Sepsis and Love

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www.sepseast2016.com
Pathomechanism of critical illness
Local insult goes systemic

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

Humoral activity
Interferon, Complement

Macrophage
TNF; IL-1, IL-6, IL-10; PAF

PMN
FR, PAF, Chemotaxis

Endothel
NO, E-selectin, NFκB

Fisiol. reactions
Fever, Metabolic changes

Sepsis, SIRS

MSOF

"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
Health = balance between the antagonistic forces

- Acid
- Pro-coagulation
- Oxidants
- Pro-inflammation

- Base
- Anti-coagulation
- Anti-oxidants
- Anti-inflammation
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

Overwhelming inflammation vs. prolonged immunosuppression: Both can be deadly!

Pro-inflammation

Anti-inflammation
### Table 2. Terminology and International Classification of Diseases Coding

<table>
<thead>
<tr>
<th>Current Guidelines and Terminology</th>
<th>Sepsis</th>
<th>Septic Shock</th>
</tr>
</thead>
<tbody>
<tr>
<td>1991 and 2001 consensus terminology</td>
<td>Severe sepsis</td>
<td>Septic shock</td>
</tr>
<tr>
<td></td>
<td>Sepsis-induced hypoperfusion</td>
<td></td>
</tr>
<tr>
<td>2015 Definition</td>
<td><strong>Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection</strong></td>
<td>Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality</td>
</tr>
<tr>
<td>2015 Clinical criteria</td>
<td>Suspected or documented infection and an acute increase of ≥2 SOFA points (a proxy for organ dysfunction)</td>
<td>Sepsis and vasopressor therapy needed to elevate MAP ≥65 mm Hg and lactate &gt;2 mmol/L (18 mg/dL) despite adequate fluid resuscitation</td>
</tr>
</tbody>
</table>

**Recommended primary ICD codes**

<table>
<thead>
<tr>
<th>ICD-9</th>
<th>995.92</th>
<th>785.52</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICD-10</td>
<td>R65.20</td>
<td>R65.21</td>
</tr>
</tbody>
</table>

**Framework for implementation for coding and research**

1. Identify suspected infection by using concomitant orders for blood cultures and antibiotics (oral or parenteral) in a specified period.
2. Within specified period around suspected infection:
   1. Identify sepsis by using a clinical criterion for life-threatening organ dysfunction
   2. Assess for shock criteria, using administration of vasopressors, MAP <65 mm Hg, and lactate >2 mmol/L (18 mg/dL)
Sepsis: From Pathophysiology to Individualized Patient Care

Ildikó László,¹ Domonkos Trásy,¹ Zsolt Molnár,¹ and János Fazakas²

A

Insult
- Infection, SIRS, surgery, trauma, burns, I-R injury, etc.
- DO₂/VO₂ imbalance

„Sepsis” triangle

Severity and outcome

Host response
- PAMP, DAMP
- Innate, adaptive immunity

B

Adjuvant therapy
(Immunoglobulins, steroids, ECMO-treatment, etc.)

Organ support
(PPV, hemodynamic, renal, nutrition, etc.)

Source control
(antibiotics, surgery, invasive radiology)

Resuscitation
(Oxygen-, fluid-therapy, catecholamines, transfusion, etc.)
Mortality
Love has been under extensive research

Mortality: 100% 😞

Willia Shakespeare: Romeo and Juliet, 1599
Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Kirs-Maija Kaukonen, MD, PhD, EDIC; Michael Bailey, PhD; Satoshi Suzuki, MD; David Pilcher, FCICM; Rinaldo Bellomo, MD, PhD

Figure 1. Mean Annual Mortality in Patients With Severe Sepsis

1,037,115 patients treated in 171 ICUs

>15% reduction in mortality!

Increase by >4 fold
# Sepsis mortality around the Globe

<table>
<thead>
<tr>
<th>Study</th>
<th>Design / data collection</th>
<th>[n]</th>
<th>Hospital Mortality</th>
<th>ICU stay (d)</th>
<th>Hospital stay (d)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kaukonen et al. (2014)</td>
<td>Retrospektive, incidence, administrative data</td>
<td>12,213</td>
<td>19,8 %</td>
<td>3,2</td>
<td>13,5</td>
</tr>
<tr>
<td>Levy et al. (2012)</td>
<td>USA, 2005-2010, Prospektive, registry, not representative</td>
<td>18,766</td>
<td>28,3 %</td>
<td>4,2</td>
<td>10,5</td>
</tr>
<tr>
<td>PROCESS (2014)</td>
<td>Retrospektive, registry, not representative</td>
<td>1,500</td>
<td>~20 %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARISE (2014)</td>
<td>Retrospektive, registry, not representative</td>
<td>1,600</td>
<td>~20 %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Europe 2005-2010</td>
<td>Prospektive, registry, not representative</td>
<td>6,609</td>
<td>41,1 %</td>
<td>7,8</td>
<td>22,8</td>
</tr>
<tr>
<td>Heublein et al. (2013)</td>
<td>Retrospektive, incidence study, administrative data</td>
<td>89,907</td>
<td>46,5 %</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Engel et al. (2004)</td>
<td>Prospektive, one-day prevalence, representative</td>
<td>415</td>
<td>55,2 %</td>
<td>12,3</td>
<td>24</td>
</tr>
<tr>
<td>Deutschland, 2003</td>
<td>Retrospektive, registry, not representative</td>
<td>415</td>
<td>55,2 %</td>
<td>12,3</td>
<td>24</td>
</tr>
<tr>
<td>Jena Sepsisregistry</td>
<td>Prospektive, monocentric, incidence study, registry</td>
<td>388</td>
<td>46,9 %</td>
<td>10</td>
<td>27</td>
</tr>
</tbody>
</table>

Do we speak the same „sepsis language”…?
Guidelines
Love is patient, love is kind.
It does not envy, it does not boast, it is not proud.
5 It does not dishonor others, it is not self-seeking, it is not easily angered, it keeps no record of wrongs.
6 Love does not delight in evil but rejoices with the truth.
7 It always protects, always trusts, always hopes, always perseveres.
8 Love never fails.

Paul’s II. Epistle to the Corinthians, 13; 4-8
Guidelines for Sepsis

Surviving Sepsis Campaign guidelines for management of severe sepsis and septic shock: 2012

R. Phillip Dellinger, MD; Mitchell M. Levy, MD; Andrew Rhodes, MB BS; Djillali Annane, MD;
Guidelines for Sepsis

- Antibiotics
- Steroids
- Immunoglobulins
- Antithrombin

The rest:
Good Medicine
In fact – following guidelines may be...

**CONFERENCE REPORTS AND EXPERT PANEL**

**Surviving Sepsis Campaign:**
**International Guidelines for Management of Sepsis and Septic Shock: 2016**

Andrew Rhodes¹, Laura E. Evans², Waleed Alhazzani³, Mitchell M. Levy⁴, Massimo Antonelli⁵

**A. INITIAL RESUSCITATION**
1. Sepsis and septic shock are medical emergencies, and we recommend that treatment and resuscitation begin immediately (BPS).
2. We recommend that, in the resuscitation from sepsis-induced hypoperfusion, at least 30 mL/kg of IV crystalloid fluid be given within the first 3 hours (strong recommendation, low quality of evidence).

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26th January:
- 54 y M
- pancreatitis
- Septis shock

On admission:
- 100% FiO2+16 PEEP
- EVLWi: 27 ml/kg
- Dg: H1N1 pneumonia
Is this patient septic or not?
I have never treated „SEPSIS” in my life!
But…

You don’t treat SEPSIS but:
Organ dysfunction +/- infection

Hemodynamic instability
Respiratory dysfunction
dysfunction

Etc, etc, etc....
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

Not good enough

Poooor!

Very late!
We need biomarkers!

WARNING!
Using biomarkers is not easy
The 3 fundamental questions to answer

1. Is there infection – should I start empirical ABs?

2. Is it effective?

More on that:
Yesterday... 😞
Patients with suspected infection = 209
Infection = 85
PCT available at T-1 = 114
No-infection = 29
Measure PCT daily, an increase can be an important signal of infection.
Is it complicated?
Thinking has no alternative!

Auguste Rodin: The Thinker, 1880
Free for junior doctors (<29)!
www.sepseast2016.com
Next time: November 2018!!