1. **Definition**
   - an agent that affects the contractility of the heart
   - may be positive (increases contractility) or negative (decreases contractility)
   - oral and intravenous agents available

2. **Indications**
   - hypotension
   - low cardiac output/congestive heart failure
   - shock (septic, cardiogenic, hypovolemic, neurogenic, anaphylactic)

3. **Desired Outcomes**
   - mean arterial pressure (MAP) > 60 mmHg
   - systolic blood pressure (SBP) > 90 mmHg
   - cardiac index (CI) > 2.1 L/min/m²

4. **Initiation of Therapy**
   - a loading dose is required for agents with long half-lives (e.g. milrinone)
   - if for low cardiac output, start low due to the risk of hypotension (e.g. dobutamine, milrinone)
   - if for hypotension, may begin at higher doses and taper as blood pressure tolerates

5. **Discontinuation of Therapy**
   - taper agents with short half-lives (dopamine, norepinephrine, epinephrine, dobutamine)
   - agents with longer half-lives may be discontinued
   - individualize according to the patient’s response

6. **Combination of Therapy**
   - if using the maximum dose of one agent, a second agent may be added (e.g. norepinephrine may be added to dopamine for refractory hypotension; milrinone may be added to dobutamine for refractory heart failure)
Dopamine Hydrochloride

1. PHARMACOLOGY

- stimulates adrenergic receptors of the sympathetic nervous system
- though primary effect is direct stimulation of $\beta_1$ and $\alpha$-adrenergic receptors, also has an indirect effect by releasing norepinephrine from its storage sites
- also stimulates dopaminergic receptors in the renal, mesenteric, coronary, and intracerebral vasculature to produce vasodilation
- dose related effects:
  - low dose (2-3 µg/kg/min) affects dopaminergic receptors
  - moderate dose (4-10 µg/kg/min) affects $\beta_1$-receptors of the heart to increase contractility, heart rate and cardiac output
  - high dose (> 10 µg/kg/min) affects $\alpha$-receptors to produce peripheral vasoconstriction

2. INDICATIONS

- hypotension
- low cardiac output in patients with low systemic vascular resistance (SVR)
- low urine output?

3. DOSAGE

- start infusion at a rate of 2-3 µg/kg/min then titrate to desired response
- maximum dose: 20 µg/kg/min

4. PREPARATION AND ADMINISTRATION

- standard peripheral concentration is made with 200 mg or 400 mg in D5W or NS 250 mL to give a concentration of 800 µg/ml and 1600 µg/ml, respectively
- for a more concentrated solution, 800 mg in D5W or NS 250 mL may be prepared for a concentration of 3200 µg/ml. MUST BE THROUGH A CENTRAL LINE

5. ADVERSE REACTIONS

- tachyarrhythmias
- hypertension
- extravasation may cause severe tissue necrosis (antidote is phentolamine – 5 to 10 mg in 10 to 15 mL of saline should be administered intradermally as soon as possible)

6. CAUTIONS/COMMENTS

- use a central line to minimize extravasation
- in patients with profound metabolic acidosis (pH ≤ 7.01), dopamine causes the release of norepinephrine from nerve terminals, which contributes to its vasoconstrictive and inotropic effects
- patients with low stores of norepinephrine (e.g. heart failure patients) may be less responsive
Norepinephrine Bitartrate (levaterenol)

1. **PHARMACOLOGY**
   - stimulates $\alpha$-adrenergic receptors inducing peripheral vasoconstriction
   - also stimulates $\beta_1$-adrenergic receptors of the heart increasing contractility, heart rate and cardiac output
   - no effect on $\beta_2$-adrenergic receptors of the lung

2. **INDICATIONS**
   - severe hypotension (e.g. patients with low SVR)

3. **DOSAGE**
   - start infusion at 2 to 4 $\mu$g/min and then titrate to desired response
   - up to 30 $\mu$g/min may be required in patients with refractory shock

4. **PREPARATION AND ADMINISTRATION**
   - standard concentration is made by adding 4 mg to D5W or NS 250 mL for a concentration of 16 $\mu$g/mL
   - for a more concentrated solution, may add 8 mg to D5W or NS 250 mL for a concentration of 32 $\mu$g/mL. MUST BE THROUGH A CENTRAL LINE

5. **ADVERSE REACTIONS**
   - tachyarrhythmias
   - hypertension
   - decreased renal perfusion
   - increased myocardial oxygen demand
   - extravasation may cause severe tissue necrosis (antidote: phentolamine 5 to 10 mg in 10 to 15 mL of saline should be administered intradermally as soon as possible

5. **CAUTIONS/COMMENTS**
   - use central line to minimize extravasation

Phenylephrine Hydrochloride

1. **PHARMACOLOGY**
   - stimulates $\alpha_1$-adrenergic receptors to cause vasoconstriction
   - little effect on $\beta_1$-adrenergic receptors of the heart at therapeutic doses (at higher doses, may see increased contractility)
   - no effect on $\beta_2$-adrenergic receptors of lung or peripheral blood vessels
   - indirect effect by releasing norepinephrine from its storage sites

2. **INDICATIONS**
   - hypotension (e.g. patients with low SVR)
3. **DOSAGE**

- a bolus of 100 µg IV push may be given if needed
- start a continuous infusion at 50 µg/min then titrate to desired response
- the recommended dosage range is 50 to 300 µg/min

4. **PREPARATION AND ADMINISTRATION**

- standard concentration is made by adding 10 or 20 mg to D5W or NS 250 mL for a concentration of 40 and 80 µg/mL, respectively
- for a more concentrated solution, may add 50 or 100 mg to D5W or NS 250 mL for a concentration of 200 or 400 µg/mL, respectively. MUST BE THROUGH A CENTRAL LINE

5. **ADVERSE REACTIONS**

- hypertension
- reflex bradycardia
- decreased cardiac output
- increased myocardial oxygen demand
- extravasation may cause severe tissue necrosis (antidote: phentolamine 5 to 10 mg in 10 to 15 mL of saline intradermally as soon as possible

6. **CAUTIONS/COMMENTS**

- use central line to minimize extravasation
- phenylephrine induced bradycardia and decreased cardiac output may be treated with atropine
- after IV push administration, the pressor effect occurs immediately and lasts for 15-20 minutes
- may be given intramuscularly or subcutaneously

**Epinephrine Hydrochloride**

1. **PHARMACOLOGY**

- directly stimulates α- and β- adrenergic receptors
- at therapeutic doses, main effects are cardiac stimulation and relaxation of smooth muscle of the lung
- dose related effects:
  - low dose – stimulate β-adrenergic receptors leading to increased contractility and heart rate
  - high dose – stimulate α-adrenergic receptors leading to vasoconstriction

2. **INDICATIONS**

- refractory hypotension
- symptomatic bradycardia
- severe anaphylaxis

3. **DOSAGE**

- start a continuous infusion at 1 µg/min then titrate to desired response
- the recommended dosage range is 1 to 12 µg/min; those with refractory hypotension may require higher doses
4. **PREPARATION AND ADMINISTRATION**

- standard concentration is made by adding 1 or 2 mg to D5W or NS 250 mL for a concentration of 4 or 8 µg/mL, respectively
- for a more concentrated solution, may add 10 or 25 mg to D5W or NS 250 mL. MUST BE THROUGH A CENTRAL LINE

5. **ADVERSE REACTIONS**

- tachyarrhythmias
- hypertension
- increased myocardial oxygen demand
- extravasation may cause severe tissue necrosis (antidote: phentolamine 5 to 10 mg in 10 to 15 mL of saline should be administered intradermally as soon as possible)

6. **CAUTIONS/COMMENTS**

- use central line to minimize extravasation
- may be given through an endotracheal (ET) tube, inhalation, or subcutaneously

**Vasopressin**

1. **PHARMACOLOGY**

- directly stimulates V₁ receptors of smooth muscles to cause vasoconstriction
- has little effect on vasoconstriction in hemodynamically normal patients

2. **INDICATIONS**

- vasodilatory shock
- diabetes insipidus
- GI hemorrhage
- cardiopulmonary resuscitation

3. **DOSAGE**

- optimum dosage remains to be established; clinical studies recommend a continuous infusion of 0.02-0.04 units/minute for vasodilatory shock
- can give 5-10 units IM or SQ 2-4 times daily as needed for diabetes insipidus
- a continuous infusion of 0.2-0.4 units/minute recommended for GI hemorrhage
- bolus 40 units as a single, one-time dose over 3-5 minutes during cardiopulmonary resuscitation

4. **PREPARATION AND ADMINISTRATION**

- standard concentration is made by adding 200 units to D5W 500 mL for a concentration of 0.4 units/mL

5. **ADVERSE REACTIONS**

- coronary artery vasoconstriction
- bradycardia
- decreased urine output
- bronchial constriction
6. **CAUTIONS/COMMENTS**
   - monitor blood pressure via arterial line
   - monitor CVP, UOP and ECG
   - when used for diabetes insipidus, monitor serum sodium and osmolality at least once daily

**Dobutamine Hydrochloride**

1. **PHARMACOLOGY**
   - directly stimulates β₁-adrenergic receptors of the heart
   - at therapeutic doses, increases contractility, heart rate and cardiac output by stimulating β₁-adrenergic receptors

2. **INDICATIONS**
   - heart failure
   - hypotension (e.g. patients with high SVR and pulmonary capillary wedge pressure)

3. **DOSAGE**
   - usual dosage is 2 to 20 µg/kg/min by continuous infusion

4. **PREPARATION AND ADMINISTRATION**
   - standard concentration is made by adding 250 or 500 mg to D5W or NS 250 mL for a concentration of 1000 µg/mL or 2000 µg/mL, respectively
   - for a more concentrated solution, may add 1000 or 2000 mg to D5W or NS 250 mL (total volume) for a concentration of 4 mg/mL and 8 mg/mL, respectively. MUST BE THROUGH A CENTRAL LINE

5. **ADVERSE REACTIONS**
   - tachyarrhythmias
   - increased myocardial oxygen demand
   - hypo/hyper- tension
   - extravasation may cause tissue ischemia or necrosis (use phentolamine for large amounts of extravasation to prevent vasoconstriction)

6. **CAUTIONS/COMMENTS**
   - slightly pink to brown colored solution is still potent

**Milrinone**

1. **PHARMACOLOGY**
   - phosphodiesterase inhibitor with both positive inotropic and vasodilatory activity
   - inotropic activity not associated with α- or β- adrenergic activity
   - vasodilatory effect due to direct action on vascular smooth muscle
2. **INDICATIONS**
- heart failure refractory to dobutamine

3. **DOSAGE**
- loading dose of 0.05 mg/kg is given over 15 to 30 minutes
- following loading dose, 0.375 to 0.75 µg/kg/min is given by continuous infusion

4. **PREPARATION AND ADMINISTRATION**
- standard concentration is made by adding 20 or 40 mg to D5W or NS to 100 and 200 mL, respectively, for a concentration of 0.2 mg/mL
- for a more concentrated solution, may add 40 mg to D5W or NS 100 mL for a concentration of 0.4 mg/mL. MUST BE THROUGH A CENTRAL LINE

5. **ADVERSE REACTIONS**
- may exacerbate myocardial ischemia
- hypotension
- nausea/vomiting
- thrombocytopenia (resolves within 1 to 2 weeks of decreasing dose or discontinuing therapy)

6. **CAUTIONS/COMMENTS**
- may be used with other inotropes to produce additive response
- rapid IV administration during loading dose may cause profound hypotension

### Hemodynamic effects of inotropic agents

<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose (mcg/kg/min)</th>
<th>HR</th>
<th>MAP</th>
<th>PCWP</th>
<th>CO</th>
<th>SVR</th>
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### Receptor effects of inotropic agents and vasopressors

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<th>β&lt;sub&gt;1&lt;/sub&gt;</th>
<th>β&lt;sub&gt;2&lt;/sub&gt;</th>
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