

# GUIDELINES OF SEPSIS MANAGEMENT: FLUID THERAPY

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# Sepsis definitions

A whiteboard with a black frame is centered in the image. The text "Sepsis definitions" is written in a bold, blue, sans-serif font. The whiteboard is placed on a light-colored wooden desk. To the left of the whiteboard, there are several books of different colors (red, white, blue) and a brown, faceted geometric object. To the right, there is a clear glass pencil holder containing a wooden pencil and blue liquid, and a black marker and a white eraser lying on the desk.

# SEPSIS-3 : New definitions for an old problem

Clinical Review & Education



The JAMA Network

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. doi:10.1001/jama.2016.0287



# EVOLUTION OF SEPSIS DEFINITIONS



Sepsis - 1

Sepsis - 2

Sepsis - 3

Life-threatening organ dysfunction caused by a dysregulated host response to infection.



2016  
Sepsis-3

**RETIRED**

**Sepsis**  
SIRS + Infection

**REDUNDANT**

**Severe Sepsis**  
Sepsis + End Organ Damage

**Septic Shock**  
Severe Sepsis + Hypotension

Temp.  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$ , HR  $>90$ , RR  $>20$  or  $\text{PaCO}_2 <32$ ,  
WBCs  $>12,000$  or  $<4,000$  or  $>10\%$  bands



## Sepsis - 3

- *Severe Sepsis*: No longer used →
- **Sepsis**: Suspected or documented infection and Acute increase of  $\geq 2$  SOFA points (a proxy for organ dysfunction)



**Septic Shock:** Sepsis and Vasopressor therapy needed to elevate MAP  $\geq 65$  mm Hg and Lactate  $> 2$  mmol/L (18 mg/dL) despite adequate fluid resuscitation

JAMA. 2016;315(8):762-774. doi:10.1001/jama.2016.0288



**Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score<sup>a</sup>**

System	Score				
	0	1	2	3	4
<b>Respiration</b>					
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
<b>Coagulation</b>					
Platelets, ×10 <sup>3</sup> /μL	≥150	<150	<100	<50	<20
<b>Liver</b>					
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)
<b>Cardiovascular</b>					
	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>
<b>Central nervous system</b>					
Glasgow Coma Scale score <sup>c</sup>	15	13-14	10-12	6-9	<6
<b>Renal</b>					
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.

<sup>c</sup> Glasgow Coma Scale scores range from 3-15; higher score indicates better neurological function.

qSOFAScore: A means of rapidly identifying ED and hospital ward (non-ICU) patients with suspected infection at increased risk

## QSOFA



JAMA. 2016;315(8):762-774. doi:10.1001/jama.2016.0288



## 3 Step Approach of Identifying Patients With Sepsis and Septic Shock (Sepsis III definition)

1. Screening of infection  
(early identification with suspected or confirmed infection)

2. Screening of organ dysfunction (qSOFA  $\geq 2$ )  
(Sepsis:  $\Delta$ SOFA  $\geq 2$ )

3. Identification of initial hypotension (Septic shock)  
(Vasopressor for MAP  $\geq 65$  mmHg & Lactate  $>2$  mmol/L)



**~ 27 000 000**

people per year develop sepsis

## Sepsis

### a global burden



**~ 19 000 000**  
people per  
year survive



**Survivors**  
may face  
lifelong  
complications



**~ 8 000 000**  
people per  
year die



**~ 6 000 000**  
neonates and  
children under  
five die of sepsis<sup>1</sup>



**Maternal Death**  
Sepsis is one of  
the most  
common causes



**Everybody**  
can develop  
sepsis following  
an infection

# Sepsis is a global healthcare challenge.

<http://www.world-sepsis-day.org/?MET=TOOLS&vPRIMNAVISELECT=6>





Global  
Sepsis  
Alliance

Surviving Sepsis  
Campaign

World  
Sepsis  
Day  
13 September



## International Recent Efforts On Sepsis

- Global Sepsis Alliance, a non- profit organization, was launched in 2010 to understand and combat sepsis better
- World Sepsis Day (on 13 September)
- In order to mitigate sepsis-associated mortality, Surviving Sepsis Campaign developed guidelines



## Surviving Sepsis Campaign: Timeline

- First edition in 2004
- Previous Revisions in 2008 and 2012
- Current revision started in 2014
- Jointly sponsored by ESICM and SCCM
- 4<sup>th</sup> edition published in 2016





Special Article

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

**March 2017 • Volume 45 • Number 3**



# Management of Severe Sepsis

Initial Resuscitation

Diagnosis

Antibiotic Therapy

Source Control

Fluid Therapy

Vasopressors

Corticosteroids

Blood Product

Glucose Control

Bicarbonate Therapy

Surviving Sepsis Campaign

Sepsis Guidelines 2016

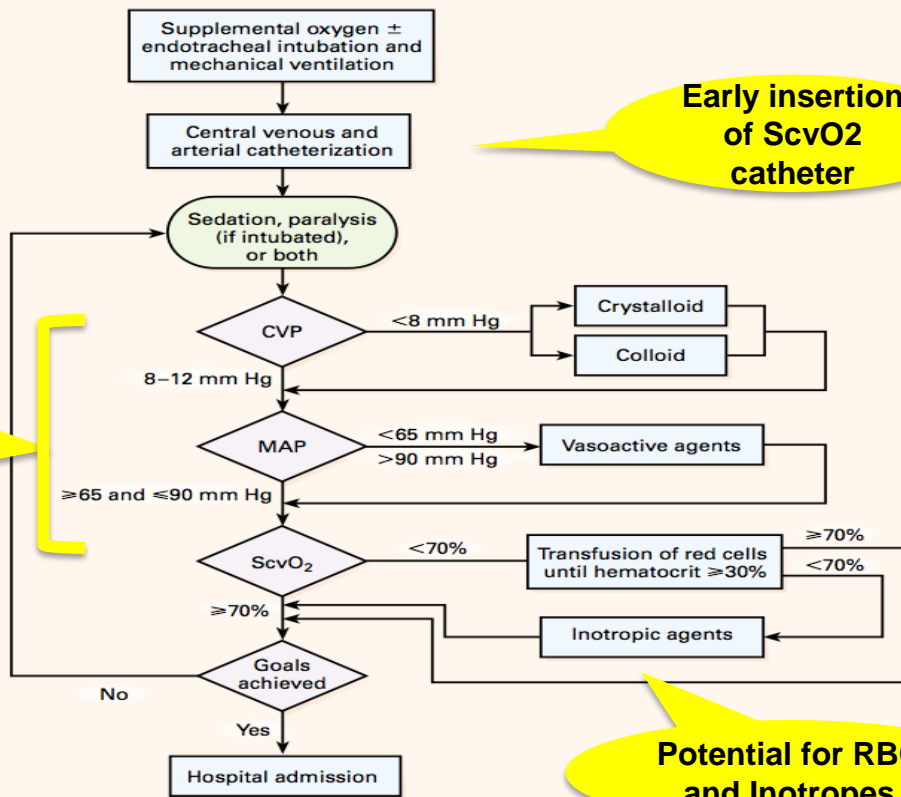
# Initial Resuscitation



Rivers et al, 2001  
EGDT

Therapy titrated to CVP, MAP and ScvO<sub>2</sub>

Early insertion of ScvO<sub>2</sub> catheter



Potential for RBC and Inotropes



# 10+ YEARS OF EARLY GOAL DIRECTED THERAPY

2001: Rivers, et.al  
published in NEJM

2002: Surviving  
Sepsis Campaign

2004: First  
guidelines  
published

2005:  
*Implementing the  
Surviving Sepsis  
Campaign (SSC)*

2008: 2<sup>nd</sup> edition  
of guidelines  
published

2012: 3<sup>rd</sup> edition of  
guidelines

ORIGINAL ARTICLE

## A Randomized Trial of Protocol-Based Care for Early Septic Shock

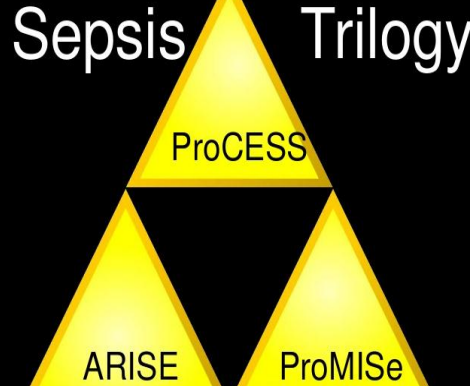
The ProCESS Investigators\*

ABSTRACT

**BACKGROUND**

In a single-center study published more than a decade ago involving patients presenting to the emergency department with severe sepsis and septic shock, mortality

The members of #  
(Donald M. Yealy, M.D., David T. Ho,



THE NEW ENGLAND JOURNAL OF MEDICINE  
ORIGINAL ARTICLE

## Goal-Directed Resuscitation for Patients with Early Septic Shock

The ARISE Investigators and the ANZICS Clinical Trials Group\*

ABSTRACT

THE NEW ENGLAND JOURNAL OF MEDICINE  
ORIGINAL ARTICLE

## Trial of Early, Goal-Directed Resuscitation for Septic Shock

Paul R. Mouncey, M.Sc., Tiffany M. Osborn, M.D., G. Sarah Power, M.Sc.,  
David A. Harrison, Ph.D., M. Zia Sadique, Ph.D., Richard D. Grievé, Ph.D.,  
Rafiq Jahani, B.A., Sheila E. Harvey, Ph.D., Derek Bell, M.D., Julian F. Bion, M.D.,  
Timothy J. Coats, M.D., Mervyn Singer, M.D., J. Duncan Young, O.M.,  
and Kathryn M. Rowan, Ph.D., for the ProMiSe Trial Investigators\*

ABSTRACT

ABSTRACT

# Primary mortality outcome of each study

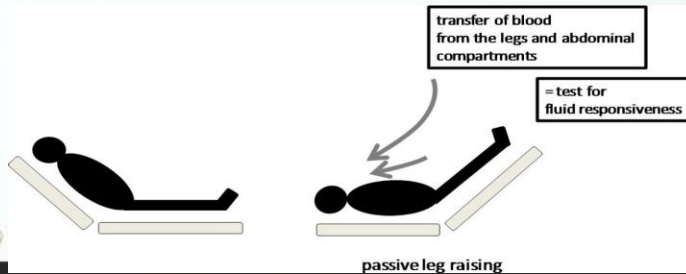
Study ID	EGDT	Events, n (%)	control	Weight
Rivers et al. (2001)	30	59/133	10.40	
Jones et al. (2010)	50	25/150	4.87	
ProCESS Investigators (2015)	39	167/902	21.78	
ARISE Investigators (2015)	792	150/796	30.71	
ProMISE Investigators (2015)	623	181/620	32.23	
Overall (I-squared = 56.0%)	2134	582/2601	100.00	



**Initial resuscitation with EGDT (or similar protocol) did not reduce 60-90 days mortality over usual care**

# New Guideline: Surviving Sepsis Campaign 2016

- at least **30 ml/kg of IV crystalloid fluid** be given within the first 3 hours (strong recommendation, low quality of evidence)
- additional fluids be guided by **frequent reassessment of hemodynamic status** (BPS)
- **dynamic over static variables** be used to predict fluid responsiveness, where available (weak recommendation, low quality of evidence)



## Volaemic Assessment Parameters

Static	Dynamic
CVP	SVV
PAOP	PPV
RVEDV	SPV
LVEDA	IVC collapse
GEDV & ITBV	PLR

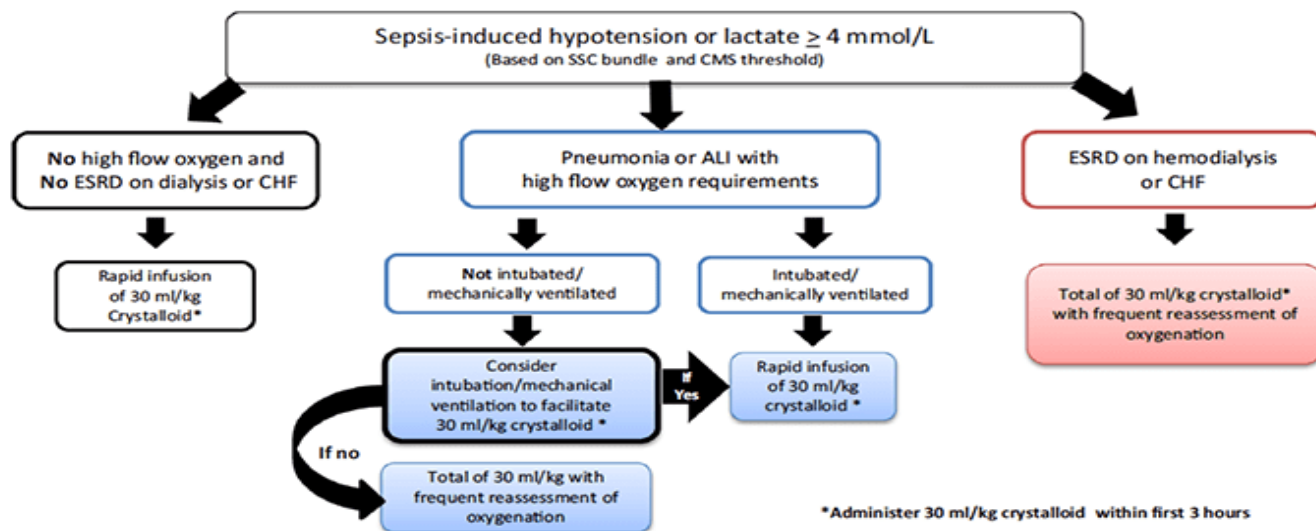


- **initial target mean arterial pressure (MAP) of 65 mm Hg** in patients with septic shock requiring vasopressors (strong recommendation, moderate quality of evidence)
- Weak suggestion to guide **resuscitation to normalize lactate**

Use clinical judgments. For instance, if patient has adequate BP and Urine output and is down titrating vasopressors, but has persistently elevated lactate, additional fluid carries the risk of over resuscitation



## Application of Fluid Resuscitation in Adult Septic Shock



### Considerations post 30ml/kg crystalloid infusion

- Continue to balance fluid resuscitation and vasopressor dose with attention to maintain tissue perfusion and minimize interstitial edema
- Implement some combination of the list below to aid in further resuscitation choices that may include additional fluid or inotrope therapy
  - blood pressure/heart rate response,
  - urine output,
  - cardiothoracic ultrasound,
  - CVP, ScvO<sub>2</sub>,
  - pulse pressure variation
  - lactate clearance/normalization or
  - dynamic measurement such as response of flow to fluid bolus or passive leg raising
- Consider albumin fluid resuscitation, when large volumes of crystalloid are required to maintain intravascular volume.

ALI=acute lung injury; CHF=congestive heart failure; CMS= US Centers for Medicare and Medicaid Services; CVP=central venous pressure; ESRD=end stage renal disease; kg=kilograms; ml=milliliters; oxyhgb=oxyhemoglobin; ScvO<sub>2</sub>=superior vena cava oxygen saturation

**Fig. 2** This figure explores the nuancing of initial administration of 30 ml/kg crystalloid for sepsis induced hypoperfusion based on patient characteristics. It also draws attention to reassessment tools following the initial fluid dose as an influence on further fluid administration or inotropic therapy

# Fluid Therapy



- **crystalloids as the fluid of choice** for initial resuscitation and subsequent intravascular volume replacement  
(strong recommendation, moderate quality of evidence)
- suggest using **albumin in addition to crystalloids** for initial resuscitation and subsequent intravascular volume replacement when patients require substantial amounts of crystalloids  
(weak recommendation, low quality of evidence)
- **against using hydroxyethyl starches (HESs)** for intravascular volume replacement (strong recommendation, high quality of evidence)



# SSC Bundles

## SURVIVING SEPSIS CAMPAIGN

### Bundles

Elements when used together, improve outcomes more than when used separately!

Evidence based





**TO BE COMPLETED WITHIN 3 HOURS OF TIME OF PRESENTATION\*:**

1. Measure lactate level
2. Obtain blood cultures prior to administration of antibiotics
3. Administer broad spectrum antibiotics
4. Administer 30ml/kg crystalloid for hypotension or lactate  $\geq 4$ mmol/L

\* "Time of presentation" is defined as the time of triage in the emergency department or, if presenting from another care venue, from the earliest chart annotation consistent with all elements of severe sepsis or septic shock ascertained through chart review.

**TO BE COMPLETED WITHIN 6 HOURS OF TIME OF PRESENTATION:**

5. Apply vasopressors (for hypotension that does not respond to initial fluid resuscitation) to maintain a mean arterial pressure (MAP)  $\geq 65$ mmHg
6. In the event of persistent hypotension after initial fluid administration (MAP < 65 mm Hg) or if initial lactate was  $\geq 4$  mmol/L, re-assess volume status and tissue perfusion and document findings according to Table 1.
7. Re-measure lactate if initial lactate elevated.

# Summary

- qSOFA – Early recognition of at risk patients
- Treatment targets – patient specific
- Targeted crystalloid resuscitation
  - 30 ml/kg initial bolus
  - Additional volumes guided by frequent reassessment of volume responsiveness
- Consider Albumin in refractory hypotension

Thank You

