Management of Shock

Supplementary Educational Material

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Management of Shock: Part 1

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    a. Why a mean arterial blood pressure of 65 mm Hg?
        i. 0135 Relationship between intraoperative mean arterial pressures and clinical outcomes after noncardiac surgery: Toward an empirical definition of hypotension
        ii. After MAP <65 patient starts to have an increase in acute kidney injury and myocardial injury
    b. 0239 SAVE THE MAP: list of organ injuries
        i. CNS: Stroke, cord injury, paralysis
        ii. CVS: MI, ischemic extremities
        iii. Respiratory: ARDS, pulmonary edema
        iv. Renal: Acute Kidney Injury, Acute Tubular Necrosis
        v. Metabolic: Acidosis, Lactate production
        vi. Hepatic: Coagulopathy, platelet dysfunction, hypoalbuminemia
        vii. GI: Pancreatitis, ischemic bowel, bacterial translocation, acalculous cholecystitis
B. 0305 What are the goals of shock?
    a. Improve perfusion
    b. Perfusion pressures
        i. Cerebral Perfusion Pressure 50-70 mm Hg
        ii. Coronary Perfusion Pressure 60-80 mm Hg
        iii. Renal Perfusion Pressure 65-70 mm Hg
    c. Cardiac output= Stroke Volume x HR
    d. Prevent ischemia to non-vital organs
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C. 0609 Epidemiology of shock (SOAP II)
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    b. Septic
    c. Non-septic
    d. Obstructive shock
    e. Hypovolemic shock
    f. Cardiogenic shock
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        i. Induce vasoconstriction
        ii. Phenylephrine, vasopressin, angiotensin II, selepressin
    b. Inotrope
        i. Increase cardiac contractility = only Beta1
    c. Inopressor
        i. Induce vasoconstriction, + increase cardiac contractility
        ii. Norepinephrine, dopamine, epinephrine
    d. Ionodilator
        i. Increase cardiac contractility + cause vasodilation
        ii. Dobutamine, milrinone, levosimendan, isoproterenol
E. 0909 Receptors
    a. Alpha 1
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    b. Beta 1
        i. Chronotropy= increase heart rate

   ii. Inotropy= increase contractility
c. Beta 2
   i. Bronchodilation (lungs)
   ii. Vasodilation (vasculature)
d. V1
   i. Vasoconstriction
e. V2
   i. (+) ADH in the kidney and increase free water absorption
f. Angiotensin II
   i. (+) aldosterone
   ii. Vasoconstriction

Management of Shock: Part 2a

A. 0101 Norepinephrine
   a. Mechanism of action
      i. Alpha 1: vasoconstriction
      ii. Beta 1: increase heart rate (chronotropic) + increase contractility (Ionotropic) = Small BUT significant
         1. 0230 beta 1 effect possibly causing arrhythmias
         2. 0253 increased inotropy
      iii. 0130 Venoconstriction: improve venous return
   b. Uses
      i. Septic shock, forms of obstructive shock, cardiogenic shock
      ii. 0324 Obstructive shock
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         1. Study Norepinephrine vs Dopamine
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      i. Starting: 0.05 mcg/kg/min
      ii. Range: 0.05mcg/kg/min – 1 mcg/kg/min
B. 0521 Epinephrine
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      ii. 0530 Beta 1: increase heart rate (chronotropic) + increase contractility (Ionotropic)
      iii. Beta 2: Bronchodilation and vasodilation
      iv. Metabolizes glucose to lactate via non-aerobic pathway
         1. 0843 insulin resistance and hyperglycemia
   b. Uses
      i. Pediatric septic shock
         1. 0806: especially less than 1 year old; cold shock
      ii. Adult septic shock
         1. 0706 Study Epinephrine vs Norepinephrine; 2nd line in septic shock guidelines
      iii. Cardiogenic shock (especially with bradycardia)
      iv. Anaphylactic shock
      v. Cardiac arrest
         1. 0732 high doses (1 mg)=> want alpha effects; beta harmful
   c. Doses
      i. 0620 <0.2 mcg/kg/min → primarily beta effects (inotrope)
      ii. 0646 e.g. hypotension related to bradycardia, cardiogenic shock
      iii. 0637 >0.2 mcg/kg/min → 0549 Alpha > Beta (vasoconstriction + iontrope)
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   a. Mechanism of Action
      i. Alpha 1: vasoconstriction
      ii. Beta 1: increase heart rate (chronotropic) + increase contractility (Ionotropic)
   b. Uses
      i. 0933 Cardiogenic shock: especially with bradycardia
         1. Norepinephrine > Dopamine in cardiogenic shock; 1005 Note: Dopamine arrhythmogenic
      ii. 0950 Septic shock?
         1. Previously used in pediatric septic shock (now epinephrine is preferred)
   c. Doses
      i. 0.5-5 mcg/kg/min→ D1/D2 receptors (coronary, cerebral, renal and splanchnic vasodilation)
      ii. 0910 5-10 mcg/kg/min → primary Beta 1 (ionotropic)
      iii. 0925 >10 mcg/kg/min → Alpha > Beta (vasoconstriction + ionotropic)
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    a. Norepinephrine vs Epinephrine
    b. Epinephrine vs Dobutamine and Norepinephrine
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            1. 1132 Possible reflex bradycardia
    b. 1142 Uses
        i. Sepsis, Refractory vasoplegia
        ii. 1215 Note: can increase both systemic and pulmonary vascular resistance = BAD w/ cardiogenic shock +/- right heart failure
    c. Dose
        i. 50 mcg/min to 300 mcg/min
G. 1228 Push dose pressors
    a. Phenylephrine
        i. Pre-made syringe where each ml contains 100 mcg of phenylephrine
        ii. Vial Contains 10 mg/ml→
            1. Draw up 1 ml (10 mg) of phenylephrine from the vial and inject 1 ml into a 100 ml bag of normal saline so each 1 ml =100 mcg
            2. Draw up 2 ml (20 mg) of phenylephrine from the vial and inject 2 ml into a 250 ml bag of normal saline so each 1 ml =80 mcg
        iii. Pharmacokinetics
            1. Onset: 1 minute
            2. Duration: 10-20 minutes
            3. Push Dose: 1-2 ml (80-200 mcg) every 2-4 minutes
    b. 1407 Epinephrine
        i. Both alpha and beta= inopressor
        ii. NEVER give 1 mg of epinephrine to someone with a pulse
        iii. Ampule contains 100 mcg/ml
            1. 1040 Take a 10 ml syringe of normal saline & get rid of 1 ml => 9 ml of normal saline + draw up 1 ml of epinephrine so each ml = 10 mcg
        iv. Pharmacokinetics
            1. Onset: 1 minute
            2. Duration: 5-10 minutes
            3. Push Dose: 1-2 ml (10-20 mcg) every 2-5 minutes

Management of Shock: Part 2b

A. 0115 Dobutamine
    a. Mechanism of action
        i. Beta 1: increase heart rate (chronotropic) + increase contractility (Ionotropic)
        ii. Beta 2: bronchodilation
    b. Uses
        i. 0146; 0215 Cardiogenic shock- mainly want the Beta 1 effect for contractility
            1. Caution: if hypotensive can vasodilate with the beta 2 effects and drop their blood pressure. In this case can start norepinephrine or epinephrine.
        ii. 0157 Septic shock- not primary agent, but 2nd or 3rd agent where they need cardiogenic support
            1. Septic cardiomyopathy: cytokine release due to sepsis
        iii. 0300 Obstructive shock (RV failure in the setting of a massive PE)
            1. Need to restore blood pressure with norepinephrine
    c. Doses
        i. 2.5-20 mcg/kg/min
        ii. Caution: arrhythmogenic
B. 0337 Milrinone
    a. Mechanism of Action
        i. Phosphodiesterase 3 inhibitor (prevents degradation of cAMP)
            1. 0445 Increases lusitropy (diastolic relaxation)
                a. Allows for a larger filling volume
            2. Increases Inotropy
            3. 0400 Can increase chronotropy- which means arrythmias are possible, but are much less common
            4. Vasodilator- decreases systemic vascular resistance and peripheral vascular resistance
    b. Uses
        i. Cardiogenic shock
            1. 0429- caution with starting or don't start if patient is in cardiogenic shock and hypotensive due to the vasodilatory effect
        ii. 0514 Obstructive shock (RV failure in the setting of massive PE)
            1. Decreases pulmonary vascular resistance
        iii. 0530 Cardiac surgery
    c. Doses
        i. 0539 0.25 – 0.75 mcg/kg/min (renally cleared)
C. 0550 Vasopressin
    a. Mechanism of action
        i. 0605 $V1_A$: Vasoconstriction
            1. Good for refractory vasoplegia
        ii. 0620 V2: Free water reabsorption
            1. Can lead to pulmonary edema
        iii. 0635 Non-catecholamine
            1. Hormone: not pH sensitivity in the setting of acidemia
            2. Can increase catecholamine sensitivity
        iv. 0805 Inhibits nitric oxide production (potent vasodilator)
    b. Uses
        i. Septic Shock
            1. 0715- Have decreased production / release of vasopressin so start low doses without titration to replace the lack of endogenous vasopressin
            2. Increase catecholamine sensitivity
            3. Inhibits nitric oxide production
            4. 0833 Monotherapy in septic shock
                a. Higher dose when compared to norepinephrine

b. Found to be as effective as norepinephrine
c. 0850 Most of the time it is added to a patient already on norepinephrine

ii. 0812 Pulmonary embolism
1. Vasoconstriction: Restore mean arterial blood pressure
2. Decrease pulmonary vascular resistance

c. Doses
i. 0.03 units/min

0935- NEW KIDS ON THE BLOCK

Manual
Management of Shock: Part 1

Learning objectives

EXPLAIN WHY HYPOTENSION IS AN EMERGENCY!

LIST OUR CATECHOLAMINE DRUGS AND THEIR MECHANISM OF ACTIONS AND USES

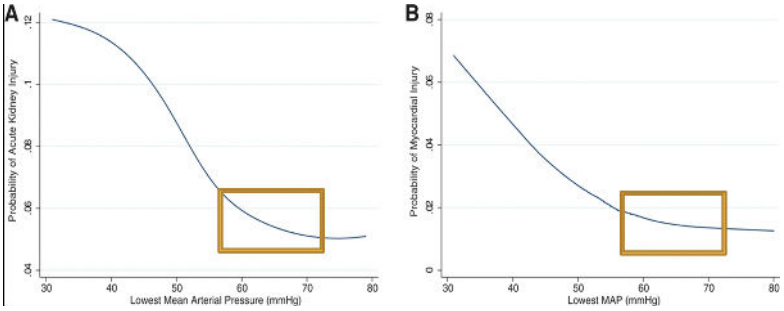
NAME SOME OF THE NEWER TREATMENTS FOR REFRACTORY VASOPLEGIA

Mean Arterial Blood Pressure
Why a mean arterial blood pressure of 65 mm Hg?

Anesthesiology. 2013 Sep;119(3):507-15. doi: 10.1097/ALN.0b013e3182a10e26.

Relationship between intraoperative mean arterial pressure and clinical outcomes after noncardiac surgery: toward an empirical definition of hypotension.

Walsh M[1], Devereaux PJ, Garg AX, Kurz A, Turan A, Rodseth RN, Cywinski J, Thabane L, Sessler DI.



- After MAP <65 start to have an increase in acute kidney injury and myocardial injury

N Engl J Med. 2014 Jul 17;371(3):283-4. doi: 10.1056/NEJMc1406276.

High versus low blood-pressure target in septic shock.

Asfar P, Teboul JL, Radermacher P.

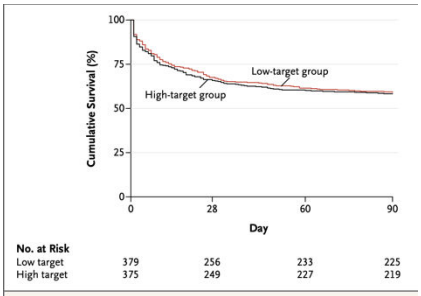


Figure 3. Kaplan–Meier Curves for Cumulative Survival.
Data for the survival analysis, which was performed in the intention-to treat population, were censored at 90 days. There was no significant difference in survival between the high-target group and the low-target group (P=0.57 at 28 days; P=0.74 at 90 days).

- MAP goals of low target(65-70) vs high target(80-95) showed no difference in mortality at 28 or 90 days in septic shock Asfar et al NEJM 2014

Save the Map-

- CNS: Stroke, cord injury, paralysis
- CVS: MI, ischemic extremities
- Respiratory: ARDS, pulmonary edema
- Renal: Acute Kidney Injury, Acute Tubular Necrosis
- Metabolic: Acidosis, Lactate production
- Hepatic: Coagulopathy, platelet dysfunction, hypoalbuminemia
- GI: Pancreatitis, ischemic bowel, bacterial translocation, acalculous cholecystitis

Goals of Shock
The goal of shock is to improve perfusion. How to determine this at the microcirculation level is the question? At this time all we can do is provide optimal MAP.

- Balance perfusion to vital organs and prevent ischemia to non-vital organs (ie gut ischemia)

Organs have critical perfusion pressures:

- Cerebral Perfusion Pressure 50-70 mm Hg
- Coronary Perfusion Pressure 60-80 mm Hg
- Renal Perfusion Pressure 65-70 mm Hg

Improve perfusion why?

- Reduce cellular hypoxia and avoid mitochondrial dysfunction = avoid organ death
- Recall from basics of shock that lactate production is not just due to lack of oxygen (cellular hypoxia) and shifting pyruvate to lactate (anaerobic process)!

Optimize hemodynamics: cardiac output= stroke volume X heart rate

- Stroke volume is determined by:
  1. Preload
  2. Afterload
  3. Contractility

The goal of giving fluids in shock is to improve stroke volume.

- Oxygen Delivery= DO_2 =
  - $Ca0_2$ x CO,
  - $Ca0_2$ (arterial oxygen content)= (1.32 x Hgb x SaO_2) + (0.003 x PaO_2)
    - In shock if Hgb is low $Pa0_2$ becomes important in the delivery of oxygen

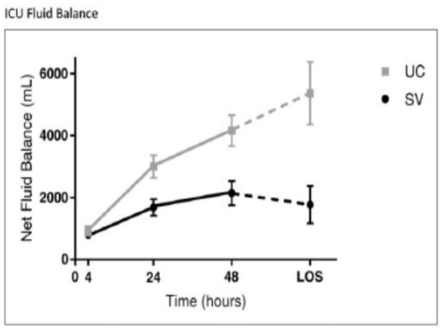
Stroke Volume Targeted Resuscitation

SV measured

- Bioreactance – non-invasive
- Pulse contour analysis – arterial line
- PA catheter

Improved

- Net fluid volume
- Time on vasopressors
- Need for dialysis
- Need for mech vent
- ICU, Hospital LOS



Latham, et al. J Crit Care, 2017

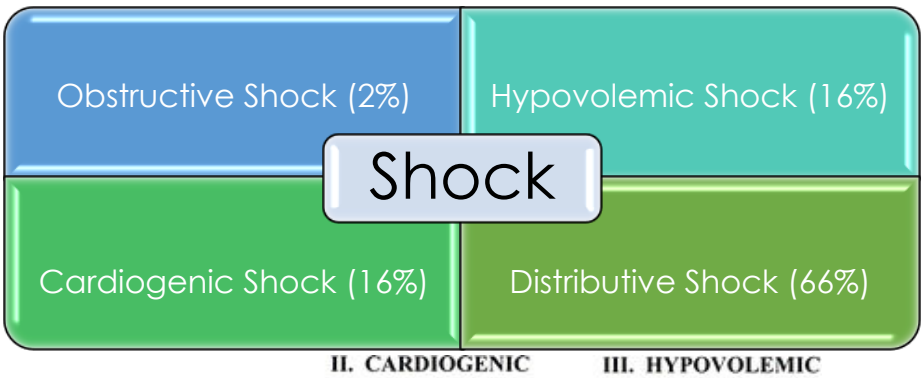
Signs of poor perfusion
Mental status
Capillary refill
Urine output
Mottles extremities
Lactate? = see basics of shock video

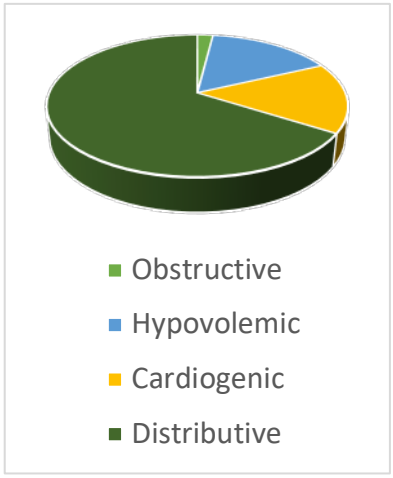
What is the cause of lactic acid elevation in septic shock?

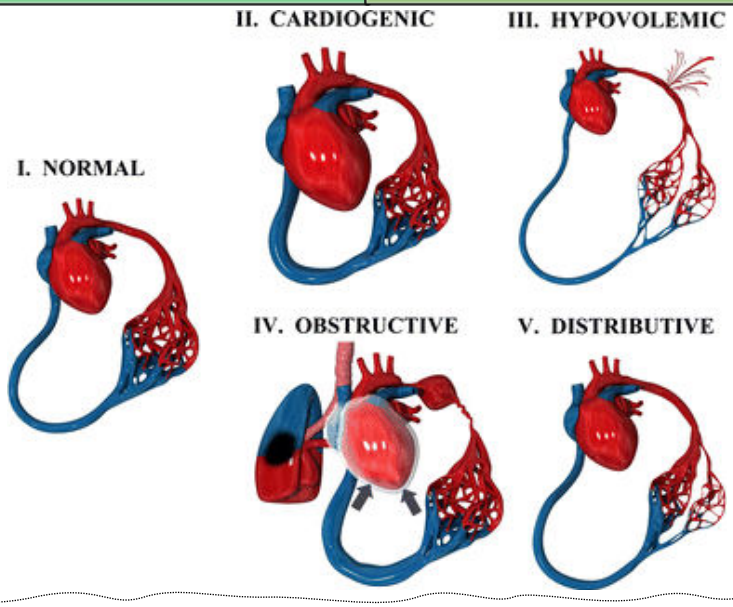
1. Anaerobic metabolism
2. Adrenergic stimulation
   - Mechanism? Epinephrine activation of B2 stimulation breaks down glycogen to glucose and mitochondria are unable to keep up with the rate of glycolysis!

Lactate then becomes an energy source for the heart and brain as well as hormone.

Epidemiology of Shock (SOAP II)







Questions to help you classify shock:

1. Is the cardiac output high of low? what are bedside clues to help you (i.e. pulse pressure, exam - pulse, skin and nail bed)
2. Is the heart full or empty? volume assessment - history, JVD, edema, CXR, pulse pressure, CVP. Invasive hemodynamic Monitoring - PA catheters, ECHO

Example: 75-year-old male with HTN and DM has MI, BP 90/70, HR 120, extremities are cool to the touch. What would be his PA catheter findings?
Increased SVR, decreased CO, increased right atrial and PA pressures. (High filling pressures due to cardiac dysfunction.)

Warm shock

Distributive shock

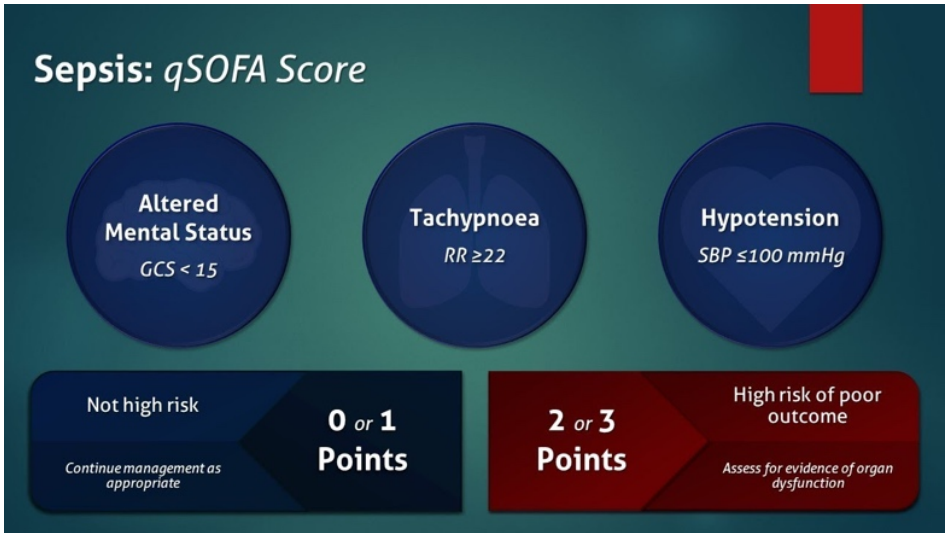
- Mechanism: problem is with the “distribution” of blood flow
  - Decrease stroke volume (i.e. decreased systolic blood pressure) **<<** decreased systemic vascular resistance (i.e. decreased diastolic blood pressure) => widened pulse pressure
- **Septic** 62% *
  - What is the new definition? What is the new literature?
    - Sepsis 3 guidelines (qSOFA - q=quick bedside assessment and SOFA)
    - Sepsis vs Septic Shock. (requiring pressors/lactate > 2)
- **Non-septic**: 4%of shock
  - Increased heart rate: anaphylaxis, liver failure, adrenal insufficiency
  - Normal heart rate: neurogenic

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP[1]; Clifford S. Deutschman, MD, MS[2]; Christopher Warren Seymour, MD, MSc[3]; et al

» Author Affiliations | Article Information

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287



SURVIVING SEPSIS CAMPAIGN RECOMMENDATION HIGHLIGHTS		
	2012	2016
SEPSIS DEFINITION	Systemic manifestation of infection + suspected infection Severe sepsis: sepsis + organ dysfunction	Life threatening organ dysfunction caused by dysregulated response to infection No severe sepsis category
INITIAL RESUSCITATION	at least 30 cc/kg in first 3 hours Crystalloid fluid (no recommendations on 0.9% NaCl vs balanced solution) Albumin if patients require "substantial" fluids (weak)	
	Protocolized care including CVP ScVO2 Normalize lactate	Use dynamic resuscitation markers (passive leg raise) Target MAP of 65mmHg Reassess hemodynamic status to guide resuscitation Normalize lactate
VASOPRESSORS	target MAP of 65 mmHg 1. Norepinephrine 2. Epinephrine if not at target MAP OR vasopressin to reduce norepinephrine requirement 3. Avoid dopamine in most patinets	
STEROIDS	Only indicated for patients with septic shock refractory to adequate fluids and vasopressors	
ANTIBIOTICS	One or more antibiotics active against presumed pathogen Combination therapy (double coverage) for neutropenic patients and pseudomonas	Initial broad spectrum antibiotics (ex: vancomycin + piperacillin-tazobactam) Against combined therapy (i.e. do not double cover pseudomonas) May use procalcitonin to guide de-escalation
SOURCE CONTROL	Achieve within 12 hours, if feasible	Achieve as soon as medically and logically feasible
VENTILATOR	6 cc/kg tidal volume prone patients with severe ARDS (P/F <150 in 2017 guideliens)	
	no recommendation	Against high frequency oscillatory ventilation (HFOV)
	weak recommendation for noninvasive ventilation in select patients with sepsis induced ARDS	Unable to make recommendation on noninvasive ventilation

Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Crit Care Med [Internet] 2017;1.

Cold shock

Obstructive shock 2%

- Decreased pre-load due to “obstruction” of venous return
- Examples: pulmonary embolism, pneumothorax, tamponade

Hypovolemic shock 16%

- Mechanism: Decreased effective intravascular volume
- Examples: Hemorrhagic (GI bleed), Fluid loss (currently Clostridium difficile is more prevalent)

Cardiogenic Shock 16%

- Mechanism: trouble with cardiac contractility
- Examples: myocardial infarction, myocarditis, arrhythmias (e.g. atrial fibrillation with RVR and ventricular tachycardia), mechanical (e.g. aortic stenosis and RV failure)

Terminology 0657

Vasopressor:

- × Induce vasoconstriction
- × Phenylephrine, Vasopressin, Angiotensin II, Selepresin

Inotrope:

- × Increase cardiac contractility= only beta 1

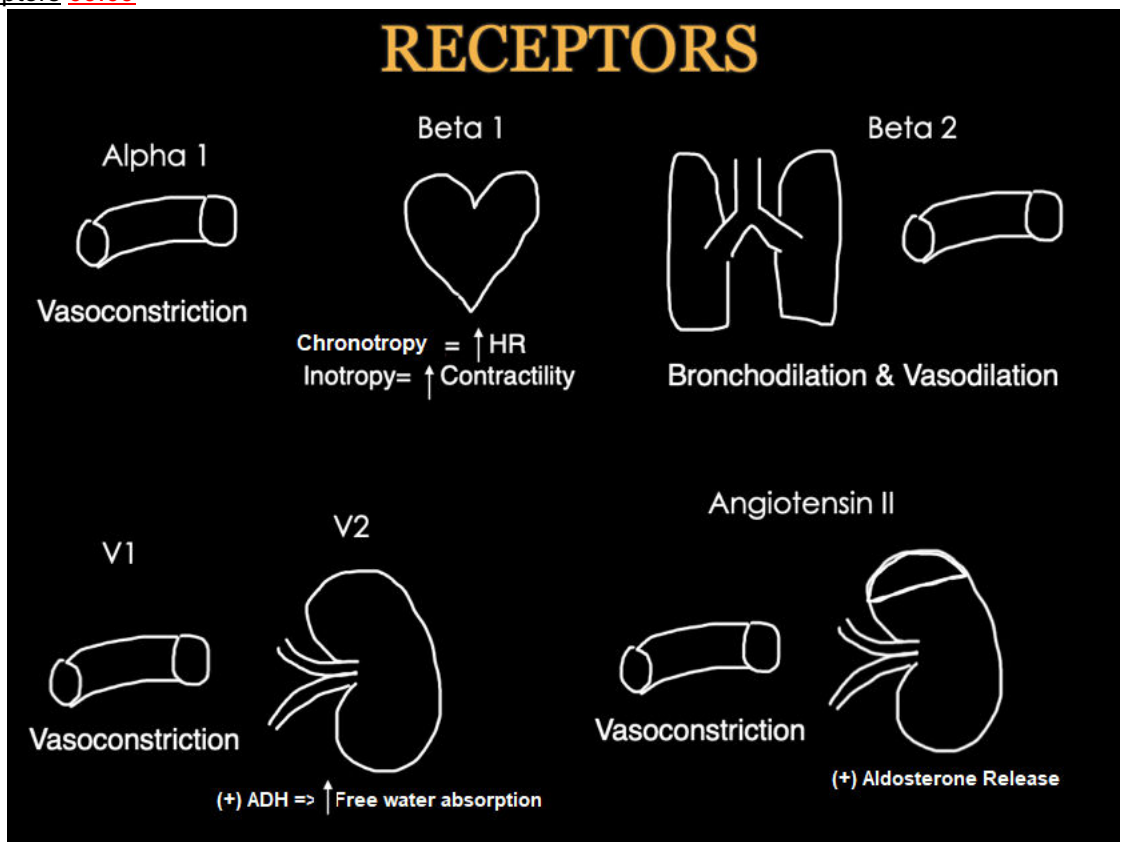
Inopressor:

- × Induce vasoconstriction & increase cardiac contractility
- × Norepinephrine, Dopamine, Epinephrine

Inodilator:

- × Increase cardiac contractility & cause vasodilation
- × Dobutamine, Milrinone, Levosimendan, isoproterenol

Receptors 09:09



Management of Shock: Part 2a

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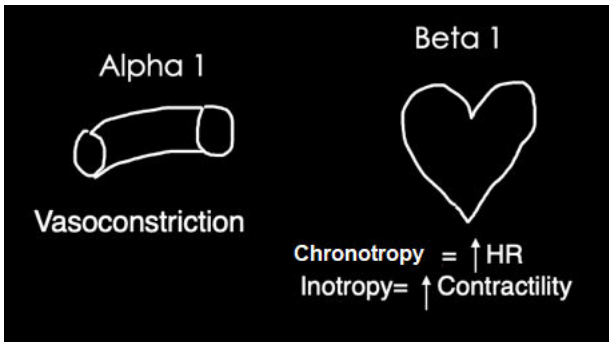
EXPLAIN WHY HYPOTENSION IS AN EMERGENCY!

LIST OUR CATECHOLAMINE DRUGS AND THEIR MECHANISM OF ACTIONS AND USES

NAME SOME OF THE NEWER TREATMENTS FOR REFRACTORY VASOPLEGIA

Norepinephrine

- Mechanism of action
  - Alpha 1: vasoconstriction
  - Beta 1: increase heart rate (chronotropic) + increase contractility (Ionotropic) = Small BUT significant
    - beta 1 effect possibly causing arrhythmias
  - increased inotropy
  - Venoconstriction: improve venous return
- Uses
  - Septic shock, forms of obstructive shock, cardiogenic shock



03:24 Obstructive Shock
03:51 Cardiogenic Shock
Doses

- Starting: 0.05 mcg/kg/min
- Range: 0.05mcg/kg/min – 1 mcg/kg/min

N Engl J Med. 2010 Mar 4;362(9):779-89. doi: 10.1056/NEJMoa0907118.

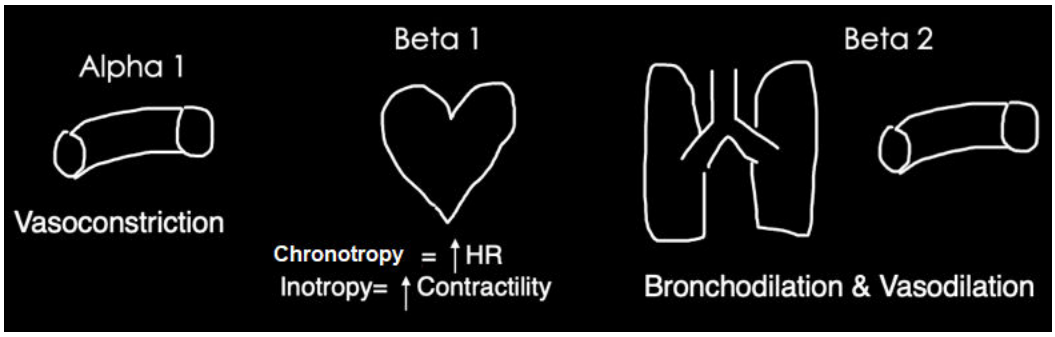
Comparison of dopamine and norepinephrine in the treatment of shock.

De Backer D[1], Biston P, Devriendt J, Madl C, Chochrad D, Aldecoa C, Brasseur A, Defrance P, Gottignies P, Vincent JL; SOAP II Investigators.

Dopamine vs Norepinephrine: No significant difference in the rate of death; the use of dopamine was associated with a greater number of adverse events

Epinephrine

- Mechanism of action
  - Alpha 1: vasoconstriction
  - Beta 1: increase heart rate (chronotropic) + increase contractility (Ionotropic)
  - Beta 2: Bronchodilation and vasodilation
  - Metabolizes glucose to lactate via non-aerobic pathway
  - Insulin resistance and hyperglycemia
    - Would consider placing on insulin drip as SQ insulin is less effective with multiple pressors
- Uses
  - Pediatric Septic Shock- especially less than 1 year old; cold shock
  - Adult Septic Shock
    - Study Epinephrine vs Norepinephrine ; 2nd line in septic shock guidelines
  - Cardiogenic shock (especially with bradycardia)
  - Anaphylactic shock
  - Cardiac arrest
- Doses
  - High doses (1 mg)=> want alpha effects; beta harmful
  - <0.2 mcg/kg/min → primarily beta effects (inotrope)
    - e.g. hypotension related to bradycardia, cardiogenic shock
  - >0.2 mcg/kg/min → Alpha > Beta (vasoconstriction + iontrope)



Intensive Care Med. 2008 Dec;34(12):2226-34. doi: 10.1007/s00134-008-1219-0. Epub 2008 Jul 25.

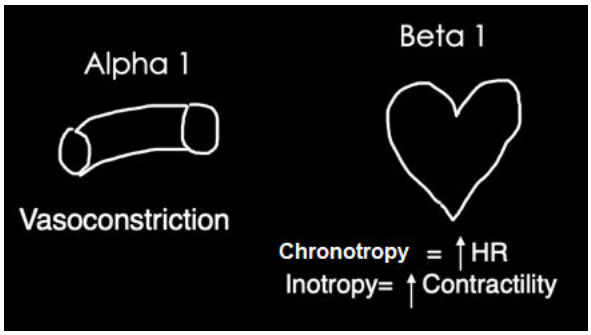
A comparison of epinephrine and norepinephrine in critically ill patients.

Myburgh JA[1], Higgins A, Jovanovska A, Lipman J, Ramakrishnan N, Santamaria J; CAT Study investigators.

Epinephrine vs norepinephrine: no difference in the achievement of a MAP goal

Dopamine

- Mechanism of Action
  - Alpha 1: vasoconstriction
  - Beta 1: increase heart rate (chronotropic) + increase contractility (Ionotropic)
- Uses
  - Cardiogenic Shock: especially with bradycardia
    - Norepinephrine > Dopamine in cardiogenic shock
  - Previously used in pediatric septic shock (now epinephrine is preferred)



- Doses
  - 0.5-5 mcg/kg/min→ D1/D2 receptors (coronary, cerebral, renal and splanchnic vasodilation)
  - 5-10 mcg/kg/min → primary Beta 1 (ionotropic)
  - >10 mcg/kg/min → Alpha > Beta (vasoconstriction + ionotropic)
- Arrhythmogenic

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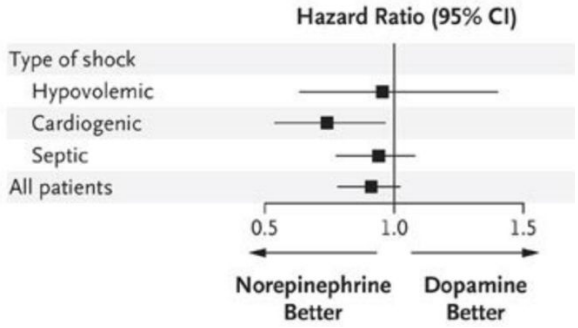
Dopamine vs Norepinephrine in cardiogenic shock: Dopamine was associated with more arrhythmias



Which Drug is BETTER?

Norepinephrine vs Epinephrine	Epinephrine vs Dobutamine and Norepinephrine
• Myburgh et al. Intensive Care Med. 2008 Dec;34(12):2226-34 • 4 Australian ICU, RCT • No 28 or 90 day mortality difference Epi vs NE • No difference in achieving MAP Goals • Epi group-needed more insulin and developed elevated lactates	• Annane et al. Lancet. 2007 Aug 25;370(9588):676-84. • N=330 patients with septic shock • No mortality difference Epi (40%) and NE (34%) • No difference in adverse effects

Intensive Care Med. 2008 Dec;34(12):2226-34. doi: 10.1007/s00134-008-1219-0. Epub 2008 Jul 25.

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Lancet. 2007 Aug 25;370(9588):676-84.

Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial.

Annane D[1], Vignon P, Renault A, Bollaert PE, Charpentier C, Martin C, Troché G, Ricard JD, Nitenberg G, Papazian L, Azoulay E, Bellissant E; CATS Study Group.

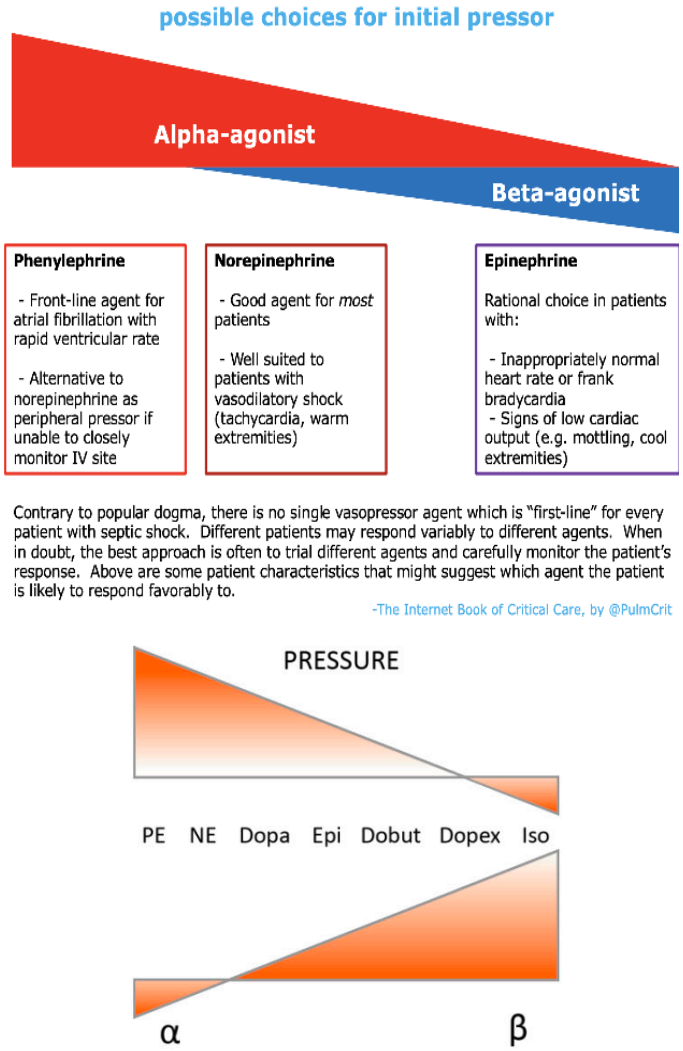
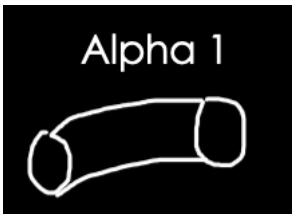


Figure 6: Effects of vasoactive agents on pressure and blood flow[22]

Phenylephrine

- Mechanism of Action
  - Alpha 1: vasoconstriction ONLY
- Possible reflex bradycardia
- Uses
  - Sepsis, Refractory vasoplegia
  - Note: can increase both systemic and pulmonary vascular resistance = BAD w/ cardiogenic shock +/- right heart failure
- Dose
  - 50 mcg/min to 300 mcg/min



Push Dose Pressors

Phenylephrine

- Pre-made syringe where each ml contains 100 mcg of phenylephrine
- Vial Contains 10 mg/ml→
  - Draw up 1 ml (10 mg) of phenylephrine from the vial and inject 1 ml into a 100 ml bag of normal saline so each 1 ml =100 mcg
  - Draw up 2 ml (20 mg) of phenylephrine from the vial and inject 2 ml into a 250 ml bag of normal saline so each 1 ml =80 mcg
- Pharmacokinetics
  - Onset: 1 minute
  - Duration: 10-20 minutes
  - Push Dose: 1-2 ml (80-200 mcg) every 2-4 minutes

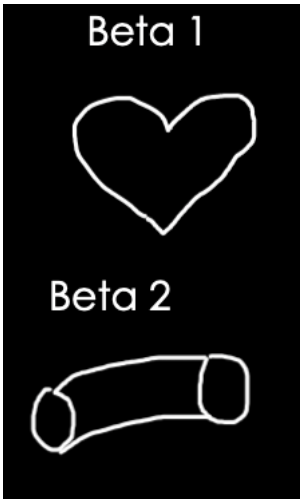
Epinephrine

- Both alpha and beta= inopressor
- NEVER give 1 mg of epinephrine to someone with a pulse
- Ampule contains 100 mcg/ml
  - Take a 10 ml syringe of normal saline & get rid of 1 ml => 9 ml of normal saline + draw up 1 ml of epinephrine so each ml = 10 mcg
- Pharmacokinetics
  - Onset: 1 minute
  - Duration: 5-10 minutes
  - Push Dose: 1-2 ml (10-20 mcg) every 2-5 minutes

Management of Shock: Part 2b

Dobutamine

- Mechanism of Action
  - Beta 1: increase heart rate (chronotropic) + increase contractility (Ionotropic)
  - Beta 2: bronchodilation
    - Caution: if hypotensive can vasodilate with the beta 2 effects and drop their blood pressures- in this case can start norepinephrine or epinephrine
- Uses
  - Cardiogenic shock- mainly want the Beta 1 effect for contractility
  - Septic shock- not primary agent, but 2nd or 3rd agent where they need cardiogenic support
    - Septic Cardiomyopathy: cytokine release due to sepsis
  - Obstructive shock (RV failure in the setting of a massive PE)
    - Need to restore blood pressure with norepinephrine
- Doses: 2.5-20 mcg/kg/min
- Caution: arrhythmogenic



Milrinone

- Mechanism of Action
  - Phosphodiesterase 3 inhibitor (prevents degradation of cAMP
  - Increases lusitropy (diastolic relaxation)
    - Allows for a larger filling volume
  - Increases inotropy
  - Can increase chronotropy
    - which means arrythmias are possible, but are much less common
  - Vasodilator- decreases systemic vascular resistance and peripheral vascular resistance
- Uses
  - Cardiogenic shock
    - caution with starting or don't start if patient is in cardiogenic shock and hypotensive due to the vasodilatory effect
  - Obstructive shock (RV failure in the setting of massive PE)
    - Decreases pulmonary vascular resistance
  - Cardiac surgery
- Doses
  - 0.25 – 0.75 mcg/kg/min (renally cleared)

Vasopressin

- Mechanism of Action
  - $V1_A$: Vasoconstriction
    - Good for refractory vasoplegia
    - Works by inhibiting nitric oxide production (potent vasodilator)
  - V2: Free water reabsorption
    - Can lead to pulmonary edema
- Non-catecholamine, and can increase sensitivity to catecholamine
- Hormone: not pH sensitivity in the setting of acidemia
- Uses
  - Septic shock - have decreased production / release of vasopressin so start low doses without titration to replace the lack of endogenous vasopressin
    - Monotherapy in septic shock
    - Higher dose when compared to norepinephrine
    - Found to be as effective as norepinephrine
    - Most of the time it is added to a patient already on norepinephrine
  - Pulmonary embolism
    - Vasoconstriction: restore mean arterial blood pressure
    - Decrease pulmonary vascular resistance
- Doses
  - 0.03 units/min

09:35- NEW KIDS ON THE BLOCK

Studies for additional reading for septic shock

- EGDT (Rivers NEJM 2001 over 16 years ago), ARISE, PROMISE, ProCESS(2014) - EGDT(2.8L) vs Usual care (2.3L) vs Fluid protocol (3.3L)- no mortality difference between the three strategies.
- Seymour et al NEJM 2017 - NY hospitals (3 hour bundle) showed 4% relative increase in death with each hour delay of antibiotics. Interestingly they found → delay of bolus or fluid resuscitation did not show any association with mortality.
- kumar 2006 - mortality 100x more likely if > 36 hours delay in antibiotics
- Whiles crit care 2007 - each hour delay of antibiotics in sepsis had an 8% incidence of progression to septic shock and 5% progression to mortality