Plasma proteins

The importance of plasma protein

- **Transport**
  - substances insoluble in water, drugs
    Albumin - Ca, Mg, Zn, thyroxin, bilirubin, drugs
    Prealbumin - thyroxine
    Ceruloplasmin - Cu
    Transferrin-Fe
    Apoprotein - lipids
- **Defense against infection**
  - Immunoglobulins, complement

The importance of plasma protein

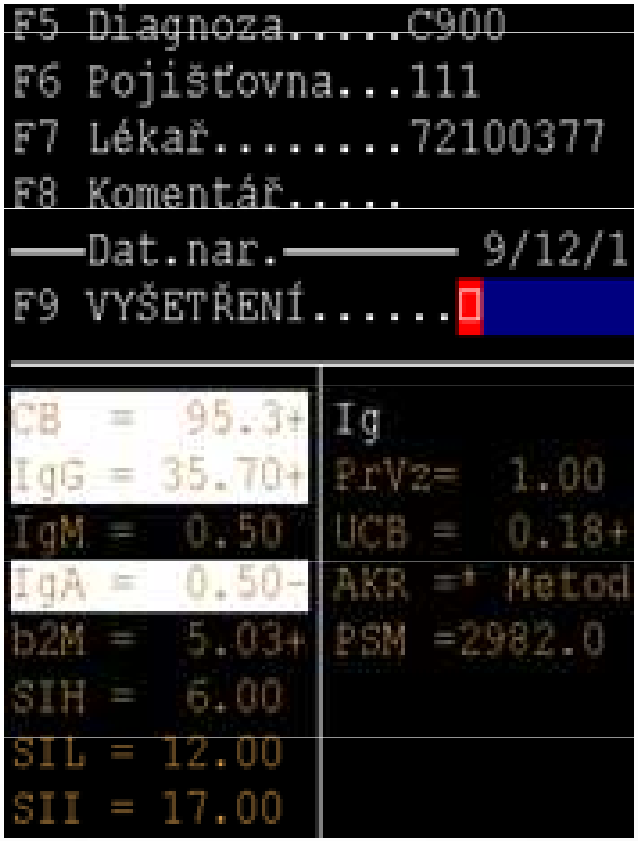
- **Oncotic pressure**
  - albumin
- **Coagulation and fibrinolysis**
  - coagulation factors and factors ensuring of dissolution of thrombus
- **Enzymes**
  - cholinesterase and ceruloplasmin
- **Protease inhibitors**
  - prevent damage by proteolytic enzymes :a1-antitrypsin, a1-antichymotrypsin and a2-macroglobulin
- **Special functions** such as protection against free radicals- inhibition of their formation (albumin, ceruloplasmin, haptoglobin, hemopexin)

Total protein: ref. range 63-84g/l

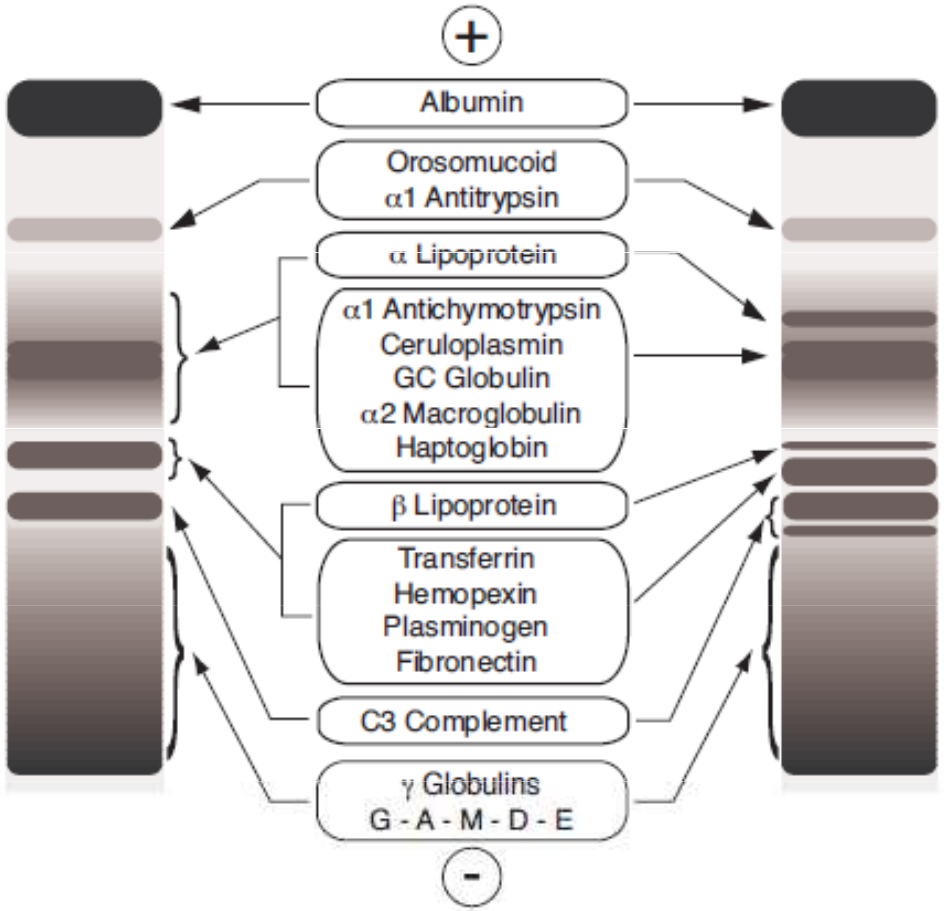
- **Decreased synthesis**
  - Hepatopathie
  - Malnutrition
- **Increased loss**
  - Urine –nefrotic syndrom
  - Faeces – exsudative enteropathy
- **Increased blood volume** (oedema,ascites)

Total proteins -hyperproteinemia

- Dehydratation
- Chronic inflammation, cirrhosis, monoclonal gammopathies



Protein electrophoresis



Prealbumin

- hepatic transport protein for thyroid hormones
- transport protein for vitamin A (to prevent loss of urine)

- ↓ = failure of protein synthesis in the liver in severe liver disease or protein malnutrition

  - Ref.ranges: 0,2-0,40 g/l
  - Half-time: 2 days

NUTRITIONAL ASSESSMENT

Laboratory

- FBC – Hemoglobin (HCMC anemia), Total Lymphocytes count
- LFT – Serum albumin
- Serum Transferrin
- Serum Prealbumin
- Others
  - Nitrogen balance
  - Electrolytes/BUSE/ creatinine

- **Albumin (T½): 20 days**
- **Transferrin (T½): 8-10 days**
- **Prealbumin (T½): 2-3 days**

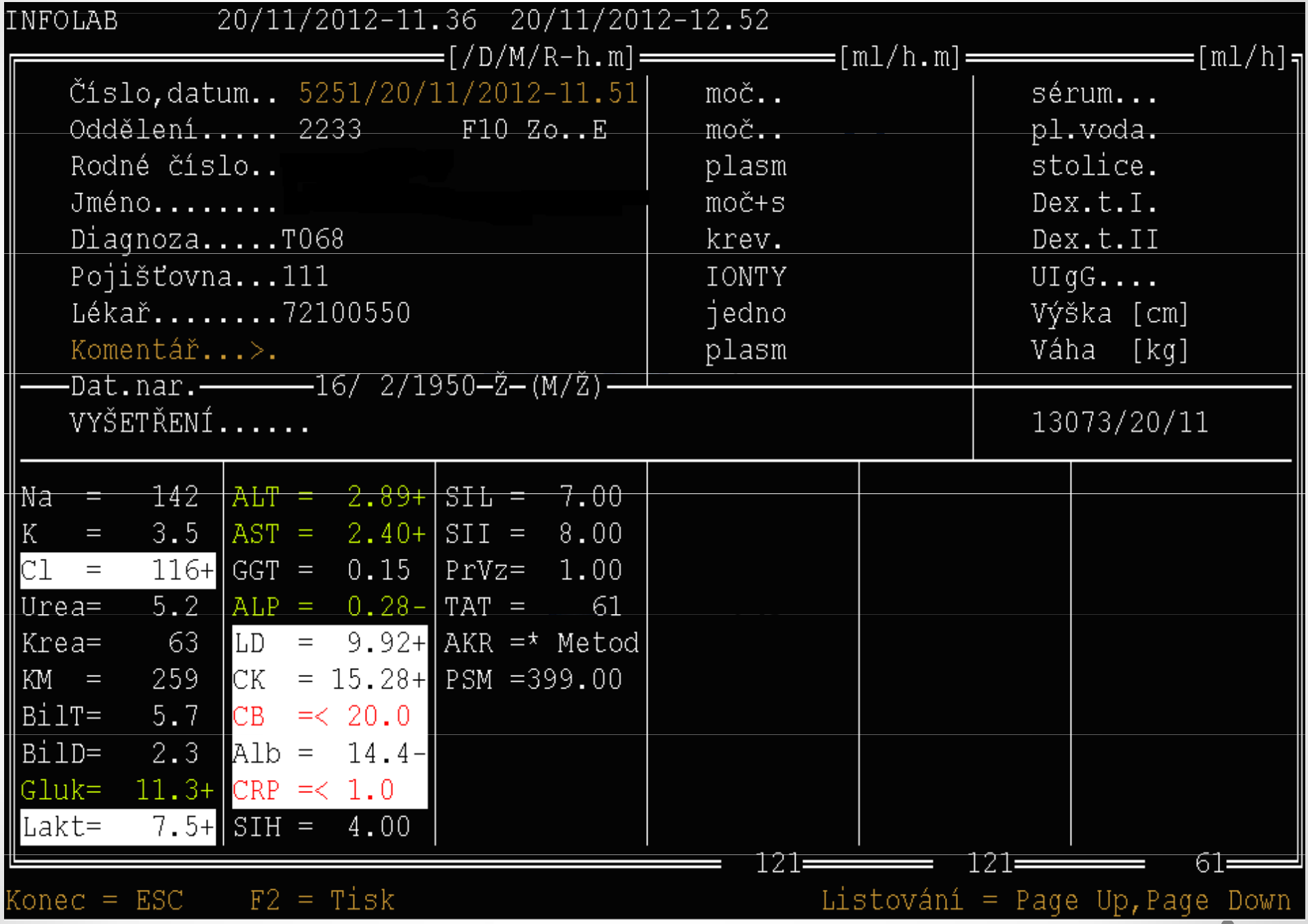
Albumin (35-53g/l)

- Formed in the liver, molecular weight 68,000

- Oncotic pressure
- Transport protein for unconjugated bilirubin, thyroid hormones, calcium, magnesium, zinc and other minerals,pharmaceuticals
- Component of the extracellular antioxidant system

- **decreased synthesis**
- hepatopathy or protein malnutrition
- increased catabolism in acute inflammation and tumors
- increased losses by kidneys (nephrotic syndrome), GIT, skin

- half-life 20 days
-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Rodné číslo..
Jméno.....
Diagnoza.....T068
Pojišťovna...111
Lékař.....72100550
Komentář...>.
moč..
moč..
plasm
moč+s
krev.
IONTY
jedno
plasm
sérum...
pl.voda.
stolice.
Dex.t.I.
Dex.t.II
UIgG....
Výška [cm]
Váha [kg]
Dat.nar. 16/ 2/1950-Ž-(M/Ž)
VYŠETŘENÍ.....
13073/20/11
Na = 142
K = 3.5
Cl = 116+
Urea= 5.2
Krea= 63
KM = 259
BilT= 5.7
BilD= 2.3
Gluk= 11.3+
Lakt= 7.5+
ALT = 2.89+
AST = 2.40+
GGT = 0.15
ALP = 0.28-
LD = 9.92+
CK = 15.28+
CB =< 20.0
Alb = 14.4-
CRP =< 1.0
SIH = 4.00
SIL = 7.00
SII = 8.00
PrVz= 1.00
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121
61
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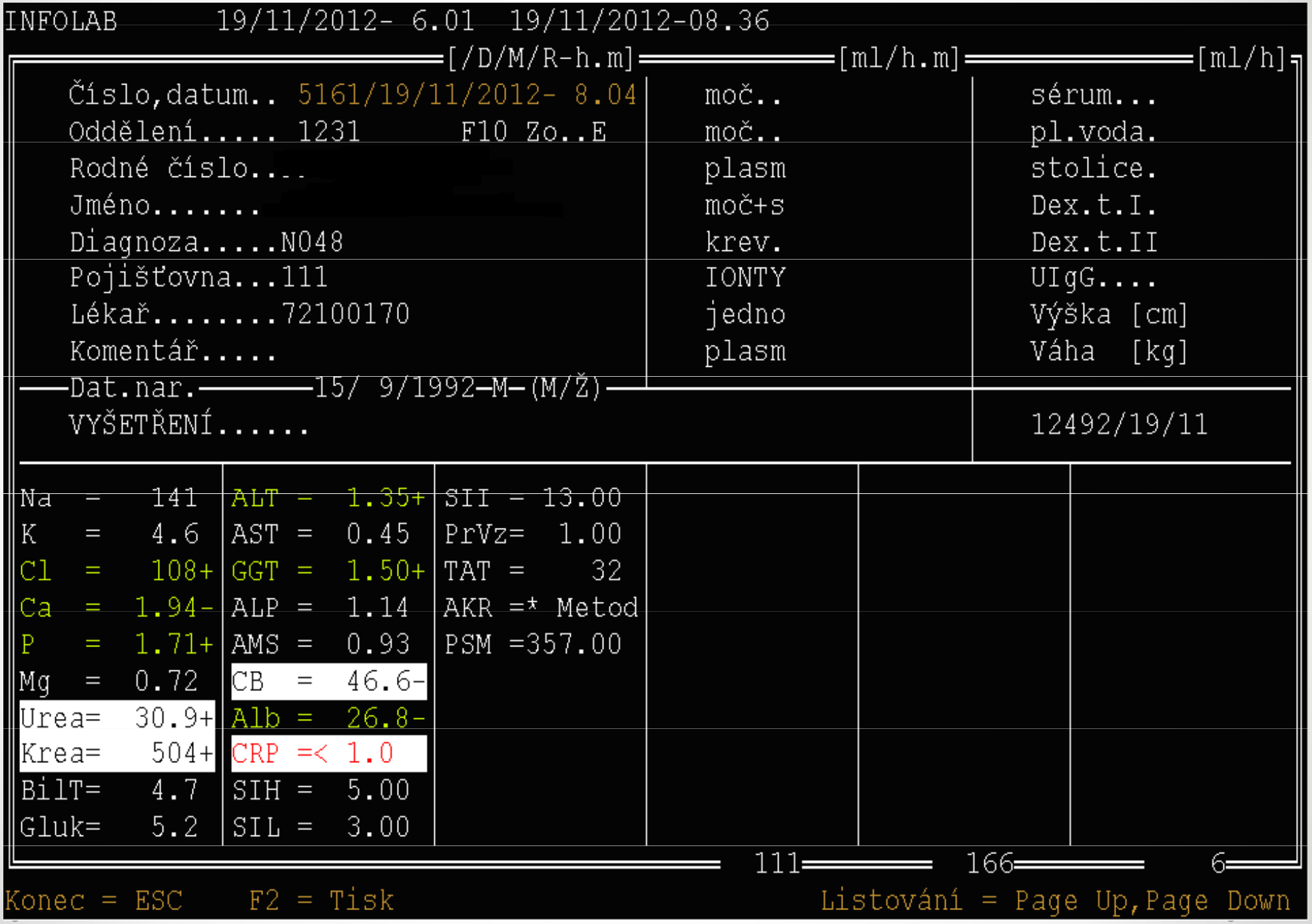
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Oddělení..... 1231 F10 Zo..E
Rodné číslo....
Jméno.....
Diagnoza.....N048
Pojišťovna...111
Lékař.....72100170
Komentář.....
Dat.nar. 15/ 9/1992-M-(M/Ž)
VYŠETŘENÍ.....
moč..
moč..
plasm
moč+s
krev.
IONTY
jedno
plasm
sérum...
pl.voda.
stolice.
Dex.t.I.
Dex.t.II
UIgG....
Výška [cm]
Váha [kg]
12492/19/11
Na = 141
K = 4.6
Cl = 108+
Ca = 1.94-
P = 1.71+
Mg = 0.72
Urea= 30.9+
Krea= 504+
BilT= 4.7
Gluk= 5.2
ALT = 1.35+
AST = 0.45
GGT = 1.50+
ALP = 1.14
AMS = 0.93
CB = 46.6-
Alb = 26.8-
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SIH = 5.00
SIL = 3.00
SII = 13.00
PrVz= 1.00
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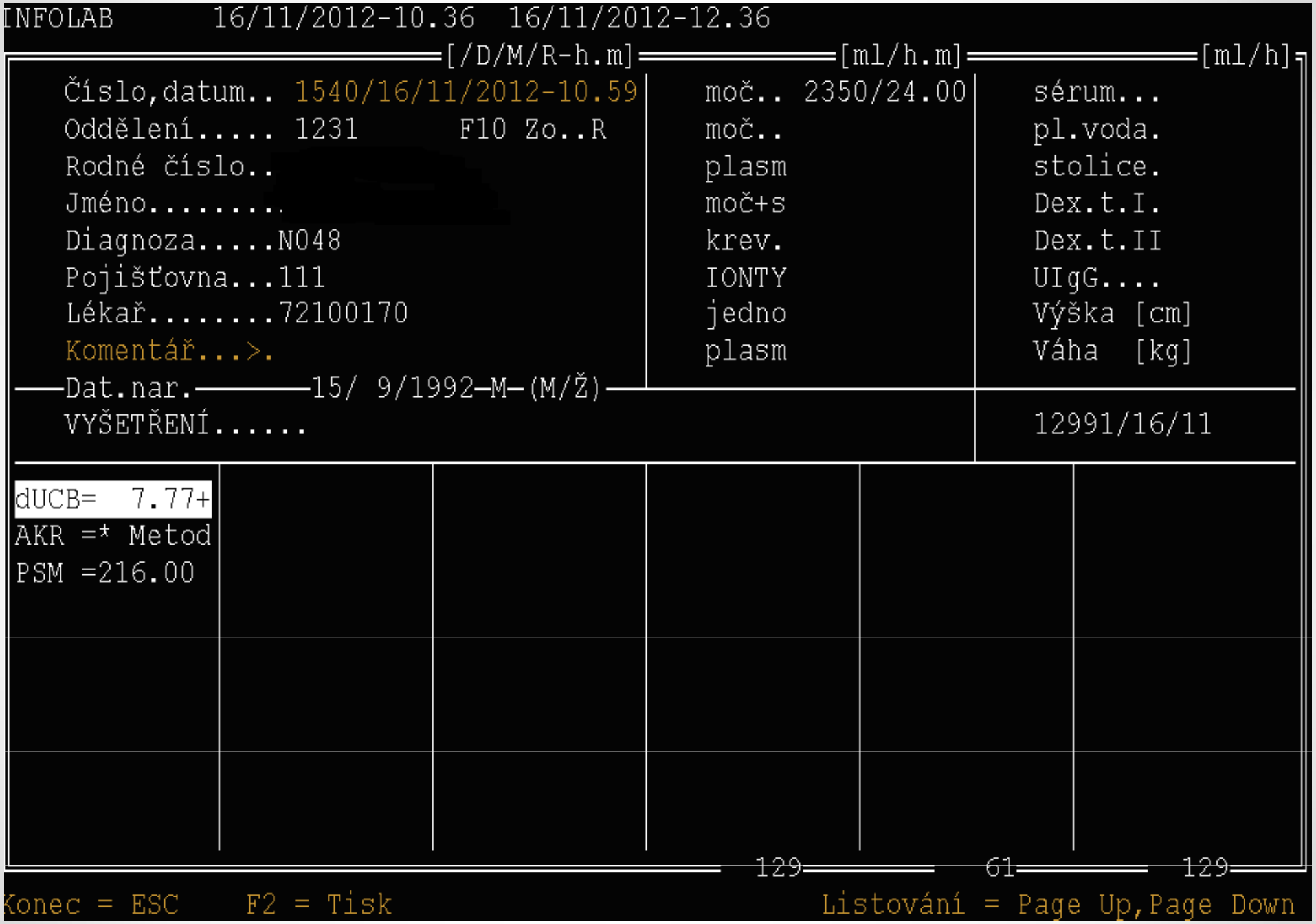
Listování = Page Up,Page Down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Oddělení..... 1231 F10 Zo..R
Rodné číslo..
Jméno.....
Diagnoza.....N048
Pojišťovna...111
Lékař.....72100170
Komentář...>.
Dat.nar.15/ 9/1992-M-(M/Ž)
VYŠETŘENÍ.....
moč.. 2350/24.00
moč..
plasm
moč+s
krev.
IONTY
jedno
plasm
sérum...
pl.voda.
stolice.
Dex.t.I.
Dex.t.II
UIgG....
Výška [cm]
Váha [kg]
12991/16/11
dUCB= 7.77+
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PSM =216.00
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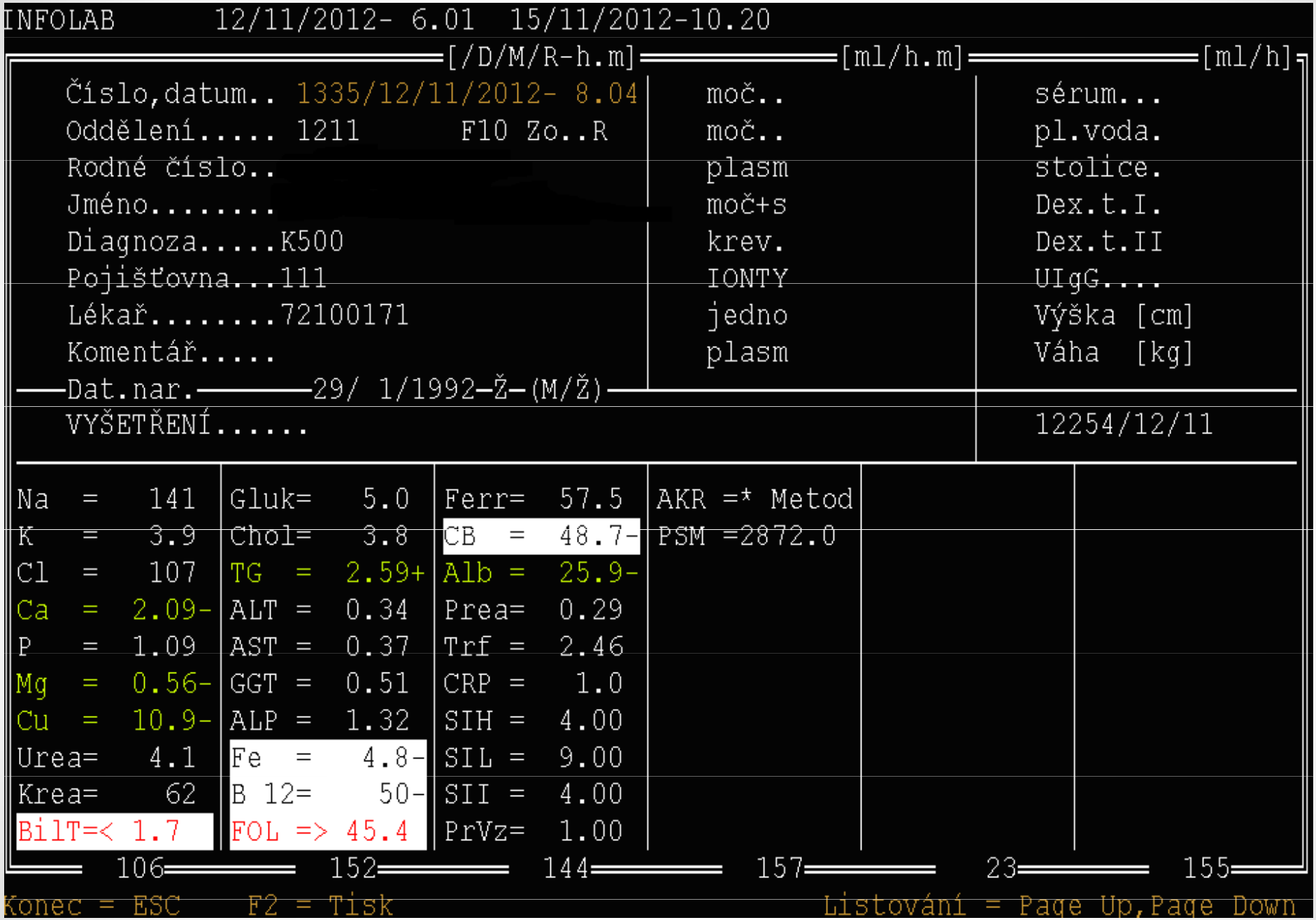
61
129
Konec = ESC F2 = Tisk
Listování = Page Up,Page Down



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   Oddělení..... 1211      F10 Zo..R     moč..          pl.voda.
   Rodné číslo..                         plasm          stolice.
   Jméno........                         moč+s          Dex.t.I.
   Diagnoza.....K500                     krev.          Dex.t.II
   Pojišťovna...111                      IONTY          UIgG....
   Lékař........72100171                 jedno          Výška [cm]
   Komentář.....                         plasm          Váha  [kg]
  Dat.nar.------29/ 1/1992-Ž-(M/Ž)
   VYŠETŘENÍ......                                      12254/12/11

Na  =   141  Gluk=   5.0  Ferr=  57.5  AKR =* Metod
K   =   3.9  Chol=   3.8  CB  =  48.7-  PSM =2872.0
Cl  =   107  TG  =  2.59+ Alb =  25.9-
Ca  =  2.09- ALT =  0.34  Prea=  0.29
P   =  1.09  AST =  0.37  Trf =  2.46
Mg  =  0.56- GGT =  0.51  CRP =   1.0
Cu  =  10.9- ALP =  1.32  SIH =  4.00
Urea=   4.1  Fe  =   4.8- SIL =  9.00
Krea=    62  B 12=    50- SII =  4.00
BilT=< 1.7   FOL => 45.4  PrVz=  1.00
   106          152          144          157          23          155
Konec = ESC    F2 = Tisk                    Listování = Page Up,Page Down
```

Acute phase proteins

- Formation in the liver parenchyma (de novo) - after washout of cytokines IL-6, TNF
- Regulators of inflammation – fever, leukocytosis, cortisol….
- Mediators of biological responses
  CRP and complement
- Binding inhibitors of proteolytic enzymes
  A1 antitrypsin

Acute phase proteins

- **With a fast response**
  Increase after 2-4 hours (IL6, Procalcitonin)
  increase after 6 hours, maximum of 48 hours,
  the rise to 1000times (CRP)

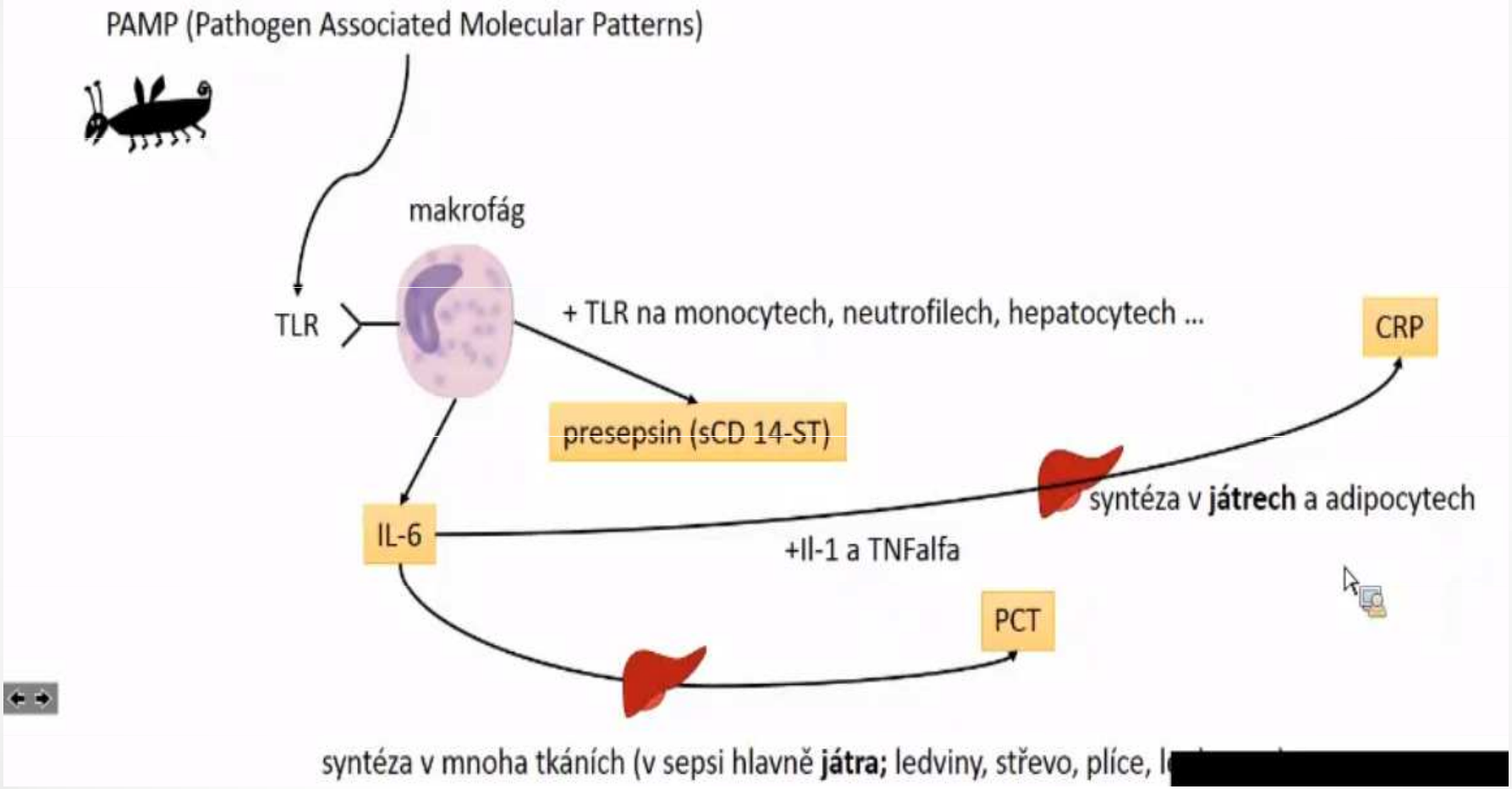
- **Slower onset and peak**
  The rise for 12 to 24 hours, peak 3-5 days (α1antitrypsin, haptoglobin)

- **Concentration is reduced**
  Prealbumin, albumin, transferrin

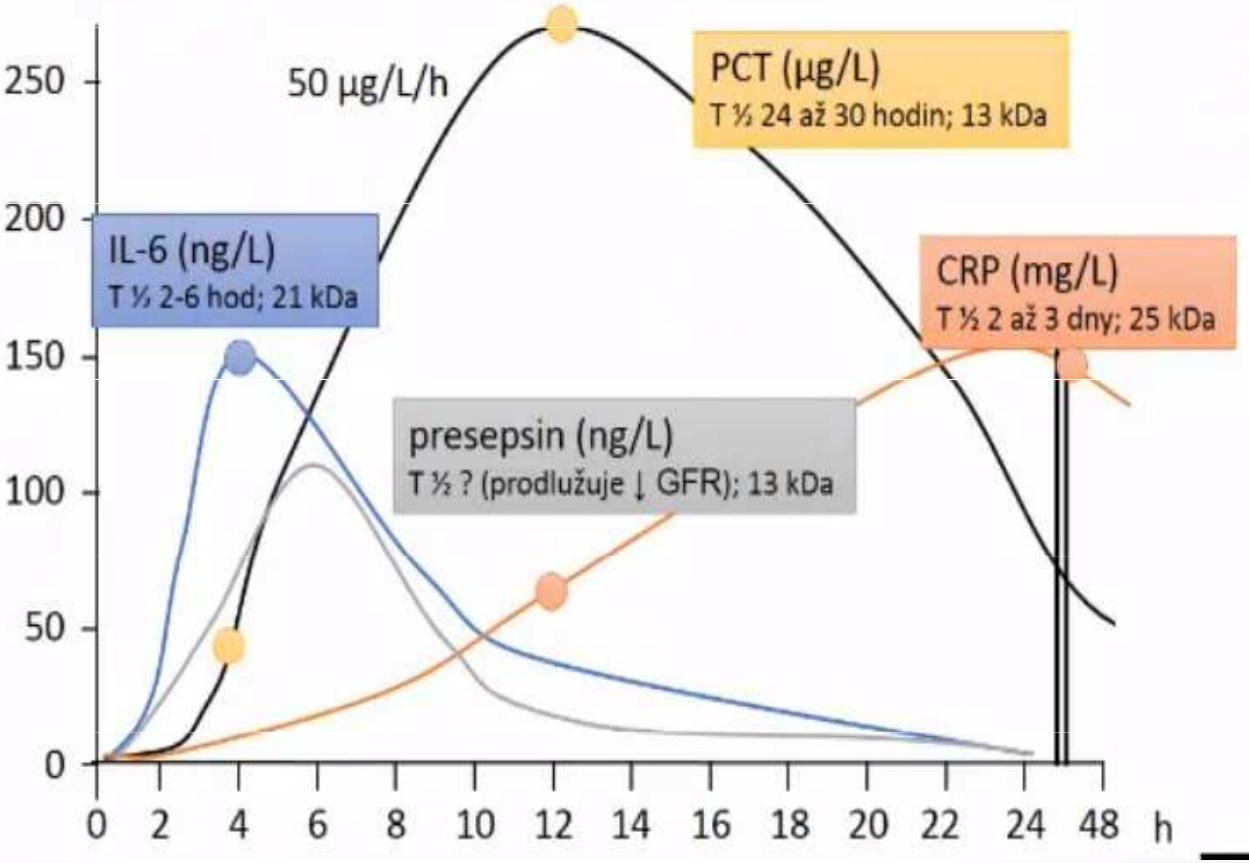
Influence of acute-phase proteins

- Genetically (ceruloplasmin, α1antitrypsin)
- Pregnancy, p.o. contraceptives (ceruloplasmin)
- Intravascular hemolysis (haptoglobin)
- Inflammatory diseases of liver – decrease of synthesis of proteins

Impulzy k produkci



Dynamika markerů zánětu



CRP

- Opsonization of structures of bacterias and demaged cells
- Activation of complement
- Imunomodulation effect

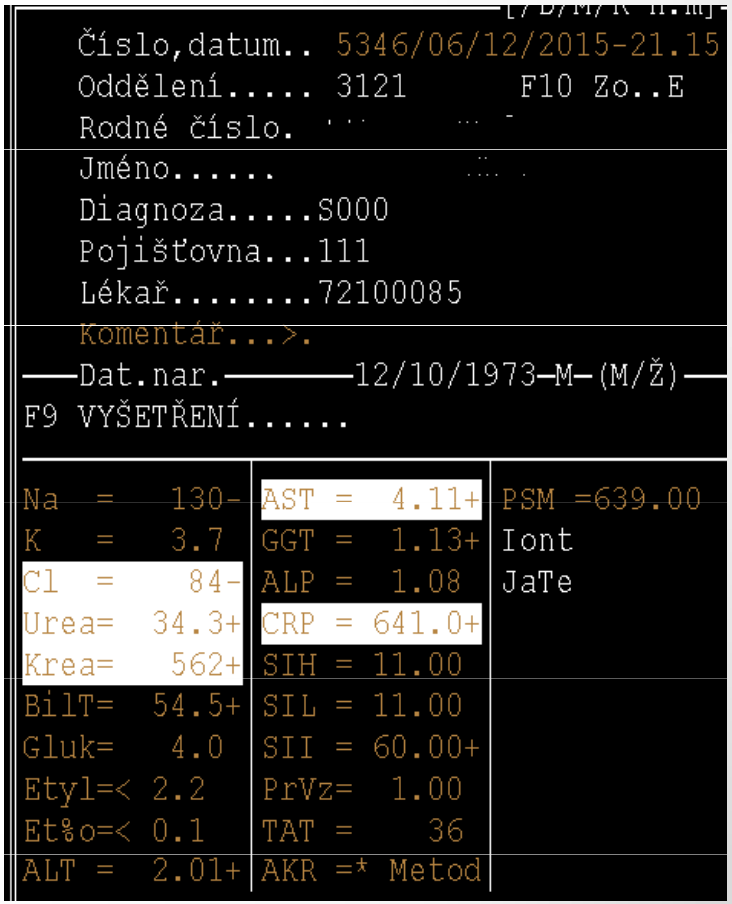
- REF.RANGE: < 5mg/l

- Increase - acute inflammation, acute conditions (rheumatic disease, malignancy, stress, post-operative conditions, etc.)

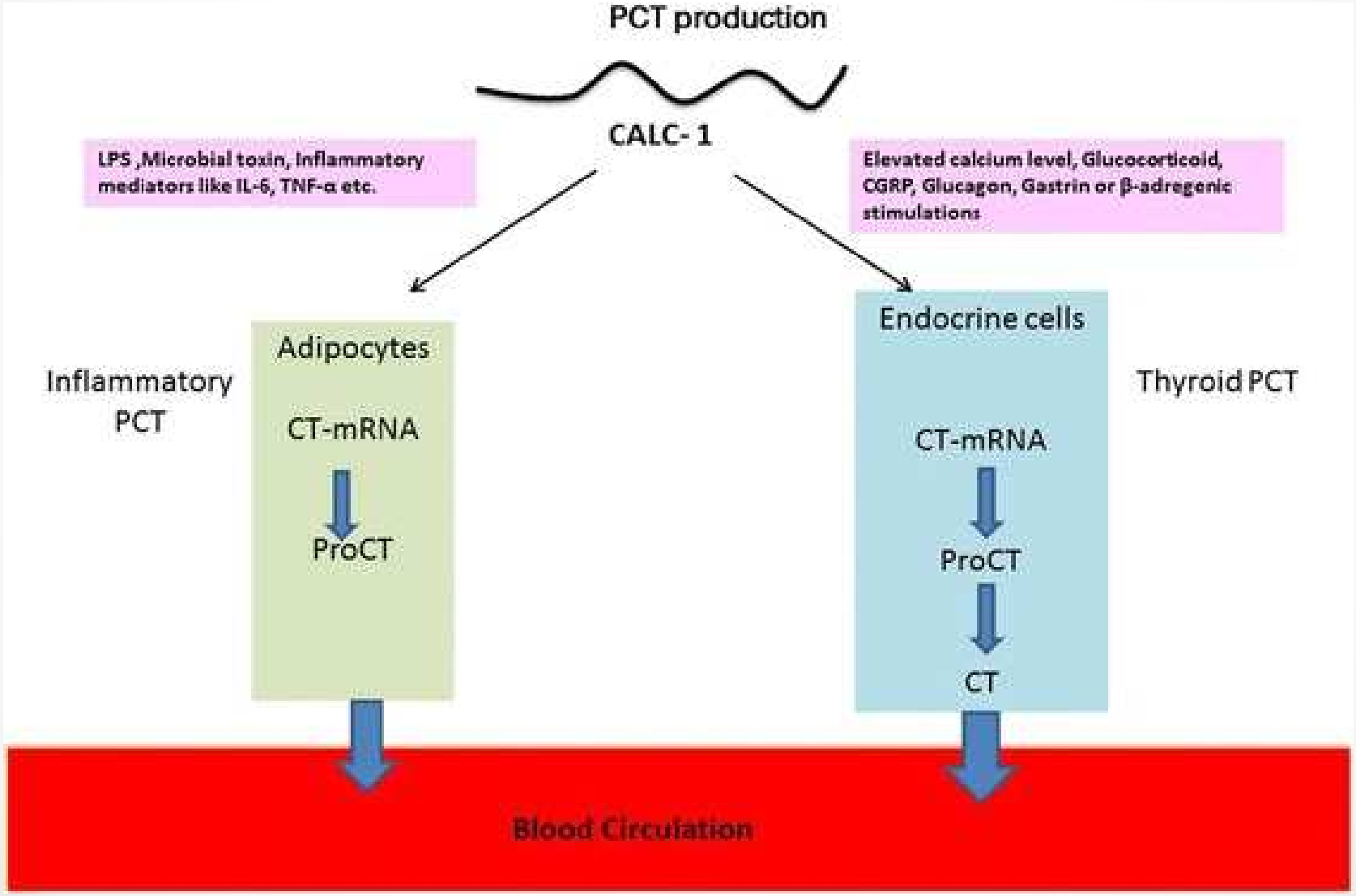
- 6- 8 hours after the onset of inflammation
  Top 1-2 days

CRP

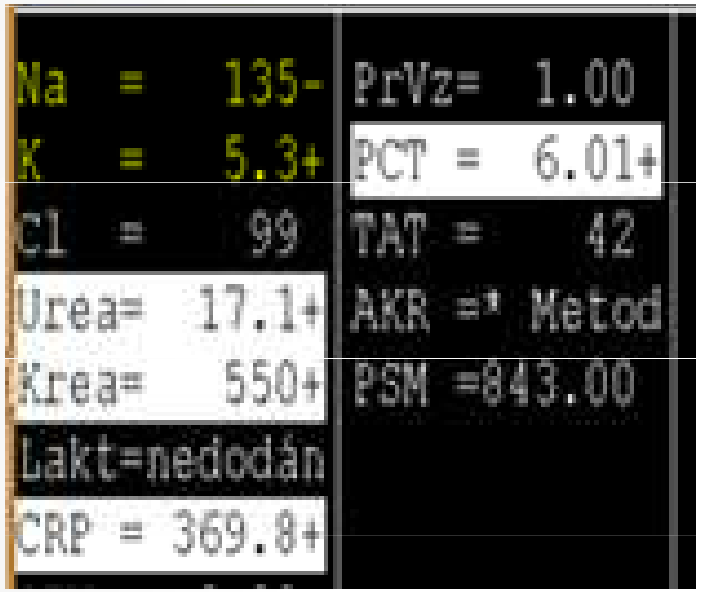
- Indication:
  Early diagnosis of bacterial infections
  Monitoring antibiotics treatment
  Differentiation of bacterial and viral etiology
    - Neonatal sepsis (with IL6)
- Late reactions to SIRS
- It does not help for differentiation between SIRS and sepsis



Prokalcitonin



Prokalcitonin



Ref.range less than 0,5 ug/l

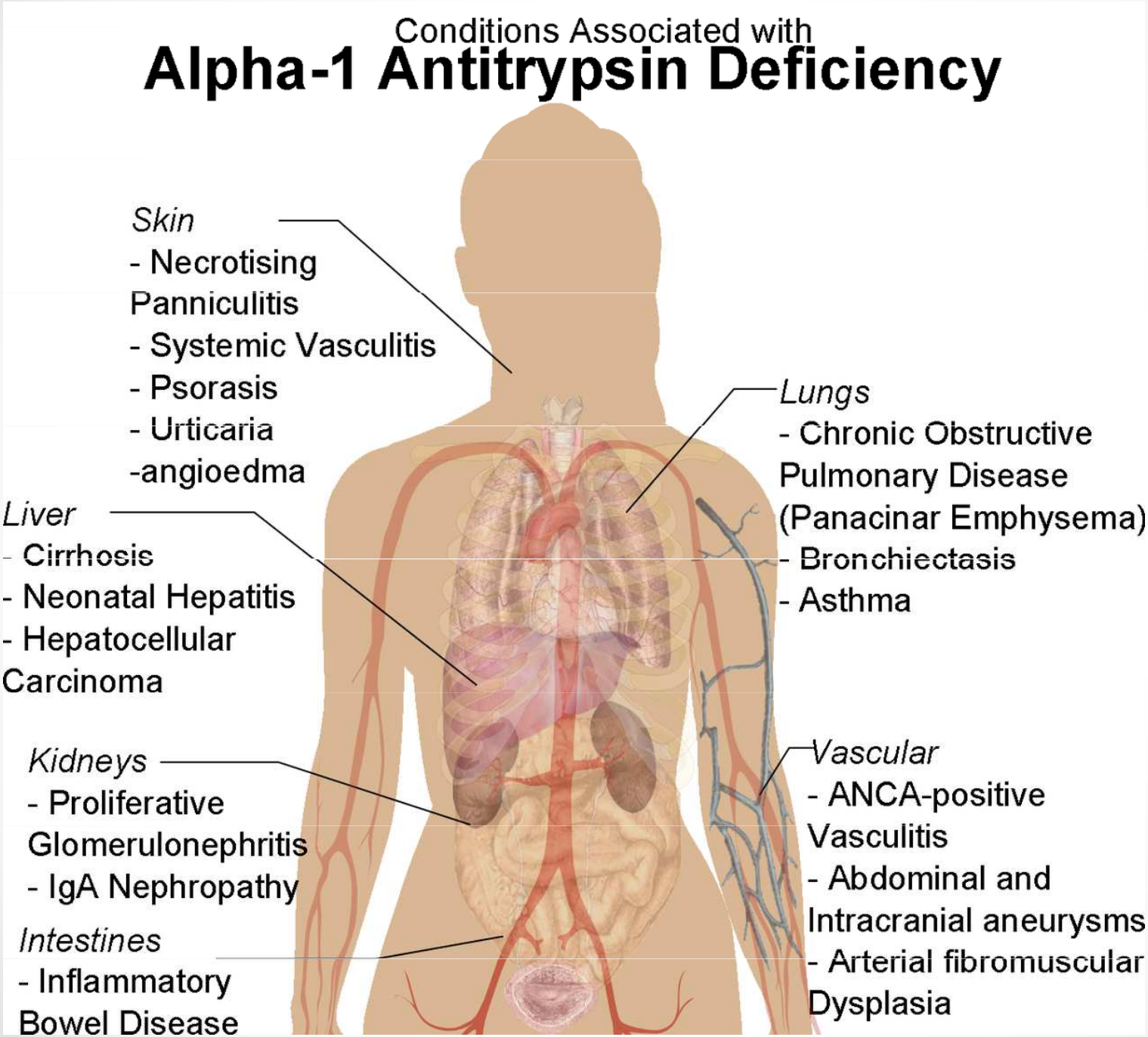
Chronic inflammation 0,5-1ug/l
Localized bacterial infection 0,5-2ug/l
SIRS 5-10ug/l
SEPSIS 10 ug/l or grater

Alfa 1 antitrypsin

- protease inhibitor,hepatic glycoprotein inhibitor of proteolytic enzymes (elastase, collagenase)
  - released during the inflammatory response
  - ↑ acute inflammation and acute severe conditions, pregnancy
  - ↓ severe hepatopathy, hereditary defect creation (liver cirrhosis, pulmonary emphysema)

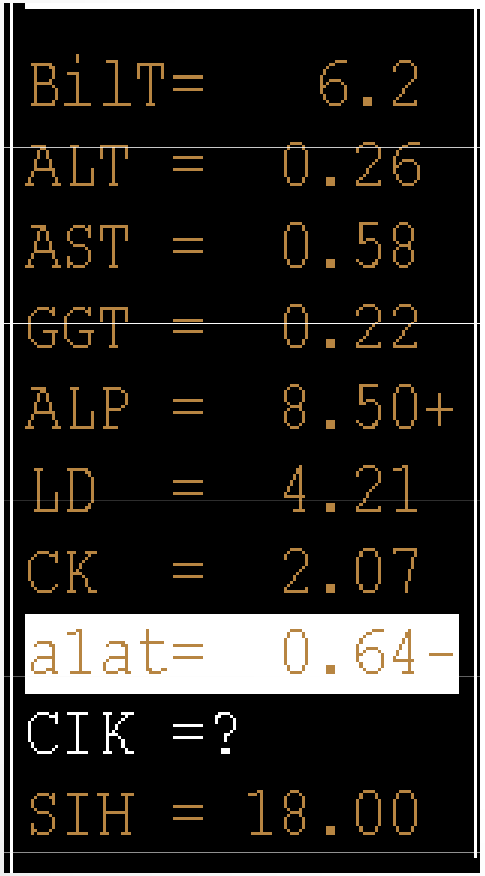
Conditions Associated with

Alpha-1 Antitrypsin Deficiency



Alfa 1 antitrypsin deficiency

Genotyp MZ



Healthy – genotyp MM

Alfa1 antitrypsin deficiency

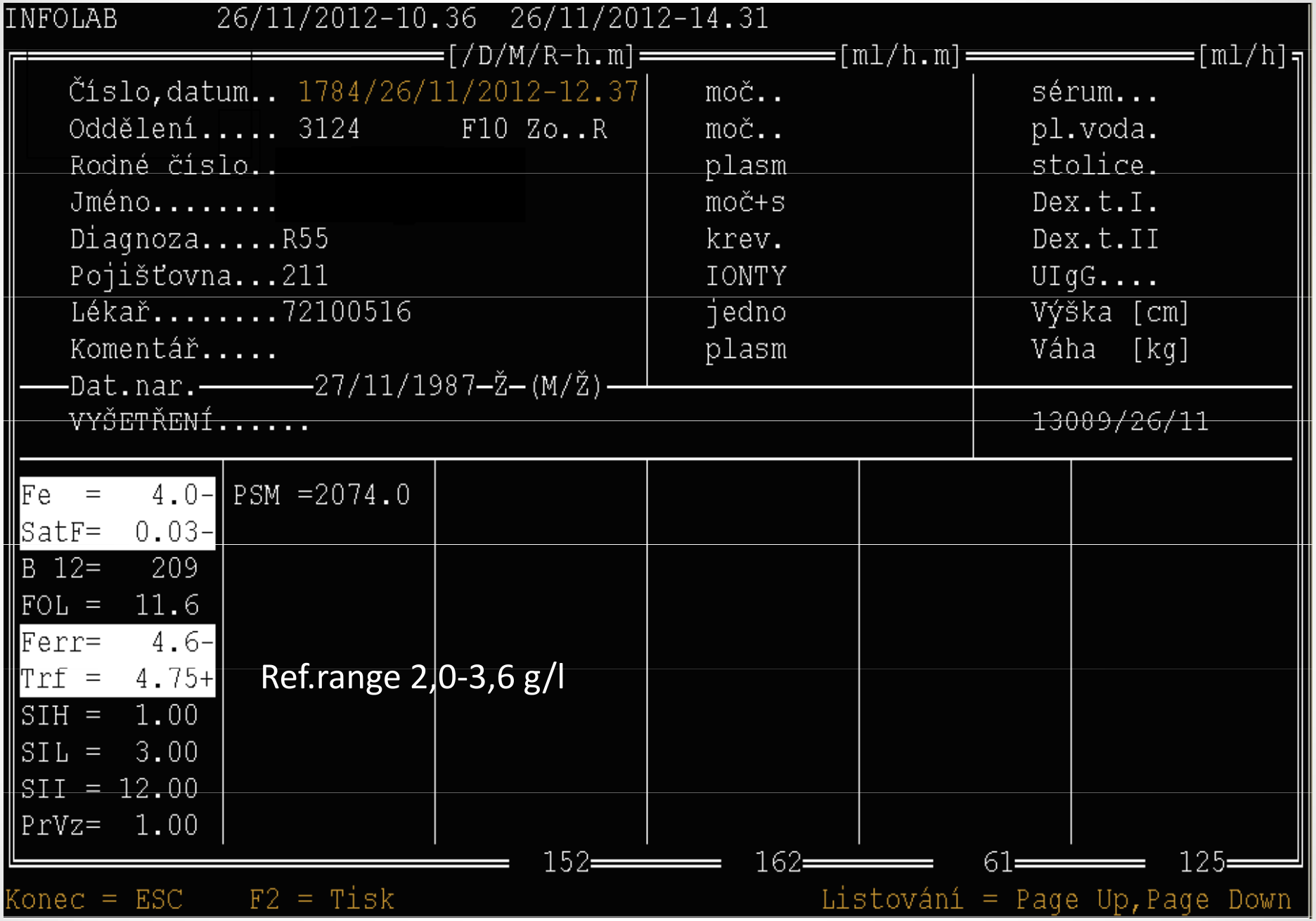
Genotyp MZ decrease to 40-60% activity
Genotyp ZZ – decrease to 15% of normal concentration

Ref.range 0,9-2,0 g/l

Transferrin

- can bind two atoms of iron (Fe 3 +), the transport protein for iron
- Increase -lack of iron in the body (with no increase in malnutrition)
- Decrease- excess body iron (hemosiderosis, hemochromatosis,impaired protein synthesis

  Carbohydrat-deficient transferrin - transferrin with a reduced proportion of sugar components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Oddělení..... 3124 F10 Zo..R
Rodné číslo..
Jméno.....
Diagnoza.....R55
Pojišťovna...211
Lékař.....72100516
Komentář.....
Dat.nar. 27/11/1987-Ž-(M/Ž)
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moč..
plasm
moč+s
krev.
IONTY
jedno
plasm
sérum...
pl.voda.
stolice.
Dex.t.I.
Dex.t.II
UIgG....
Výška [cm]
Váha [kg]
13089/26/11
Fe = 4.0-
SatF= 0.03-
B 12= 209
FOL = 11.6
Ferr= 4.6-
Trf = 4.75+
SIH = 1.00
SIL = 3.00
SII = 12.00
PrVz= 1.00
PSM =2074.0
Ref.range 2,0-3,6 g/l
152
162
61
125
Konec = ESC F2 = Tisk
Listování = Page Up,Page Down

Haptoglobin

- Haptoglobin binds very tightly hemoglobin molecule, the resulting complex is rapidly cleared from the circulation

- Reducing the oxidative potential of free hemoglobin
- Anti-inflammatory effects (inhibition of chemotaxis, phagocytosis ...)

  Increase: acute inflammation
  Decrease:intravascular haemolysis

INFOLAB 26/11/2012- 9.01 26/11/2012-14.31

[/D/M/R-h.m] [ml/h.m] [ml/h]

Číslo,datum.. 1729/26/11/2012-12.01	moč..	sérum...
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Rodné číslo.	plasm	stolice.
Jméno.....	moč+s	Dex.t.I.
Diagnoza.....D580	krev.	Dex.t.II
Pojišťovna...211	IONTY	UIgG....
Lékař.....72100653	jedno	Výška [cm]
Komentář.....	plasm	Váha [kg]
Dat.nar. 5/10/2010-M-(M/Ž)		
VYŠETŘENÍ.....		12960/26/11

Urea= 3.3	SIL = 19.00
Krea= 29	SII = 27.00+
KM = 182	PrVz= 1.00
BilT= 17.4	AKR =* Metod
ALT = 0.32	PSM =950.00
AST = 0.68+	
LD = 5.62+	
Ferr= 34.1	
Hpl =< 0.03	
SIH = 15.00	

Ref. range 0,3-2,0 g/l

106 38 125

Konec = ESC F2 = Tisk Listování = Page Up,Page Down

Ceruloplasmin

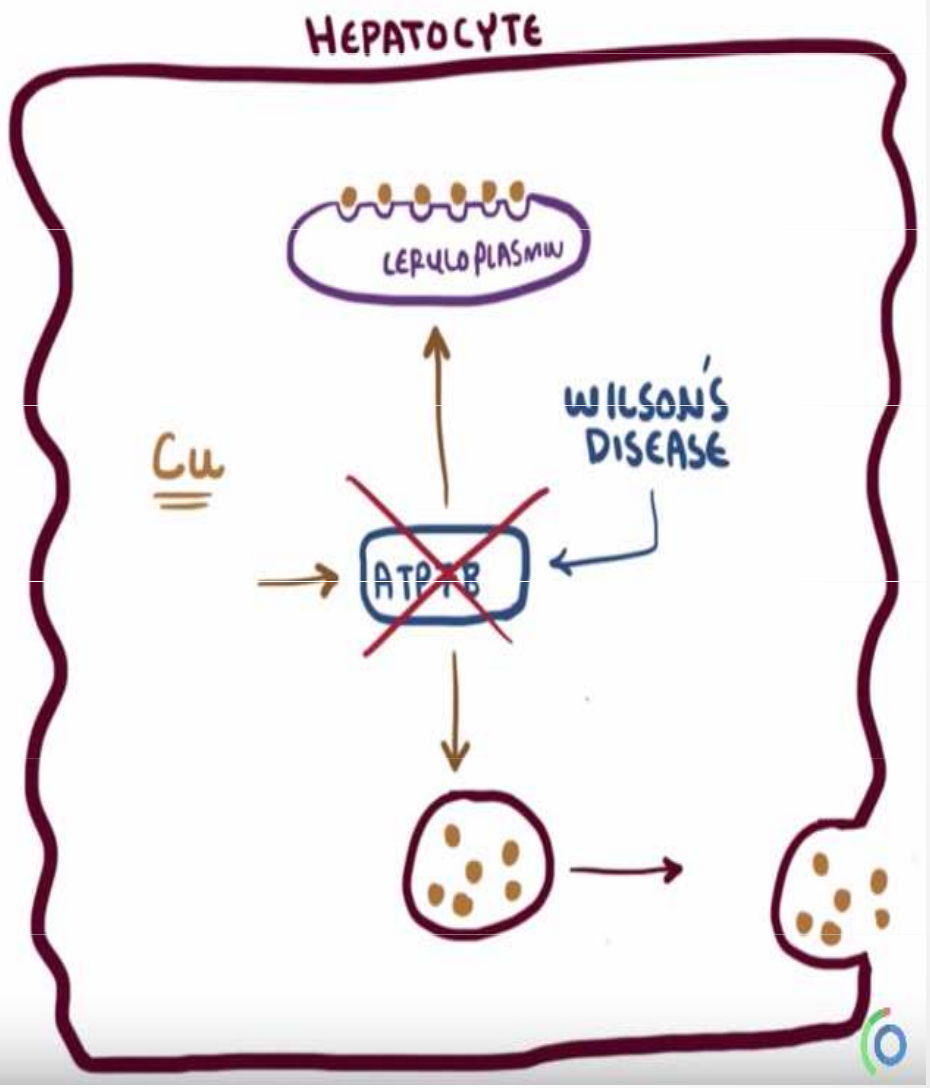
- 6-8 atoms of copper (Cu)
- Transport of copper
- Ferroxidase activity - Fe^{2+} Fe^{3+}
- Antioxidative effect

- Increase: inflammation, gravidity
- Decrease: Wilson disease

WILSON'S DISEASE

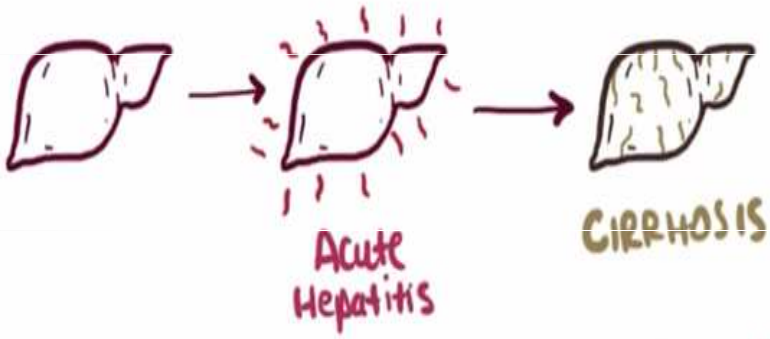
ATP7B

1. BIND Cu to APOCERULOPLASMIN
   - ↳ Cu-carrying protein
2. Package into vesicles for exocytosis to BILE



WILSON'S DISEASE

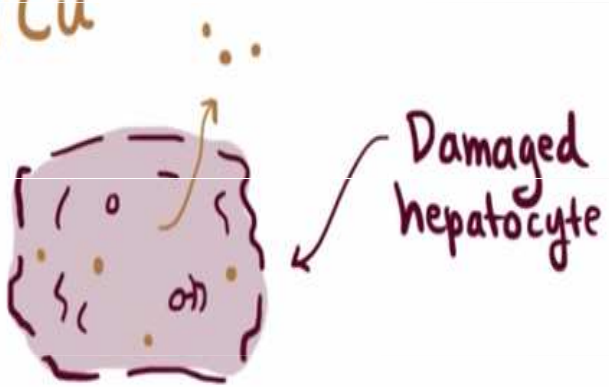
LIVER DAMAGE



- symptoms ~ late childhood

BLOOD

1. ↓ ceruloplasmin
2. ↑ Cu



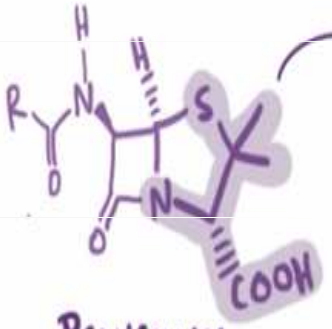
URINE

1. ↑ Cu

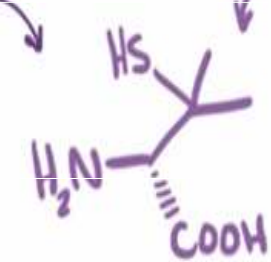
WILSON'S DISEASE

TREATMENTS

PENICILLAMINE



PENICILLIN



- No antibiotic properties
- copper-chelating agent

ZINC + Ammonium tetrathionolybdate

↓ Cu reabsorption

Cu — Penicillamine → EXCRETE in URINE

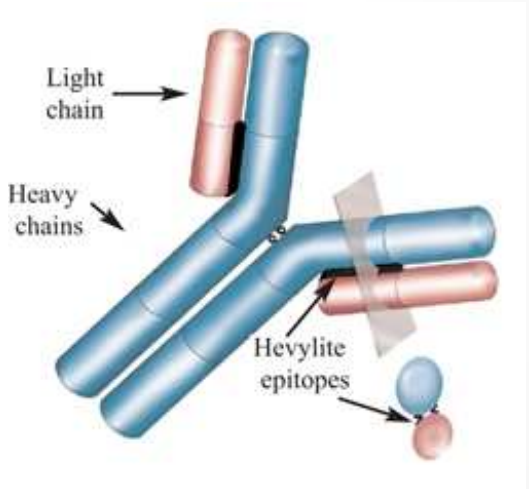
LIVER TRANSPLANT

Imunoglobulines

Secretion product of differentiated plasma cells

Composition 2 heavy (H) and 2 light chains (L)
Types of light chains kappa, lambda

Class (isotype) IgG, A, M, D, E
Part constant, part variable

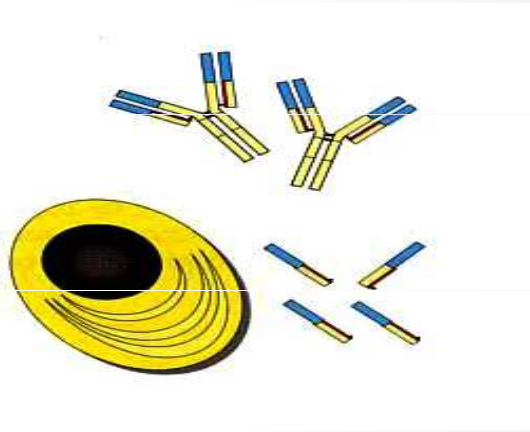


Polyclonal immunoglobulins
different idiotypes

Monoclonal immunoglobulin
product of one plasma cell clone
the same isotype and idiotype
a molecule of the same physical and chemical properties

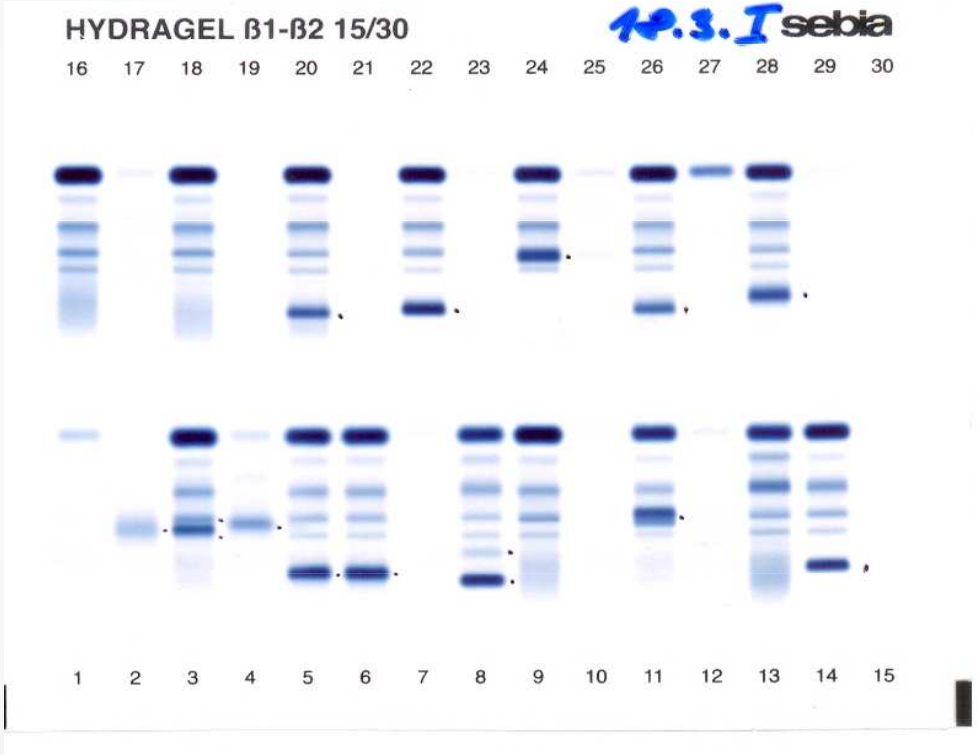
Monoclonal gammopathies

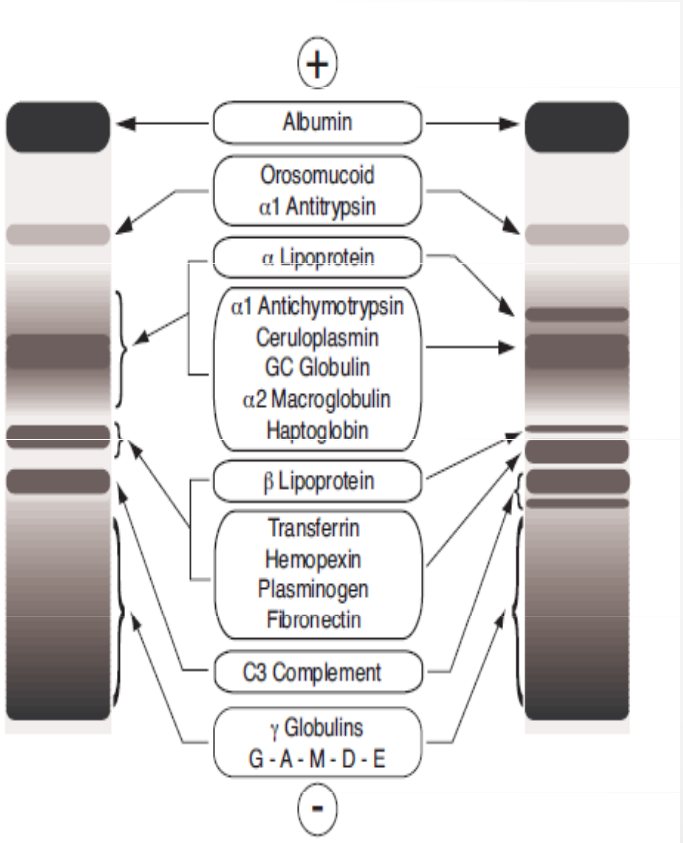
- Malignant monoclonal gammopathies
  - Multiple myeloma
  - Morbus Waldenström
  - Amyloidosis



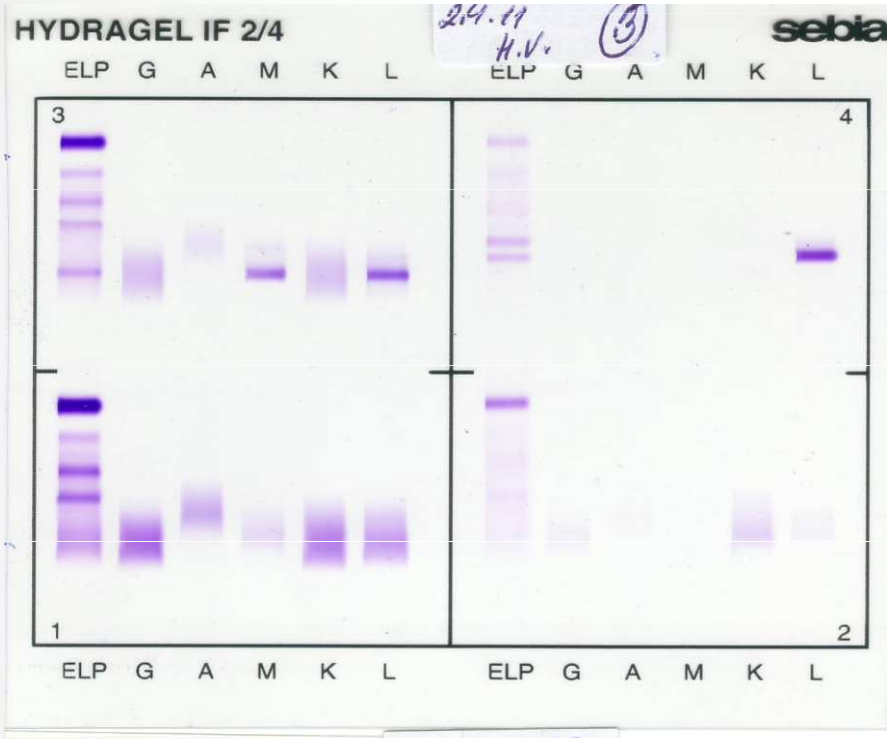
- Monoclonal gammopathies of undetermined significance (MGUS)

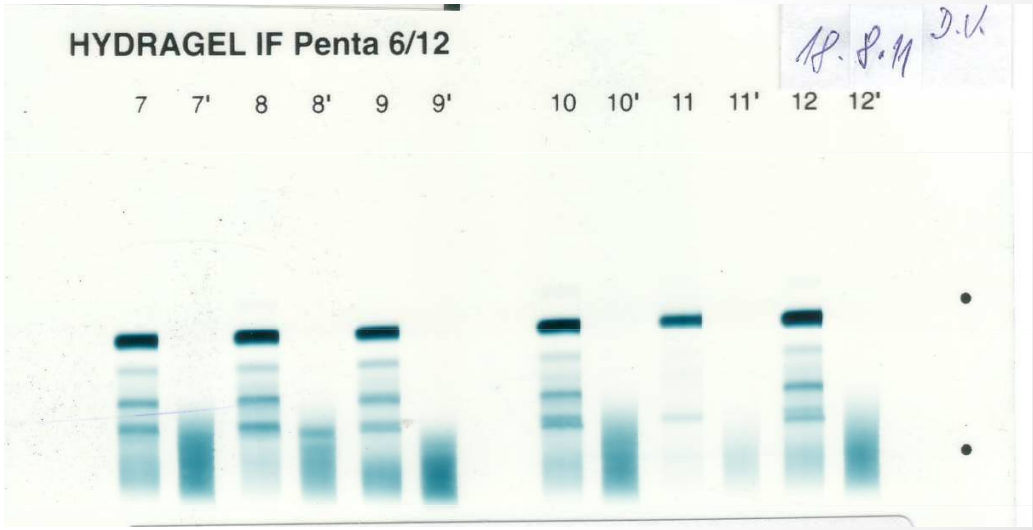
ELFO serum and urine





Elektroforesis with immunofixation

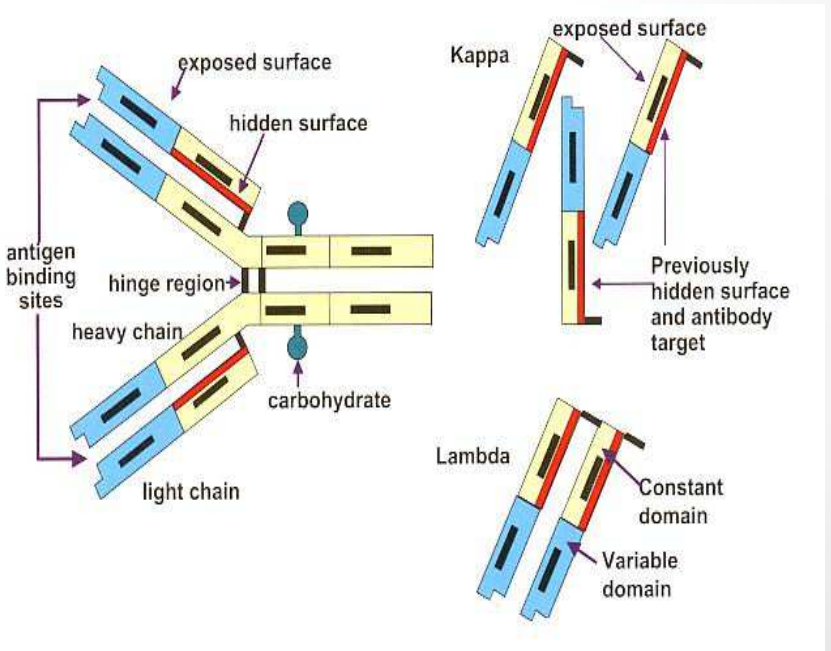




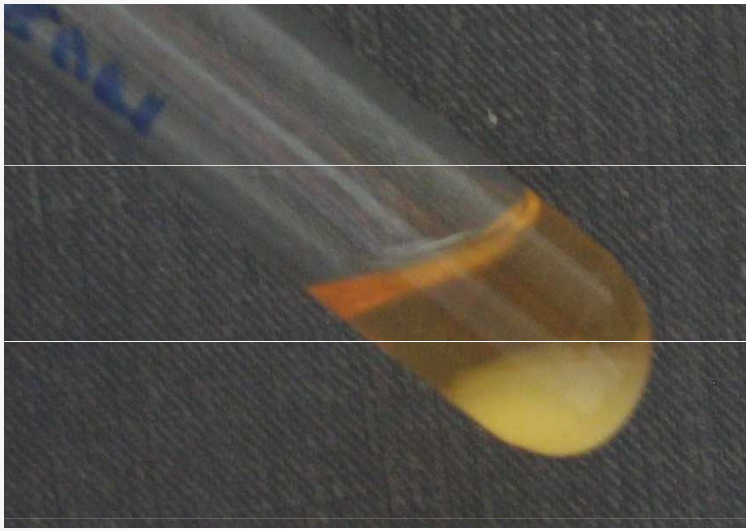
Free light chains

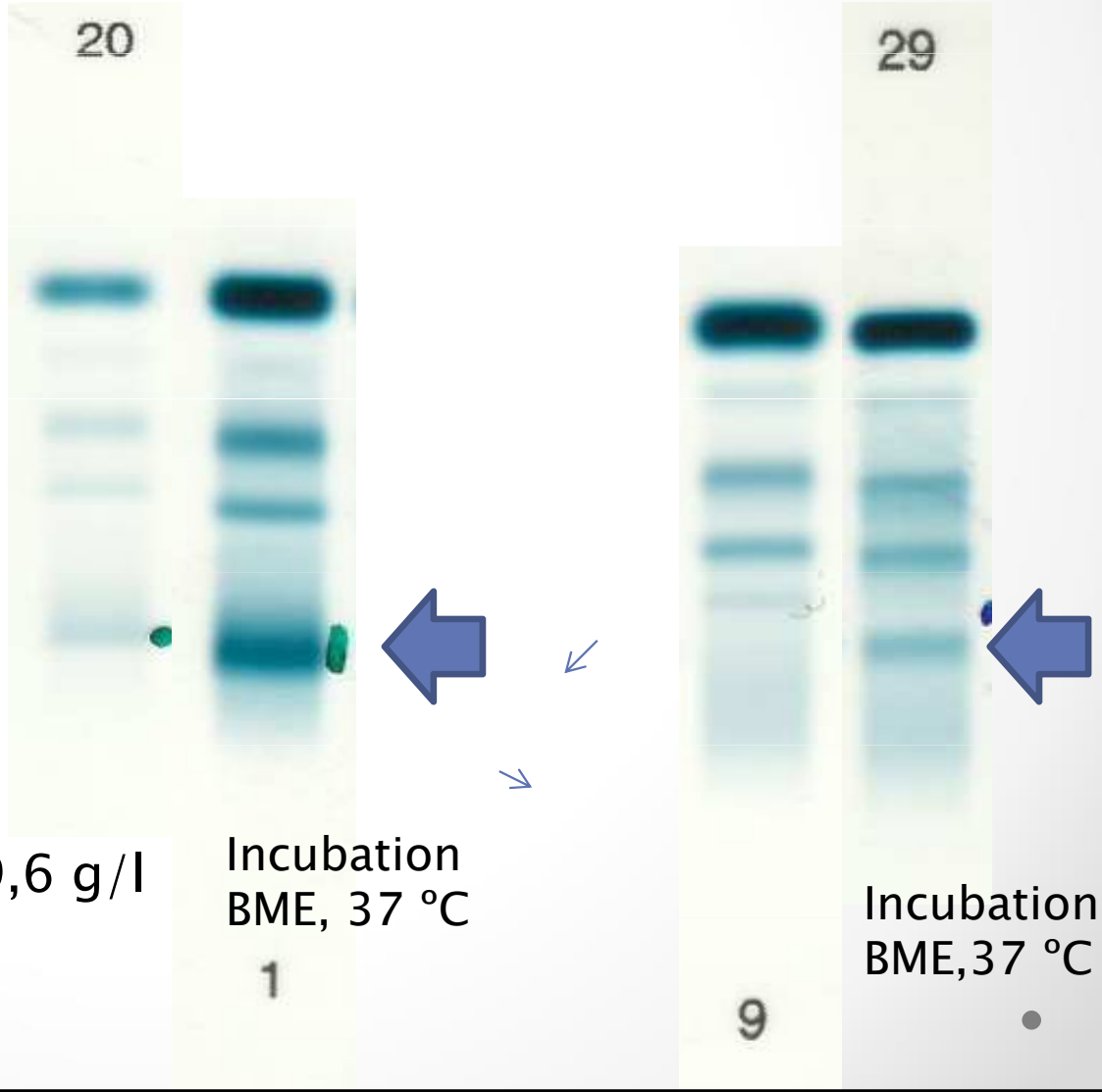
- Set FreeLite firmy BindingSite
- Analyzer IMMAGE 800 (Beckman Coulter) imunoturbidimetrie (NIPIA)
- antibodies are directed against internal epitopes light chains, which are hidden in the complete molecule

- Kappa free 3,3-19,4mg/l
- Lambda free 5,7-26,3 mg/l
- ratio κ/λ 0,26-1,65



Cryoprecipitation





CB=89,6 g/l

Incubation
BME, 37 °C

Incubation
BME,37 °C

Anamnesis

- Male 60 y.o.
- 7 months back pain, pain in ribs, even during inhalation – diagnosed as Tietze syndrome, classification of pain VAS 6-7, increased back pain, common analgesics with no effect, Doreta (paracetamol+tramadol) with partial effect, additionally strong fatigue
- Is treated for hypertension
- FA: Prestarium

Laboratory results

Parametes	14.7.201	30.7.2015	Units
S-urea	7,9	9,8	mmol/l
S-creatinine	128	153	umol/l
S-uric acid	499	446	umol/l
S-CRP	3,8		mg/l
S-TP		71	g/l
S-beta2microglobuline		4,38	mg/l
S-Ca		2,65	mmol/l
U-CB		2,95	g/l
Urine sediment	protein 1		arb.j.
CBC			
Erythrocytes (RBCs)	$3,46*10^{12}$	3,23	l
Hemoglobin	124	106	g/l
Hematocrit	0,33	0,3	
Leukocytes (WBCs)	$7,4*10^{9}$	9,14	l
Lymphocytes	35,80%	30,8	%
Granulocytes	54,90%	58,6	%
Thrombocytes	$335*10^{9}$	366	l
Sedimentation FW	30/50		

- Increased retention of nitrogen in serum
- Hypercalcemia

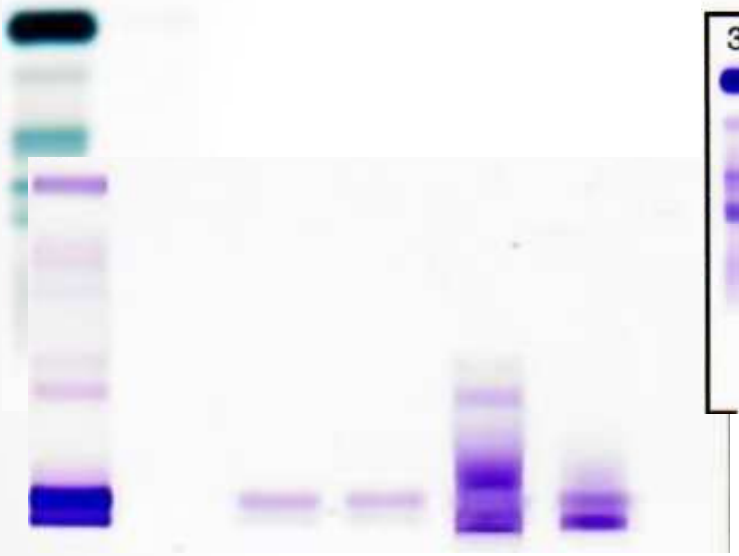
- Discrepant finding of protein in urine
  - quantitatively significant proteinuria
  - Semi-qualitatively with dry chemistry strips +1 (detects albumin only)
- Progression of anemia

Next steps?

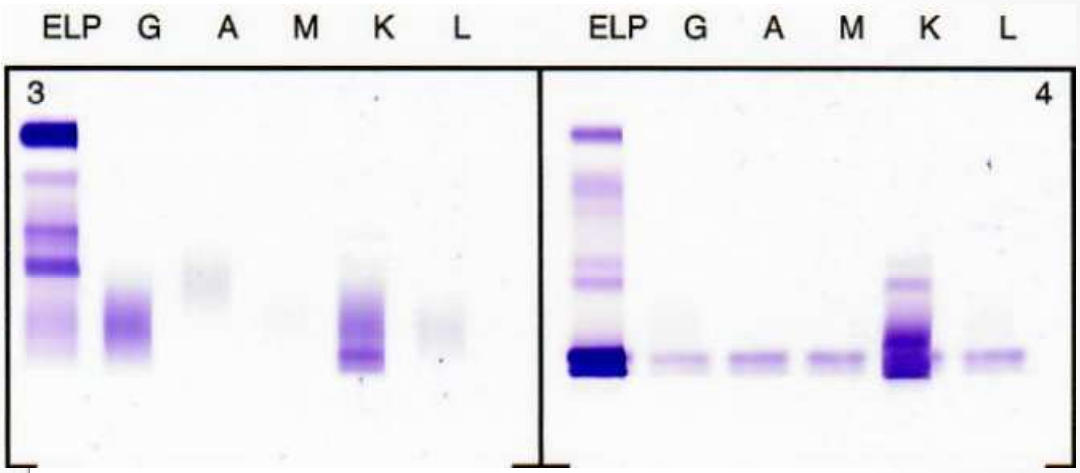
Laboratory results

Electrophoresis

serum urine



Immunofixation – serum



Immunofixation urine

S-ifix: positive FLC κ in serum
U-ifix: FLC κ 2.9g/24 hours

FLC κ kvant. in serum> 18000 mg/l (3.3-19.4 g/l)
FLC ʎ kvant. in serum 1.0 mg/l (5.7-26.3 mg/l)

IgD IgE κ celk.

κfree

More examinations

- **RTG of skeleton**
  - Multiple lytic deposits in skull skeleton, both claviculae, humeri, scapulae, bilateral ribs, in smaller scale both femura
- **Trepanobiopsy**
  - Massive infiltration of plasmatic cells with pathologic morphology, reduction of granulopoesis

Final diagnosis – therapy, monitoring

- **Multiple myeloma III A (DS)**
- Symptomatic – anemia, hypercalcemia, impending renal damage

Therapy:

6 cycles CHT (effect – reached VGPR- very good partial response – more than 90% decrease in FLC urine excretion in 24 hours)

1. Autologous transplantation – CR (complete remission) – no monoclonal protein in serum or urine and normalization of FLC in serum