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Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

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Speaker Introduction

- Aaron grew up in Nixa, Missouri. He received his pharmacy degree in 2020 from the University of Missouri-Kansas City School of Pharmacy and completed his PGY1 residency at Nebraska Medical Center in Omaha, Nebraska. He is now the PGY2 critical care resident at the University of Utah. He career interest includes emergency response, cardiovascular medicine, and having fun.
- Today he is going to present on a topic that summarizes the limited and wild evidence behind salvage therapy for vasoplegia.

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UTAH SOCIETY OF HEALTH-SYSTEM PHARMACISTS

Aaron Hunsaker, PharmD
November 16, 2021

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Blues Clues – What To Do When You Wish You Knew. Salvage Therapy For Vasoplegia

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Disclosure

- Relevant Financial Conflicts of Interest
  - **CE Presenter, Aaron Hunsaker:**
    - None
  - **CE mentors, Laura Steffens and Lauren Flieller:**
    - None
- Off-Label Uses of Medications
  - Hydroxocobalamin
  - Methylene blue

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Learning Objectives – Pharmacist

1. Describe the pathophysiology of vasoplegia
2. Interpret the literature surrounding the medications commonly used to treat vasoplegia
3. Apply the literature to make recommendations

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Learning Objectives – Pharmacy technicians

1. List common causes of vasoplegia
2. Differentiate the different medications used for vasoplegia
3. Recognize common side effects of medications used to treat vasoplegia

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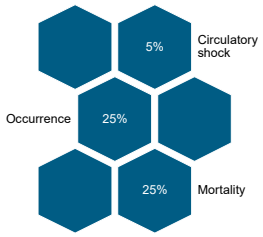
Epidemiology



Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

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Risk factors

Prehospital medications
- Antihypertensive

Large number of comorbidities
- Cardiac (i.e heart failure, hypertension, history of myocardial infarction)

Cardiac bypass
- Warmer core temperatures
- Longer duration on cardiac bypass

Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

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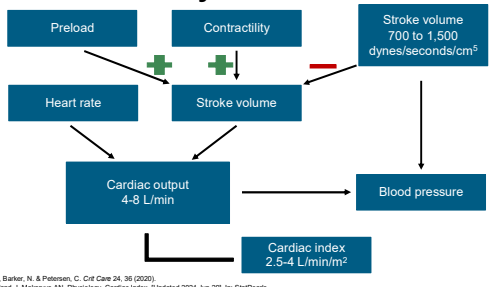
Normal hemodynamic markers



Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).
Patel N, Durland J, Makaryus AN. Physiology, Cardiac Index. [Updated 2021 Jun 29]. In: StatPearls

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Characteristics of vasoplegia

- Significant arterial hypotension
- Low systemic vascular resistance
- Normal or high cardiac output/index
- Significant vasopressor requirements

Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

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Potential definitions of vasoplegia

- MAP < 60 mmHg
- SVR < 800 dyn*sec/cm5
- CI > 2.2 L/min/m2
- Non-responsiveness to adequate volume administration
- Norepinephrine equivalent ≥ 0.2-0.5 µg/kg/min

SVR= systemic vascular resistance
MAP = mean arterial pressure
CI= cardiac index

Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

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Guidelines

Surviving Sepsis Campaign	No definition, favors steroid addition
ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery	No definition of vasoplegia or treatment

Hillis LD et al. 2011 Nov 7. Erratum in: *Circulation*. 2011 Dec 20;124(25):e956.
Evans L et al. *Intensive Care Med*. 2021 Oct 2:1–67

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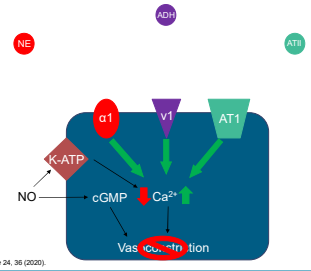
Normal physiology



Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

NE= norepinephrine
ADH = antidiuretic hormone
AT II = angiotensin II
NO = nitric oxide

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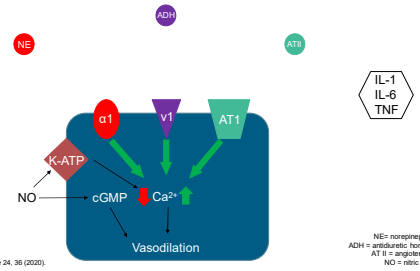
Pathophysiology of vasoplegia



Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

NE= norepinephrine
ADH = antidiuretic hormone
AT II = angiotensin II
NO = nitric oxide

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Review of vasopressors

Agent	Mechanism	Dosing
Norepinephrine	α-1 agonism Moderate β-1 agonism	0.01-3 µg/kg/min
Epinephrine	α-1 agonism Significant β-1 agonism	0.01-1 µg/kg/min
Phenylephrine	Significant α-1 agonism No β-1 agonism	0.1- 5 µg/kg/min
Dopamine	Dose dependent	1-20 µg/kg/min
Vasopressin	V1 agonism	0.03 – 0.04 U/min
Angiotensin II	Angiotensin II receptor agonist	10 ng/kg/min, max 80 ng/kg/min

α-1 agonism = vasoconstriction
β-1 agonism = increase heart and contractility
V1 agonism = vasoconstriction

Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

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Clinical scenario

- CH is a 65-year-old male admitted for a CABG who arrives to your unit intubated and on max doses of norepinephrine, epinephrine, and vasopressin
- Spent 362 minutes on the bypass machine
- PMH : hypothyroidism
- Infection work up is negative
- SVR is 500 dyn*sec/cm^5, MAP is 50 mmHg, CI = 2.8 L/min/m^2

SVR= systemic vascular resistance
MAP = mean arterial pressure
CI= cardiac index

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Clinical scenario

65 year old male admitted for a CABG, on max doses of norepinephrine, epinephrine, and vasopressin

SVR is 500 dyn*sec/cm^5
MAP is 59 mmHg
CI = 2.8 L/min/m^2

What to do next?

Stay on max dose vasopressor

Reach for another medication

SVR= systemic vascular resistance
MAP = mean arterial pressure
CI= cardiac index

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Vasopressor use

Long term use

- Arrythmias and renal failure
- Ischemia

Pathophysiological considerations

- Need for a multimodal approach

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Salvage therapy medications

- **Vitamin C and Thiamine**
  - Co-factors
- **Hydrocortisone**
  - Mineralocorticoid activity
- **Methylene blue and hydroxocobalamin**
  - Acts on the nitric oxide system
- **Angiotensin II**
  - Vasoconstrictor and increases aldosterone release

Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

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Methylene blue – pharmacology

- Inhibits guanylate to decrease cGMP production, also competes with nitric oxide to activate cGMP
- Vd: 255 liters
- Metabolized by CYP 1A2, 2C19, and 2D6
  Half life: 24 hours
- Approximately 40% is excreted in the urine unchanged

Methylene blue. Package insert. Provepharm; 2016

Vd = volume of distribution

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Hydroxocobalamin – pharmacology

- Binds nitric oxidie and inhibits nitric oxide synthase
- Vd: 280 – 349 liters and is significantly protein bound
- Does not undergo metabolism
  Half life: 26-31 hours
- Excreted primarily in the urine

Hydroxocobalamin. Package Insert. Merk 2018

Vd = volume of distribution

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Slide 23

AH15 Perhaps not on this slide but in general I think it would be SUPER helpful to put together a table comparing the three agents you are discussing: MOA, usual dose, max dose if applicable, side effects
Aaron Hunsaker, 10/4/2021

Angiotensin II – pharmacology

- Fast pressor response (sympathetic response)
  Slow pressor response (RAAS activation)
  Non-hemodynamic effects (cardiac remodeling)
- Vd: unknown
- Half life: < 1 minute
- Unknown mechanism of excretion

Angiotensin II. Package Insert. La Jolla Pharmaceutical 2018

Vd = volume of distribution
RAAS= renin angiotensin-aldosterone system

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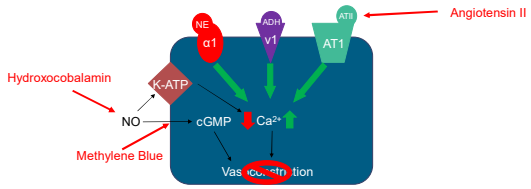
Mechanisms of action



Busse, L.W., Barker, N. & Petersen, C. *Crit Care* 24, 36 (2020).

NE= norepinephrine
ADH = antidiuretic hormone
AT II = angiotensin II
NO = nitric oxide

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The literature

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The literature

- Methylene blue monotherapy
  - Kirov et al 2001
- Methylene blue vs hydroxocobalamin
  - Feih et al 2019
  - Furnish et al 2020
- Angiotensin II
  - Khanna et al 2017

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Kirov et al 2001

Methylene blue vs placebo

Kirov MY et al. *Crit Care Med.* 2001 Oct;29(10):1860-7.

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Study design

- Pilot, randomized, controlled study
- Methylene blue vs placebo
- 10 patients in the methylene blue group
  10 patients in the control group
- 1 Hemodynamic parameters were used to evaluate effectiveness

Kirov MY et al. *Crit Care Med.* 2001 Oct;29(10):1860-7.

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Methylene blue dosing

2 mg/kg for 15 minutes → Increasing rates of 0.25 mg, 0.5, 1 and 2 mg/kg/hr for 1 hour → Goal MAP 70-90 mmHg

Kirov MY et al. *Crit Care Med.* 2001 Oct;29(10):1860-7.

MAP = mean arterial pressure

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AH16

Inclusion and exclusion

Inclusion	Exclusion
• Severe sepsis (<72 hours) and septic shock (<24 hours) • Mechanical ventilation	• <18 years old • Pregnant • Receiving steroids • Immunosuppressed

Kirov MY et al. *Crit Care Med.* 2001 Oct;29(10):1860-7.

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Slide 33

AH2 I will read out loud how they define sepsis and shock. They use old definitions so I don't know the utility of listing their long defintions for the audience. I welcome your thoughts too
Aaron Hunsaker, 9/19/2021

AH16 Don't love this SmartArt -- I feel like many of these slides could be compressed and that formatting would be more streamlined - Lauren
Aaron Hunsaker, 10/4/2021

AH3

Patient demographics

Methylene blue	Control
55 years old, 50% females	59 years old, 40% females
SOFA: 10.1 Number of organ dysfunctions: 2.4	SOFA: 10.5 Number of organ dysfunctions: 2.4
Medical: 6 Surgical: 4	Medical: 5 Surgical: 5

Kirov MY et al. *Crit Care Med.* 2001 Oct;29(10):1860-7.

SOFA = Sequential Organ Failure Assessment

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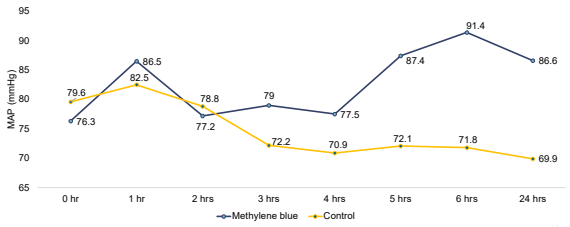
AH4

Hemodynamic outcomes – MAP



Kirov MY et al. *Crit Care Med.* 2001 Oct;29(10):1860-7.

MAP = mean arterial pressure

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Adrenergic support

Methylene blue decreased:

- Norepinephrine by 87%
- Epinephrine by 81%
- Dopamine by 40%

No difference in morbidity or mortality

Kirov MY et al. *Crit Care Med.* 2001 Oct;29(10):1860-7.

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Slide 34

AH3 I am not sure what USHP thinks but I don't like making a table and listing off the whole demographics. So I do my best to include what I think helps paint a picture of the pateint population
Aaron Hunsaker, 9/19/2021

Slide 35

AH4 The authors evaluate like every hemodynamic parameter, so I was just going to include three graphs on them to help with visualization. I will have the other two graphs on the PPT by the next round of edits
Aaron Hunsaker, 9/19/2021

Limitations

- Small retrospective pilot study
- Goal MAP of 70-90
- Old definitions of sepsis and septic shock
- Excluded patients who were immunosuppressed

Kirov MY et al. *Crit Care Med*. 2001 Oct;29(10):1860-7.

MAP = mean arterial pressure

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Conclusions

Methylene blue monotherapy in medical patients → Associated with a decrease in adrenergic support → No difference in morbidity or mortality

Kirov MY et al. *Crit Care Med*. 2001 Oct;29(10):1860-7.

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Feih et al 2019

Methylene blue monotherapy vs combination with hydroxocobalamin

Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

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Study design

- Retrospective, observational, cohort study
- Methylene blue monotherapy (n=14)
  Combination therapy with hydroxocobalamin (n=6)
- Patients who underwent cardiac surgery
- 1 Ability to maintain MAP > 60 mmHg at least 1 hour after study drug administration

Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

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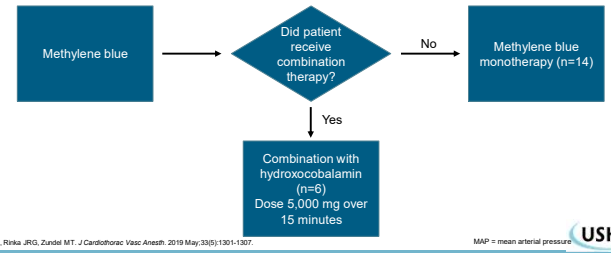
Group stratification



Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

MAP = mean arterial pressure

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Inclusion and exclusion

Inclusion	Exclusion
• Norepinephrine equivalent > 0.1 µg/kg/min while on vasopressin at 0.4 U/min	• CI < 2.2 L/min/m² • Supported with temporary mechanical circulatory device

Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

CI = cardiac index

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Patient demographics

Methylene blue (n=14)	Combination therapy (n=6)
63 YO, 29% female	67 YO, 17% female
Bypass time: 292 min	Bypass time: 217 min
Baseline NEE: 0.29 µg/kg/min	Baseline NEE: 0.3 µg/kg/min

Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

NEE = norepinephrine equivalent

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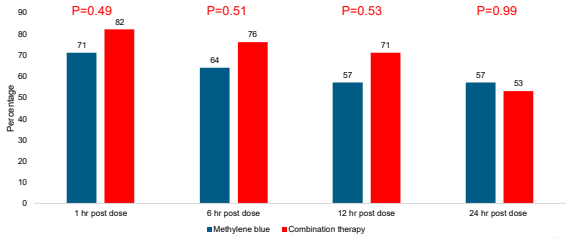
Primary outcome – ability to maintain MAP



Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

MAP = mean arterial pressure

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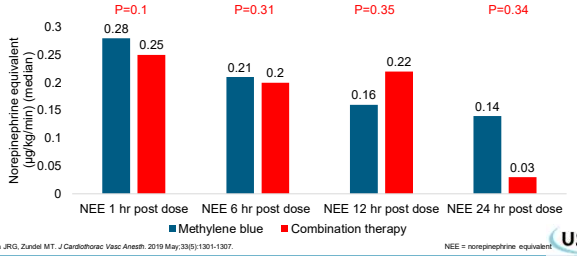
Secondary outcomes – vasopressor requirements



Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

NEE = norepinephrine equivalent

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Limitations

- Small retrospective cohort study
- Only investigated post cardiac patients
- Definition of vasoplegia was not established
- Excluded patients on temporary mechanical support

Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

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Conclusion

No significant findings were found between the two groups in surgical patients

Monotherapy and combination showed a decrease in vasopressor requirements

No evaluation of morbidity or mortality

Feih JT, Rinka JRG, Zundel MT. *J Cardiothorac Vasc Anesth*. 2019 May;33(5):1301-1307.

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Furnish et al 2020

Hydroxocobalamin vs methylene blue

Furnish C et al *J Cardiothorac Vasc Anesth*. 2020 Jul;34(7):1763-1770..

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Study design

- Retrospective, cohort study
- Methylene blue (n=16)
  Hydroxocobalamin (n=19)
- Vasoplegia in cardiothoracic surgery
- Change in time-averaged norepinephrine equivalent

Furnish C et al *J Cardiothorac Vasc Anesth*. 2020 Jul;34(7):1763-1770..

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Time-averaged norepinephrine equivalent equation used

Time-averaged norepinephrine equivalent 1-hour **post** intervention (µg/kg/min) − Time-averaged norepinephrine equivalent 1-hour **pre** intervention (µg/kg/min) = Change in time-averaged norepinephrine equivalent (µg/kg/min)

Norepinephrine at 0.03 µg/kg/min post intervention – Norepinephrine at 0.1 µg/kg/min = - 0.7 µg/kg/min

Furnish C et al *J Cardiothorac Vasc Anesth*. 2020 Jul;34(7):1763-1770..

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Norepinephrine equivalent dosing conversions

Drug	Dose	Norepinephrine Equivalent
Epinephrine	0.1 µg/kg/min	0.1 µg/kg/min
Norepinephrine	0.1 µg/kg/min	0.1 µg/kg/min
Dopamine	15 µg/kg/min	0.1 µg/kg/min
Phenylephrine	1 µg/kg/min	0.1 µg/kg/min
Vasopressin	0.04 U/min	0.1 µg/kg/min

Furnish C et al *J Cardiothorac Vasc Anesth*. 2020 Jul;34(7):1763-1770..

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Baseline characteristics

Methylene blue	Hydroxocobalamin
60 years old, 6% female	57 years old, 26% female
APACHE II: 29.8 MAP: 52.2	APACHE II: 22.2 MAP: 59.4
Methylene blue dose: 123 mg	Hydroxocobalamin dose: 5 g

Furnish C et al *J Cardiothorac Vasc Anesth*. 2020 Jul;34(7):1763-1770..

MAP = mean arterial pressure

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Inclusion

Inclusion
- If they received either medication for suspected vasoplegic syndrome

Exclusion
- If patient received both medications for a single vasoplegia occurrence
- Non cardiac transplant

Furnish C et al *J Cardiothorac Vasc Anesth*. 2020 Jul;34(7):1763-1770..

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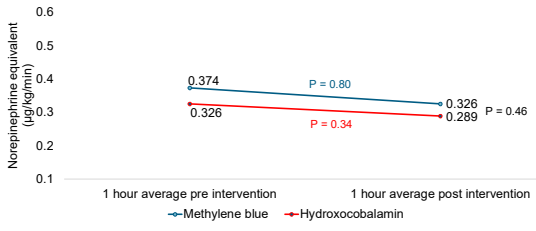
Primary outcome – change in time-averaged norepinephrine equivalent



Furnish C et al *J Cardiothorac Vasc Anesth*. 2020 Jul;34(7):1763-1770..

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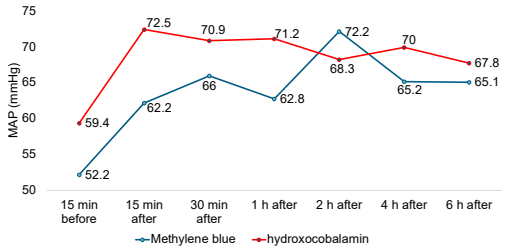
AH6

Secondary outcome – MAP



Furnish C et al *J Cardiothorac Vasc Anesth.* 2020 Jul;34(7):1763-1770..

MAP = mean arterial pressure

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Secondary outcomes

	Methylene blue (n=16)	Hydroxocobalamin (n=19)	P value
Time free from ICU, days	3.5 ± 4.5	4.9 ± 4.9	0.40
Time free from mechanical ventilation, days	6.4 ± 6.6	7.4 ± 6.5	0.65
Mortality, %	50	36.8	0.51

Furnish C et al *J Cardiothorac Vasc Anesth.* 2020 Jul;34(7):1763-1770..

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Limitations

- Retrospective cohort
- Only included post surgical patients
- Dosing of methylene blue varied
- APACHE II scores at baseline was higher in the methylene blue group

Furnish C et al *J Cardiothorac Vasc Anesth.* 2020 Jul;34(7):1763-1770..

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Slide 55

AH6 I will make this into a graph before the next round of edits
Aaron Hunsaker, 9/20/2021

Conclusion

No difference existed between methylene blue and hydroxocobalamin in surgical patients

Monotherapy with either product significantly increase MAP from baseline

No difference in morbidity or mortality

Furnish C et al *J Cardiothorac Vasc Anesth.* 2020 Jul;34(7):1763-1770..

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Audience Response Question 4

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Khanna et al 2017

Angiotensin II - ATHOS III

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

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Study design

- International, randomized, double-blind, placebo controlled
- Synthetic human angiotensin II (n=163)
  Placebo (n=158)
- Treatment was not limited to medicine or surgical populations
- 1 Mean arterial pressure response at hour 3 (MAP > 70 mmHg or an increase from baseline of >10 mmHg

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

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Inclusion and exclusion

Inclusion	Exclusion
• 18 years of age • Vasodilatory shock* despite fluid resuscitation with 25 mL/kg • Administration of high dose vasopressors *	• Burns covering > 20 % BSA • ACS • Liver failure • Active bleeding • AAA

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

BSA = body surface area
AAA = abdominal aorta aneurysm

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Trial definitions

Vasodilatory shock	High dose vasopressors
CI > 2.3 L/min/m² or	Norepinephrine > 0.2 µg/kg/min or equivalent
CVO2 >70% with CVP > 8 mmHg and MAP 50-70 mmHg	For at least 6 hours but less than 48 hours

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

MAP = mean arterial pressure
CVP = central venous pressure
CI= cardiac index
CVO2 = central venous oxygen

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Angiotensin II dosing

Initiated at 20 ng/kg/min → Adjusted during first 3 hours to a MAP of 75 mmHg → Max rate 200 ng/kg/min

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

MAP = mean arterial pressure

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Baseline demographics

Angiotensin II	Placebo
63 years old, 46% female	65 years old, 35% female
APACHE II: 27 MAP: 66.3	APACHE II: 29 MAP: 66.3
Sepsis: 79%	Sepsis: 79%

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

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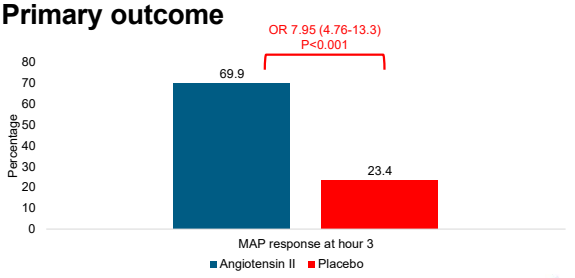
Primary outcome



Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

MAP = mean arterial pressure

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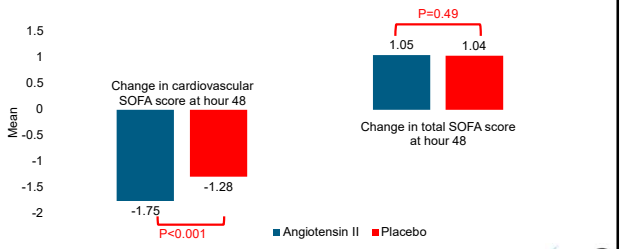
Slide 64

AH7 I feel like this max infusion rate is wrong but I think that's what the article says?
Aaron Hunsaker, 9/20/2021

AH10 okay I hated not knowing this but the supplement has dosing at 200 max within the first three hours then down to 40 max afterwards
Aaron Hunsaker, 9/22/2021

Secondary end points



Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

SOFA = Sequential Organ Failure Assessment

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Additional end points

Change in norepinephrine dose from baseline to 3 hours

- Angiotensin II = - 0.03
- Placebo = 0.03
- P-value <0.001

All cause mortality at day 7 or day 28

- No difference existed between the two groups

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

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Adverse events

Event	Angiotensin II	Placebo
Adverse event of any grade	142 (87.1%)	145 (91.8%)
Adverse event leading to discontinuation	23 (14.1%)	34 (21.5%)
Intestinal ischemia	1 (0.6%)	3 (1.9%)

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

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Limitations

- Included a limited amount of surgical patients
- Lacks long term follow up
- Primary outcome significance and high angiotensin II infusion rate
- Targeted a MAP of 75 mmHg

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

MAP = mean arterial pressure

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Conclusion

Angiotensin II compared to placebo → Significantly achieved a MAP target of 75 mmHg at 3 hours → No difference in mortality

Khanna A et al. *New Engl J Med.* 2017. 377:419-30.

MAP = mean arterial pressure

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Putting it all together

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Clinical scenario

65 year old male admitted for a CABG, on max doses of norepinephrine, epinephrine, and vasopressin

→

SVR is 500 dyn*sec/cm^5
MAP is 59 mmHg
CI = 2.8 L/min/m^2

→

What to do next?

SVR= systemic vascular resistance
MAP = mean arterial pressure
CI= cardiac index

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Trial summaries

Kirov et al 2001	Khanna et al 2017	Feih et al 2019	Furnish et al 2020
MB vs placebo	Angiotensin II vs placebo	MB monotherapy vs combination with HCB	MB vs HCB
Decrease in adrenergic support	Significantly achieved a MAP target	No difference in ability to achieve MAP	No difference between the two groups

No difference in mortality

MAP = mean arterial pressure
MB = methylene blue
HCB = hydroxocobalamin

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Considerations – angiotensin II

Physiological side effects	Uses
• Thrombosis • Tachycardia • Thrombocytopenia	• Only approved for distributive shock • Utility in surgical patients remains uncertain

Khanna A et al. *New Engl J Med*. 2017. 377:419-30.
Angiotensin II. Package Insert. La Jolla Pharmaceutical 2018

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Considerations – methylene blue

Physiological side effects	Equipment effects	Contraindications
• Increased pulmonary vascular pressures • Green/blue urine and skin coloration • Hemolytic anemia	• O2 sat readers are no longer accurate after use	• G6PD deficient • Caution in combination with MAOIs • Serotonergic medications

Prashant R et al. J Anaesthesiol Clin Pharmacol. 2010 Oct-Dec; 26(4): 517–520.
Chan ED et al. Respir Med. 2013 Jun;107(6):789-99

G6PD = glucose-6-phosphate-dehydrogenase
MAOI = monoamine oxidase inhibitor

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Considerations – hydroxocobalamin

Physiological side effects	Equipment effects	Lab values
• Erythema • Acneiform rash • Hypokalemia • Vitamin B12 deficiency • Deep blood red, almost purple discolroation	• False blood leak alarm on dialysis machine	• Hemoglobin elevated for 12 hours • Scr, glucose, alk phos elevated for up to 24 hours • Bilirubin elevated for up to 4 days • aPPT, PT, INR changed for up to 1-2 days

Shapeton AD et al. J Cardiothorac Vasc Anesth. 2019 Apr;33(4):894-901

Scr = serum creatine
aPPT = activated partial thromboplastin time
PT= prothrombin time
INR = international normalize ratio.

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Audience Response Question 6

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Cost

Angiotensin II	• $1,800 per vial
Methylene blue	• $50 per 50 mg vial
Hydroxocobalamin	• $1,000 per kit

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Other considerations

Pathophysiology
- A multimodal approach
- Avoiding down regulation of angiotensin II receptor

Population
- Surgical vs medical
- Lack of data with angiotensin II in surgery patients

Shortages
- Hydroxocobalamin

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Conclusion

- The pathology of vasoplegia is complex and not well known
- Many causes are thought to cause vasoplegia
- A wide variety of medications exists to treat vasoplegia
- Evidence is lacking in order to make strong recommendations
- Each medication has its own special consideration

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- **Instructions:**
- Review questions and answers with attendees in whichever format you prefer. If you have multiple-choice questions, please use the Audience Response Cards that will be provided to attendees.
  - We will utilize Poll Everywhere for audience responses when doing virtual presentations
  - https://www.polleverywhere.com/videos
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