SHOCK

HYPOTENSION MANAGEMENT: INTRODUCTION TO VASOPRESSORS

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DISCLOSURE

- No conflicts to disclose.

DEFINITION OF SHOCK

" Shock is a life-threatening condition of circulatory failure, causing inadequate oxygen delivery to meet cellular metabolic needs and oxygen consumption requirements, producing **cellular and tissue hypoxia.**" (Gaieski & Mikkelsen, 2020).

Cellular and tissue hypoxia occurs due to:

1) Reduced oxygen delivery
2) Increased oxygen consumption
3) Inadequate oxygen utilization

Although we typically think of shock as persistent hypotension, it is more about a lack of perfusion/oxygen delivery. A person can actually be in shock but still have a normal BP.

INADEQUATE TISSUE PERFUSION

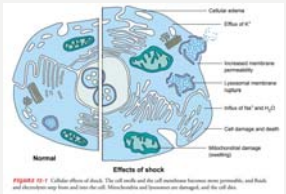
Physiology of oxygen transport:
- Oxygen delivery (DO_2) is the volume of oxygen delivered (mL/minute) from the left ventricle each minute.

- $DO_2 = CO \times CaO_2 \times 10$
  - CO = Cardiac Output
  - CaO_2 = arterial content of oxygen

- Arterial content of oxygen = $(1.34 \times Hgb \times SaO_2) + (0.0031 \times PaO_2)$

INADEQUATE TISSUE PERFUSION

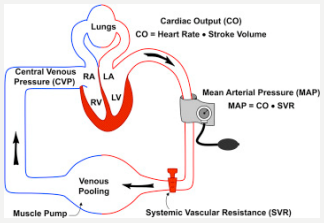
- What happens when tissue is inadequately perfused??
  - Let's look at a cellular level.



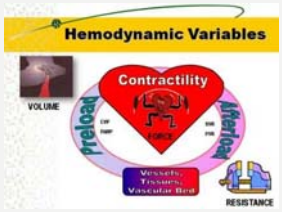
HEMODYNAMIC BASICS…A REVIEW

- Cardiac output- the amount of blood that is pumped out of the ventricles in one minute.
  - Normal = 4-8 L/minute
  - HR x SV = CO
- Stroke volume- the amount of blood pumped out of the ventricle with each contraction
  - Normal = 60-100 mL/minute
  - Volume is altered by heart rate or rhythm (relates to ability of ventricle to completely fill)

(Rn.com, 2016)



- Preload- the volume required to stretch the cardiac muscle fibers in the atrial and ventricles (to accommodate fluid in the chambers).
  - Right sided preload = CVP; normal 2-8 mm/Hg
  - Left sided preload = PAWP (pulmonary artery wedge pressure); normal 4-12 mm/Hg
- Afterload (i.e. systemic vascular resistance)- the resistance or pressure the ventricular heart muscle must overcome to open the aortic valve and eject volume
  - Normal SVR is 800-1200
  - Hypertension = increased SVR,
  - Hypotension = decreased SVR



TYPES OF SHOCK

1) Hypovolemic shock

2) Cardiogenic shock

3) Distributive shock

4) Obstructive shock

HYPOVOLEMIC SHOCK

- A state of decreased intravascular volume with resultant decreases in preload and cardiac output
  - The body compensates by increasing peripheral vascular tone, cardiac contractility and heart rate which initially are beneficial but eventually result in a hypermetabolic state and localized tissue ischemia.
  - Increased vascular tone may also result in tissue ischemia d/t inconsistent microcirculatory flow.

(Todd et al., 2009)

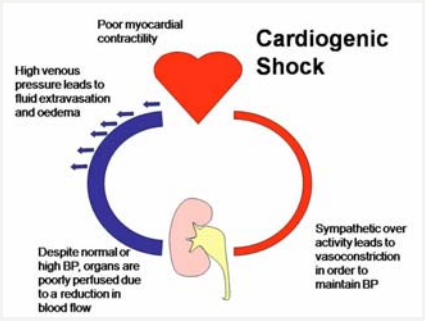
HYPOVOLEMIC SHOCK

Causes include:
- Hemorrhagic:
  - Internal or external bleeding
- Non-hemorrhagic:
  - Significant GI losses (emesis, fistula, diarrhea)
  - Significant urinary losses (hyperosmolar state)
  - Third spacing (capillary leakage)
  - Malnutrition
  - Open wounds (e.g. burns, open abdomen)

CARDIOGENIC SHOCK

- PUMP FAILURE!
- Inadequate tissue perfusion due to primary ventricular failure
  - Most common cause of mortality from coronary artery disease

(Todd et al., 2009)



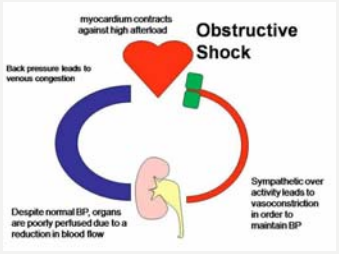
CARDIOGENIC SHOCK

- Causes:
  - MI –once 40% of the myocardium has been irreversibly damaged, cardiogenic shock may occur.
  - Myocarditis
  - Cardiomyopathies
  - Valvular disease
  - Arrhythmias

OBSTRUCTIVE SHOCK

- Caused when forces compress the chambers or the heart, the great vessels (superior vena cava, inferior vena cava, pulmonary arteries) or a combination of these.
  - Impairs diastolic filling OR systolic contraction of the heart
  - Decreases forward flow of blood and it backs up.

(Todd et al., 2009)



OBSTRUCTIVE SHOCK

- Causes:
  - Pericardial tamponade
  - Constrictive pericarditis
  - Pulmonary embolic
  - Aortic dissection
  - Large intrathoracic tumors
  - Tension pneumothoraces

DISTRIBUTIVE SHOCK

- Characterized by decrease in peripheral vascular tone (vasodilation).
  - Decreased systemic vascular resistance→ relative hypovolemia (empty tank because the tank is big!)

(Todd et al., 2009)

DISTRIBUTIVE SHOCK

- Causes:
  - Sepsis
  - Anaphylaxis
  - Neurogenic
  - Pharmacologic (e.g. sedating medications)
  - Endocrinologic (e.g. adrenal insufficiency)

HEMODYNAMIC VARIABLES

	Cardiac Output	SVR	Preload (PAWP)
Hypovolemic Shock	↓	↑	↓
Cardiogenic Shock	↓	↑	↑
Obstructive Shock	↓	↑	↑
Distributive Shock			
pre-resuscitation	↓	↑	↓
post-resuscitation	↑	↓	↔

SIGNS/SYMPTOMS OF END-ORGAN DYSFUNCTION

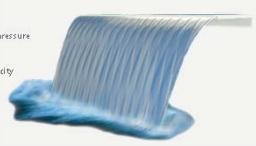
Organ System	Symptoms of signs
Central nervous system	Mental status changes: agitation, obtundation, coma
Cardiovascular	Tachycardia or other dysrhythmias, hypotension, elevated or depressed JVD, disparate peripheral pulses
Lungs	Tachypnea, cyanosis, respiratory failure
GI	Decreased bowel sounds (ileus), signs of liver dysfunction
Renal	Oliguria
Skin	Cool, clammy

MANAGEMENT OF SHOCK

- The underlying goal of shock management is to improve tissue oxygen perfusion.
  - Step #1: Determine type of shock and it's cause!
  - Special considerations and treatments depending on type of shock
    - Obstructive shock: Remove/treat obstruction (e.g. needle decompression of tension pneumothorax, pericardiocentesis for cardiac tamponade.)
    - Distributive (septic) shock: Source control (e.g. antibiotics, I&D of abscess)
    - Hypovolemic shock: Identify source of hemorrhage and stop bleeding (e.g. surgically).
    - Cardiogenic shock: Various causes require different treatments (e.g. revascularization in shock caused by MI, IABP for severe aortic stenosis).

MANAGEMENT OF SHOCK

- Step # 2:
  - Give fluids!! Give them early!
    - Restores perfusion
    - Replaces volume lost via hemorrhage, capillary leak or redistribution
  - Options:
    - Crystalloid (e.g. normal saline, lactated ringers)
      - Expand blood volume
    - Colloids (e.g. albumin)-
      - Expand blood volume more rapidly due to higher oncotic pressure
    - Blood products
      - Higher oncotic pressure and increase oxygen carrying capacity but this doesn't necessarily translate into improved survival unless blood is specifically needed (e.g. Hgb < 7.0)



MANAGEMENT OF SHOCK

•Step #3: Use the big guns

VASOPRESSOR →

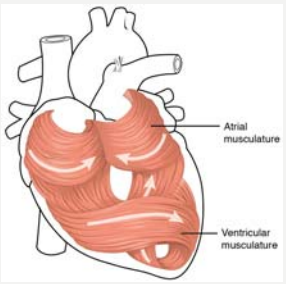
VASOPRESSORS

- Cause vasoconstriction in a variety of ways:
  - **Alpha adrenergic receptors-** located in vascular walls and activation induces significant vasoconstriction.
  - **Beta adrenergic receptors-**
    - Beta-1 receptors: most common in the heart and mediate increases in inotropy (contraction) and chronotropy (heart rate) with minimal vasoconstriction.
    - Beta-2 receptors: Induce vasodilation in blood vessels
  - **Dopamine receptors-** present in the renal, splanchnic (mesenteric), coronary and cerebral vascular beds. Stimulation leads to vasodilation. A second subtype of dopamine receptors cause vasoconstriction by inducing norepinephrine release.

(Manaker, S., 2018)

INOTROPES

- Agents that augment cardiac output by increasing contractility
  - Some vasopressors have inotropic effects.
  - Dobutamine is not a pressor but an inotrope.



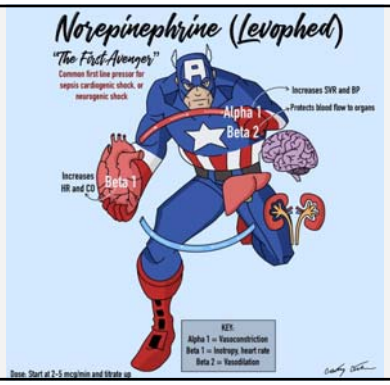
EFFECTS OF CATECHOLAMINE DRUGS ON ADRENERGIC RECEPTORS:

Catecholamine	Alpha	Beta-1	Beta -2
Dobutamine	--	++	+
Dopamine (mod. dose)	--	+++	+++
Dopamine (high dose)	++	+++	+++
Epinephrine	+++	++++	+++
Norepinephrine	+++	+	--
Phenylephrine	+++	--	--

(Marino, P., 2014)

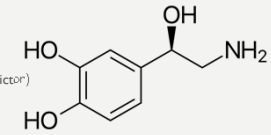
3 FUNDAMENTAL CONCEPTS OF VASOPRESSORS/INOTROPES

1) One drug, many receptors: A drug often has multiple effects because it binds to more than one type of receptor.
2) Dose-response curve: Certain adrenergic receptors are activated based on dosage.
3) Direct vs. reflex actions. A drug can affect MAP by direct actions on receptors and reflex actions triggered by the pharmacologic response.



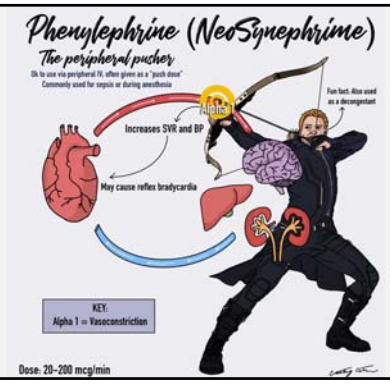
(Cichon, 2019)

NOREPINEPHRINE



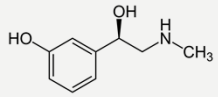
- Potent alpha adrenergic effects (potent vasoconstrictor)
  - Increased systolic and diastolic pressure
  - Increased venous return
  - Increased cardiac filling pressure
- Less potent beta-1 adrenergic stimulation
  - Increased chronotropic function (limited by the baroreflex of vasoconstriction resulting in little change in heart rate).
- Pressor of choice for septic shock (because fewer adverse effects than dopamine or epinephrine).
- Also helpful in other distributive shocks and a temporizing agent in cardiogenic shock

(Todd et al., 2009)



(Cichon, 2019)

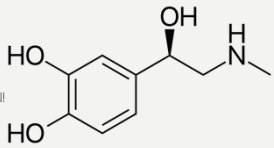
PHENYLEPHRINE



- Pure alpha adrenergic stimulation
- Increases MAP primarily by increasing systemic vascular resistance (increases afterload!)
- Increase in SVR impairs cardiac output (increases afterload) so not a good choice for cardiogenic shock.
- Used for distributive shock if tachyarrhythmias are a concern.
- Adverse effects include bradycardia, low cardiac output (usually in patients with cardiac dysfunction) and renal hypoperfusion.

(Cichon, 2019)

EPINEPHRINE

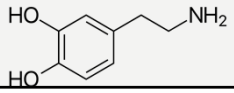


- MAXIMUM CATECHOLAMINE STIMULATION!
- Potent beta-1 adrenergic receptor activity
- Moderate beta-2 and alpha-1 activity.
- Low dose epi increases cardiac output due to beta-1 receptor inotropic and chronotropic effects
- Higher dose epi plays mostly to alpha-1 receptors increasing SVR in addition to increased CO.
- Used most often in the treatment of anaphylaxis (also blunts mast cell response!).
- Causes lactic acidosis.
- Use as vasoconstrictor often limited by tachycardia.
- Important part of ACLS in cardiac arrest (drug of choice in extreme situations).

(Cichon, 2019)

DOPAMINE

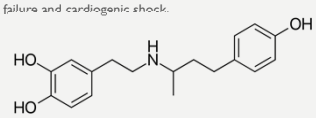
- Dose dependent effects
- Lowest dose (1-2 mcg/kg/min)- acts on dopamine 1 receptors in the renal, mesenteric, cerebral and coronary beds resulting in selective vasodilation.
  - Dopamine increases urine output by augmenting renal blood flow but "renal dose dopamine" doesn't actually help or protect the kidneys.
- Doses between 2 and 5 mcg/kg/min have variable effects depending on the patient. Mildly increases SVR and MAP.
- Moderate dose (5-10 mcg/kg/min)- also stimulates beta-1 adrenergic receptors for inotropic effects.
- High dose (10-20 mcg/kg/min)- predominantly effects alpha receptors and produces vasoconstriction with an increased SVR. However, weaker than norepinephrine at this.
- Can use dopamine to treat bradycardia.

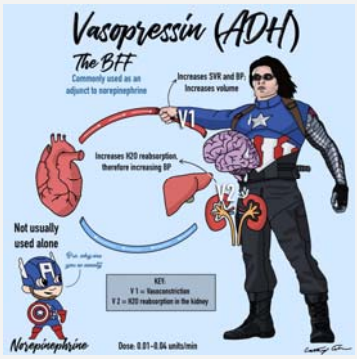


(Cichon, 2019)

DOBUTAMINE

- Not a pressor but an inotrope→ actually causes vasodilation.
- Predominantly beta-1 effects increasing inotropy, chorontropy and reducing left ventricular filling pressure
  - In heart failure patients, this causes a reduction in cardiac sympathetic activity (gives the heart a break from working too hard!)
- Minimal alpha and beta-2 effects result in overall vasodilation→ increased cardiac output plus decreased SVR +/- a small reduction in blood pressure.
- Used in severe, medically refractory heart failure and cardiogenic shock.

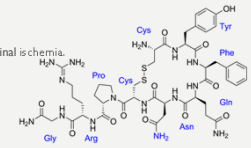




(Cichon, 2019)

VASOPRESSIN

- Not a traditional pressor but a hormone! (Antidiuretic hormone)→ used as hormone replacement as ADH is deficient in hemorrhagic and vasodilatory shock.
- Causes vasoconstriction and anti-diuretic effects (increases preload!)
- Synergistic with pressors (helps them work better!)
- Also allows for pressor titration reducing the risk of deleterious effects.
- Has less effect on pulmonary arteries than other pressors so good for treating patients with pulmonary hypertension/RV failure.
- Potential adverse effects:
  - Hyponatremia
  - Splanchnic vasoconstriction- slightly higher risk of intestinal ischemia.
    This risk is increased with doses > 0.06 units/min



VASOPRESSOR COMPLICATIONS

- Hypoperfusion- caused by excessive vasoconstriction (especially if the patient has not been adequately resuscitated) resulting in inadequate perfusion of the extremities, mesenteric organs or kidneys. (e.g. ischemic limbs, kidney failure, gastritis, shock liver, ischemic bowel, translocation of gut flora with resultant bacteremia).
  - However, renal and mesenteric blood flow during excessive vasoconstriction is not as bad as that during the untreated hypotension so the benefit outweighs the risk, especially given the life-saving potential of these drugs.
- Dysrhythmias- specifically caused by activation of beta-1 adrenergic receptors leading to tachyarrhythmias (including atrial fibrillation and ventricular tachycardias).
  - The incidence of dysrhythmias is worse with dopamine vs. norepinephrine. Epinephrine is also a frequent offender.

(S. Manaker, 2018)

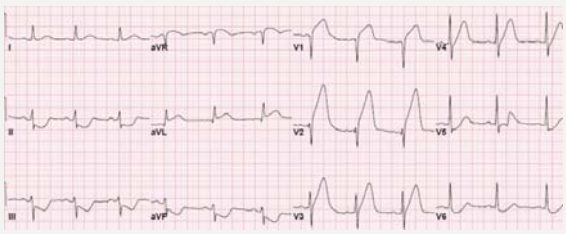
COMPLICATIONS CONTINUED…

- Myocardial Ischemia- increased chronotropy and inotropy can increase myocardial oxygen consumption and despite coronary vasodilation, perfusion may not be adequate enough to meet demand.
- Local tissue damage- extravasation of vasopressors can lead to local vasoconstriction and tissue ischemia. Recommended central line administration but what evidence is there??
- Hyperglycemia – due to inhibition of insulin secretion. Usually mild. Norepinephrine and epinephrine are worse offenders than dopamine.

CASE #1

- Mr. C is a 63-year-old male patient with previous medical history of tobacco abuse, hypertension and GERD who presents to the emergency department with chest and back pain as well as diaphoresis.
  - Vital signs are: BP 86/49, HR 114, RR 24, O2 sat 95%. His blood pressure improves initially with a 500 mL normal saline bolus.

This is Mr. C's EKG….what's going on?



They take Mr. C straight to the cath lab and find severe, multi-vessel CAD including L main disease with an EF of 30%. They are unable to stent him so ask CV surgery to see him.

Mr. C is in the cath lab recovery room with when he begins to decompensate again with the following vital signs:
BP: 79/42
HR: 120
RR 30
O2 sat 91%

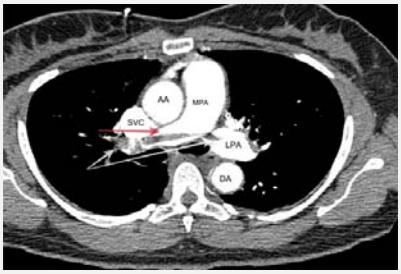
They give the patient another 500 mL fluid bolus which helps a little. However, his extremities are cold and clammy and hypotension returns. Norepinephrine is started through a peripheral IV while anesthesia places a RIJ central line. The cardiologist requests a measured venous saturation which returns at 40. They decide to float a swan to get some more information and find the patient's cardiac output is 1.4. SVR is 1800. PAWP is 20.

What kind of shock is this? What should we do about it?

CASE #2

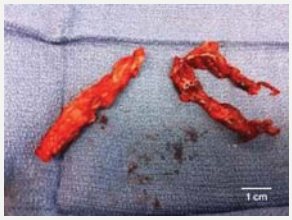
- Mr. O is a 63-year-old male patient with previous medical history of tobacco abuse, hypertension and GERD who presents to the emergency department with chest and back pain as well as diaphoresis.
  - Vital signs are: BP 86/49, HR 114, RR 24, O2 sat 92%. His blood pressure improves initially with a 500 mL normal saline bolus.

Mr. O. also mentions that he's had a a few episodes of hemoptysis over the last several days and is getting winded easily. His EKG has no ST elevations but this is his chest CT:



After getting back from CT, Mr. O. develops acute respiratory distress and hypoxia with O2 sats in the low 80s. His blood pressure has dropped to 79/42. The ED doc orders norepinephrine and after a short trial of biPAP, he intubates Mr. F. and orders heparin and a stat echocardiogram. The echocardiogram reveals severe right ventricular dysfunction and tPA is ordered.

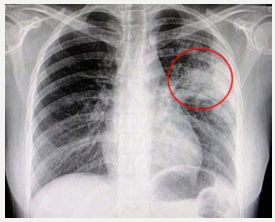
What kind of shock does Mr. O have??



CASE #3

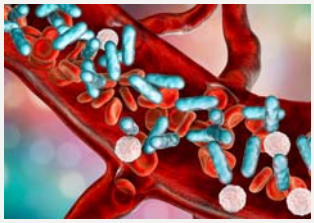
- Mr. C is a 63-year-old male patient with previous medical history of tobacco abuse, hypertension and GERD who presents to the emergency department with chest and back pain as well as diaphoresis.
  - Vital signs are: BP 86/49, HR 114, RR 24, O2 sat 88%. His blood pressure improves initially with a 500 mL normal saline bolus.

Mr. D is put on 2 L of oxygen and chest x-ray is obtained which looks like this…



- Mr. O is also noted to have a fever of 103 in the ED and has a productive cough. He is put on 4 L nasal cannula with improvement in O2 sat. After he returns from chest x-ray, he becomes hypotensive again with pressure of 79/42. Since he ruled in for sepsis, he is given 30 mL/kg fluid bolus and antibiotics are initiated for community acquired pneumonia. His pressure does not improve significantly with further fluid resuscitation so levophed is initiated.

What kind of shock is this??



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