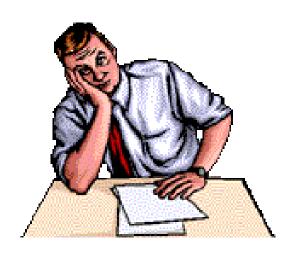
### ΠΜΣ «Λοιμωξιολογία» 12/02/2024

## Sepsis 1 - 2 - 3... ή μια "επιστημολογική" προσέγγιση



### Απόστολος Αρμαγανίδης

Ομότιμος Καθηγητής Πνευμονολογίας – Εντατικής Θεραπείας Ιατρικής Σχολής ΕΚΠΑ

Evidence Based Medicine (αρκεί?)

### "Conflict" of "interest" (ενδια- ή συμ-φέρον)

Τίποτε που να αναφορά τη σημερινή παρουσίαση (μόνο interest χωρίς conflict)

#### MEDICAL GRAND ROUNDS

CME CREDIT **EDUCATIONAL OBJECTIVE:** Readers will consider the recommendations of the Surviving Sepsis Campaign when treating patients with sepsis

R. PHILLIP DELLINGER, MD, MSc, MCCM

Orofessor and Chair of Medicine, Cooper Medical School of Rowan University, Camden, 193, Director, Adult Health Institute, and Senior Critical Care Attending, Cooper University Hospital, Camden, NJ; Steering Committee, Surviving Sepsis Campaign TAKE-HOME
POINTS FROM
LECTURES BY
CLEVELAND
CLINIC
AND VISITING
FACULTY

## The Surviving Sepsis Campaign: Where have we been and where are we going?

CLEVELAND CLINIC TOURNAL OF MEDICINE

VOLUME 82 • NUMBER 4

**APRII 2015** 

### Abstract

Chest. 1992 Jun;101(6):1644-55.

Definitions for sepsis and organ failure and guidelines ACCP/SCCM Consensus Conference Committee. Amer Care Medicine.

Bone RC1, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, Schein RN

## Modified from: Martin-Loeches I, Levy M., Artigas A Drug Design, Development and Therapy 2015:9 2079–2088

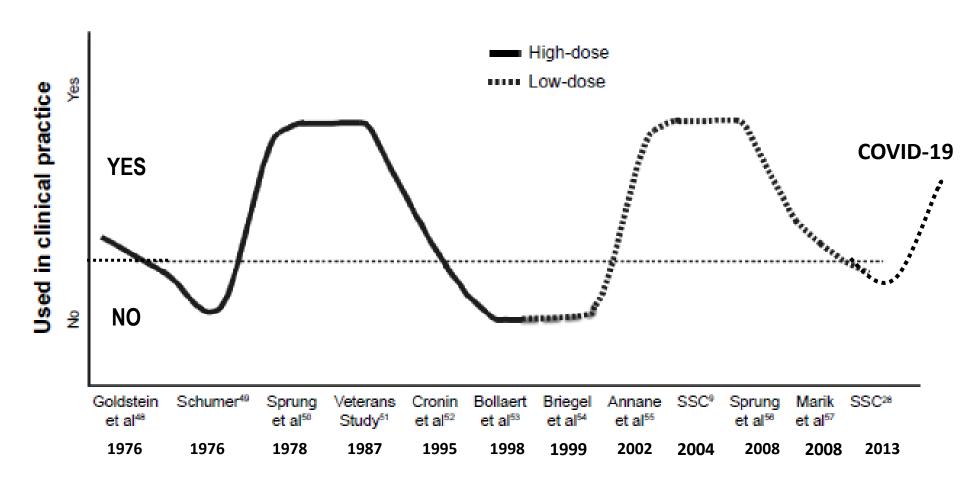


Figure 2 Steroids for treatment of infections, sepsis, and septic shock – ups and downs. Abbreviations: SSC, Surviving Sepsis Campaign.

Emanuel P. Rivers, MD, MPH, IOM,

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

Richard Rissmiller, MD, Internal Medicine, Carolinas Medical Center, Charlotte, NC

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

### Crit Care Med 2006 Vol. 34, No. 11 The authors reply:

Emanuel P. Rivers, MD, MPH, IOM,

... sepsis management is less than 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 <u>lack of compliance</u> to <u>base practice sepsis recommendations</u> is associated with increased mortality (8, 9).

### Martin-Loeches I, Levy M., Artigas A

Drug Design, Development and Therapy 2015:9 2079–2088

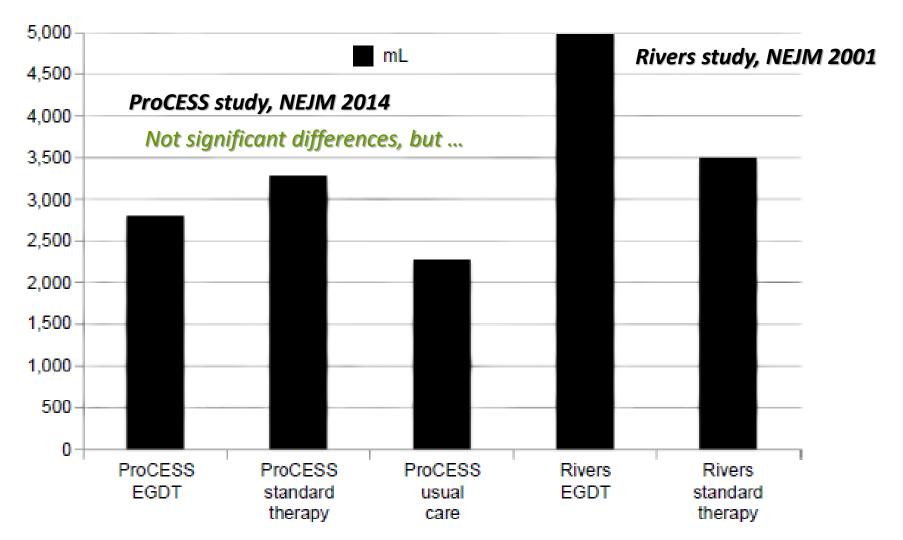


Figure 1 Fluid administration between 0 and 6 hours.

Abbreviations: ProCESS Protocolized Care for Early Septic Shock; EGDT, Early Goal-Directed Therapy.

## Key points (I)



• Σημασία του case-mix στις RCTs με βάση τις οποίες δημιουργούνται τα Guidelines

Crit Care Med. 1992 Jun;20(6):864-74.

American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference: definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis.

[No authors listed]

### **Abstract**

### **OBJECTIVE:**

To define the terms "sepsis" and "organ failure" in a precise manner.

### **DATA SOURCES:**

Review of the medical literature and the use of expert testimony at a consensus conference.

### **SETTING:**

American College of Chest Physicians (ACCP) headquarters in Northbrook, IL.

#### **PARTICIPANTS:**

Leadership members of ACCP/Society of Critical Care Medicine (SCCM).

#### **RESULTS:**

An ACCP/SCCM Consensus Conference was held in August of 1991 with the goal of agreeing on a set of definitions that could be applied to patients with sepsis and its sequelae. New definitions were offered for some terms, while others were discarded. Broad definitions of sepsis and the systemic inflammatory response syndrome were proposed, along with detailed physiologic variables by which a patient could be categorized. Definitions for severe sepsis, septic shock, hypotension, and multiple organ dysfunction syndrome were also offered. The use of severity scoring methods were recommended when dealing with septic patients as an adjunctive tool to assess mortality. Appropriate methods and applications for the use and testing of new therapies were recommended.

#### **CONCLUSION:**

The use of these terms and techniques **should assist clinicians and researchers who deal with sepsis** and its sequelae.

Intensive Care Med. 2003 Apr;29(4):530-8. Epub 2003 Mar 28.

2001 SCCM/ESICM/ACCP/ATS/SIS International Sepsis Definitions Conference.

Levy MM1, Fink MP, Marshall JC, Abraham E, Angus D, Cook D, Cohen J, Opal SM, Vincent JL, Ramsay G; International Sepsis Definitions Conference.

Author information Mitchell\_Levy@brown.edu

Rhode Island Hospital, 593 Eddy Street, MICU Main 7, Providence RI 02903, USA. Abstract OBJECTIVE:

In 1991, the American College of Chest Physicians (ACCP) and the Society of Critical Care Medicine (SCCM) convened a "Consensus Conference," the goals of which were to "provide a conceptual and a practical framework to define the systemic inflammatory response to infection, which is a progressive injurious process that falls under the generalized term 'sepsis' and includes sepsis-associated organ dysfunction as well. The general definitions introduced as a result of that conference have been widely used in practice and have served as the foundation for inclusion criteria for numerous clinical trials of therapeutic interventions. Nevertheless, there has been an impetus from experts in the field to modify these definitions to reflect our current understanding of the pathophysiology of these syndromes.

### **DESIGN:**

Several North American and European intensive care societies agreed to revisit the definitions for sepsis and related conditions. This conference was sponsored by the Society of Critical Care Medicine (SCCM), The European Society of Intensive Care Medicine (ESICM), The American College of Chest Physicians (ACCP), the American Thoracic Society (ATS), and the Surgical Infection Society (SIS).

#### **METHODS:**

29 participants attended the conference from Europe and North America. In advance of the conference, subgroups were formed to evaluate the following areas: signs and symptoms of sepsis, cell markers, cytokines, microbiologic data, and coagulation parameters. The present manuscript serves as the final report of the 2001 International Sepsis Definitions Conference.

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### **CONCLUSION:**

- 1. Current concepts of sepsis, severe sepsis and septic shock remain useful to clinicians and researchers.
- 2. These definitions do not allow precise staging or prognostication of the host response to infection. 3. While SIRS remains a useful concept, the diagnostic criteria for SIRS published in 1992 are overly sensitive and non-specific. 4. An expanded list of signs and symptoms of sepsis may better reflect the clinical response to infection. 6. PIRO, a hypothetical model for staging sepsis is presented, which, in the future, may better characterize the syndrome on the basis of predisposing factors and premorbid conditions, the nature of the underlying infection, the characteristics of the host response, and the extent of the resultant organ dysfunction.

remain a useful concept *Definition for what purpose? Useful for what – for who??? Researchers*OR clinicians?

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

JAMA. 2016;315(8):801-810.

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

### Conclusions

These updated definitions and clinical criteria should clarify long-used descriptors and <u>facilitate earlier recognition and more timely management of patients with sepsis or at risk of developing it.</u> This process, however, remains a work in progress. As is done with software and other coding updates, the task force recommends that the new definition be designated Sepsis-3, with the 1991 and 2001 iterations being recognized as Sepsis-1 and Sepsis-2, respectively, to emphasize the need for future iterations.

## Key points (II)



- Σημασία του case-mix στις RCTs με βάση τις οποίες δημιουργούνται τα Guidelines (\*)
- Διαφορετικοί ορισμοί ανάλογα με το σκοπό για τον οποίο δημιουργούνται(\*) αλλά και με το επίπεδο επιστημονικής γνώσης + κατανόησης



Dellinger et al CCM 2004
Vol. 32, No 11
(Suppl)
Introduction

A clinician armed with a sepsis change bundle, attacks the three heads of sepsis (hypotension, hypoperfusion, and organ dysfunction).

Inspired by Hercules Kills Cerberus, Renato Pettinato

Implications for optimizing antimicrobial therapy

**Anand Kumar** 

- Current paradigm: Immunologic Model
- The classic paradigm: Microbiologic Primacy
- A new Composite Model: Integrating Shock

Implications for optimizing antimicrobial therapy

**Anand Kumar** 

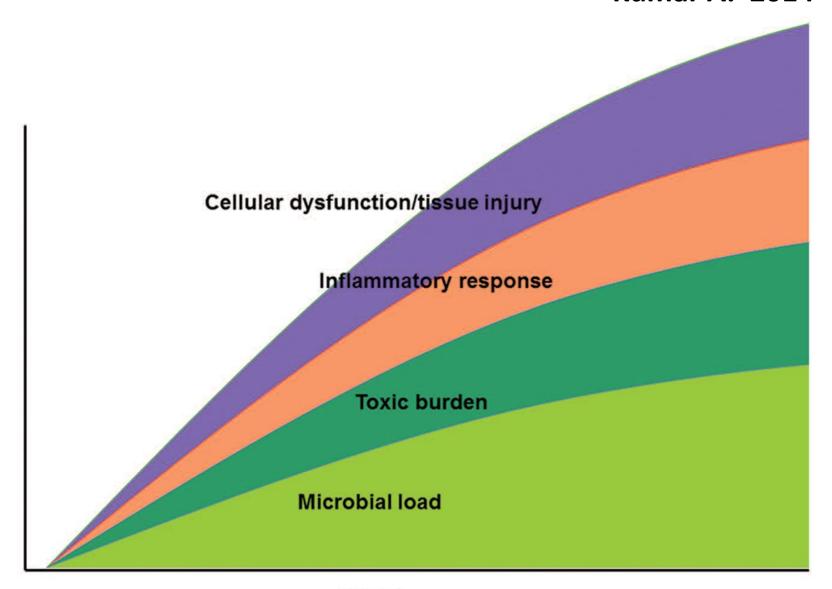
A key deficiency of this immunologic model of sepsis is that most pathogens cannot be eliminated quickly despite bactericidal antimicrobial therapy and likely persist during the period that immunomodulatory therapies (most of which are, in fact, immunosuppressive) might be initiated. A recent autopsy study of sepsis suggested that a persistent septic focus could be found in approximately 75% of 235 surgical ICU patients who died of sepsis/septic shock and in almost 90% of those succumbing in ICU after at least 7 days of treatment [26, 27, 28]

Implications for optimizing antimicrobial therapy

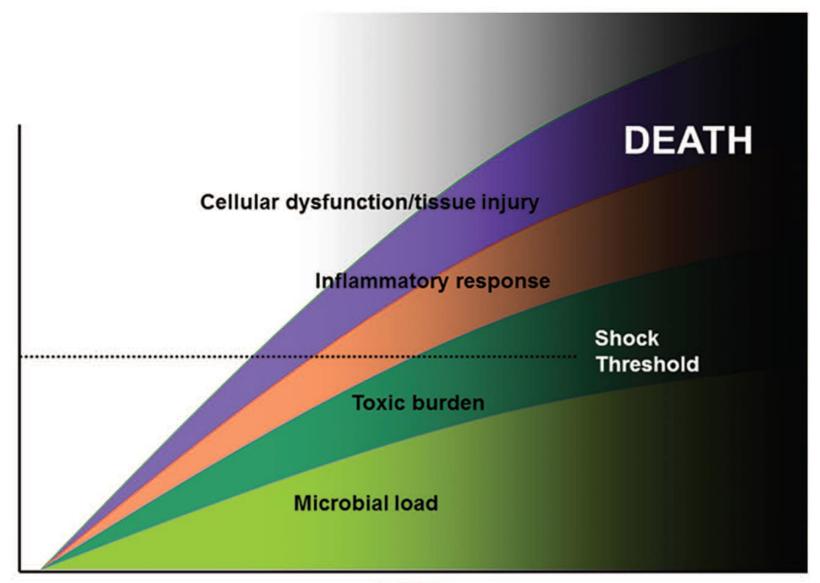
**Anand Kumar** 

- Current paradigm: Immunologic Model
- The classic paradigm: Microbiologic Primacy
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### Microbiologic view of sepsis and septic shock Kumar A. 2014



### Composite Microbiologic view of sepsis and septic shock Kumar A. 2014

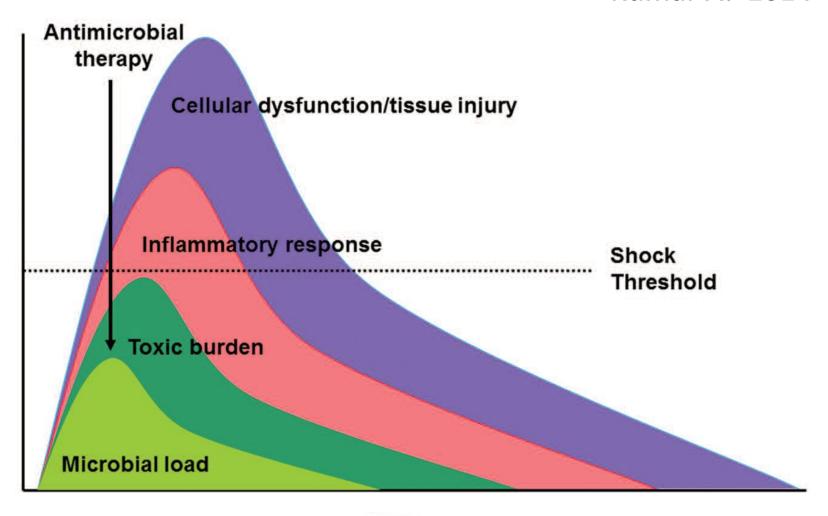


Implications for optimizing antimicrobial therapy

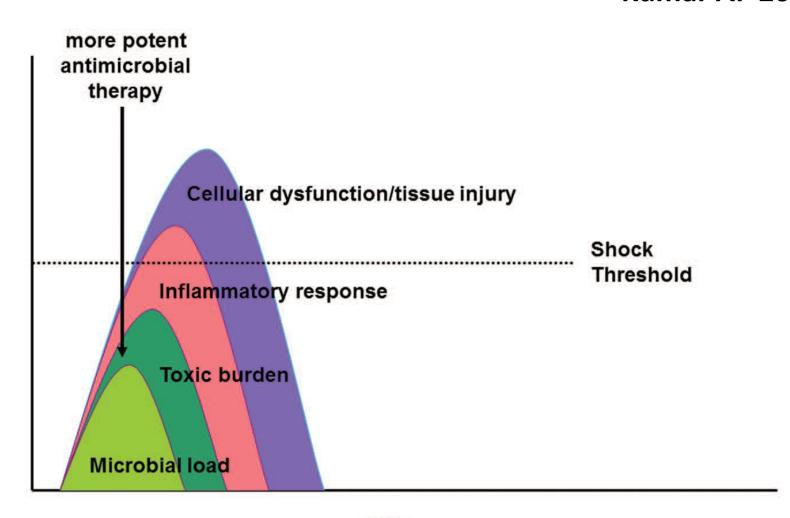
**Anand Kumar** 

- Current paradigm: Immunologic Model
- The classic paradigm: Microbiologic Primacy
- A new Composite Model: Integrating Shock (a more complex multifactorial model)

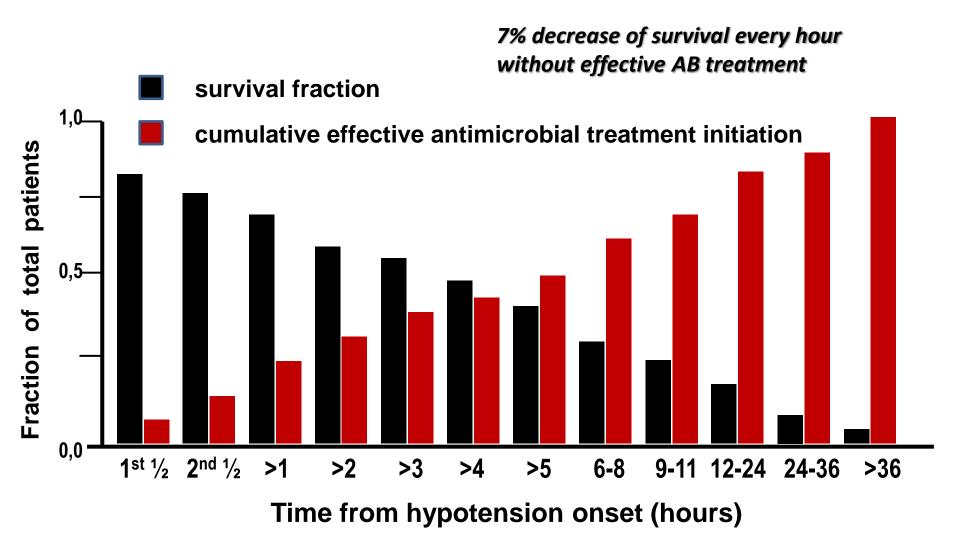
# Impact of <u>appropriate</u> antimicrobial therapy in sepsis and septic shock. Kumar A. 2014



# Impact of more potent antimicrobial therapy in sepsis and septic shock. Kumar A. 2014

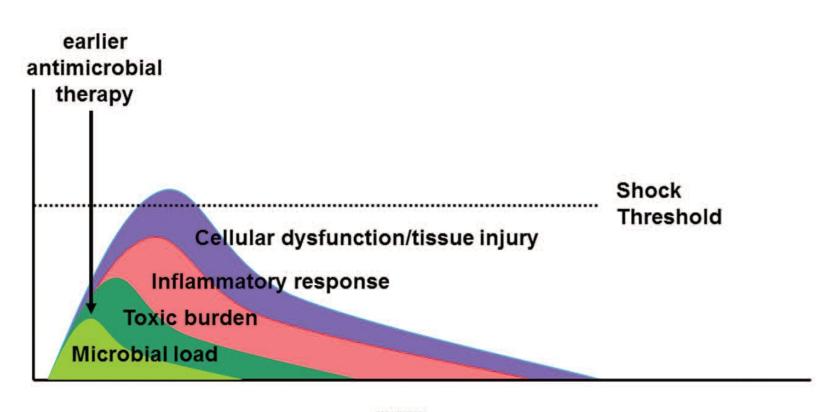


### In severe sepsis and septic shock, time is life

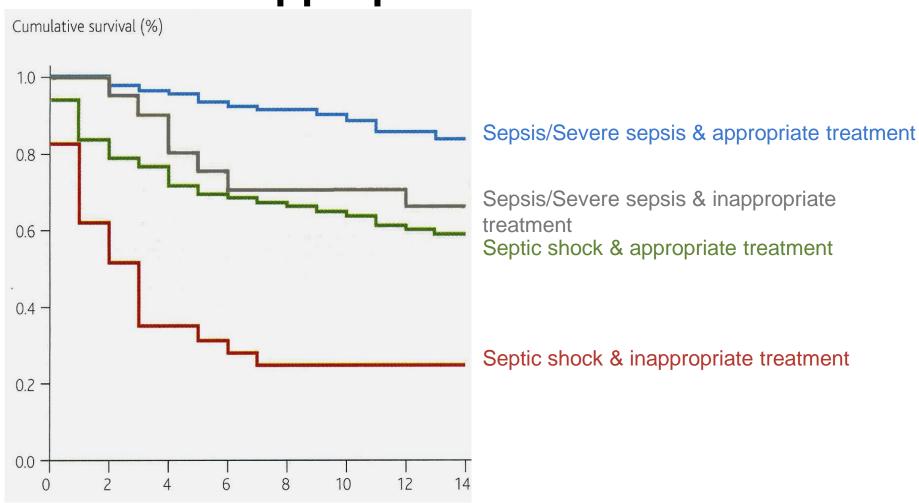


Modified from: Kumar A, Robert D, Wood KE, Critical Care Med 2006; 34: 1589–1596

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



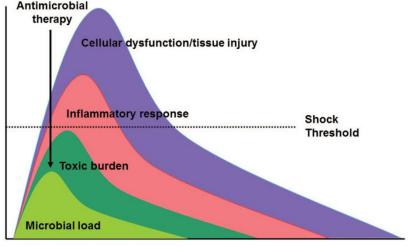
# Survival with appropriate OR inappropriate treatment



Days

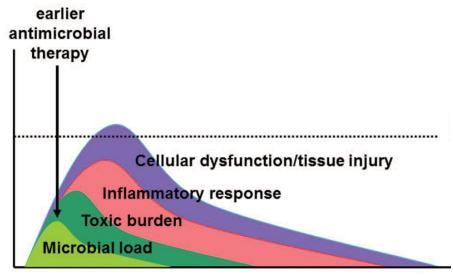
Valles A, et al. Chest 2003; 123:1615-24

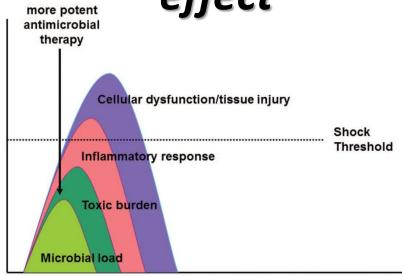
Microbiologic view of sepsis and septic shock Kumar A. 2014



Variability related to treatment effect



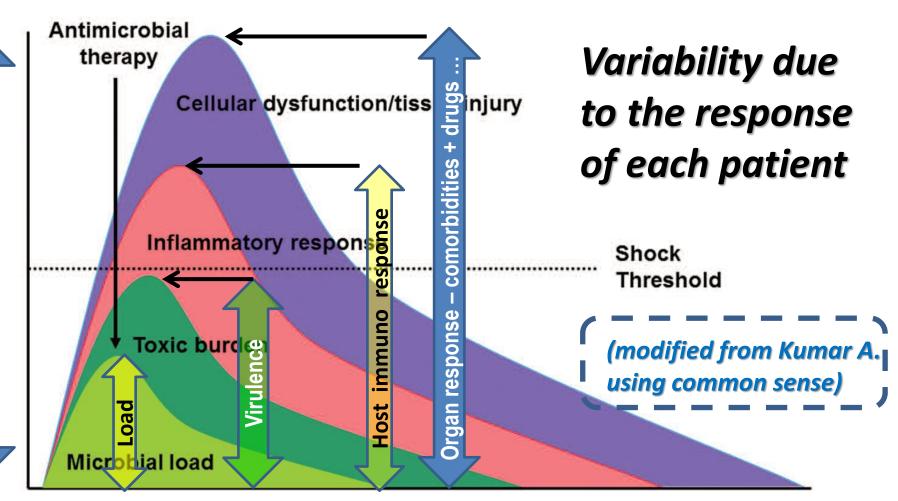


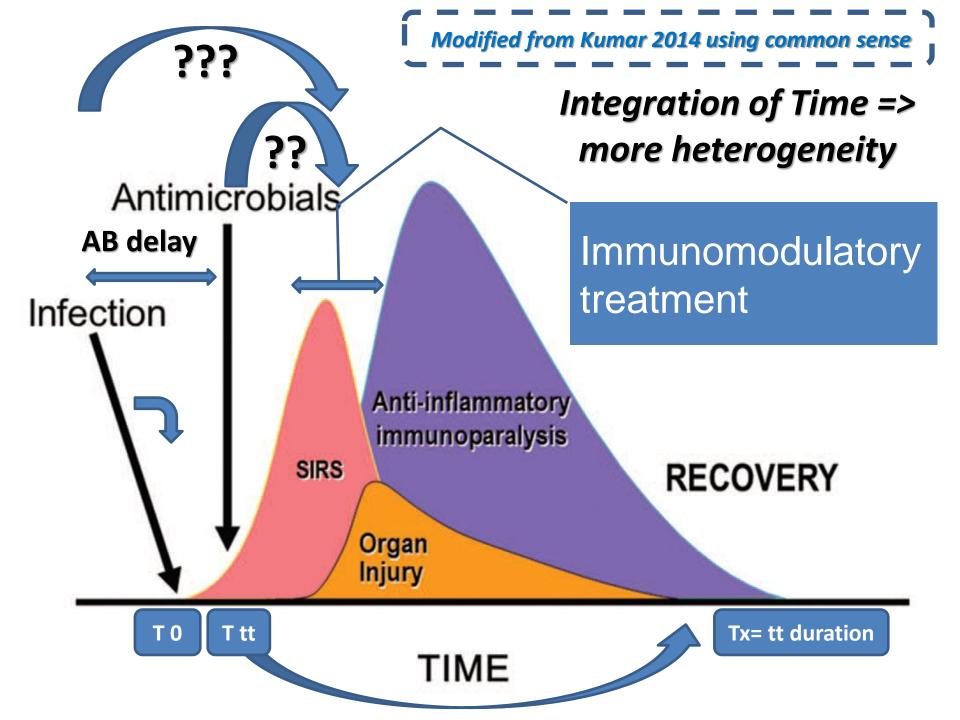


TIME

## Impact of appropriate antimicrobial therapy in patients with sepsis OR septic shock.

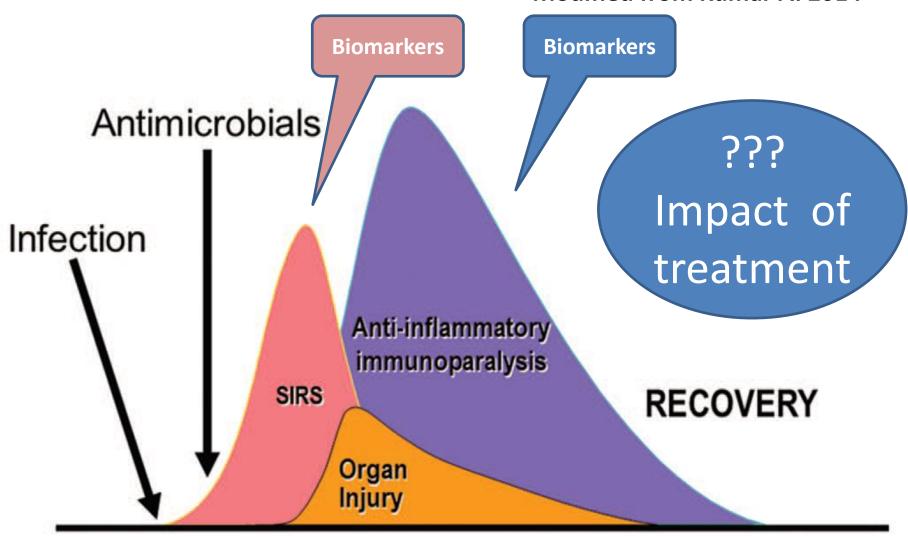
Kumar A. 2014





### Immunologic view of sepsis and septic shock





TIME

"In the Real Word"
Clinical practice in the ICU
IS NOT simple at all

"Everything should be made as simple as possible, but not simpler".

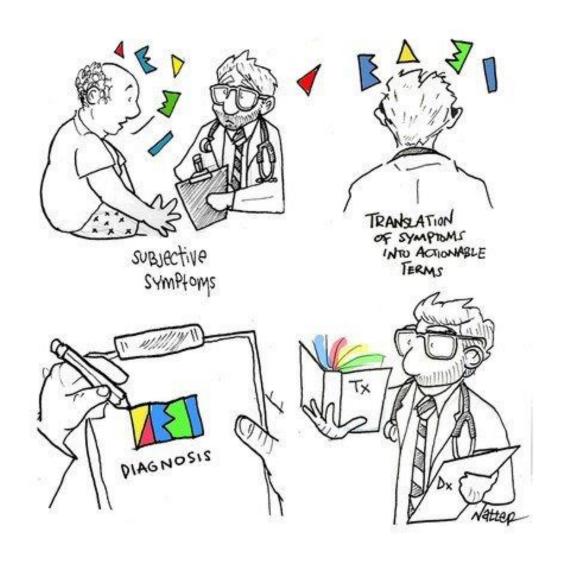
Albert Einstein

## Key points (III)



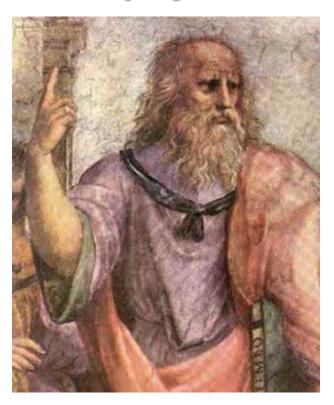
- Σημασία του case-mix στις RCTs με βάση τις οποίες δημιουργούνται τα Guidelines
- Διαφορετικοί ορισμοί ανάλογα με το σκοπό για τον οποίο δημιουργούνται αλλά και με το επίπεδο επιστημονικής <u>γνώσης + κατανόησης</u>
- Πολυπλοκότητα των «μοντέλων» στον πραγματικό κόσμο (in the real word) => αναγκαιότητα της personalized medicine \*\*\*
  - ΕΠΙΣΤΗΜΟΛΟΓΙΚΗ ΠΡΟΣΕΓΓΙΣΗ =>

## «Υπαρξη» της νόσου (σαν «ιδέας») ΕΞΩ και ΑΣΧΕΤΑ από τον ασθενή



## Philosophy / Epistemology (Part I)

# Theory of Ideas OR Theory of Forms



428 – 348 before JC

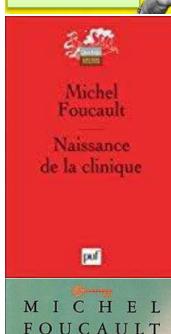
Plato applies this concept to all things. According to Plato, there must be a form of the **tree itself** in somewhere. Trees that we can see in our lives share the property of the **Form of the tree itself**.

The reason why trees are trees is that they participate in the Form of the three itself.

The reason why other things are not trees is that they don't participate in the Form of the tree itself.



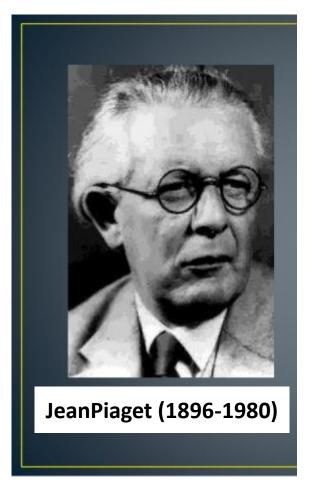
## Philosophy / Epistemology (II)

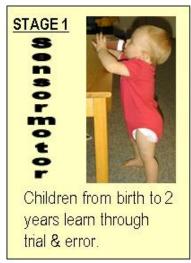


What Foucault is telling us is that the clinic (the doctor's office) is built around the idea that the patient's body is doing the talking and the doctor is only an objective observer. The doctor uses his expert training to spot the signs of disease or disorder in the patient's body and then he objectively translates these signs into a diagnosis and a treatment plan.

Diseases exist somewhere like Plato's "Ideas" or "Forms" "Know the name of the Evil Spirit to be able to face it "Diagnostic boxes=> automatically treatment instructions?

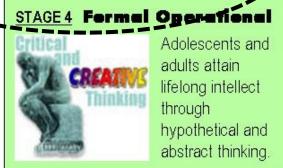
### Philosophy / Epistemology (Part IIIa)







Cognitive Development STAGE 3 Logical thinking and concrete referencing develops from 7 to 11 years.



Adolescents begin to think more as a scientist thinks, devising plans to solve problems and systematically test opinions.[40] They use hypothetical-deductive reasoning, which means that they develop hypotheses or best guesses, and systematically deduce, or conclude, which is the best path to follow in solving the problem.[40]

**Concrete Operational** 



## Philosophy / Epistemology (Part IVa)

## Two forms of intelligence according to Piaget:

### Figurative intelligence

is the more or less <u>static aspect</u> of intelligence involving all means of representation <u>used to retain in mind the states</u> (i.e., successive forms, shapes, or locations) that intervene between transformations. Therefore, it involves perception, imitation, mental imagery, drawing, and language. [10]

### **Operative intelligence**

is the active aspect of intelligence. It involves all actions, undertaken in order to follow, recover, or anticipate the transformations of the objects or persons of interest. [9]



## Philosophy / Epistemology (Part IVb)

Two forms of intelligence according to Piaget:

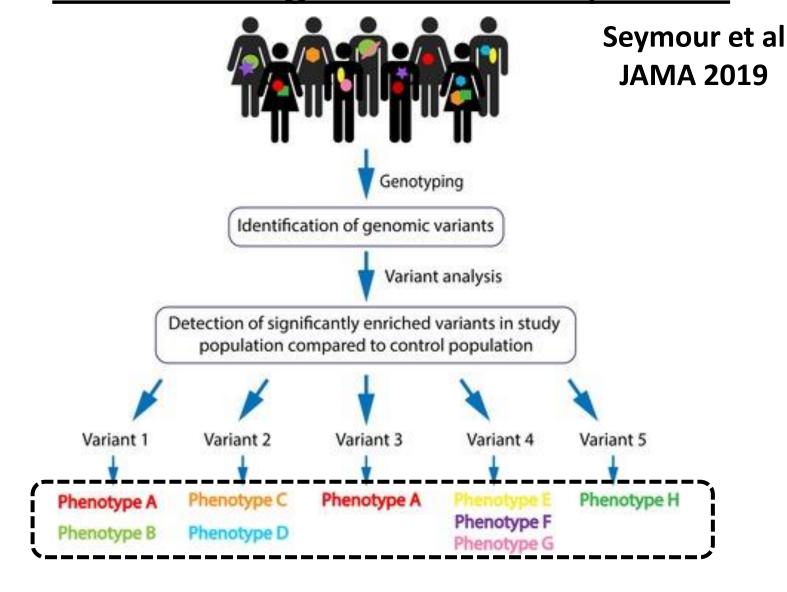
Piaget stated that figurative aspects of intelligence are subservient to its operative and dynamic aspects, and therefore,

understanding essentially derives from the operative aspect of intelligence.

THINKING OUT OF THE "BOX"

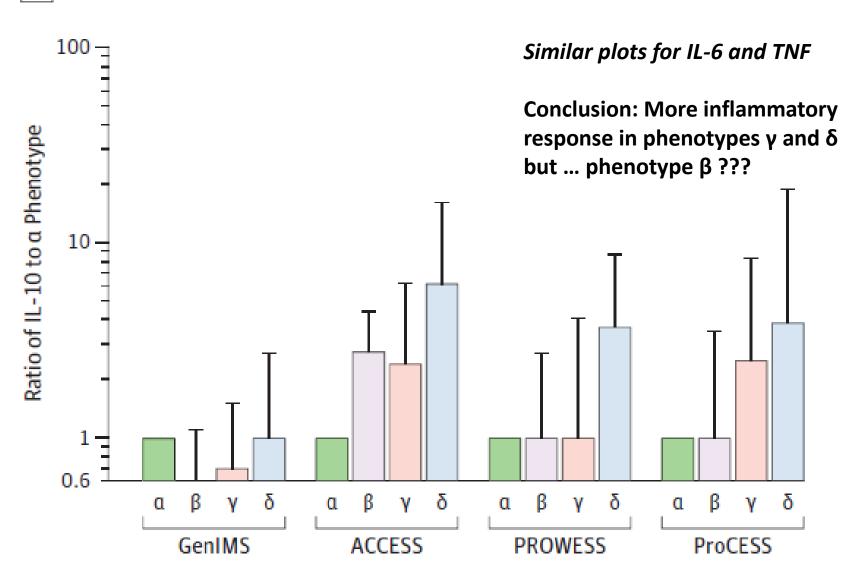
OR WITHOUT FORMS

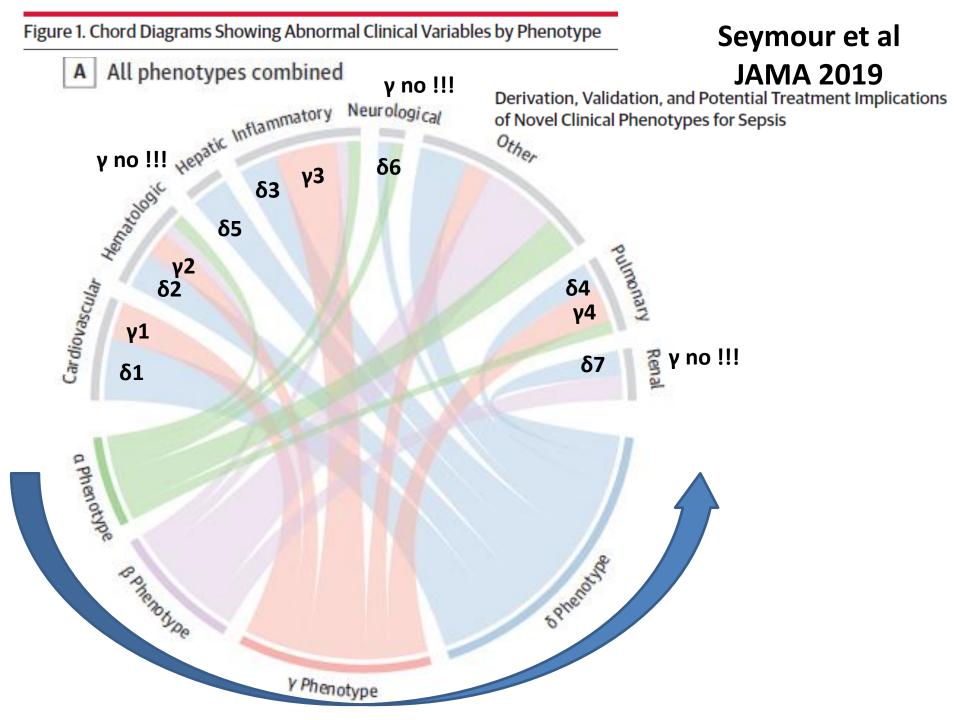
# The usefulness of "phenotypes" in "medical cognitive development"



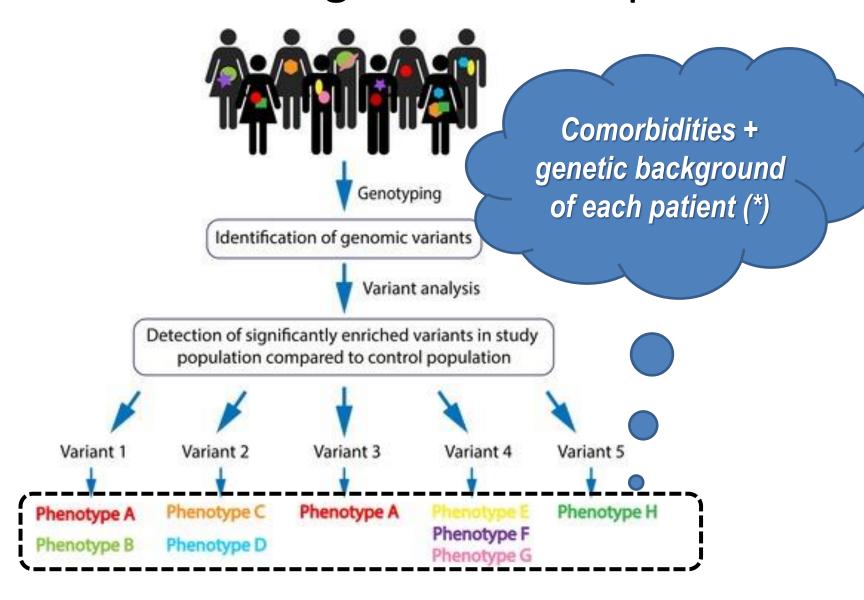
Seymour et al JAMA 2019

B Ratio of IL-10 to α phenotype





# The usefulness of "phenotypes" in "medical cognitive development"



# The diagnosis of sepsis revisited - a challenge for young medical scientists in the 21st century

Lawrence A Lynn



Expert opinion

Lynn Patient Safety in Surgery 2014, 8:1 http://www.pssjournal.com/content/8/1/1

#### **Abstract**

In 1991, a well-meaning consensus group of thought leaders derived a simple definition for sepsis which required the breach of only a few static thresholds. More than 20 years later, this simple definition has calcified to become the gold standard for sepsis protocols and research. Yet sepsis clearly comprises a complex, dynamic, and relational distortion of human life. Given the profound scope of the loss of life worldwide, there is a need to disengage from the simple concepts of the past. There is an acute need to develop 21st century approaches which engage sepsis in its true form, as a complex, dynamic, and relational pattern of death.

### There is a need

to disengage from the simple concepts of the past and to develop 21<sup>st</sup> century approaches which engage sepsis in its true form, a <u>complex-dynamic-relational</u> pattern of death.

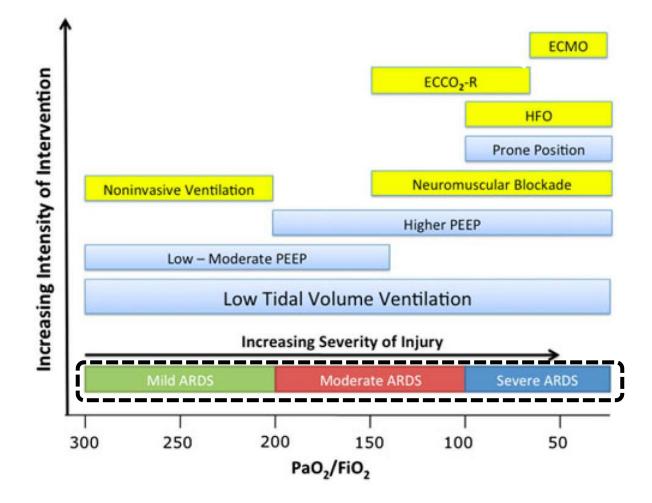
## American European Consensus Conference Criteria for ALI & ARDS

Clinical Variable	ALI	ARDS
Onset	Acute	Acute
Hypoxemia	PaO2/FiO2 ≤300	PaO2/FiO2≤200
Chest X-ray	B/L infiltrates Consistent with pul. Edema	B/L infiltrates Consistent with pul. Edema
Non-cardiac cause	No clinical e/o left atrial HTN or pulm artery occlusion pressure ≤18 mmHg	No clinical e/o left atrial HTN or pulm artery occlusion pressure ≤18 mmHg

Bernard et al 1994

Niall D. Ferguson **Eddy Fan** Luigi Camporota Massimo Antonelli **Antonio Anzueto** Richard Beale Laurent Brochard **Rov Brower** Andrés Esteban Luciano Gattinoni Andrew Rhodes Arthur S. Slutsky Jean-Louis Vincent Gordon D. Rubenfeld **B.** Taylor Thompson V. Marco Ranieri

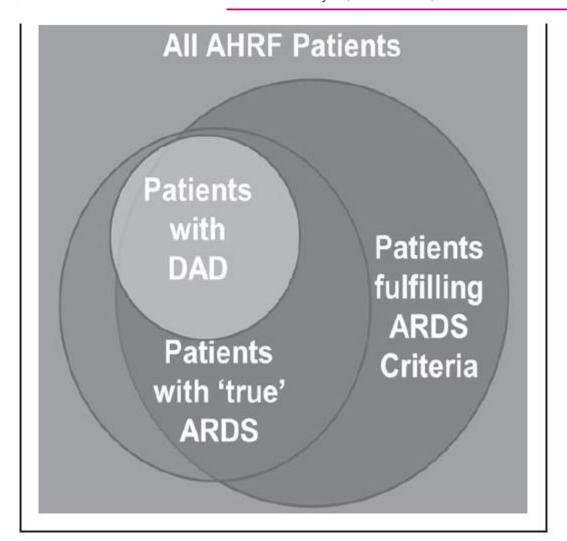
# The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material





# Continued under-recognition of acute respiratory distress syndrome after the Berlin definition: what is the solution?

John G. Laffey<sup>a,b</sup>, Tài Pham<sup>c</sup>, and Giacomo Bellani<sup>d,e</sup>



# Definitions follow Purpose

Patients with the "disease"

Curr Opin Crti Care 2017 Feb; 23(1):10-17.

# Key points (IV)



- Σημασία του case-mix στις RCTs με βάση τις οποίες δημιουργούνται τα Guidelines
- Διαφορετικοί ορισμοί ανάλογα με το σκοπό για τον οποίο δημιουργούνται αλλά και με το επίπεδο επιστημονικής <u>γνώσης</u> + κατανόησης
- Πολυπλοκότητα των «μοντέλων» στον πραγματικό κόσμο (in the real word) => αναγκαιότητα της *personalized* medicine \*\*\*
- Αναγκαιότητα για operational intelligence στην εξέλιξη της ιατρικής γνώσης- αντίληψης
- Decision making in the Real Word =>

# An alternate pathophysiologic paradigm of sepsis and septic shock

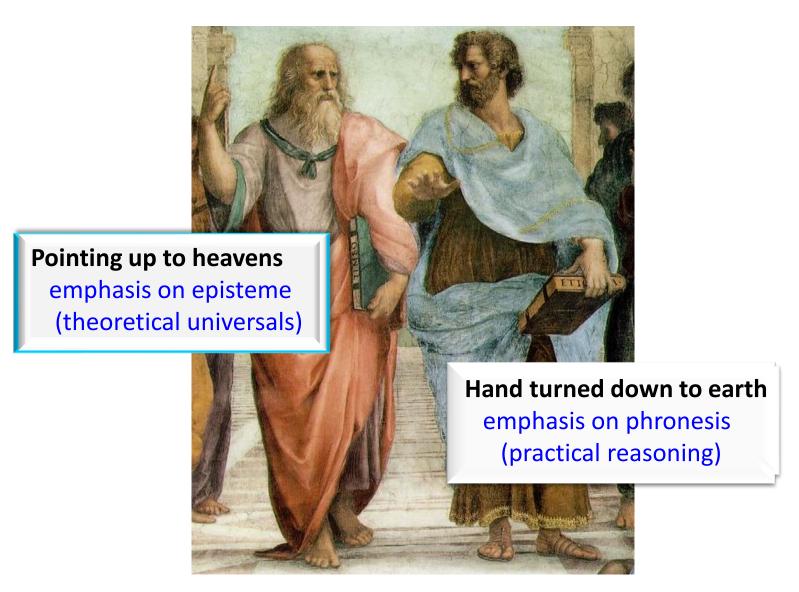
Implications of individual response variability

A new paradigm (modified from Anand Kumar )

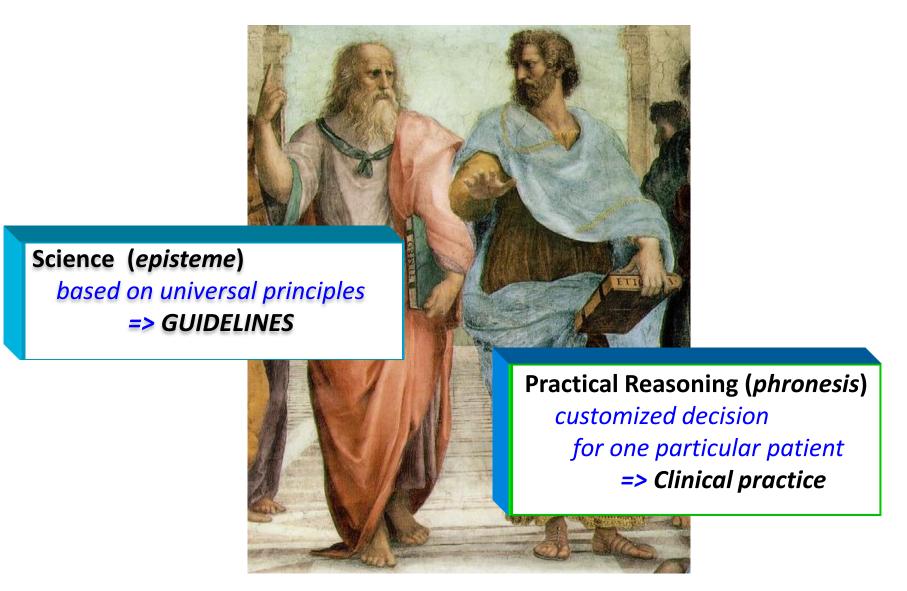
- Current paradigm: Immunologic Model
- The classic paradigm: Microbiologic Primacy
- A new Composite Model: Integrating Shock
- We need a more Composite Model = use a Dialectic Approach integrating:
  - a) Time effect and variability in the real world
  - b) risk /benefit analysis => risk of adverse effects in the individual patient (comorbidities ?)
  - c) re-evaluation after response to treatment?



Dialectic approach (Διαλεκτική προσέγγιση)
Raphael 1483-1520: The school of Athens 1510-11, Vaticano



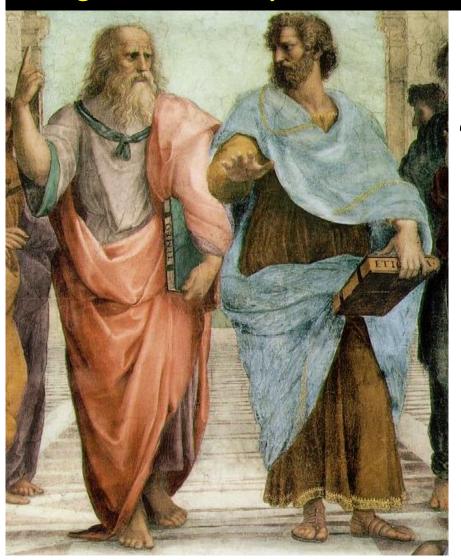
Plato, 427-347 BC Aristotle, 384-322 BC



Plato, 427-347 BC Aristotle, 384–322 BC

# "Clinical Practice Guidelines"

# We need a dialectic approach using both Theory and Phronesis



for a
"customized"
decision
making
in the
individual
patient

Plato, 427-347 BC Aristotle, 384–322 BC

#### Crit Care Med 2006 Vol. 34, No. 11

Patients are not airplanes and doctors are not pilots

Richard Rissmiller, MD, Internal Medicine, Carolinas Medical Center, Charlotte, NC

#### 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

## The authors reply:

Emanuel P. Rivers, MD, MPH, IOM,

Although co-morbidities make each patient unique, making the management of sepsis an art and a science, they also add a higher level of complexity requiring an orderly approach to patient care.

In the absence of order, chaos reigns, which benefits no one, including the patients we serve.

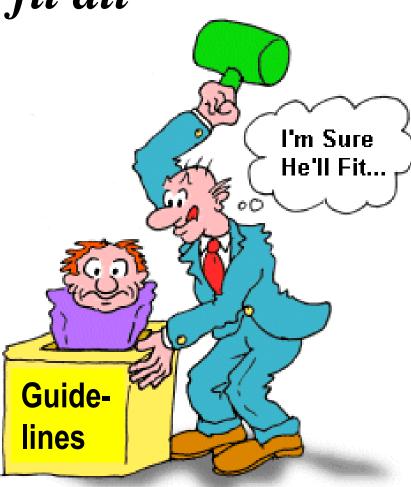
# EMERGENCY MEDICINE DECISION MAKING

Critical Choices in Chaotic Environments

SCOTT WEINGART PETER WYER



# One size DOES NOT fit all



# Expert (and my) Opinion

Russell Burck Rush University Medical Center, Chicago, IL

**Editorial in Critical Care Medicine 2004** 

"Clearly, the reality of the science of critical care is that it is a messy.



### TAILORED Consortium Meeting:

### TAILORED-Treatment scientists are discussing project strategy and results

Erasmus University Medical Centre in Rotterdam, Netherlands 2015

COORDINATOR Dr John P. Hays



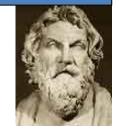
## «Αρχή σοφίας η των ονομάτων επίσκεψις» Αντισθένης (445 -360 π.Χ.)

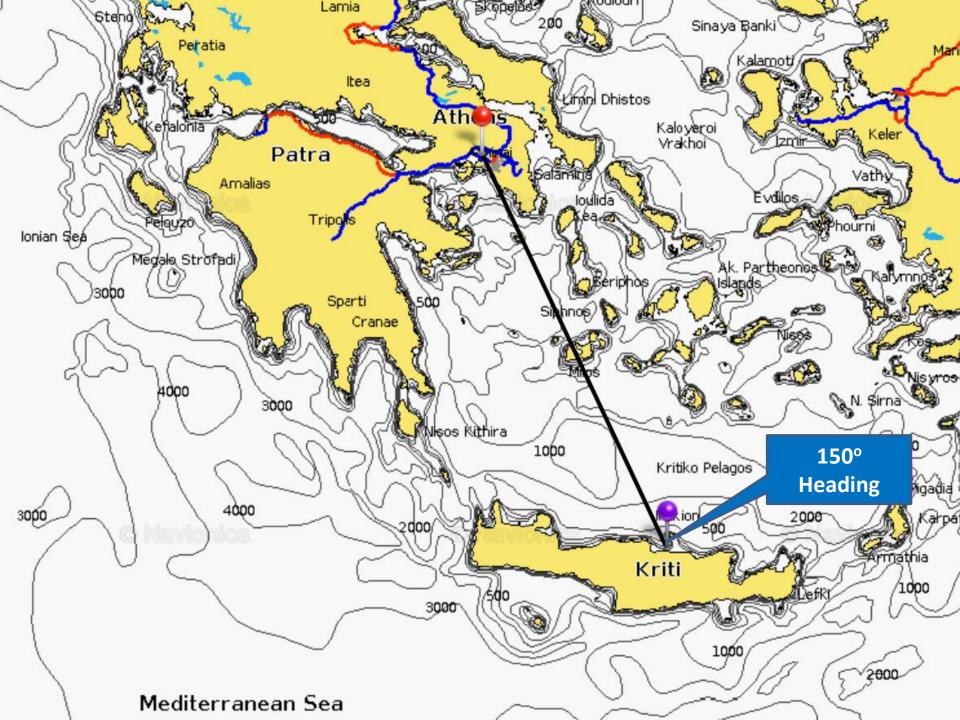
## Guidelines ΔΕΝ σημαίνει:

- Κανόνες ; (rules)
- Αρχές αντιμετώπισης ; (principles)
- Οδηγίες; (instructions manual ?)

## Σημαίνει: ΚΑΤΕΥΘΥΝΤΗΡΙΕΣ ΓΡΑΜΜΕΣ

- Σημασία μετάφρασης: οικονομικά + νομικά θέματα αλλά και θέματα που έχουν σχέση με τη διδασκαλία, την κατανόηση των εννοιών «νόσος» και «σύνδρομο» και της παθοφυσιολογικής προσέγγισης και της διαλεκτικής αντιμετώπισης «ασθενών με νόσο Χ» και όχι «της νόσου Χ»
- Παράδειγμα πλοήγηση για Κρήτη=κατεύθυνση 150°





http://www.inc.com/josh-linkner/compasses-over-maps.html



## Why You Need to Give Your Team a Compass, **Not a Map**

Shifting terrain, unexpected roadblocks, and surprise attacks can be conquered only by travelers who can think and act without detailed instructions.



BY JOSH LINKNER Entrepreneur, author, VC, Jazz gultarist 🍏 @JoshLinkner



WRITE A COMMENT

# Why You Need to Give Your Team a Compass, Not a Map

IT

Management-by-operating-manuals worked fine back in the days when markets were local, customers were homogenous,

product cycles occurred over decades, and complexity was minimal. \*

Workers didn't need to think all that much on their own, as long as following the map would ensure their safe arrival.

Boy, has the world changed.

# Why You Need to Give Your Team a Compass, Not a Map

When teams or organizations turn off their brains and simply follow the map, progress shrivels.

Shifting terrain, unexpected roadblocks, and surprise attacks can be conquered only by travelers who can think and act without detailed instructions.

Compasses over maps.
Creativity over compliance.
Empowerment over control.
Thinking over following.

Operative vs. Figurative Intelligence

## ΣΥΝΟΨΗ ΠΑΡΟΥΣΙΑΣΗΣ

- Η σημασία του «δείγματος ασθενών» (casemix)
- Η λογική δημιουργίας ορισμών νόσων
- Η πολυπλοκότητα της παθοφυσιολογίας στον «πραγματικό κόσμο» (RCTs vs real word studies)
- Επιστημολογική προσέγγιση σαν εξήγηση των δυσκολιών κατανόησης της πραγματικότητας (personalized medicine)
- Διαλεκτική προσέγγιση για λήψη αποφάσεων (decision making in clinical practice)

## Evidence Based Medicine: the wolf in sheep's clothing Cassiere et al 1998

"Decisions must be made by clinicians and not by reviewers,

who combine experience, judgement and a thoughtful review of the literature".



It is more important to know the patient than the disease <u>Hippocrates</u>

The good physician *The good clinician* treats the disease; *follows the Guidelines* the great physician treats the patient who has the disease.

William Osler
1849-1919



(personalized ≠precision medicine)

Πέρασε ο Φίλλιπος για να δεί τι διδάσκει ο Αριστοτέλης στον Μέγα Αλέξανδρο. Τον ρώτησε λοιπόν:

"Μαθηματικά τον διδάσκεις;" - Όχι απάντησε ο Αριστοτέλης

"Γραφή;" - Όχι απάντησε ο Αριστοτέθης

"Τι τον διδάσκεις ποιπόν;" είπε εκνευρισμένος ο Φίππιπος

-Τον διδάσκω πως να σκέπτεται απάντησε ο Αριστοτέθης!

# ΕΥΧΑΡΙΣΤΩ ΓΙΑ ΤΗΝ ΠΡΟΣΟΧΗ ΣΑΣ

