBRANE DEFECT (*spectrin*
or other proteins)



Talassaemia, sickle cell anaemia

- **Talassaemia (alfa, beta – major, minor)**
- production of globin chains is not quantitatively matched
- clinica (phenotypic) manifestation differs
- **Sickle cell anaemia (HbS)**
- the most frequent *hemoglobinopathy*
- ischemic episodes, pain, CNS and other organs damage

Thalassaemias

	Hb A (%)	Hb F/A2 %	Jiný Hb	Symptoms
normal Hb (a healthy person)	90–98	2–3/2–3		none
talasaemia α (4 alely pro α -řetězec hemoglobinu)				
- α / α α	90–98	2–3/2–3		žádné
- - / α α (- α / - α)	90–98	2–3/2–3		žádné, hypochromní erytrocyty/mikrocyty bez anémie
- - / - α^*	60–70	2–5/2–3	30–40 H	anémie (100–70 g Hb/l)
- - / - -	0	0	H/Bartův	hydrops fetalis
talassaemia β (2 alely pro β -řetězec)				
β^0/β nebo β^+/β^{**}	90–95	2–10/5–7		žádné, mírná anémie
β^+/β^{***}	15–75	20–80/2–5		anémie (90–70 g Hb/l), hepato-, splenomegalie
β^0/β^{****}	0	95–98/2–5		těžká anémie, poruchy vývoje, patologické fraktury kostí, velká potřeba transfúzí
hemoglobin Lepore („L“)				
(fúze genů pro β - a δ -řetězce)				
– heterozygot	70–80	5–20/1–2	5–15 „L“	mírná anémie
– homozygot	0	70–90/0	10–30 „L“	těžká anémie a jako u thalassaemia major

* označovaná též jako „nemoc hemoglobinu H“

** thalassaemia minor

*** thalassaemia intermedia

**** thalassaemia major

Talassaemia β

	Hb A (%)	Hb F/A ₂	Manifestation
β^0/β nebo β^+/β^{**} mírná anémie	90–95	2–10/5–7	none, a mild anaemia
β^+/β^{****} Hb/I),	15–75	20–80/2–5	anaemia (90–70 g hepatosplenomegaly
β^0/β^0****	0	95–98/2–5	severe anaemia, transfusions, developmental anomalies

** thalassaemia minor

*** thalassaemia intermedia

**** *thalassaemia major*

EXTRACORPUSCULAR HAEMOLYTIC ANAEMIAS (mostly acquired)

ANTIBODIES AGAINST RED BLOOD CELLS

- autoantibodies
- anti-Rh antibodies (e.g. fetal erythroblastosis)
- isoagglutinins

DAMAGE FROM PHYSICAL OR TOXIC FACTORS

- mechanical damage (DIC, heart valve prosthesis, march haemoglobinuria)
- extensive burns
- bacterial toxins
- parasitic infection (malaria)
- severe plasma hypotonia

Etiologic (casual) classification of anaemias

Causes of a decreased production of red blood cells or increased red blood cell losses are numerous.

Their identification allows for a rational, etiologically based (causative) therapy, if possible.

Summary of the most important items of the lecture.

- Anaemia may be symptom, sign or disease depending on level of the diagnostic procedure
- Anemia results from losses of red blood cells exceeding their production
- A new balance between losses and production of red blood cells may result in „stable“ – chronic anaemia
- Identification of the cause of anaemia allows **casual therapy**
- Transfusions of red blood cells are only a **symptomatic therapy**