

# SEPSIS

What is new and what is old ?



Szederjesi Janos

10.January.2018



# Learning objectives

- Understand sepsis
- Learn the new definition of sepsis and septic shock



# The Rory story !!!

## THE RORY STAUNTON FOUNDATION

FOR SEPSIS PREVENTION

- In March 2012, Rory Staunton, a 12-year-old boy in Queens, New York, cut his arm playing basketball in school. The next day, his parents, worried about his fever and leg pain, took him to see his pediatrician and then, the day after, to the emergency department at Langone Medical Center. He was discharged with a diagnosis of an upset stomach and dehydration but died 3 days later from sepsis

*An infection , unnoticed , turn Unstoppable*

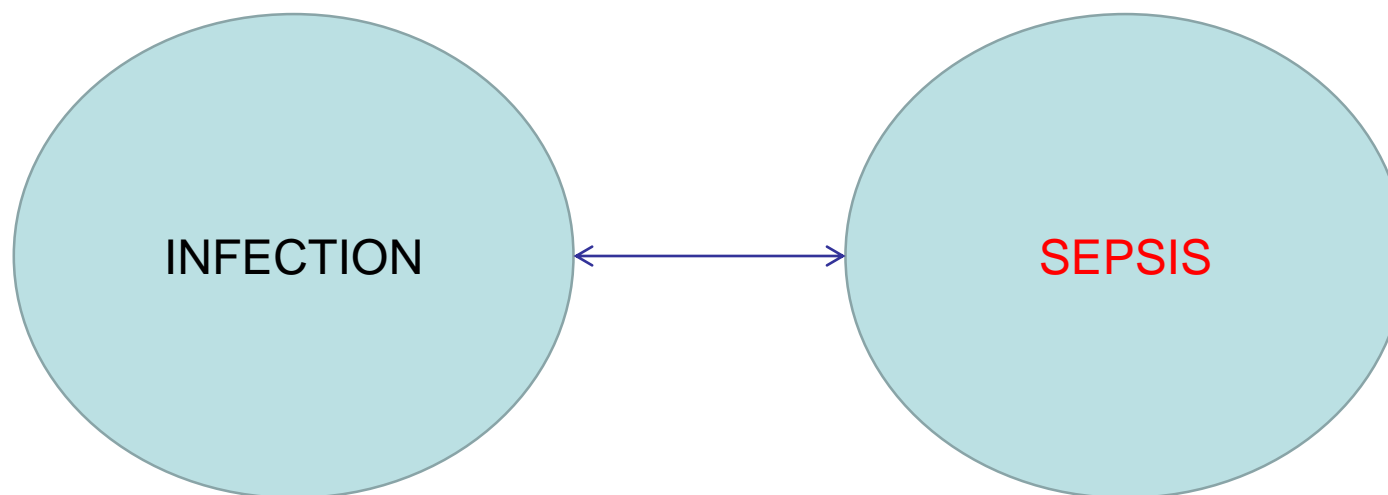
About New York

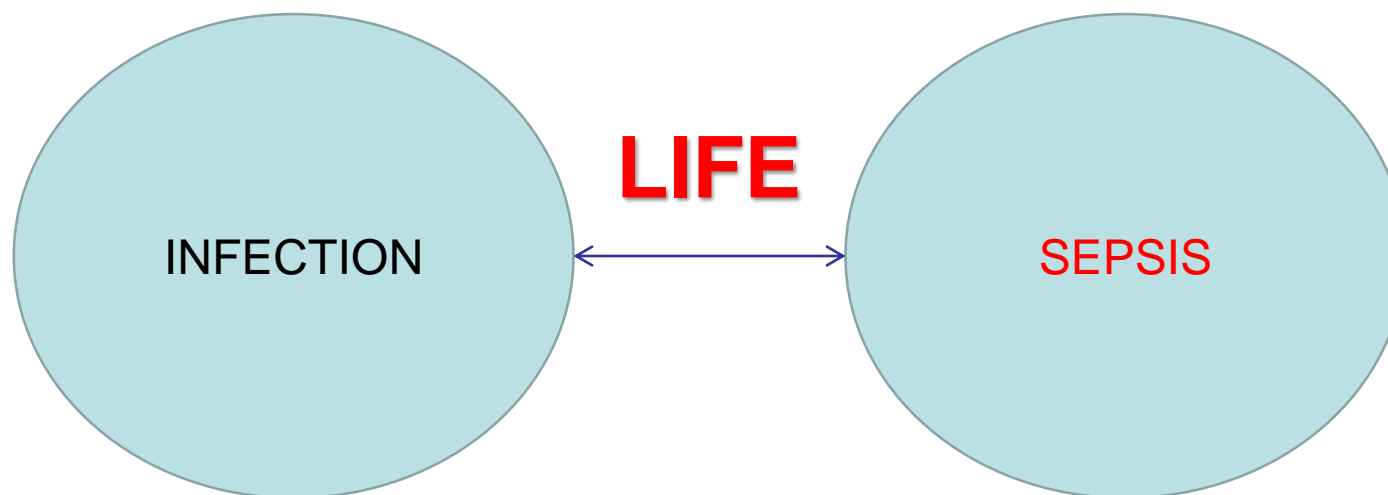
By JIM DWYER JULY 11, 2012



Rory Staunton taking his first flying lesson in 2011.







Why Sepsis again !!

Why new definitions !!

Why new scoring system !!





## The 10 most expensive conditions treated in U.S. hospitals in 2011

Condition	Total spending	Percentage of total costs	Number of hospital discharges
1 Sepsis (except in labor)	\$20.3 billion	5.2%	1.1 million
2 Osteoarthritis	\$14.8 billion	3.8%	964,000
3 Complication of device, implant or graft	\$12.9 billion	3.3%	699,000
4 Liveborn	\$12.4 billion	3.2%	3.8 million
5 Acute myocardial infarction	\$11.5 billion	3.0%	612,000
6 Spondylosis, intervertebral disc disorders, other back problems	\$11.2 billion	2.9%	667,000
7 Pneumonia (except TB or STDs)	\$10.6 billion	2.7%	1.1 million
8 Congestive heart failure, nonhypertensive	\$10.5 billion	2.7%	970,000
9 Coronary atherosclerosis	\$10.4 billion	2.7%	605,000
10 Respiratory failure, insufficiency, arrest (adult)	\$8.7 billion	2.3%	404,000

Source: Agency for Healthcare Research and Quality

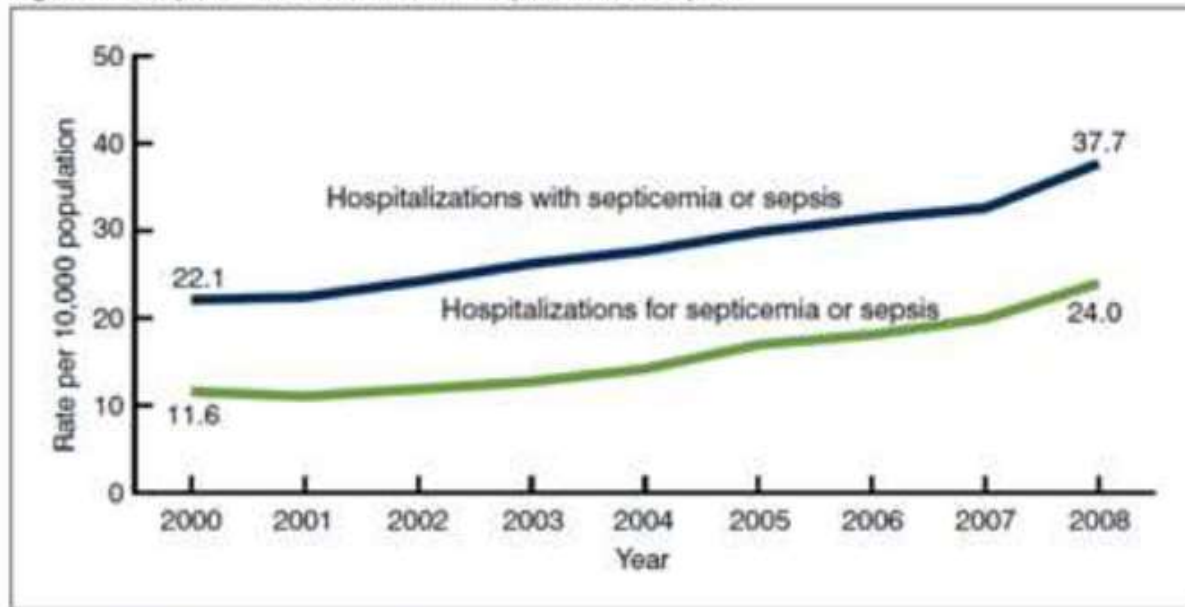
Greg Cross / The Bulletin



# Hospitalization rates

**Hospitalization rates for septicemia or sepsis more than doubled from 2000 through 2008.**

Figure 1. Hospitalizations for and with septicemia or sepsis



NOTE: Significant linear trend from 2000 through 2008 for both categories.  
SOURCE: CDC/NCHS, National Hospital Discharge Survey, 2000-2008.



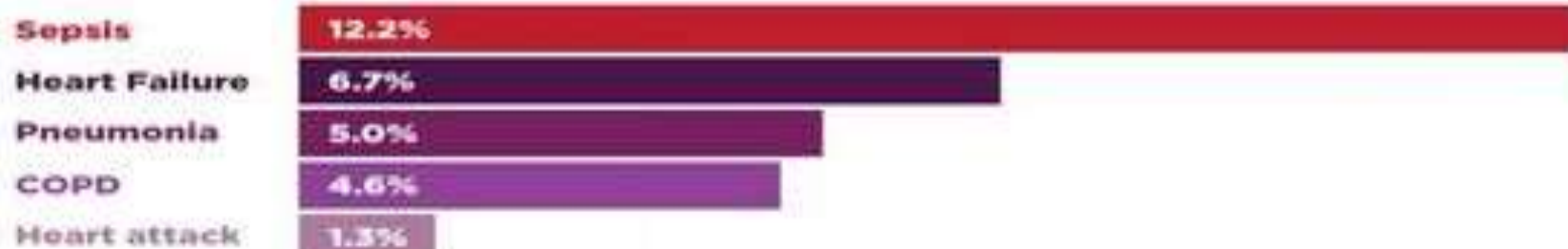
# Sepsis Readmission Rates



## Sepsis is the No. 1 killer of hospital patients.

It is a condition that arises when the body's response to an infection injures its own tissues and organs. Nationally, hospital readmissions\* of patients who suffered sepsis far outpace the four medical conditions that the federal government tracks to gauge hospital performance.

### Percentage of hospital readmissions

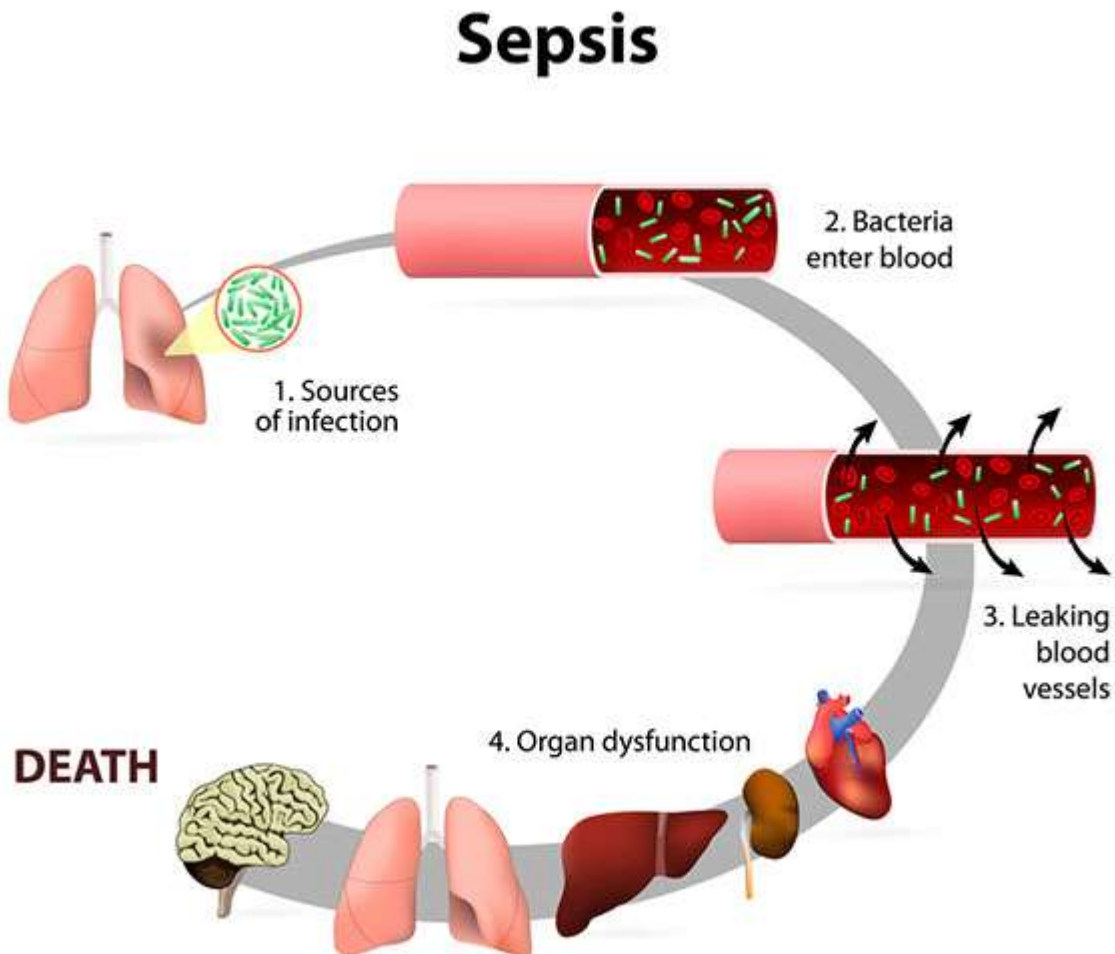


### Estimated average cost per readmission



\*30-day readmission, 2013 Nationwide Readmissions Database  
Source: Mayr, et al., JAMA, 2017

# What is the sepsis ?



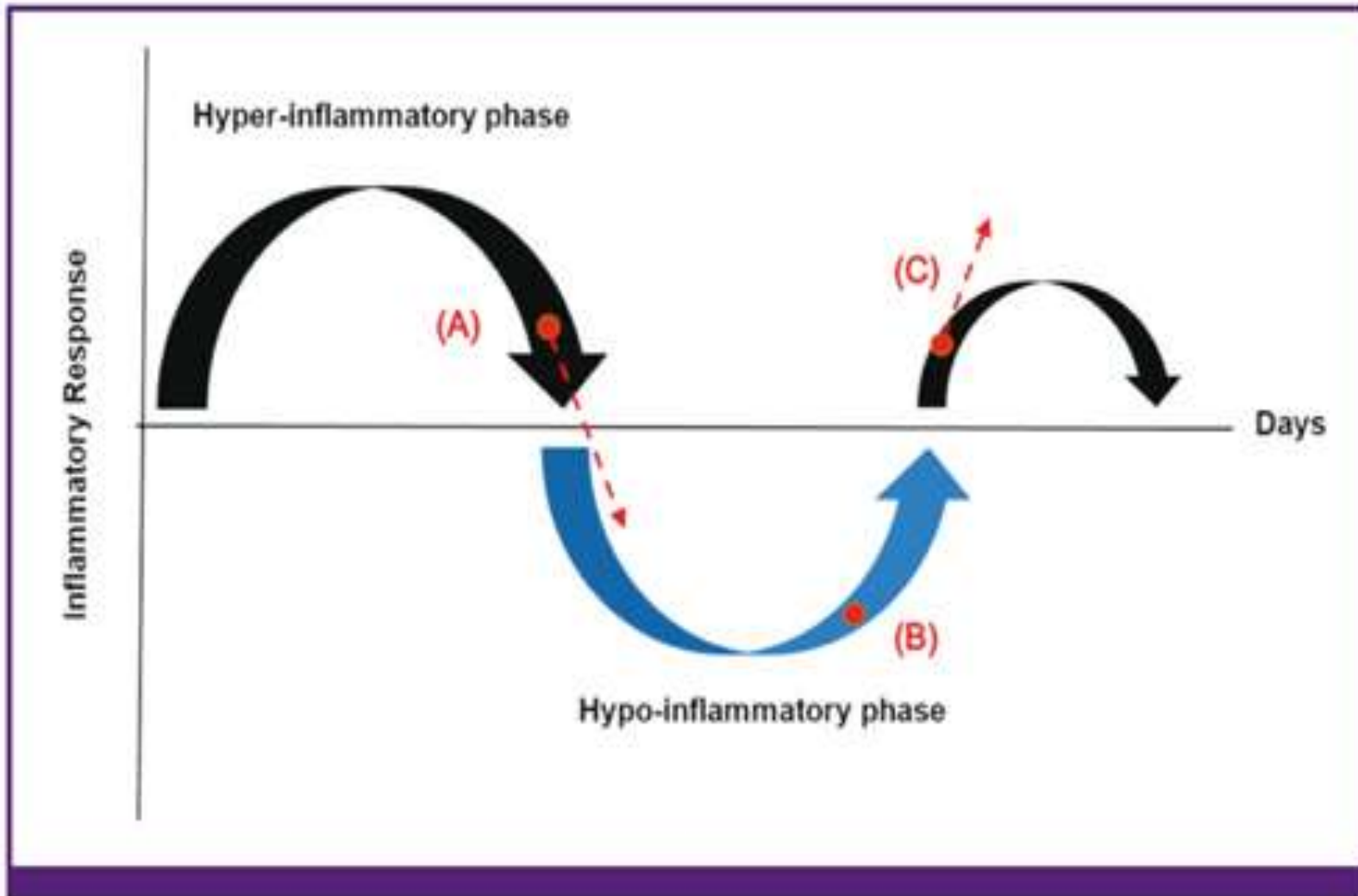
- A dysregulated immune response to infection
- Regulated
  - Innate & Adaptive
    - Cellular: Dendritic cells, T-cells, B-cells
    - Molecular: complement, acute phase, cytokines
    - Anti-viral: Interferon, local cellular immunity, apoptosis



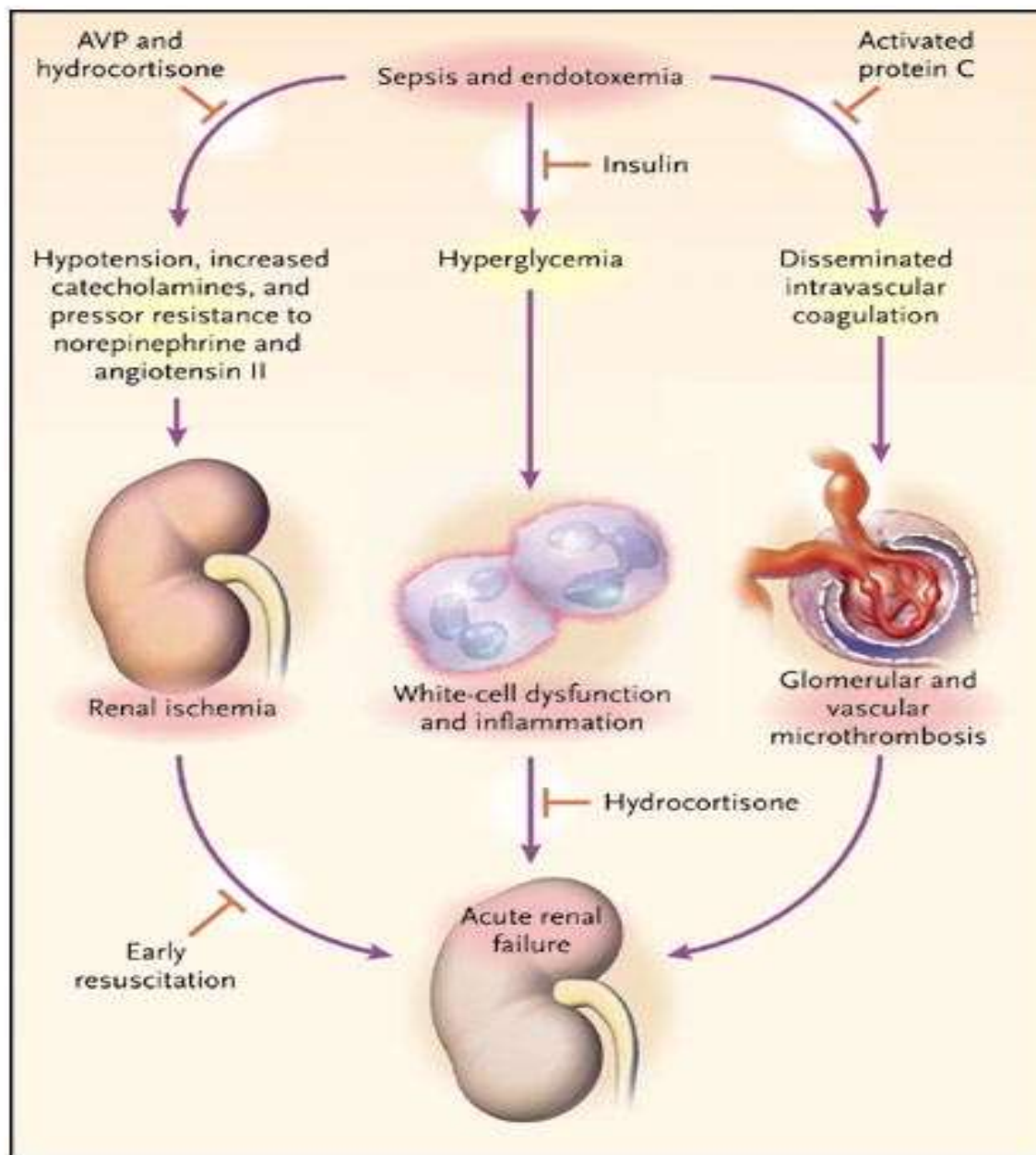
# Regulated?

- Local inflammation
  - Vasodilation, capillary leak
- Systemic inflammation
  - SIRS, CARS (compensatory anti-inflammatory response)





Bone 1996





# Actors

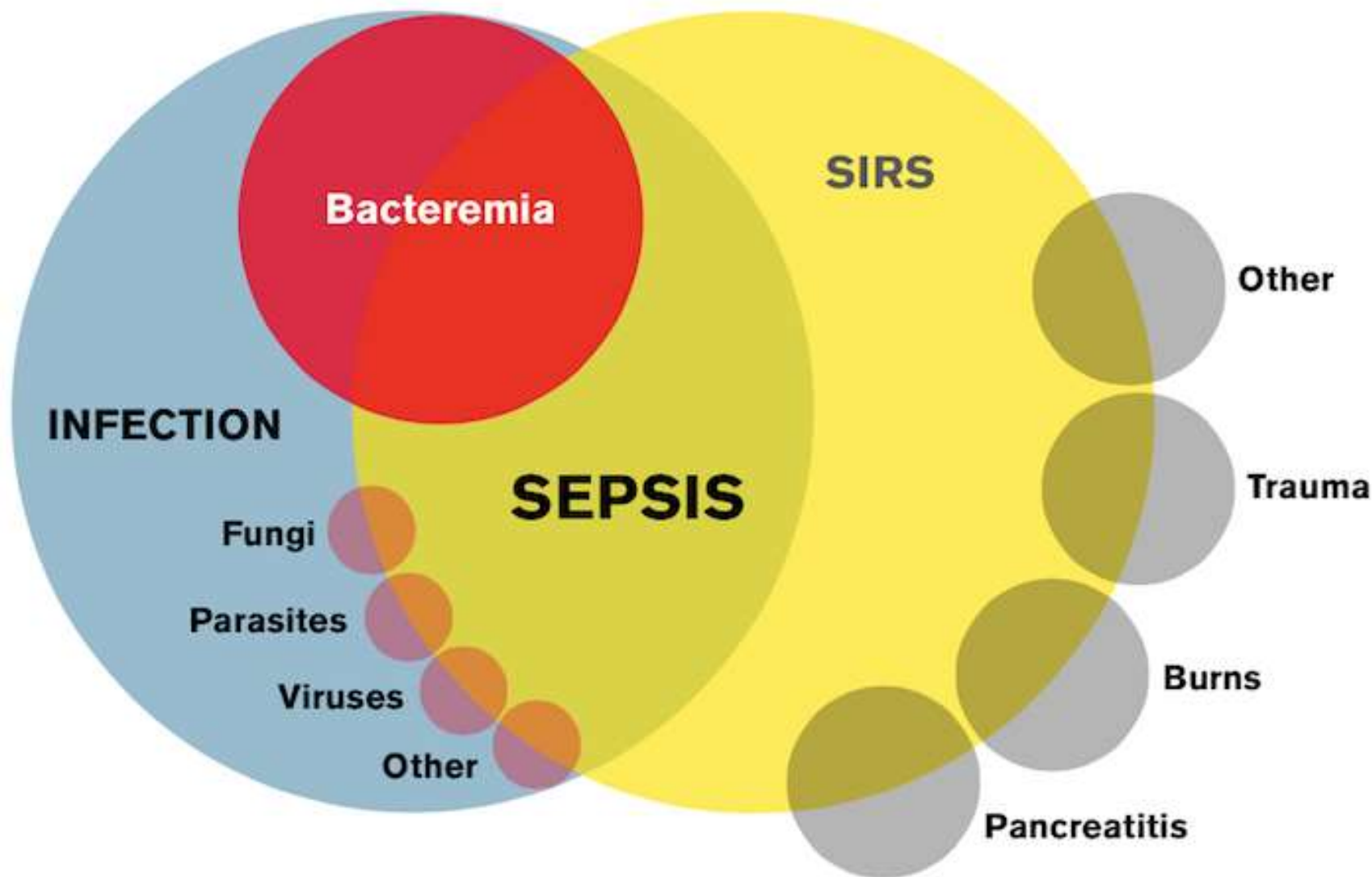
- **Micro-organism**
  - Virulence
  - Innoculation dose
  - Multi-drug resistance
- **Host**
  - Genetic polymorphisms
  - Co-morbidities
    - Age
    - Chronic health status
    - Immuno-modulatory medications



# Dysregulated?

- Multi-organ dysfunction then failure
  - Little necrosis
    - Apoptosis of the cellular immune system
    - Anti-inflammatory phase ‘immunoparalysis’
    - D4 persistent lymphopenia
    - ‘Stimulate immune system improve outcome’





# SIRS Criteria

- Two or more of:
  - Temperature  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$
  - Heart rate  $>90/\text{min}$
  - Respiratory rate  $>20/\text{min}$  or  $\text{PaCO}_2 <32 \text{ mm Hg}$  (4.3 kPa)
  - White blood cell count  $>12\,000/\text{mm}^3$  or  $<4000/\text{mm}^3$  or  $>10\%$  immature bands
- Bone et al. *Crit Care Med.* 1992;20(6):864-874.



# The old definitions

Defining criteria of ACCP/SCCM named conditions.

ACCP/SCCM named condition	Defining criteria
SIRS	Core body temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$ HR $\geq 90$ bpm Respirations $\geq 20/\text{min}$ (or $\text{PaCO}_2 < 32$ mmHg) WBC $\geq 12,000/\mu\text{l}$ or $\leq 4000/\mu\text{l}$ or $>10\%$ immature forms
Sepsis	At least two SIRS criteria caused by known or suspected infection
Severe sepsis	Sepsis with acute organ dysfunction (including hypoperfusion and hypotension) caused by sepsis
Septic shock	Sepsis with persistent or refractory hypotension or tissue hypoperfusion despite adequate fluid resuscitation
MODS	The presence of organ dysfunction in an acutely ill patient such that homeostasis cannot be maintained without intervention.

ACCP: American College of Chest Physicians; HR: Heart rate; MODS: Multiple organ dysfunction syndrome;  $\text{PaCO}_2$ : Partial pressure of carbon dioxide in the blood; SCCM: Society of Critical Care Medicine; SIRS: Systemic inflammatory response syndrome; WBC: White blood cell.



# Why new definitions !!

- To know what distinguishes sepsis from uncomplicated infection as simple infection (which could simply controlled by rest and cup of hot tea!! ) SIRS criteria basically could be the same

*“We need to differentiate a straightforward infection from one that can cause organ dysfunction or death”*





February 23, 2016, Vol 315, No. 8 >

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Special Communication | February 23, 2016

CARING FOR THE CRITICALLY ILL PATIENT

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

Mervyn Singer, MD, FRCP<sup>1</sup>; Clifford S. Deutschman, MD, MS<sup>2</sup>; Christopher Warren Seymour, MD, MSc<sup>3</sup>; Manu Shankar-Hari, MSc, MD, FFICM<sup>4</sup>; Djillali Annane, MD, PhD<sup>5</sup>; Michael Bauer, MD<sup>6</sup>; Rinaldo Bellomo, MD<sup>7</sup>; Gordon R. Bernard, MD<sup>8</sup>; Jean-Daniel Chiche, MD, PhD<sup>9</sup>; Craig M. Coopersmith, MD<sup>10</sup>; Richard S. Hotchkiss, MD<sup>11</sup>; Mitchell M. Levy, MD<sup>12</sup>; John C. Marshall, MD<sup>13</sup>; Greg S. Martin, MD, MSc<sup>14</sup>; Steven M. Opal, MD<sup>12</sup>; Gordon D. Rubenfeld, MD, MS<sup>15,16</sup>; Tom van der Poll, MD, PhD<sup>17</sup>; Jean-Louis Vincent, MD, PhD<sup>18</sup>; Derek C. Angus, MD, MPH<sup>19,20</sup>

- The team analyzed 148,907 patients with suspected infection, and evaluated how well the existing and the new criteria predicted sepsis mortality in these patients.

**"We now have a scientifically based classification that will give the clinician at the bedside new and more effective ways to recognize the septic patient and the severely septic patient so as to afford the earliest possible intervention,"**

Timothy Buchman, MD, from Emory University in Atlanta



# Sequential [Sepsis-Related] Organ Failure Assessment Score

System	Score				
	0	1	2	3	4
Respiration					
Pao <sub>2</sub> /Fio <sub>2</sub> , mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, ×10 <sup>3</sup> /μL	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular					
MAP ≥70 mm Hg		MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose) <sup>b</sup>	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1 <sup>b</sup>	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1 <sup>b</sup>
Central nervous system					
Glasgow Coma Scale score <sup>c</sup>	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

Abbreviations: Fio<sub>2</sub>, fraction of inspired oxygen; MAP, mean arterial pressure; Pao<sub>2</sub>, partial pressure of oxygen.

<sup>a</sup> Adapted from Vincent et al.<sup>27</sup>

<sup>b</sup> Catecholamine doses are given as μg/kg/min for at least 1 hour.

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**P/F**

$\text{PaO}_2$  = partial pressure of oxygen in arterial blood (Hgmm)

$\text{FiO}_2$  = inspiratory oxygen concentration



----- XXXX Diagnostics -----

Blood	Gas	Report
248	05:36	Jul 22 2000
Pt ID	2570 / 00	

Measured	37.0° C	
pH	7.463	
pCO <sub>2</sub>	44.4	mm Hg
pO <sub>2</sub>	113.2	mm Hg

Corrected	38.6° C	
pH	7.439	
pCO <sub>2</sub>	47.6	mm Hg
pO <sub>2</sub>	123.5	mm Hg

Calculated Data		
TPCO <sub>2</sub>	49	
HCO <sub>3</sub> act	31.1 mmol / L	
HCO <sub>3</sub> std	30.5	mmol / L
BE	6.6	mmol / L
O <sub>2</sub> CT	14.7	mL / dl
O <sub>2</sub> Sat	98.3	%
ct CO <sub>2</sub>	32.4	mmol / L
pO <sub>2</sub> (A - a)	32.2	mm Hg
pO <sub>2</sub> (a / A)	0.79	

Entered Data		
Temp	38.6	°C
ct Hb	10.5	g/dl
FiO <sub>2</sub>	30.0	%



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# Glasgow Coma Scale

EYE OPENING		VERBAL RESPONSE		MOTOR RESPONSE	
					
Spontaneous	> 4	Orientated	> 5	Obey commands	> 6
To sound	> 3	Confused	> 4	Localising	> 5
To pressure	> 2	Words	> 3	Normal flexion	> 4
None	> 1	Sounds	> 2	Abnormal flexion	> 3
		None	> 1	Extension	> 2
				None	> 1

## GLASGOW COMA SCALE SCORE

**Mild**  
**13-15**

**Moderate**  
**9-12**

**Severe**  
**3-8**

MEDIC  TESTS #1 EMT & PARAMEDIC EXAM PREP

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Cardiovascular					
MAP ≥70 mm Hg		MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose) <sup>b</sup>	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1 <sup>b</sup>	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1 <sup>b</sup>
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## New definitions ( the screening tool )

- 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,
  - Respiratory rate  $\geq 22/\text{min}$
  - Altered mentation
  - Systolic blood pressure  $\leq 100\text{mmHg}$
  - **The presence of at least two of these criteria strongly predicts the likelihood of poor outcome in out-of-ICU patients with clinical suspicion of sepsis.**





# New definitions

- Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.
- NB:
  - **The SIRS criteria have been removed**
  - It may present in simple, non-complicated infection, or in response to non infectious-triggers (i.e. trauma, pancreatitis, post-cardiac arrest syndrome),
  - Or may even be absent in critically ill patients with obvious evidence of a life-threatening infection.



## New definitions

- Organ dysfunction can be identified as an acute change in total SOFA score  $> 2$  points consequent to the infection.
- A SOFA score  $> 2$  reflects an overall mortality risk of approximately 10% in a general hospital population with suspected infection
- The baseline SOFA score can be assumed to be zero or in patients not known to have preexisting organ dysfunction.



# New definitions

- **Septic shock** is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality.
  - **Clinical criteria identifying such condition include the need for vasopressors to obtain a  $MAP \geq 65\text{mmHg}$  and an increase in lactate concentration  $> 2\text{ mmol/L}$ , despite adequate fluid resuscitation.**

Terms like Severe Sepsis/Septicemia has been removed



# Controversies and limitations

- Most data extracted from US database
- q SOFA and SOFA can miss occult organ dysfunction
- Specific infections can cause local organ dysfunction without dysregulated systemic host response
- Non-availability of lactate measurements in resource poor settings
- Task force focused on adult patients

# What about biomarkers?


- PCT
- CRP
- IL
- More than 50 others ...





**THE GUIDELINES:  
IMPLEMENTATION FOR  
THE FUTURE**



 American College of  
Emergency Physicians®

**Tiffany M. Osborn, MD**

University of Virginia

ACEP Chair Critical Care  
Section

ACEP Representative  
Surviving Sepsis Campaign



# Take home message !

- Infection plus two or more sequential organ failure assessment points, and the use of quick sepsis-related organ failure assessment score as a prompt to identify patients likely to be septic early on,.



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- Infection plus two or more sequential organ failure assessment points, and the use of quick sepsis-related organ failure assessment score as a prompt to identify patients likely to be septic early on,.

**THANK  
YOU!**

