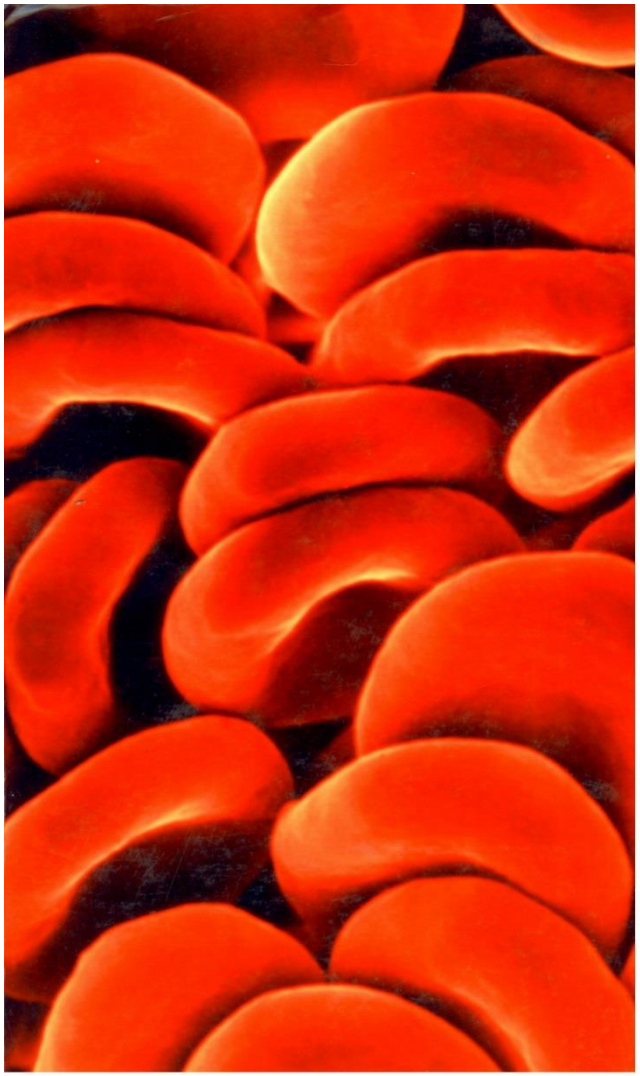
ANAEMIA 1



Emanuel Nečas
necas@cesnet.cz

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?

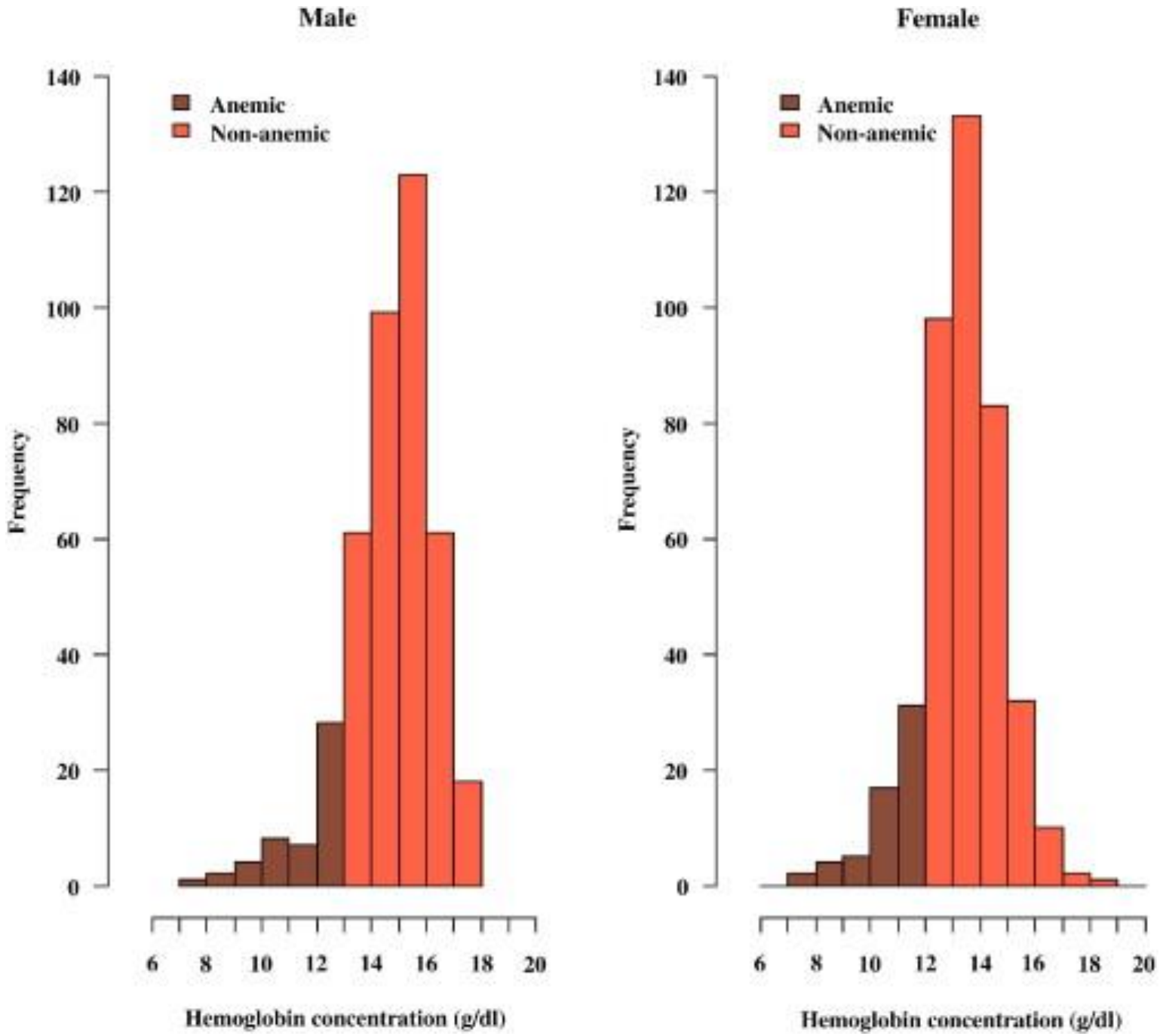
The anaemia is pathological condition characterized by **specific signs** and **symptoms.**

Symptoms of anaemia

- fatigue
- shortness of breath
- pale skin and muccosae
- 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
Anemic
Non-anemic
Frequency
0
20
40
60
80
100
120
140
6
8
10
12
14
16
18
20
Hemoglobin concentration (g/dl)

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.

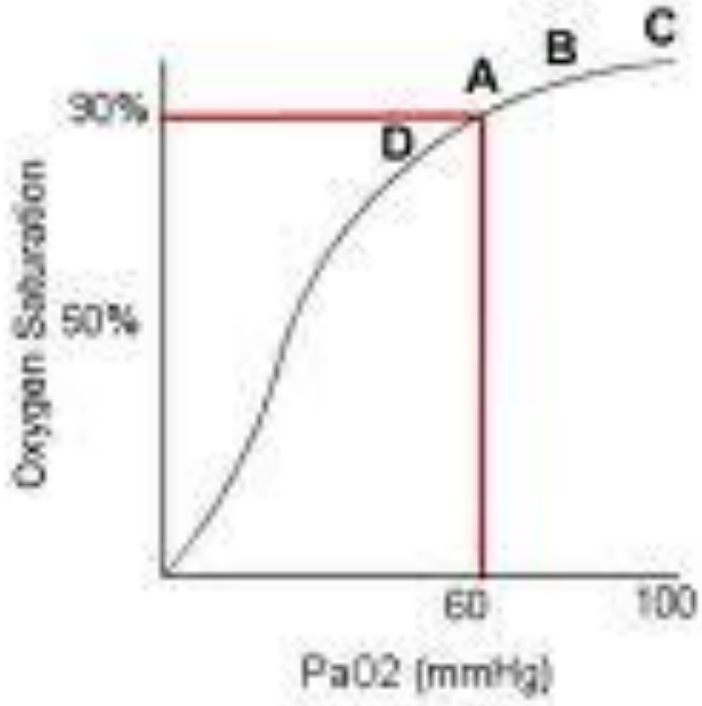
Adaptive, compensatory mechanisms in acute and chronic anaemia

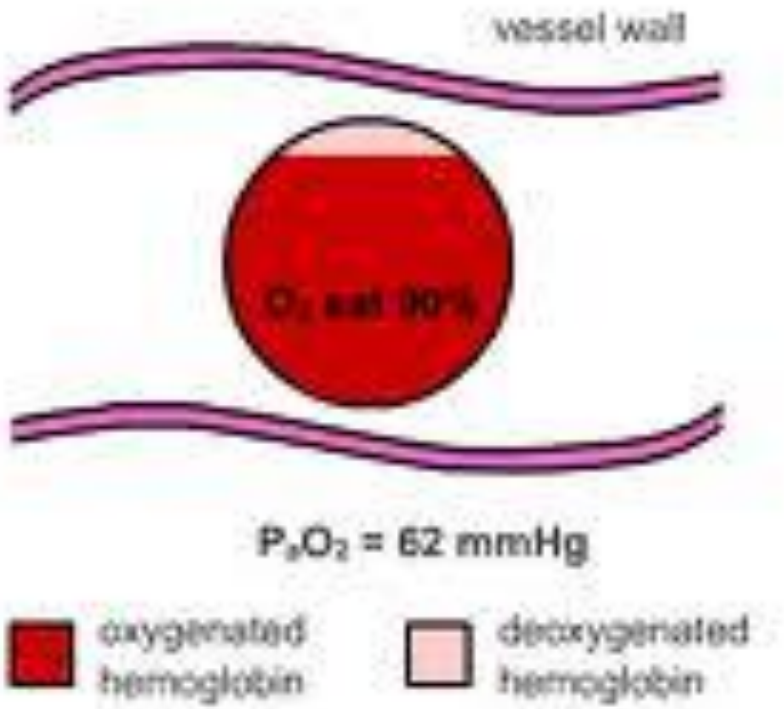
Acute anaemia:

- 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)


A
B
C
D
90%
50%
Oxygen Saturation
60
100
PaO2 (mmHg)


vessel wall
P_aO_2 = 62 mmHg
oxygenated hemoglobin
deoxygenated hemoglobin

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_disaease

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 immflamatory 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?

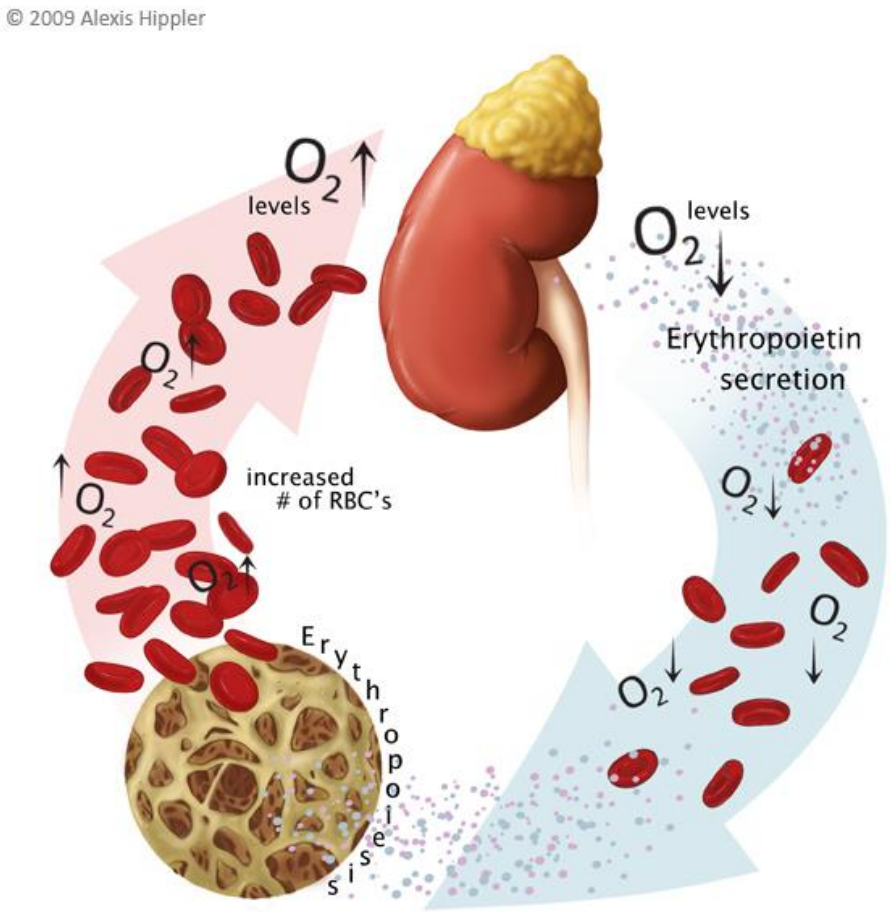
Losses and production of red blood cells are normally well balanced ...

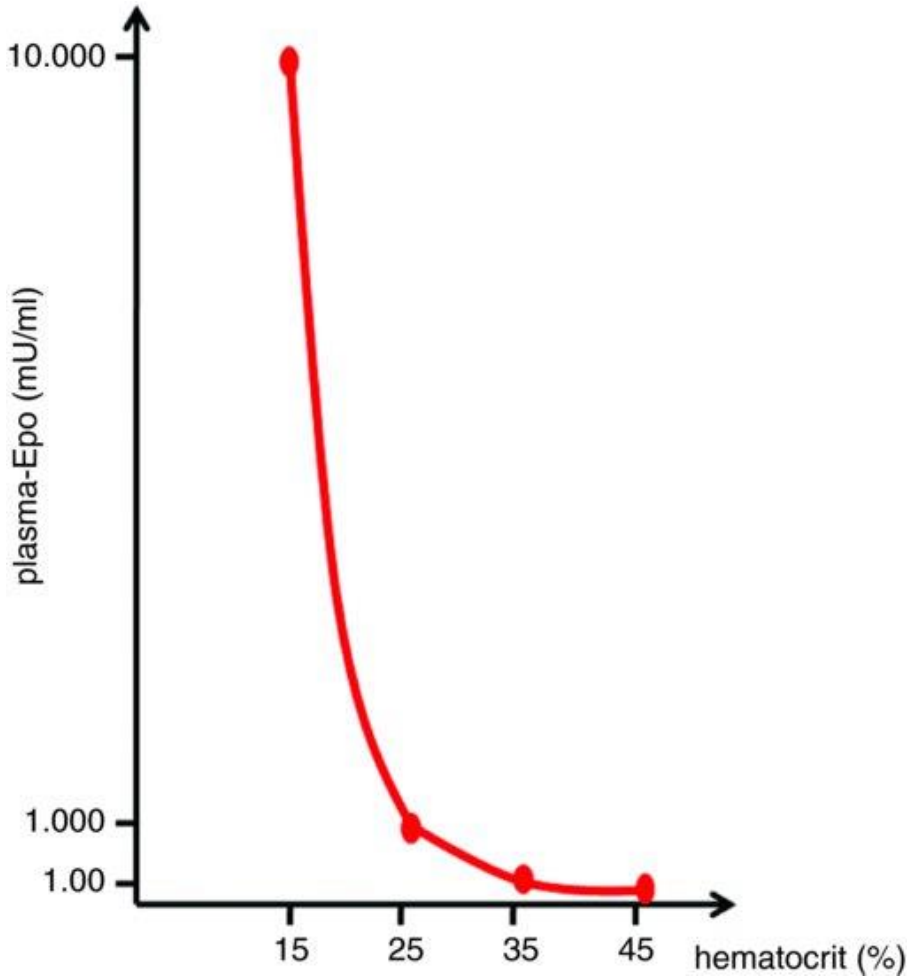
Anaemia results from

the losses of red blood cells outweighing

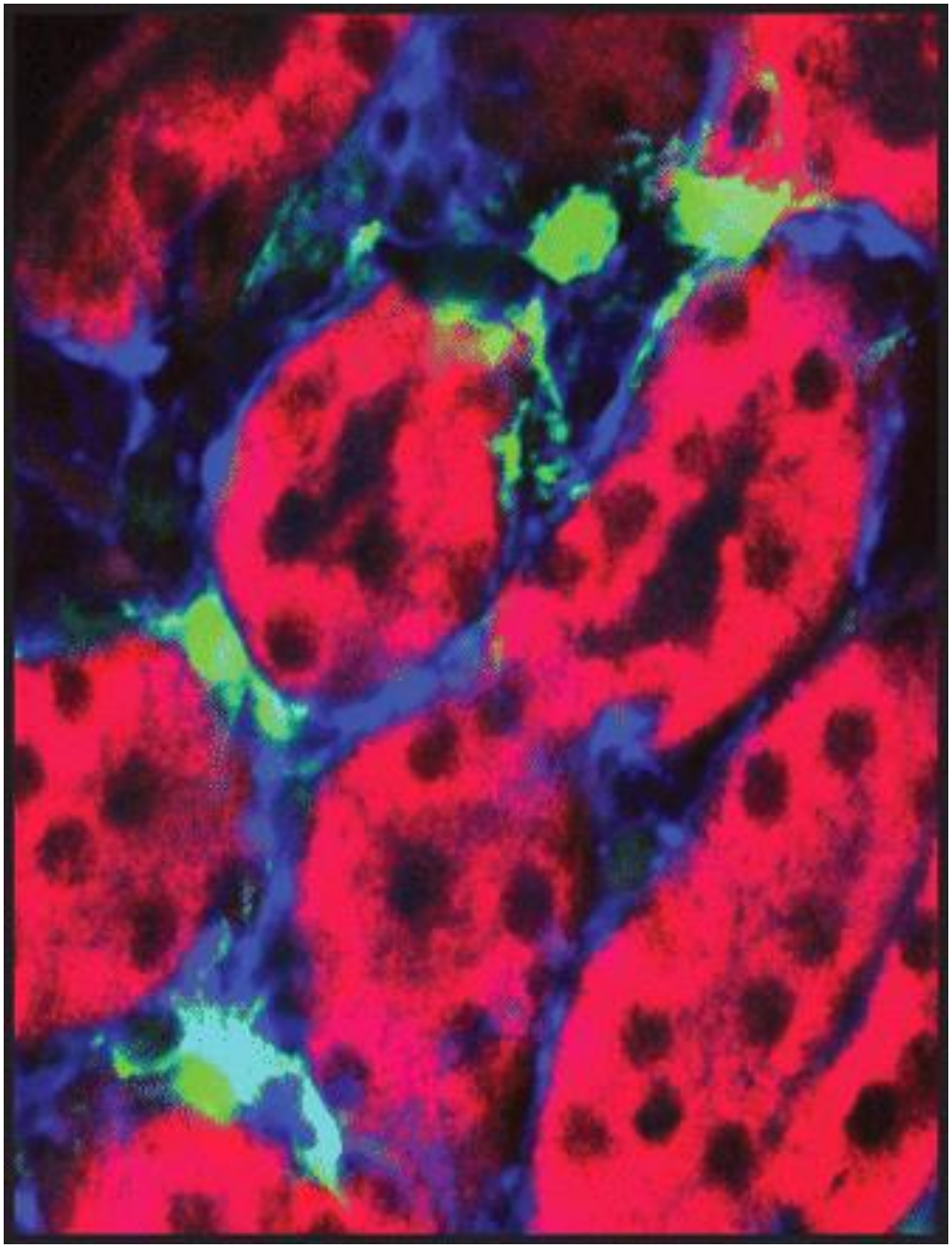
their production rate.

Control of the Red Blood Cell Production

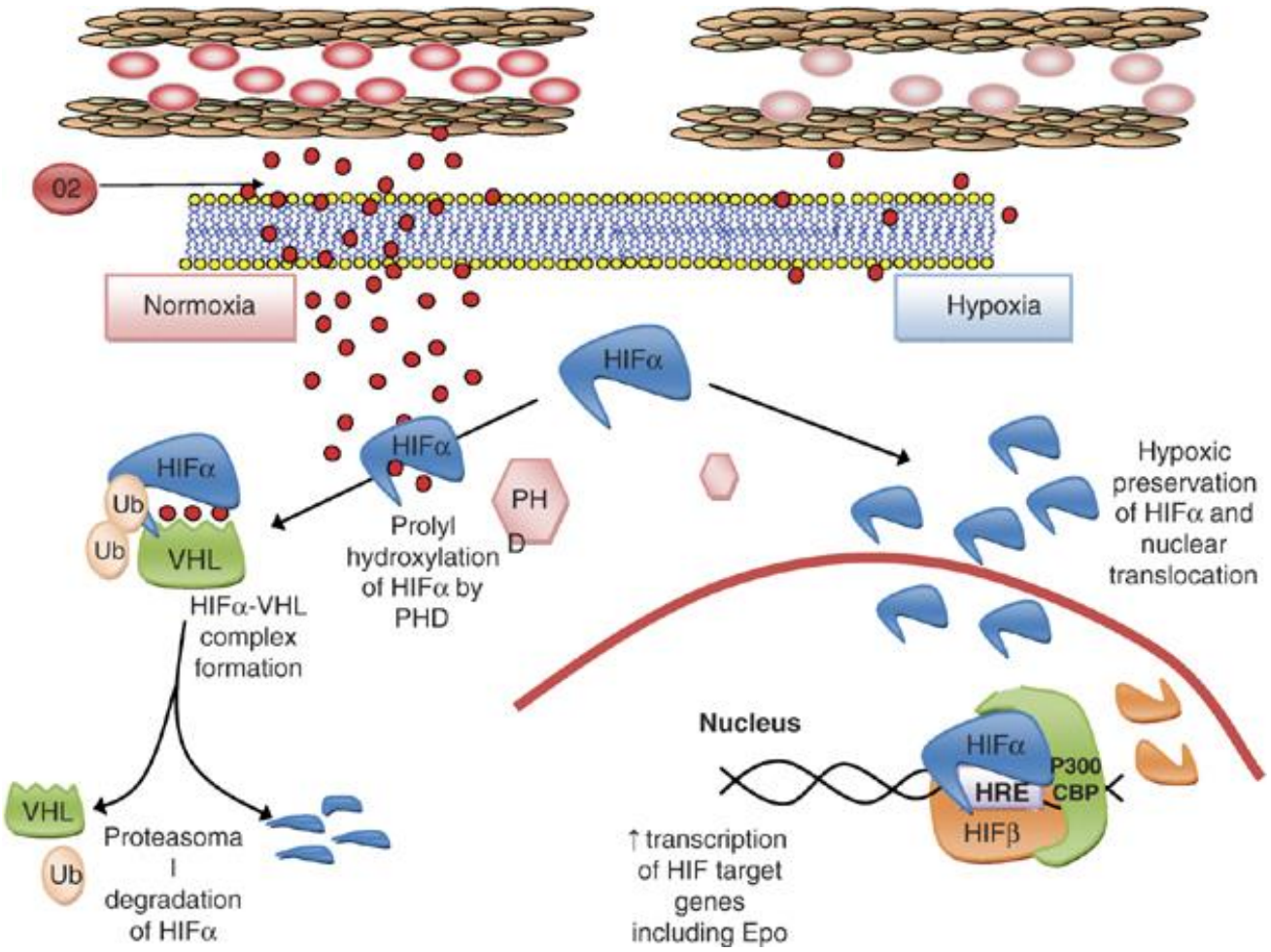




Cells producing erythropoietin in the kidney according to oxygen availability



Oxygen sensing mechanism governing erythropoietin production



COMPUTER SIMULATION

Aneamia may improve, may worsen, may be stable.

- **A new equillibrium**, 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

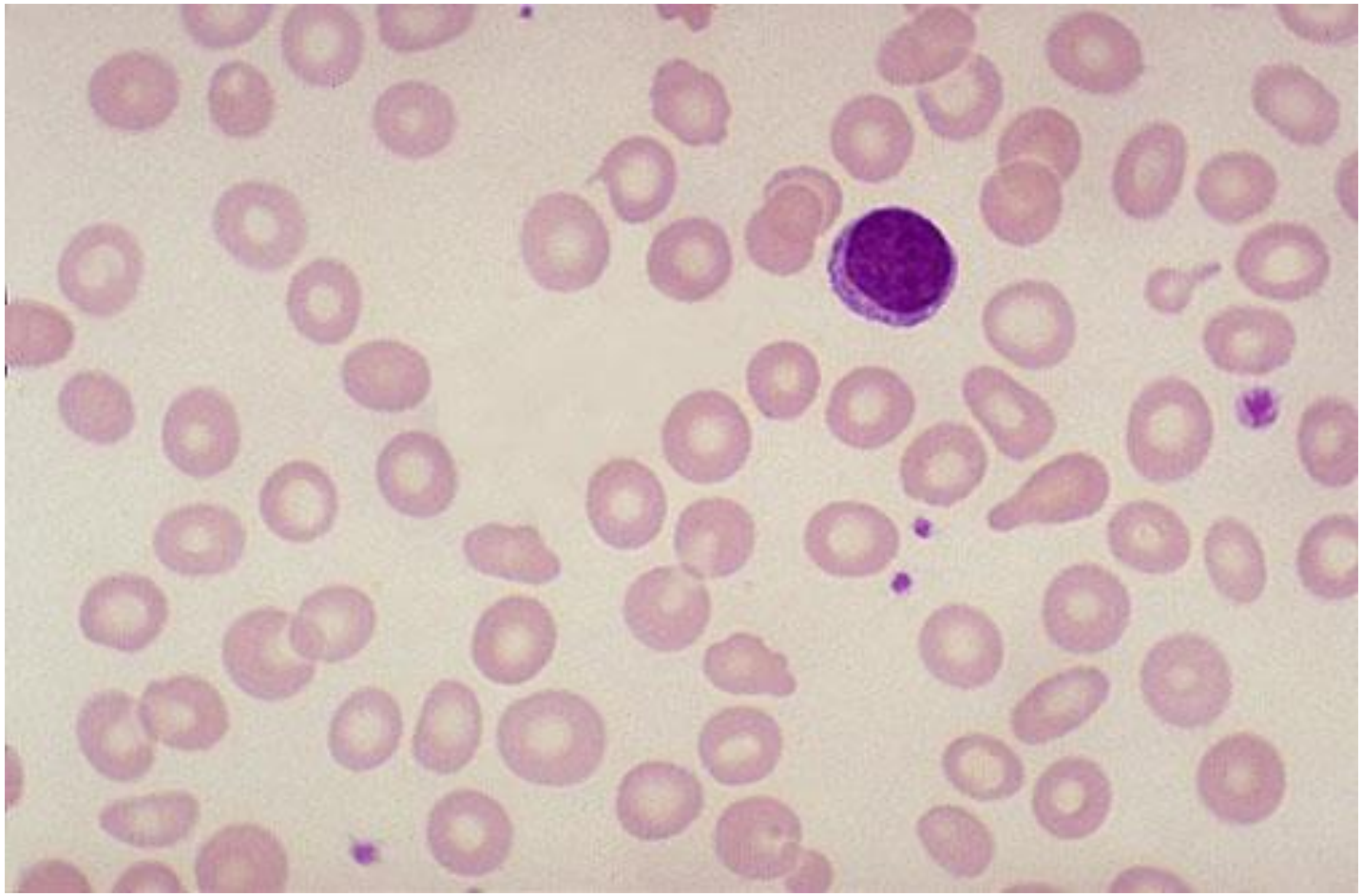
Makrocytic anaemia (MCV higher than 95 fL)

- megaloblastic anaemia (folic acid or vitamin B_{12} deficit
- anaemia accompanying hypothyreosis, high number of reticulocytes in the blood

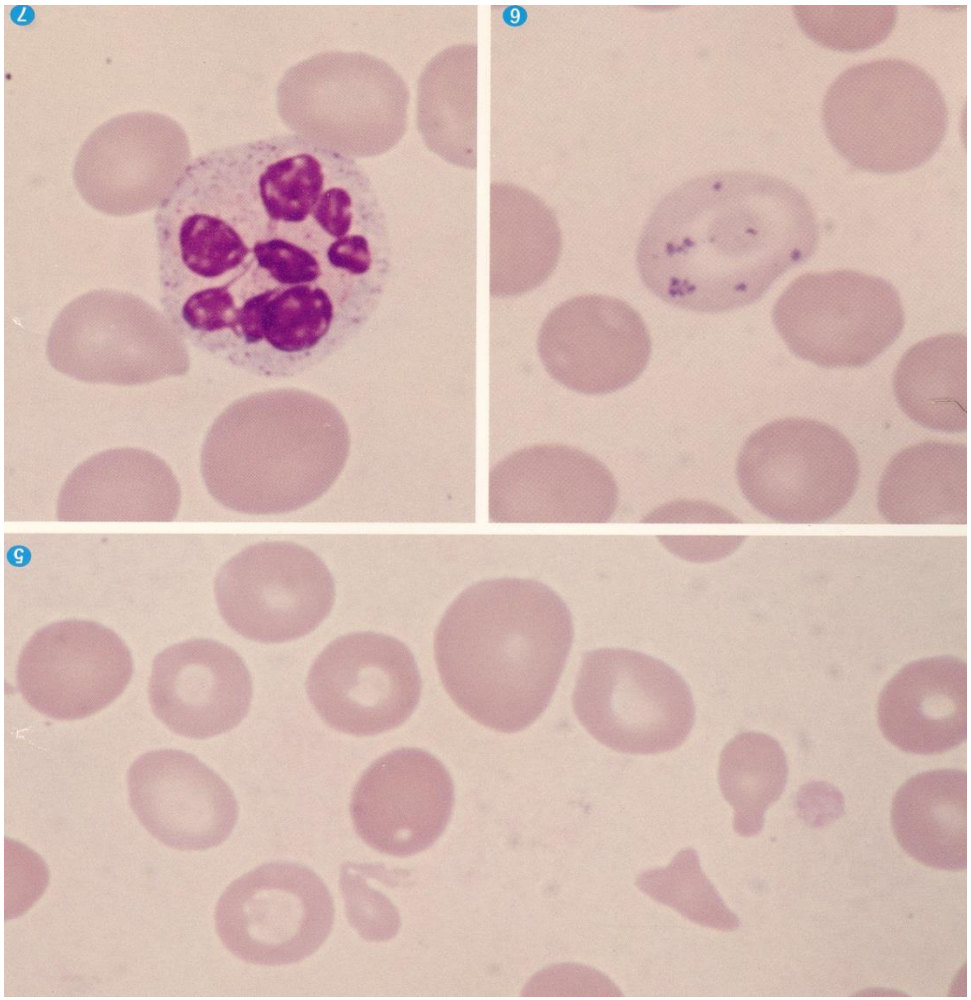
Mikrocytic anaemia (MCV less than 80 fL)

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

Mikrocytic (MCV < 80 fL) hypochromic anaemia

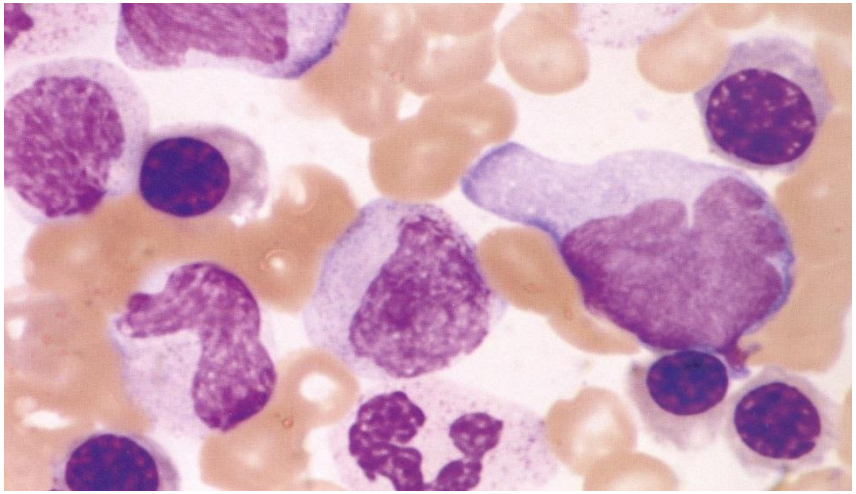


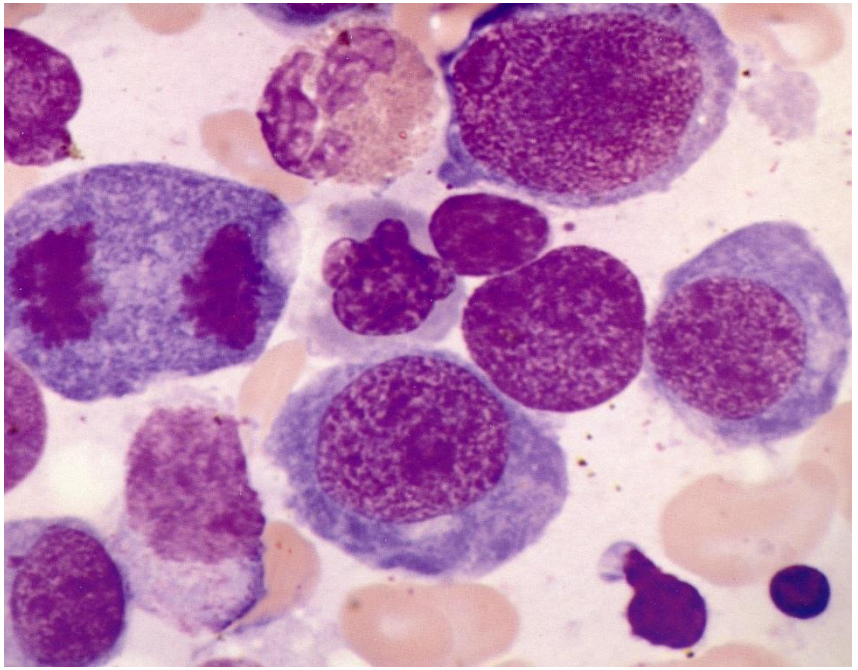
MACROCYTIC ANAEMIA (MCV > 95 fL)
anisocytosis, poikilocytosis



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

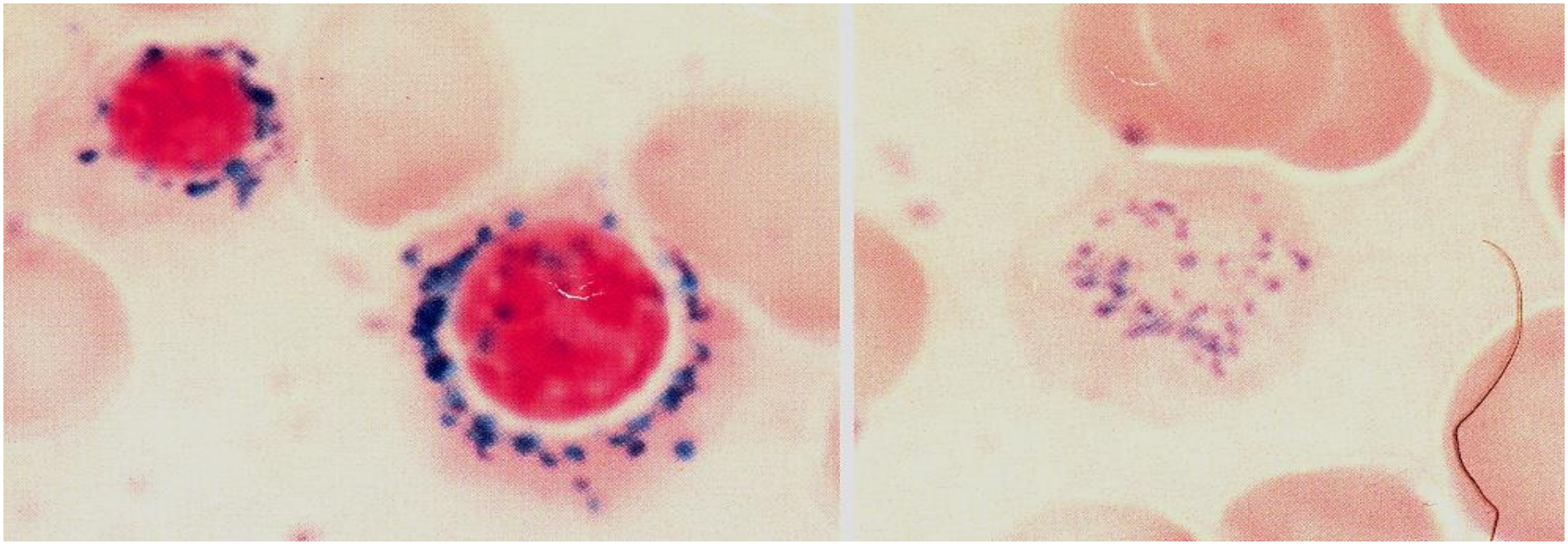
Normochromic anaemia (MCHC is 300–350 g/L of packed red blood cells)

- **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

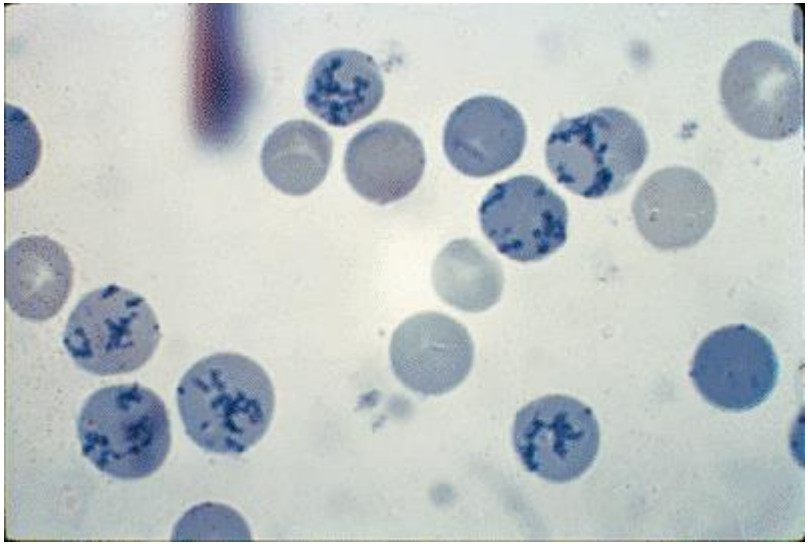
1. Anaemias caused by
insufficient (low, decreased)
red blood cell production.

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 inflitration of the bone mrrow

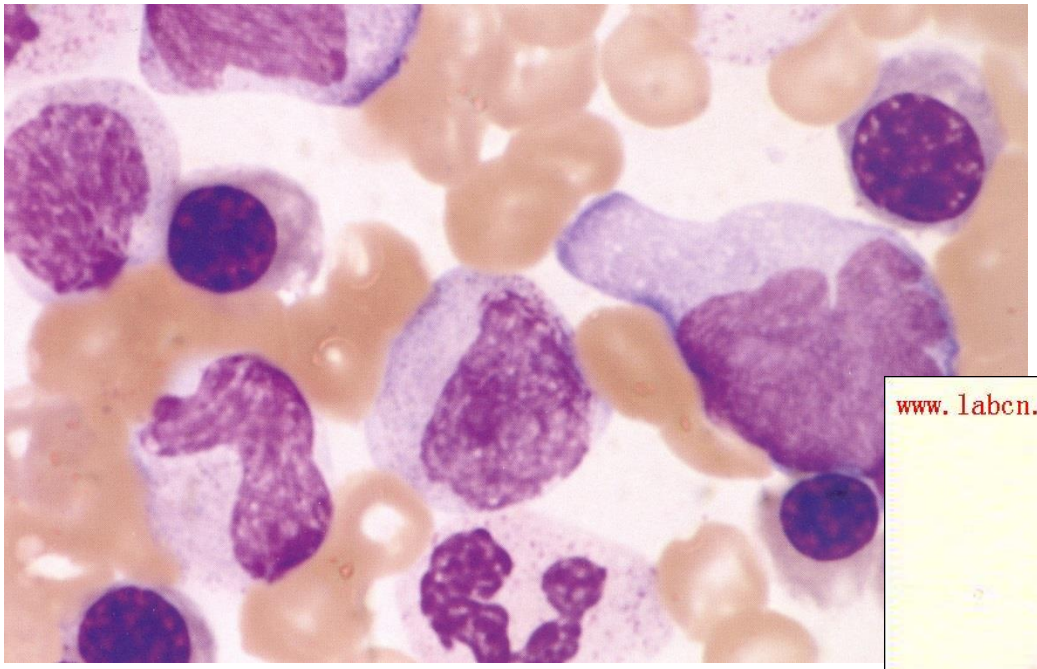
2. DEFICIENCY OF ESSENTIAL FACTORS

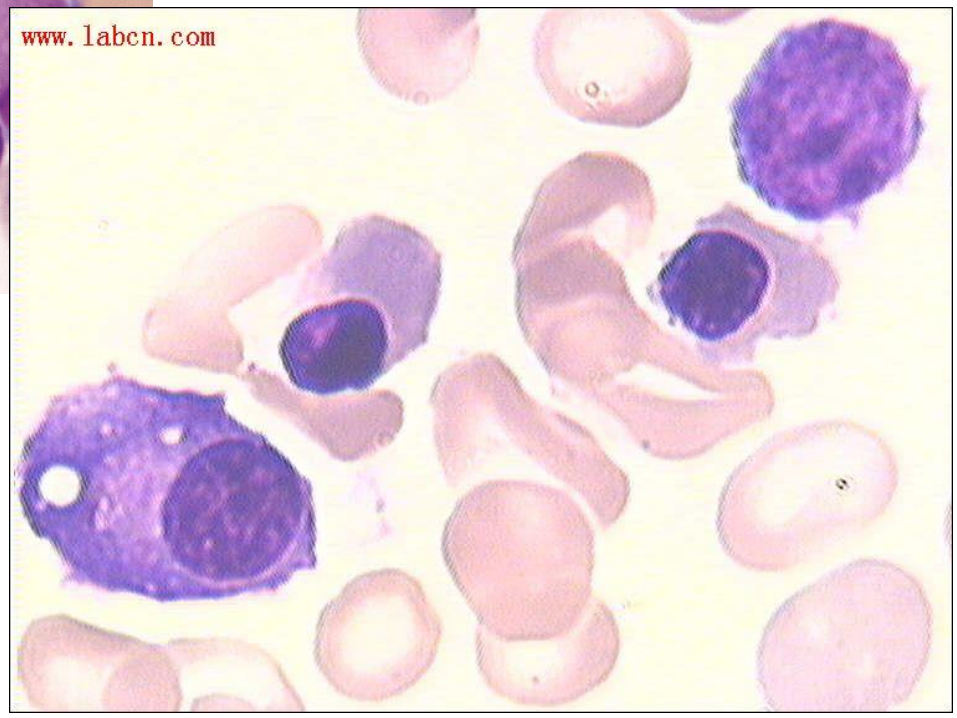
- iron deficiency
- folic acid or vitamine B12 deficiency
- severe protein malnutrition

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

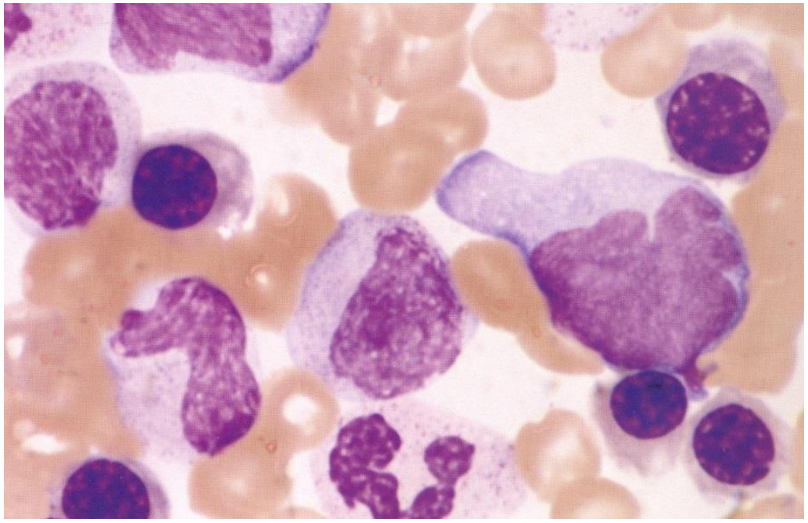
- **bone marrow:** contains enough hematopoietic cells (precursors of blood cells), they look abnormal (large – megaloblasts, changed nucleus-cytoplasmic ratio, little hemoglobin in the cytoplasm ...

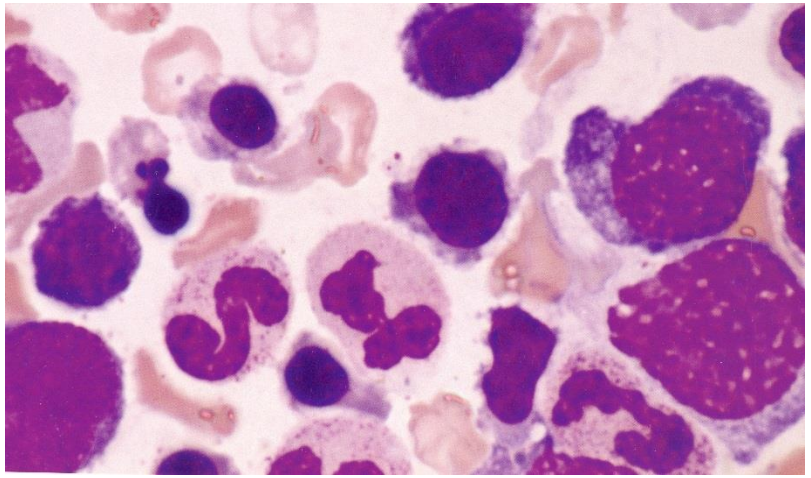
Iron deficiency anaemia
(a microcytic hypochromic anaemia)

- 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 intensivelly recycled.

IRON DEFICIENCY - BONE MARROW





Vitamin B_{12} and folic acid deficiency anaemia

- folic acid and vitamin B12 are needed for synthesis desoxynucleotides
- cells in the bone marrow divide intensivelly 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

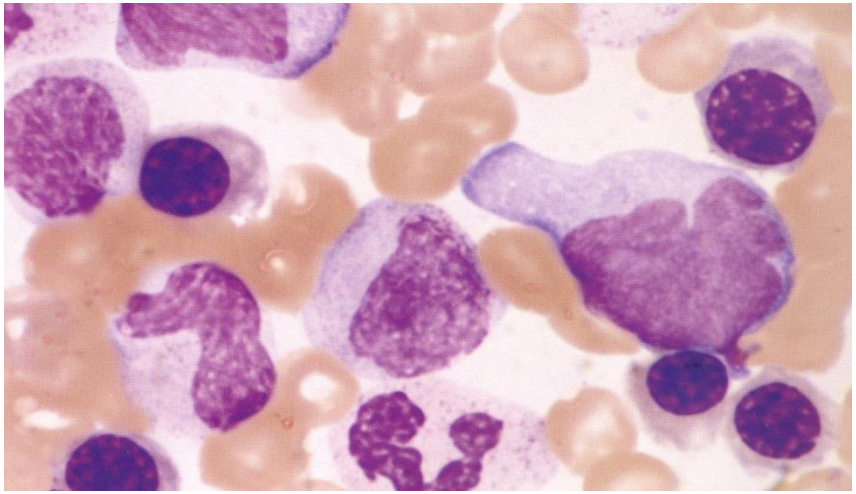
Pernicious anaemia

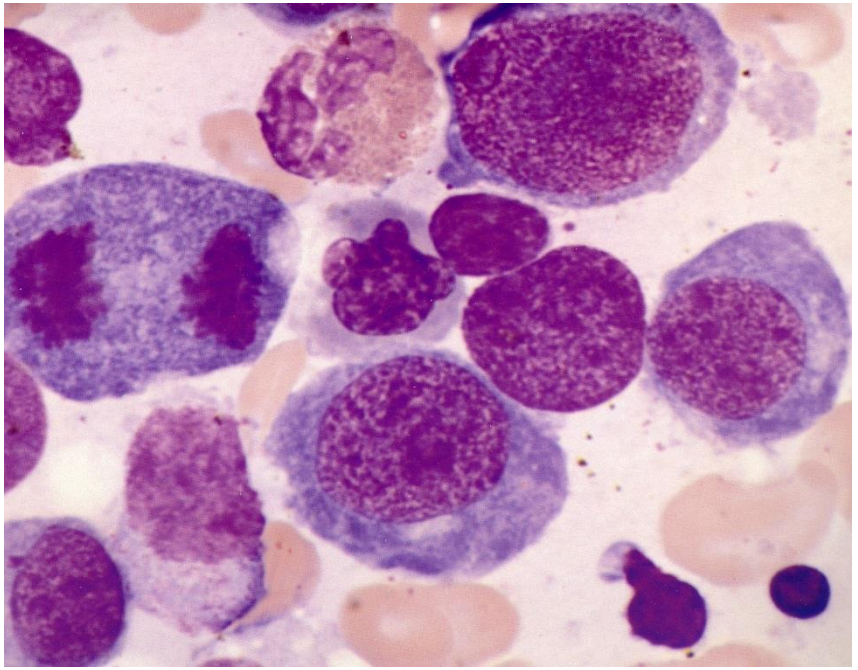
- there is a deficit in vitamin B12 absorption due to lack of the intrinsic factor produced normally by gastric mucosa

- 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, epitocytosis
- paroxysmal nocturnal haemoglobinuria (acquired)

DEFECTS OF ENERGY METABOLISM

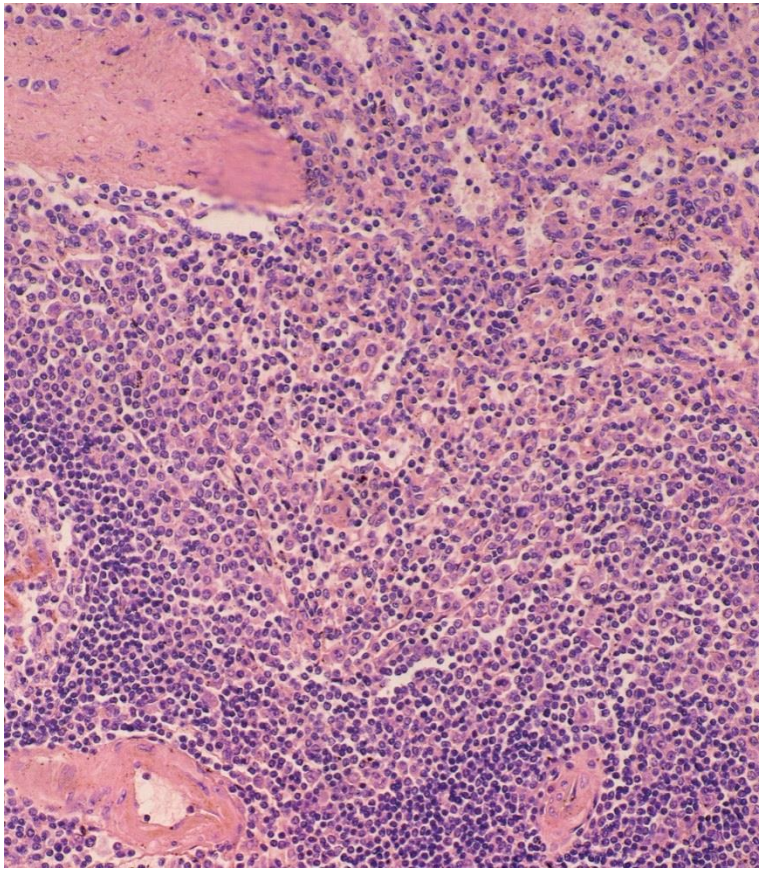
- defects of enzymes of the pentose cycle (glucose-6-phosphate-dehydrogenase, glutathion-reductase)

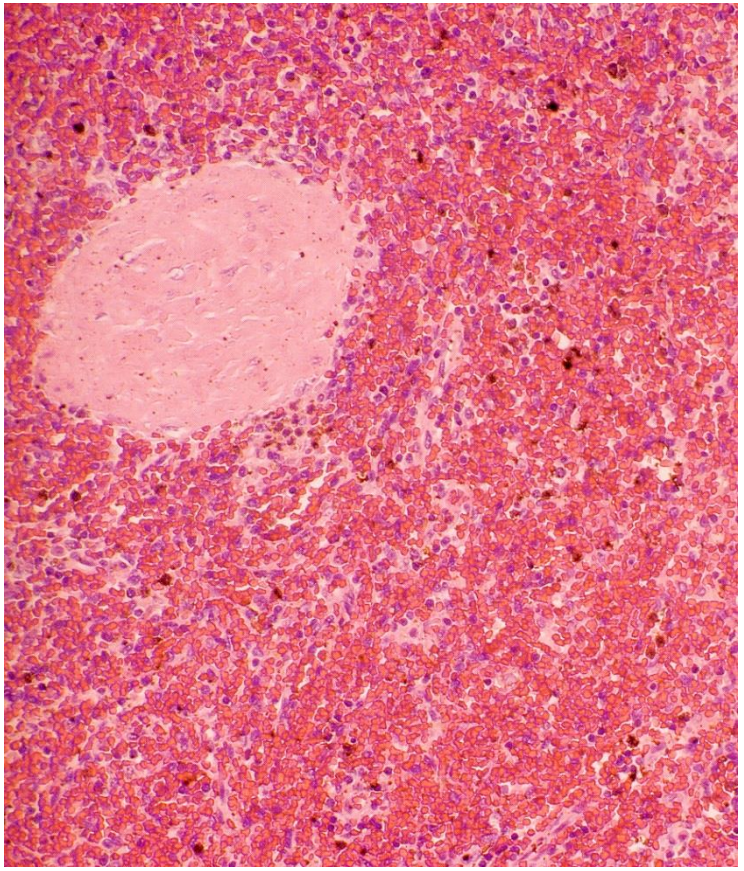
- defects of enzymes of the Embden-Mayerhof cycle (hexokinase, 2,3-difosfoglycerate-mutase, pyruvátkinase)

DEFECTS OF HAEMOGLOBIN SYNTHESIS OR HAEMOGLOBINOPATHIES

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

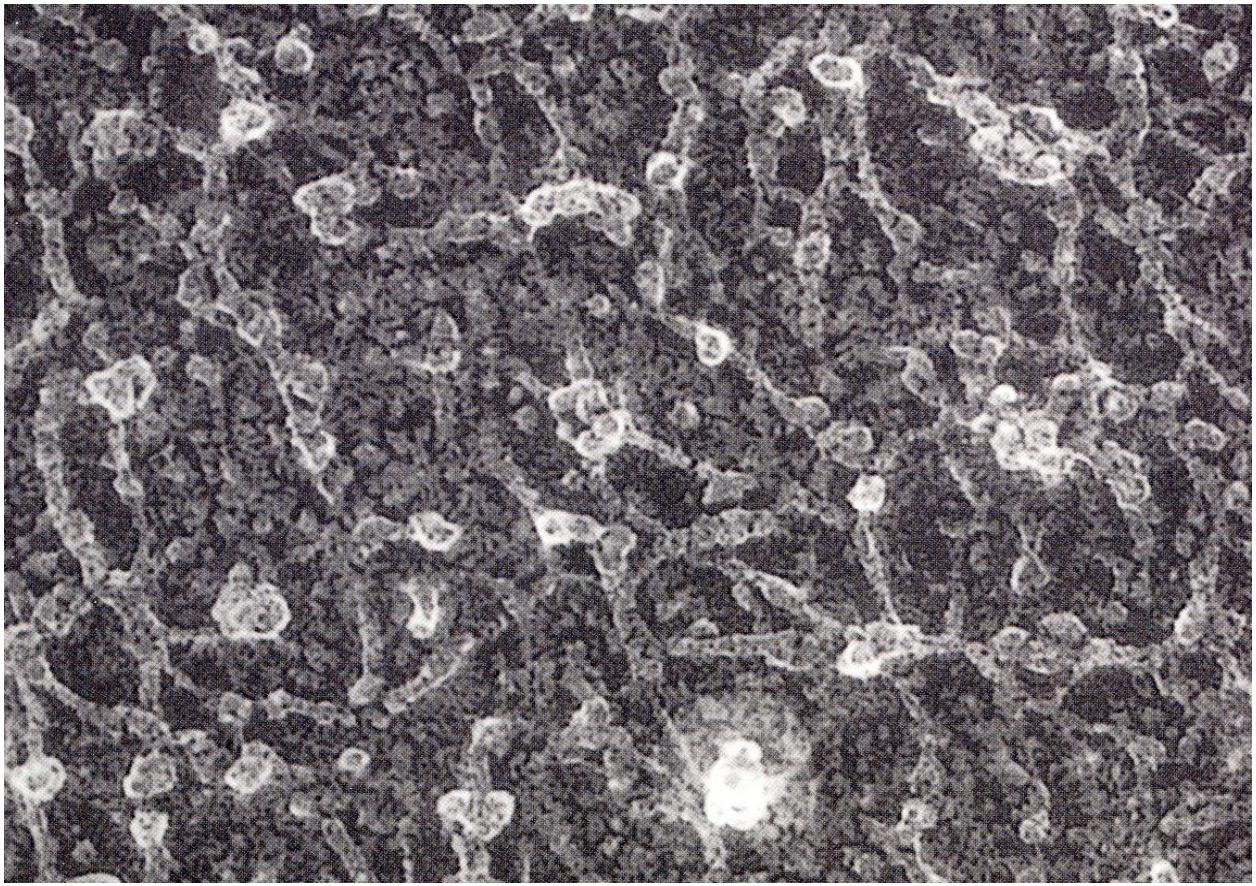
Hereditary spherocytosis, epiptocytosis – spleen histology (***splenomegaly)***





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****	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/l),	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)**
- **isoaglutinins**

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, etiologicaly 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 precedure
- 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