


Schieleho nahota - biomarkery sepsy, operace a imunosuprese



Antonín Jabor, Janka Franeková, Marek Protuš,
Eva Kieslichová, Aleš Březina,
Institut klinické a experimentální medicíny, Praha



Why English texts?

- Some of our speakers understand Hungarian,



- some understand Czech, some Slovak...

- **...but everybody understands English!**

Why nudes by Schiele?

- Biomarkers of sepsis are dressed
- Let's make them nude!

- How?
- Let's try to reveal their strong and weak points

Why Egon Schiele?

Španělská chřipka

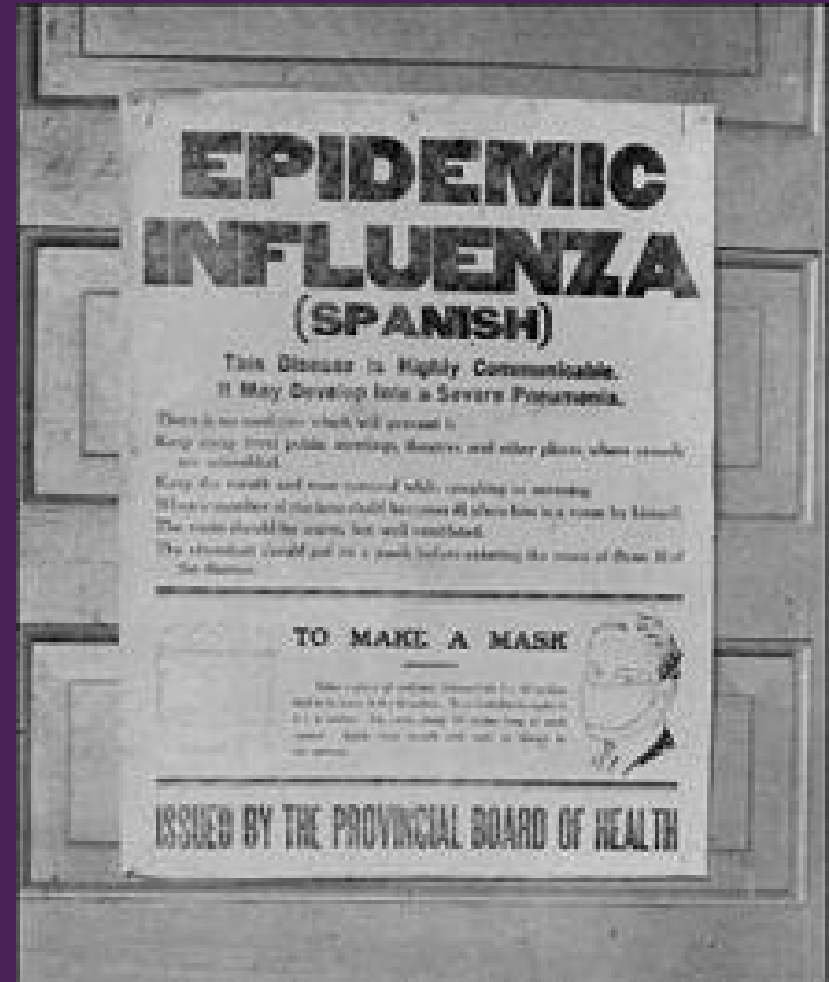
1918 – 1920

50 až 100 milionů

obětí

většinou ve věku

20 – 40 let



Presepsin



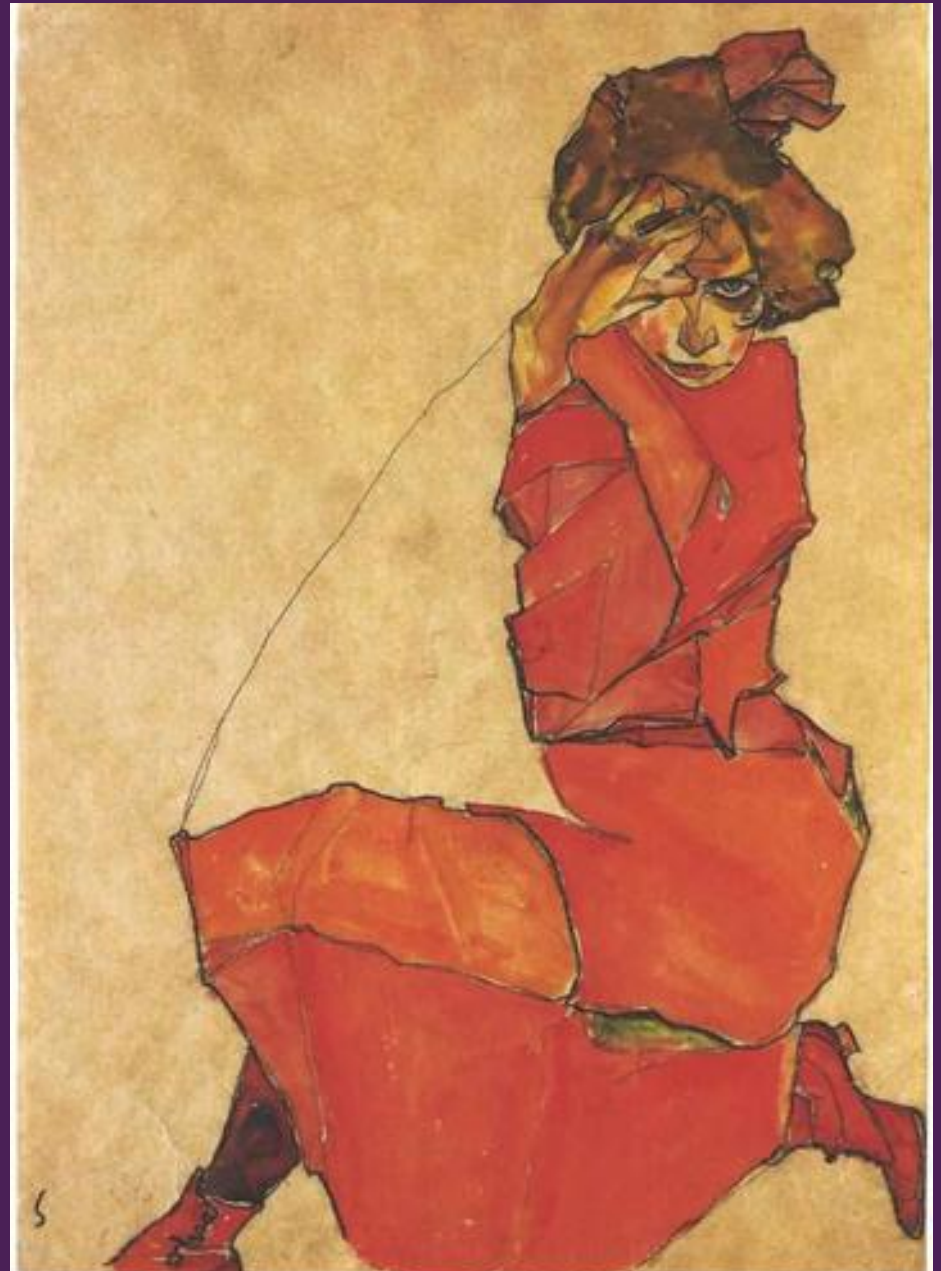
IL-6 and CRP



Procalcitonin

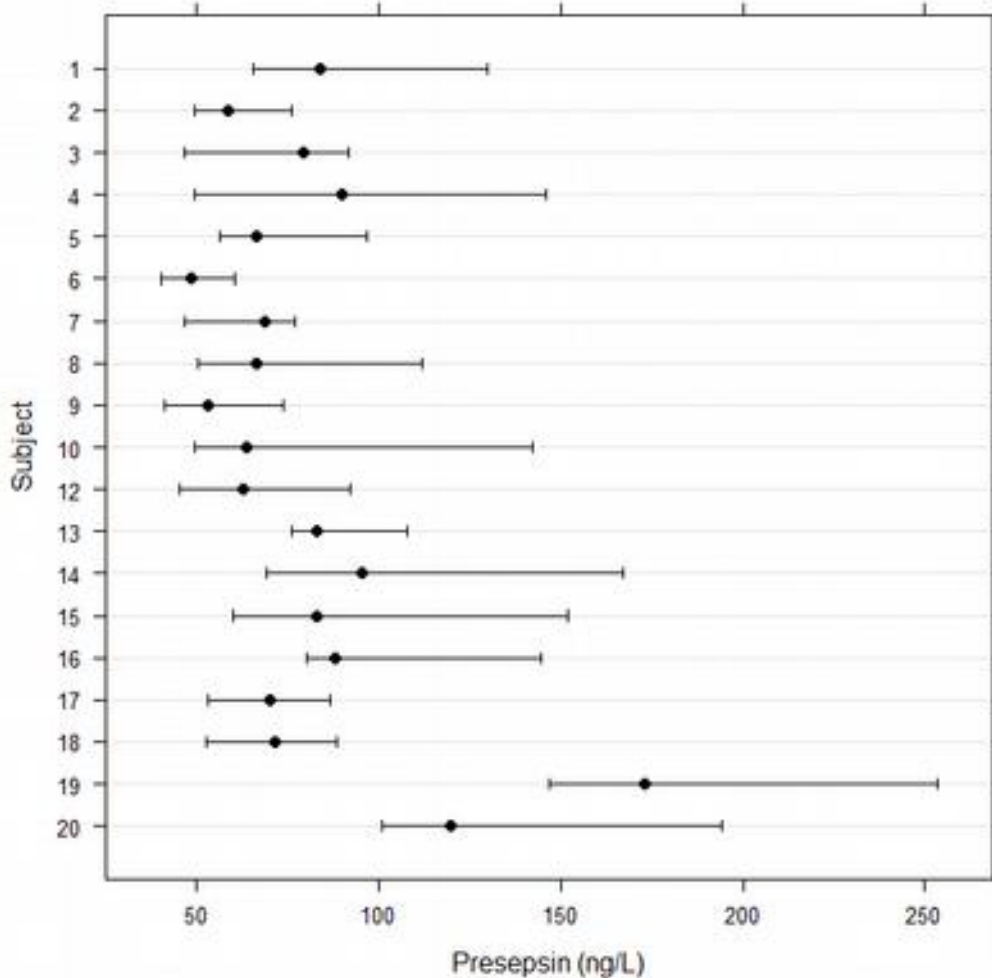


Leukocytes



Part I

- Biological variation (presepsin and IL-6)
 - CV_I
 - CV_G
 - Index of individuality
 - Reference change value (critical difference)
 - ... and reference range



Presepsin - biological variation

Within-subject

CV_I 22%

Between-subject

CV_G 21%

Index of individuality

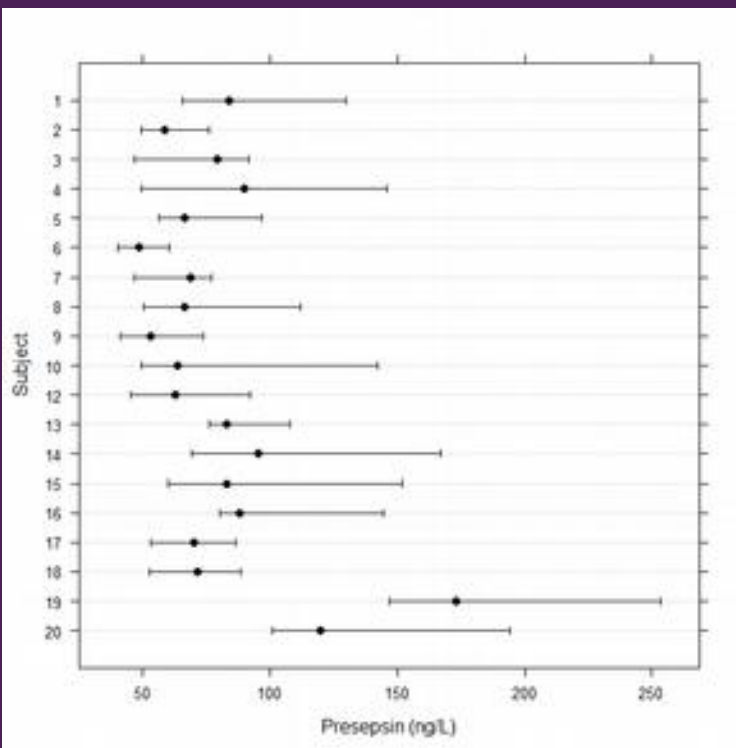
II 1.1

Reference change value

RCV 70%

Experiment - healthy subjects
 6-week experiment, 20 subjects
 Total of 20*7=140 values





Presepsin - healthy subjects

Within-subject

CV_i 22%

Between-subject

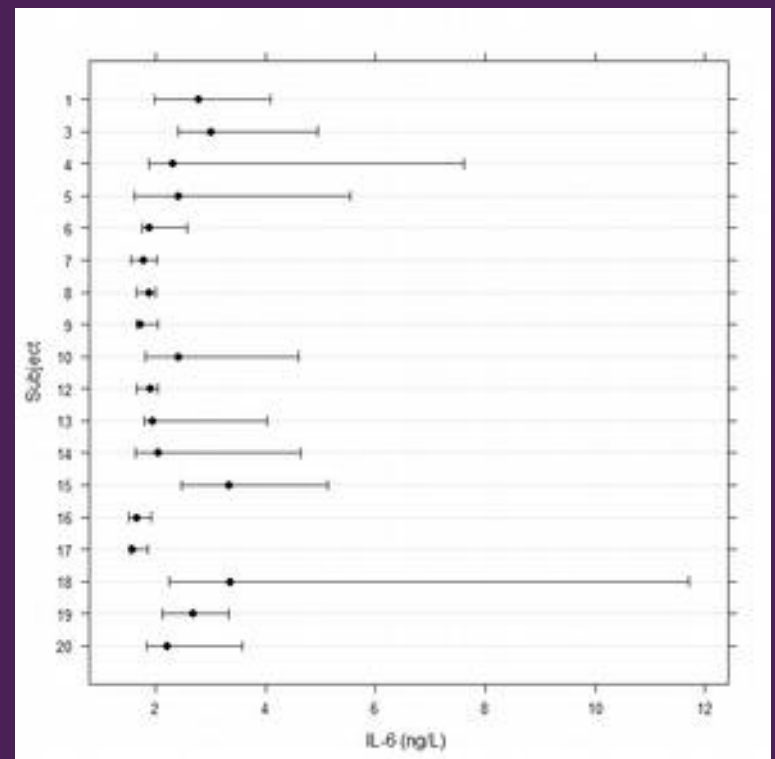
CV_G 21%

Index of individuality

II 1,1

Reference change value

RCV 70%



IL-6 - healthy subjects

Within-subject

CV_i 40%

Between-subject

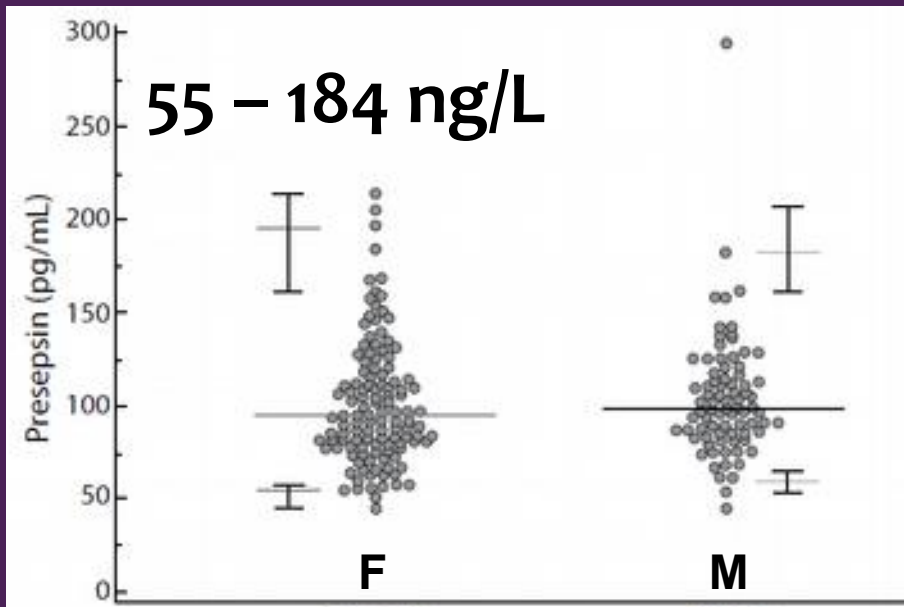
CV_G 18%

Index of individuality

II 2,2

Reference change value

RCV 111%



Giavarina, 2015

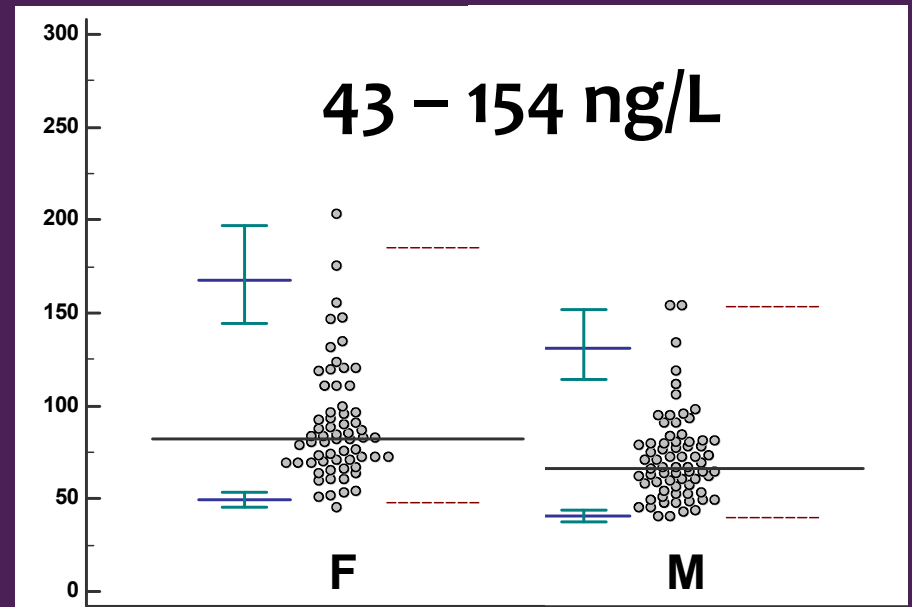
Left: females (N=120)

Right: males (N=80)

(CLSI C28-A3c)



„The upper reference limit for the presepsin is much lower than every cut-off limit so far proposed, both for sepsis and also for systemic inflammatory response syndrome.“



IKEM

Left: females (N=9*7)

Right: males (N=10*7)

(CLSI C28-A3)



„Maybe even lower!“

Good news! Dynamic range between „normals“ and „pathology“ increases.

Part I – Conclusions for presepsin

- ❑ RCV of 70% means that the increase (or decrease) of approx. 2/3 of previous value is significant
- ❑ reference intervals (<200 ng/l) of presepsin are lower in Caucasian population and increased sensitivity can be expected



Part II

□ Postoperative SIRS

- presepsin
- PCT
- CRP
- leukocytes
- IL-6

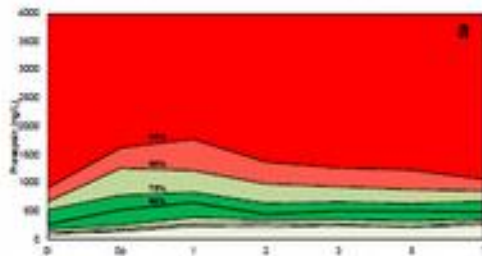
Cohort of patients

- a group of **86** consecutive patients
- major abdominal and chest surgery
- no signs of infection or sepsis up to 10 days post surgery, survival at least 30 days
- without immunosuppression therapy
- blood samples taken before surgery, +3 hours, +1, +2, +3, +5, +7 days

Cohort of patients – Major surgery

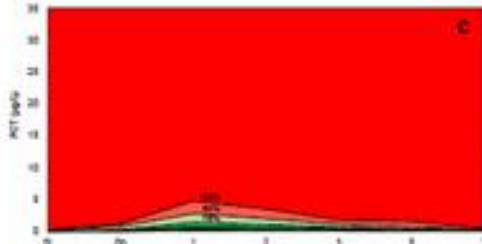
	Major surgery (N=86) Median (IQR) or N (%)
Age (years)	65.5 (59.0 – 73.0)
Men (N, %)	51 (59%)
APACHE II	9 (6.0 – 13.0)
Length of surgery (min)	230 (185 – 295)
Blood loss (mL)	200 (100 – 600)
Length of stay (days)	9.0 (7.0 – 12.0)
Without any infection up to 7 days (N, %)	86 (100%)
Without any infection up to 10 days (N, %)	84 (98%)
Without any infection till discharge (N, %)	81 (94%)

Non-Tx patients



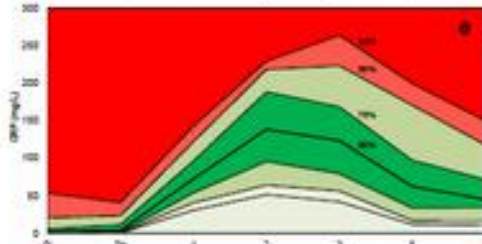
Presepsin

peak: 1st day
95% of values up to
1368 ng/L



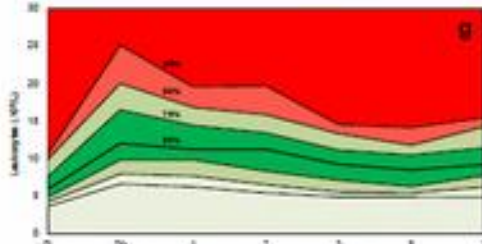
PCT

peak: 1st day
95% of values up to
3.49 μ g/L



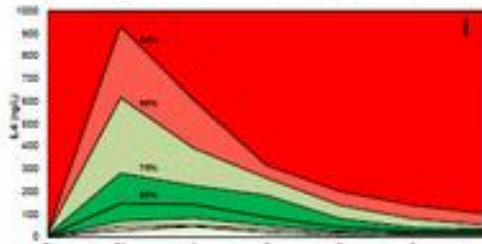
CRP

peak: 3rd day
95% of values up to
229 mg/L



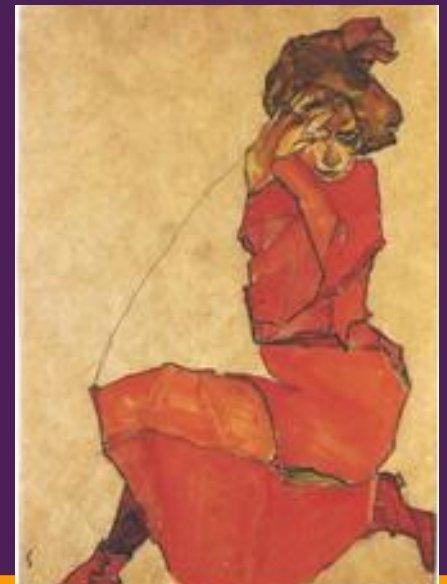
Leukocytes

peak: +3 hours
95% of values up to
22,9 $\cdot 10^9$ /L



IL-6

peak: +3 hours
95% of values up to
317 ng/L



Part II - Conclusions

- SIRS significantly increases all biomarkers
- now we know „reference limits“
- biomarkers are different in terms of
 - peaks
 - multiplies of an increase
 - rate of normalization
- presepsin
 - in „normals“ up to 200 ng/L
 - in SIRS 250 – 1 000 ng/L (major surgery!)

Part III

- Postoperative SIRS, transplantation and immunosuppression
 - presepsin
 - PCT
 - CRP
 - leukocytes
 - IL-6

Cohort of patients

- a group of **54** consecutive patients
- Tx of kidney, liver, pancreas (+kidney)
- no signs of infection or sepsis up to 10 days post Tx, survival at least 30 days, no organ rejection
- induction immunosuppression during surgery (antithymocyte globuline, ATG; or corticosteroids; or basiliximab/rituximab)
- combined maintenance immunosuppression
 - tacrolimus
 - prednisone
 - mycophenolate mofetil
- blood samples taken before Tx, +3 hours, +1, +2, +3, +5, +7 days

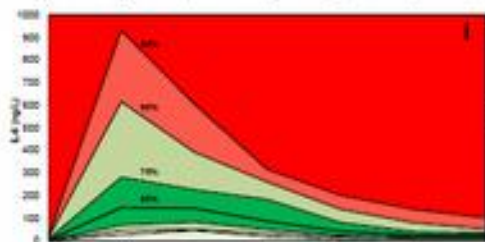
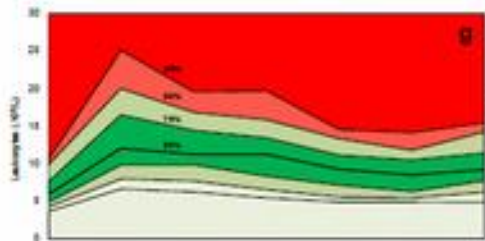
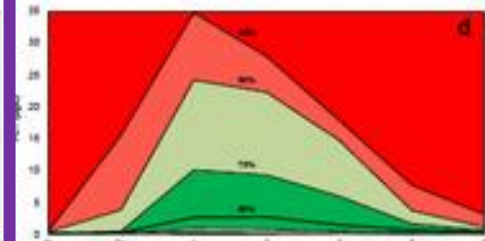
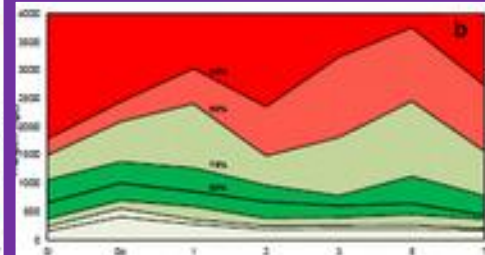
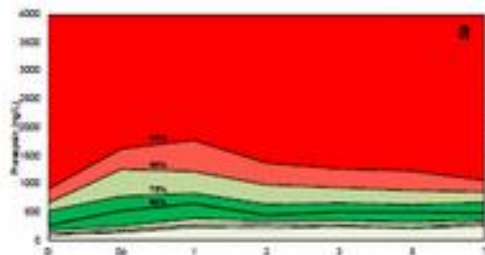
Cohort of patients – Transplantation

	Transplantation (N=54) Median (IQR) or N (%)
Age (years)	54.5 (43.0 – 65.0)*
Men (N, %)	39 (72%)
APACHE II	13 (10.0 – 15.0)*
Length of surgery (min)	190 (160 – 270)*
Blood loss (mL)	200 (100 – 500)
Length of stay (days)	13.0 (11.0 – 15.0)
Without any infection up to 7 days (N, %)	54 (100%)
Without any infection up to 10 days (N, %)	53 (98%)
Without any infection till discharge (N, %)	46 (85%)

* different from non-Tx group; these Tx patients were younger, with higher APACHE II and shorter surgery time

Non-Tx patients

Tx patients



Higher presepsin

Higher PCT

Lower CRP

Comparable leukocytes

Lower IL-6

Transplanted patients in comparison to major non-Tx surgery

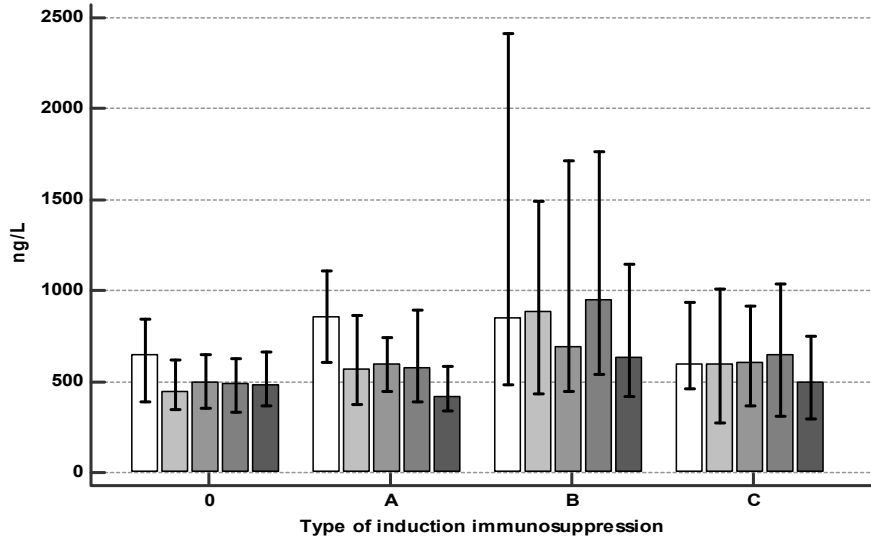
Kidney, liver, pancreas
N=54

No signs of infection or sepsis up to 10 days after surgery

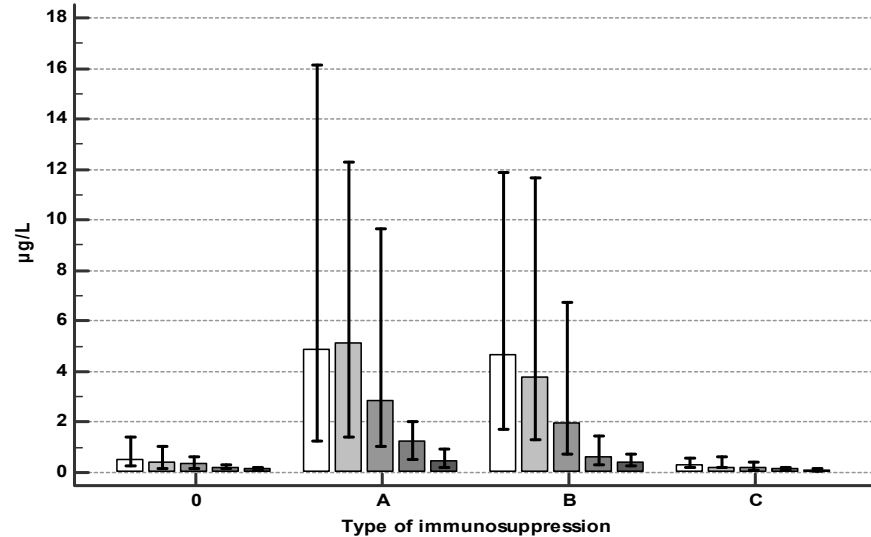
Survival at least 30 days
No organ rejection

Samples: before, +3h, +1,+2,+3,+5,+7 days

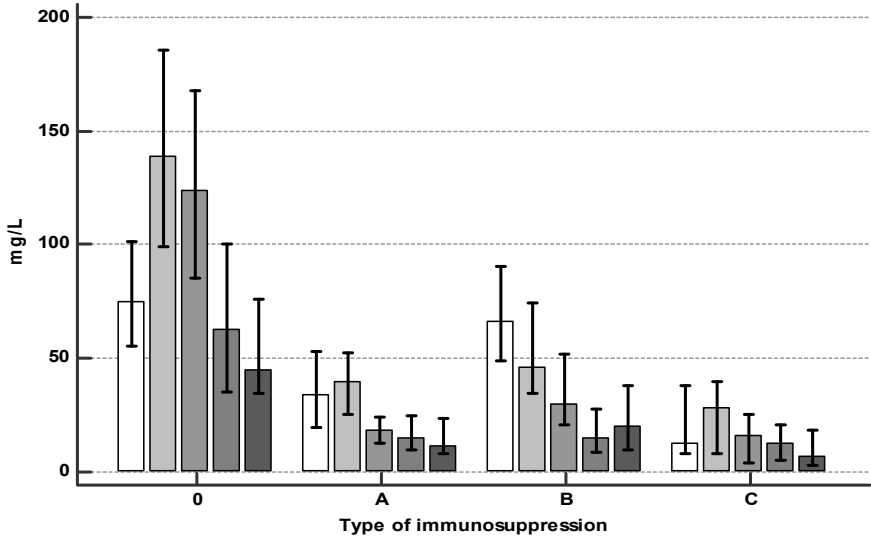
Presepsin (Days 1, 2, 3, 5, 7)



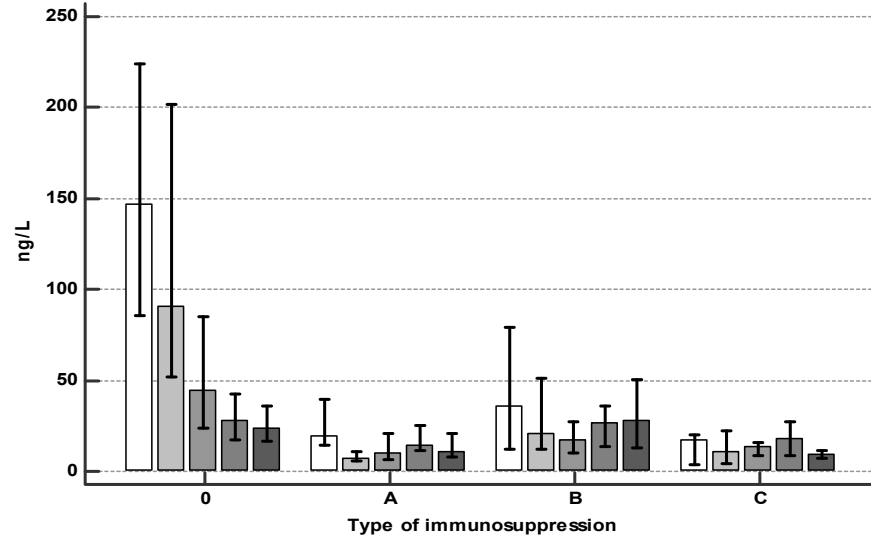
PCT (Day 1, 2, 3, 5, 7)



CRP (Day 1, 2, 3, 5, 7)



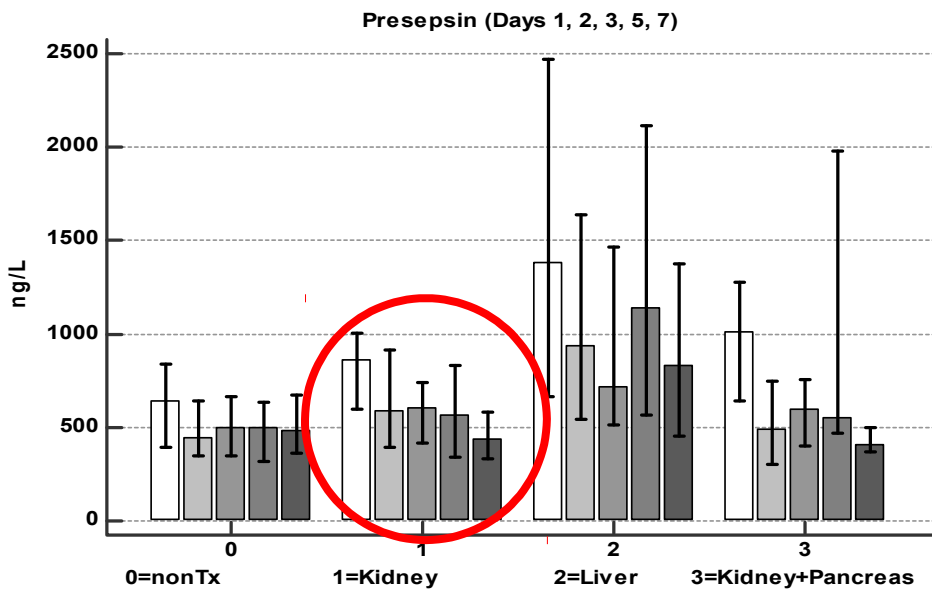
IL-6 (Day 1, 2, 3, 5, 7)



none ATG Corticoids Bmab/Rmab

none ATG Corticoids Bmab/Rmab

ATG: antithymocyte globulin, Bmab/Rmab: basiliximab/rituximab



Navzdory literárním údajům nebyl presepsin významně ovlivněn po Tx ledviny

(ale byl vyšší po Tx jater – starší pacienti, vyšší APACHE II, delší výkon, větší krevní ztráty)

Part III - Conclusions

- completely different changes in biomarkers in Tx patients
- the probable reason is immunosuppression
- presepsin is less influenced by immunosuppression
- PCT is increased by ATG and corticosteroid induction
- CRP and IL-6 are decreased by all types of immunosuppression

Conclusions

Presepsin

- cut-off 1100 ng/L for all time points (1st – 10th Day)
- lower reference limits (<200 ng/l)
- medium-size biological variation
- minimal influence of immunosuppressant therapy
- surprisingly not influenced after kidney Tx
- higher values after liver Tx

Conclusions

Procalcitonin

- cut-offs depend on postoperative day
- influenced by ATG and corticosteroids

Conclusions

CRP

- cut-offs depend on postoperative day
- significantly decreased by immunosuppression

IL-6

- cut-offs depend on postoperative day
- significantly decreased by immunosuppression

Conclusions

Multimarker strategy in a clinical context

Monitoring

Specific interpretative zones

- **time**
- **treatment**
- **renal function**
- **type of surgery**
- **clinical complications**
- **etc.**

A multimarker strategy: at least two nude biomarkers



**But
sometimes
three nude
biomarkers
are better**



Thank you, Mr. Egon Schiele.



1890 - 1918



Selfportrait 1912