Laboratory diagnosis of plasma proteins and plasma enzymes
# Functions of plasma proteins

<table>
<thead>
<tr>
<th>Function</th>
<th>Example</th>
</tr>
</thead>
<tbody>
<tr>
<td>• transport</td>
<td>thyroxine-binding globuline, (and other hormon-binding globulines)</td>
</tr>
<tr>
<td></td>
<td>apolipoproteins (cholesterol, triglyceride)</td>
</tr>
<tr>
<td></td>
<td>transferrin (iron)</td>
</tr>
<tr>
<td>• humoral immunity</td>
<td>immunoglobulins</td>
</tr>
<tr>
<td>• enzymes</td>
<td>renin, clotting factors, complement proteins</td>
</tr>
<tr>
<td>• protease inhibitors</td>
<td>α₁-antitrypsin</td>
</tr>
<tr>
<td>• maintenance of oncotic pressure</td>
<td>all proteins, particularly albumin</td>
</tr>
<tr>
<td>• buffering</td>
<td>all proteins</td>
</tr>
</tbody>
</table>
Causes of changes in total plasma protein concentration

normal range: 60-80 g/l

Increase:
- Protein synthesis ↑:
  - hypergammaglobulinemia,
  - paraproteinemia
- Volume of distribution ↓:
  - dehydration
- Artefactual:
  - hemoconcentration due to stasis of blood during venepuncture

Decrease:
- Protein synthesis ↓:
  - malnutrition, malabsorption, liver disease
- Volume of distribution ↑:
  - overhydration, increased capillary permeability
- Excretion ↑, Catabolism ↑:
  - protein-losing states, catabolic states
Pathologic changes of plasma proteins

**Dysproteinemia:** total plasma protein concentration is normal, but the normal ratio of its components is changed.
*example: acute inflammation, chronic inflammation.*

**Defectdysproteinemia:** total absence of a certain plasma protein.
*example: lack of albumin, lack of alfa-1 antitrypsin, lack of ceruloplasmin*

**Paraproteinemia:** There is a protein in the plasma, which can not be detected under normal conditions.
*example: monoclonal gammopathy*
### Principal plasma proteins

<table>
<thead>
<tr>
<th>Class:</th>
<th>Protein:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>prealbumin</td>
</tr>
<tr>
<td></td>
<td>albumin</td>
</tr>
<tr>
<td>(\alpha_1)-globulin</td>
<td>(\alpha_1)-antitrypsin,</td>
</tr>
<tr>
<td></td>
<td>(\alpha_1)- acid glycoprotein</td>
</tr>
<tr>
<td>(\alpha_2)-globulin</td>
<td>haptoglobins</td>
</tr>
<tr>
<td></td>
<td>(\alpha_2)-macroglobulin</td>
</tr>
<tr>
<td></td>
<td>ceruloplasmin</td>
</tr>
<tr>
<td></td>
<td>transferrin</td>
</tr>
<tr>
<td>(\beta)-globulin</td>
<td>low density lipoprotein</td>
</tr>
<tr>
<td></td>
<td>Complement components</td>
</tr>
<tr>
<td>(\gamma)-globulins</td>
<td>IgG, IgM, IgD, IgE, IgA</td>
</tr>
</tbody>
</table>
Causes of hypoalbuminemia

**Decreased synthesis:**
- malnutrition
- malabsorption
- liver disease

**Increased volume of distribution:**
- overhydration
- increased capillary permeability: septicemia, hypoxemia

**Increased excretion / degradation:**
- nephrotic syndrome
- protein-losing enteropathies
- burns
- hemorrhage
- catabolic states: severe sepsis, fever, trauma, malignant disease
Plasma protein electrophoresis
normal profile
Plasma protein electrophoresis
normal profile

Albumin

α-1 glycoprotein acid
α-1 antitrypsin
haptoglobin
α-2 macroglobulin
 transferrin
C3
γ-globulins
Plasma protein electrophoresis
Acute inflammation
Plasma protein electrophoresis
Acute inflammation

Alb  α-1  α-2  β-1  β-2  γ
Plasma protein electrophoresis
Chronic inflammation

Alb  α1  α2  β1  β2  γ
### Laboratory Diagnosis of Inflammatory Diseases

<table>
<thead>
<tr>
<th>Test</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>qualitative and quantitative</td>
</tr>
<tr>
<td>Erythrocyte Sedimentation Rate (Westergren)</td>
<td>aspecific</td>
</tr>
<tr>
<td>CRP</td>
<td>rapid and sensitive</td>
</tr>
</tbody>
</table>

#### Changes of plasmaproteins:
- albumin $\downarrow$
- IgG, IgA, IgM: $\uparrow$ $A/G$ $\downarrow$
- Protein electrophoresis: $\alpha_1$, $\alpha_2$ $\uparrow$

#### Acute phase proteins:
- $\uparrow$
  - $\alpha_1$-antitrypsin
  - fibrinogen
  - haptoglobin
  - ceruloplasmin
  - CRP
- $\downarrow$
  - albumin
  - transferrin

**Procalcitonin:** increases in severe bacterial, mycotic and parasitic diseases, also in sepsis
Plasma protein electrophoresis nephrotic syndrome
Plasma protein electrophoresis
liver cirrhosis

β-γ block
Plasma protein electrophoresis
hyper- and hypogammaglobulinemia
Plasma protein electrophoresis
monoclonal gammopathy
Laboratory findings in multiple myeloma

**Biochemical:**

**Serum:**
- presence of paraprotein
- normal immunoglobulins $\downarrow$
- urea $\uparrow$
- creatinine $\uparrow$
- $\beta_2$-microglobulin $\uparrow$
- calcium $\uparrow$
- urate $\uparrow$
- normal alkaline phosphatase activity

**Urine:**
- presence of Bence-Jones protein

**Hematological:**
- erythrocyte sedimentation rate $\uparrow$
- anemia (usually normochromic, normocytic)
- rouleaux formation
Clinical enzymology
Classification of plasma enzymes

• Plasma-specific enzymes:
  
  *clotting factors, elements of complement-system, etc.*

• Exocrin enzymes:
  
  *amilase, lipase, peptidases etc.*

• Intracellular, non-plasma-specific enzymes:
  
  *ASAT, ALAT, GGT, ALP, LDH, CK etc.*
ISOENZYMES

LDH: 5 isoenzymes:
LDH$_1$: heart, RBC, renal cortex
LDH$_2$: heart, RBC, renal cortex
LDH$_3$: lungs, lymphocytes
LDH$_4$: liver, skeletal muscle
LDH$_5$: liver, skeletal muscle

ALP:
intestinal tract
placental origin
non-specific isoforms: bones, liver, kidneys, granulocytes

CK: 3 isoenzymes
CK-BB: central nervous system, intestinal tract
< 1%
CK-MM: skeletal muscle
> 94%
CK-MB: heart
< 6%
Most Important Enzymes in Laboratory Diagnosis I.

**AST:** mainly from heart, skeletal muscle and liver

**ALT:** mainly from liver

**De Ritis formula:**
- \( \text{AST/ALT} < 1 \): injury caused by inflammation
- \( \text{AST/ALT} > 1 \): severe necrotic liver disease

**GGT:** its clinical importance is monitoring hepatobiliary diseases and alkohol-abuse

**ALP:** hepatobiliary diseases, bone diseases
Most Important Enzymes in Laboratory Diagnosis II.

**Amylase:** pancreatic disorders
salivary gland disorders

**Lipase:** specific for pancreatic disorders