

# Sepsis 2021

Rebecca M. Baron, M.D.

Associate Professor of Medicine, Harvard Medical School

Associate Physician, Brigham and Women's Hospital

Pulmonary and Critical Care Division

2021

# Conflict of Interest

- Advisory Board for Merck
- Consultant for Genentech

# Case

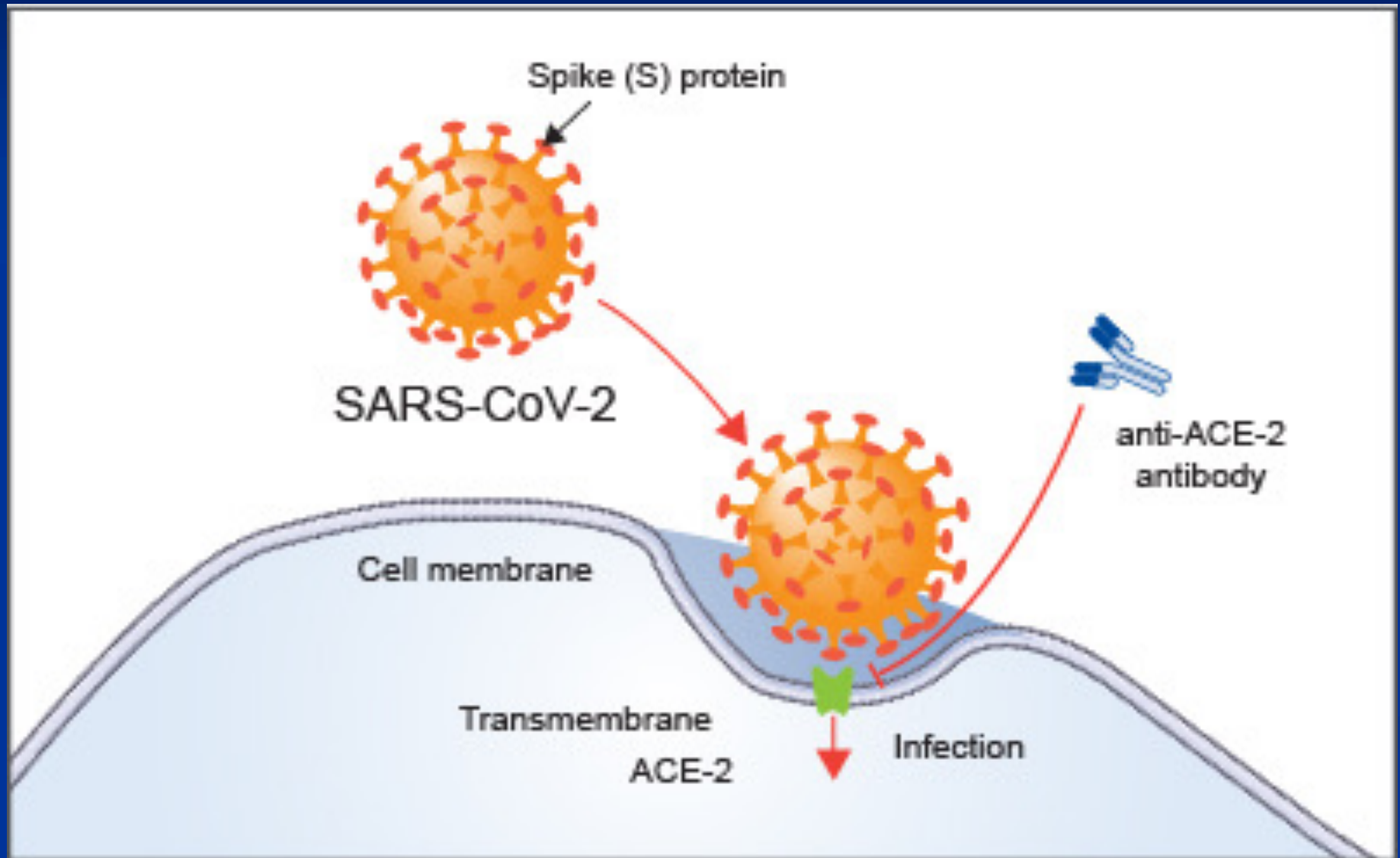
A 47 yo woman with alcoholic cirrhosis is brought to your ER with fevers, confusion, shortness of breath, and worsening ascites. Temp is 37°C, SBP is 50 mmHg, HR 150 bpm, RR 40/min, CVP 4 mm Hg, and O<sub>2</sub> sat 90% (RA). CXR shows diffuse infiltrates, and peritoneal fluid returns with a leukocyte count of 1000/ $\mu$ L (95% polys).

# Question #1:

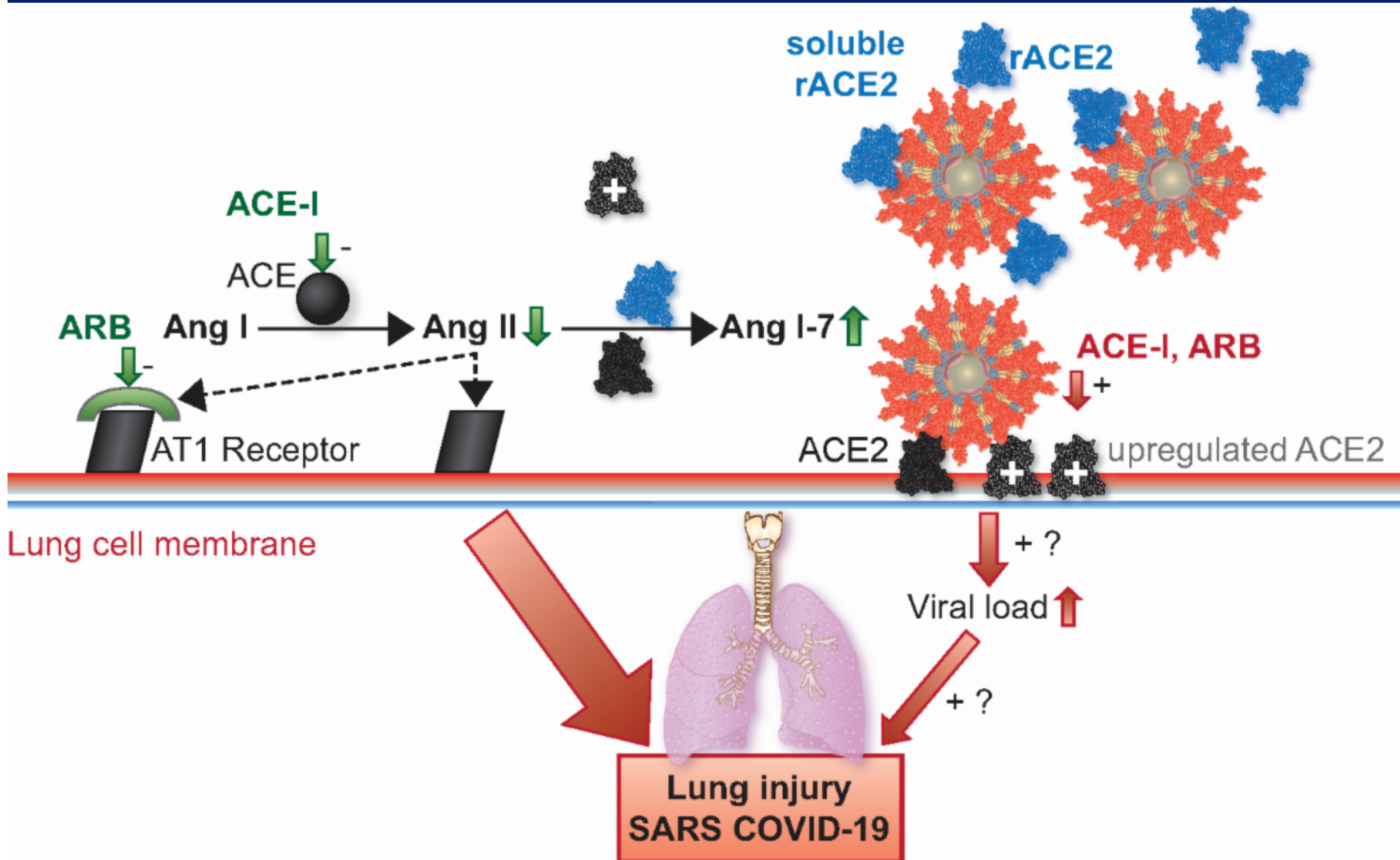
**Does this patient have sepsis?**

**By what criteria?**

# Question #1 revised: Does this patient have COVID?



# COVID Treatment thoughts: Targeting the virus and/or specific pathways?



# What is Sepsis (2001-15)?

- Systemic Inflammatory Response Syndrome (SIRS):
  - Temp  $>38^{\circ}\text{C}$  or  $<36^{\circ}\text{C}$
  - Heart Rate  $> 90$  bpm
  - Resp Rate  $> 20/\text{min}$
  - WBC  $>10000$ ,  $<4000$ , or Bandemia  $>10\%$
- Sepsis: SIRS + Infection
- Severe Sepsis: Sepsis+ Organ Dysfunction
- Septic Shock: Sepsis+Refractory Hypotension

# 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: (>10% mortality)
  - Life-threatening organ dysfunction
  - Caused by *dysregulated response* to infection
  - Increase SOFA score of  $\geq 2$
- SHOCK: (>40% mortality)
  - Vasopressors for MAP  $\geq 65$  mmg Hg
  - Lactate  $> 2$  mmol/L
  - In absence of hypovolemia

# SOFA Score: 6 Organ Systems, 0-4 Points

<i>Points</i>	<b>0</b>	<b>1</b>	<b>2</b>	<b>3</b>	<b>4</b>
<b>PaO<sub>2</sub>/FiO<sub>2</sub></b>	≥400	<400	<300	<200 + mechanical ventilation	<100 + mechanical ventilation
<b>Platelets</b>	≥150	<150	<100	<50	<20
<b>Bilirubin</b>	<1.2	1.2-1.9	2.0-5.9	6.0-11.9	>12.0
<b>Blood Pressure</b>	MAP ≥70	MAP <70	Dopamine <5 or Dobutamine	Dopamine 5.1-15 or Epinephrine <0.1 or Norepinephrine <0.1	Dopamine >15 or Epinephrine >0.1 or Norepinephrine >0.1
<b>Glasgow Coma Scale</b>	15	13-14	10-12	6-9	<6
<b>Creatinine</b>	<1.2	1.2-1.9	2.0-3.4	3.5-4.9 or <500cc urine/d	>5.0 or <200cc urine/d

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## qSOFA

- Out of hospital, ED, Ward settings
- *Worse outcomes* predicted from sepsis with 2 of:
  - Respiratory Rate  $\geq 22/\text{min}$
  - Altered mental status (GCS  $\leq 13$ )
  - SBP  $\leq 100$  mmHg
- Ongoing inquiry as to its validation
- *LESS SENSITIVE* but *MORE SPECIFIC* than SIRS  
for sepsis screening.

# Limitations

- Lab testing required (lactate, SOFA) not feasible in low-resource settings
- Prospective validation underway for qSOFA score vs. other metrics
- No use of biologic markers of sepsis to help define subgroups or predictors
- Practicality of definition for screening patients vs. billing vs. epidemiologic vs. research tools, etc.

# In the future: Machine Learning/Artificial Intelligence?

JAMA | Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

## Derivation, Validation, and Potential Treatment Implications of Novel Clinical Phenotypes for Sepsis

Christopher W. Seymour, MD, MSc; Jason N. Kennedy, MS; Shu Wang, MS; Chung-Chou H. Chang, PhD; Corrine F. Elliott, MS; Zhongying Xu, MS; Scott Berry, PhD; Gilles Clermont, MD, MSc; Gregory Cooper, MD, PhD; Hernando Gomez, MD, MPH; David T. Huang, MD, MPH; John A. Kellum, MD, FACP, MCCM; Qi Mi, PhD; Steven M. Opal, MD; Victor Talisa, MS; Tom van der Poll, MD, PhD; Shyam Visweswaran, MD, PhD; Yoram Vodovotz, PhD; Jeremy C. Weiss, MD, PhD; Donald M. Yealy, MD, FACEP; Sachin Yende, MD, MS; Derek C. Angus, MD, MPH

Used 'big data' machine learning approaches to derive 4 sepsis subphenotypes not otherwise predicted from conventional severity indices. \*\*Big data playing a big role in COVID epi studies and growing role in sepsis.

JAMA. 2019;321(20):2003-2017. doi:10.1001/jama.2019.5791  
Published online May 19, 2019.

# Surviving Sepsis Campaign

Surviving Sepsis Campaign Responds to Sepsis-3

March 1, 2016

SSC's approach: essentially no different than before!

- Step 1: Screen for Infection
  - *SIRS may be a sign of infection*
- Step 2: Screen for Organ Dysfunction
  - Use organ dysfunction to target initial treatment and qSOFA to target closer monitoring for deterioration from sepsis
- Step 3: If hypotensive or lactate  $\geq 2.0 \rightarrow 30$  ml/kg crystalloid, with reassessment of volume responsiveness or tissue perfusion

**My bottom line: DON'T MISS SEPSIS. SCREEN with SIRS, PROGNOSTICATE with qSOFA, Dx SEPSIS w SOFA**

# Case, Question #2

A 47 yo woman with alcoholic cirrhosis is brought to your ER with fevers, confusion, shortness of breath, and worsening ascites. Temp is 37°C, SBP is 50 mmHg, HR 150 bpm, RR 40/min, CVP 4 mm Hg, and O<sub>2</sub> sat 90% (RA). CXR shows diffuse infiltrates, and peritoneal fluid returns with a leukocyte count of 1000/ $\mu$ L (95% polys). You initiate your sepsis bundle. Initial management of hemodynamics should entail use of:

- a. Vasopressin
- b. Norepinephrine
- c. Norepinephrine + Furosemide
- d. Intravenous fluids
- e. Dobutamine

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- b. Norepinephrine
- c. Norepinephrine + Furosemide
- d. Intravenous fluids**
- e. Dobutamine

## Question #2:

**What are we supposed to be doing with fluids in sepsis?**

# Sepsis: Source Control

- EARLY, BROAD, EMPIRIC antibiotic therapy
  - Not the time to be elegant!
- Think of sources needing SURGICAL INTERVENTION
  - Catheter / device → Remove it
  - Soft tissue abscess → Drain it
  - Empyema → Chest tube
  - Cholangitis → ERCP
  - Endocarditis → Abx/Valve replacement
  - Septic arthritis → Joint debridement
- Narrow therapy after 48 – 72H of cultures

**\*\*COVID: Remdesivir shortened time to recovery in less sick patients, perhaps**

# Septic Shock: *EARLY* Goal-Directed Therapy 2001-2014

The New England Journal of Medicine

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## EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S.,  
ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D.,  
FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP\*

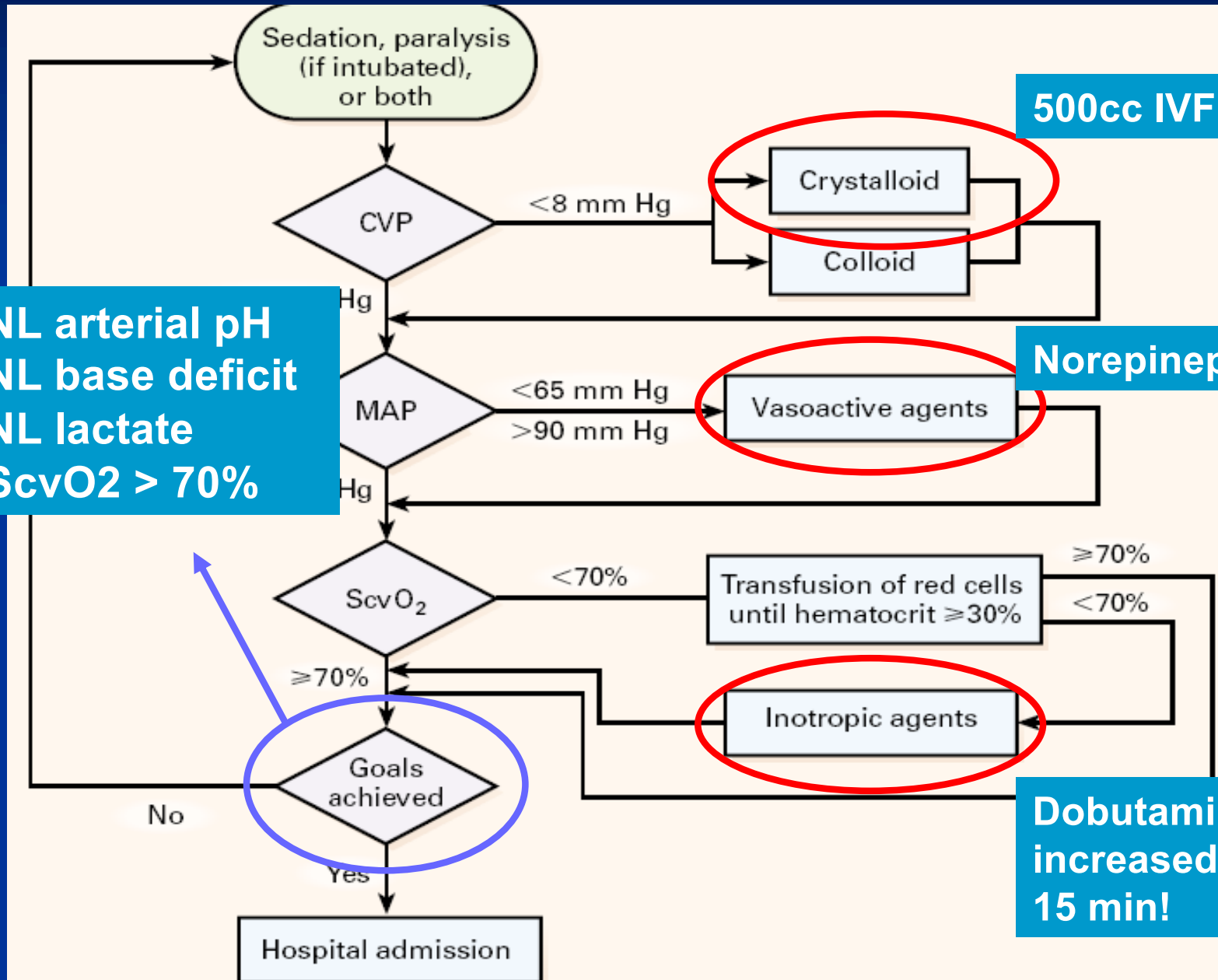
\*Treatment began in E.D.: 6-hours

\*A-line, Central line insertion

\*Monitored: Mean arterial BP (MAP)  
Central venous pressure (CVP)  
Central venous O<sub>2</sub> sat (S<sub>CV</sub>O<sub>2</sub>)  
Hematocrit

# EARLY Goal-Directed Therapy

## INTERVENTION



500cc IVF Q 30 min!

NL arterial pH  
NL base deficit  
NL lactate  
ScvO<sub>2</sub> > 70%

Norepinephrine

Dobutamine: dose increased 2.5 mcg Q 15 min!

# EARLY Goal-Directed Therapy

## HOW'D THEY DO THAT??

TREATMENT	HOURS AFTER THE START OF THERAPY		
	0-6	7-72	0-72
Total fluids (ml)			
Standard therapy	3499 ± 2438	10,602 ± 6,216	13,358 ± 7,729
EGDT	4981 ± 2984	8,625 ± 5,162	13,443 ± 6,390
P value	<0.001	0.01	0.73
Red-cell transfusion (%)			
Standard therapy	18.5	32.8	44.5
EGDT	64.1	11.1	68.4
P value	<0.001	<0.001	<0.001
Any vasopressor (%)†			
Standard therapy	30.3	42.9	51.3
EGDT	27.4	29.1	36.8
P value	0.62	0.03	0.02
Inotropic agent (dobutamine) (%)			
Standard therapy	0.8	8.4	9.2
EGDT	13.7	14.5	15.4
P value	<0.001	0.14	0.15

# EARLY Goal-Directed Therapy

## IT WORKED!!

VARIABLE	STANDARD THERAPY (N=133)	EARLY GOAL-DIRECTED THERAPY (N=130)	RELATIVE RISK (95% CI)	P VALUE
	no. (%)			
In-hospital mortality†				
All patients	59 (46.5)	38 (30.5)	0.58 (0.38–0.87)	0.009
Patients with severe sepsis	19 (30.0)	9 (14.9)	0.46 (0.21–1.03)	0.06
Patients with septic shock	40 (56.8)	29 (42.3)	0.60 (0.36–0.98)	0.04
Patients with sepsis syndrome	44 (45.4)	35 (35.1)	0.66 (0.42–1.04)	0.07
28-Day mortality†	61 (49.2)	40 (33.3)	0.58 (0.39–0.87)	0.01
60-Day mortality†	70 (56.9)	50 (44.3)	0.67 (0.46–0.96)	0.03

However, what are the key components and broader applicability of EGDT?

# The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

MAY 1, 2014

VOL. 370 NO. 18

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

The ProCESS Investigators\*

1341 Patients, Compared:

1. EGDT, vs.
2. Protocolized care *without* CVC, inotropes, blood, vs.
3. Usual care

**NO DIFFERENCE** in Primary outcome of 60d in-hospital mortality or other outcomes

# ProCESS\*: What does it mean?

- Mortality in usual care group substantially lower than in EGDT in first trial (18% vs. 46%), thus “usual care” has evolved.
- Severe sepsis without septic shock wasn't studied in ProCESS.
- This trial and general practice supports *early* antibiotics and fluids and uncertain re: CVC for everyone, PRBCs\*\*, dobutamine.
- Targeted fluid resuscitation now the goal.

# Application of Fluid Resuscitation in Adult Septic Shock

Sepsis-induced hypotension or lactate  $\geq 4$  mmol/L  
(Based on SSC bundle and CMS threshold)

No high flow oxygen and  
No ESRD on dialysis or CHF

Rapid infusion  
of 30 ml/kg  
crystalloid

Pneumonia or ALI with  
high flow oxygen requirements

Not intubated/  
mechanically ventilated

Intubated/  
mechanically ventilated

Consider  
intubation/mechanical  
ventilation to facilitate  
30 ml/kg crystalloid infusion

If  
Yes

Rapid infusion  
of 30 ml/kg  
crystalloid

If no

Total of 30 ml/kg with  
frequent reassessment of  
oxygenation

ESRD on hemodialysis  
or CHF

Total of 30 ml/kg crystalloid  
with frequent reassessment of  
oxygenation

**CMS: (3h: plus  
LA, cx, Abx)  
(6h: f/u LA)**

## 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
  - 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

CRITICAL CARE MEDICINE

## From: Will This Hemodynamically Unstable Patient Respond to a Bolus of Intravenous Fluids?

JAMA. 2016;316(12):1298-1309. doi:10.1001/jama.2016.12310

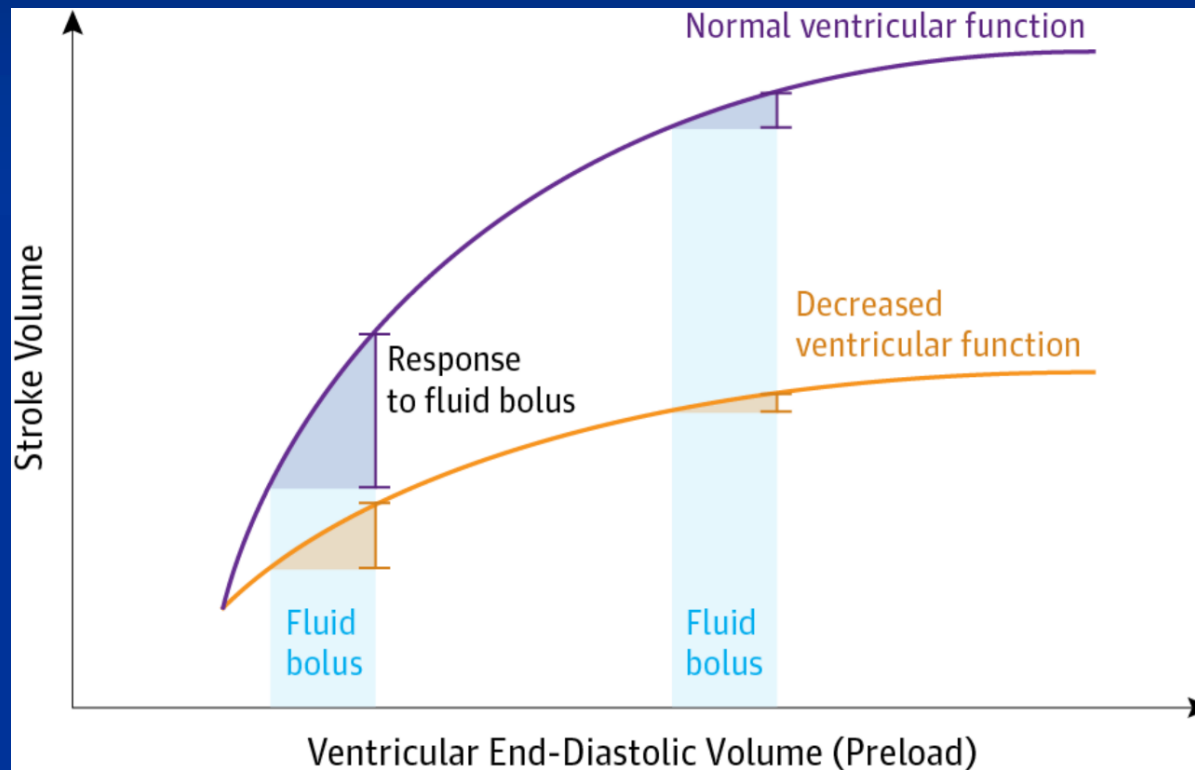


Figure Legend:

**Effect of Increase in Preload on Stroke Volume of Ventricles With Normal and Decreased Contractility. Frank-Starling curves illustrate that the effect of a given increase in preload on stroke volume is dependent both on ventricular contractility and on baseline preload.**

# Fluid Response Evaluation in Sepsis Hypotension and Shock

## A Randomized Clinical Trial



*Ivor S. Douglas, MD; Philip M. Alapat, MD; Keith A. Corl, MD; Matthew C. Exline, MD, MPH;  
Lui G. Forni, PhD; Andre L. Holder, MD; David A. Kaufman, MD; Akram Khan, MD; Mitchell M. Levy, MD;  
Gregory S. Martin, MD; Jennifer A. Sahatjian, PsyD; Eric Seeley, MD; Wesley H. Self, MD;  
Jeremy A. Weingarten, MD; Mark Williams, MD; and Douglas M. Hansell, MD*



Fluid responsiveness assessed by Passive Leg Raise to guide fluid resuscitation (n=83) vs. Usual Care (n=41). With intervention:

- Lower net positive fluid balance
- Lower risk of renal replacement and mechanical ventilation

# Enrolling now at an ICU near you: CLOVER trial design (PETAL Network)

## GROUP ASSIGNMENT

You will receive either a **medicine to raise blood pressure** and then fluids (if needed) OR a **larger amount of fluids** first and then medicine to raise blood pressure (if needed).

This is assigned by chance (like a coin flip).



## Medicine to Raise Blood Pressure First

One group will get **medicine to raise blood pressure** **pressure** FIRST and then fluids (if needed).  
Both are given through a tube in the vein (IV).



## Fluids First

One group will get a **larger amount of fluids** FIRST and then medicine to raise blood pressure (if needed).  
Both are given through a tube in the vein (IV).

**Small studies recently examining earlier pressors initiation and suggest volume overload not beneficial.**

# What 'flavor' of fluid should we be using in sepsis?

NO: Hetastarch

Mostly NO: Albumin

Yes: Crystalloid...moving toward favoring LR over saline

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Balanced Crystalloids versus Saline in Critically Ill Adults

Matthew W. Semler, M.D., Wesley H. Self, M.D., M.P.H., Jonathan P. Wanderer, M.D., Jesse M. Ehrenfeld, M.D., M.P.H., Li Wang, M.S., Daniel W. Byrne, M.S., Joanna L. Stollings, Pharm.D., Avinash B. Kumar, M.D., Christopher G. Hughes, M.D., Antonio Hernandez, M.D., Oscar D. Guillaumondegui, M.D., M.P.H., Addison K. May, M.D., Liza Weavind, M.B., B.Ch., Jonathan D. Casey, M.D., Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D., and Todd W. Rice, M.D., for the SMART Investigators and the Pragmatic Critical Care Research Group\*

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Balanced Crystalloids versus Saline in Noncritically Ill Adults

Wesley H. Self, M.D., M.P.H., Matthew W. Semler, M.D., Jonathan P. Wanderer, M.D., Li Wang, M.S., Daniel W. Byrne, M.S., Sean P. Collins, M.D., Corey M. Slovis, M.D., Christopher J. Lindsell, Ph.D., Jesse M. Ehrenfeld, M.D., M.P.H., Edward D. Siew, M.D., Andrew D. Shaw, M.B., Gordon R. Bernard, M.D., and Todd W. Rice, M.D., for the SALT-ED Investigators\*

NEJM March 1, 2018

# **FLUIDS in SEPSIS BOTTOM LINE:**

**Bolus crystalloid, but don't overdo it.**

**Find your favorite way(s) to target resuscitation.**

# Case, Question #3

You have administered broad-spectrum antibiotics to treat presumed spontaneous bacterial peritonitis, give her supplemental O<sub>2</sub> (now saturating 90% on 100% FM), and after fluid resuscitation with 3L of crystalloid, her HR comes down to 100 bpm, her SBP has risen to 65 mm Hg with a mean arterial pressure (MAP) of 50 mm Hg, and the CVP is 13 mm Hg. You next order:

- a. Vasopressin
- b. Norepinephrine
- c. Norepinephrine + Furosemide
- d. 1 Unit of PRBCs
- e. Dobutamine

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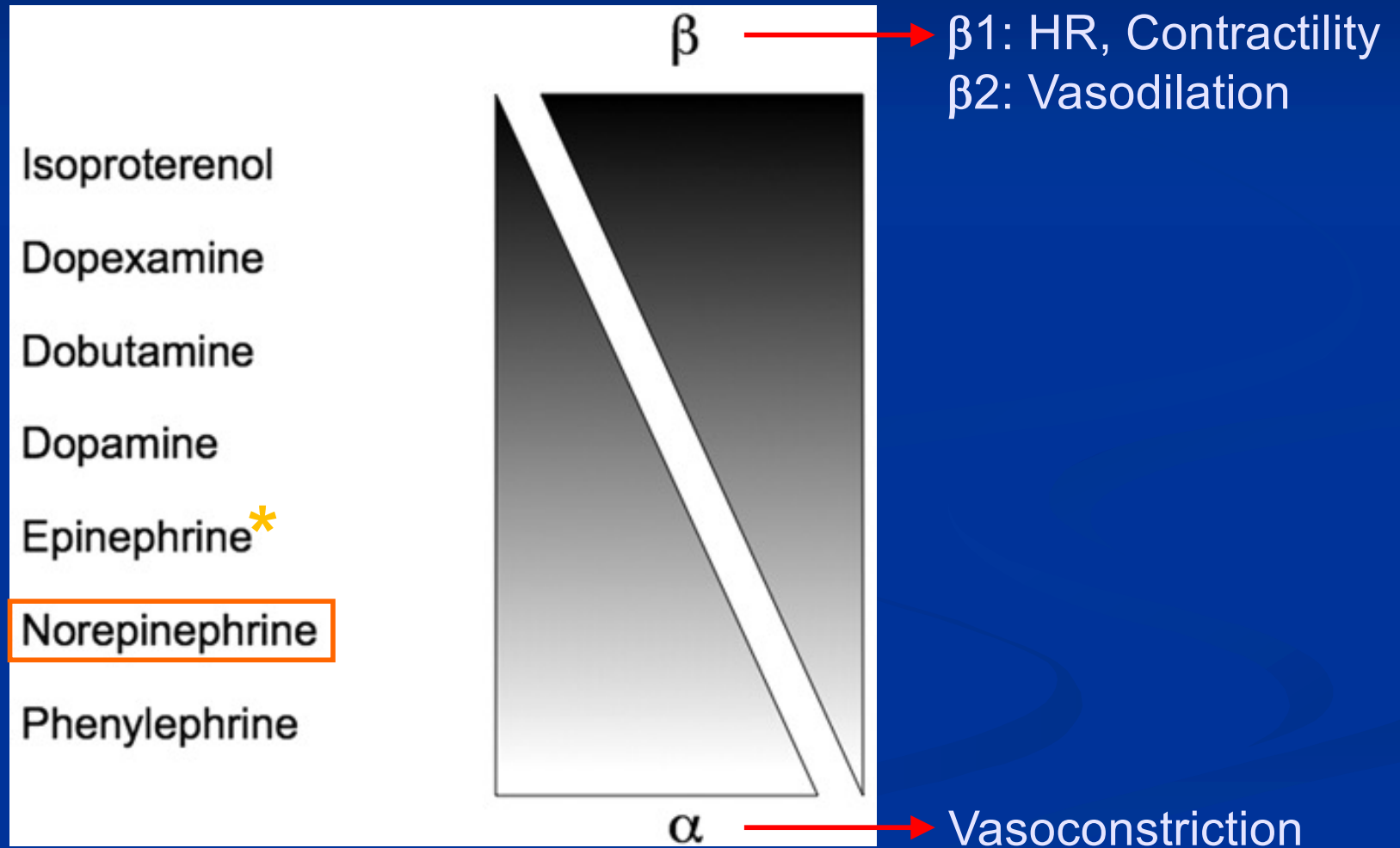
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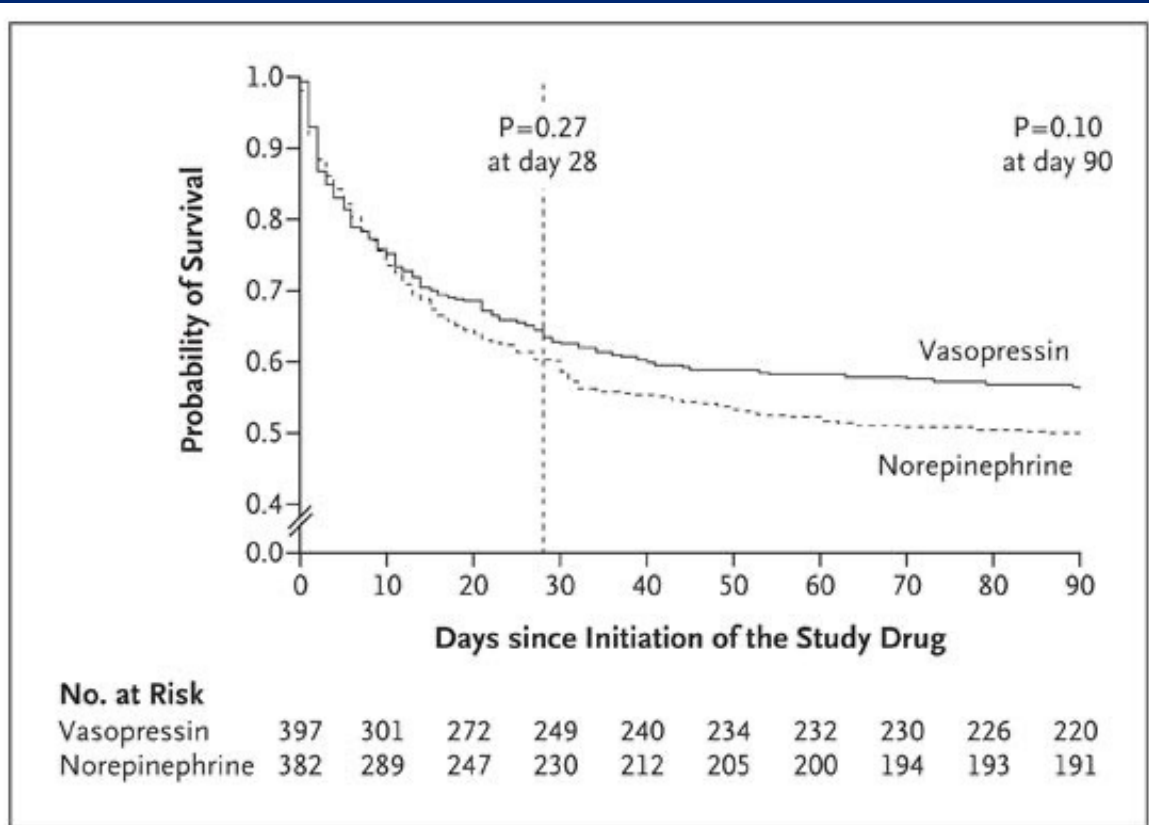
# Question #3:

**What about Vapressors?**

# Action of Vasoactive Catecholamines 2001- 2008



# Vasopressin as a 'Pressor'



- Multi-center RCT with ~800 patients
- No significant mortality benefit in adding vasopressin to norepinephrine
- Less sick people did better with addition of vasopressin
- Widespread use as an adjunctive support with norepinephrine

## VASST Trial

Russell et al. NEJM 2008; 358:877-887, Feb 28, 2008.

JAMA. 2016;316(5):509-518. doi:10.1001/jama.2016.10485

# New kid on the block:

## *The* NEW ENGLAND JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

AUGUST 3, 2017

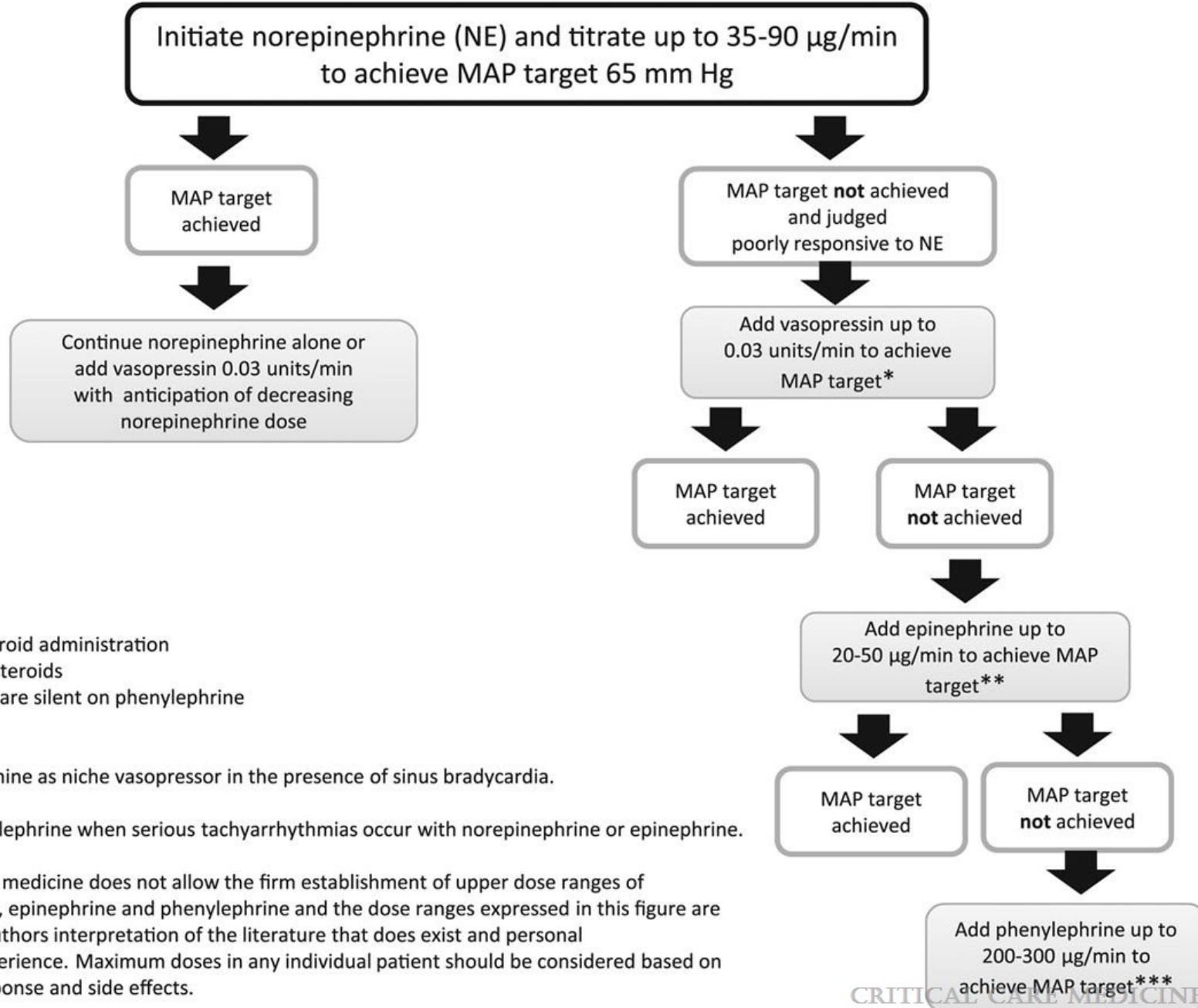
VOL. 377 NO. 5

### Angiotensin II for the Treatment of Vasodilatory Shock

Ashish Khanna, M.D., Shane W. English, M.D., Xueyuan S. Wang, M.D., Kealy Ham, M.D., James Tumlin, M.D., Harold Szerlip, M.D., Laurence W. Busse, M.D., Laith Altaweel, M.D., Timothy E. Albertson, M.D., M.P.H., Ph.D., Caleb Mackey, M.D., Michael T. McCurdy, M.D., David W. Boldt, M.D., Stefan Chock, M.D., Paul J. Young, M.B., Ch.B., Ph.D., Kenneth Krell, M.D., Richard G. Wunderink, M.D., Marlies Ostermann, M.D., Ph.D., Raghavan Murugan, M.D., Michelle N. Gong, M.D., Rakshit Panwar, M.D., Johanna Hästbacka, M.D., Ph.D., Raphael Favory, M.D., Ph.D., Balasubramanian Venkatesh, M.D., B. Taylor Thompson, M.D., Rinaldo Bellomo, M.D., Jeffrey Jensen, B.S., Stew Kroll, M.A., Lakhmir S. Chawla, M.D., George F. Tidmarsh, M.D., Ph.D., and Adam M. Deane, M.D., for the ATHOS-3 Investigators\*

- Multi-center RCT with 344 patients (mostly sepsis; but NOT low output states)
- *Add-on* to conventional pressors increased MAP to 75 within 3h (69% vs. 23%,  $p < 0.001$ )
- Similar rates of adverse events
- Intriguing as a new class of vasopressors (?? Role in COVID)

## Vasopressor Use for Adult Septic Shock (with guidance for steroid administration)



# Question #4:

**What are we supposed to be doing with steroids in sepsis?**

# RELATIVE Adrenal Insufficiency

## Basic Background

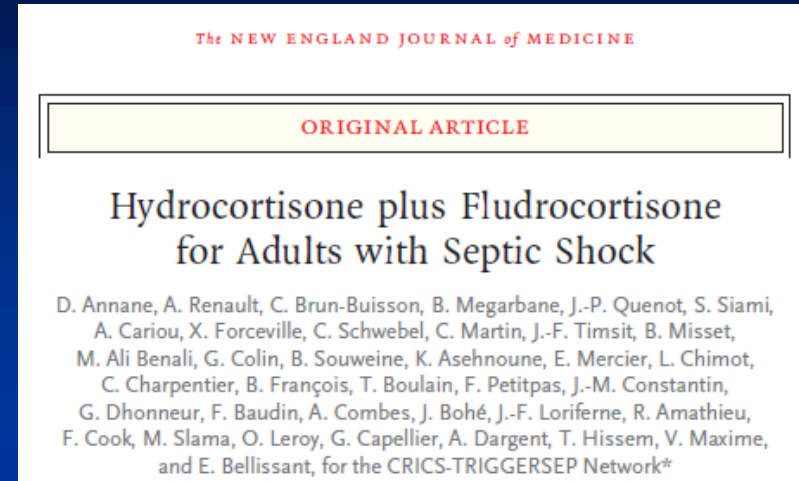
- “High-dose” corticosteroids DO NOT improve sepsis outcomes<sup>1</sup>
- Absolute adrenal insufficiency in sepsis is RARE
- What about RELATIVE adrenal insufficiency?
  - 2002-2008: Cort-stim to select ‘nonresponders’ based upon a subgroup analysis
  - 2008: low dose steroids hastened shock reversal in those in whom shock was reversed

<sup>1</sup>NEJM 1984 311: 1137; Crit Care Med 1995 23: 1430; JAMA 2002; NEJM<sup>8</sup>2008

# Low-Dose Steroids in Sepsis, 2018:



- 3800 patients, RCT
- Less sick patients
- HC continuous infusion
- No fludrocortisone
- No mortality benefit 90d
- Faster resolution of shock
- Fewer blood transfusions with steroids (unclear why)



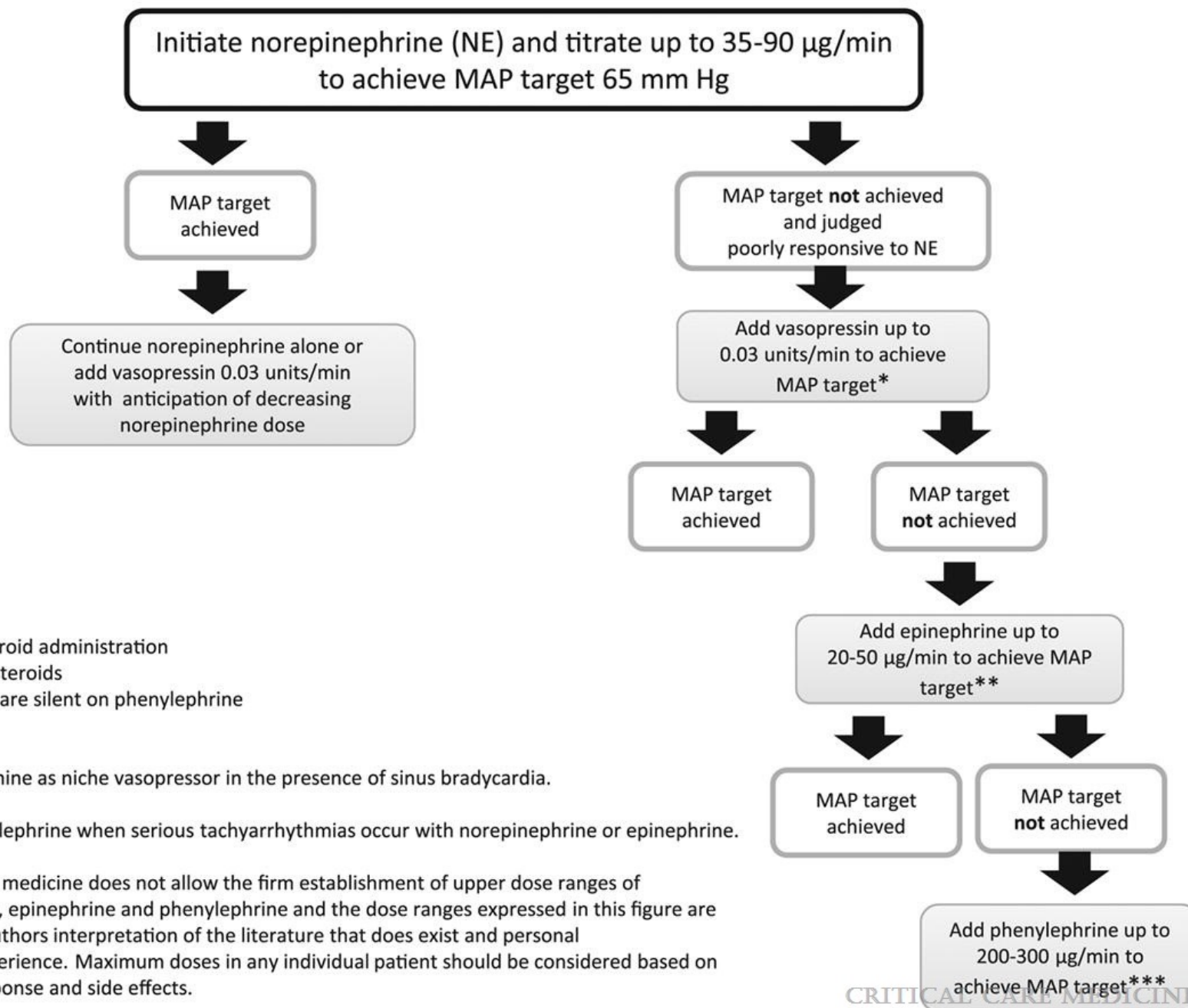
- 1241 patients, RCT
- Activated Protein C removed
- Sicker patients
- Included fludrocortisone
- 90d mortality benefit
- Similar infections though more viral with HC/FC
- More hyperglycemia with HC

# Steroids in Sepsis Bottom Line?

“It is unlikely that in the near future sufficiently powered trials will provide us with better data. Thus, clinicians will have to use these data and subsequent meta-analyses to decide how best to treat patients with septic shock. Estimating 90-day mortality at the bedside is not practical. It is likely that some practitioners caring for a patient with a deteriorating condition who is receiving escalating doses of vasopressors, in whom other core interventions have been instituted (i.e., appropriate antibiotics and adequate volume resuscitation and source control), will consider that the short-term benefits of low-dose hydrocortisone may exceed any risks (e.g., antiinflammatory effects) as an added therapy in selected patients.”

# Vasopressor Use for Adult Septic Shock

→ (with guidance for steroid administration)



\* Consider IV steroid administration  
 \*\* Administer IV steroids  
 \*\*\* SSC guidelines are silent on phenylephrine

- Notes:
- Consider dopamine as niche vasopressor in the presence of sinus bradycardia.
  - Consider phenylephrine when serious tachyarrhythmias occur with norepinephrine or epinephrine.
  - Evidence based medicine does not allow the firm establishment of upper dose ranges of norepinephrine, epinephrine and phenylephrine and the dose ranges expressed in this figure are based on the authors interpretation of the literature that does exist and personal preference/experience. Maximum doses in any individual patient should be considered based on physiologic response and side effects.

## Preliminary Communication

Caring for the Critically Ill Patient

October 1, 2019

**Effect of Vitamin C Infusion on Organ Failure and Biomarkers of Inflammation and Vascular Injury in Patients With Sepsis and Severe Acute Respiratory Failure**

The CITRIS-ALI Randomized Clinical Trial

## Preliminary Communication

Caring for the Critically Ill Patient

January 17, 2020

**Effect of Vitamin C, Hydrocortisone, and Thiamine vs Hydrocortisone Alone on Time Alive and Free of Vasopressor Support Among Patients With Septic Shock The VITAMINS Randomized Clinical Trial**

**At least 5 trials negative for primary endpoint. One single center study with faster shock resolution only (HAT). Still unclear benefit of Vitamin C.**

# JAMA

# Adjunctive Sepsis Care

- Tight Glucose Control<sup>2</sup>
  - Target glucose  $\leq 180$  mg/dl rather than tighter control.
- Low Tidal Volume Ventilation in ARDS<sup>3</sup>
- Judicious Fluid Management in Acute Lung Injury<sup>4</sup>
- Protocolized Central Line Insertion and Care and attention to ICU 'bundles' and prophylactic care<sup>5,6,7</sup>

<sup>1</sup>NEJM 2008;358:111; <sup>2</sup>NEJM 2009;360:1283; <sup>3</sup>NEJM 2000;342:1301;

<sup>4</sup>NEJM 2006;354:2564; <sup>5</sup>NEJM 2006;355:2725; <sup>6</sup>JAMA 2009;301:1231; <sup>7</sup>CCM 2016

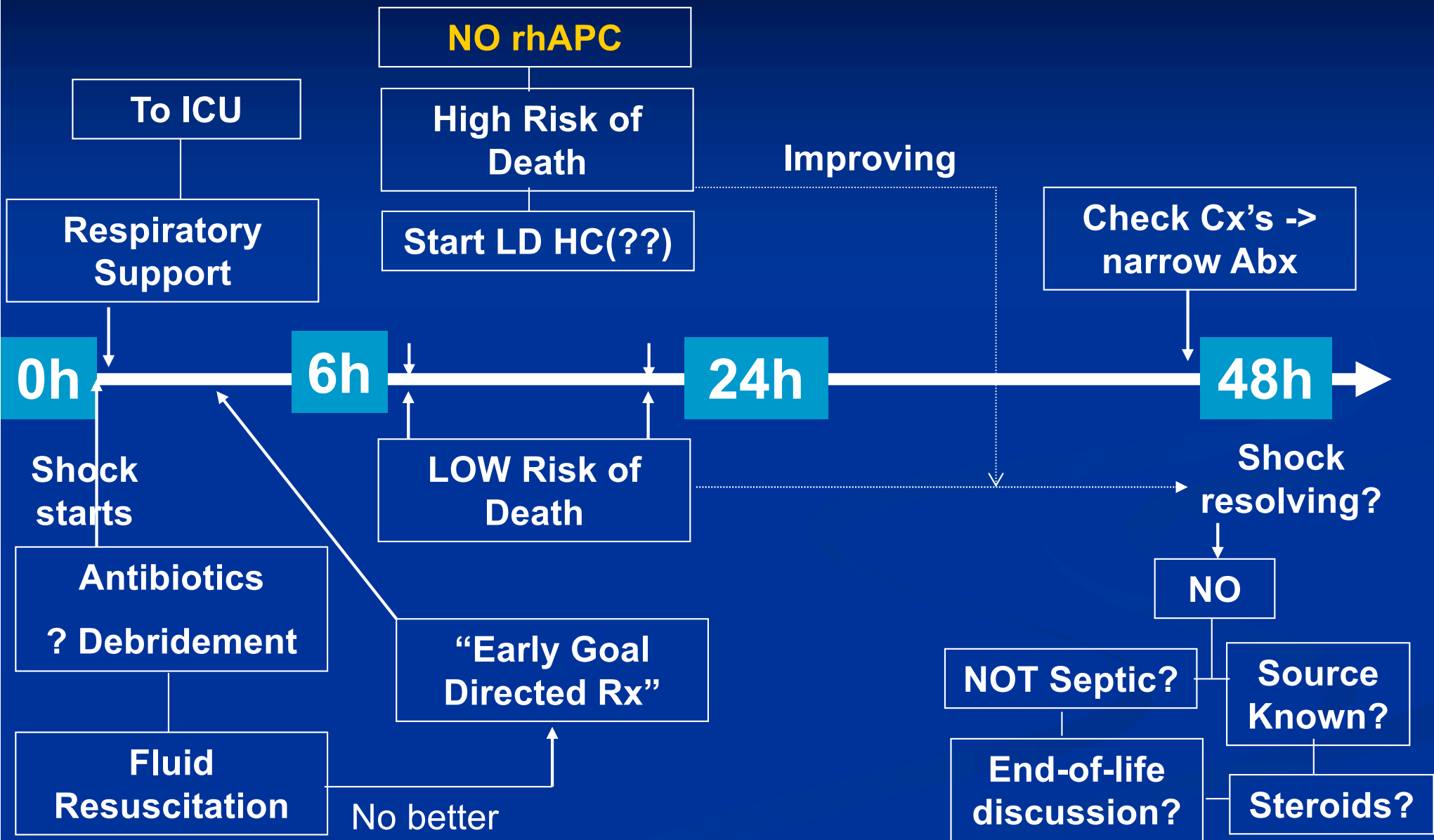
# Take-Home Points

- Early Identification of Patients with Sepsis\*
- Source Control and Early Broad-Spectrum Antibiotics
- Early fluid resuscitation, primarily with crystalloid (“Early Goal Directed Therapy” targeted fluids)
- Norepinephrine as First Pressor of Choice
- Consider Addition of Vasopressin to Norepinephrine
- Consider Epinephrine as 2<sup>nd</sup>-line Agent for Refractory Hypotension to Norepinephrine
- Limited role for Dopamine and Neosynephrine as initial agents of choice; Angiotensin II is new.

# Take-Home Points, Cont'd

- Activated Protein C is no longer available.
- Consider low-dose hydrocortisone for patients with sepsis-induced refractory hypotension despite fluids and pressors (without use of ACTH stim test to guide decision-making) – perhaps in the sicker patients.
- Uncertain goal of glucose control, but target  $\leq 180$  mg/dL (instead of tighter control) suggested until more data available. Hourly monitoring of glucose levels while on an insulin drip is critical, and avoid hypoglycemia.
- Attention to standard ICU care (e.g., ventilator bundle, DVT and GI prophylaxis, central line care, etc).

# Sepsis: Summary



# Selected Key References

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