Evidence Based Medicine: Pro and Cons (in septic ICU pts)

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Disclosures

• Honoraria for lectures and advisory boards:
  Astellas, Bayer, Gilead, Janssen, MSD, Novartis, Pfizer, BIANEΞ,

• Research Grands (ELKE of Athens University):
  Astellas, Gilead, MSD, Pfizer
Two key points to discuss

• RCTs conclusions and Guidelines usefulness in everyday clinical practice in a “Real Word setting”

• Pathophysiologic paradigms of sepsis and septic shock AND diagnostic approach and treatment (= decision making) in septic pts
The Surviving Sepsis Campaign:

Definitions for sepsis and organ failure and guidelines

ACCP/SCCM Consensus Conference Committee

Care Medicine.

Bone RC¹, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, S
Figure 2 Steroids for treatment of infections, sepsis, and septic shock – ups and downs. Abbreviations: SSC, Surviving Sepsis Campaign.
Guidelines for severe infections: are they useful?
Ismail Cinel and R. Phillip Dellinger

*Current Opinion in Critical Care* 2006, 12:483–488

Protocols: Do they work?
Marco Ranieri
Lecture in Berlin, ESICM Lives 2015
What a sepsis pilot must consider before taking flight with your next patient. *Crit Care Med* 2006; 34:1247

Patients are not airplanes and doctors are not pilots

To the Editor:

While I do not claim to have the research experience of Drs. Kortgen and colleagues (1) and Dr. Rivers (2), I do have a fair amount of experience treating sepsis. I am tiring of the ongoing analogy of the airline industry or of a jet pilot in regard to
... sepsis management is less then optimal. A recent survey has shown that:

• early goal directed therapy was performed in 17% of academic emergency departments, (2)
• protective lung strategies provided in 39% of patients on day 2 of acute lung injury (3), and
• aggressive glycemic control is provided 19% of the time with routine insulin protocols (4).
• the administration of recombinant human activated protein C ranged from 4% to 33% of patients in other studies examining the effectiveness of a sepsis protocol (5–7).

No matter what analogy is used, the lack of compliance to base practice sepsis recommendations is associated with increased mortality (8, 9).
Randomized controlled trials do not reflect reality: Real-world analyses are critical for treatment guidelines!

Martin T. R. Grapow, MD, Robert von Wattenwyl, MD, Ulrich Guller, MD, Friedhelm Beyersdorf, MD, PhD, and Hans-Reinhard Zerkowski, MD

study by Hannan and coworkers\(^1\) by analyzing 59,314 patients in New York’s cardiac registries who underwent either CABG or PCI (all with stents) from 1997 through 2000. Risk adjustment was performed by using both multivariable and propensity-score analysis.

In summary, only by considering both results from RCTs and large cohort studies can real-life clinical situations be reflected to a degree capable of providing applicable treatment guidelines useful in a daily clinical setting.
An alternate pathophysiologic paradigm of sepsis and septic shock

Implications for optimizing antimicrobial therapy

Anand Kumar

- **Current paradigm: Immunologic Model**
- **The classic paradigm: Microbiologic Primacy**
- **A new Composite Model: Integrating Shock**
An alternate pathophysiologic paradigm of sepsis and septic shock

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SIRS, sepsis, severe sepsis, and septic shock
Kumar A. 2014
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Microbiologic view of sepsis and septic shock

Kumar A. 2014
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Impact of appropriate antimicrobial therapy in sepsis and septic shock.

Kumar A. 2014
Impact of appropriate antimicrobial therapy in sepsis and septic shock.
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Kumar A. 2014
Integration of Time $\Rightarrow$ more heterogeneity

Immunomodulatory treatment
“Everything should be made as simple as possible, but not simpler”.

*Albert Einstein*
An alternate pathophysiologic paradigm of sepsis and septic shock

Implications for optimizing antimicrobial therapy

Anand Kumar

- Current paradigm: Immunologic Model
- The classic paradigm: Microbiologic Primacy
- A new Composite Model: Integrating Shock
- We need a more Composite Model = use a Dialectic Approach integrating:
  a) Time and variability in the real world
  b) calculated risk of adverse effects
  c) response to treatment
Dialectic approach (Διαλεκτική προσέγγιση)

Raphael 1483-1520: The school of Athens 1510-11, Vaticano
Pointing up to heavens
emphasis on episteme
(theoretical universals)

Hand turned down to earth
emphasis on phronesis
(practical reasoning)

Plato, 427-347 BC    Aristotle, 384–322 BC
Science (episteme)

based on universal principles

GUIDELINES

Practical Reasoning (phronesis)
customized decision
for one particular patient

Clinical practice

Plato, 427-347 BC  Aristotle, 384–322 BC
Evidence Based Medicine must be used as a tool and not as a substitute of decision making.

Conclusion: this is not a PRO – CON debate but a debate on “appropriate use” of EBM.
One size **DOES NOT** fit all
Evidence-based medicine or fuzzy logic

Dreyffus and Salmon, Editorial in ICM 2002

- Evidence-based medicine
- Experience-based medicine
- Medical Decision Making
- Comprehensive medicine
- Cook-book based medicine

Medicine based evidence?
There is a need
to disengage from the simple concepts of the past
and to develop 21st century approaches
which engage sepsis in its true form,
a complex-dynamic-relational pattern of death.
We need a dialectic approach using both Theory and Phronesis
Thank you very much for your attention
The investigation of the meaning of words is the beginning of wisdom

*Αντισθένης (Antisthenis) (445 -360 B.C.)*

Guidelines are NOT:

- Κανόνες ; *(rules)*
- Αρχές αντιμετώπισης ; *(principles)*
- Οδηγίες ; *(instructions)* of a manual

Σημαίνει: ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΓΡΑΜΜΕΣ

means *lines which give us a direction (guidance)*

- Sailing from Athens to Crete you must follow a route (a cap) around 160° but ...
The role of Guidelines

The recommendations in this document are intended to provide guidance for the clinician caring for a patient with severe sepsis or septic shock.

Recommendations from these guidelines cannot replace the clinician’s decision-making capability when he is presented with a patient’s unique set of clinical variables.


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