Procalcitonin kinetics guided antibiotic management of the critically ill patient

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19/11/2016, XXXVII Turkish Congress of Microbiology
Epidemiology of sepsis

- Sepsis has severe impact on all health care
- Rates increased in USA between 2004-2009:

Improvement in sepsis

- Mortality results are decreasing
- Recognition of sepsis is increasing
- Novel interventions
- New pharmacotherapeutical strategies
- Surviving Sepsis Campaign
What is sepsis?
Sepsis is not a definitive diagnosis

• “Sepsis-syndrome” and Las Vegas - 1980:
  • Fever or hypothermia (> 38.3°C or < 35.0 °C)
  • Tachycardia (>90/min)
  • Leukocytosis or leukopenia (> 12 000cells/mm³, < 4000cells/mm³, or > 10% immature forms)
  • Hypotension (<90mmHg)
Sepsis is not a definitive diagnosis

• “Sepsis-syndrome” and Las Vegas - 1980:
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  • Tachycardia (>90/min)
  • Leukocytosis or leukopenia (> 12 000cells/mm³, < 4000cells/mm³, or > 10% immature forms)
  • Hypotension (<90mmHg)

Sepsis syndrome: A valid clinical entity

ROGER C. BONE, MD; CHARLES J. FISHER, JR, MD; TERRY P. CLEMMER, MD; GUS J. SLOTMAN, MD; CRAIG A. METZ, MS; ROBERT A. BALK, MD: THE MethylPREDNISOLONE SEVERE SEPSIS STUDY GROUP*
Sepsis is not a definitive diagnosis

- Consensus conference ACCP/SCCM:
  - Infection
  - Bacteraemia
  - Systemic inflammatory response syndrome (SIRS)
  - Sepsis = SIRS + Infection
  - Severe sepsis (Sepsis + one organ dysfunction)
  - Septic shock (hypoperfusion despite adequate fluid load)
  - Multiple System Organ Failure (MSOF)

ACCP/SCCM. Crit Care Med 1992; 20: 864
Sepsis definitions: time for change

Jean-Louis Vincent, Steven M Opal, John C Marshall, Kevin J Tracey

*Lancet* 2013; 381: 774-75

<table>
<thead>
<tr>
<th>Infection, documented or suspected, and some of the following:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General variables</strong></td>
</tr>
<tr>
<td>Fever (&gt;38.3°C)</td>
</tr>
<tr>
<td>Hypothermia (core temperature &lt;36°C)</td>
</tr>
<tr>
<td>Heart rate &gt;90/min or more than two x above the normal value for age</td>
</tr>
<tr>
<td>Tachypnea</td>
</tr>
<tr>
<td><strong>Plasma C-reactive protein</strong> more than two x above the normal value</td>
</tr>
<tr>
<td><strong>Plasma procalcitonin</strong> more than two x above the normal value</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hemodynamic variables</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypotension (MAP &lt;70 mm Hg) or SBP &lt;90 mm Hg or MAP &lt;70 mm Hg or SBP &lt;90 mm Hg or decreased cardiac output</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sepsis definitions: time for change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis is not a „disease” but a „consensus”</td>
</tr>
</tbody>
</table>
Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

Organ dysfunction can be identified as an acute change in total SOFA score ≥2 points consequent to the infection.

- The baseline SOFA score can be assumed to be zero in patients not known to have preexisting organ dysfunction.
- A SOFA score ≥2 reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection. Even patients presenting with modest dysfunction can deteriorate further, emphasizing the seriousness of this condition and the need for prompt and appropriate intervention, if not already being instituted.

- In lay terms, sepsis is a life-threatening condition that arises when the body’s response to an infection injures its own tissues and organs.
- Patients with suspected infection who are likely to have a prolonged ICU stay or to die in the hospital can be promptly identified at the bedside with qSOFA, i.e., alteration in mental status, systolic blood pressure ≤100 mm Hg, or respiratory rate ≥22/min.
- Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.

- Patients with septic shock can be identified with a clinical construct of sepsis with persisting hypotension requiring vaspressors to maintain MAP ≥65 mm Hg and having a serum lactate level >> mmol/L (≥8 mg/dL) despite adequate volume resuscitation. With these criteria, hospital mortality is in excess of 40%.
Pathomechanism
Pathomechanism

Insult
Endotoxin, Trauma, Sterile inflammation, Operation, etc.

Humoral activity
Interferon, Complement

Veno-venous haemofiltration in the treatment of sepsis and the multiple organ dysfunction syndrome

It isn't the insult, but host response what determines severity and outcome

“Except on few occasions, the patients seems to die from the body’s response to infection rather than from it.”

Sir William Osler; The Evolution of Modern Medicine 1904

Molnár and Shearer Br J Int Care Med 1998; 8: 12
DAMP = Damage Associated Molecular Pattern
PAMP = Pathogen Associated Molecular Pattern

„DAMP → SIRS“ versus „PAMP → SIRS“

- DAMP = Damage Associated Molecular Pattern
- PAMP = Pathogen Associated Molecular Pattern

Surgery, Trauma, Pancreatitis, Isch-reperf.

G+
G-
F

TLR2
Evolution
Mitochondrion

Tissue injury
Alteration of extracellular matrix
Necrotic cell
Inflammatory contents

ARN
ADN
Uric acid crystal
HMGB-1
High mobility group box

ATP
HSI
Heat shock
IL
Hyaluronan fragment
Heparan sulfate
Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy

Richard S. Hotchkiss¹, Guillaume Monneret² and Didier Payen³

Nature Reviews | Immunology Volume 13 | December 2013 | 862-874

Pro-inflammation

Anti-inflammation

Early deaths due to overwhelming inflammation

Late deaths due to intractable inflammation-induced organ injury
Overwhelming inflammation vs. prolonged immunosuppression: Both can be deadly!
Is this patient septic or not?
I have never treated „SEPSIS” in my life!
But…
Does the patient have *infection* or not?

Infection = ABs

No infection = No ABs
Signs of infection

• Clinical signs:
  • Most important

• Fever (>38°C), WBC (>12 000):
  • Low sensitivity (~50%)

Galicier L and Richet H. Infect Control Hosp

• Microbiology:
  • Results: 24 hours or more
Pathogen → PAMPs
Tissue Injury → DAMPs

Leucocyte, lymphocyte, endothelial cells, parenchymal cells
MBL, NOD protein, P substance

Dysregulated, generalized immune response

<table>
<thead>
<tr>
<th>Coagulation</th>
<th>Complement system</th>
<th>Cytokines and chemokines</th>
<th>Acute phase proteins</th>
<th>Stress hormones</th>
<th>Hormonkines</th>
<th>Cytoplasmatic factors</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN-γ</td>
<td>IL-2</td>
<td>IL-1β endothelin</td>
<td>α1-glycoprotein</td>
<td>ACTH</td>
<td>ADM</td>
<td>HS protein</td>
</tr>
<tr>
<td>IL-4</td>
<td>IL-5</td>
<td>IL-6 chemokines</td>
<td>Ferritin</td>
<td>AVP</td>
<td>CGRP</td>
<td>HMG-1</td>
</tr>
<tr>
<td>IL-7</td>
<td>IL-8</td>
<td>IL-11 elastase</td>
<td>Fibronectin</td>
<td>GH</td>
<td>IL-6</td>
<td>IL-8</td>
</tr>
<tr>
<td>IL-11</td>
<td>IL-12 growth factors</td>
<td>IL-6 chemokines</td>
<td>Haptoglobin</td>
<td>Cortisol</td>
<td>Leptin</td>
<td>Leptin</td>
</tr>
<tr>
<td>IL-16</td>
<td>IL-18 ETs</td>
<td>IL-10</td>
<td>LPS prot.</td>
<td>Proctolin</td>
<td>PCG</td>
<td>MIF</td>
</tr>
<tr>
<td>IL-23 NO</td>
<td>IL-16</td>
<td>IL-11</td>
<td>SAA</td>
<td>Histamine</td>
<td>PCG</td>
<td>NO</td>
</tr>
<tr>
<td>TNFα protease</td>
<td>IL-18</td>
<td>IL-12</td>
<td>CRP</td>
<td>Noradrenaline</td>
<td>PCG</td>
<td>NO</td>
</tr>
<tr>
<td>IFNγ FCs</td>
<td>IL-18RA</td>
<td>IL-13</td>
<td>IL-16</td>
<td>Adrenaline</td>
<td>PCG</td>
<td>NO</td>
</tr>
<tr>
<td>ROI</td>
<td>IL-1RA</td>
<td>IL-14</td>
<td>IL-23 NO</td>
<td>Endorphin</td>
<td>PG</td>
<td>NO</td>
</tr>
<tr>
<td>MIF</td>
<td>IL-4</td>
<td>IL-15</td>
<td>TNF</td>
<td></td>
<td>PCG</td>
<td>NO</td>
</tr>
<tr>
<td>TBS</td>
<td>IL-1β</td>
<td>IL-17</td>
<td></td>
<td></td>
<td>PCG</td>
<td>NO</td>
</tr>
</tbody>
</table>

Procalcitonin (PCT)

- CD16, CD14 expression
- increases leucocyte-derived cytokins
- effects leucocyte migration
- augments nitric-oxid secretion
**TABLE 1: Comparison of CRP versus PCT (advantages and disadvantages).**

<table>
<thead>
<tr>
<th>CRP</th>
<th>PCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Differentiating bacterial infection from SIRS</td>
<td>– [27]</td>
</tr>
<tr>
<td>Response to infection</td>
<td>Slower (days) [27]</td>
</tr>
<tr>
<td>Peak response after infection</td>
<td>2-3 days [27]</td>
</tr>
<tr>
<td>Half-life</td>
<td>Several days [27]</td>
</tr>
<tr>
<td>Plasma kinetic</td>
<td>Slow [27]</td>
</tr>
<tr>
<td>Price</td>
<td>+</td>
</tr>
<tr>
<td>Correlating disease severity and progression</td>
<td>Slightly [27]</td>
</tr>
<tr>
<td>Correlating effective therapy</td>
<td>+</td>
</tr>
<tr>
<td>Prognostic factor for mortality</td>
<td>Weak or nonexistent [27]</td>
</tr>
<tr>
<td>Differentiating G+ from G–</td>
<td>– [35]</td>
</tr>
<tr>
<td>Virus, autoimmune diseases, local infections, surgery, trauma [27]</td>
<td></td>
</tr>
<tr>
<td>Response to other factors</td>
<td></td>
</tr>
<tr>
<td>Fungal infection</td>
<td>same as bacterial [35]</td>
</tr>
<tr>
<td>Immunosuppression</td>
<td>Formation can be changed [27]</td>
</tr>
<tr>
<td>Biological effect</td>
<td>Opsonin for phagocytosis [27]</td>
</tr>
<tr>
<td>Sensitivity/specificity</td>
<td>Sensitive but nonspecific [27]</td>
</tr>
<tr>
<td>General use</td>
<td>Outpatient care [27]</td>
</tr>
</tbody>
</table>
Differential diagnostic value of procalcitonin in surgical and medical patients with septic shock

Medical patients:
- SIRS: PCT = 0.3 (0.1-1.0) ng/ml
- Septic shock: PCT = 8.4 (3.6-76.0) ng/ml

Surgical patients:
- SIRS: PCT = 5.7 (2.6-8.4) ng/ml
- Septic shock: PCT = 34 (7-76) ng/ml

Clec’h et al. *Crit Care Med* 2006; 34:102-107
In clinical practice

<table>
<thead>
<tr>
<th>61 years old male</th>
<th>47 years old female</th>
</tr>
</thead>
<tbody>
<tr>
<td>past medical history: unwell for 2 days, cough, yellowish sputum</td>
<td>past medical history: breast reconstruction surgery with free flap yesterday, feeling unwell</td>
</tr>
<tr>
<td>fever – yes: 38.6 °C</td>
<td>fever – yes: 38.1 °C</td>
</tr>
<tr>
<td>leucocytosis – no: WCC 4520/ml</td>
<td>leucocytosis – yes: WCC 13120/ml</td>
</tr>
<tr>
<td>organ failure – yes: respiratory</td>
<td>organ failure – no</td>
</tr>
<tr>
<td>PCT: 1.2 ng/ml</td>
<td>PCT: 3.7 ng/ml</td>
</tr>
</tbody>
</table>

Sepsis ≠ homogenous group of patients

*ie*

One size does not fit all
The diagnostic challenge

- **COLORFUL** manifestation

RECOGNISING THE SEPTIC PATIENT

- initiating supportive therapy
- decision making:
  - SIRS or sepsis?
- initiating proper antibiotics
Delay in antibiotic therapy

Optimal antibiotic treatment

- 30-60 % of antibiotics prescribed on ICUs are:
  - unnecessary
  - inappropriate
  - suboptimal

  Luyt CE et al. Crit Care, 2014

  ↓

- dissemination of antimicrobial-resistant microorganisms
Questions are

- Should we initiate antibiotic treatment?
- Is it an appropriate antibiotic?
- For how long should I administer the antibiotic?
PCT response to consequent infectious insults

Research Article

Delta Procalcitonin Is a Better Indicator of Infection Than Absolute Procalcitonin Values in Critically Ill Patients: A Prospective Observational Study

Domonkos Trásy, Krisztián Tánczos, Márton Németh, Péter Hankovszky, András Lovas, András Mikor, Edit Hajdú, Angelika Osztroluczki, János Fazakas, and Zsolt Molnár
ΔPCT as an indicator of infection

### Demographics of the investigation

<table>
<thead>
<tr>
<th>Condition</th>
<th>Total</th>
<th>NI-group</th>
<th>I-group</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever ((&lt;36^\circ\text{C}; &gt;38^\circ\text{C})</td>
<td>55 (48.2%)</td>
<td>13 (44.8%)</td>
<td>42 (49.4%)</td>
<td>0.670</td>
</tr>
<tr>
<td>WBC ((&gt;12\text{ or }&lt;4 \times 10^9/\text{L}))</td>
<td>82 (71.9%)</td>
<td>22 (75.9%)</td>
<td>60 (70.6%)</td>
<td>0.585</td>
</tr>
<tr>
<td>Impaired gas exchange</td>
<td>82 (71.9%)</td>
<td>18 (62.1%)</td>
<td>64 (75.3%)</td>
<td>0.171</td>
</tr>
<tr>
<td>Impaired consciousness</td>
<td>59 (51.8%)</td>
<td>9 (31.0%)</td>
<td>50 (58.8%)</td>
<td>0.010</td>
</tr>
<tr>
<td>Hemodynamic instability</td>
<td>74 (64.9%)</td>
<td>13 (44.8%)</td>
<td>61 (71.8%)</td>
<td>0.009</td>
</tr>
<tr>
<td>PCT (ng/mL)</td>
<td>3.37 (9.22)</td>
<td>1.12 (1.36)</td>
<td>4.62 (10.72)</td>
<td>0.018</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>182.75 (158.5)</td>
<td>147.60 (156.50)</td>
<td>208.80 (140.60)</td>
<td>0.301</td>
</tr>
</tbody>
</table>
Absolute values of PCT, CRP, temperature and WCC

ΔPCT as an indicator of infection
Sepsis/Infection

Early procalcitonin kinetics and appropriateness of empirical antimicrobial therapy in critically ill patients

A prospective observational study

Domonkos Trázy, MD a,*, Krisztián Tánczos, MD a, Márton Németh, MD a, Péter Hankovszky, MD a, András Lovas, MD a, András Mikor, MD a, Ildikó László, MD a, Edit Hajdú, MD b, Angelika Osztroluczki a, János Fazakas, MD c, Zsolt Molnár, MD a The EProK study group
Early PCT kinetics may indicate effective empirical antibiotic therapy

Early PCT kinetics may indicate effective empirical antibiotic therapy

Best cut-off values to indicate inappropriate antibiotic treatment:

- PCT increase of > 55% during the first 16 hours
- PCT increase of > 70% during the first 24 hours

Trásy et al. under review
CRP kinetics in the same study
Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial

Background of the investigation:

- duration of AB treatment is associated with growing resistance
- safety of PCT guided therapy is scarce
- assessment of efficiency and safety of PCT guided AB therapy on ICU

Efficacy and safety of PCT guiding

• satisfactory drop in PCT might help to discontinue AB
• is it a safe practice?
• Stop Antibiotics on Procalcitonin Guidance Study

Study design:
• 1546 patients
• stop antibiotics if:
  • PCT decreased by 80%
  • absolute value < 0.5 μg/L

Results of SAPS I.

<table>
<thead>
<tr>
<th></th>
<th>Procalcitonin-guided group (n=761)</th>
<th>Standard-of-care group (n=785)</th>
<th>Between-group absolute difference in means (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Antibiotic consumption (days)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Daily defined doses in first 28 days</td>
<td>7.5 (4.0 to 12.8)</td>
<td>9.3 (5.0 to 16.5)</td>
<td>2.69 (1.26 to 4.12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Duration of treatment</td>
<td>5.0 (3.0 to 9.0)</td>
<td>7.0 (4.0 to 11.0)</td>
<td>1.22 (0.65 to 1.78)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antibiotic-free days in first 28 days</td>
<td>7.0 (0.0 to 14.5)</td>
<td>5.0 (0.0 to 13.0)</td>
<td>1.31 (0.52 to 2.09)</td>
<td>0.0016</td>
</tr>
<tr>
<td><strong>Mortality (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>28-day mortality</td>
<td>149 (19.6%)</td>
<td>196 (25.0%)</td>
<td>5.4% (1.2 to 9.5)</td>
<td>0.0122</td>
</tr>
<tr>
<td>1-year mortality</td>
<td>265 (34.8%)</td>
<td>321 (40.9%)</td>
<td>6.1% (1.2 to 10.9)</td>
<td>0.0158</td>
</tr>
<tr>
<td><strong>Adverse events</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reinfecion</td>
<td>38 (5.0)</td>
<td>23 (2.9)</td>
<td>-2.1% (-4.1 to -0.1)</td>
<td>0.0492</td>
</tr>
<tr>
<td>Repeated course of antibiotics</td>
<td>175 (23.0)</td>
<td>173 (22.0)</td>
<td>-1.0% (-5.1 to 3.2)</td>
<td>0.67</td>
</tr>
<tr>
<td>Time (days) between stop and reinstitution of antibiotics</td>
<td>4.0 (2.0 to 8.0)</td>
<td>4.0 (2.0 to 8.0)</td>
<td>-0.22 (-1.31 to 0.88)</td>
<td>0.96</td>
</tr>
<tr>
<td><strong>Costs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total cumulative costs of antibiotics</td>
<td>€150 082</td>
<td>€181 263</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Median cumulative costs antibiotics per patient</td>
<td>€107.5 (51 to 229)</td>
<td>€129 (66 to 273)</td>
<td>€33.6 (2.5 to 64.8)</td>
<td>0.0006</td>
</tr>
<tr>
<td><strong>Length of stay (days)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>On the intensive care unit</td>
<td>8.5 (5.0 to 17.0)</td>
<td>9.0 (4.0 to 17.0)</td>
<td>-0.21 (-0.92 to 1.60)</td>
<td>0.56</td>
</tr>
<tr>
<td>In hospital</td>
<td>22.0 (13.0 to 39.3)</td>
<td>22.0 (12.0 to 40.0)</td>
<td>0.39 (-2.69 to 3.46)</td>
<td>0.77</td>
</tr>
</tbody>
</table>

Data are median (IQR), n (%), or mean (95% CI). Between-group absolute differences were calculated using the mean values, percentage differences, and 95% CIs. NA=not applicable.
Results of SAPS II.

PCT guided treatment can significantly reduce antibiotic exposure with a significant survival benefit.
Case Report

Extreme Procalcitonin Elevation without Proven Bacterial Infection Related to Amphetamine Abuse

András Lovas,1 Zsuzsanna Ágoston,1 Klára Késmárky,1,2 Péter Hankovszky,1 and Zsolt Molnár1

Table 1: Blood chemistry results and their kinetics during stay in intensive care unit.

<table>
<thead>
<tr>
<th></th>
<th>Reference range</th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 4</th>
<th>Day 6</th>
<th>Day 10</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCT (ng/mL)</td>
<td>&lt;0.5</td>
<td>1432</td>
<td>1640</td>
<td>1007</td>
<td>170.6</td>
<td>15.18</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>&lt;5</td>
<td>8.5</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
<td>n/a</td>
</tr>
<tr>
<td>WCC (cells/μL)</td>
<td>3700–9500</td>
<td>22690</td>
<td>18160</td>
<td>13960</td>
<td>11250</td>
<td>15950</td>
</tr>
<tr>
<td>PLT (cells/μL)</td>
<td>143000–332000</td>
<td>340000</td>
<td>204000</td>
<td>120000</td>
<td>115000</td>
<td>405000</td>
</tr>
<tr>
<td>INR</td>
<td>1.33</td>
<td>1.61</td>
<td>1.22</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
</tr>
<tr>
<td>LDH (U/L)</td>
<td>&lt;530</td>
<td>2010</td>
<td>4754</td>
<td>7240</td>
<td>5150</td>
<td>n.a.</td>
</tr>
<tr>
<td>GOT (U/L)</td>
<td>&lt;37</td>
<td>651</td>
<td>2016</td>
<td>4207</td>
<td>1442</td>
<td>n.a.</td>
</tr>
<tr>
<td>GPT (U/L)</td>
<td>&lt;40</td>
<td>144</td>
<td>384</td>
<td>2016</td>
<td>463</td>
<td>n.a.</td>
</tr>
<tr>
<td>CK (U/L)</td>
<td>&lt;195</td>
<td>42960</td>
<td>125500</td>
<td>92700</td>
<td>20580</td>
<td>1325</td>
</tr>
<tr>
<td>Trop-T (μg/mL)</td>
<td>&lt;0.04</td>
<td>0.117</td>
<td>0.192</td>
<td>n/a</td>
<td>n/a</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

PCT: procalcitonin; CRP: C-reactive protein; WCC: white cell count; PLT: platelet count; INR: international normalised ratio; LDH: lactate dehydrogenase; GOT: glutamic oxaloacetic transaminase; GPT: glutamic pyruvic transaminase; CK: creatine kinase; Trop-T: troponin-T.
Conclusions I

• Sepsis is NOT a definitive diagnosis
• New definitions of sepsis approximates us to the underlying pathophysiology
• Rather the response of the body than the infection on its own causes the harm
• There is grave overlap between response to infection and sterile cell injury
Conclusions II

- Biomarkers can help us in decision making
- PCT has high sensitivity and specificity

Nothing will ever replace the well trained, experienced, thinking human
Conclusions III.

• Defining and diagnosing sepsis are challenges
• Overlapping pathomechanism in sepsis and SIRS (DAMP, PAMP)
• Initiating adequate empiric antibiotic treatment in time is crucial
Conclusions IV.

- PCT can help the decision making
- Early PCT kinetics may indicate effective empirical antibiotic therapy
- PCT kinetics can be useful in the cessation of antibiotic treatment
Thank you for your attention