Physiology of the blood

- General characteristics of the blood
- Haematocrit
- Viscosity
- Role of the blood
- Blood volume

The role of blood

- Transport (gases, nutrients, waste products, hormones and vitamins, heat)
- *To keep milieu interieur* (chemical substances, pH, temperature)
- Decreasing loss of blood (bleeding and clotting time)
- Immune functions
- Communication (hormones)
Variations in blood volume

- Age
- Physical Position (venous stagnation)
- Physical work
- Temperature
- Body weight
- Hypoxia
- Gravidity
- Dry-out
- Bleeding
- Shock

Sedimentation rate of RBCs (by Westergren)

In the blood RBCs sediment by the gravity(if the blood is still and some anticoagulant is applied).

Normal value: men: 2-6 mm/h, women: 8-10 mm/h

Accelerated sedimentation:
  - RBC precipitation
  - increased level of globulin or fibrinogen in the plasma
<table>
<thead>
<tr>
<th>Type</th>
<th>Percentage of leukocytes</th>
<th>Mean count (in 1 µl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leukocytes</td>
<td></td>
<td>4000-10 000</td>
</tr>
<tr>
<td>Granulocyte</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neutrophil</td>
<td>60-80</td>
<td></td>
</tr>
<tr>
<td>Eosinophil</td>
<td>1-5</td>
<td></td>
</tr>
<tr>
<td>Basophil</td>
<td>0-1</td>
<td></td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>20-30</td>
<td></td>
</tr>
<tr>
<td>Monocyte</td>
<td>2-6</td>
<td></td>
</tr>
<tr>
<td>Red blood cells (Erythrocyte)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>woman:</td>
<td>4,8 million</td>
<td></td>
</tr>
<tr>
<td>man:</td>
<td>5,4 million</td>
<td></td>
</tr>
<tr>
<td>Platelets (thrombocyte)</td>
<td></td>
<td>150 000 - 300 000</td>
</tr>
</tbody>
</table>
Life span of the cells:
Some hours: neutrophil granulocyte
Some months: RBC
Years: certain lymphocytes

RBC are formed in:
embryo – spleen, liver
adult - red bone marrow (1,5 kg)
    proximal epiphysis of the long bones
    ribs
    sternum
    vertebrae

Red bone marrow
Red Blood Cells (RBC)

Life span: 120 days

Thickness: 2.5 µm
Diameter: 7-8 µm

Shape: biconcave disc (donut shape)

Count:
- man 5.4 million / µl
- woman 4.8 million / µl
- 4.3-5.2 T/l

Bürker chamber, counting RBC and WBC, Automated counters, CellSorter
Erythropoiesis

- **Location:**
  - in embryos:
    - liver and spleen
    - from 6th months: mainly in bone marrow
  - After 5 years of age: red bone marrow, sternum, ribs, humerus, tibia)

- **Process type:**
  - differentiation
  - **reticulocyte crisis:** reticulocyte count increases after a forced production of erythrocytes
  - normal value: 0.7-1.5%

Development of RBC

- Erythropoietin sensitivity
- Hemoglobin content
Mean retikulocyte percentage is 0.4 – 1.5%

Increases after blood loss

**Retikulocyte**

**Development:**

**Erythropoetin** (Glycoprotein)

**Production:** Kidney (90 %), Liver (10 %).

Erythropoetin acts on erythropoetin-sensitive cells in bone marrow.

Potentiated by androgens, thyroid hormone, growth hormone.

**Other factors:** vitamin B$_{12}$, folic acid
Factors reducing oxygen level
1. smaller blood volume
2. decrease in RBC count
3. decrease in hemoglobin content
4. slower blood flow
5. Lung disorder
6. Height above sea level

Cyanocobalamin (vitamin B₁₂)
Extrinsic factor: B₁₂ vitamin
Intrinsic factor: transcorrin (glycoprotein) produced by parietal cells of the stomach

Folic acid
Source: vegetables, liver
Anaemia

= Loss of more than 1% of RBCs

Causes:
  – production ↓ or loss ↑
    • Iron deficiency
    • Vitamine B\textsubscript{12} deficiency
    • Folic acid deficiency
    • Increased degradation of RBCs (radiation)
Anemias

1. **Blood loss anemia**: acute and chronical
2. **Aplastic anemia**: because of radiation
3. **Megaloblastic anemia**:
   - anaemia perniciosa (hyperchrom macrocyter)
4. **hemolitic anemia**:
   - spherocytosis
   - neonatal
5. **Iron deficiency anemia**: hypochrom, microcyter

<table>
<thead>
<tr>
<th>Normal</th>
<th>Macrocyter</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anaemia perniciosa</strong></td>
<td></td>
</tr>
<tr>
<td>Anisocytosis – size differences</td>
<td></td>
</tr>
<tr>
<td>Poikilocytosis – shape differences</td>
<td></td>
</tr>
</tbody>
</table>
Lack of nucleus, endoplasmic reticulum, Golgi-apparatus, mitochondria

Presence of cell membrane (blood group antigens), membrane proteins (glucose transporter), enzymes (carbo-anhydrase), (Na-K pump)

The structure of RBC

hemoglobin
intracellular net of proteins (spectrin, actin, ankyrin)

double lipid layer
Cl/HCO₃⁻ exchanger (kapnoforin)
Ankyrin
Spectrin-dimer
Actin
4.1-band protein
Glycophorin

The osmotic resistency of RBC

0.9% NaCl-solution is „isotonic” solution

RBCs in hypotonic solution
Iron metabolism

Iron content of a man is: ~4000 mg

Plasma iron: man: 23 μmol/l (1.3 mg/l)
            woman: 19 μmol/l (1.1 mg/l)

Stored iron ~ 1000 mg (ferritin), mainly in the liver

„functional iron” ~3000 mg
  • Hb in th RBC (70%)
  • myoglobin (3%)
  • in enzymes (peroxidases, catalyses, cytochromes)
Iron transport

- Protein carries iron: transferrin
- Daily requirement of iron:
  - compensation of iron lost
  - increased need of iron (pregnancy)
- From eroded enterocytes: 1 mg
  - in women at period: 2-3 mg
  - in children: 2-3 mg

Iron supplement

- **Forms of Iron supplement**: 10-20 mg/day
  - anorganic Fe$^{3+}$ (ferri) by food
  - hemoprotein of animal origin: hem is deliberated in the intestine, absorbed by enterocyte, iron deliberated intracellulary
- **Absorption of iron**
  - active process
  - duodenum, prox. jejunum
  - Fe$^{2+}$ (reducing agents eg. vitamine C)
  - Mucosal block
- Excessive iron supplement: in **LISOSOMES**: ferritin aggregated = hemosiderin
Absorption of iron
Iron transport

- **LUMINAL MEMBRANE:**
  - Fe$^{2+}$ binds to a protein in the mucosa, that carries trough the brush border of mucous cell
- **ENTEROCYTE:**
  - iron binds to apoferritin = ferritin => iron storage or elimination
  - iron release (unknown)
- **BLOOD:**
  - transferrin (physiological saturation: 35%)

Types of hemoglobin

- 1. **OxiHb** (oxygenated)
- 2. **DezoxiHb** (deoxygenated - reduced), dark color
- 3. **MetHb**
  - by oxydative agents Fe$^{2+}$ → Fe$^{3+}$
  - dark blood, cyanotic skin
  - Physiologically the NADH-methemoglobin-reductase transforms it back to normal Hb
- 4. **CarboxiHb** (CO)
  - affinity to CO is 200x stronger than O$_2$
  - decreases the oxygene transport capacity of blood
- 5. **CarbaminoHb**
  - a Hg bound carbondioxyde
Degradation of Hb

- RBC life span: 120 days
- Cause of dysfunction: decreased membrane flexibility

- decomposition: in spleen, by phagocytes: HEM + GLOBIN

- Hem → biliverdin (blue-green), bilirubin (orange-red)

- Blood: bilirubin-albumin complex indirect/unconjugated/bound bilirubin

- Liver: conjugated with glucoronic acid → direct/conjugated/free bilirubin → bile
Liver Blood Bile canal

- bile → small intestine (bacteria) → urobilinogen → urobilin (orange), stercobilinogen → stercobilin (golden yellow)
- feces: stercobilin ~ 200 mg/ day
- portal circulation → 1. kidney ~ 1-2 mg/day → 2. liver (enterohepatic circulation)
Icterus (jaundice)

**Cause:** hyperbilirubinaemy $\Rightarrow$ elevated bilirubin level in the tissues (sclera, skin)

- norm: bilirubin: $< 17 \mu$mol/l
- jaundice: bilirubin $> 34-43 \mu$mol/l

a) **hemolytic** $\sim$: hemolysis increased; indirect bilirubin level $\uparrow$
   (embryo, newborn)

b) **hepatocellular** $\sim$: primary disease of the liver cells, disfunctional secretion of bile $\Rightarrow$ conjugated bilirubin enter sinusoids,
   level of direct and indirect bilirubin raised.

c) **obstructional** $\sim$: jam of bile ducts out of liver $\Rightarrow$ acholic feces,
   lack of UBG in urine

- **physiological jaundice:** some days after birth
  - Cause: the life span of the foetal RBCs is approx. 80 days,
    many of them degraded at the same time, and the bilirubin-conjugation capacity of foetal liver is low.
Human blood types
Only compatible blood types can be transfused

- ABO system
- Rh system
- Others: MNs, Kelly, Duffy…

<table>
<thead>
<tr>
<th></th>
<th>europid</th>
<th>negrid</th>
<th>mongoloid</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>41%</td>
<td>28%</td>
<td>38%</td>
</tr>
<tr>
<td>B</td>
<td>11%</td>
<td>17%</td>
<td>22%</td>
</tr>
<tr>
<td>0</td>
<td>45%</td>
<td>51%</td>
<td>30%</td>
</tr>
<tr>
<td>AB</td>
<td>3%</td>
<td>4%</td>
<td>10%</td>
</tr>
</tbody>
</table>

- Antigenes on RBC membrane
  - H, A, B
- Natural antibodies (IgM) in blood plasma:
  - produced after oral intake of A or B chains from plants and meat during the 1st year
  - antibody production against unknown chains
- Antigen chains are also found in: saliva, tears, gastric juice, sweat…

ABO-system
The ABO Blood System

<table>
<thead>
<tr>
<th>Blood Type (genotype)</th>
<th>Type A (AA, AO)</th>
<th>Type B (BB, BO)</th>
<th>Type AB (AB)</th>
<th>Type O (OO)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Red Blood Cell Surface Proteins (phenotype)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A agglutinogens only</td>
<td>A agglutinogens only</td>
<td>A and B agglutinogens</td>
<td>No agglutinogens</td>
<td></td>
</tr>
<tr>
<td><strong>Plasma Antibodies (phenotype)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>b agglutinin only</td>
<td>a agglutinin only</td>
<td>No agglutinin</td>
<td>a and b agglutinin</td>
<td></td>
</tr>
</tbody>
</table>
antibodies/serums: anti-A anti-B anti-A+B

blood type

- B
- A
- AB
- 0

Rh(esus) group

- **Rh factor**: C, D, E, c, d, e antigens

- **RhD+ and RhD− blood groups**
  - RhD+ (85%)  D-antigen present,  no antibody
  - RhD− (15%)  no D-antigen,  no antibody

- **Sensibilisation - Ig G immunoglobulin production**
  - transfusion
  - Rh- incompatibility!!
Rh-incompatibility

- Rh- mother carrying an Rh+ fetus

- small amount of Rh+ fetal blood leaks into the maternal circulation during delivery (or abortion), and the mother develops significant titer (concentration) of anti-Rh agglutinins of IgG class

- during the next pregnancy with Rh+ fetus, IgG antibodies cross the placenta and hemolyses the fetal erythrocytes → erythroblastosis fetalis (fetal death, severe illness: hydrops fetalis, kernicterus)

- Prevention: after delivery anti-Rh agglutinins are injected into the mother to hemolys the fetal erythrocytes and prevent immunisation