Let's Get Critical: Critical Care Pharmacotherapy You Should Know

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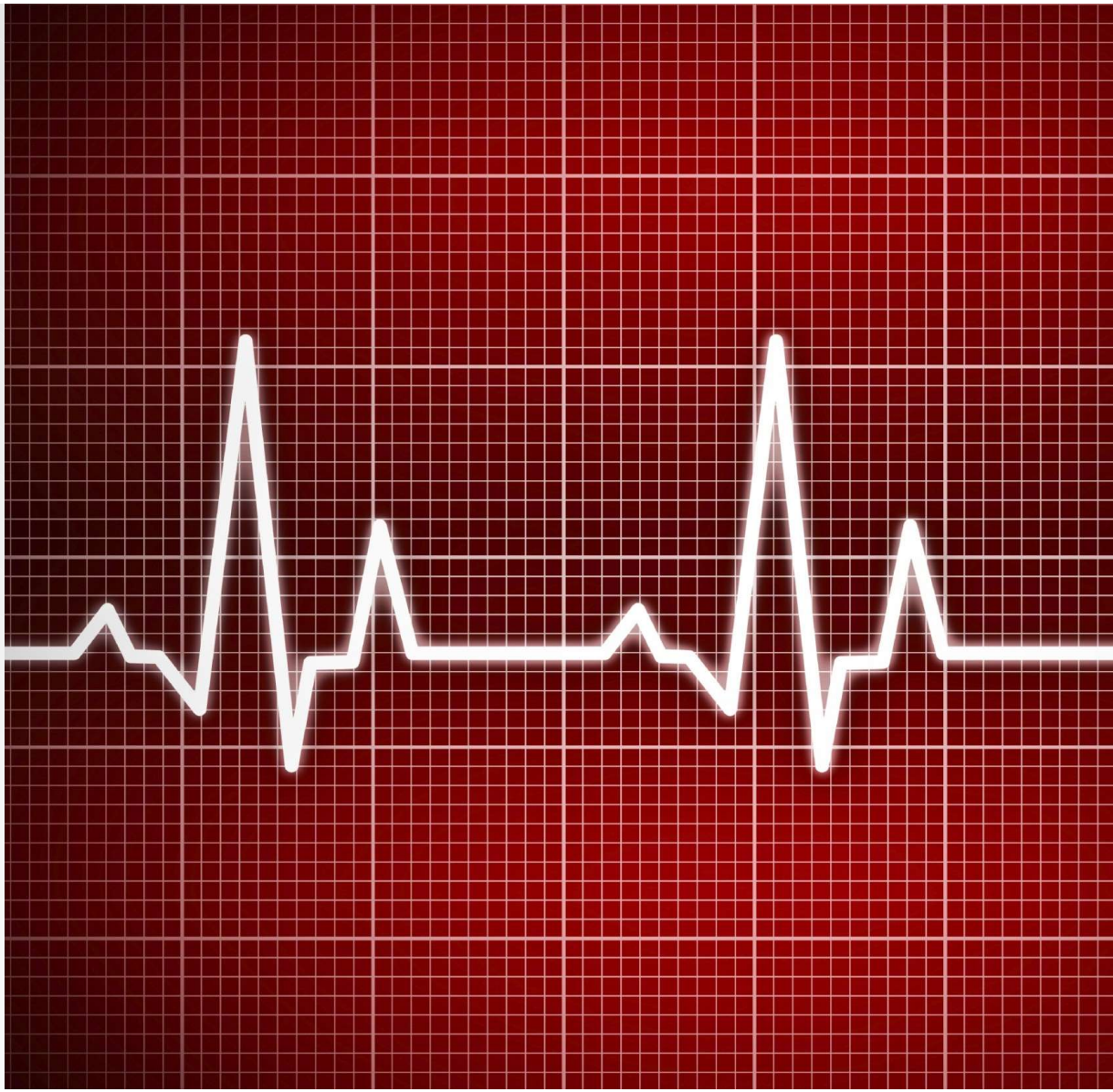


Disclosures

- I have no relevant relationships with ineligible companies to disclose.

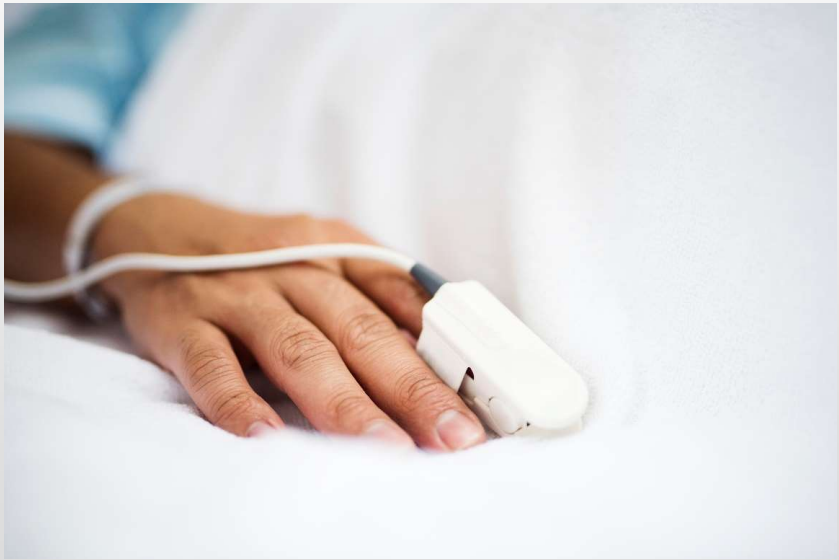
Objectives

At the conclusion of this session, participants should be able to:

- Discuss medications used for hemodynamic support of the patient in shock
- Create a pharmacotherapy plan for rapid sequence intubation
- Select the best antiarrhythmic medication(s) for new-onset arrhythmias

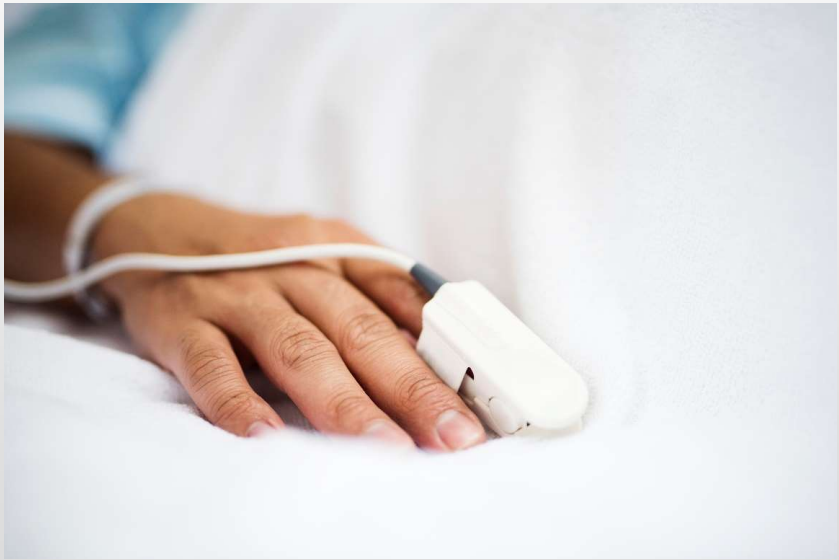
Patient Case

- LM is a 68-year-old female
- PMH: type 2 diabetes, ischemic cardiomyopathy (EF 40%), peripheral vascular disease
- Chief complaint: increased shortness of breath x 1 week, fatigue
- Admitted to internal medicine floor for treatment of fluid overload, AKI



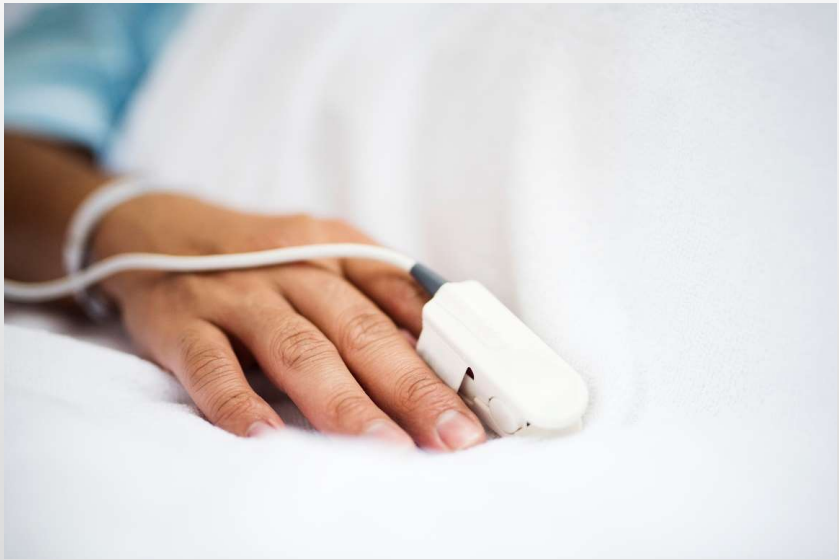
Patient Case (cont)

- Hospital Day 2: LM is orthostatic per RN, complaining of chest discomfort. Provider notified and begins workup
- LM becomes more tachycardic throughout the day & is started on nasal cannula for O_2 sat of 91%. ECG with sinus tach, SvO_2 60%. Given a dose of diuretic
- LM is found unresponsive @ 1145. CODE BLUE called



Patient Case (cont)

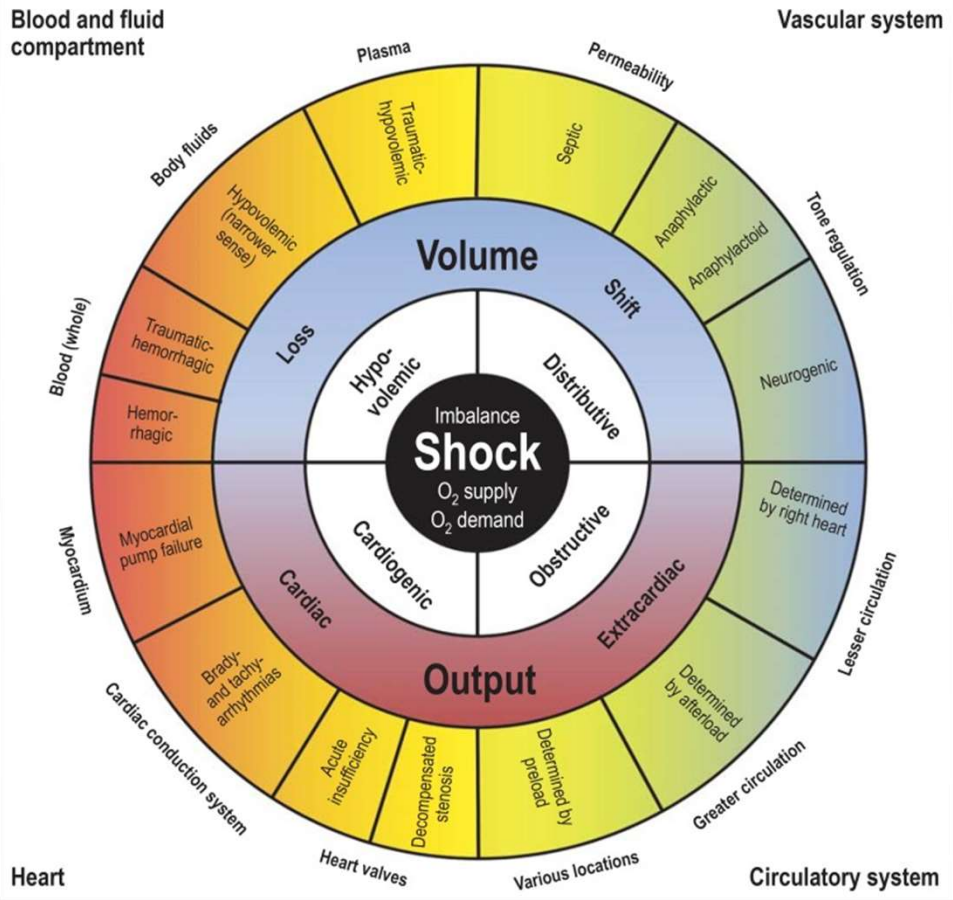
- ICU team decides to intubate – which medications should this patient be given?
- After intubation the patient is hypotensive – how do we correct blood pressure?
- The patient is started on medication for hemodynamic support and develops a new tachycardia. ECG reveals atrial fibrillation – how do we treat the patient?



Hemodynamic Support of The Patient In Shock

What kind of shock are we treating?

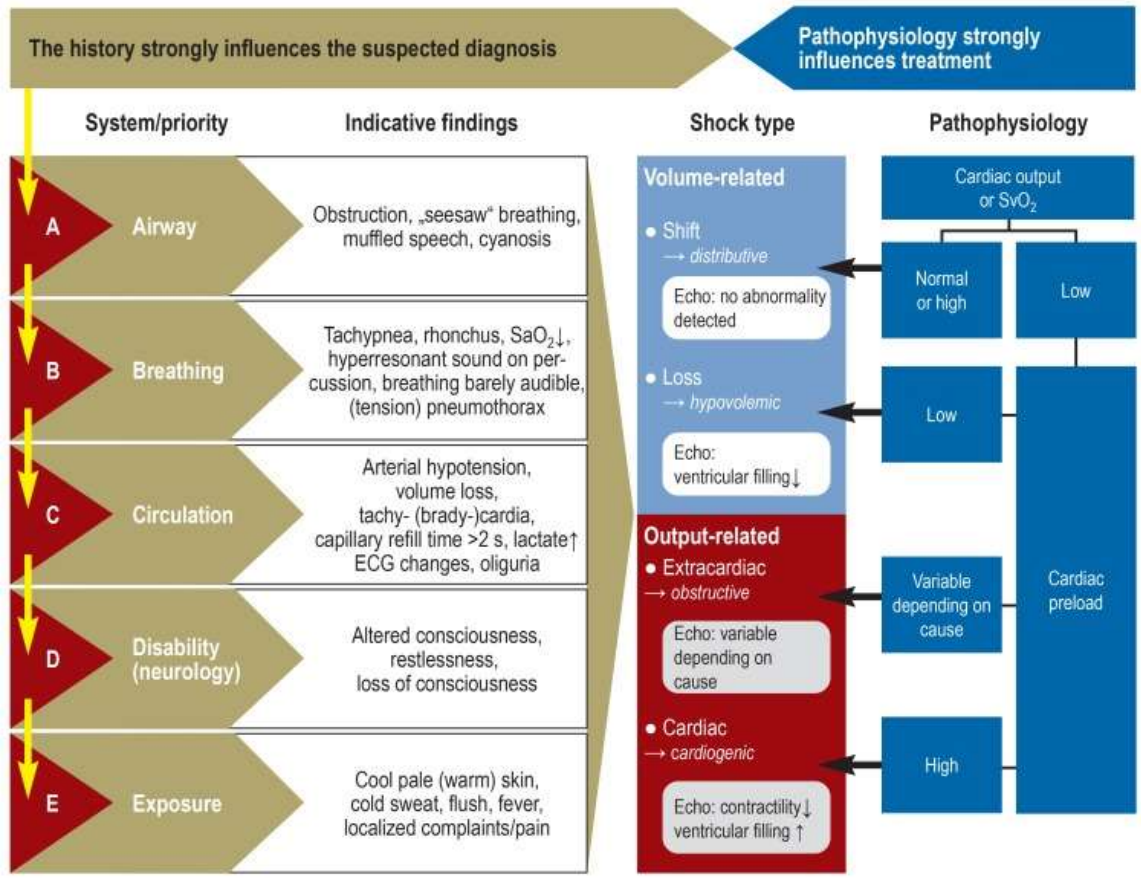
Classification of Shock Types



- Hypovolemic Shock
- Cardiogenic Shock
- Obstructive Shock
- Distributive Shock

Standl T, et al. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6323133/figure/F1/?report=objectonly.

Differential Diagnosis



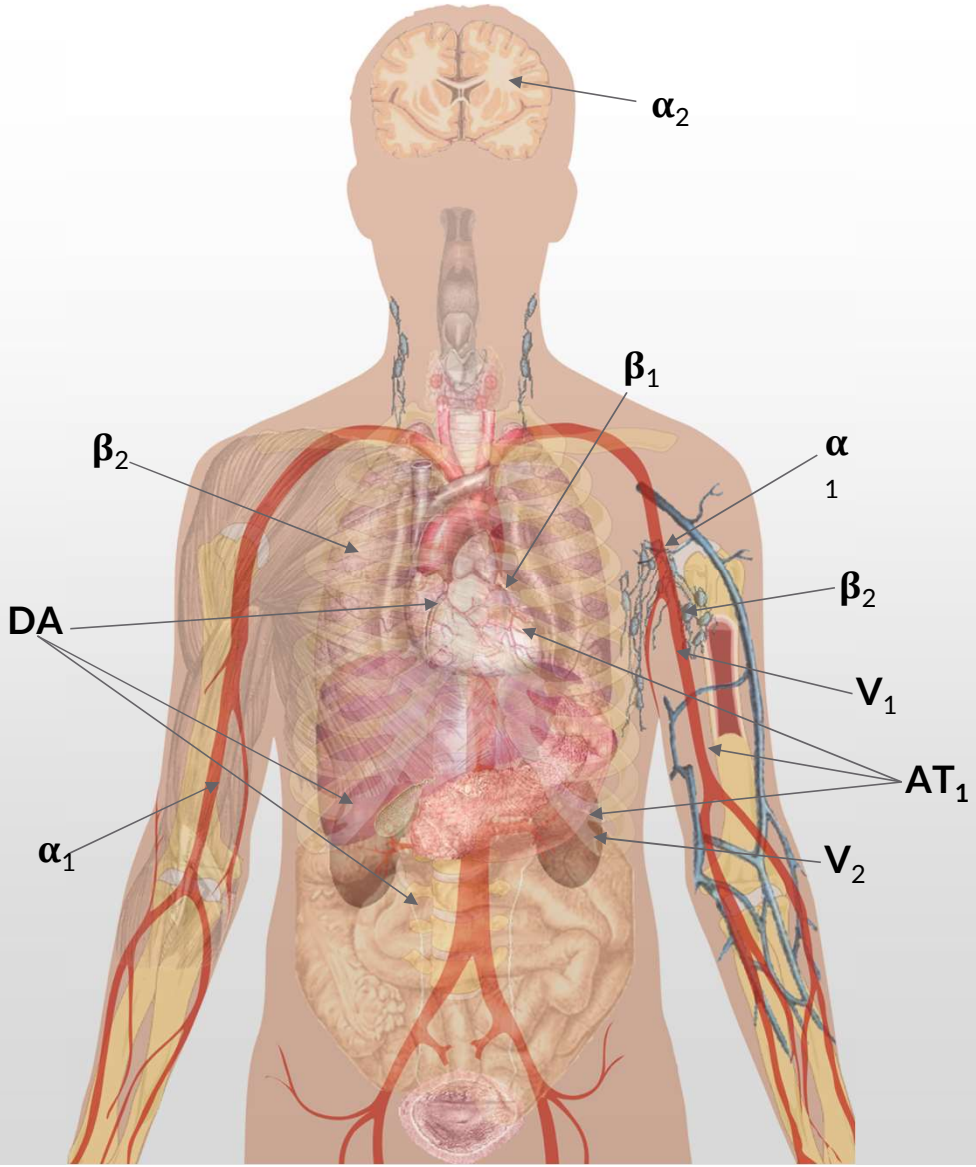
Standl T, et al. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6323133/figure/F1/?report=objectonly.

Resuscitation Goals

Improve blood flow to vital organs

Prevent irreversible tissue damage

A Review of Adrenergic Receptors


α2
β1
β2
α1
β2
DA
V1
AT1
α1
V2

Adrenergic Receptors

Receptor	Location	Activity
α_1	vascular smooth muscle	vasoconstriction (↑ SVR)
α_2	postsynaptic CNS neurons	decreased sympathetic outflow
β_1	cardiac muscle	chronotropy, inotropy (↑ CO)
β_2	lung tissue vascular smooth muscle	bronchodilation vasodilation (↓ SVR)
Dopamine (DA)	cardiac muscle mesentery renal vessels	coronary artery dilation mesenteric and renal vessel dilation

SVR: systemic vascular resistance
CO: cardiac output

Overgaard, et al. *Circulation*. 2008;118:1047–1056.

Other Receptors

Receptor	Location	Activity
Vasopressin-1 (V_1)	vascular smooth muscle (mesentery, systemic, renal)	vasoconstriction (↑ SVR)
Vasopressin-2 (V_2)	distal tubule and renal collecting ducts	fluid retention
Angiotensin II type 1 (AT_1)	vascular smooth muscle cardiac muscle adrenal cortex kidney	vasoconstriction (↑ SVR) and fibrosis cardiac hypertrophy and fibrosis aldosterone synthesis/secretion sodium reabsorption, ↓ renin secretion

SVR: systemic vascular resistance

Overgaard, et al. *Circulation*. 2008;118:1047–1056.
Sharman, et al. *Continuing Education in Anaesthesia Critical Care and Pain*. 2008; 8: 134–137.
Burnier. *Circulation*. 2001; 103: 904-912.

PHARMACOLOGY OF VASOACTIVES

Vasoactive Agents

Drug	Indication	Main effect	Important adverse effects	Dosage
Norepinephrine	All types of shock with reduced peripheral resistance, 1st line septic shock	α1 β1 (higher dose)	Peripheral ischemia, cardiac arrhythmias, tachycardia	IV Infusion: 1-30 mcg/min; titrate by 1 mcg/min
Epinephrine	All types of shock, when use of other catecholamines fails to achieve adequate blood pressure and increased inotropy, ACLS, 1st line anaphylactic shock	β1 α1 (higher dose) β2 (higher dose)	Myocardial ischemia, stress cardiomyopathy, tachyarrhythmias, oliguria/anuria, elevated lactate, hyperglycemia	IV Infusion: 1-10 mcg/min; titrate by 1 mcg/min Anaphylaxis: 0.3–0.5 mg IM every 5-15 min ACLS: 1 mg IV every 3–5 min
Phenylephrine	Distributive shock with reduced peripheral resistance; hypotension during RSI; Hypotension with severe AS; Hypotension associated with PDE inhibitors	α1	Reflex bradycardia, myocardial ischemia, decreased cardiac output, severe peripheral ischemia	IV Infusion: 10-100 mcg/min; titrate by 10 mcg/min Intubation: 50-100 mcg increments

RSI: rapid sequence intubation
ACLS: advanced cardiac life support
AS: aortic stenosis
PDE: phosphodiesterase

Overgaard, et al. *Circulation*. 2008;118:1047–1056.
Rhodes, et al. *Crit Care Med*. 2017; 45: 486-552.
Standl, et al. *Dtsch Arztebl Int*. 2018; 115: 757-768.

Vasoactive Agents

Drug	Indication	Main effect	Important adverse effects	Dosage
Vasopressin	Shock states, especially septic shock, when norepinephrine alone does not achieve the required vasoconstriction; catecholamine sparing strategies	V1-mediated vasoconstriction	Digital and mesenteric ischemia, fluid retention	IV Infusion: 0.01-0.04 units/min
Dopamine	All types of shock, when use of other catecholamines fails to achieve adequate blood pressure and increased inotropy	DA (low dose) β1 (higher dose) α1 (highest dose)	High risk for tachycardia / tachyarrhythmias, digital ischemia, polyuria, increased mortality in RCTs	Low: 0-5 mcg/kg/min Medium: 5-10 mcg/kg/min High: 10-20 mcg/kg/min
Angiotensin II	Refractory shock after inadequate response to other vasopressor agents; AVOID in cardiogenic shock!	AT1	Peripheral ischemia, tachycardia, acidosis, hyperglycemia, thromboembolism, delirium, fungal infection	IV Infusion: 1.25-80 ng/kg/min; titrate by 5-10 ng/kg/min

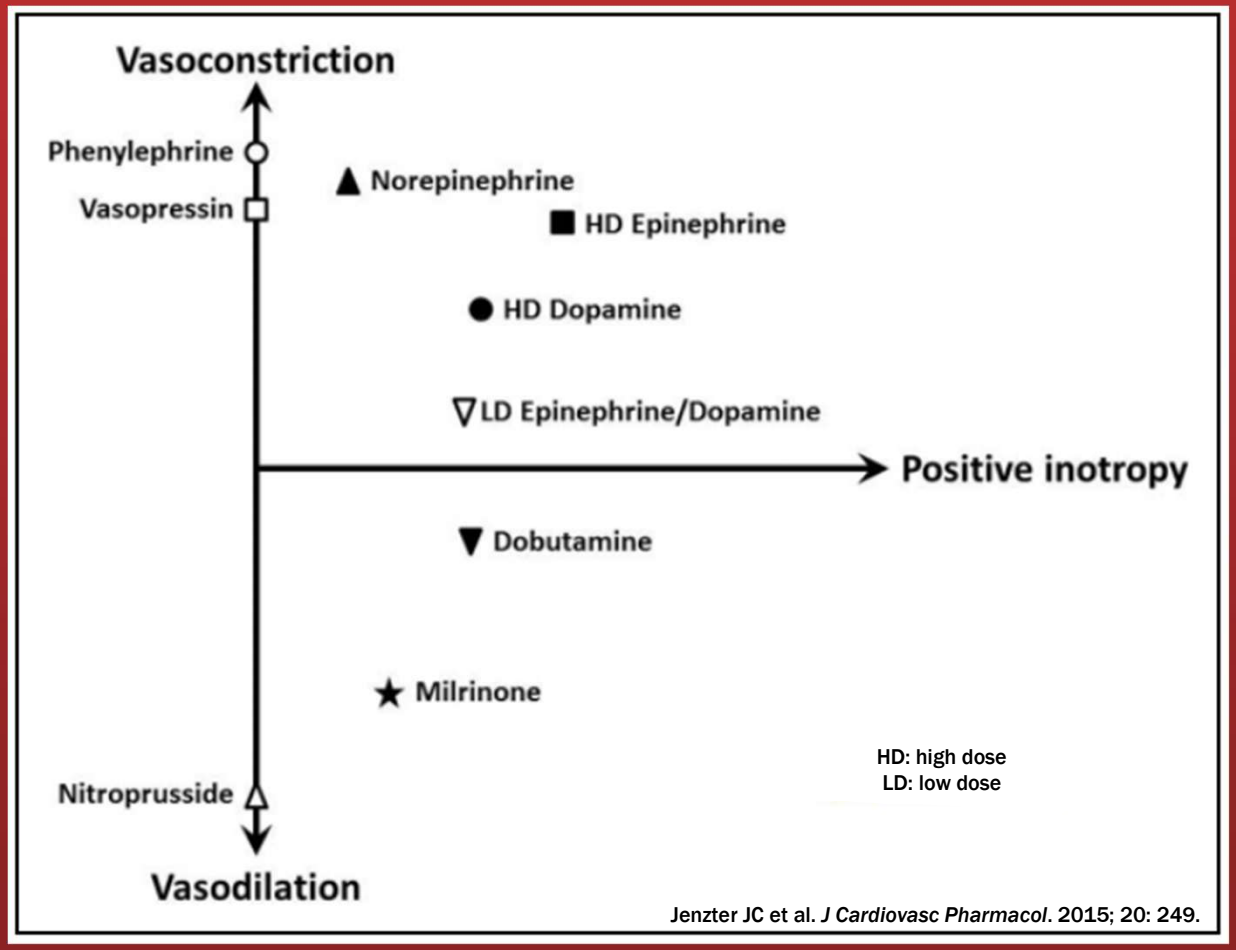
Overgaard, et al. *Circulation*. 2008;118:1047–1056.
Rhodes, et al. *Crit Care Med*. 2017; 45: 486-552.
Standl, et al. *Dtsch Arztebl Int*. 2018; 115: 757-768.

Vasoactive Agents

Drug	Indication	Main effect	Important adverse effects	Dosage
Milrinone	Cardiogenic shock, especially for patients on beta-blocker therapy	PDE-3 enzyme inhibitor: positive inotropic, lusitropic & vasodilatory effect	Ventricular ectopic beats and tachycardia, ventricular fibrillation, headache, hypotension, RENAL clearance	IV Infusion: 0.125–0.75 mcg/kg/min
Dobutamine	Cardiogenic shock, all types of shock with insufficient ventricular pump function (i.e. septic shock)	β1–mediated inotropy β2 (higher dose) α1 (highest dose)	Tachycardia, hypertension, headache, cardiac arrhythmias, possible hypertension with β2 receptor agonism	IV Infusion: 1-10 mcg/kg/min
Sodium nitroprusside	Cardiogenic shock, for rapid reduction in both preload and afterload	Breaks down in circulation to produce NO, which causes vasodilation	Risk of cyanide & thiocyanate toxicity with hepatic and renal dysfunction, respectively	IV Infusion: 1-10 mcg/kg/min (AVOID doses > 2 mcg/kg/min for > 24 hours)

PDE-3: phosphodiesterase-3
NO: nitric oxide

Amado, et al. *Rev Port Cardiol*. 2016; 35: 681-695.
Holme et al. Sodium Nitroprusside. *StatPearls*. Last updated May 24, 2022.



Jenzter JC et al. *J Cardiovasc Pharmacol*. 2015; 20: 249.

So What Do I Start? Cardiogenic Shock

- RV dysfunction?
  - Milrinone > dobutamine
- Hypotension?
  - Add norepinephrine
- Increased after load or LV filling pressure?
  - Add nitroprusside
- No RV dysfunction?
  - Dobutamine
- Persistent hypotension despite norepinephrine?
  - Add vasopressin

So What Do I Start? Septic Shock

- 1st line: norepinephrine
- 2nd line: vasopressin
- 3rd line: take your pick!
  - Epinephrine
  - Phenylephrine
  - Angiotensin II
- Selection often depends on other clinical parameters
  - Arrhythmias
  - Distal ischemia
  - Other medical contraindications…

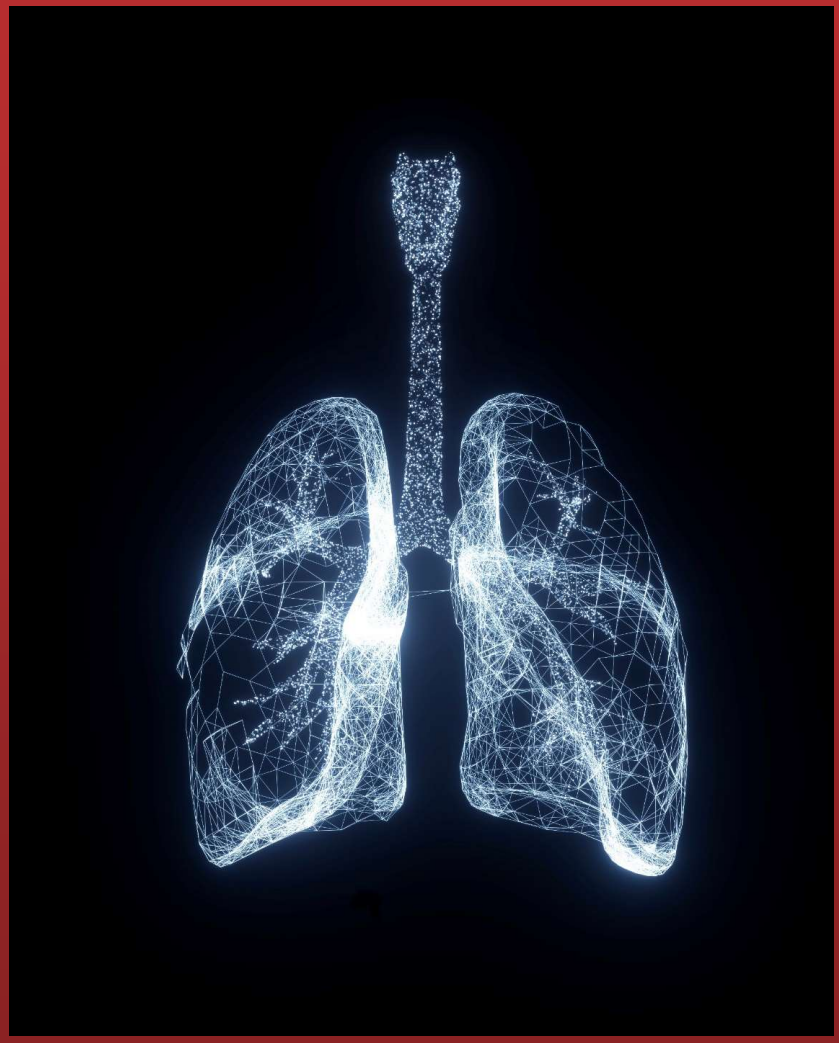
“HELP!
I Have No Central Line!”

- Vasoactives that can be given via peripheral line (temporarily):
  - Phenylephrine
  - Norepinephrine
  - Epinephrine
  - Dobutamine

- Tran et al: “Out of 1835 patients, 7% had complications of peripheral vasopressor administration, of which 96% were minor”

Tran et al. *Am J Emerg Med*. 2020; 38: 2434-2443.

Rapid Sequence Intubation (RSI)



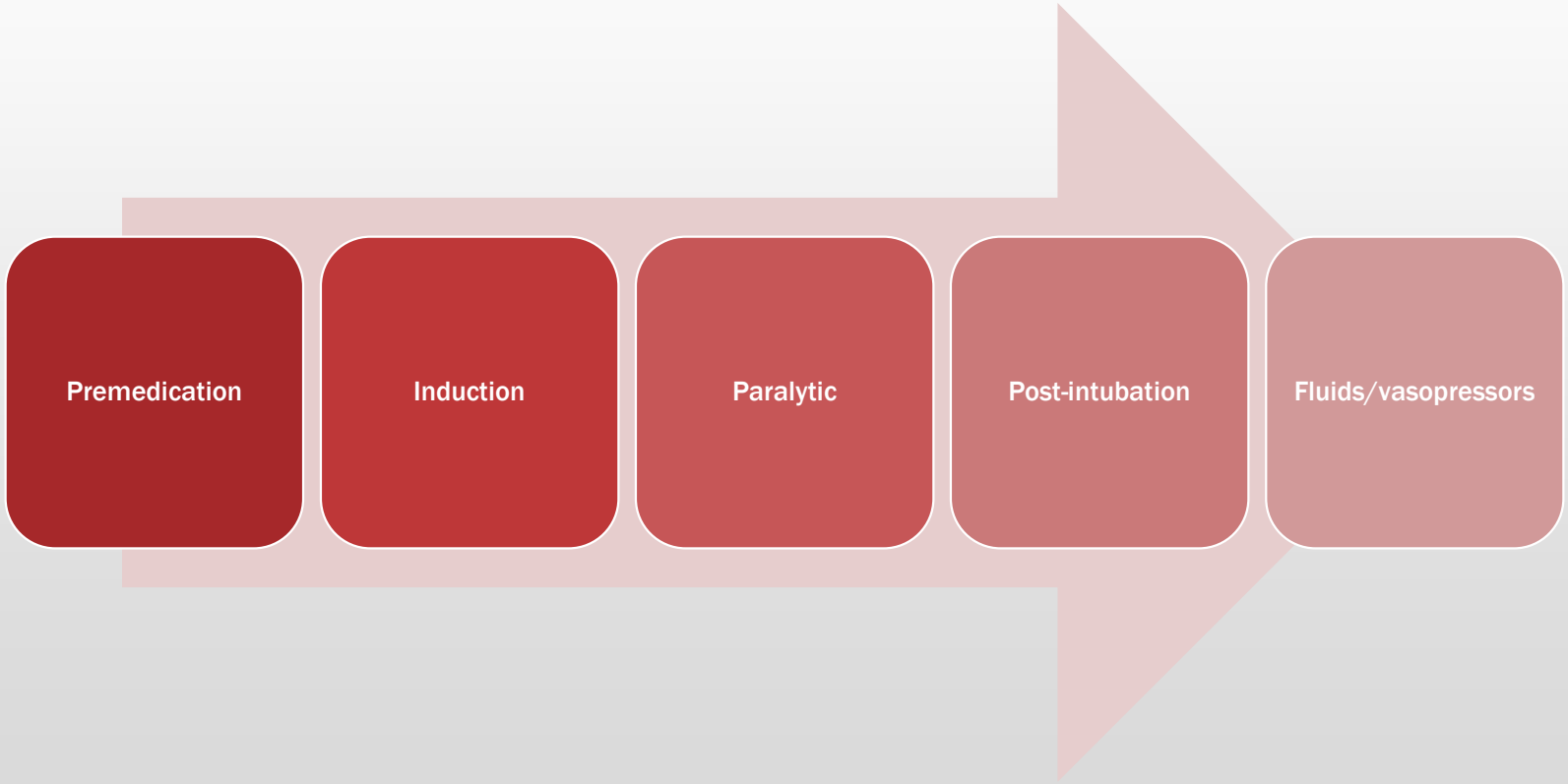
Why RSI?

- Almost all patients in the emergency setting who require intubation and are not in cardiac arrest should be intubated using RSI for rapid control of the airway

- Used when patients have not been prepared for procedure by being NPO and/or for patients who might be at risk for aspiration

Rapid Sequence Intubation Pharmacology. *ACEP Now*. Updated September 1, 2010. Accessed July 31, 2022.

RSI Pharmacotherapy



Premedication

- "Non-essential" step in RSI
  - Must be initiated *at least* 3 minutes prior to induction
  - Used to prevent harmful effects of physiologic response to laryngoscopy and endotracheal tube insertion (sympathetic stimulation)

- Consider for the following conditions:

High airway resistance (e.g. asthma)	Increased intracranial pressure	Aortic dissection	Acute coronary syndromes

Rapid Sequence Intubation Pharmacology. *ACEP Now*. Updated September 1, 2010. Accessed July 31, 2022.

Premedication = “LOAD”

- **L**idocaine
- **O**pioids
- **A**tropine
- **D**efasciculating dose

No longer supported based on available literature!

Rapid Sequence Intubation Pharmacology. *ACEP Now*. Updated September 1, 2010. Accessed July 31, 2022.

Premedication

- Lidocaine
  - Some evidence that administration decreases likelihood of bronchospasm
  - Suppresses cough reflex and prevents increase in ICP
  - Dose: 1.5 mg/kg IV given 2 – 3 minutes before induction
  - AVOID in cases of high-grade heart block (Mobitz type II or 3rd degree), hypotension, and amide allergy

Rapid Sequence Intubation Pharmacology. *ACEP Now*. Updated September 1, 2010. Accessed July 31, 2022.

Premedication

- Fentanyl
  - Blunts sympathetic response to intubation
    - Useful for cases of ICH, increased ICP, cardiac ischemia, aortic aneurysm
  - Dose: 1-3 mcg/kg (IBW) IV at least 3 minutes prior to induction
  - AVOID if patient is in shock

Rapid Sequence Intubation Pharmacology. *ACEP Now*. Updated September 1, 2010. Accessed July 31, 2022.

Induction Agents

- Cause amnesia and blunt sympathetic response prior to paralysis and intubation.

Ketamine	Etomidate	Propofol	Midazolam
• MOA: NMDA antagonist, produces state of dissociation • Weak opioid receptor agonism also produces analgesia • Bronchodilator	• MOA: GABA agonist • Does *not* produce analgesia or blunt sympathetic response → generally given with fentanyl	• MOA: GABA agonist • Does *not* produce analgesia	• MOA: GABA agonist • Does *not* produce analgesia • Has antiseizure activity; good for status epilepticus

MOA: mechanism of action

Bergen JM, et al. *J Emerg Med*. 1997; 15: 221.

Induction Agents

Ketamine	Etomidate	Propofol	Midazolam
• Dose: 0.5 - 2 mg/kg IV • Duration of action: 10 – 20 mins • Onset: 30 seconds • Notes: no effect on respiratory drive, can increase sympathetic tone (HR, BP), increases salivation and feelings of euphoria, avoid in cardiac ischemia	• Dose: 0.3 mg/kg • Duration of action: 3 - 12 mins • Onset: 15-30 seconds • Notes: Decreases ICP, possible lowering of seizure threshold & adrenal suppression, most hemodynamically neutral	• Dose: 1.5 - 2.5 mg/kg • Duration of action: 5 - 10 mins • Onset: 45 seconds • Notes: Hypotension, good agent for patients with seizures	• Dose: 0.1 – 0.3 mg/kg • Duration of action: 15 – 30 mins • Onset: 30 – 90 seconds • Notes: moderate hypotension, slowest onset of action

ICP: intracranial pressure

Bergen JM, et al. *J Emerg Med*. 1997; 15: 221.
Schrader M et al. StatPearls. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560592. Accessed July 20, 2022.
Ketamine. Micromedex Solutions. http://micromedex.com. Updated June 22, 2022. Accessed July 24, 2022.
Etomidate. Micromedex Solutions. http://micromedex.com. Updated July 28, 2021. Accessed July 24, 2022.
Propofol. Micromedex Solutions. http://micromedex.com. Updated May 18, 2022. Accessed July 24, 2022.

Randomized Controlled Trial > Intensive Care Med. 2022 Jan;48(1):78-91.
doi: 10.1007/s00134-021-06577-x. Epub 2021 Dec 14.

Etomidate versus ketamine for emergency endotracheal intubation: a randomized clinical trial

Study Question	Which agent is associated with improved survival at day 7 when used for RSI?
Study Design	Single-center, unblinded, RCT
Patient Population	801 critically ill adult patients requiring emergency intubation
Exclusion Criteria	<18 years old, RSI without sedation (cardiac arrest), neurologically obtunded, awake intubation
Study Drug	Etomidate 0.2–0.3 mg/kg (n = 400) or ketamine 1–2 mg/kg (n = 401)

Matchett, et al. *Intensive Care Med*. 2022; 48: 78-91.

Randomized Controlled Trial > Intensive Care Med. 2022 Jan;48(1):78-91.
doi: 10.1007/s00134-021-06577-x. Epub 2021 Dec 14.

Etomidate versus ketamine for emergency endotracheal intubation: a randomized clinical trial

Primary Outcome	Day 7 survival was significantly lower in the etomidate arm (77.3% versus 85.1%, p = 0.005). Day 28 survival rates for the two groups were not significantly different (etomidate 64.1%, ketamine 66.8%, p = 0.294)
Conclusions	More information is needed to determine if there is a clinically meaningful difference between ketamine & etomidate for induction
Limitations	Generalizability unknown, use of highly skilled airway teams for RSI, did not quantitatively assess hemodynamics/supportive medications before & after induction, unblinded, allowed to screen-out patients (enrollment bias), unconventional endpoint

De Backer, et al. *N Engl J Med*. 2010 Mar 4;362: 779-89.

Paralytics

- Essential for creating optimal intubation conditions
  - Intubation without paralytics has been proven to be more difficult with significantly higher failure and complication rates
- Sedation must be provided before paralytics are administered

Succinylcholine	Rocuronium	Vecuronium
• MOA: depolarizing analog of ACh • Contraindications: rhabdomyolysis, myopathy, known or suspected hyperkalemia, personal or family history of malignant hyperthermia	• MOA: non-depolarizing; competitive inhibition of ACh receptor • Does not cause fasciculations • No contraindications	• MOA: non-depolarizing; competitive inhibition of ACh receptor • Does not cause fasciculations • Requires priming dose • No contraindications

MOA: mechanism of action
ACh: acetylcholine

Schrader M et al. StatPearls. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560592. Accessed July 20, 2022.
Li J, et al. *Am J Emerg Med*. 1999; 17: 141.

Paralytics

Succinylcholine

- Dose: 1.5 mg/kg IV
- Duration of action: 6 – 10 mins
- Onset: 45 - 60 seconds
- Notes: causes hyperkalemia in setting of burns, myopathies, & crush injuries, bradycardia, and MH

Rocuronium

- Dose: 1 – 1.5 mg/kg IV
- Duration of action: 30 – 60 mins
- Onset: 60 seconds
- Notes: Longer duration of action

Vecuronium

- Dose: 0.01 mg/kg IV "priming dose", followed by 0.15 mg/kg IV
- Duration of action: 30 – 75 minutes
- Onset: 1.5 – 3 mins

MH: malignant hyperthermia

Bergen JM, et al. *J Emerg Med*. 1997; 15: 221.
Schrader M et al. StatPearls. Available at: https://www.ncbi.nlm.nih.gov/books/NBK560592. Accessed July 20, 2022.
Naguib M, et al. *Anesth Analg*. 2006; 102: 151.

Post-Intubation

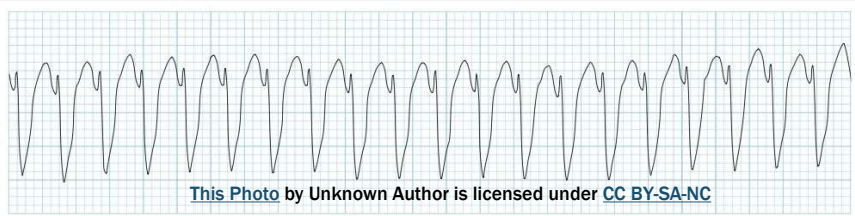
- Hypotension is common & generally resolves with IV fluids; push-dose phenylephrine can be used
- Continue to provide analgesia and sedation/anxiolysis
  - Patient will not be able to communicate
  - Paralytic duration may last longer than induction agent (monitor HR and BP – may be signs of inadequate sedation)

Bergen JM, et al. *J Emerg Med*. 1997; 15: 221.

Antiarrhythmics

Background

- Common causes of arrhythmias are:
  - Infection
  - Electrolyte abnormalities
  - Medications
  - Ischemia
  - Anemia
  - Hypoxia
  - Changes in volume status



- Tachycardias are more common than bradycardias and atrial arrhythmias are more common than ventricular arrhythmias
- Incidence of arrhythmias = 12% in the general ICU population

Annane D, et al. *Am J Respir Crit Care Med* 2008; 178: 20–25.
Gupta D, et al. Arrhythmia Diagnosis and Management. Available at: https://accessmedicine.mhmedical.com/content.aspx?bookid=1944&sectionid=143517105. Accessed July 20, 2022.

Background

- Major source of morbidity
- Increase hospital length of stay

- Urgency and type of treatment are determined by the physiological impact of the arrhythmia as well as underlying cardiac status

Tarditi DJ, et al. *Semin Respir Crit Care Med.* 2006; 27: 221–229.

If hemodynamically unstable, cardiovert!

Classes of Antiarrhythmic Medications

Class Ia

- Disopyramide
- Quinidine
- Procainamide

Class Ib

- Lidocaine
- Mexiletine

Class Ic

- Flecainide
- Propafenone

Class II

- Beta blockers

Class III

- Amiodarone
- Sotalol
- Ibutilide

Class IV

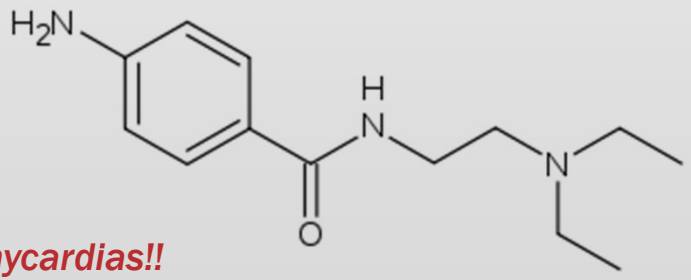
- Diltiazem
- Verapamil

Miscellaneous:

- Digoxin
- Atropine
- Adenosine

Procainamide

- Class 1a: voltage gated Na+ channel blocker
- Increases effective refractory period and electrical stimulation threshold → reduces impulse conduction velocity and excitability in the atria, His-Purkinje fibers and ventricular muscle of the heart
  - Can decrease cardiac contractility / inotropy
- Uses:
  - Ventricular arrhythmias



** Procainamide will terminate between 50% and 80% of ventricular tachycardias!!*

Procainamide. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.
Ventricular tachycardia. Stat Pearls. Available at: https://www.ncbi.nlm.nih.gov/books/NBK532954. Accessed August 13, 2022.

Procainamide

- Dose:

Load: 100mg IV every 5 mins until the arrhythmia is suppressed, hypotension ensues, or the QRS complex is prolonged by 50% from its original duration; MAX loading dose 17 mg/kg

Maintenance infusion rate: 1 to 4 mg/min

- Adverse Effects:

Bone marrow depression	Hepatotoxicity
Lupus-related syndrome	Widened QRS / arrhythmia
Myasthenia gravis	Positive ANA

ANA: antinuclear antibody

Procainamide. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.

Lidocaine

- Class 1b: weak Na+ channel blocker
- Also an amide anesthetic
- Suppresses automaticity by increasing the electrical stimulation threshold of the ventricles and the His-Purkinje system; increases spontaneous depolarization of the ventricles during diastole and shortens effective refractory period
- Uses:
  - Ventricular arrhythmias

Lidocaine. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.

Lidocaine

- Dose:

Load: 1 – 1.5 mg/kg IV bolus; MAX 200 mg

Maintenance infusion rate: 1 to 4 mg/min

- Adverse Effects:

Edema	Erythema
Headache	Methemoglobinemia
Pruritis	Nausea/vomiting

Lidocaine. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.

Beta Blockers

- Class II: Bind beta-adrenergic receptors and block binding of catecholamines (sympatholytic)
  - Most common drugs: metoprolol, esmolol, propranolol
- Decrease sinus rate & conduction velocity and inhibit aberrant pacemaker activity
- Increase action potential duration and the effective refractory period
- Uses:
  - Atrial fibrillation
  - Supraventricular tachycardia
  - Chronic management of ischemic heart disease with VT
  - Symptomatic NSVT

VT: ventricular tachycardia
NSVT: non-sustained ventricular tachycardia

Metoprolol. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.
Ventricular tachycardia. Stat Pearls. Available at: https://www.ncbi.nlm.nih.gov/books/NBK532954. Accessed August 13, 2022.

Beta Blockers

- Dosing:

Metoprolol

- 2.5 – 10 mg IV push

Propranolol

- 10 – 40 mg PO, repeat 3-4 x daily
- 1 – 3 mg IV, (max 1 mg/min); may repeat after 2 mins

Esmolol

- 500 mcg/kg IV bolus over 1 minute
- 50 mcg/kg/min IV infusion; increase infusion rate by 50 mcg/kg/min every 4 minutes based on ventricular response; MAX 200 mcg/kg/min

- Adverse Effects:

Heart block	Acute decompensated heart failure
Hypotension	Dizziness
Pruritis	Nausea/vomiting

Metoprolol. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.
Propranolol. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.
Esmolol. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.

Amiodarone

- Class III: inhibits adrenergic stimulation (both alpha- and beta-blocking properties); affects sodium, calcium, and potassium channels

- Prolongs the action potential and refractory period in myocardial tissue

- Uses:
  - Atrial fibrillation
  - Supraventricular tachycardia
  - Ventricular arrhythmias

Amiodarone. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.

Amiodarone

- Dose:

Load:

- VF/pulseless VT: 300 mg IV push; may repeat with 150 mg IV push
- VT with pulse: 150 mg IV over 10 mins
- AF/SVT: 150 mg IV over 10 mins

Maintenance infusion rate:
1 mg/min for 6 hours, followed by 0.5 mg/min for 18+ hours

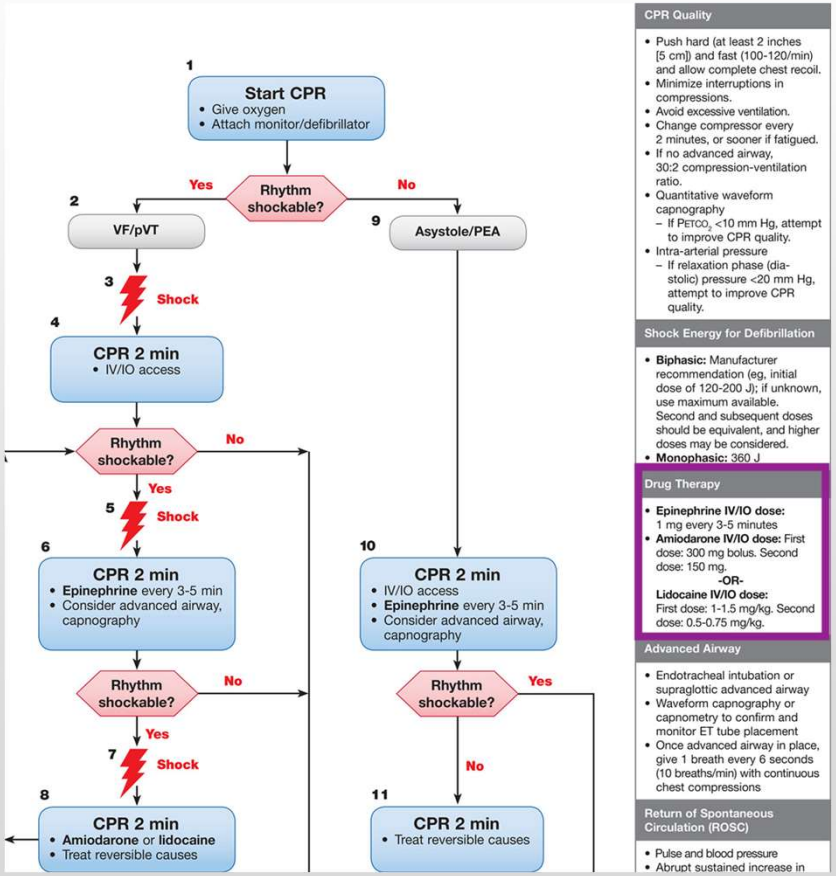
- Adverse Effects:

- Bradycardia
- Heart block
- Hypotension (IV > PO)
- Thyroid dysfunction
- Nausea/vomiting
- Hepatic & pulmonary toxicity

VF: ventricular fibrillation
VT: ventricular tachycardia
AF: atrial fibrillation
SVT: supraventricular tachycardia

Amiodarone. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated June 24, 2022. Accessed July 22, 2022.

Amiodarone vs Lidocaine for ACLS??



Panchal AR, et al. *Circulation*. 2018; 138: e740-e749.

Effect of amiodarone and lidocaine on shock-refractory cardiac arrest: a systematic review and meta-analysis

Study Question	Is there a difference between amiodarone and lidocaine on survival and neurological outcome after shock-refractory cardiac arrest?
Study Design	Systematic review & meta-analysis
Patient Population	Adults with in-hospital and out-of-hospital cardiac arrest due to *shockable* rhythms
Exclusion Criteria	Case studies, pediatrics
Study Drug	Amiodarone vs placebo; lidocaine vs placebo; amiodarone vs lidocaine

Ludwin K, et al. *Kardiol Pol.* 2020; 78: 999-1007.

Effect of amiodarone and lidocaine on shock-refractory cardiac arrest: a systematic review and meta-analysis

Primary Outcome	• No significant difference in ROSC • Survival to hospital discharge was slightly higher with amiodarone • No significant difference in survival with favorable neurologic outcome
Conclusions	Use of lidocaine should not be limited to cases where amiodarone is not available because the drugs have similar efficacy for shock-refractory cardiac arrest
Limitations	Only 3 RCTs, only 2 studies used blinding

Ludwin K, et al. *Kardiol Pol.* 2020; 78: 999-1007.

Amiodarone vs Lidocaine for ACLS??

2018 AHA Recommendations:

2018 Recommendations for Use of Antiarrhythmic Drugs During Resuscitation From Adult VF/pVT Cardiac Arrest

Amiodarone and Lidocaine Recommendation—Updated

1. **Amiodarone or lidocaine may be considered for VF/pVT that is unresponsive to defibrillation. These drugs may be particularly useful for patients with witnessed arrest, for whom time to drug administration may be shorter (*Class IIb; Level of Evidence B-R*).**

Panchal AR, et al. *Circulation*. 2018; 138: e740-e749.

Diltiazem

- Class IV: slow calcium channel blocker (non-dihydropyridine)
- Induces a moderate slowing in heart rate, slows down AV conduction, with a risk of atrioventricular block
- No negative inotropic effect has been demonstrated on a healthy myocardium; AVOID in HFrEF or structural heart disease – increases mortality!
- Uses:
  - Atrial fibrillation
  - Supraventricular tachycardia
  - Symptomatic NSVT unresponsive/intolerant to beta-blockers

HFrEF: heart failure with reduced ejection fraction
NSVT: non-sustained ventricular tachycardia

Ventricular tachycardia. Stat Pearls. Available at: https://www.ncbi.nlm.nih.gov/books/NBK532954. Accessed August 13, 2022.

Diltiazem

- Dose:

Load:

- AF/SVT: 0.25 mg/kg IV over 2 mins (up to 25 mg)

Maintenance infusion rate: 5 – 15 mg/min; MAX duration 24 hrs

- Adverse Effects:

- Bradycardia
- Heart block
- Peripheral edema
- Dizziness

AF: atrial fibrillation
SVT: supraventricular tachycardia

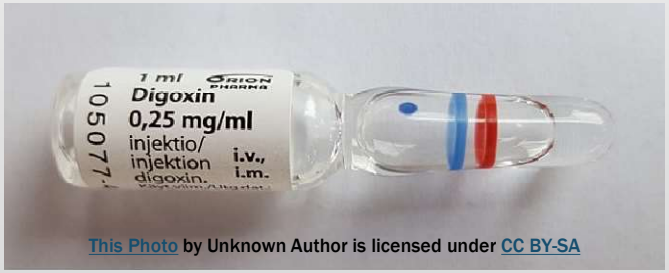
Diltiazem. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated July 25, 2022. Accessed July 31, 2022.

Digoxin

- Inhibits Na+/K+/ATPase pump ⟶ increases intracellular Na+ and Ca2+, resulting in increased contractility

- Vagomimetic action leads to increased inotropy, with decreased sympathetic tone & heart rate
  - Slows conduction through AV node

- Uses:
  - Atrial fibrillation



AV: atrioventricular

Digoxin. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated July 25, 2022. Accessed July 31, 2022.

Digoxin

- Dose:

Load:

- 8 to 12 mcg/kg given as 500 mcg x 1, then 250 mcg q6 hrs x 2 doses (MAX 1.5 mg)

Decrease load in renal failure!

- 250 mcg doses with levels checked 6 hrs after each bolus

- Adverse Effects:

Bradycardia	Headache
Thrombocytopenia	Nausea/vomiting

AF: atrial fibrillation
SVT: supraventricular tachycardia

Digoxin. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated July 25, 2022. Accessed July 31, 2022.

Atropine

- Competitively blocks the effects of acetylcholine at muscarinic cholinergic receptors on smooth muscle & cardiac muscle (anticholinergic)
- Vagolytic agent- removes parasympathetic input to the heart
- Of note: does NOT work on transplanted hearts!
- 1st line therapy for symptomatic bradycardia per guidelines
  - Especially useful in cases of high vagal tone and AV node block
  - Not as useful for heart block beyond AV node

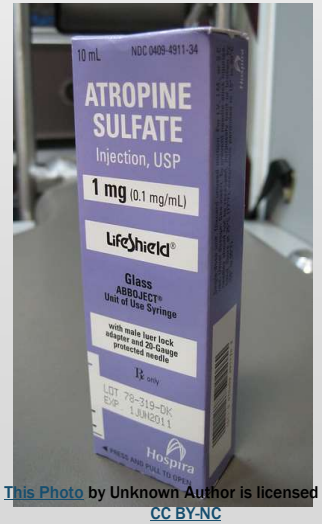
Atropine. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated July 18, 2022. Accessed July 31, 2022.

Atropine

- Dose:

Bradycardia

- 0.5 - 1 mg IV every 3 – 5 mins; MAX 3 mg



- Adverse Effects:

Palpitations	Flushing
Nausea/vomiting	Headache/dizziness
Blurred vision	Anhidrosis

Atropine. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated July 18, 2022. Accessed July 31, 2022.

Adenosine

- Endogenous nucleoside primarily formed as a degradation product of adenos
- Slows impulse for le & conduction time through the
- Depresses left ver se of its short half-life, it can be nction

Adenosine. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated November 6, 2021. Accessed July 31, 2022.

Adenosine

- Dose:

Initial:

- 6 mg IV rapid bolus over 1 to 2 seconds followed by 20 mL saline flush

Repeat:

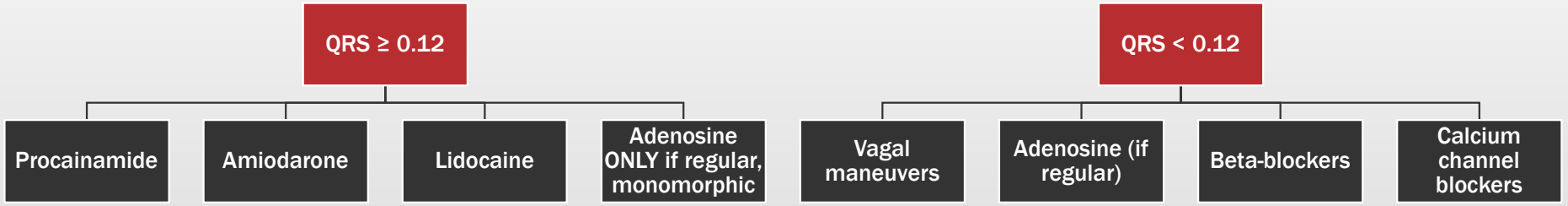
- 12 mg every 1 to 2 minutes as needed for 2 doses; MAX 12 mg/dose

- Adverse Effects:

Chest pain	Flushing
Abdominal pain	Headache
Dyspnea	Cardiac Arrest

Adenosine. Micromedex Solutions. Greenwood Village, CO: Truven Health Analytics. http://micromedex.com/. Updated November 6, 2021. Accessed July 31, 2022.

Tachyarrhythmia Management



If hemodynamically unstable, synchronized cardioversion!

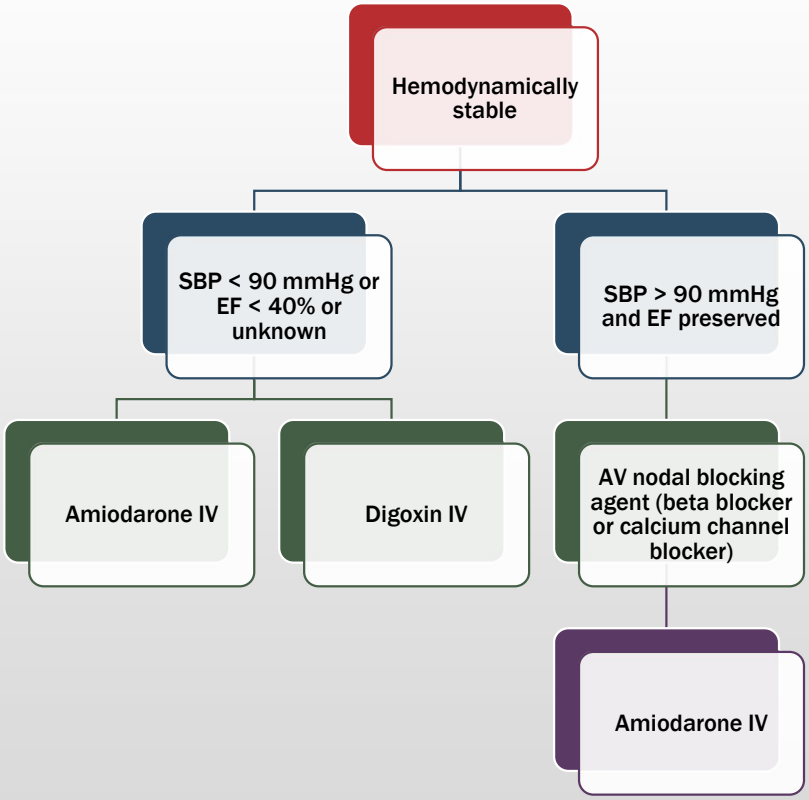
American Heart Association. Tachycardia with a pulse algorithm. Available at: cpr.heart.org/-/media/CPR-Files/CPR-Guidelines-Files/Algorithms/AlgorithmACLS_Tachycardia_200612.pdf. Accessed August 11, 2022.

Bradyarrhythmia Management

- For *symptomatic* bradycardia:

Atropine	Dopamine	Epinephrine	Transcutaneous pacing
• Initial dose 1 mg IV • Repeat every 3-5 mins up to 3 mg total	• 5-20 mcg/kg/min IV infusion	• 2-10 mcg/min IV infusion	• Specialist consultation

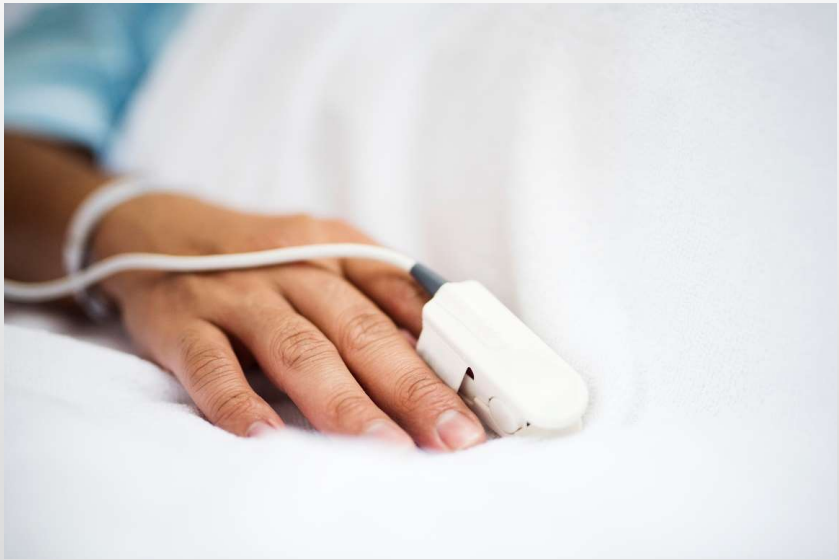
New-Onset Atrial Fibrillation



If hemodynamically unstable, synchronized cardioversion!

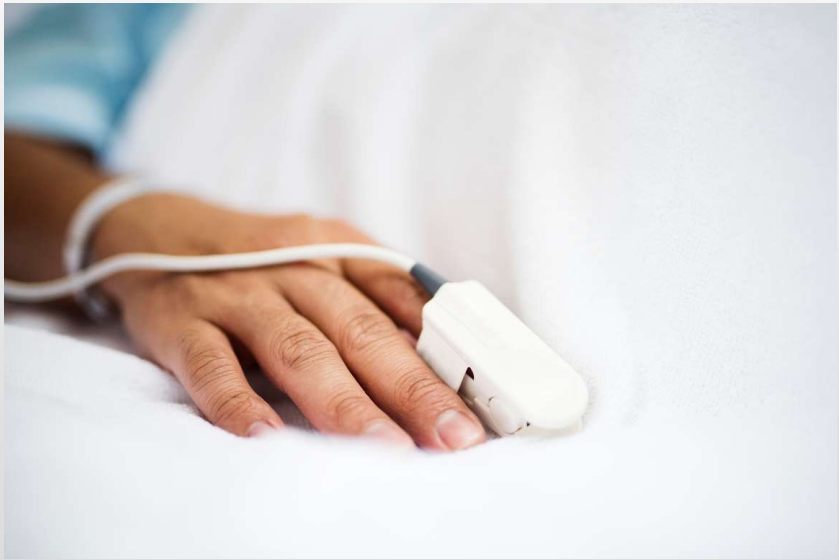
Patient Case

- 68-year-old female
- PMH: type 2 diabetes, ischemic cardiomyopathy (EF 40%), peripheral vascular disease
- Chief complaint: increased shortness of breath x 1 week, fatigue
- Admitted to internal medicine floor for treatment of fluid overload, AKI



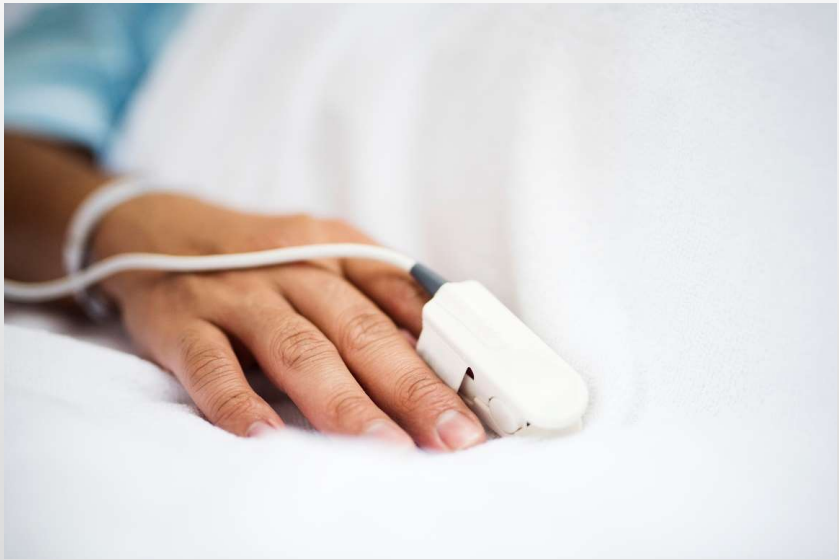
Patient Case (cont)

- Hospital day 2: patient orthostatic per RN, complaining of chest discomfort. Provider notified and begins workup
- Becoming more tachycardic throughout the day, started on nasal cannula for O_2 sat of 91%. ECG with sinus tachycardia, SvO_2 60%. Given a dose of diuretic
- Patient found unresponsive @ 1145; pulse present. CODE BLUE called



Patient Case (cont)

- ICU team decides to intubate – which medication could this patient be given?
- After intubation the patient is hypotensive – how do we correct blood pressure?
- The patient is started on medication for hemodynamic support and develops a new tachycardia. ECG reveals atrial fibrillation – how do we treat the patient?



Patient Case (cont)

- ICU team decides to intubate – which medication *could* this patient be given?

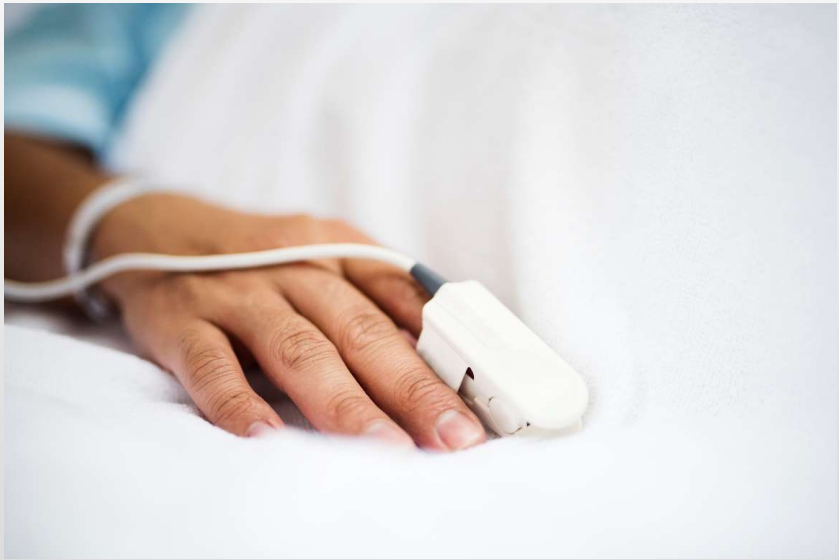
  A. Etomidate 0.3 mg/kg

  B. Ketamine 1 mg/kg

  C. Propofol 2 mg/kg

  D. Midazolam 0.3 mg/kg

  E. All of the above



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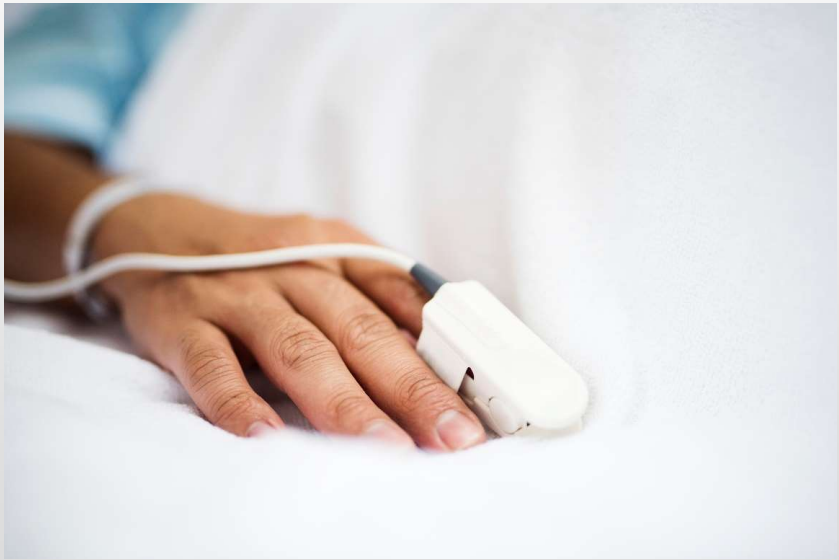
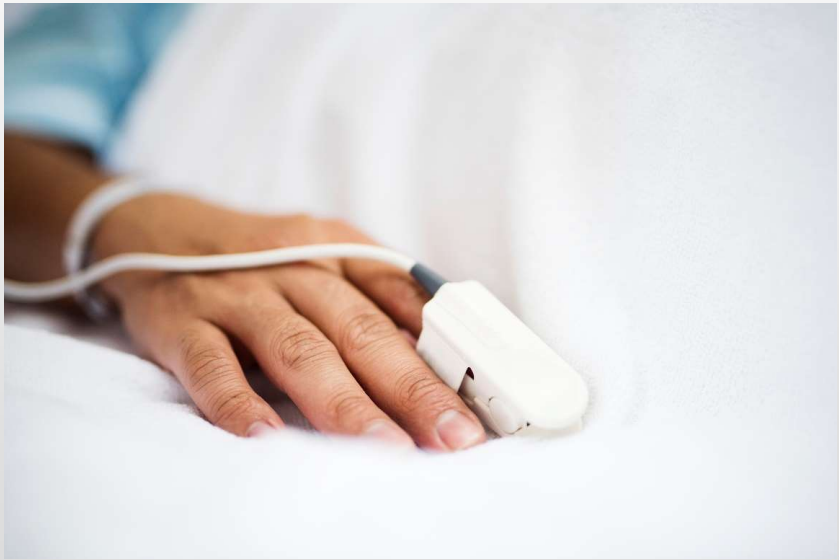


Patient Case (cont)

- After intubation the patient is hypotensive – how do we correct blood pressure?
  A. Phenylephrine IV push in 100 mcg increments
  B. Norepinephrine infusion at 5 mcg/min
  C. Dopamine infusion at 5 mcg/kg/min
  D. IV fluid bolus
  E. A, B, and D
  F. All of the above



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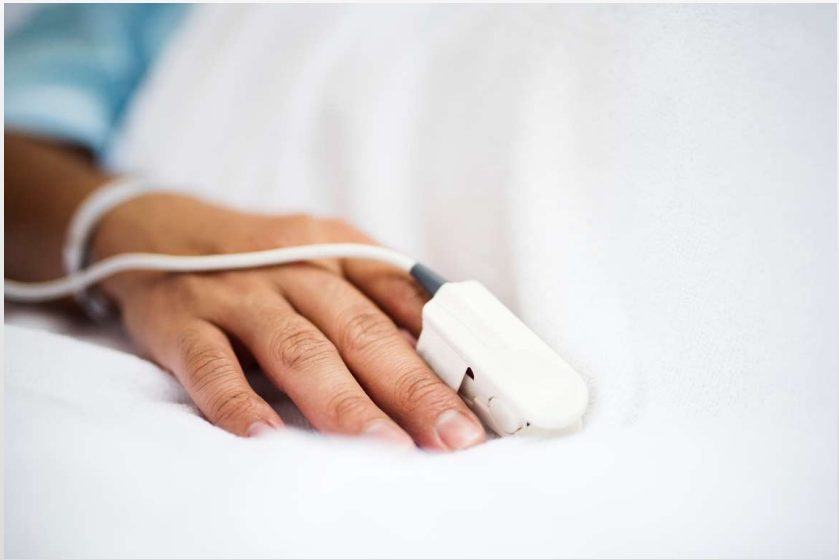
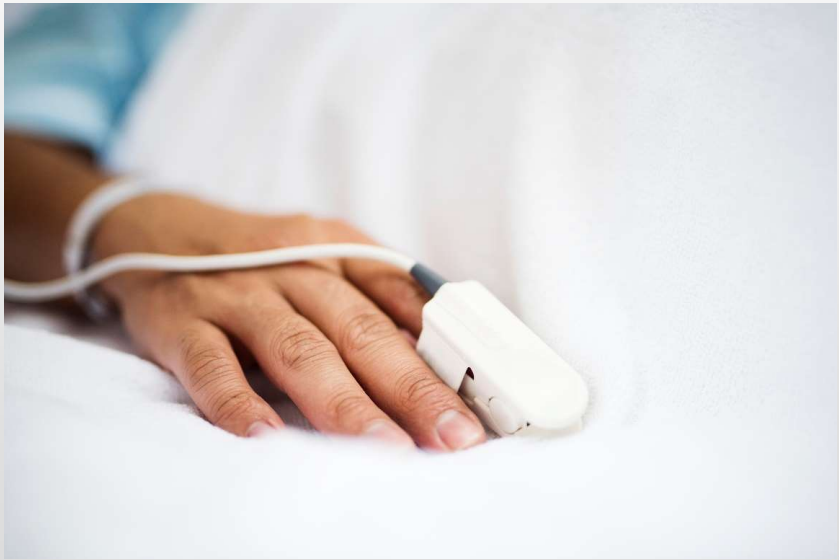


Patient Case (cont)

- The patient is started on medication for hemodynamic support and develops a new tachycardia. ECG reveals atrial fibrillation – how do we treat the patient?
  A. Amiodarone 300 mg IV push
  B. Amiodarone 150 mg IV over 10 min, followed by infusion at 1 mg/min
  C. Diltiazem 15 mg IV bolus
  D. Metoprolol 5 mg IV push



Take Home Points

- Vasoactives vary in their amount of pressor effect and inotropic effect. Selection depends on clinical presentation and comorbidities.
- When performing RSI, induction should *always* be given before paralysis. You may not always have time to administer premedications. Be prepared to follow RSI with further sedation & analgesia.
- Tachyarrhythmias are more common than bradyarrhythmias. Pharmacologic therapy is based on the classification of the arrhythmia itself, as well as patient comorbidities.

Questions?

Let's Get Critical: Critical Care Pharmacotherapy You Should Know

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AAPA BOOT CAMP SEPTEMBER 2022