I’m Shocked: Adjunctive Vasoactive Therapies in Septic Shock

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2023 ICHP ANNUAL MEETING

Disclosures

- SB: serves on the speaker's bureau for LaJolla Pharmaceutical Company. All relevant conflicts have been resolved.

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Objectives

1. Illustrate a classic presentation of septic shock.

2. Interpret hemodynamic variable alterations and compensatory mechanisms associated with septic shock.

3. Explain adjunctive therapies and considerations for use.

AUDIENCE ENGAGEMENT ACTIVITY #1

Framing of Outcomes in Septic Shock

Conceptualizing Septic Shock

- Sepsis = *sēpein*
- Shock = state in which there is failure of the circulatory system to maintain adequate cellular perfusion and/or oxygen delivery
- Three vital components
  - Arterial hypotension (absolute or relative)
  - Clinical signs of hypoperfusion
  - Abnormal cellular oxygen metabolism (hyperlactatemia)

N Eng J Med. 2013; 369:1726-1734.

Epidemiology of Septic Shock

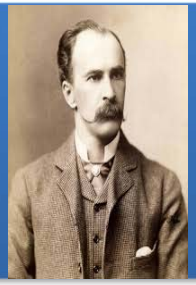
- > 750,000 cases of severe sepsis/septic shock annually
- Sepsis accounts for 6-30% ICU admissions
  - Severe sepsis/septic shock ~10%
  - Type of ICU dependent
- Morality is associated with progression within disease continuum
  - 600 deaths per day from severe sepsis/septic shock
- Mortality is time dependent
  - Significantly increases if undetected for > 6 hours

N Eng J Med. 2003; 348:1546
Crit Care Med. 2004; 32:2207

History of Septic Shock has evolved to implicate the host response

"…hectic fever, at its inception, is difficult to recognize but easy to treat; left unattended it becomes easy to recognize and difficult to treat."

Dr. William Osler



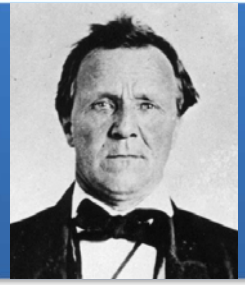
1513

1900

" Patients appear to die from the body's response rather than from the infection itself."

"They will invade and replicate if given the chance… but it is our response to their presence that makes the disease." -Germs

Dr. Lewis Thomas



1972

1991

ACCP/SCCM named condition	Defining criteria
SIRS	Core body temperature >38°C or <36°C HR ≥90 bpm Respirations ≥20/min (or $PaCO_2$ <32 mmHg) WBC ≥12,000/μl or ≤4000/μl 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

2002

Surviving Sepsis Campaign

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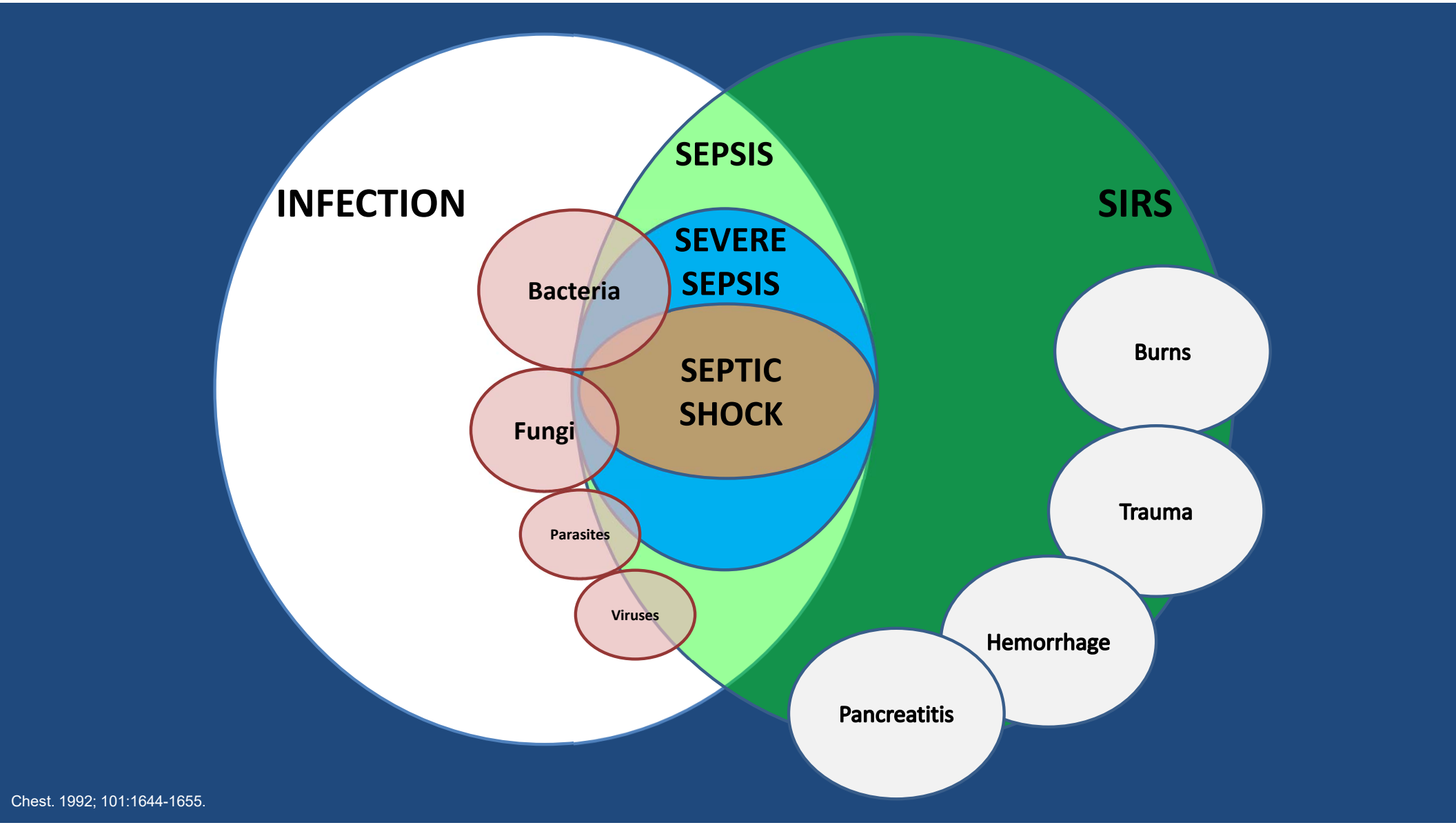
Expert Rev Anti Infect Ther. 2012;10:(6).



Chest. 1992; 101:1644-1655.

Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

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

ONLINE SPECIAL ARTICLE

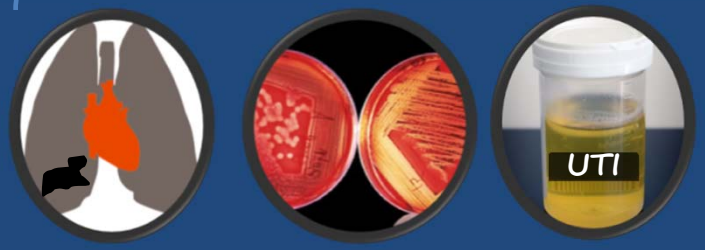
Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock 2021

KEY WORDS: adults; evidence-based medicine; guidelines; sepsis; septic shock

Laura Evans[1]
Andrew Rhodes[2]
Waleed Alhazzani[3]

Sepsis-3: Sepsis

INFECTION



+

CHANGE IN:

Sequential

Organ

Failure

Assessment

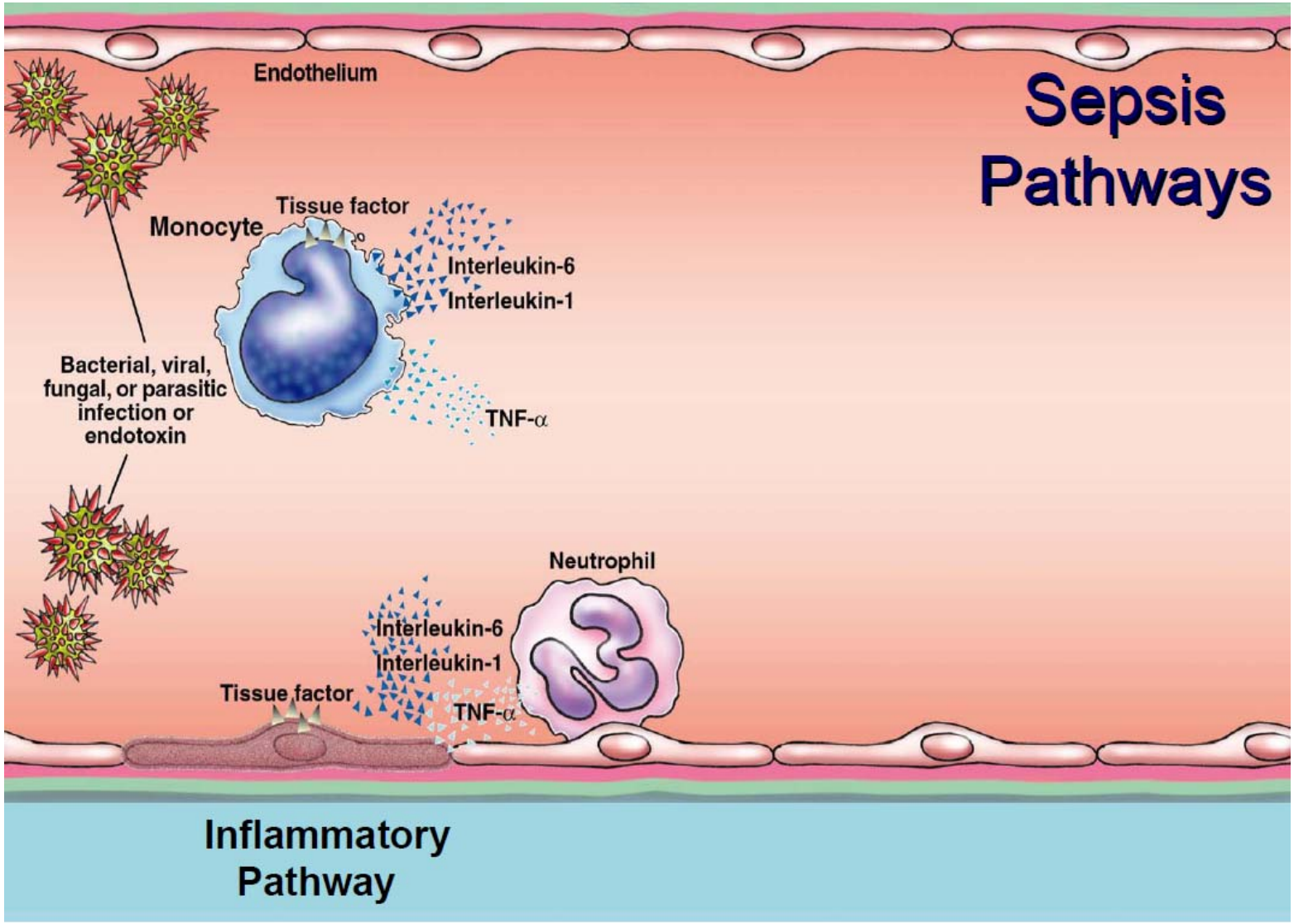
≥2

JAMA. 2016; 315(8): 801-810.

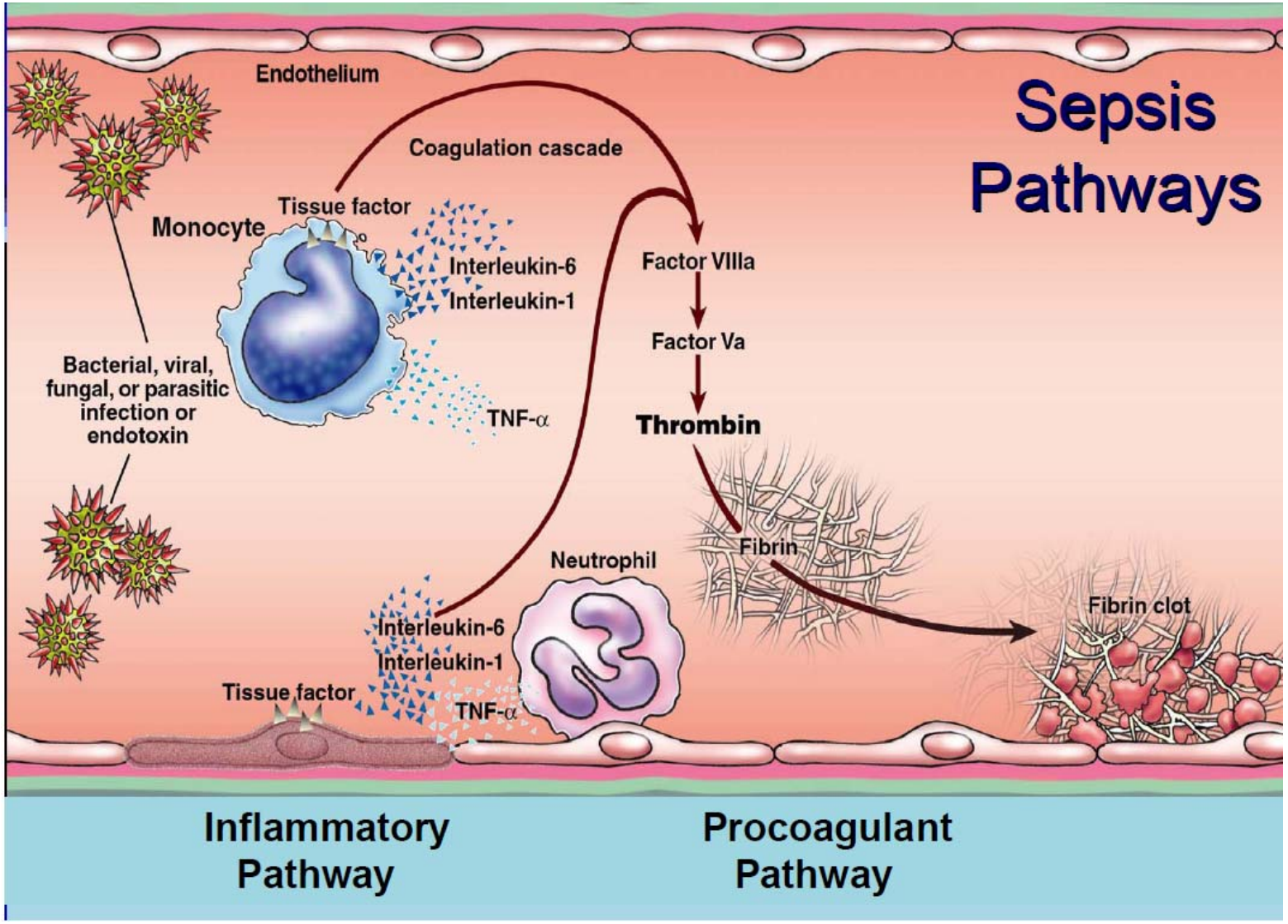
Pathophysiology

- Involves multiple interactions
  - Infecting microorganism
  - Host immune response
  - Inflammatory cascade
  - Procoagulant cascade
  - Anti-fibrinolysis cascade

N Eng J Med 2003;348:1546



Ann Pharmacother. 1995; 29: 892-905. N Engl J Med. 2008; 358: 1037-1052. N Engl J Med 2006; 355:1699-1713



Ann Pharmacother. 1995; 29: 892-905. N Engl J Med. 2008; 358: 1037-1052. N Engl J Med 2006; 355:1699-1713

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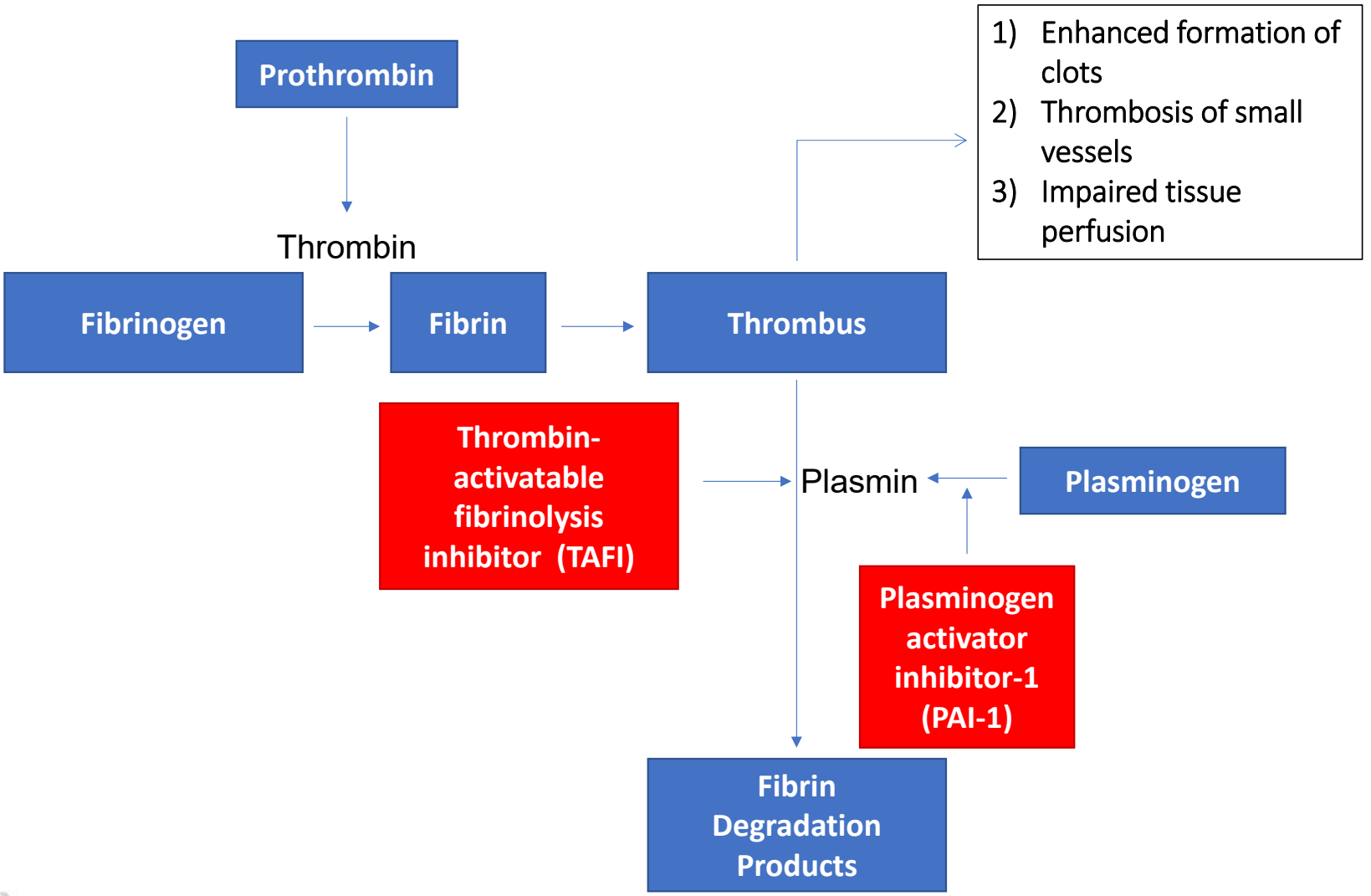
When poll is active respond at **PollEv.com/ichp3** Send **ichp3** to **22333**

1. The pathophysiology of septic shock requires the interaction of the infecting microorganism and the:

0

0%	0%	0%	0%
Host immune response	Environmental adaptive response	Host fibrinolytic cascade	Host anti-inflammatory cascade



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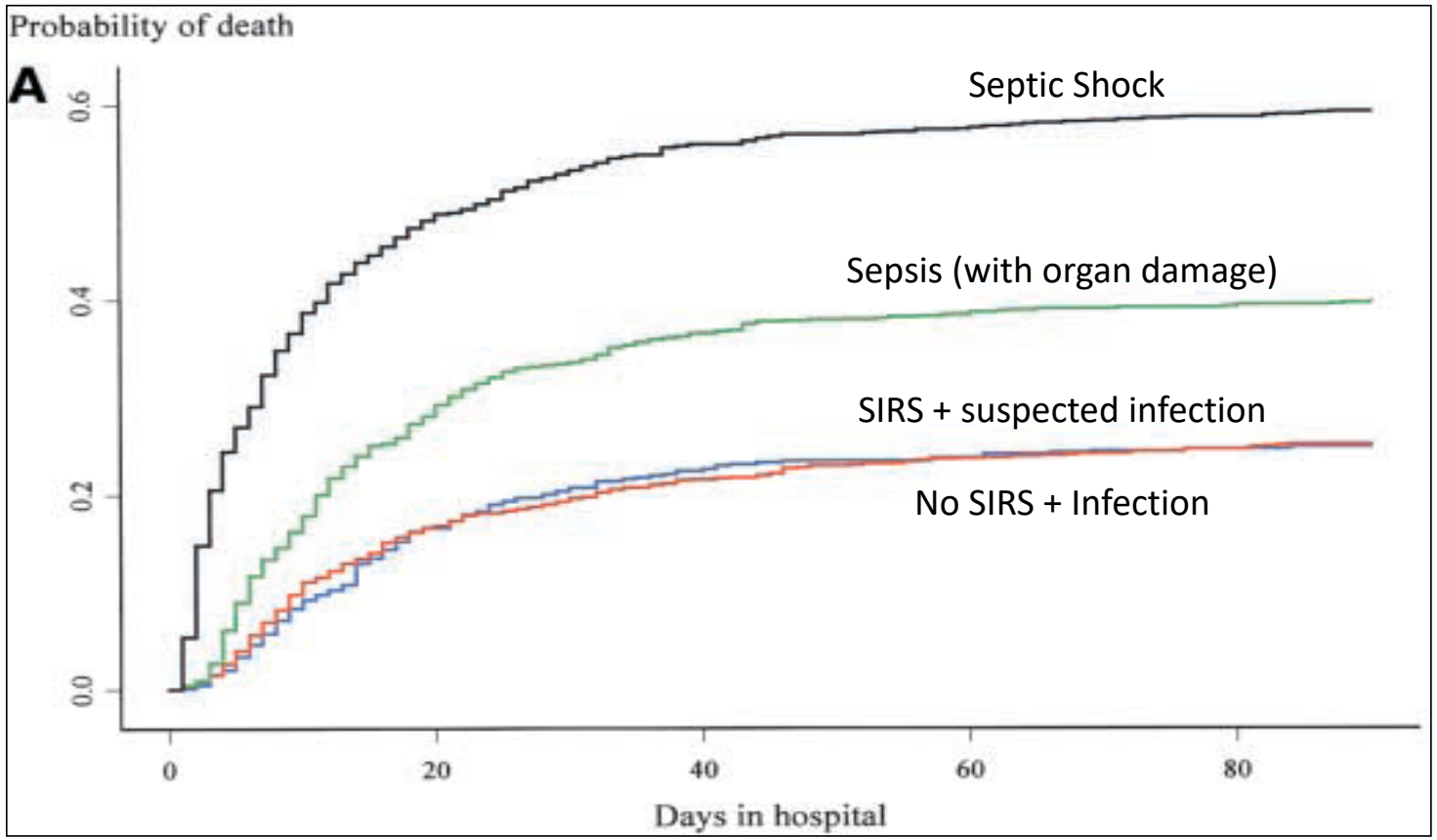
Ann Pharmacother. 1995; 29: 892-905. N Engl J Med. 2008; 358: 1037-1052. N Engl J Med 2006; 355:1699-1713

ORGAN	SEQUENTIAL ORGAN FAILURE ASSESSMENT SCORE				
	0	1	2	3	4
CV	MAP ≥ 70 mmHg	MAP < 70 mmHg	DA < 5 or DB	DA 5.1-15 or EPI/NE ≤ 0.1	DA > 15 or EPI/NE > 0.1
RESP (PaO_2:FiO_2)	≥400 mmHg	< 400 mmHg	< 300 mmHg	< 200 mmHg w/ support	< 100 mmHg w/ support
RENAL -SCr -UOP	< 1.2 mg/dL	1.2-1.9 mg/dL	2-3.4 mg/dL	3.5-4.9 mg/dL < 500 mL/24hr	> 5 mg/dL < 200 mL/24hr
HEPATIC	< 1.2 mg/dL	1.2-1.9 mg/dL	2-5.9 mg/dL	6-11.9 mg/dL	> 12 mg/dL
COAG (Plt x 10^3)	≥ 150 /mcL	< 150 / mcL	< 100 /mcL	< 50 / mcL	< 20 /mcL
CNS (GCS)	15	13-14	10-12	6-9	< 6

JAMA. 2016; 315(8): 801-810.

Disease Continuum vs. Mortality

Probability of Death in the Sepsis Continuum



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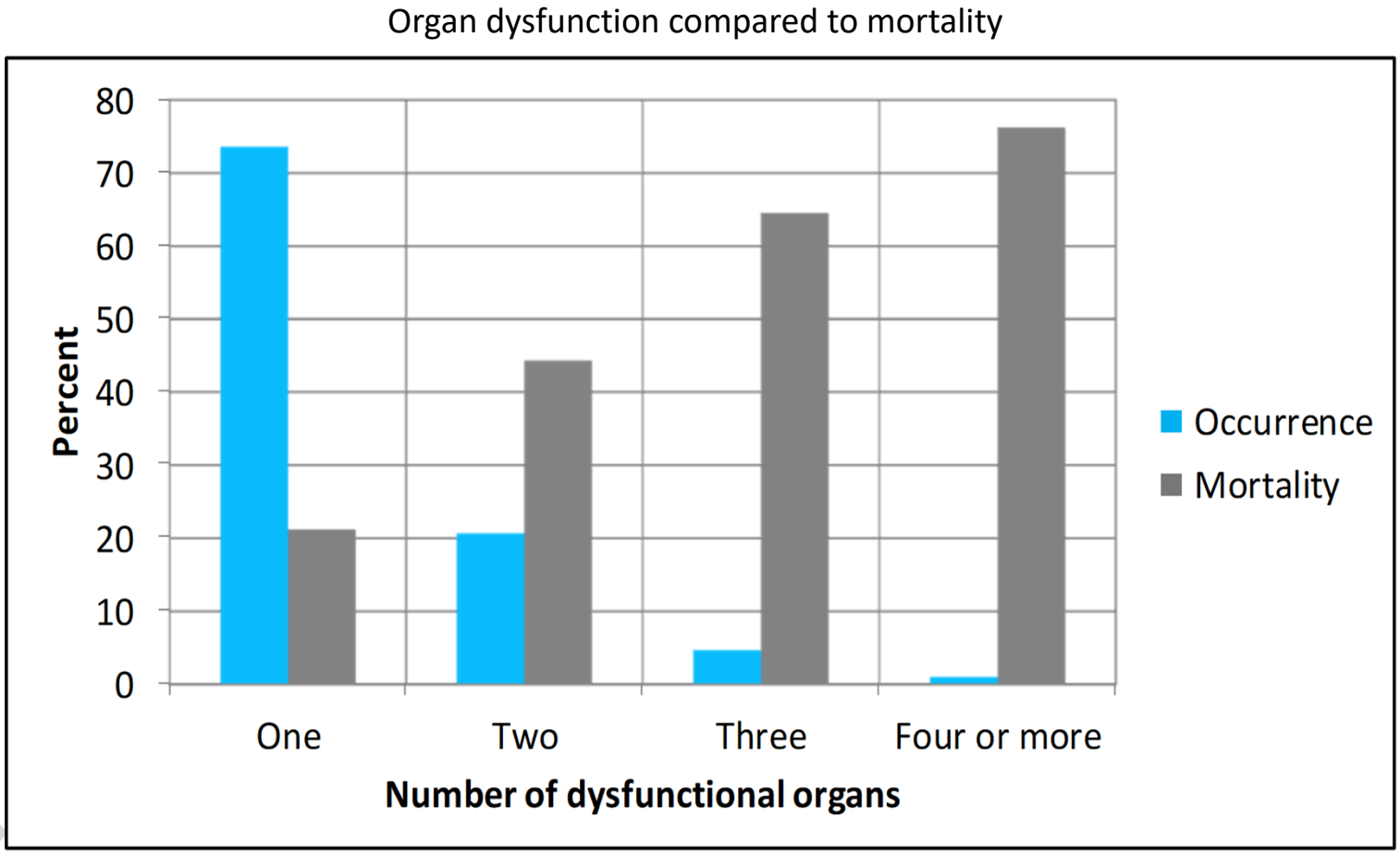
Am J Resp Crit Care Med 2003;168:77.

Organ Dysfunction vs. Mortality



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Crit Care Med 2001; 29: 1303.

Audience Response Question
Case A

HPI: Patient is a 72 y/o M who is POD4 from a planned admission for extensive abdominal surgery (abdominal exenteration with ileal conduit) and POD1 pelvic reconstruction. The nurse is calling the team to report fever and that his urine output has dropped to 0.3 mL/kg/hr.

PMH:

- **Colon cancer s/p resection, chemotherapy, and radiation (2010)**
- **HTN**
- **HLD**
- **Stroke (2000, 2011)**
- **L hemiparesis**
- **Hypothyroidism**
- **IDDM**

Allergies: NKDA

Anthropometrics: Weight 95kg

Vital Signs:

Temperature: 39.2◦C (max 39.5◦C)

HR: 135 beats/min

RR: 38 breaths/min

BP: 87/51 mmHg

Labs:

139 | 109 | 40 / 120

3.7 | 23 | 1.69 (baseline 0.4)

20 \ 8.2 / 90

/ 23.9

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Moderate | Visual settings | Edit

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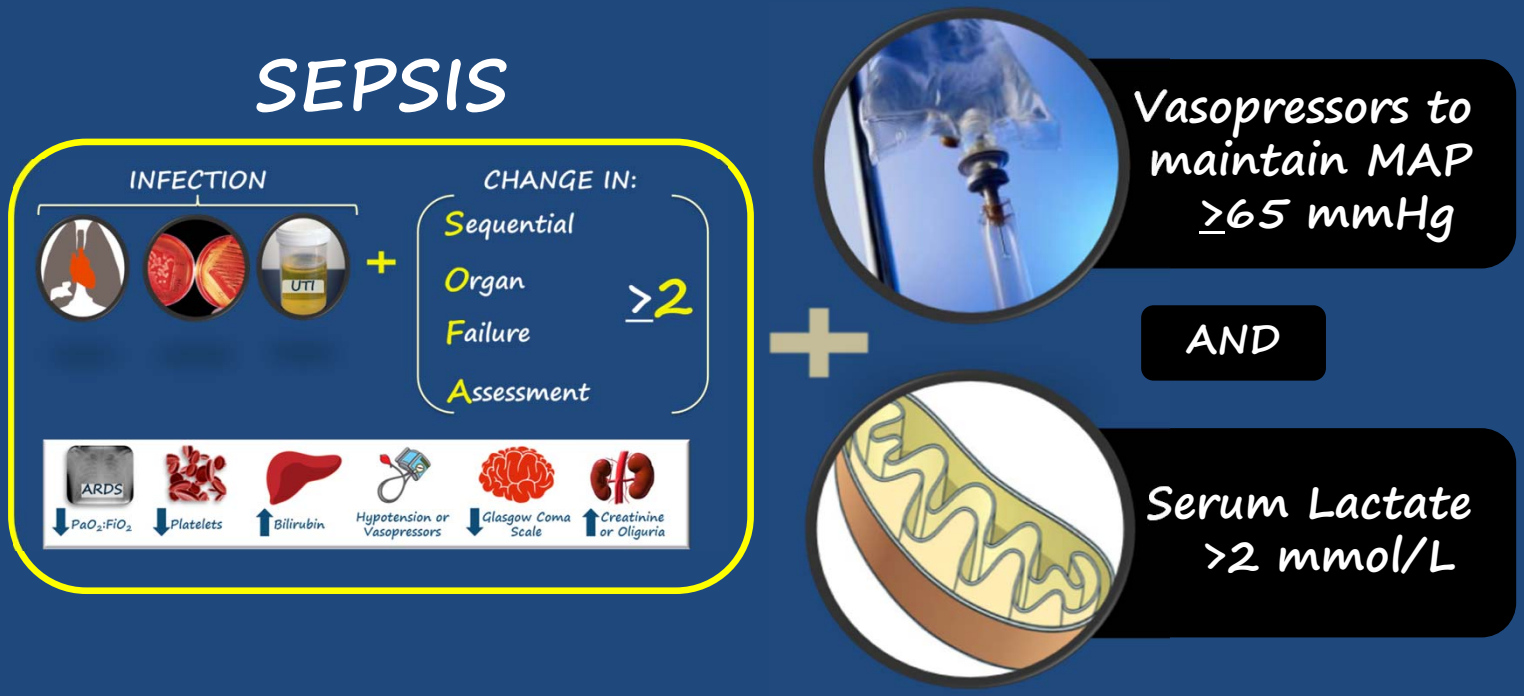
What part of this patient case raises the suspicion of sepsis?

0

Nobody has responded yet.

Hang tight! Responses are coming in.

Sepsis-3: Septic Shock



JAMA. 2016; 315(8): 801-810.

Shock States

Cardiogenic:

Acute myocardial infarction
End-stage cardiomyopathy
Advanced valvular heart disease
Myocarditis
Acute arrhythmias

Hypovolemic:

Internal or external blood loss

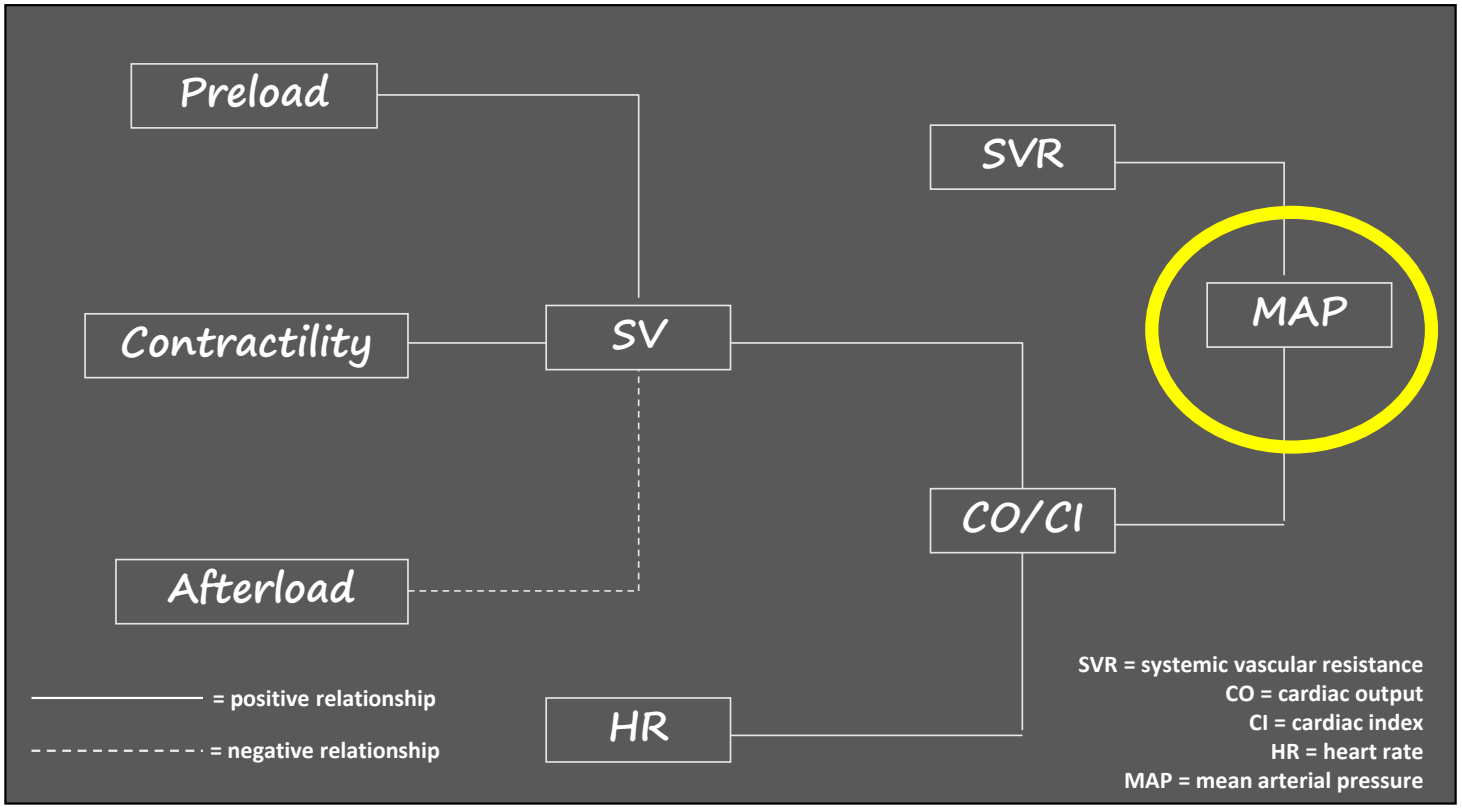
Obstructive:

Pulmonary embolism
Cardiac tamponade
Tension pneumothorax

Distributive:

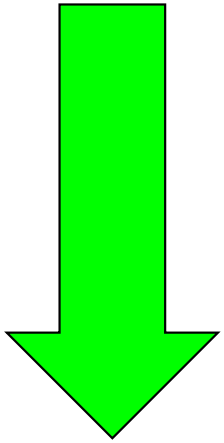
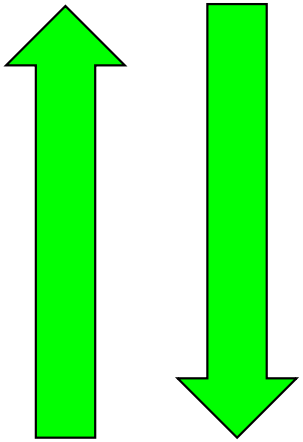
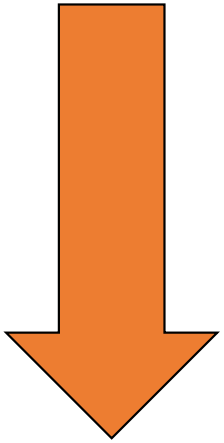
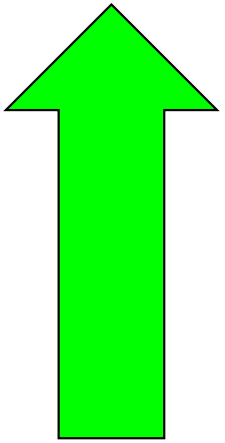
Anaphylaxis
Neurogenic
SEPTIC SHOCK

Global Hemodynamic Interactions



N Eng J Med 1974; 290: 1124.-1129.

Hemodynamic Compensation

Preload (CVP, PAOP)*	CO	SVR	HR
	EARLY LATE 		

*Relative hypovolemia due to increase in the "tank" size (massive vasodilation)

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2. The underlying hemodynamic dysfunction in septic shock primarily involves:

0

Cardiac output	Contractility	Systemic vascular resistance	Heart rate
0%	0%	0%	0%

Audience Response Question
Case B

HPI:

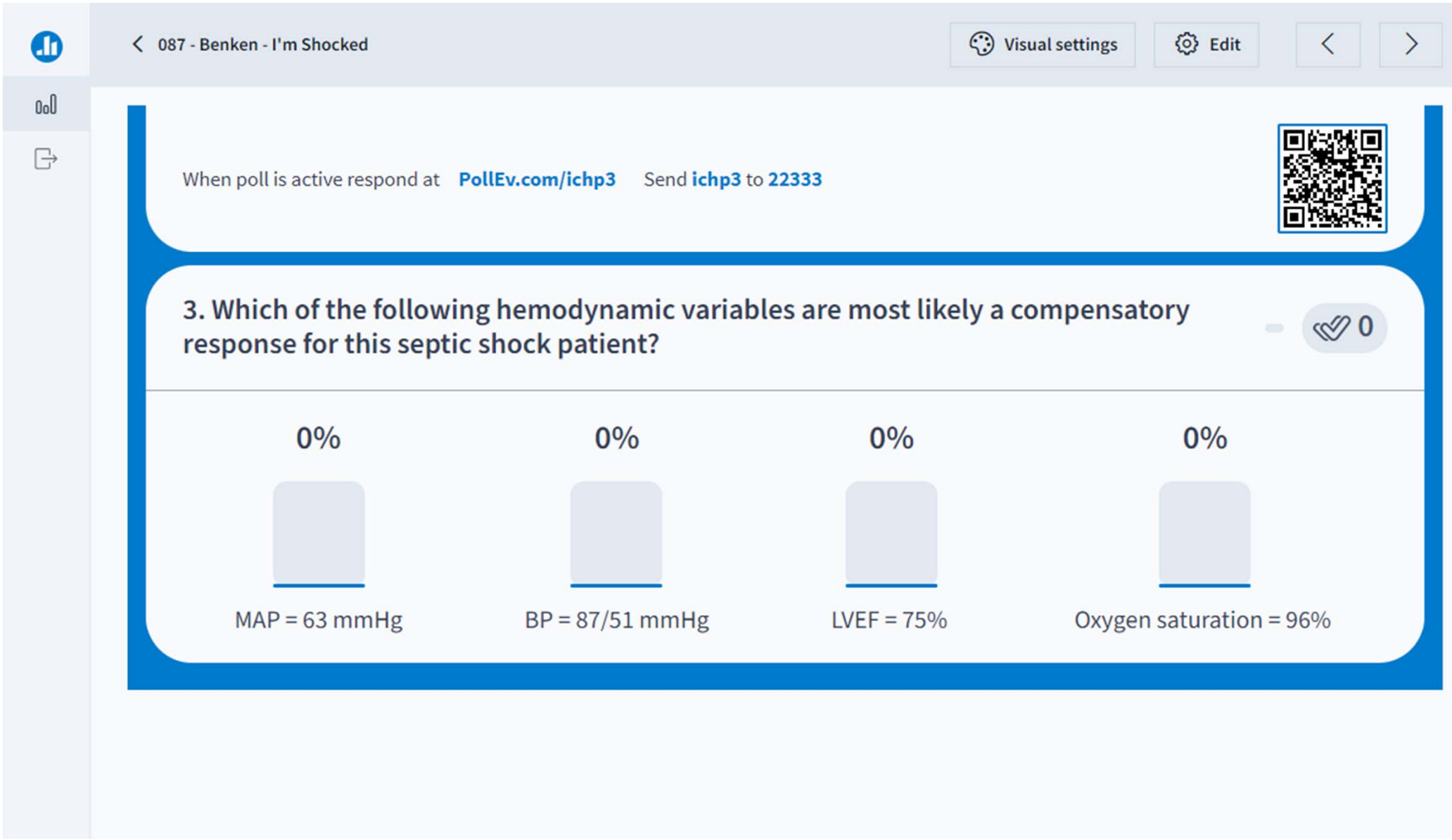
Patient is a 72 y/o M who is POD4 from a planned admission for extensive abdominal surgery (abdominal exenteration with ileal conduit) and POD1 pelvic reconstruction. The nurse is calling the team to report fever and that his urine output has dropped to 0.3 mL/kg/hr.

Diagnostics:
TTE demonstrating LVEF 75%

Arterial Line:
MAP 63 mmHg
HR: 135 beats/min

Cuff blood pressure:
BP: 87/51 mmHg

Pulse oximeter:
SpO2 = 96%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When poll is active respond at PollEv.com/ichp3 Send ichp3 to 22333
3. Which of the following hemodynamic variables are most likely a compensatory response for this septic shock patient?
0
0%
0%
0%
0%
MAP = 63 mmHg
BP = 87/51 mmHg
LVEF = 75%
Oxygen saturation = 96%

Treatment of Septic Shock

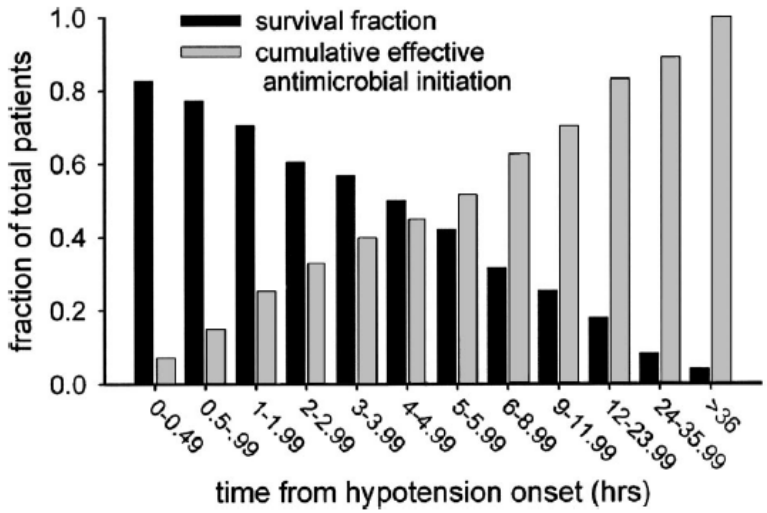
Antimicrobial Therapy

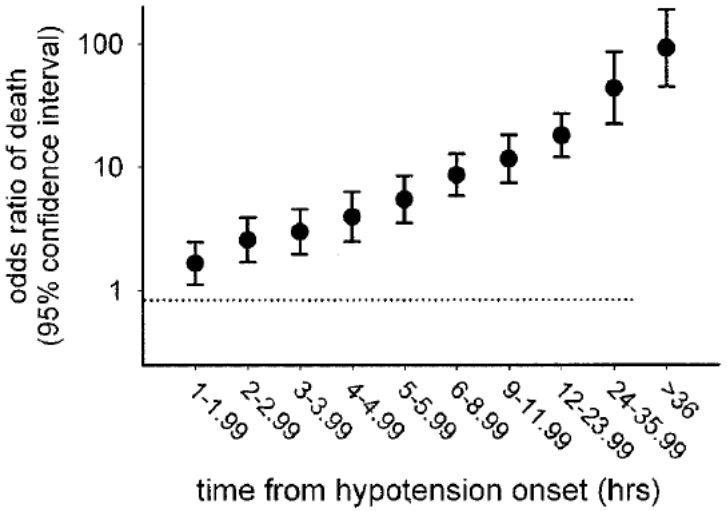
EARLY GOAL DIRECTED THERAPY

Adjunctive Therapy

Antibiotic therapy

- Goal:
  - Administration of **effective** antibiotics within the **first hour** of recognition





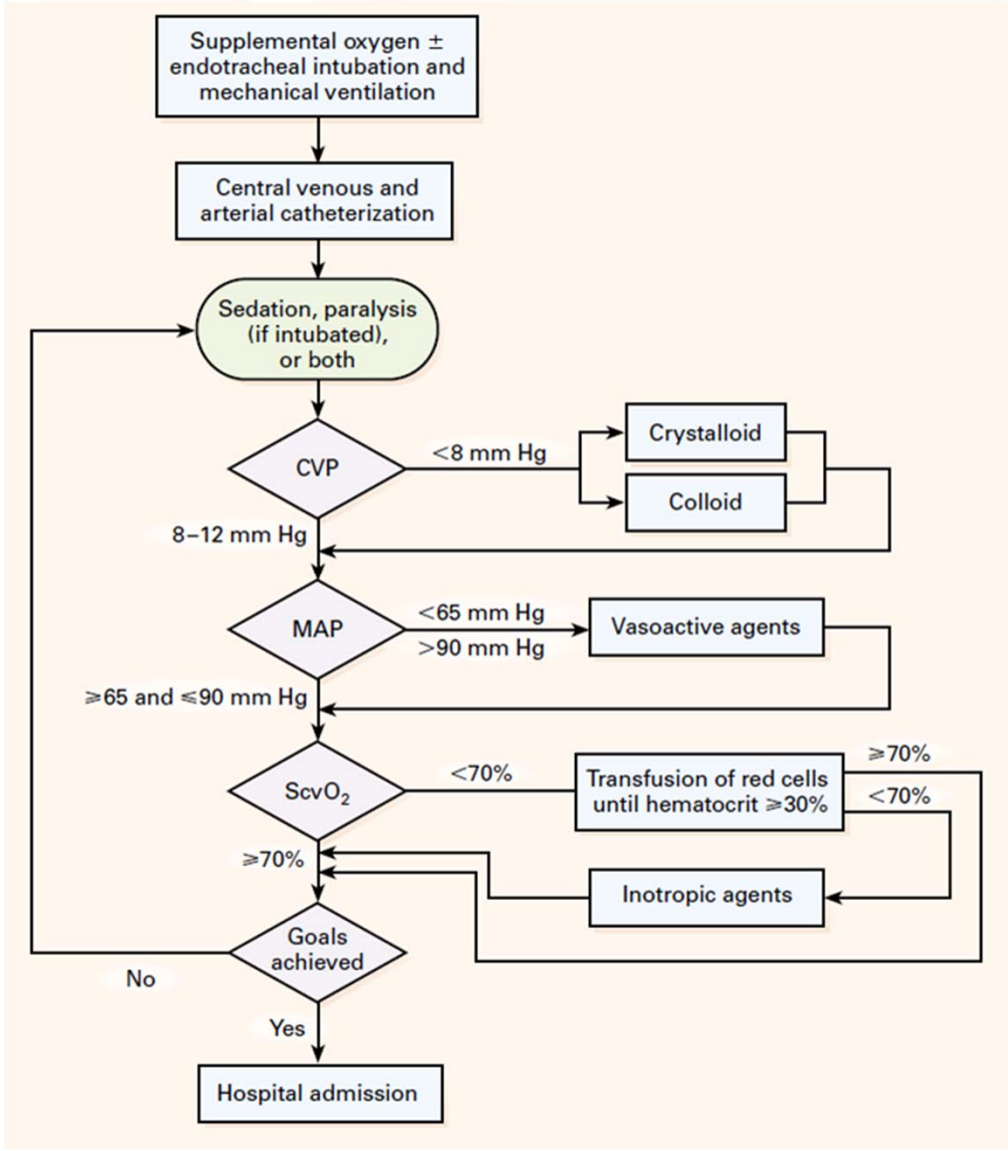
Critical Care Med 2006; 34(6) 1589-1596

Antibiotic therapy

- Additional considerations:
  - Activity against likely pathogens
  - Penetrate adequately to presumed tissues

- *Source control*
  - Rapidly identify sources
  - Intervene to control source as soon as feasible (ideally within 12 hours)
    - Exception – peripancreatic necrosis
  - Consider hemodynamic instability
    - Least physiologic insult (eg. percutaneous interventions vs. surgical)
  - Removal of infected devices as able

Critical Care Med 2006; 34(6) 1589-1596



N Eng J Med. 2001; 345: 1368.

EARLY GOAL DIRECTED THERAPY

Fluid Resuscitation

- Crystalloids first line
  - 30 mL/kg as **initial** intravenous bolus over minutes
  - Within the **first 3 hours** of diagnosis
  - Balanced crystalloids instead of normal saline for resuscitation (weak recommendation)

- Followed with “hemodynamic” techniques
  - Non-invasive
  - Invasive

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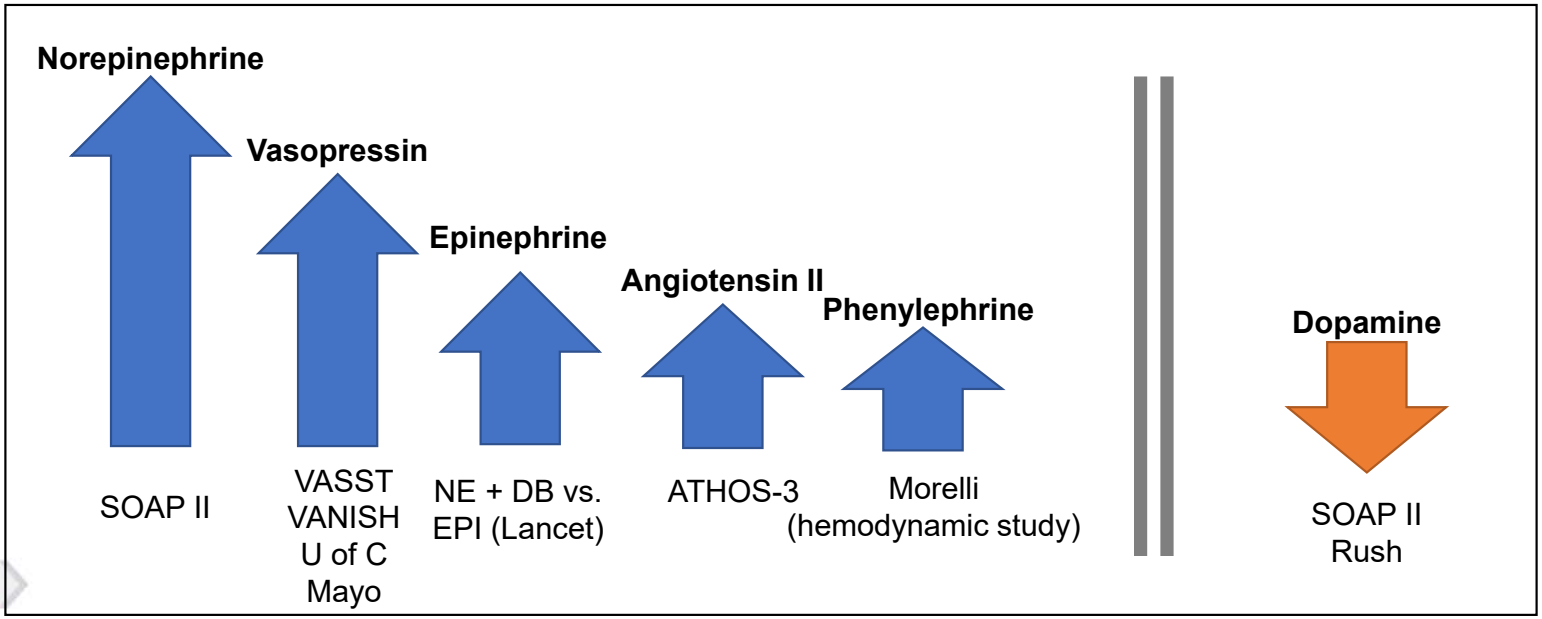
Crit Care Med 2013; 41(2): 580-637.
Intensive Care Med 2021; 47: 1181–1247

EARLY GOAL DIRECTED THERAPY

Vasopressors

- Fluid refractory
- Goal:
  - MAP ≥ 65 mmHg
  - **Should be individualized: "normal" BP and comorbidities**

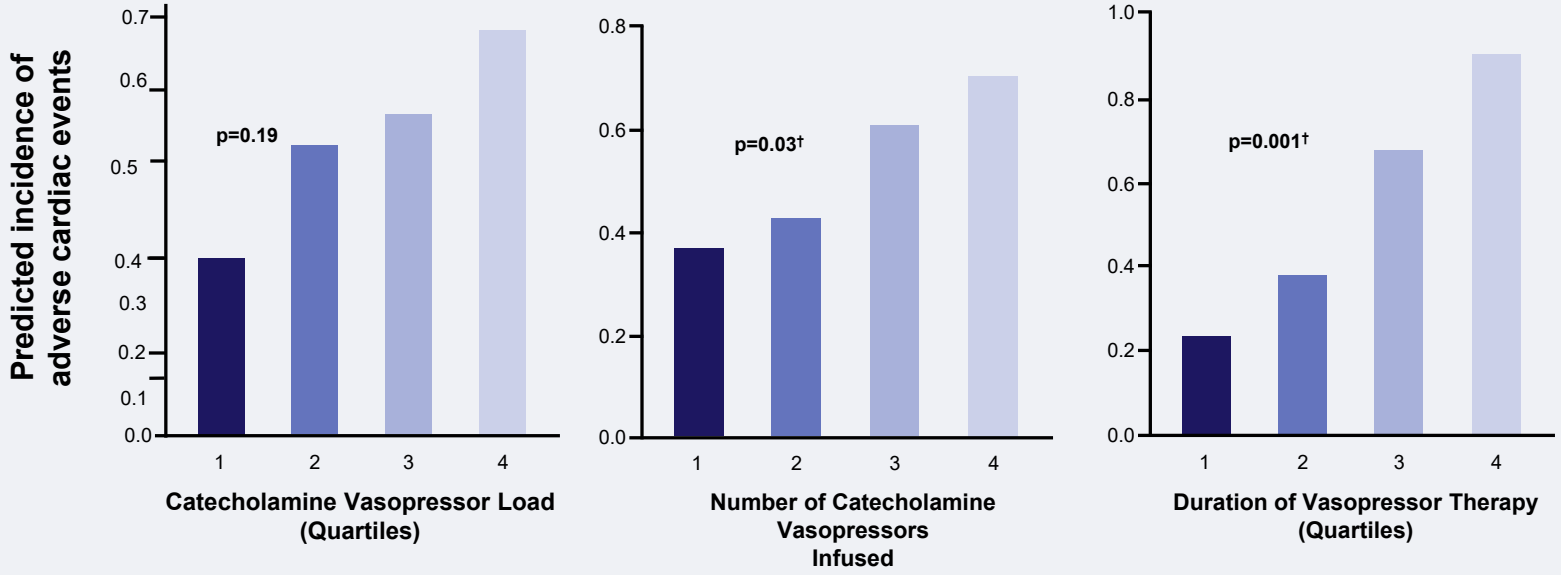


Crit Care Med 2013; 41(2): 580-637

EARLY GOAL DIRECTED THERAPY

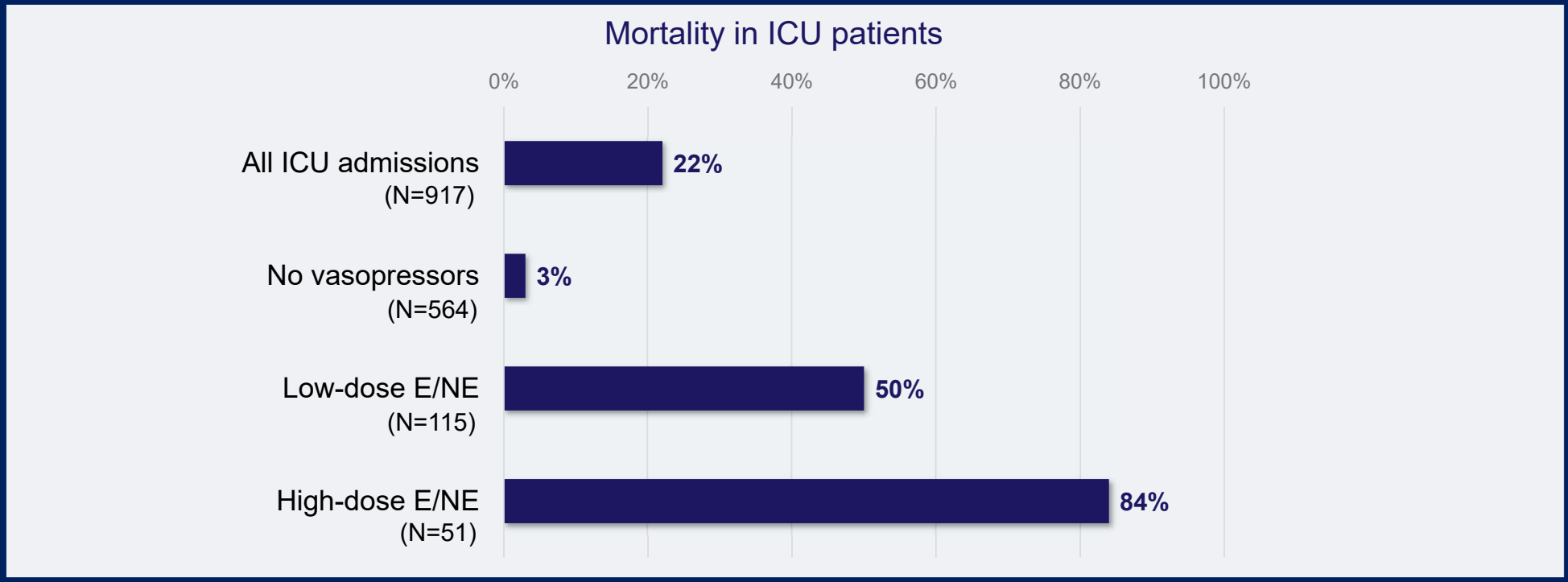
Catecholamine Vasopressor Therapy & AE's

- In a prospective observational study of 112 SICU patients, catecholamine vasopressor therapy* was associated with greater adverse event rates
- 48.2% experienced cardiac AEs during catecholamine vasopressor therapy
  - Number of agents infused and duration of therapy independently associated with cardiac AEs‡
  - Cardiac AEs associated with greater morbidity and mortality



*Epinephrine, NE, dopamine, and phenylephrine. †Independent association with the occurrence of cardiac AEs
‡ New-onset tachyarrhythmia [49.1%], prolonged elevated heart rate [23.7%], myocardial cell damage [17.5%]
SICU=surgical intensive care unit; AE=adverse event, NE=Norepinephrine.
Intensive Care Med. 2012;38:950-958.

Catecholamine Vasopressor Therapy & Mortality



In patients treated with high-dose catecholamines at any time during their ICU stay, the odds ratio of mortality was 5.1 (CI, 2.02–12.9; p=0.001)

E/NE=epinephrine/norepinephrine; CI=confidence interval.

J Crit Care. 2014;29:157-160.

Adjunctive Therapy

- Steroids
- “Fruit Cocktail”
- Blood product administration (goal Hgb > 7 g/dL)
- Mechanical ventilation in ARDS
- Sedation, analgesia, and paralysis
- Glucose control (<180mg/dL)
- Renal replacement therapy
- DVT prophylaxis and SUP
- Nutrition
- Goals of care

Crit Care Med 2013; 41(2): 580-637

AUDIENCE ENGAGEMENT ACTIVITY #2

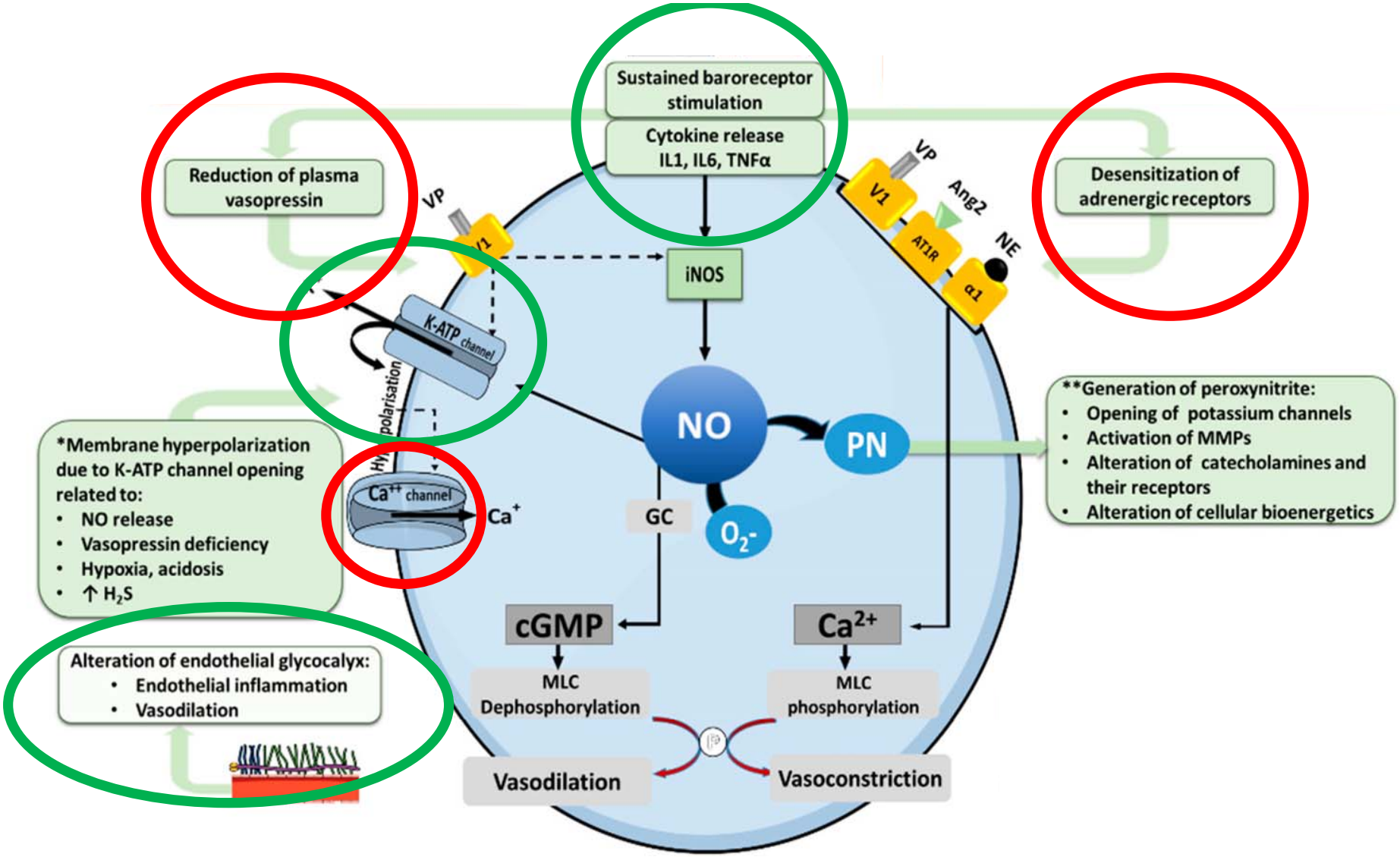
RE-framing of Outcomes in Septic Shock

Inadequate or Ineffective Natural Vasoconstrictive Response

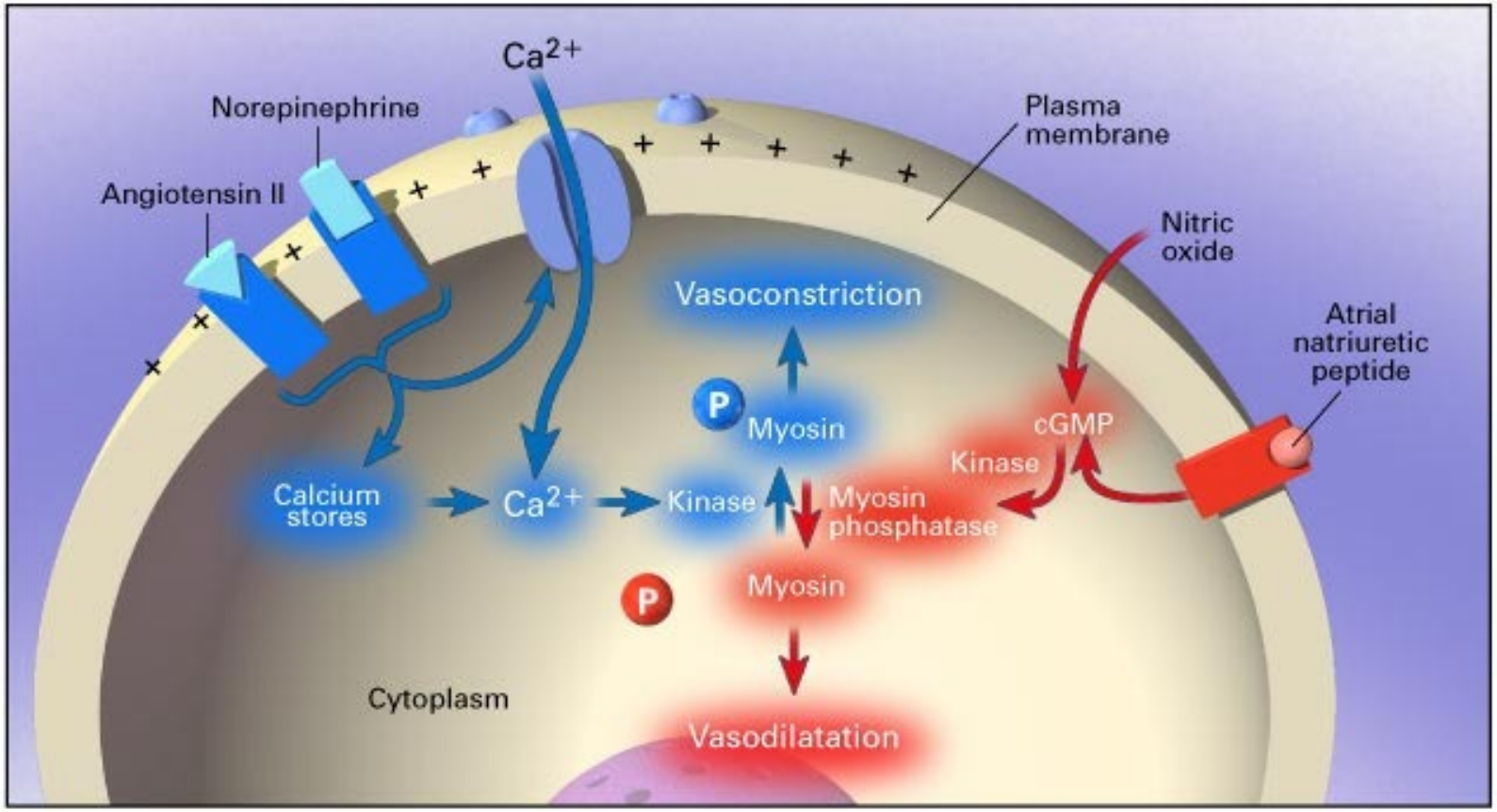
- Peripheral levels of catecholamines are dramatically increased but **decreased responsiveness to natural vasoconstrictors**
- Evidence of activation of the renin–angiotensin system - **? inconsistent interpatient response**.
- **Deficiency in vasopressin** - Vasopressin is a nonapeptide potent vasopressor hormone released by the posterior pituitary gland in response to hypotension

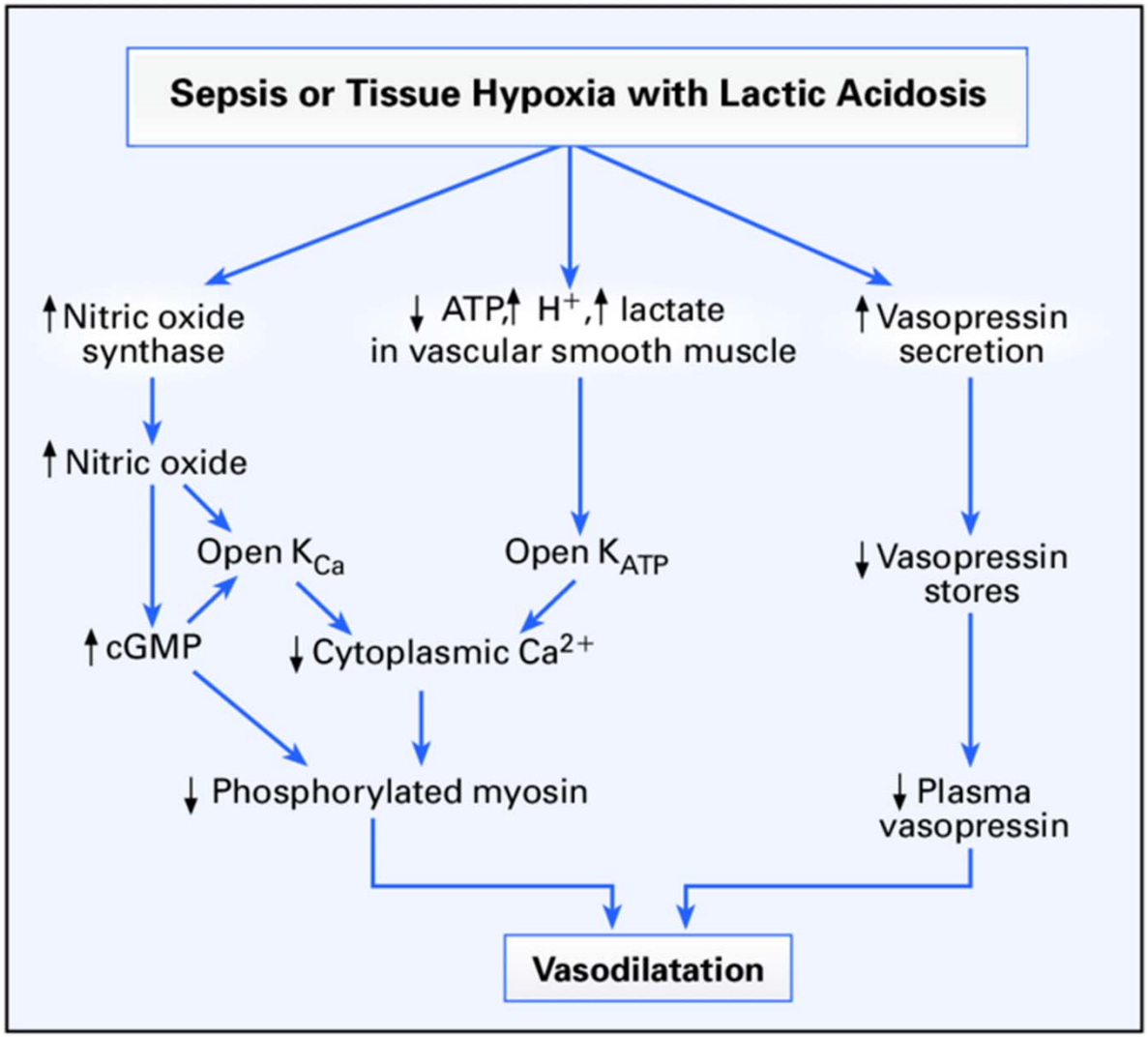
Induced Vasodilatory Response

- Nitric oxide (NO)
- Prostacyclin synthesis
- Adrenomedullin
- Activation of the transient receptor potential vanilloid type 4 (TRPV4)



Journal of Clinical Medicine. 2022; 11(21):6407


Ca2+
Norepinephrine
Angiotensin II
Plasma membrane
Nitric oxide
Vasoconstriction
Atrial natriuretic peptide
P
Myosin
cGMP
Kinase
Calcium stores
Ca2+
Kinase
Myosin phosphatase
P
Myosin
Cytoplasm
Vasodilatation


Sepsis or Tissue Hypoxia with Lactic Acidosis
↑ Nitric oxide synthase
↓ ATP, ↑ H+, ↑ lactate in vascular smooth muscle
↑ Vasopressin secretion
↑ Nitric oxide
Open KCa
Open KATP
↓ Vasopressin stores
↑ cGMP
↓ Cytoplasmic Ca2+
↓ Phosphorylated myosin
↓ Plasma vasopressin
Vasodilatation

Proposed Adjunctive Therapies

- Ascorbic Acid (Vitamin C)
- Hydroxocobalamin (Cyanokit)
- Methylene Blue (ProvayBlue)
- **Goals of these therapies?**

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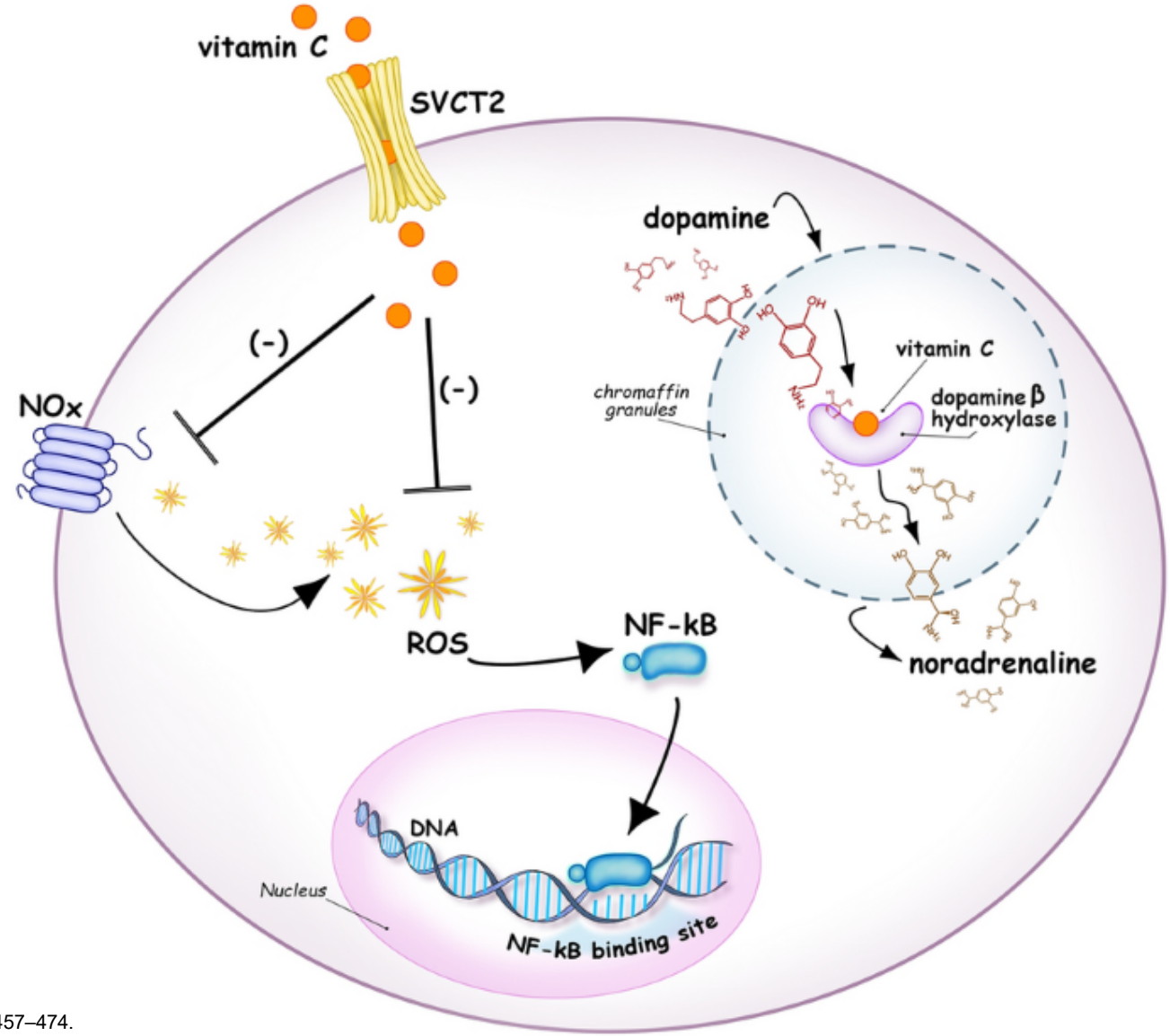
Ascorbic Acid (Vitamin C)

Proposed benefit

- Cofactor in the biosynthesis of cortisol, norepinephrine (restoring receptor sensitivity)
- Critically ill patients are at risk of low plasma ascorbic acid due to decreased intake, absorption, and acutely increased metabolism
- Clinical studies have investigated its use in septic shock among various ICU populations



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Nutr Clin Pract 2016; 31:457–474.

ANIMAL MODEL OF SEPSIS

Exogenous vitamin C increases perfused capillary density and arteriolar vasoconstrictor responsiveness

Free Radic Biol Med 2004, 37(8):1282–1289

EARLY EXCITEMENT – MARIK HAT STUDY

Before–after study assessing the combination of IV vitamin C (1.5 g every 6 h), hydrocortisone (50mg every 6 h), and thiamine (200mg every 12 h) in 94 patients with severe sepsis or septic shock

Hospital mortality
-4 (8.5%) vs. 19 (40.4%) – $p < 0.001$

-Duration of pressors
-18.3 ± 9.8 vs. 54.9 ± 28.4 – $p < 0.001$

-RRT for AKI3
-3/31 (10%) vs. 11/30 (33%) – $p = 0.02$

Chest. 2017; 151(6):1229–1238

ATESS STUDY

Prospective RCT to evaluate effect of Vitamin C (50mg/kg q12hr) and Thiamine (200mg q12hr) on organ function in first 72 hours (SOFA score) and outcomes of shock reversal and mortality

111 of 116 randomized patients were included in the analysis

Delta SOFA score
-3 (1 to 5) vs. 3 (0–4) - p = 0.96

7-day, 28-day, and 90-day mortality,
-9.4% vs. 10.3%, p = 0.87
-20.8% vs. 15.5%, p = 0.47
-32.1% vs. 27.6%, p = 0.61

No differences in RRT for AKI, mechanical ventilation free days, shock reversal, vasopressor free days (p > 0.05)

Intensive Care Med. 2020 Nov;46(11):2015-2025

VITAMINS STUDY

Effect of Vitamin C, Hydrocortisone, and Thiamine vs Hydrocortisone Alone on Time Alive and Free of Vasopressor Support Among Patients With Septic Shock

216 patients – IV vitamin C (1.5 g every 6 hours), hydrocortisone (50mg every 6 hours), and thiamine (200mg every 12 hours) vs. IV hydrocortisone (50mg every 6 hours) alone until shock resolution or up to 10 days.

Alive and vasopressor free at 7 days
- 122.1 hours (76.3-145.4) vs.124.6 hours (82.1-147) (95%CI, –8.3 to 7.2 hours; p = 0.83).

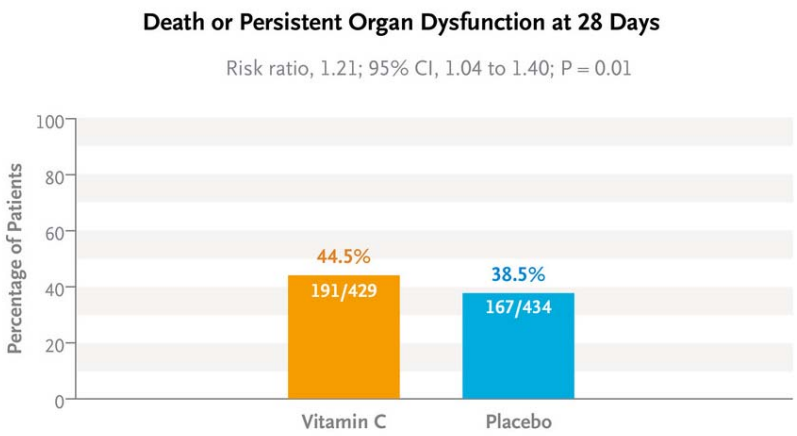
Change in SOFA score at 3 days
– 2 (–4 to 0) vs. –1 (–3 to 0), p = 0.02

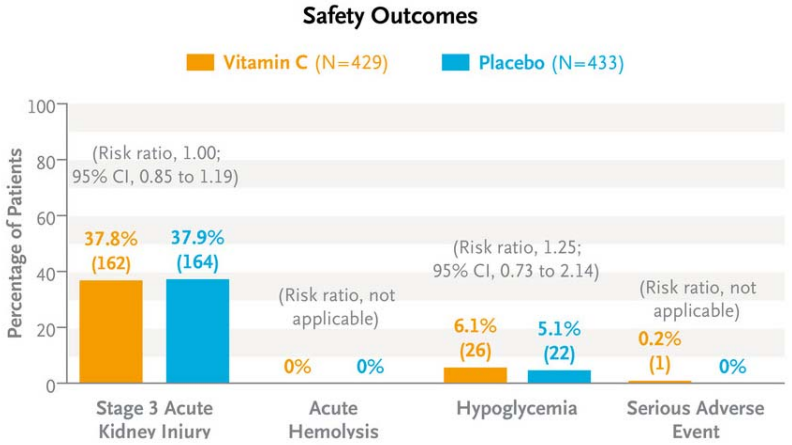
No difference in mortality, mechanical ventilation free days, RRT for AKI free days, ICU LOS, mortality (p > 0.05)

JAMA. 2020;323(5):423-431.

LOVIT Trial: Intravenous Vitamin C in Adults with Sepsis in the Intensive Care Unit

- RCT infection + vasopressor within 24 hours of diagnosis
- Infusion of either ascorbic acid (50 mg/kg) or matched placebo administered every 6 hours for up to 96 hours



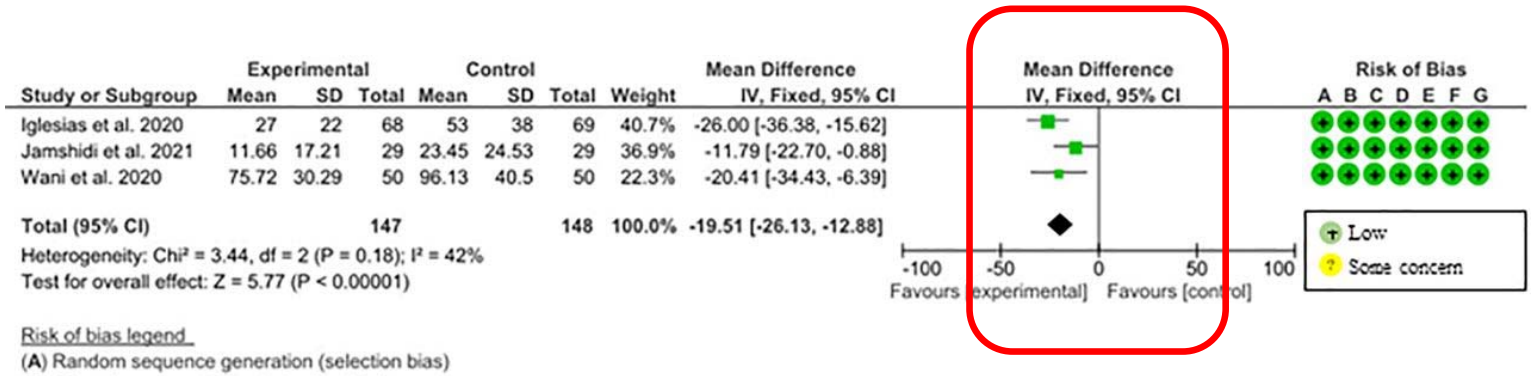


N Engl J Med 2022; 386:2387-2398

Meta analysis

- Nine RCTs were identified and included in the outcome evaluation.

- HAT therapy did not improve the 28-day and ICU mortality, new-onset AKI, ICU-LOS, or SOFA scores.



Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Fixed, 95% CI
Iglesias et al. 2020	27	22	68	53	38	69	40.7%	-26.00 [-36.38, -15.62]
Jamshidi et al. 2021	11.66	17.21	29	23.45	24.53	29	36.9%	-11.79 [-22.70, -0.88]
Wani et al. 2020	75.72	30.29	50	96.13	40.5	50	22.3%	-20.41 [-34.43, -6.39]
Total (95% CI)			147			148	100.0%	-19.51 [-26.13, -12.88]

Heterogeneity: Chi² = 3.44, df = 2 (P = 0.18); I² = 42%
Test for overall effect: Z = 5.77 (P < 0.00001)

Risk of bias legend
(A) Random sequence generation (selection bias)
(B) Allocation concealment (selection bias)
(C) Blinding of participants and personnel (performance bias)
(D) Blinding of outcome assessment (detection bias)
(E) Incomplete outcome data (attrition bias)
(F) Selective reporting (reporting bias)
(G) Other bias

In Vivo. 2023 May-Jun;37(3):1236-1245.

Ascorbic Acid Takeaways

- No improvement in mortality
- Inconsistent results surrounding organ function
- Potential impact on vasopressor duration

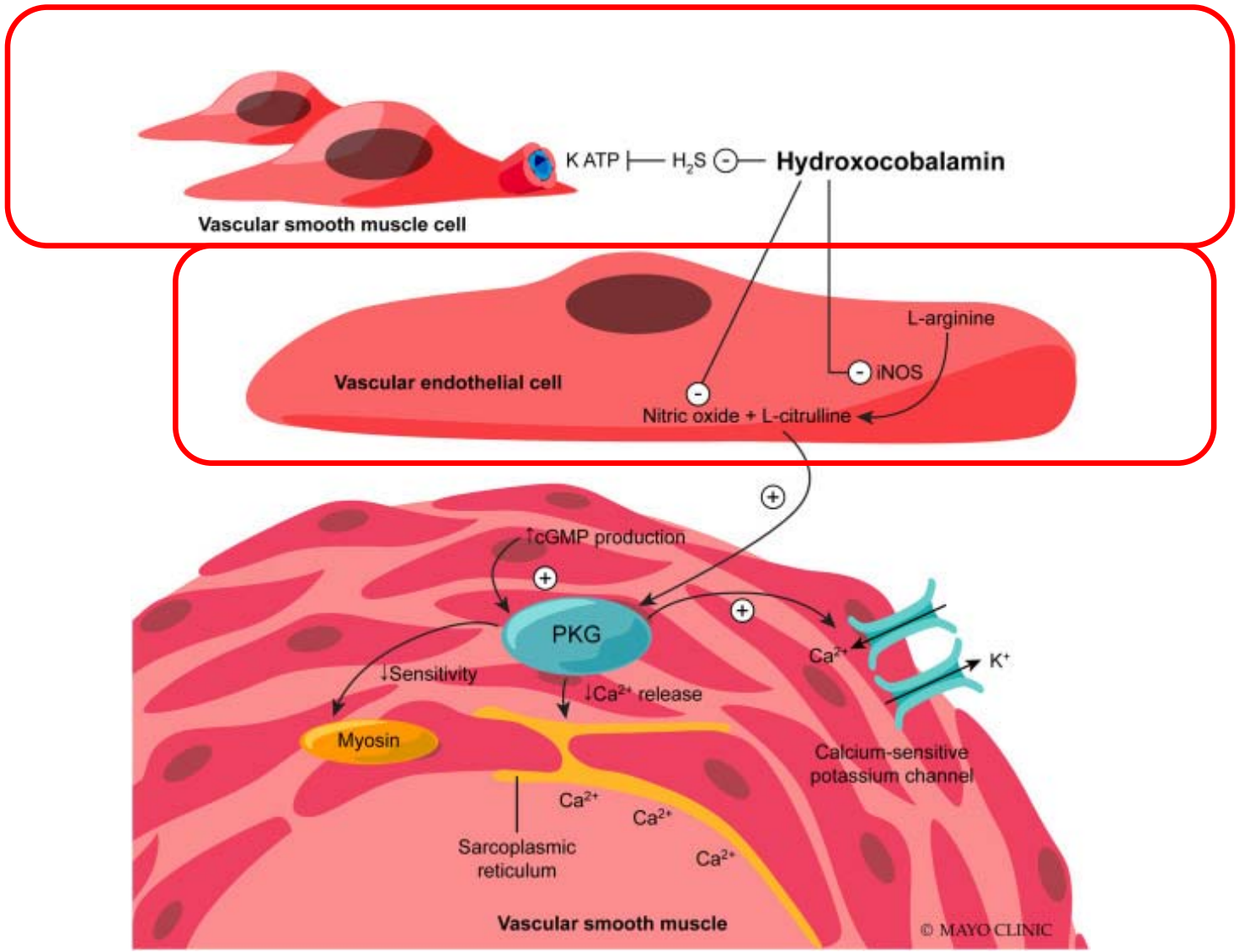
Hydroxocobalamin (Vitamin B12)

- Directly inhibits NO and iNOS, which prevents myosin dephosphorization minimizing the vasodilatory effects of these pathways

- Binds to hydrogen sulfide (H_2S), an endogenous vasodilator, by modifying potassium channels and amplifying its elimination

Science. 2008 Oct 24;322(5901):587-90.

Scientific reports. 2016 Feb 15;6(1):20831.



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Science. 2008 Oct 24;322(5901):587-90.

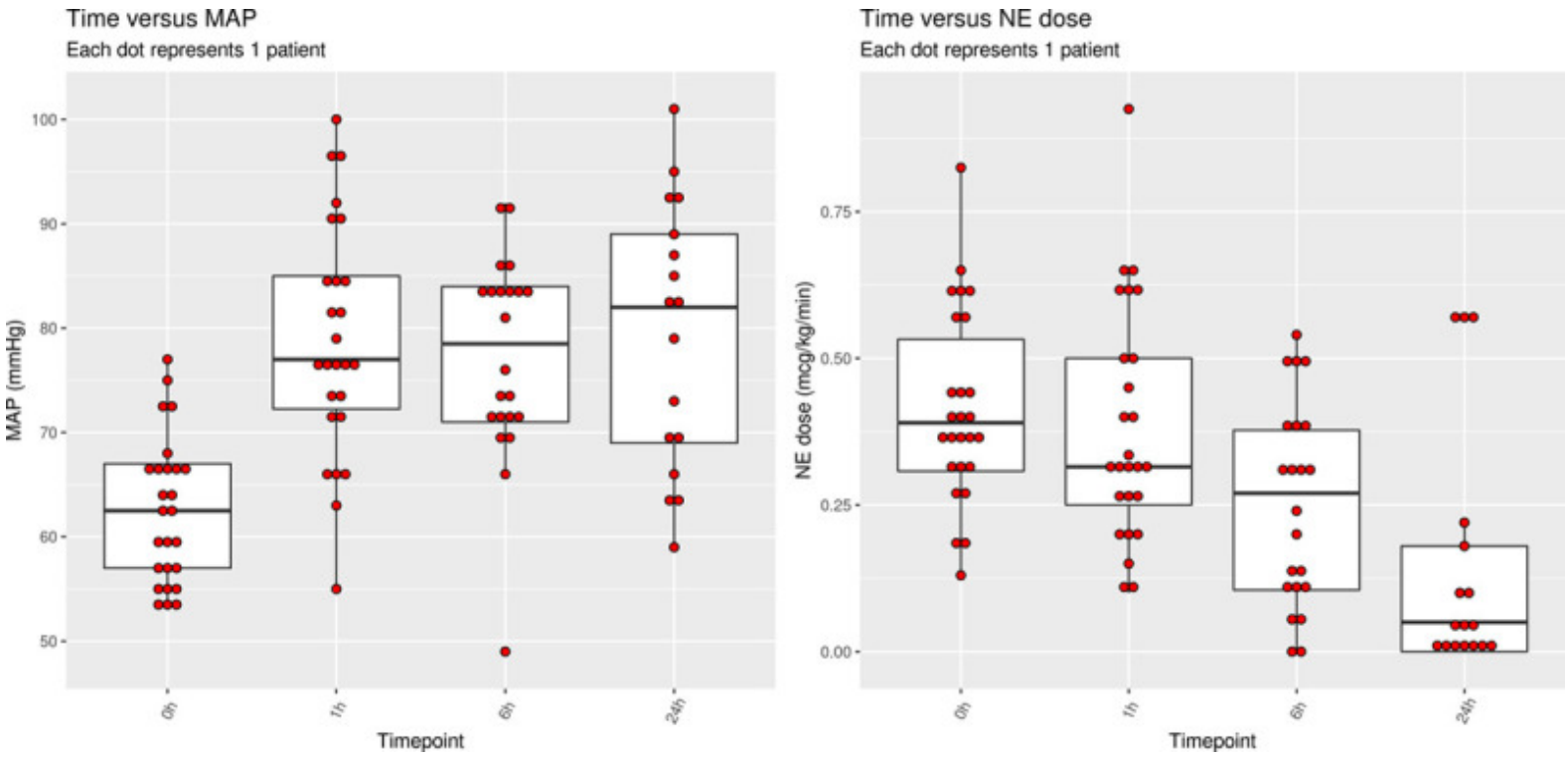
Scientific reports. 2016 Feb 15;6(1):20831.

Hydroxocobalamin in refractory septic shock: a retrospective case series.

- Case report and case series of 26 patients in refractory septic shock
- At least one dose of 5 g IV over 15 minutes
- Primary outcomes were the change from baseline in MAP and NE at 1, 6, and 24 hours after hydroxocobalamin administration.

Critical Care Explorations. 2021 Apr;3(4).

Hydroxocobalamin in refractory septic shock: a retrospective case series.



Critical Care Explorations. 2021 Apr;3(4).

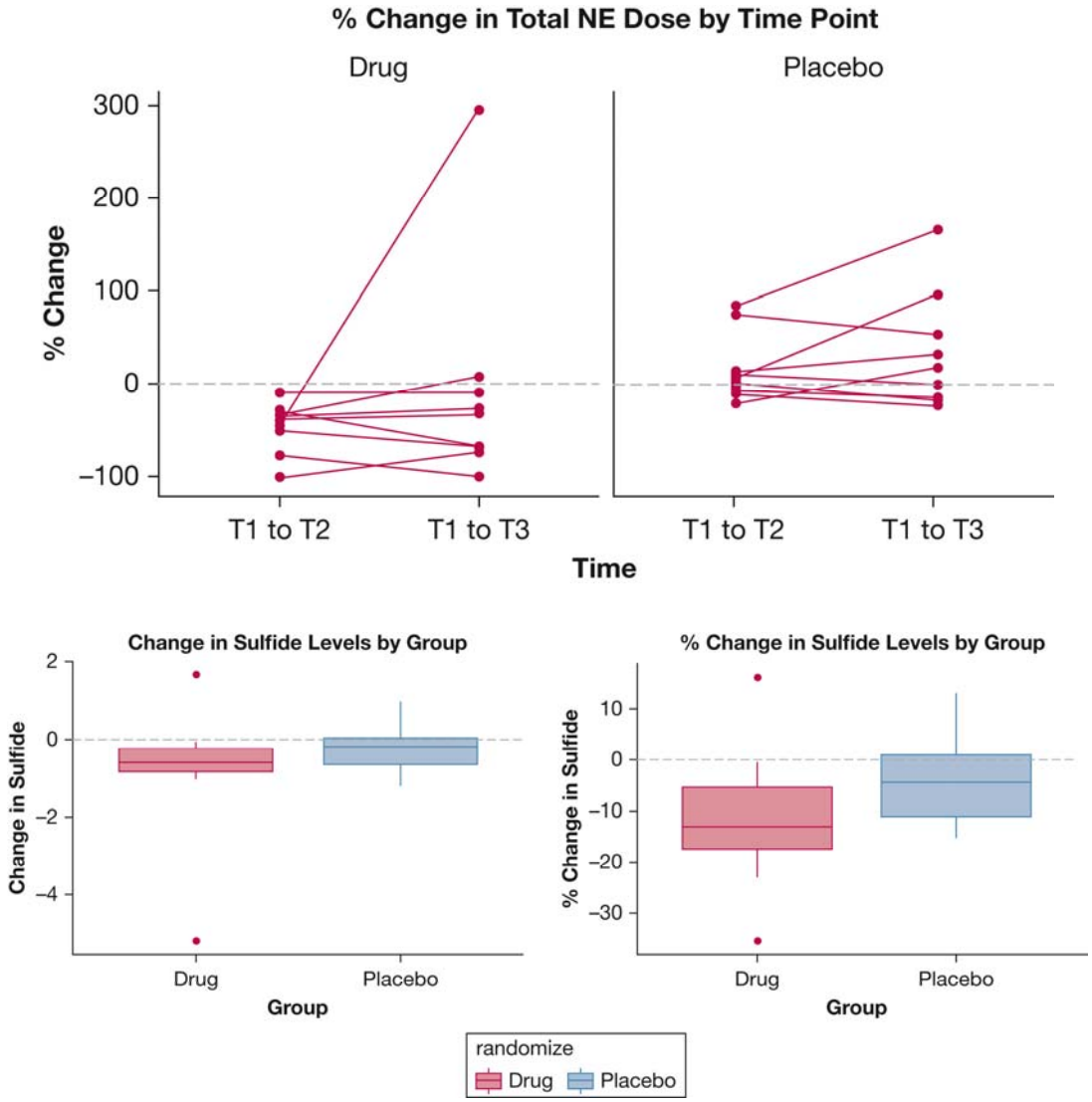
The Intravenous Hydroxocobalamin in Septic Shock Trial

- Phase 2 single-center, double-blind, allocation-concealed, placebo-controlled, parallel-group pilot randomized controlled trial comparing high-dose IV hydroxocobalamin with placebo in critically ill adults with septic shock

- The primary outcome was study feasibility (enrollment rate, clinical and laboratory compliance rate, and contamination rate).

- Secondary outcomes included between-group differences in plasma H_2S concentrations and vasopressor dose before and after infusion.

Chest. 2023 Feb 1;163(2):303-12.



Chest. 2023 Feb 1;163(2):303-12.

Hydroxocobalamin (Vitamin B12) Takeaways

- Decrease in short-term vasopressor load
- Increase in MAP or “relative” MAP
- No glaring signals surrounding oxalate nephropathy but limitations of small total sample

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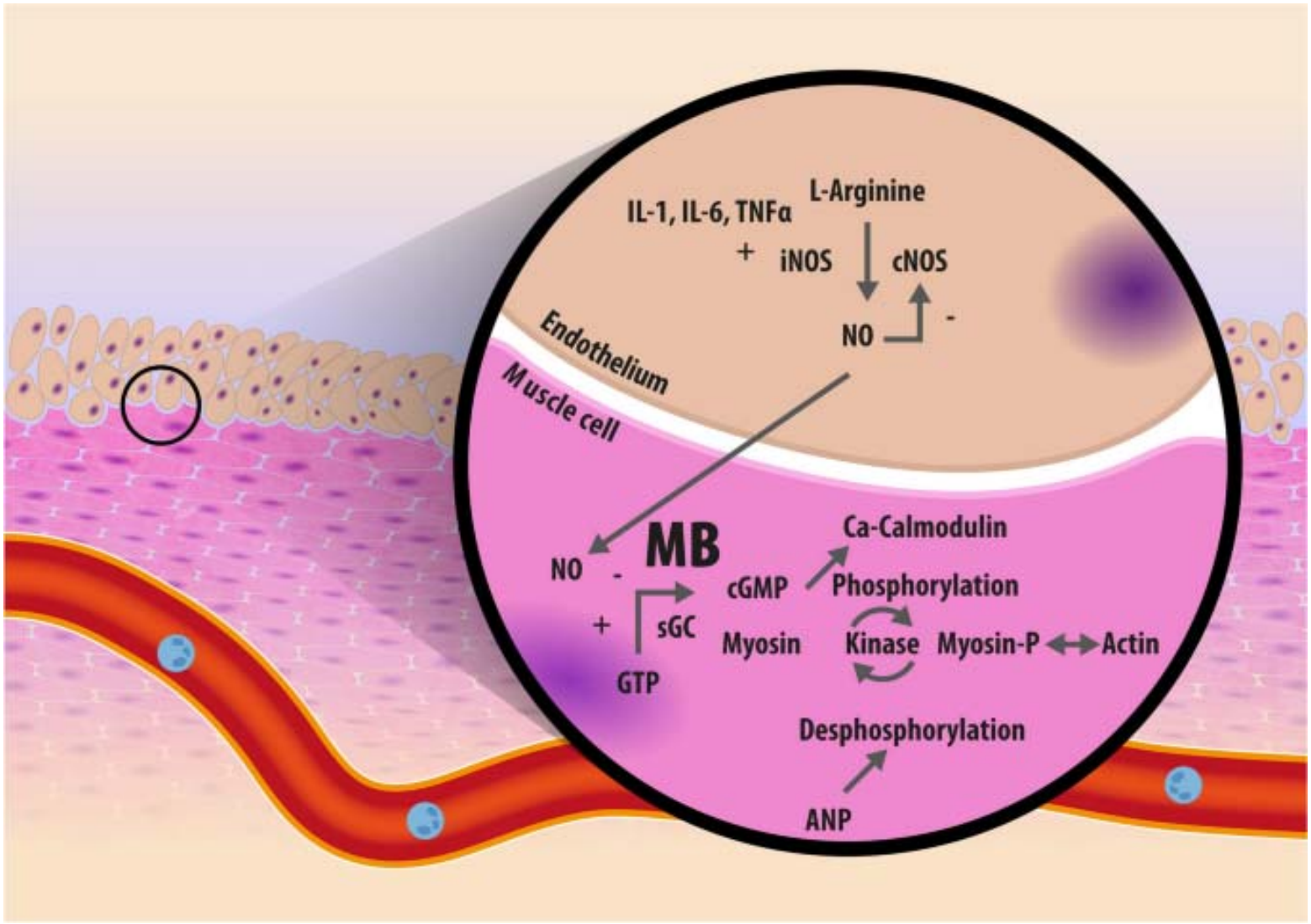
Methylene Blue

- Methylene blue inhibits guanylate cyclase, blocks the formation of cyclic guanosine monophosphate (cGMP), which prevents smooth muscle relaxation by NO.

- Direct inhibitory effect on eNOS and possibly iNOS by oxidation of enzyme-bound ferrous iron.

J Med Toxicol. 2013 Sep; 9(3): 242–249



J Med Toxicol. 2013 Sep; 9(3): 242–249

Refractory septic shock

Original investigation

Use of methylene blue in patients with refractory septic shock: Impact on hemodynamics and gas exchange

Max Andresen, Alberto Dougnac, Orlando Diaz, Glen Hernandez, Luis Castillo, Guillermo Bugedo, Manuel Alvarez, Jorge Dagnino

Journal of critical care. 1998 Dec 1;13(4):164-8.

Use of Methylene Blue in Sepsis: A Systematic Review

Edmund S. H. Kwok, MSc*
Daniel Howes, MD, FRCPC†

Journal of intensive care medicine. 2006 Dec;21(6):359-63.

Methylene Blue for the Treatment of Septic Shock

Christopher A. Paciullo, Pharm.D., Deanna McMahon Horner, Pharm.D., Kevin W. Hatton, M.D., and Jeremy D. Flynn, Pharm.D.

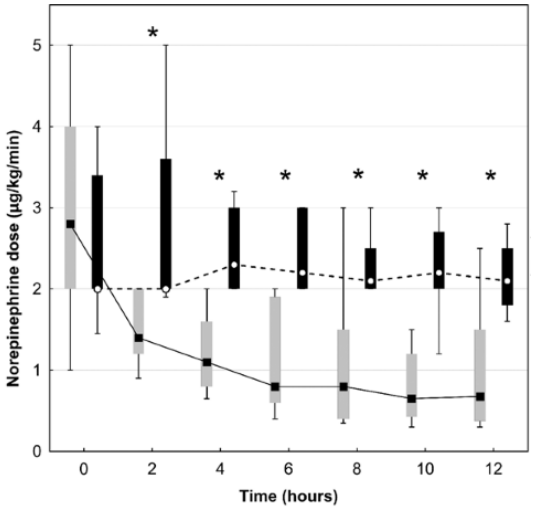
Pharmacotherapy. 2010 Jul;30(7):702-15.

Article | Open Access | Published: 04 February 2020

Methylene blue administration in patients with refractory distributive shock – a retrospective study

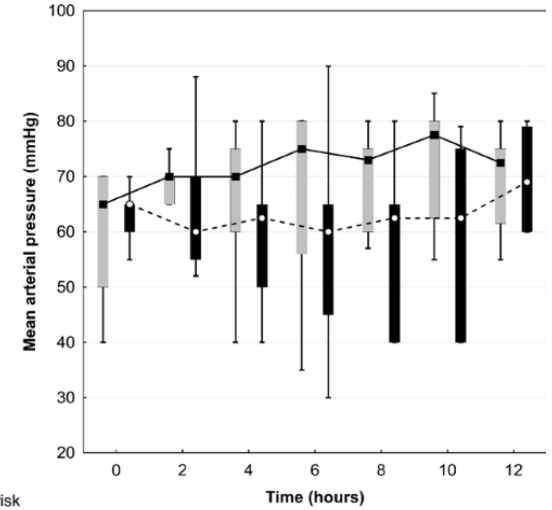
Michal Porizka, Petr Kopecky, Helena Dvorakova, Jan Kunstyr, Michal Lips, Pavel Michalek & Martin Balik

Scientific Reports **10**, Article number: 1828 (2020) | Cite this article



No. at risk

Responders	9	9	9	9	9	8	8
Non-responders	11	11	10	7	7	4	4



No. at risk

Responders	9	9	9	9	9	8	8
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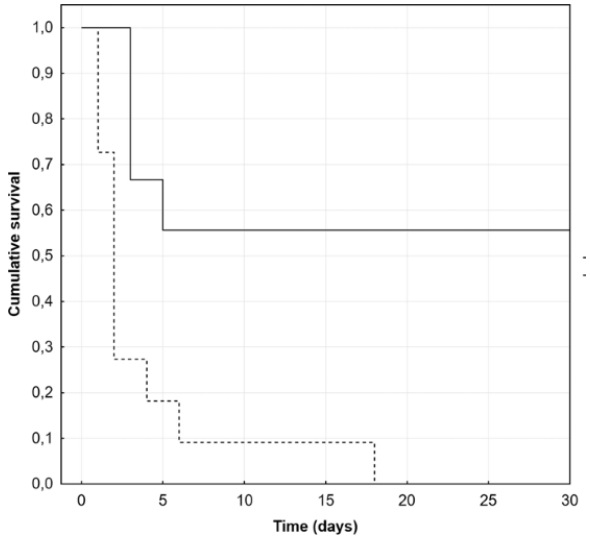


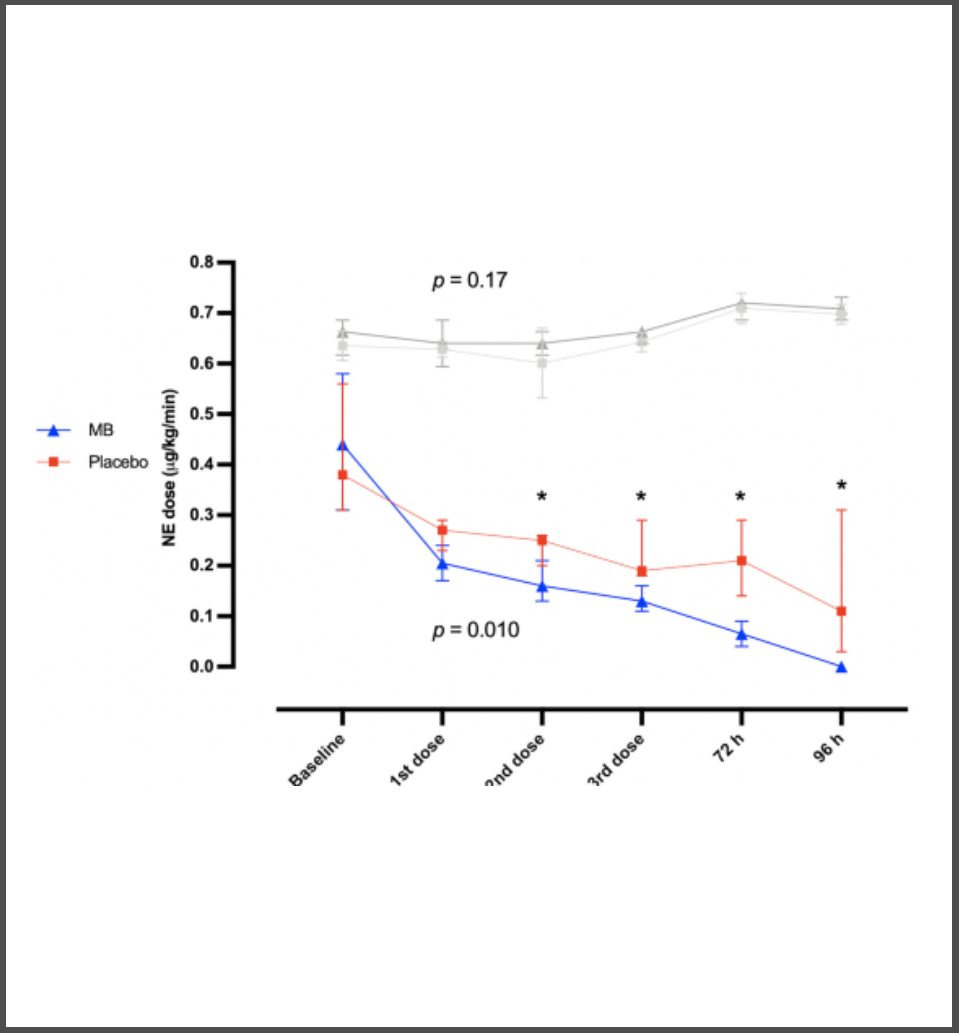
Scientific Reports. 2020 Feb 4;10(1):1828.

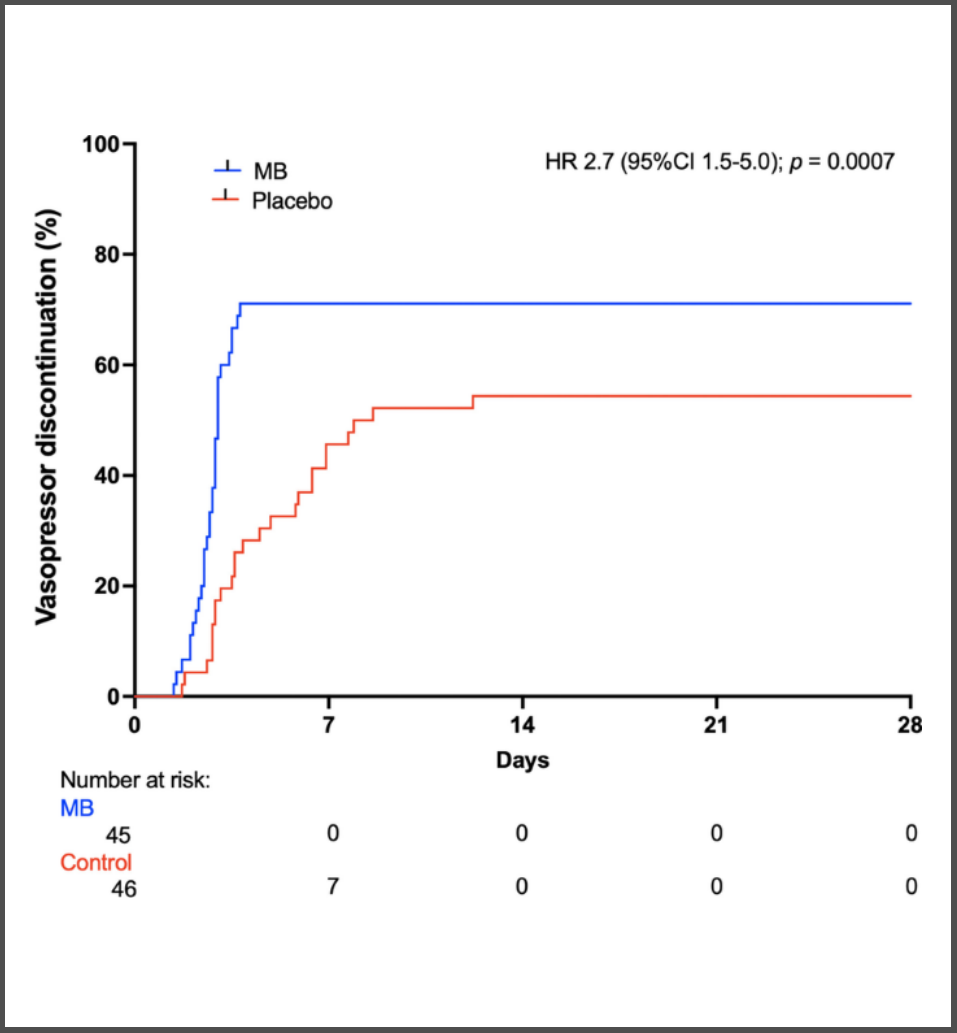
Early adjunctive methylene blue in patients with septic shock: a randomized controlled trial

- 100 mg of methylene blue over six hours, once a day for a total of three doses/days
- Primary outcome: Time to vasopressor discontinuation
- Secondary outcome: Vasopressor free days at 28 days

2023 ICHP ANNUAL MEETING

Critical Care. 2023 Dec;27(1):1-0.





Critical Care. 2023 Dec;27(1):1-0.

Early adjunctive methylene blue in patients with septic shock: a randomized controlled trial

- Methemoglobin saturation between the two groups.... This did not cause any clinical effects.

Critical Care. 2023 Dec;27(1):1-0.

Methylene Blue Takeaways

- Decrease in short-term vasopressor load and earlier discontinuation

- Possible decrease in vasopressor free days which could impact ICU length of stay and hospital length of day

087 - Benken - I'm Shocked

Visual settings | Edit

When poll is active respond at **PollEv.com/ichp3** Send **ichp3** to **22333**

4. Studies surrounding early high dose ascorbic acid as part of HAT therapy in septic shock have consistently shown:

00:20 | 0

Mortality benefit	Vasopressor benefit	Significant toxicities	Organ function improvement
0%	0%	0%	0%

087 - Benken - I'm Shocked

Visual settings | Edit

When poll is active respond at **PollEv.com/ichp3** Send **ichp3** to **22333**

5. Studies surrounding hydroxocobalamin in refractory septic shock have primarily demonstrated:

0

0%	0%	0%	0%
Increased rates of oxalate nephropathy	Improved mortality	Decrease in vasopressor load	Decrease in mean arterial pressure

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Visual settings | Edit

When poll is active respond at **PollEv.com/ichp3** Send **ichp3** to **22333**

6. Studies surrounding methylene blue in both early and refractory septic shock have demonstrated:

0

0%	0%	0%	0%
Improved survival	Unacceptable rates of serotonin syndrome	Organ function improvement	Decreased vasopressor duration

Summary

- Ascorbic acid, hydroxocobalamin, and methylene blue all appear to have a positive impact on vasopressors
- Unclear clinical impact of these findings
- Strong consideration in refractory septic shock
- MORE RESEARCH NEEDED

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Moderate | Visual settings | Edit

When poll is active respond at **PollEv.com/ichp3** Send **ichp3** to **22333**

Questions?

0

Nobody has responded yet.

Hang tight! Responses are coming in.

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