# Fluids During septic Shock Olfa Hamzaoui Medical ICU Teaching Hospital of Reims France



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### Fluid resuscitation during early sepsis: a need for individualization

Mathieu JOZWIAK <sup>1, 2</sup>, Olfa HAMZAOUI <sup>3</sup>, Xavier MONNET <sup>1, 2</sup>, Jean-Louis TEBOUL <sup>1, 2</sup> \*

Minerva Anestesiologica 2018 August;84(8):987-92

Pt presenting with **septic shock** 



ne patient presented at the ED with fever, fatigue, and shortness of breath











#### INES

ving sepsis campaign: international elines for management of sepsis and septic < 2021

Intensive	Care Med (2021) 47:1181–12	247
		HEMODYNAMIC MANAGEMENT
	MODERATE	For adults with sepsis or septic shock, we <b>recommend</b> using crystalloids as first-line fluid for resuscitation.





### **GUIDELINES**

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Intensive Care Med (2021) 47:1181–1247



5 For patients with sepsis induced hypoperfusion or septic shock we suggest that at least 30 mL/kg of intravenous (IV) crystalloid fluid should be given within the first 3 hours of resuscitation.

# 2016 STATEMENT

"We **recommend** that in the initial resuscitation from sepsis-induced hypoperfusion, at least 30ml/kg of intravenous crystalloid fluid be given within the first 3 hours."





### Pneumonia: relative hypovolemia and increased capillary leak



### Peritonitis or abdominal sepsis: severe absolute hypovolemia







We recommend **individualizing** initial fluid resuscitation. No single formula can be applied to all patients, as **fluid requirements vary** substantially (depending on the source of sepsis and preexis cardiovascular function).



# Fluid resuscitation during early sepsis: a need for individualization Mathieu JOZWIAK <sup>1,2</sup>, Olfa HAMZAOUI <sup>3</sup>, Xavier MONNET <sup>1,2</sup>, Jean-Louis TEBOUL <sup>1,2</sup>\* Minerva Anestesiologica 2018 August;84(8):987-92 Pt presenting with septic shock Decrease infusion rate if: . Worsening of tachypnea

. Abdominal sepsis Low PP

Importance of individualizing

within the **first hour** 

. Fall in  $O_2$  saturation

the initial **fluid therapy** 



• RT-PCR SARS-CoV-2: positive

# He had 30ml/Kg of fluids and antibiotherapy



# He had 30ml/Kg of fluids and antibiotherapy



# He had 30ml/Kg of fluids and antibiotherapy

nhn

EMERGENCY

William Producer

123

9(

 $\mathbf{1}$ 

## 1. Fluids

- 2. Norepinephrine
- 3. Dobutamine
- 4. Nothing else

### Pression artérielle(mmHg)







### Peripheral **resistance**

- related to peripheral DAP (r = 0.71) (p<0.001)</li>
- but not related to peripheral
   SAP (r<sup>2</sup> = 0.04) and PP (r<sup>2</sup> = 0.02)



**Review Article** 

### Early norepinephrine use in septic shock

Olfa Hamzaoui<sup>1</sup>, Rui Shi<sup>2,3</sup> Thor

Thorac Dis 2020;12(Suppl 1):S72-S77

Table 1 Arguments in	favor of the early	use of norepinephrin	e in septic shock

Consequences of early use of norepinephrine	Rational	References
Prevention of prolonged severe hypotension	Septic shock is characterized by a depressed arterial tone. fluid administration alone cannot be sufficient to correct severe hypotension	(10,11)
Increase in cardiac output	Increase in cardiac preload due to an increase in stressed blood volume	(12-16)
	Increase in cardiac contractility	(17)
Improvement of microcirculation	Improvement of microvascular blood flow in pressure-dependent vascular beds through increase in MAP in severely hypotensive patients	(13)
Prevention of fluid overload	Early administration of norepinephrine limits the volume of fluids infused	(18)
Improvement of outcome	Likely in relation to the preceding effects	(18,19)



#### Critical Care 2010, 14:R142

#### RESEARCH

**Open Access** 

Early administration of norepinephrine increases cardiac preload and cardiac output in septic patients with life-threatening hypotension

Olfa Hamzaoui, Jean-François Georger, Xavier Monnet, Hatem Ksouri, Julien Maizel, Christian Richard, Jean-Louis Teboul $^{\ast}$ 

• NE increases preload

• NE decreases the degree of preload dependency

By redistributing the "non stressed" volume into the "stressed" volume

Exactly like fluids !

Without infusing fluids!

**Review Article** 

### Early norepinephrine use in septic shock

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#### CLINICAL INVESTIGATION

# Norepinephrine exerts an inotropic effect during the early phase of human septic shock

O. Hamzaoui<sup>1,\*</sup>, M. Jozwiak<sup>2</sup>, T. Geffriaud<sup>2</sup>, B. Sztrymf<sup>1</sup>, D. Prat<sup>1</sup>, F. Jacobs<sup>1</sup>, X. Monnet<sup>2</sup>, P. Trouiller<sup>1</sup>, C. Richard<sup>2</sup> and J.L. Teboul<sup>2</sup>

British Journal of Anaesthesia, 120 (3): 517–524 (2018)



In spite of the increase in LV afterload, all the indices of systolic function improved with

38 septic shock pts

with MAP< 65mmHg

**Repeated TTE** 

resuscitated < 3 hrs and

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•

early NE suggesting an improved cardiac contractility

**Review Article** 

### Early norepinephrine use in septic shock

Olfa Hamzaoui<sup>1</sup>, Rui Shi<sup>2,3</sup> Thorac

Thorac Dis 2020;12(Suppl 1):S72-S77

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	Improvement of outcome	Likely in relation to the preceding effects	(18,19)			

### Effects of very early start of norepinephrine in patients with septic shock: a propensity score-based analysis

Gustavo A. Ospina-Tascón<sup>1,2\*</sup>, Glenn Hernandez<sup>3</sup>, Ingrid Alvarez<sup>1</sup>, Luis E. Calderón-Tapia<sup>1</sup>, Ramiro Manzano-Nunez<sup>1</sup>, Alvaro I. Sánchez-Ortiz<sup>1</sup>, Egardo Quiñones<sup>1</sup>, Juan E. Ruiz-Yucuma<sup>1</sup>, José L. Aldana<sup>1,2</sup>, Jean-Louis Teboul<sup>4</sup>, Alexandre Biasi Cavalcanti<sup>5</sup>, Daniel De Backer<sup>6</sup> and Jan Bakker<sup>3,7,8,9</sup>

Critical Care (2

(2020) 24:52



# He had 3 litres of fluids and 0.3 microgramme/Kg/min of NE



# He had 3 litres of fluids and 0.3 microgramme/Kg/min of NE







High incidence of ARDS in cases of SARS-CoV-2

## Why do we need to predict fluid responsiveness?

> Not all the patients are fluid responsive



### critical care review

# Predicting Fluid Responsiveness in ICU Patients\*

A Critical Analysis of the Evidence

Frédéric Michard, MD, PhD; and Jean-Louis Teboul, MD, PhD

CHEST 2002; 121:2000-2008

Source	Patients, No.	FC, No.	Fluid Infused	Volume Infused, mL	Speed of FC, min	Definition of Response	Rate of Response, %
Calvin et al <sup>2</sup>	28	28	5% Alb	250	20-30	$\Delta SV > 0\%$	71
Schneider et al <sup>3</sup>	18	18	FFP	500	30	$\Delta SV > 0\%$	72
Reuse et al <sup>4</sup>	41	41	4.5% Alb	300	30	$\Delta \text{CO} > 0\%$	63
Magder et al <sup>5</sup>	33	33	9% NaCl	100 - 950		$\Delta \text{CO} > 250$	52
						mL/min	
Di∈							59
<b>Only 52%</b>	6 of pa	tier	nts <b>incr</b>	ease the	eir <b>ca</b>	rdiac	$\frac{40}{56}$
	in rocr	onc	o to flu	id admi	inistra	tion	60
	micsh			ilu aunn	IIIISUC		45
<b>WI</b> a							40
Tousignam et ar-	υr	UE	11110	000	LU.	ADY - 4070	40
Michard et al <sup>12</sup>	40	40	HES	500	30	$\Delta \text{CO} > 15\%$	40
Feissel et al <sup>13</sup>	19	19	HES	8 mL/kg	30	$\Delta \text{CO} > 15\%$	53
Total	334	406		0			52

# Why do we need to predict fluid responsiveness?

> Not all the patients are fluid responsive

> Fluid responsiveness is a dynamic phenomenon



## Why do we need to predict fluid responsiveness?

- > Not all the patients are fluid responsive
- > Fluid responsiveness is a dynamic phenomenon
- Fluid overload is harmful

Sepsis in European intensive care units: Results of the SOAP study\*

Jean-Louis Vincent, MD, PhD, FCCM; Yasser Sakr, MB, BCh, MSc; Charles L. Sprung, MD; V. Marco Ranieri, MD; Konrad Reinhart, MD, PhD; Herwig Gerlach, MD, PhD; Rui Moreno, MD, PhD; Jean Carlet, MD, PhD; Jean-Roger Le Gall, MD; Didier Payen, MD; on behalf of the Sepsis Occurrence in Acutely III Patients Investigators

Crit Care Med 2006; 34:344–353

Table 7. Multivariate, forward stepwise logistic regression analysis in sepsis patients (n = 1177), with intensive care unit mortality as the dependent factor

	OR (95% CI)	p Value
SAPS II score <sup>a</sup> (per point increase)	1.0 (1.0–1.1)	<.001
Cumulative fluid balance <sup><math>b</math></sup> (per liter increase)	1.1(1.0-1.1)	.001
Age (per year increase)	1.0(1.0-1.0)	.001
During sepsis: positive is an independent factor	cumulative fluid ba	lance rtality
Female gender	1.4(1.0-1.8)	.044

## Why do we need to predict fluid responsiveness?

- > Not all the patients are fluid responsive
- > Fluid responsiveness is a dynamic phenomenon
- Fluid overload is harmful
- > Use of **fluid responsiveness** tests is associated with improved **outcome**

Characteristics of resuscitation, and association between use of dynamic tests of fluid responsiveness and outcomes in septic patients: results of a multicenter prospective cohort study in Argentina

Arnaldo Dubin<sup>1\*</sup>, Cecilia Loudet<sup>2</sup>, Vanina S. Kanoore Edul<sup>3</sup>, Javier Osatnik<sup>4</sup>, Fernando Ríos<sup>5</sup>, Daniela Vásquez<sup>6</sup>, Mario Pozo<sup>7</sup>, Bernardo Lattanzio<sup>8</sup>, Fernando Pálizas<sup>7</sup>, Francisco Klein<sup>9</sup>, Damián Piezny<sup>5</sup>, Paolo N. Rubatto Birri<sup>1</sup>, Graciela Tuhay<sup>9</sup>, Analía García<sup>10</sup>, Analía Santamaría<sup>11</sup>, Graciela Zakalik<sup>12</sup>, Cecilia González<sup>13</sup> and Elisa Estenssoro<sup>2</sup> on behalf of the investigators of the SATISEPSIS group

Ann. Intensive Care (2020) 10:40

- National, multicenter prospective cohort study (n = 787) fulfilling Sepsis-3 definitions
- Examine the association between the use of dynamic tests of fluid responsiveness and outcome

### Only 584 patients received fluids

# Table 4 Independent determinants of mortality according to logistic regression analysis

Variable	Odds ratio	[Cl 95%]	Р
Charlson score	1.21	[1.07–1.36]	0.002
SOFA score	1.16	[1.07–1.26]	< 0.0001
Serum lactate	1.21	[1.08–1.37]	0.001
Mechanical ventilation	12.2	[5.73-26.00]	< 0.0001
Dynamic tests of fluid responsiveness	0.37	[0.21–0.67]	0.001



We recommend **individualizing** initial fluid resuscitation. No single formula can be applied to all patients, as **fluid requirements vary** substantially (depending on the source of sepsis and preexis cardiovascular function).

We recommend **individualizing** fluid therapy using **dynamic challenges**.



### GUIDELINES

Surviving sepsis campaign: international guidelines for management of sepsis and septic shock 2021

Intensive Care Med (2021) 47:1181–1247

. For adults with sepsis or septic shock, we **suggest** using dynamic measures to guide fluid resuscitation, over physical examination or static parameters alone

Veak recommendation, very low-quality evidence

# emarks

)ynamic parameters include response to a passive leg raise or a fluid bolus, using stroke volume (SV), stroke volume variation (SVV), pulse pressure variation (PPV), or echocardiography, where available

## Patient in the ICU: 2 hours later



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Minerva Anestesiologica 2018 August;84(8):987-92







Improved Outcome Based on Fluid Management in Critically III Patients Requiring Pulmonary Artery Catheterization<sup>1-3</sup>

JOHN P. MITCHELL, DAN SCHULLER, FRANK S. CALANDRINO, and DANIEL P. SCHUSTER

AM REV RESPIR DIS 1992; 145:990-998



Intensive Care Med (2007) 33:448–453	ORIGINAL
Xavier Monnet Nadia Anguel David Osman Olfa Hamzaoui Christian Richard Jean-Louis Teboul	Assessing pulmonary permeability by transpulmonary thermodilution allows differentiation of hydrostatic pulmonary edema from ALI/ARDS





Higher is the PVPI higher is the risk to develop PE

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Restriction of Intravenous Fluid in ICU Patients with Septic Shock





ORIGINAL ARTICLE

### Early Restrictive or Liberal Fluid Management for Sepsis-Induced Hypotension

The National Heart, Lung, and Blood Institute Prevention and Early Treatment of Acute Lung Injury Clinical Trials Network\*

Table 3. Outcomes.*								
Outcome	Restrictive Fluid Group (N=782)		Liber	Difference (95% Cl)†				
	No. of Patients	Mean (95% CI)	No. of Patients	Mean (95% CI)				
Death before discharge home by day 90 — % of patients <u>:</u>	782	14.0 (11.6 to 16.4)	781	14.9 (12.4 to 17.4)	–0.9 (–4.4 to 2.6)§			
No. of days free from organ-support therapy at 28 days	778	24.0 (23.4 to 24.6)	778	23.6 (23.0 to 24.3)	0.3 (-0.5 to 1.2)			
No. of days free from ventilator use at 28 days	773	23.4 (22.7 to 24.1)	771	22.8 (22.0 to 23.5)	0.6 (-0.4 to 1.6)			
No. of days free from renal-replace- ment therapy at 28 days	737	24.1 (23.4 to 24.8)	738	23.9 (23.2 to 24.6)	0.2 (-0.8 to 1.2)			
No. of days free from vasopressor use at 28 days¶	778	22.0 (21.4 to 22.7)	778	21.6 (20.9 to 22.3)	0.4 (-0.5 to 1.3)			
No. of days out of the ICU from day 1 to day 28	778	22.8 (22.2 to 23.4)	778	22.7 (22.0 to 23.3)	0.1 (-0.8 to 1.0)			
No of days out of the hospital by day 28	778	16.2 (15.4 to 17.0)	778	15.4 (14.6 to 16.2)	0.8 (-0.3 to 1.9)			





How can we blindy randomise patients without estimating the individual need of fluids ???



Some others who need less fluids will be in the wrong liberal strategy and will have increased risk of mortality

### Fluid resuscitation during early sepsis: a need for individualization Mathieu JOZWIAK 1, 2, Olfa HAMZAOUI 3, Xavier MONNET 1, 2, Jean-Louis TEBOUL 1, 2 \* Minerva Anestesiologica 2018 August;84(8):987-92 Individualise the Pt presenting with septic sho initial fluid bolus **Decrease** infusion rate if: Infuse around 10 mL/kg Increase infusion rate if: crystalloids . Worsening of tachypnea . Fluid losses . Mottling or ↗ CRT within the first hour . Fall in $O_2$ saturation . Abdominal sepsis Low PP Consider early use of NE (low DAP)

#### Fluid resuscitation during early sepsis: a need for individualization Mathieu JOZWIAK <sup>1, 2</sup>, Olfa HAMZAOUI <sup>3</sup>, Xavier MONNET <sup>1, 2</sup>, Jean-Louis TEBOUL <sup>1, 2</sup> \* Minerva Anestesiologica 2018 August;84(8):987-92 Individualise the Pt presenting with septic shoc initial fluid bolus **Decrease** infusion rate if: Infuse around 10 mL/kg Increase infusion rate if: . Worsening of tachypnea crystalloids . Fluid losses . Mottling or ↗ CRT . Fall in O<sub>2</sub> saturation within the **first hour** . Abdominal sepsis Low PP **Consider Early** use of NE PLR PPV If shock persists, SVV EEO $\triangleright$ test preload responsiveness $V_{T}$ challenge IVC diameter variation $\triangleright$ Consider dynamic indicators of preload responsiveness

# Fluid resuscitation during early sepsis: a need for individualization Mathieu JOZWIAK 1-2, Olfa HAMZAOUI 3, Xavier MONNET 1-2, Jean-Louis TEBOUL 1-2 \* Minerva Anestesiologica 2018 August;84(8):987-92 Pt presenting with septic shoc





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