



Sepsis and Love



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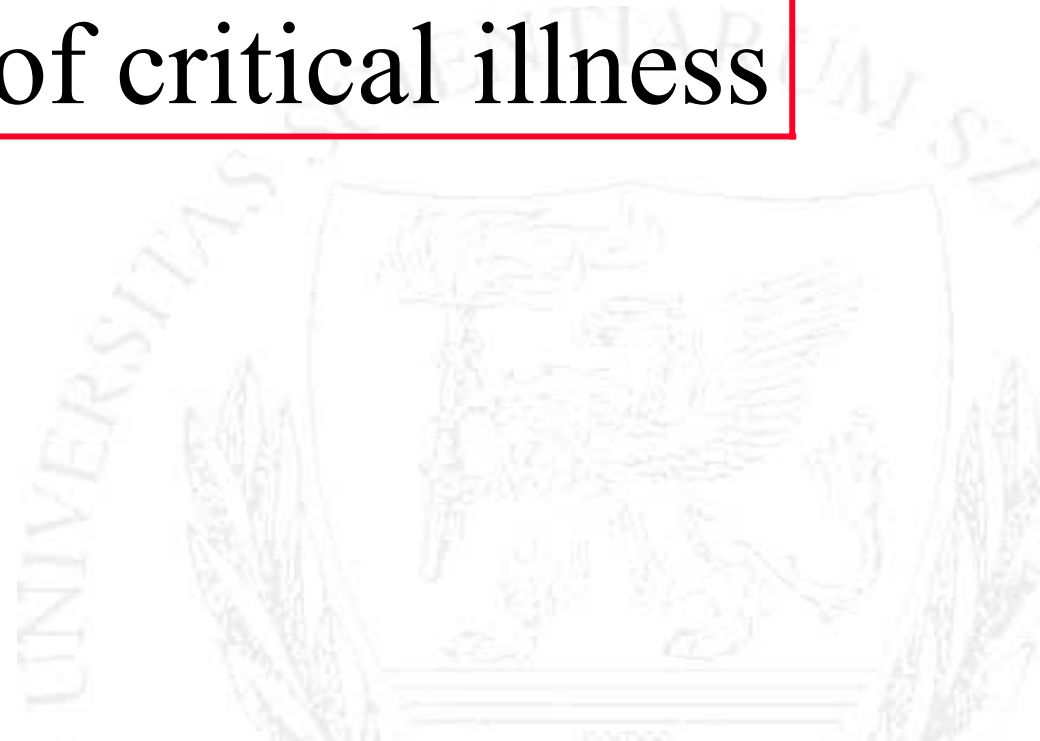
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Pathomechanism of critical illness



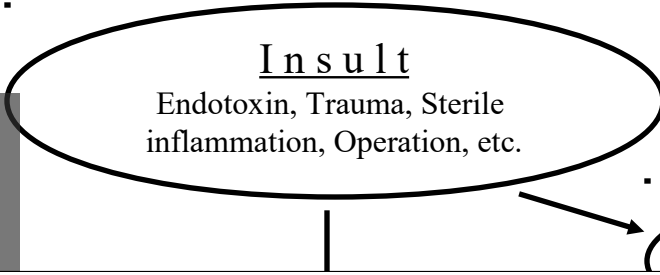


Local insult goes systemic

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

Z Molnár MD, DEAA, E Shearer FRCA. *Anaesthesia and Intensive Care, Fazakerley Hospital, Liverpool*

The incidence of sepsis has increased by 137% over the past decade.¹ Due to antimicrobial therapy, the mortality associated with sepsis and its end result, multiple organ dysfunction syndrome (MODS), reported at levels from 85-100% in the past, more organs have failed.²⁻⁴ There is concern that the high mortality



„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





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

DAMP

PAMP

Tissue Alteration extracellular

Sepsis

Trauma

Pancreatitis

Ischemia

Uric acid

Heparane s

Eukaryotic cell

Mitochondria

Evolution

Trauma

Sepsis

PAMPs

DAMPs

Bacterial DNA

Mitochondrial DNA

Formyl peptides

FPR1

p38 MAPK

Neutrophil chemotaxis

Acute lung injury

Dectin-1





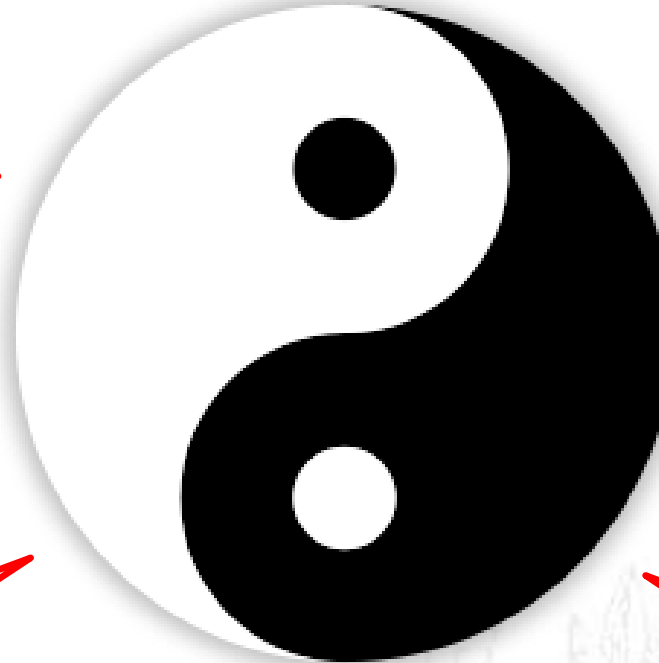
Health=balance between the antagonistic forces

Acid

Pro-coagulation

Oxidants

Pro-inflammation



Base

Anti-coagulation

Anti-oxidants

Anti-inflammation

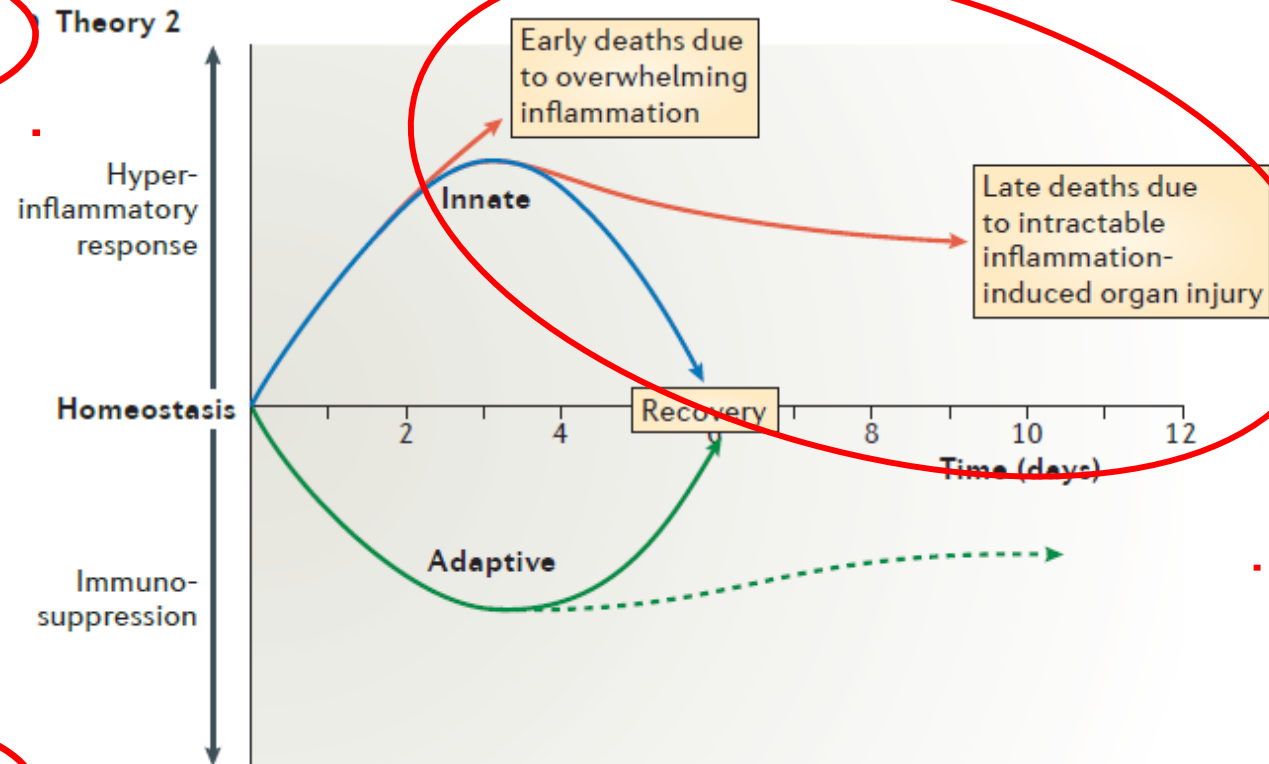


Sepsis-induced immunosuppression: from cellular dysfunctions to immunotherapy

Richard S. Hotchkiss¹, Guillaume Monneret² and Didier Payen³

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

Pro-inflammation



Anti-inflammation

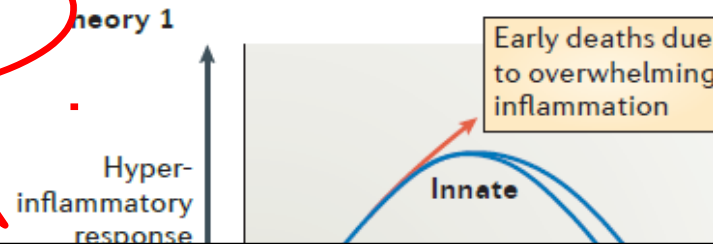


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Pro-inflammation



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



Anti-inflammation



The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

Table 2. Terminology and *International Classification of Diseases* Coding

Current Guidelines and Terminology	Sepsis	Septic Shock
1991 and 2001 consensus terminology ^{9,10}	Severe sepsis Sepsis-induced hypoperfusion	Septic shock ¹³
2015 Definition	Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection	Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality
2015 Clinical criteria	Suspected or documented infection and an acute increase of ≥ 2 SOFA points (a proxy for organ dysfunction)	Sepsis ^a and vasopressor therapy needed to elevate MAP ≥ 65 mm Hg and lactate > 2 mmol/L (18 mg/dL) despite adequate fluid resuscitation ¹³
Recommended primary ICD codes ^a		
ICD-9	995.92	785.52
ICD-10 ^a	R65.20	R65.21
Framework for implementation for coding and research	Identify suspected infection by using concomitant orders for blood cultures and antibiotics (oral or parenteral) in a specified period ^b Within specified period around suspected infection ^c : 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) ^d	

Good! 😊

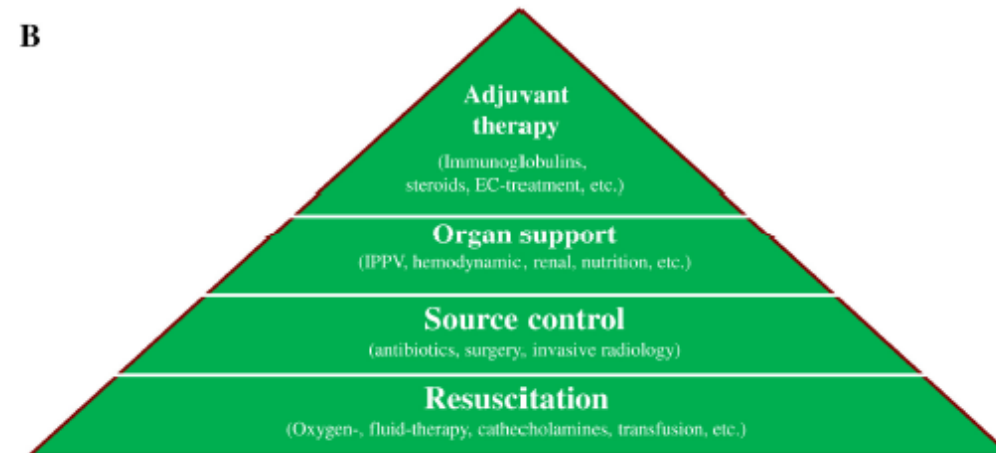
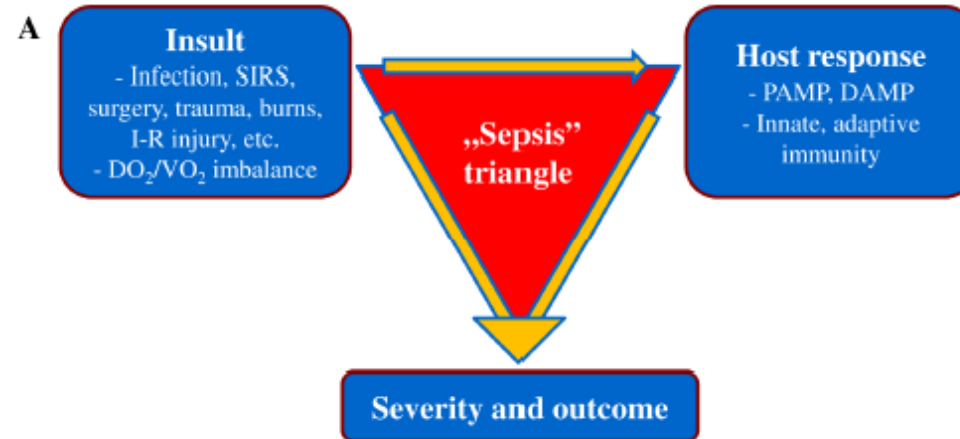




Sepsis: From Pathophysiology to Individualized Patient Care

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

Journal of Immunology Research
Volume 2015, Article ID 510436, 13 pages
<http://dx.doi.org/10.1155/2015/510436>





Mortality





Love has been under extensive research

THE
MOST EX-
cellent and lamentable
Tragedie of Romeo

Mortality: 100% ☹️


LONDON
Printed by Thomas Creede, for Iohn Iamby, and are to
be sold at his shop neere the Exchange.
1599

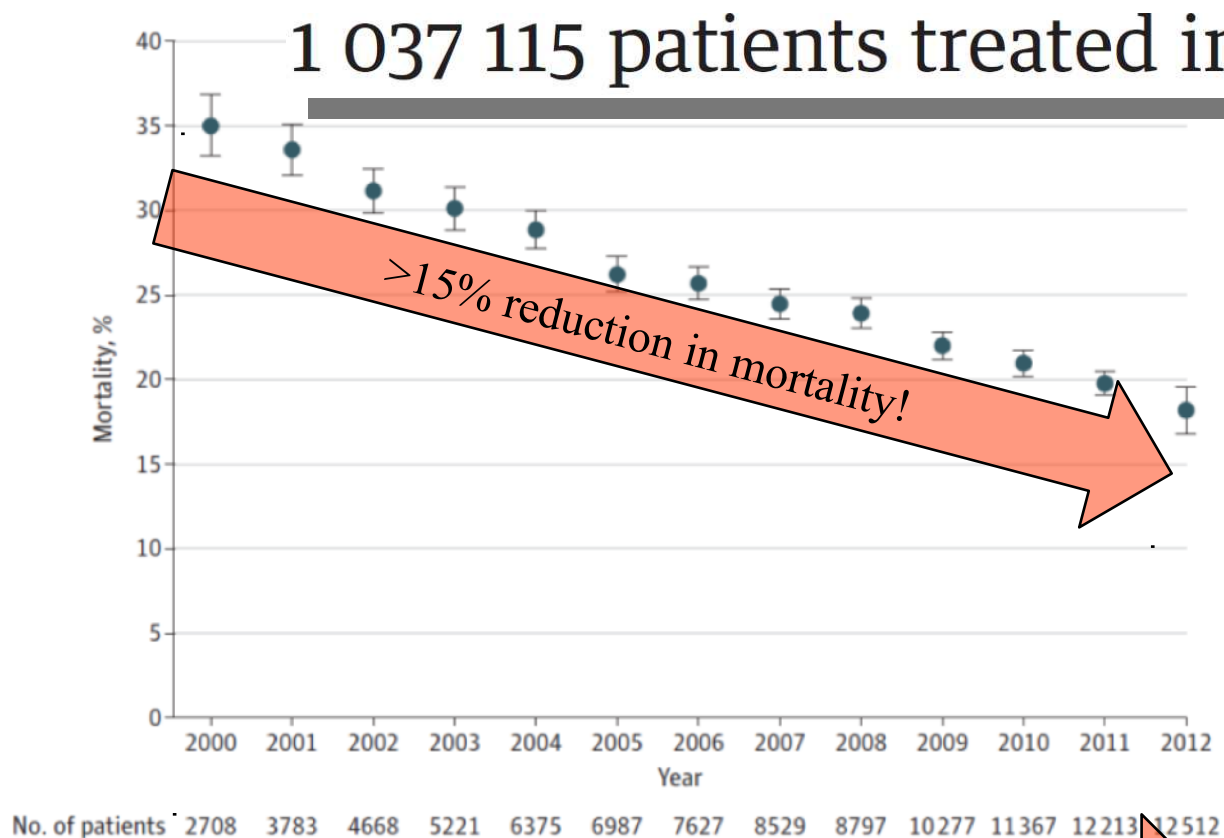
Willial Shakespeare: Romeo and Juliet, 1599



Mortality Related to Severe Sepsis and Septic Shock Among Critically Ill Patients in Australia and New Zealand, 2000-2012

Kirsi-Majja 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



>15% reduction in mortality!

Increase by >4 fold



Sepsis mortality around the Globe

Study	Design / data collection	[n]	Hospital Mortality	ICU stay (d)	Hospital stay (d)
Kaukonen et al. (2014)	Retrospektive, incidence, administrative data	12,213	19,8 %	3,2 (1,6-6,9)	13,5 (7,0-25,9)

Do we speak the same „sepsis language”...?

<i>Europe 2005-2010</i>	Prospektive, registry, not representative	6,609	41,1%	7,8 (3,4-17,2)	22,8 (11,1-43,3)
Heublein et al. (2013)	Retrospektive, incidence study, administrative data	89,907	46,5%	-	-
Engel et al. (2004) <i>Deutschland, 2003</i>	Prospektive, one-day prevalence, representative	415	55,2%	12,3 (6-16)	24 (13-38)
Jena Sepsisregistry <i>Deutschland (Jena), 2011</i>	Prospektive, monocentric, incidence study, registry	388	46,9%	10 (4-23)	27 (16-43,2)



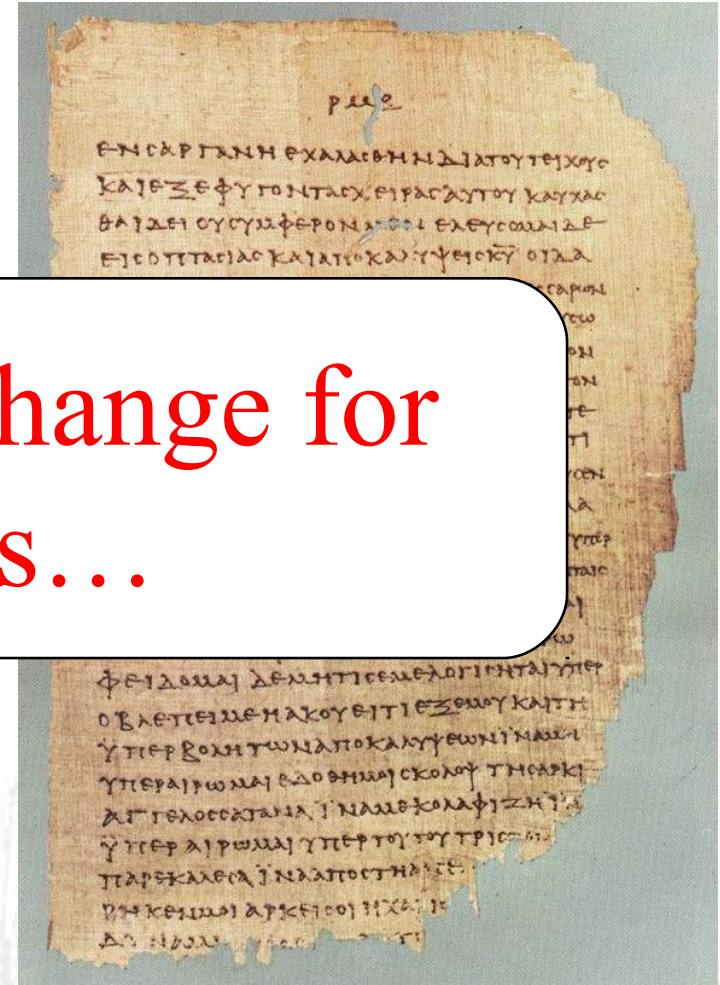
Guidelines





„Guidelines” for Love

Love is patient, love is kind.
It does not envy, it does not boast, it is not proud.



This hasn't and won't change for thousands of years...

⁵ It
se
it
of
⁶ L

with the truth.

⁷ It always protects, always trusts, always hopes,
always perseveres.

⁸ Love never fails.



Guidelines for Sepsis

Special Articles

Surviving Sepsis Campaign guidelines for management of severe

Intensive Care Med (2008) 34:17–60
DOI 10.1007/s00134-007-0934-2

SPECIAL ARTICLE

R. Phillip Dellinger

Surviving Sepsis Campaign:

Surviving Sepsis Campaign: International Guidelines for Management of Severe Sepsis and Septic Shock: 2012

R. Phillip Dellinger, MD¹; Mitchell M. Levy, MD²; Andrew Rhodes, MB BS³; Djillali Annane, MD⁴;



Guidelines for Sepsis

CONFERENCE REPORTS AND EXPERT PANEL



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

Andrew Rhodes^{1*}, Laura E. Evans², Waleed Alhazzani³, Mitchell M. Levy⁴, Massimo Antonelli⁵, Ricard Ferrer⁶,

Results: The Surviving Sepsis Guideline panel provided 93 statements on early management and resuscitation of patients with sepsis or septic shock. Overall, 32 were strong recommendations, 39 were weak recommendations, and 18 were best-practice statements. No recommendation was provided for four questions.

- 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 Rhodes^{1*}, Laura E. Evans², Waleed Alhazzani³, Mitchell M. Levy⁴, Massimo Antonelli⁵, et al.

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).

30 ml/kg/3h

26th January:

-54 y M

-?pancreatitis

-Septic shock

On admission:

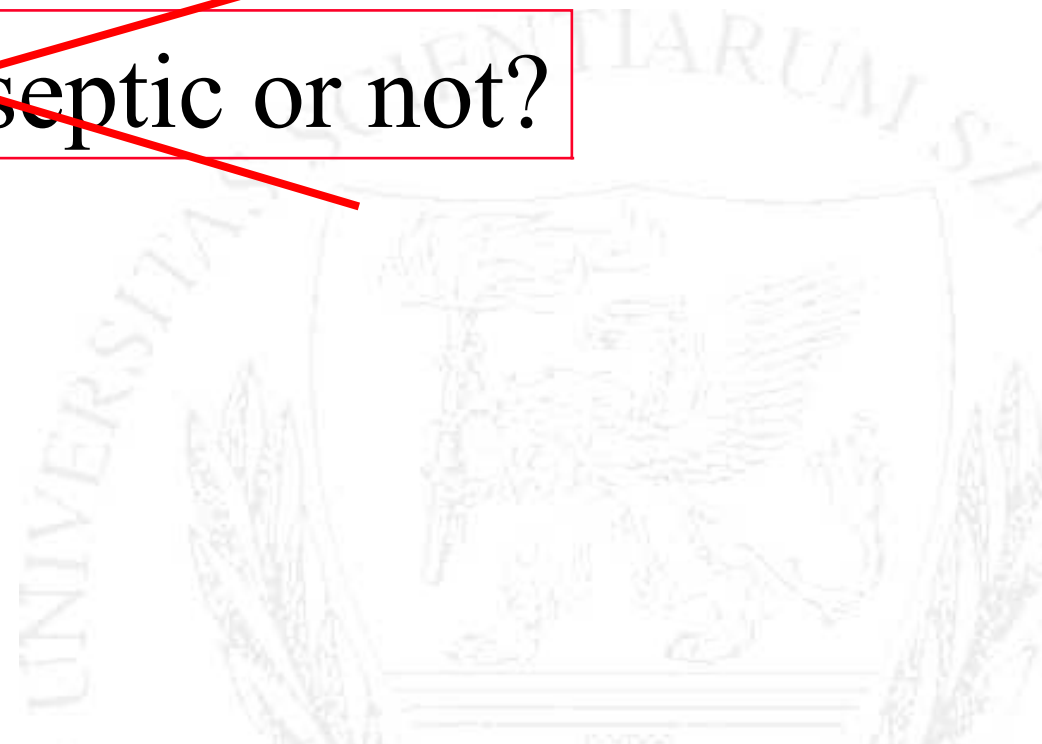
-100% FiO₂+16 PEEP

- EVLWi: 27 ml/kg

- Dg: H1N1 pneumonia



~~Is this patient septic or not?~~





I have never treated „SEPSIS” in my life!
But...

Hemodynamic
instability

Respiratory
dysfunction

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

Renal 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 ($>38^{\circ}\text{C}$), WBC ($>12\ 000$):
 - Low sensitivity ($\sim 50\%$)
- Microbiology:
 - Results: 24 hours or more

Not good enough

Pooooor!

Very late!

Galicier L and Richet H. Infect Control Hosp



We need biomarkers!

Pierrakos and Vincent *Critical Care* 2010, 14:R15

<http://ccforum.com/content/14/1/R15>



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... ☹️**



Research Article

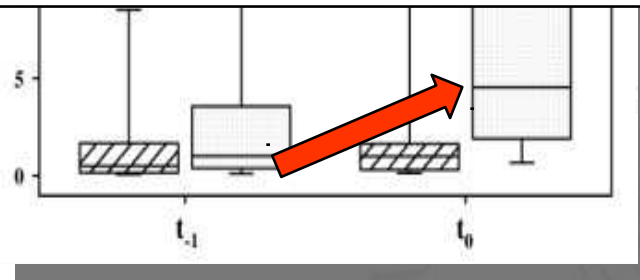
Delta Procalcitonin Is a Better Indicator of Infection Than Absolute Procalcitonin Values in Critically Ill Patients: A Prospective Observational Study

Domonkos Trásy,¹ Krisztián Tánzos,¹ Márton Németh,¹ Péter Hankovszky,¹ András Lovas,¹ András Mikor,¹ Edit Hajdú,² Angelika Osztroluczki,¹ János Fazakas,³ and Zsolt Molnár¹



Journal of Immunology Research
Volume 2016, Article ID 3530752, 9 pages
<http://dx.doi.org/10.1155/2016/3530752>

Measure PCT daily, an increase can be an important signal of infection.



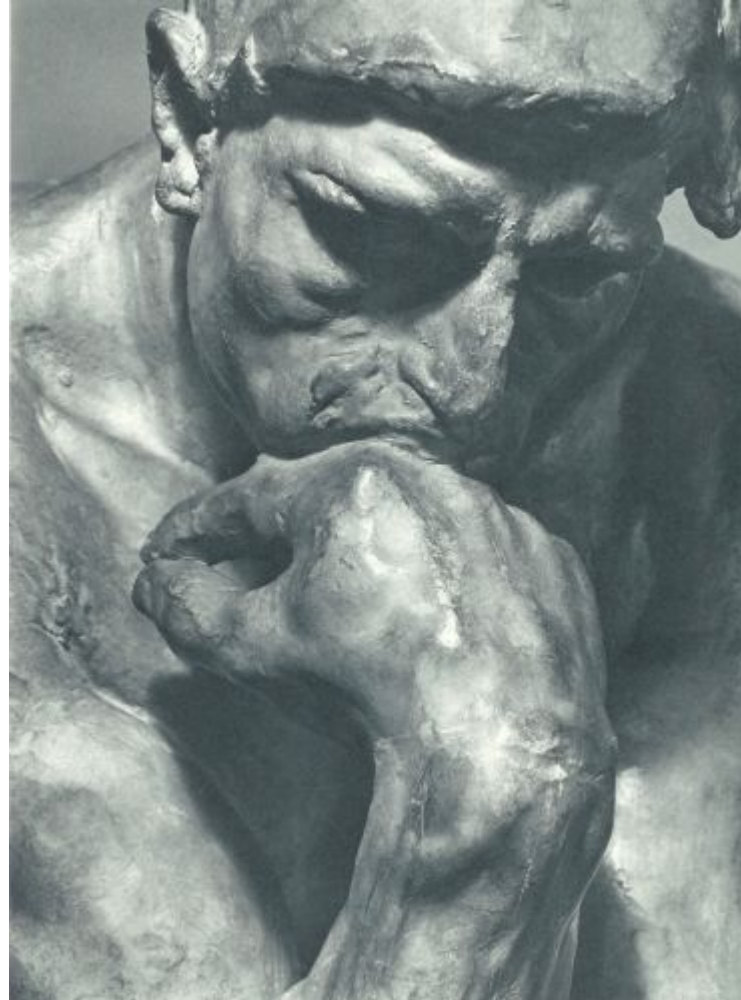


Is it complicated?





Thinking has no alternative!



Auguste Rodin: The Thinker, 1880

Free for junior doctors (<29)!

www.sepseast2016.com

Next time: November 2018!!





SepsEast 2016

3rd Central and Eastern European Sepsis Forum



YouTube: [oncall@jate](https://www.youtube.com/channel/UC...)