

Evaluation des nouvelles définitions du sepsis



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Service de Réanimation Médicale
CHU La Rabta de Tunis

16-17 Février 2018 - Hôtel Le Royal Hammamet

09h00-09h30

Plan

1

Introduction

2

History of sepsis

3

Définitions du sepsis

4

Validation du sepsis-3

5

Les points forts

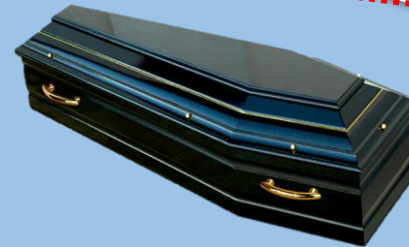
6

Les points faibles

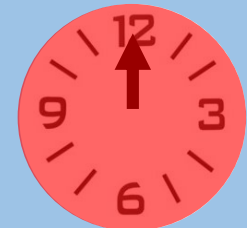
7

Conclusions

ICU costs in the United States



One person dying every **2** minutes





40 percent of all ICU costs

Six times greater than that for ICU patients that do not have sepsis

62 percent readmission rate



(Sutton & Friedman, 2013; Sepsis Alliance, 2014)



2015

The **most expensive** condition treated in US hospitals

\$23.7 billion



(Torio and Andrews, 2015)

31.5 million people are treated each year

5.3 million end up dying

Most expensive condition treated in US hospitals

Pour bien le traiter, il faut l'étudier

Sepsis

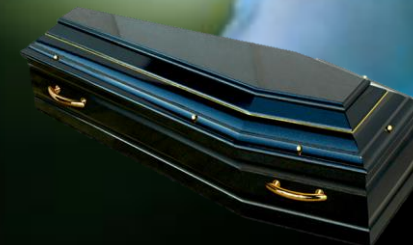


40 % of all ICU costs

62 %
readmission rate

Pour bien l'étudier il faut le définir

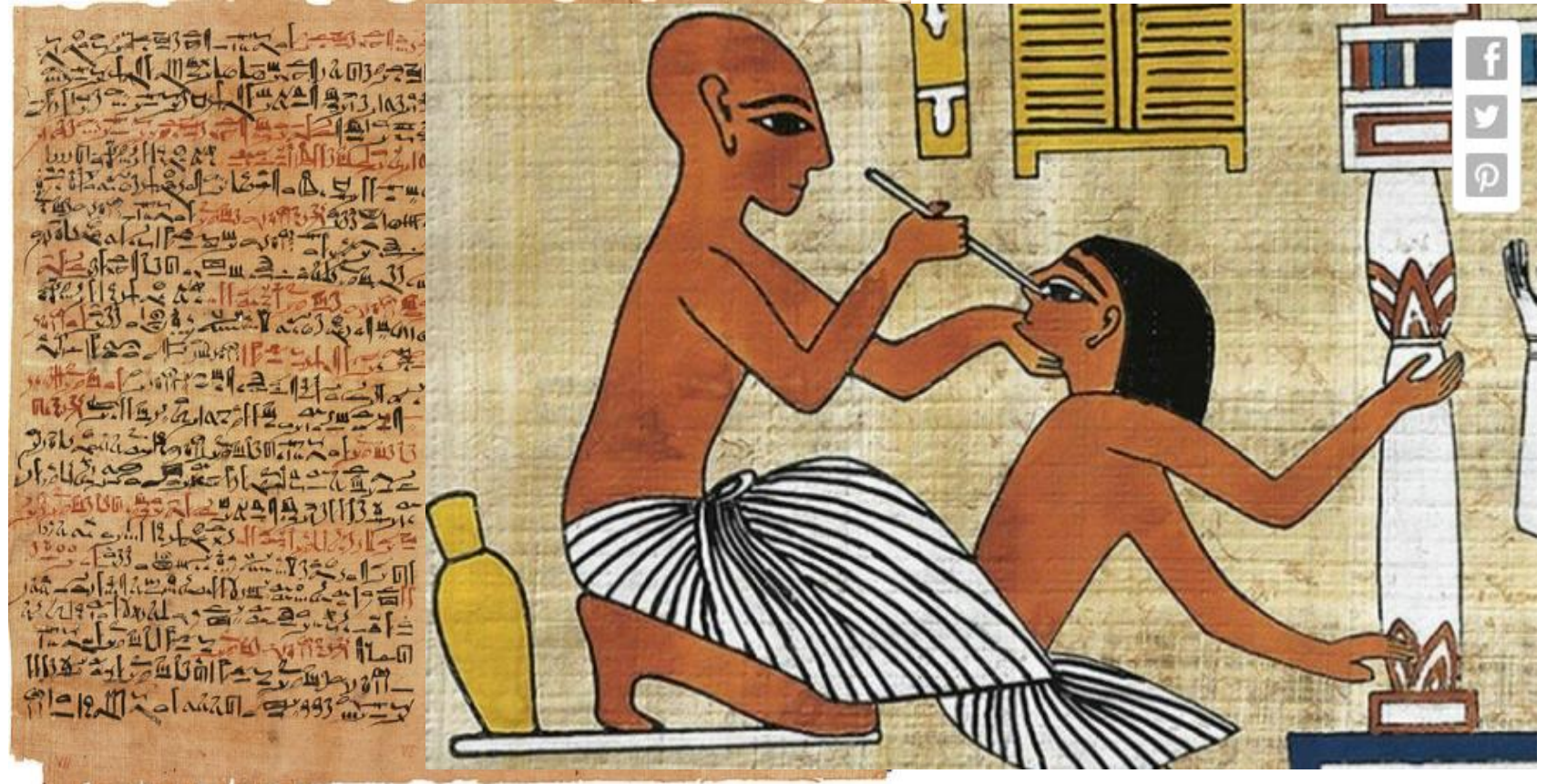
One person dying every **2 minutes**



History of sepsis



First descriptions of sepsis are found in Egyptian papyrus as early as **1600 BC**



Le papyrus Edwin Smith They used **honey** and **human brains** to cure eye infections



Hippocrate



460-470 av. JC

Galien



130-200

Avicenne



979-1037 BC

Sepsis (σήψις) =
« putréfaction »

« *Pus bonum
et laudabile* »

**Coincidence of
blood putrefaction
and fever**

Greek word

Sipsis

Make rotten

Faire pourrir

Pepsis

Good digestion

Bonne digestion



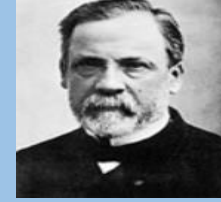
Semmelweiss

Pasteur

Robert Koch



1818-1865



1870

Hungary



Théorie des germes

Les processus d'infection et de suppuration étaient causés par des micro-organismes

Le terme de sepsis devenant synonyme d'infection invasive.



HUGO Schottmuller

1867-1936 Germany

Modern definition of
sepsis (1914)

Le sepsis survenait si des **germes pathogènes** envahissaient d'une façon constante ou périodiquement la **circulation sanguine** à partir d'un **foyer infectieux** et provoquaient des **symptômes** subjectifs et objectifs

Le traitement ne doit pas être dirigé contre les **bactéries** dans le sang, mais contre les **toxines bactériennes libérées**



Rising incidence,
new etiologies

Changing
demographics

= the **most
common cause of
death** in the
noncoronary
intensive care unit

↗ use of **ATB**,
immunosuppressive
agents, and invasive
technology in the
treatment



Bactériémie

Septicémie

Définition opérationnelle et universelle

American College Of Chest Physicians

Society of Critical Care Medicine

1992

SEPSIS-1



accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Table 1—Definitions

Infection = microbial phenomenon characterized by an inflammatory response to the presence of microorganisms or the invasion of normally sterile host tissue by those organisms.

Bacteremia = the presence of viable bacteria in the blood.

Systemic inflammatory response syndrome (SIRS) = the systemic inflammatory response to a variety of severe clinical insults. The response is manifested by two or more of the following conditions: (1) temperature $>38^{\circ}\text{C}$ or $<36^{\circ}\text{C}$; (2) heart rate >90 beats per minute; (3) respiratory rate >20 breaths per minute or PaCO_2

Température $< 36^{\circ}\text{C}$ ou $\geq 38,5^{\circ}\text{C}$

FC > 90 battements/minute

FR $> 20/\text{mn}$ ou $\text{PaCO}_2 < 32 \text{ mmHg}$

GB $> 12000/\text{mm}^3$ ou $< 4000/\text{mm}^3$
ou cellules immatures $> 10\%$

Severe sepsis = sepsis associated with organ dysfunction, hypoperfusion, or hypotension. Hypoperfusion and perfusion abnormalities may include, but are not limited to lactic acidosis, oliguria, or an acute alteration in mental status.

Septic shock = sepsis-induced with hypotension despite adequate fluid resuscitation along with the presence of perfusion abnormalities that may include, but are not limited to, lactic acidosis, oliguria, or an acute alteration in mental status. Patients who are receiving inotropic or vasopressor agents may not be hypotensive at the time that perfusion abnormalities are measured.

Sepsis-induced hypotension = a systolic blood pressure $<90 \text{ mm Hg}$ or a reduction of $\geq 40 \text{ mm Hg}$ from baseline in the absence of other causes for hypotension.

Multiple organ dysfunction syndrome (MODS) = presence of altered organ function in an acutely ill patient such that homeostasis cannot be maintained without intervention.

In 2001, a second consensus conference validated most of the previous concepts

but drew attention to the fact that systemic inflammatory response is not specific of sepsis and could be seen in many diseases.



accp/sccm consensus conference

Definitions for Sepsis and Organ Failure and
Guidelines for the Use of Innovative Therapies in
Sepsis

CHEST / 101 / 6 / JUNE, 1992

THE ACCP/SCCM CONSENSUS CONFERENCE COMMITTEE:

Roger C. Bone, M.D., F.C.C.P., Chairman

Robert A. Balk, M.D., F.C.C.P.

Frank B. Cerra, M.D.

R. Phillip Dellinger, M.D., F.C.C.P.

Alan M. Fein, M.D., F.C.C.P.

William A. Knaus, M.D.

Roland M. H. Schein, M.D.

William J. Sibbald, M.D., F.C.C.P.

1992

2001

SEPSIS-1

Peu sensible

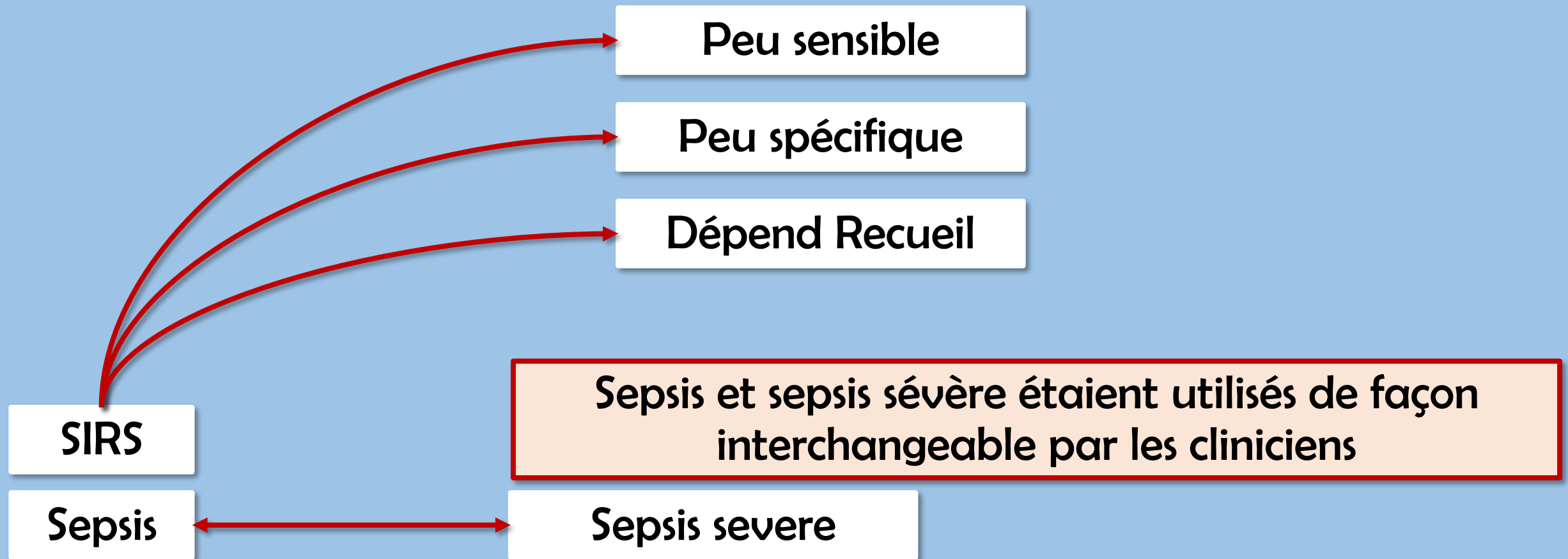
SIRS criteria are **missing**
in **1 in 8** patients

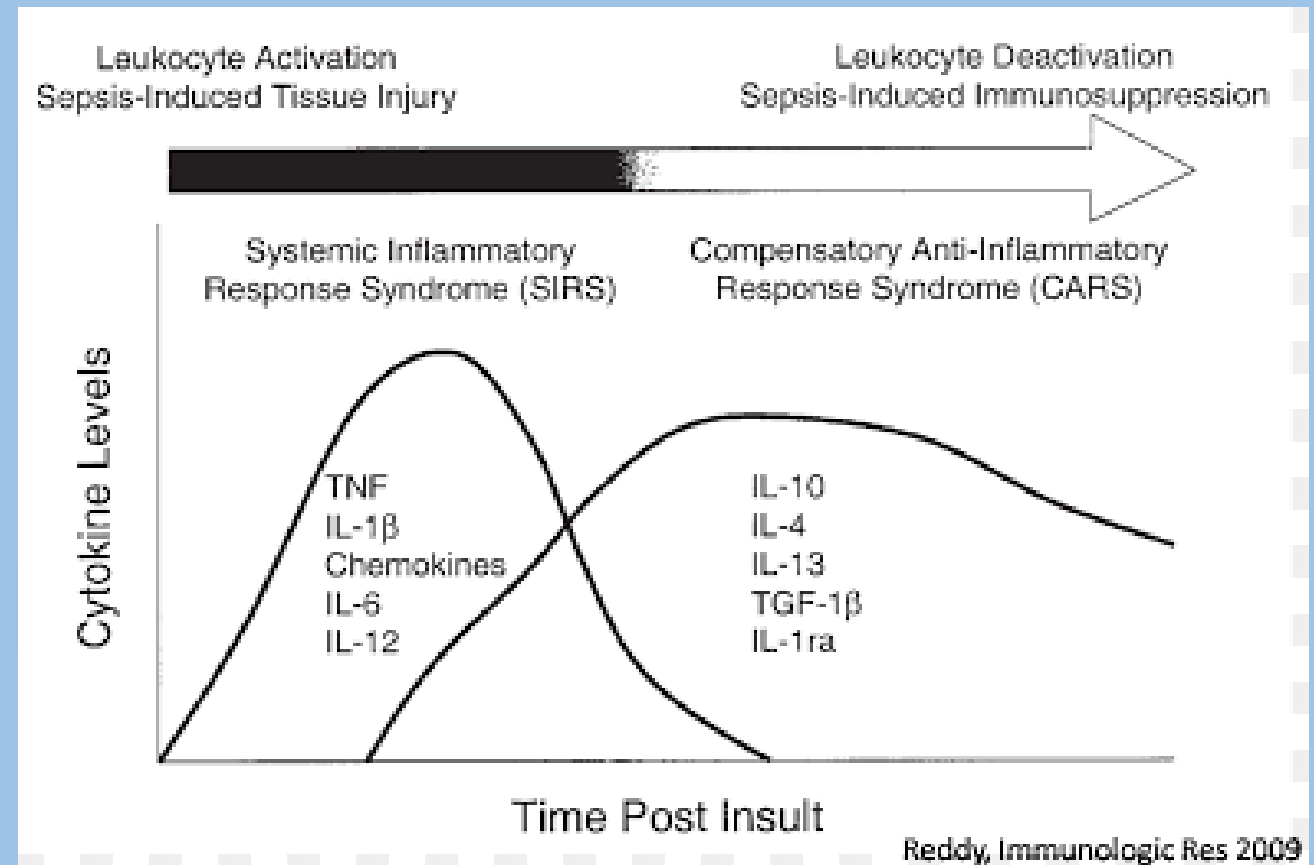
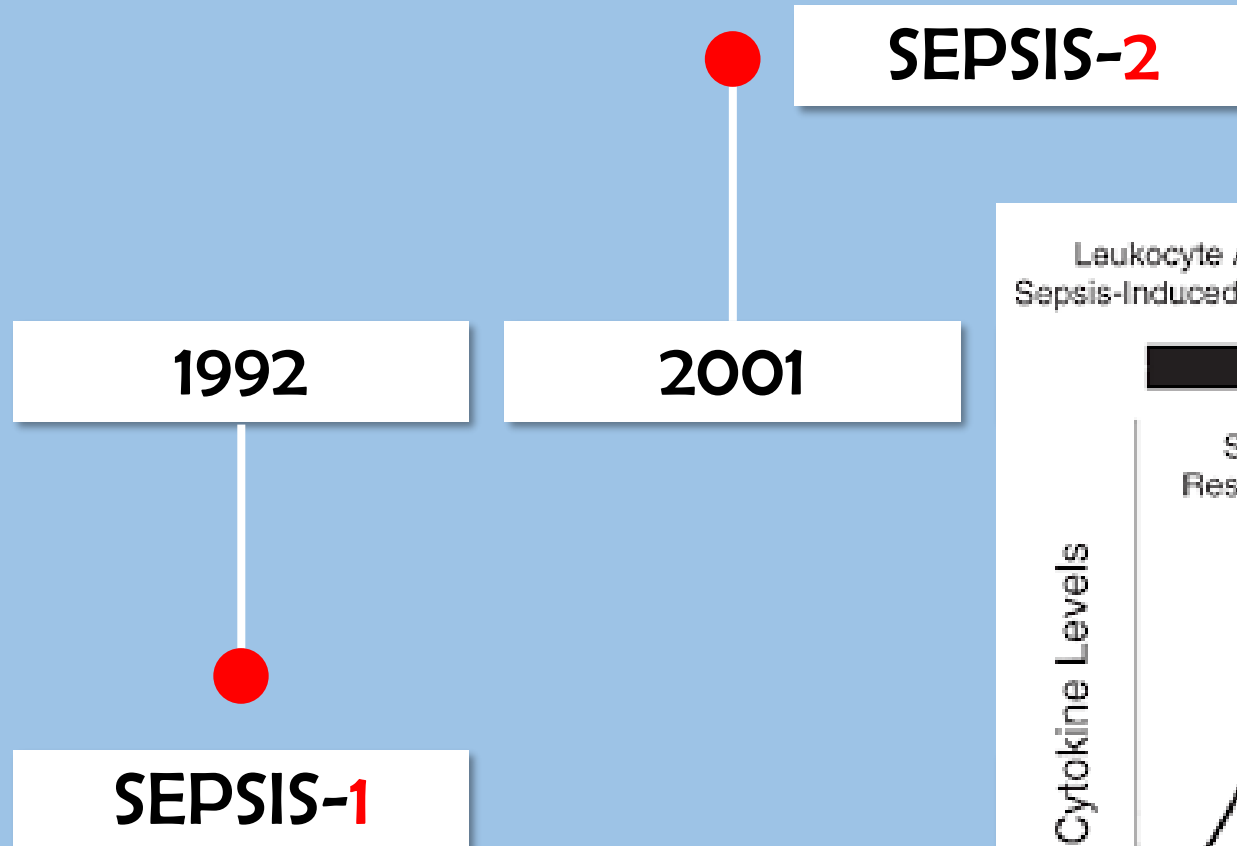
SIRS

Table 1. Baseline Characteristics and Hospital Outcomes of Patients with Severe Sepsis, According to Status with Respect to Criteria for the Systemic Inflammatory Response Syndrome (SIRS).*

Characteristic	All Patients <i>no. of patients with data</i>	Patients with SIRS-Positive Sepsis <i>no. of patients with data</i>	Patients with SIRS-Negative Sepsis <i>no. of patients with data</i>	P Value
Hospital outcome — no. (%)	109,663	96,385	13,278	
Death	25,713 (23.4)	23,577 (24.5)	2136 (16.1)	<0.001

This lack of positivity was
associated with **highest** hospital
morbidity and **mortality**





NEW

Un groupe international de 19 experts

Données issues de l'analyse rétrospective

Plusieurs cohortes de patients américains et allemands

Recrutés dans différents services

Patients porteurs d'infections nosocomiales

Absence de validation aux urgences

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;
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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

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

Sepsis

=

Dysfonction d'organe secondaire à une **réponse**
inappropriée de l'hôte envers une infection

SEPSIS - 3

SEPSIS 1 et 2

Sepsis

=

~~SIRS~~

+

Infection

On oublie le SIRS

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score^a

System	Score				
	0	1	2	3	4
Respiration					
Pao ₂ /Fio ₂ , 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 ³ /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) ^b	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1 ^b	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1 ^b
Central nervous system					
Glasgow Coma Scale score ^c	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: Fio₂, fraction of inspired oxygen; MAP, mean arterial pressure; Pao₂, partial pressure of oxygen.

^a Adapted from Vincent et al.²⁷

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

^c Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

La complexité du score SOFA

Prélèvements biologiques

Limitent son utilisation Une version simplifiée du SOFA en réanimation

Altération de la conscience

FR ≥ 22 /min

PAS ≤ 100 mmHg



1

1

1

quick SOFA = qSOFA

Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock

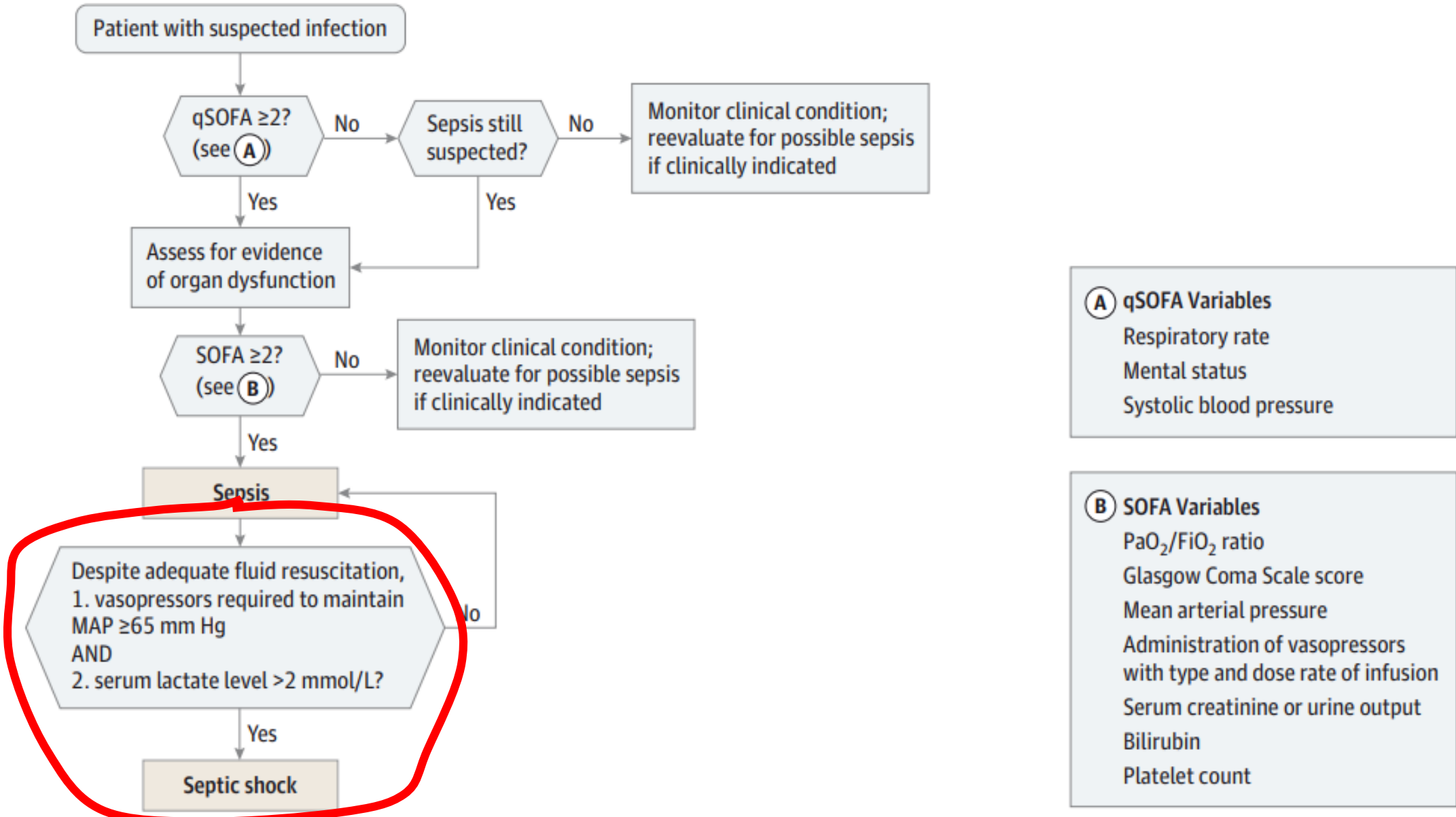


qSOFA

Cette stratification du risque a pour but de mettre l'accent sur la précocité de la prise en charge

Identification rapide patients les + graves/susceptibles de s'aggraver

Figure. Operationalization of Clinical Criteria Identifying Patients With Sepsis and Septic Shock



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Validation des critères SEPSIS-3



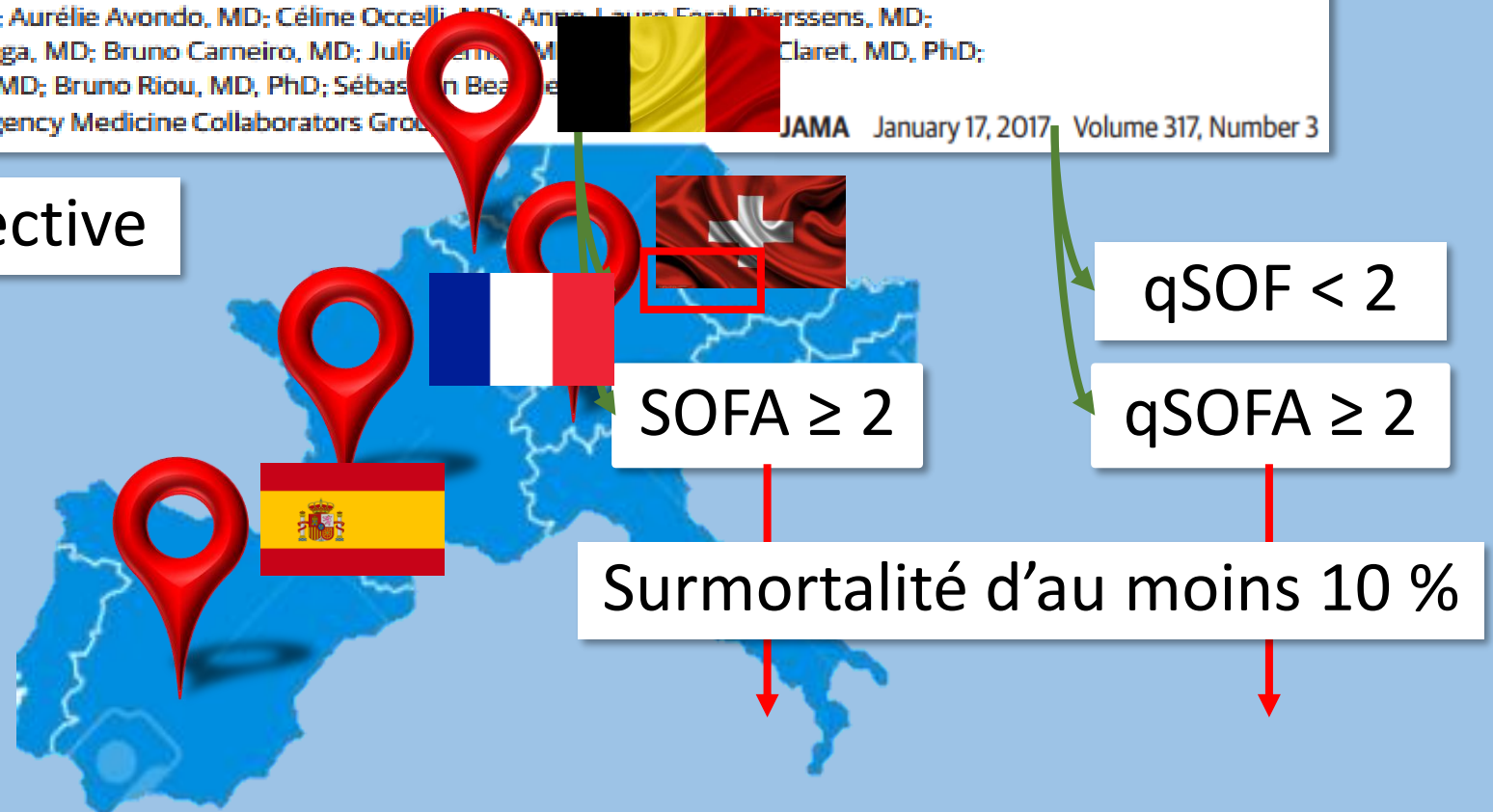
JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Prognostic Accuracy of Sepsis-3 Criteria for In-Hospital Mortality Among Patients With Suspected Infection Presenting to the Emergency Department

Yonathan Freund, MD, PhD; Najla Lemachatti, MD; Evguenia Krastinova, MD, PhD; Marie Van Laer, MD; Yann-Erick Claessens, MD, PhD; Aurélie Avondo, MD; Céline Occelli, MD; Anne-Laure Foral, MD; Pieter Dierckx, MD, PhD; Jennifer Truchot, MD; Mar Ortega, MD; Bruno Carneiro, MD; Julie Claret, MD, PhD; Fabrice Dami, MD; Ben Bloom, MD; Bruno Riou, MD, PhD; Sébastien Beuret, MD, PhD; for the French Society of Emergency Medicine Collaborators Group

JAMA January 17, 2017 Volume 317, Number 3

Étude de cohorte prospective



Prognostic Accuracy of the SOFA Score, SIRS Criteria, and qSOFA Score for In-Hospital Mortality Among Adults With Suspected Infection Admitted to the Intensive Care Unit

Eamon P. Raith, MBBS, MACCP; Andrew A. Udy, MBChB, PhD, FCICM; Michael Bailey, PhD; Steven McGloughlin, BMed FRACP, FCICM, MPHTM; Christopher MacIsaac, MBBS, PhD, FRACP, FCICM; Rinaldo Bellomo, MD, FRACP, FCICM, FAHMS; David V. Pilcher, MBBS, FRACP, FCICM; for the Australian and New Zealand Intensive Care Society (ANZICS) Centre for Outcomes and Resource Evaluation (CORE)

Étude rétrospective

190 000 patients

182 services de réanimation

2000 - 2015

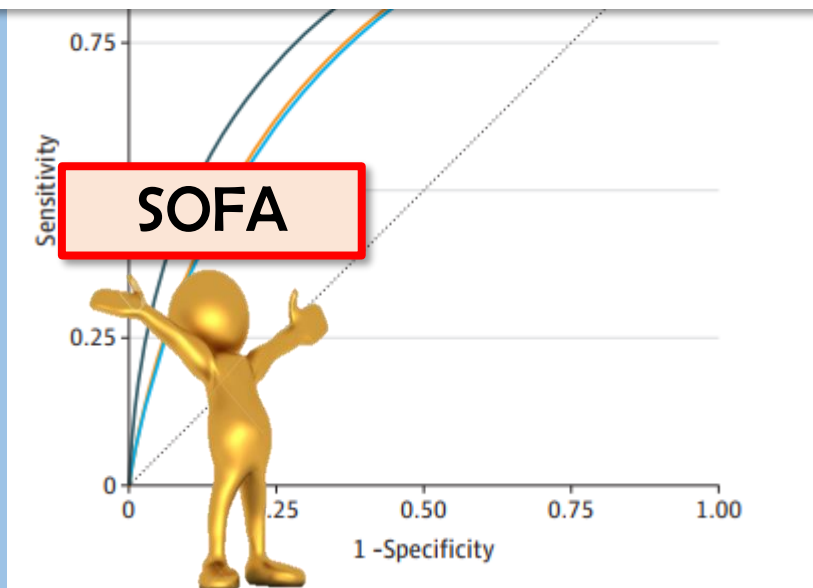
Les performances **pronostiques** de l'item diagnostique **score SOFA ≥ 2**

2 critères ou plus de SIRS

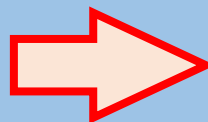
qSOFA ≥ 2

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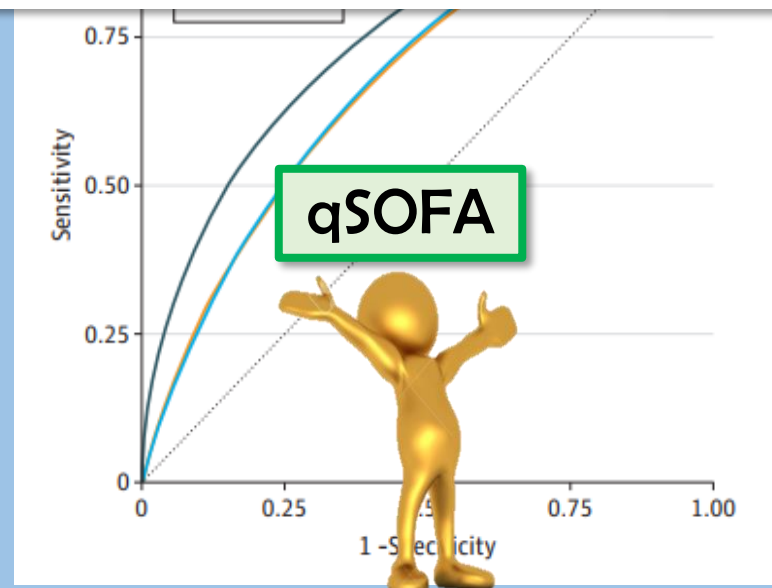
SOFA 0,811-0,818)



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JAMA January 17, 2017 Volume 317, Number 3



SOFA 0,761-0,764)

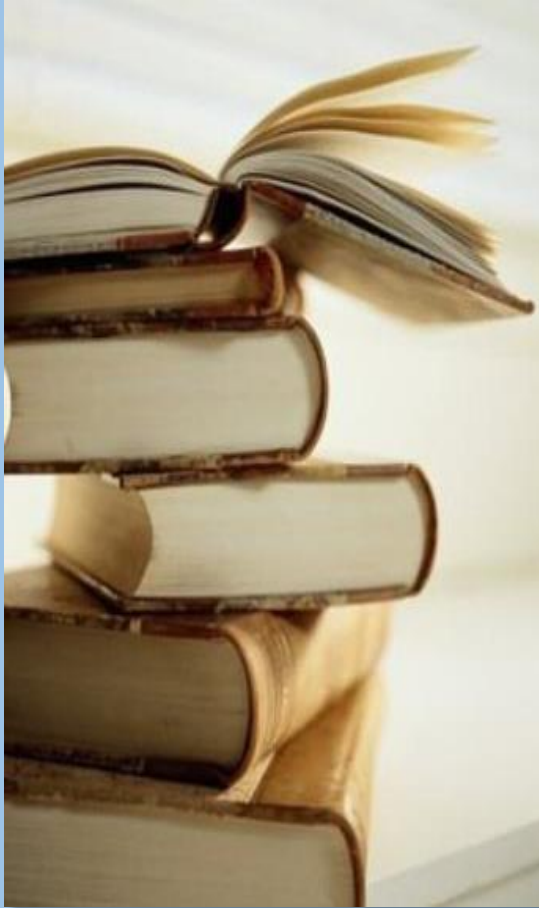


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The good





La définition du sepsis



Physiopathologie (SOFA)

EDC septique

Pas de SIRS ni de sepsis sévère

qSOFA



qSOFA et SOFA



Meilleure comparabilité des études



Infection

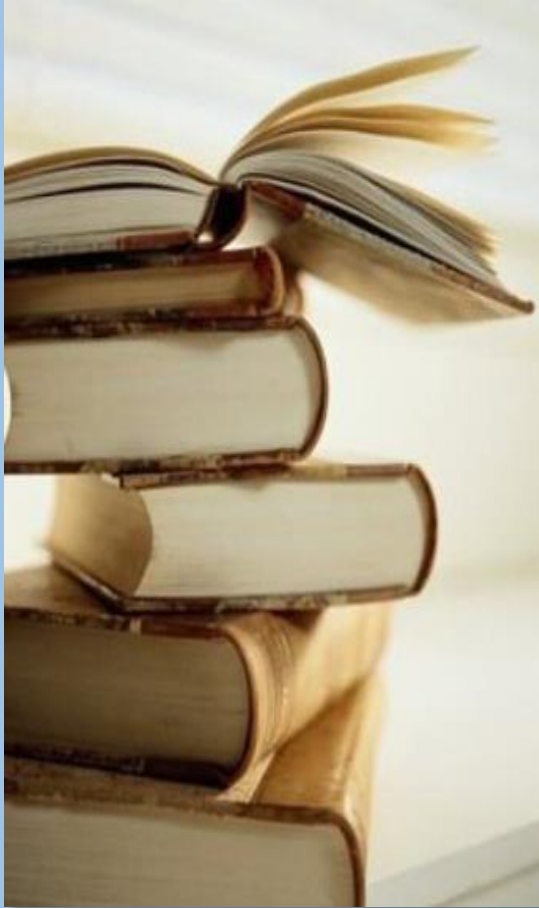
Un rôle important attribué à la **réaction de l'hôte**

Réponse **inadaptée**
Dysfonctionnement organique

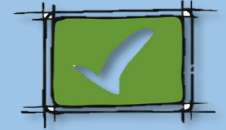
Sepsis – état de choc septique

Réponse adaptée
(hyperleucocytose, fièvre)

Les critères SIRS



La définition du sepsis

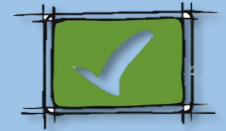


Physiopathologie (SOFA)

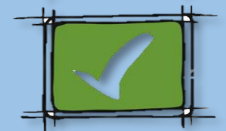
EDC septique

Pas de SIRS ni de sepsis sévère

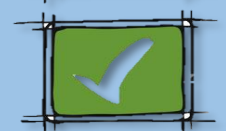
qSOFA



qSOFA et SOFA



Meilleure comparabilité des études



Déterminé à partir d'analyses de **grandes bases de données**

Trois éléments cliniques

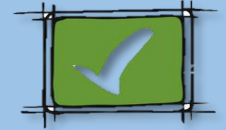
Simple et facile à retenir

Médecin et surtout par les non-medecins (infirmières +++)

Rôle important dans la **détection signes précoces** de sepsis
(leur fréquence présence au chevet du patient)



La définition du sepsis

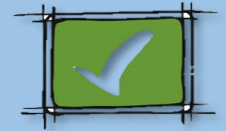


Physiopathologie (SOFA)

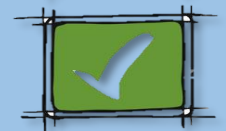
EDC septique

Pas de SIRS ni de sepsis sévère

qSOFA



qSOFA et SOFA



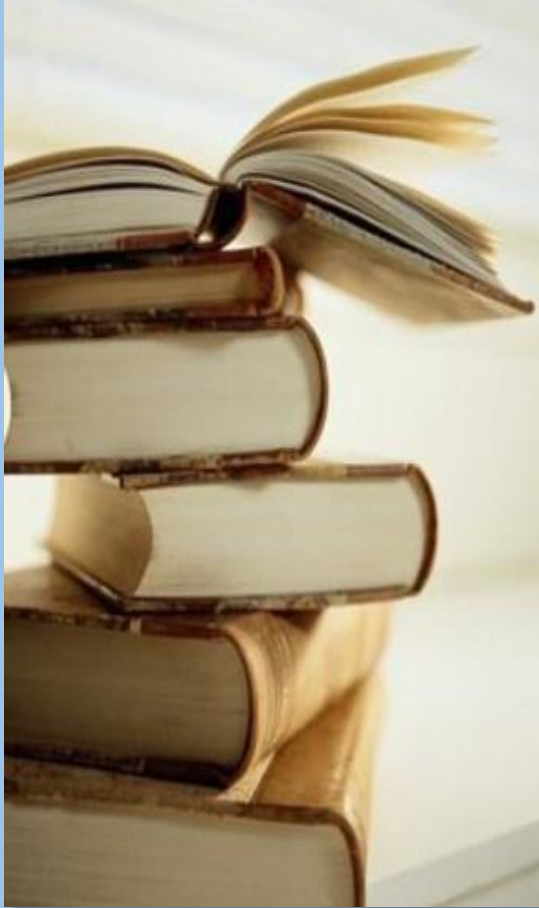
Ils présentent deux avantages: leurs **mesures** peut être **automatisés** et il peut être réalisé **rétrospectivement**

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The bad





La définition du sepsis



Physiopathologie (SOFA)

EDC septique

Pas de SIRS ni de sepsis sévère

qSOFA

qSOFA et SOFA

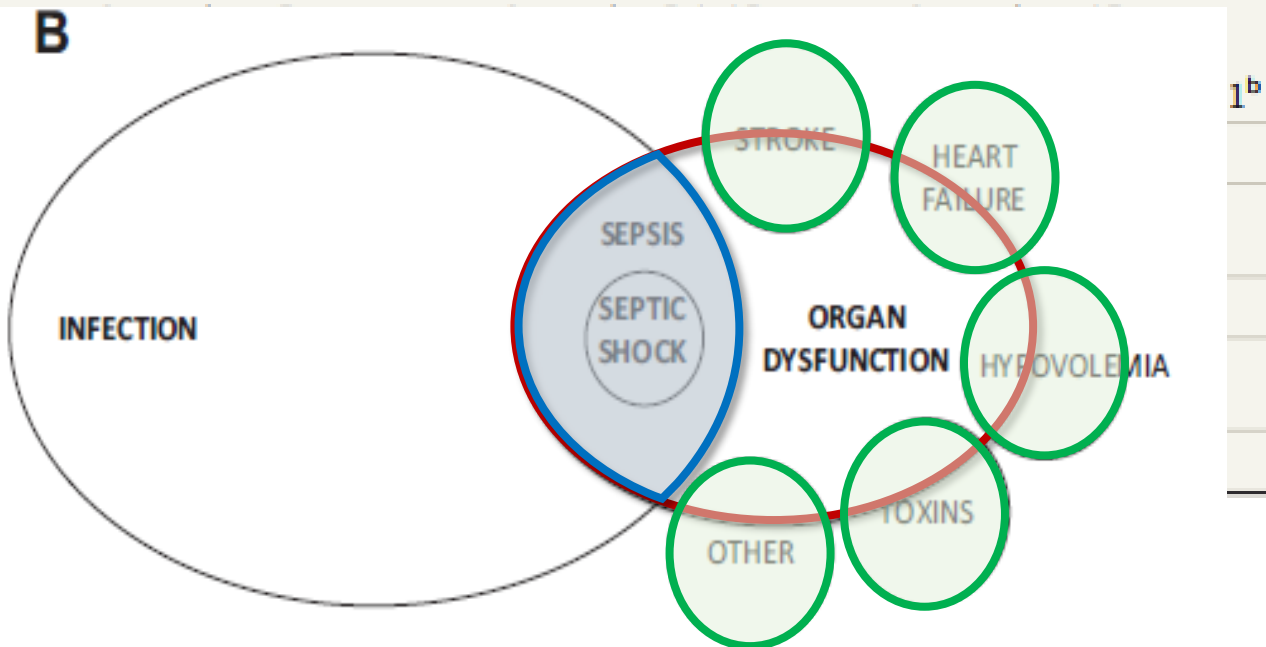
Meilleure comparabilité des études

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score^a

System	Score				
	0	1	2	3	4
Respiration					
PaO ₂ /FiO ₂ , 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 ³ /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			
Central nervous system					
Glasgow Coma Scale score ^c	15	13-14			
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9			
Urine output, mL/d					

Abbreviations: FiO₂, fraction of inspired oxygen; MAP, mean arterial pressure; PaO₂, partial pressure of oxygen.

^a Adapted from Vincent et al.²⁷



Détecter un dysfonctionnement organique

Sepsis

=

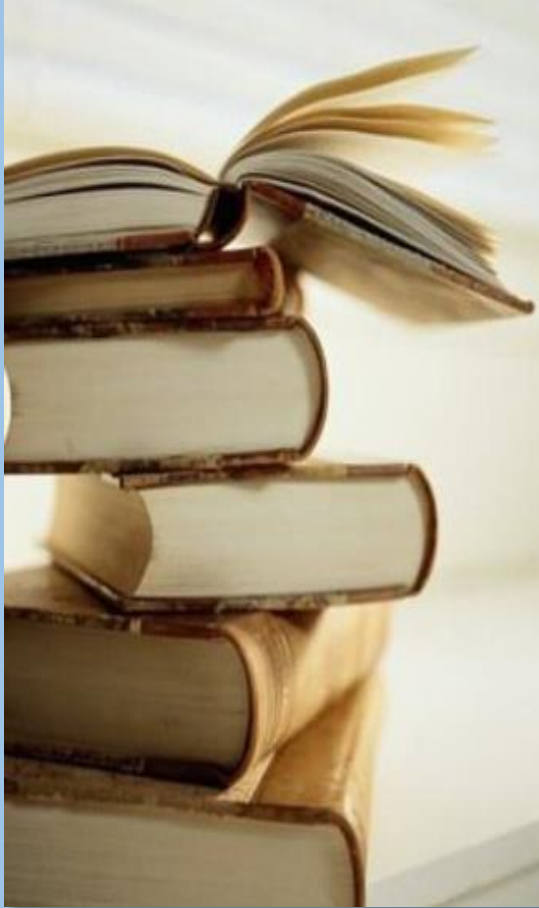
Dysfonction d'organe secondaire à une réponse
inappropriée de l'hôte envers une infection

Avec l'espoir qu'elle a été
causée par une infection

Ce patient est-il infecté ou non?

Les nouvelles définitions n'offrent aucune indication sur
l'identification de l'infection

Des progrès importants ont été réalisés ces dix dernières
années dans l'utilisation de biomarqueurs (Dg et ATBpie)



La définition du sepsis

Physiopathologie (SOFA)

EDC septique

Pas de SIRS ni de sepsis sévère

qSOFA

qSOFA et SOFA

Meilleure comparabilité des études



Choc septique = forme grave et continuum du sepsis

Infection

~~SIRS~~

Sepsis

~~Sepsis sévère~~

Choc septique

Lactate Level Versus Lactate Clearance for Predicting Mortality in Patients With Septic Shock

TABLE 2. Prognostic Value of Measuring the Serum Lactate Level and Clearance After 6 Hours of Septic Shock

6 hr From Shock	Receiver Operating	Sensitivity	Specificity	Predictive	Predictive	Positive	Negative
	Characteristic			Value	Value	Likelihood	Likelihood
						Ratio	Ratio
Lactate (mmol/L)							
Lactate over 2						1.26	0.40
Lactate over 3						1.60	0.60
Lactate over 4	0.64 (0.60–0.68)	55.9	72.3	40.2	83.1	1.39	0.42
Clearance (%)							
Clearance under 10						1.78	0.72
Clearance under 15						1.63	0.68
Clearance under 20	0.60 (0.50–0.67)	54.5	69.0	32.0	82.0	1.50	0.60

Volémie adéquate?

Évaluation HD invasive?
Non invasive?

Perte de temps % transfert
en USI (pronostic)

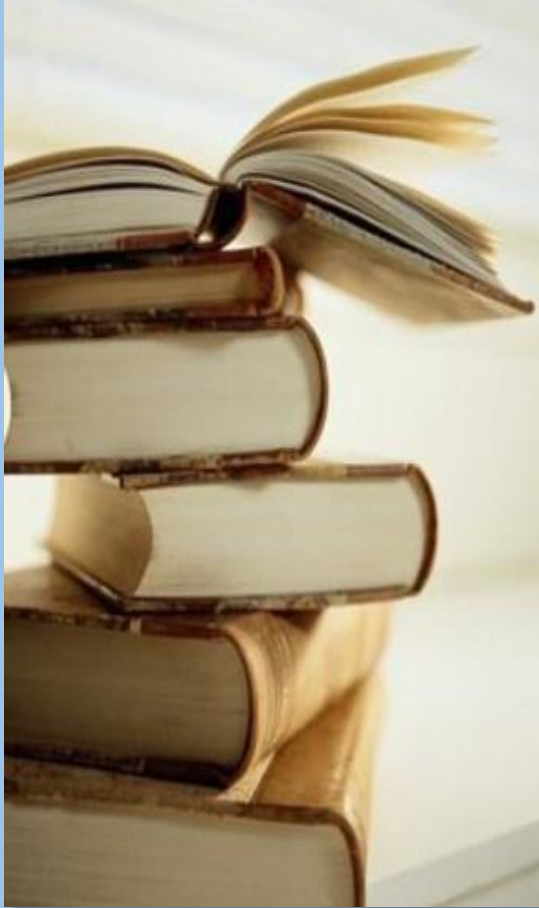
Vasopresseurs

PAM $\geq$ 65 mmHg

Lactate >2 mmol/L
(18 mg/dL)

Malgré la correction
d'une hypovolémie

Figure 1
with sep
for prognosis of septic shock patients who were treated with
protocol-driven resuscitation bundle therapy.



La définition du sepsis



Physiopathologie (SOFA)

EDC septique

Pas de SIRS ni de sepsis sévère

qSOFA

qSOFA et SOFA

Meilleure comparabilité des études

Systemic Inflammatory Response Syndrome, Quick Sequential Organ Function Assessment, and Organ Dysfunction

Insights From a Prospective Data Editorial

Julian M. Williams, MBBS; Jaimi H. Greenslade, PhD
Anthony F. T. Brown, MBChB; and Jeffrey Lipman, MD

Systemic Inflammation, Quick Sequential Organ Function Assessment, and Insights From a Prospective Data

Julian M. Williams, MBBS; Jaimi H. Greenslade, PhD
Anthony F. T. Brown, MBChB; and Jeffrey Lipman, MD

RESULTS: We enrolled 8,871 patients, with

CONCLUSIONS: SIRS was associated with organ dysfunction and mortality, and abandoning the concept appears premature. A qSOFA score ≥ 2 showed high specificity, but poor sensitivity may limit utility as a bedside screening method. Although mortality for organ dysfunction was comparable between Sepsis-2 and Sepsis-3, more prognostic and clinical information is conveyed using Sepsis-2 regarding number and type of organ dysfunctions. The SOFA score may require recalibration.

CHEST 2017; 151(3):586-596

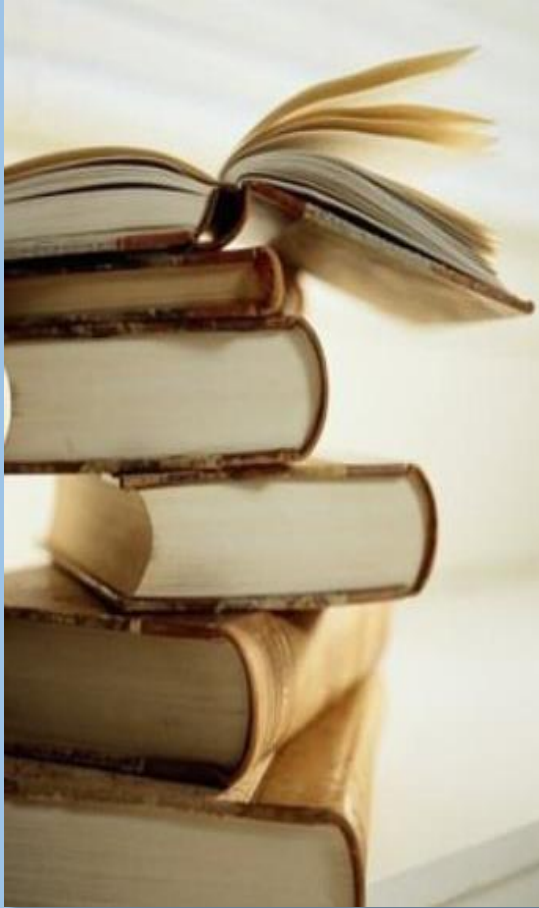
The SOFA score may require recalibration.

CHEST 2017; 151(3):586-596

KEY WORDS: emergency medicine; infection; organ dysfunction; qSOFA; SIRS

Table 1 Sensitivity and specificity for mortality of diagnostic criteria for sepsis/severe sepsis in non-ICU settings

Criteria	Source	Sensitivity (%)	Specificity (%)
SIRS ≥ 2	Sepsis-3	64.0	65.0
	U of C	93.8	12.3
qSOFA ≥ 2	Sepsis-3	55.0	84.0
	U of C	68.7	63.5
		86.6	47.5
		71.4	65.0
		92.0	84.0



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qSOFA



GCS < 15



FR $\geq 22/\text{min}$



PAS $\leq 100 \text{ mmHg}$

Comorbidities



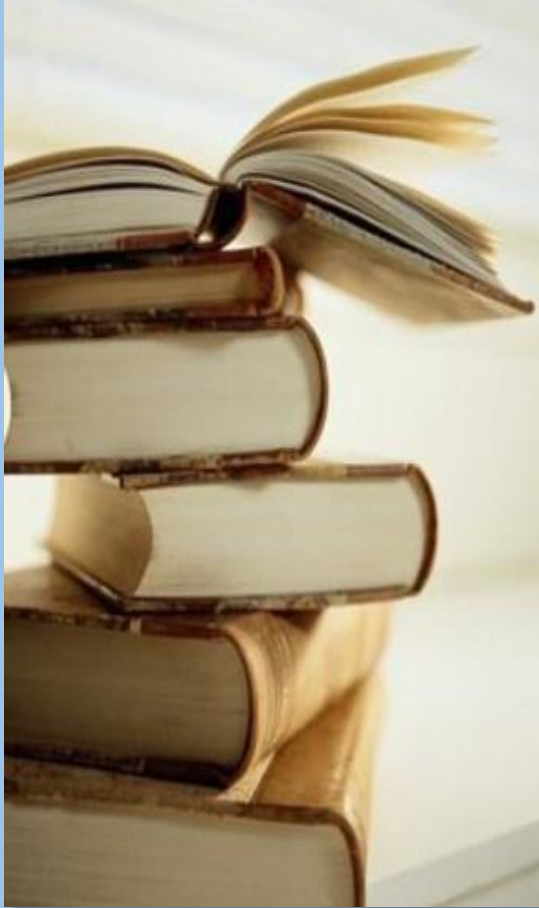
Age

qSOFA peut remplacer le SIRS?



Churpek MM, Snyder A, Han X, et al. qSOFA, SIRS, and early warning scores for detecting clinical deterioration in infected patients outside the ICU. Am J Respir Crit Care Med. 2017;45(10): 1677-1682.

Prédiction **tardive** de la détérioration clinique



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Meilleure comparabilité des études



Retards potentiels dans l'identification précoce et le traitement

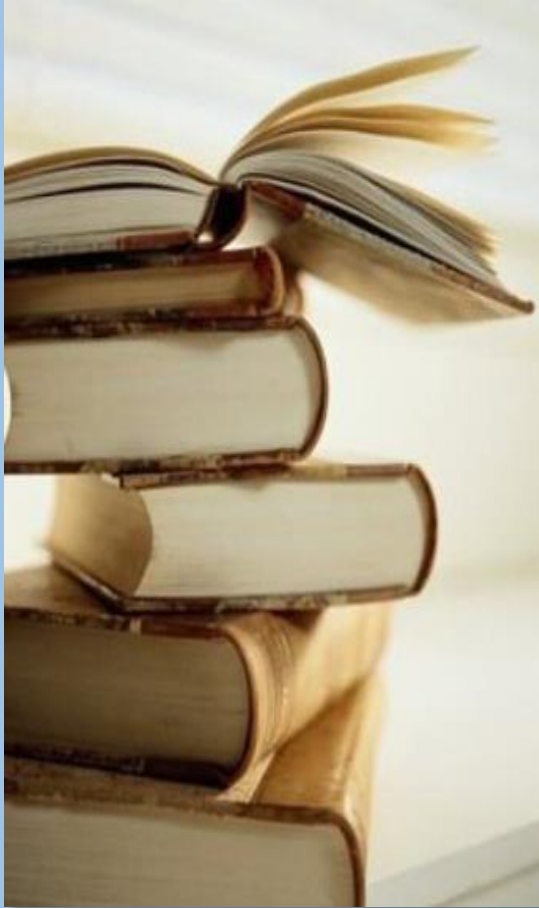
Simpson SQ. New sepsis criteria: a change we should not make. Chest 2016; 149(5):1117–8.

Cortes-Puch I, Hartog CS. Opening the debate on the new sepsis definition change is not necessarily progress: revision of the sepsis definition should be based on new scientific insights. Am J Respir Crit Care Med 2016;194(1):16–8.

Le calcul du score SOFA doit inclure des mesures biologiques.

Coûts associés + temps (Pc)

Ni qSOFA ni le SOFA ne permettent d'identifier l'infection



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qSOFA et SOFA

Meilleure comparabilité des études



Comparabilité avec les anciennes études

Travaux

1992

SEPSIS 1-2

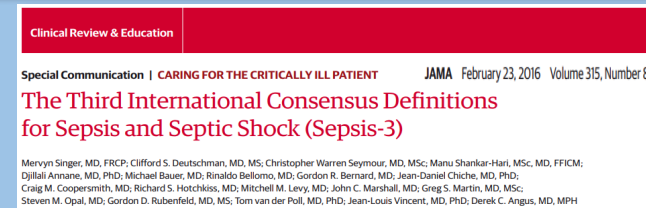
2002

2016

SEPSIS 3

1^{ère} définitions
consensuelles

Ajoutés bibliothèque
de codage



*The International Classification
of Diseases Coding library*

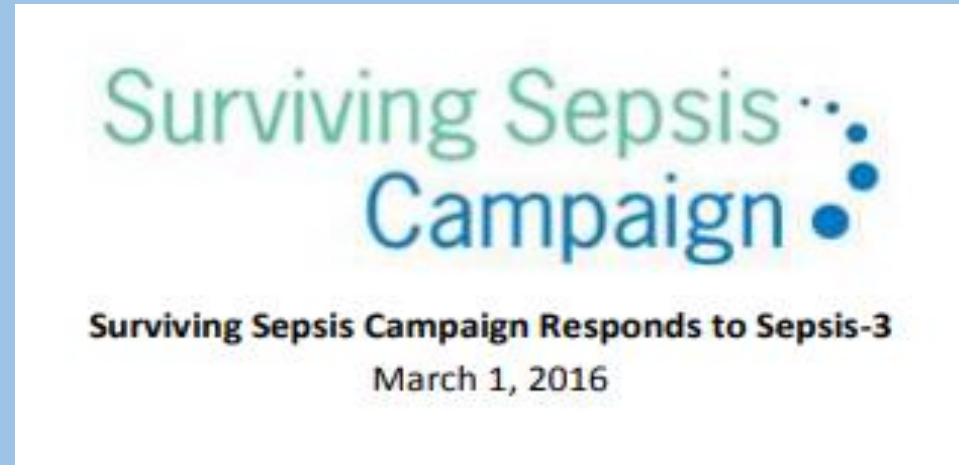
Centers for Medicare & Medicaid Services

Il faut toujours les anciennes définitions du sepsis et des travaux à conserver l'ancienne terminologie

Townsend SR, Rivers E et al. Definitions for sepsis and septic shock. JAMA 2016;316(4):457–8.

Impact sur le traitement

Nouvelles recommandations basées sur ces nouvelles définitions



Conclusion

Once hospitals have adequately prepared for change, sepsis team leaders should reinforce the message that the new definitions do not change the primary focus of early sepsis identification and initiation of timely treatment in the management of this vulnerable patient population.

Les nouvelles définitions ne doivent pas modifier l'objectif principal qui est l'identification précoce du sepsis et l'initiation d'un traitement rapide dans la gestion de ces patients vulnérables

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

Définition plus proche de la physiopathologie du sepsis

Critères simples et facile à retenir

Le risque de **minimiser la gravité du sepsis**

Le risque d'anéantir les efforts déployés depuis plusieurs décennies dans le cadre de la ***Surviving Sepsis Campaign***

MERCI DE VOTRE ATTENTION



**SOCIÉTÉ TUNISIENNE DE
PATHOLOGIE INFECTIEUSE**

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5
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RENCONTRES EN INFECTIOLOGIE