Disclosure

- “I have no relevant financial relationships with the manufacturer(s) of any commercial product(s) and/or provider of commercial services discussed in this CME activity.”

- “I do not intend to discuss an unapproved/investigative use of a commercial product/device in my presentation.”
Cardiovascular System

• Low pressure pulmonary and high pressure systemic circulations connected in series

• Function: Deliver oxygen and nutrients to tissues

• Two phases of cardiac cycle
  • Systole – contraction- Ejection
  • Diastole – relaxation- Filling
What Determines BP?

- Remember *Ohm’s Law*: 
  - “\( V = I \times R \)”
- Pressure = Flow x Resistance
  - Systemic BP = SBF x SVR
  - Pulmonary BP = PBF x PVR
  - For patients with normal cardiac anatomy, SBF = PBF = Cardiac Output
Balance between Pressure & Flow

- **Pressure is needed**
  - BP = CO x SVR
  - Organ perfusion pressure
    - Renal = MAP – CVP
    - Brain = MAP – ICP
    - Heart = DBP – CVP

- **Flow is what matters**
  - CO = SV x HR
Blood Pressure

- BP is essential to allow the heart to deliver blood, containing oxygen and nutrients required throughout the body. To get the blood to travel that far, fast enough, it has to be under pressure.

- This pressure is created by the relationship between three elements:
  - the heart’s pumping action
  - the size and stretchiness of the blood vessels
  - the thickness of the blood itself
Blood Pressure

- Gestation and postnatal age are the dominant influences on BP

- The number of the mean BP in mmHg should be higher than the number of weeks of the baby’s gestation at the time of birth (Lee et al, 1999)
Mean Arterial Pressure “MAP”

- It is used to judge the normality of data obtained from the indwelling arterial line
- Less artifact caused by resonance, thrombi, and air bubbles
- The lower limits of mean BP during the first day of life are approximately similar to the gestational age of the infant
- Most preterm infants, even at 24-26 weeks' gestation, have a mean BP of 30 mm Hg or greater by the third day of life

Mean arterial pressure (MAP) = Systolic BP + 2 (diastolic BP) / 3
Clinical Relevance

- Why do we care about BP?
  - Adequate perfusion pressure is needed to supply blood to all tissues of the body

- Why do we care about SBF?
  - Adequate blood flow is required to provide enough oxygen to tissues

- Why do we care about SVR/PVR?
  - It directly influences SBF and BP
Clinical Relevance

- Cardiac output, blood pressure and resistance are all interrelated and all important.
- Why do we focus so much on BP?
  - Because it is the easiest to measure!
- It is important to recognize that cardiac output may be the most physiologically relevant variable.
Cardiac output (CO) is the quantity of blood delivered to the systemic circulation per unit time:

\[
\text{Cardiac output (CO)} = \text{Ventricular stroke volume (L/beat)} \times \text{heart rate (beats/min)} = \text{L/min}
\]
Estimation of cardiac output - Clinical Examination

- Vitals:
  - Hyperthermia, tachycardia, tachypnea, hypotension, narrow pulse pressure

- Mental status:
  - Lethargy, decreased responsiveness

- Perfusion:
  - Cool temperature, prolonged capillary refill, poor pulses
Estimation of cardiac output - Bedside monitoring

- EKG tracing:
  - Rate and rhythm

- Organ blood flow (Near-infrared spectroscopy “NIRS”)

- Echocardiography (measuring systemic blood flow)

- Arterial wave form:
  - Narrow wave form with “spiked” tracing is often sign of low output

- Atrial pressure/CVP:
  - very low with hypovolemia,
  - high with ventricular dysfunction

- Urine output:
  - < 1 cc/kg/hr may indicate poor renal perfusion and low CO
Pulse Pressure

- SBP – DBP (30-40 mm Hg)
- **WIDE (> 40 mmHg)**
  - Thyrotoxicosis
  - Run-off lesions (AI, PDA)
  - Sepsis (∨ SVR)
  - Anemia

- **NARROW (< 25 mmHg)**
  - Pericardial effusion
  - Constrictive pericarditis

- Respiratory variations
Estimation of cardiac output

Laboratory Data

- Acid-Base balance:
  - Decreased serum bicarbonate
  - Increased serum lactate
  - Tissue hypoxia/anaerobic metabolism
  - Not very useful in quantifying CO

- Renal function:
  - BUN/Creatinine
  - Hyperkalemia

- Liver enzymes:
  - May be elevated, but generally with very low output
Determinants of Cardiac Output

- Heart rate and rhythm
- Preload
- Afterload
- Contractility
- Distensibility
Hypotension

- When BP is lower than the expected reference range
- Normal physiologic range for BP is defined by the presence of normal organ blood flow. This is not well studied in the newborn population
- In clinical practice, the reference range BP limits are defined as the gestational age–dependent and postnatal age–dependent BP values between the 5\textsuperscript{th} (or 10\textsuperscript{th}) and 95\textsuperscript{th} (or 90\textsuperscript{th}) percentiles
Hypotension

- Hypotension frequently, but not always, accompanies shock

- Sole reliance on BP will lead to inaccurate and sometimes significantly delayed diagnosis of circulatory compromise, especially in very preterm infants immediately after birth
Neonatal Shock - Risk Factors

- Umbilical cord accident
- Placental abnormalities
- Fetal or neonatal hemolysis
- Fetal or neonatal hemorrhage
- Maternal infection
- Maternal anesthesia, hypotension
- Intrauterine asphyxia, intrapartum asphyxia
- Neonatal sepsis
- Pulmonary air leak syndromes
- Lung overdistension during positive pressure ventilation
- Cardiac arrhythmias
Neonatal Shock - Causes

- **Hypovolemic shock** is caused by acute blood loss or fluid and electrolyte losses.
- **Distributive shock** is caused by sepsis, vasodilators, myocardial depression, or endothelial injury.
- **Cardiogenic shock** is caused by cardiomyopathy, heart failure, arrhythmias, or myocardial ischemia.
- **Obstructive shock** is caused by tension pneumothorax or cardiac tamponade.
- **Dissociative shock** is caused by profound anemia or methemoglobinemia.
Pharmacologic Therapy
Inotropes vs Pressors

- **Inotrope:** Pharmacologic agent that increases force of myocardial contraction

- **Pressor:** Pharmacologic agent that increases blood pressure
Inotropes vs Pressors

- Although many inotropes are pressors (e.g. dopamine, epi), not all are (e.g. milrinone)
- Some pressors have little inotropic effect (e.g. phenylephrine)
- Distinction is important and need to use the agent appropriate for the patient’s physiology
Sites of catecholamine receptors

<table>
<thead>
<tr>
<th>Site</th>
<th>Receptor Type</th>
<th>Stimulation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Heart</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sinus node</td>
<td>$\beta_1$</td>
<td>Increased heart rate</td>
</tr>
<tr>
<td>Atroventricular node</td>
<td>$\beta_1$</td>
<td>Increased heart rate</td>
</tr>
<tr>
<td>Atria + ventricles</td>
<td>$\beta_1$</td>
<td>Increased contractility</td>
</tr>
<tr>
<td>Coronary circulation</td>
<td>$\alpha$</td>
<td>Vasoconstriction</td>
</tr>
<tr>
<td>Coronary circulation</td>
<td>DA</td>
<td>Vasodilatation</td>
</tr>
<tr>
<td><strong>Peripheral Vasculature</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>$\alpha$</td>
<td>Vasoconstriction</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>$\alpha$</td>
<td>Vasoconstriction</td>
</tr>
<tr>
<td>Renal</td>
<td>DA</td>
<td>Vasodilatation</td>
</tr>
<tr>
<td>Mesenteric + splanchnic</td>
<td>$\beta_2$, DA</td>
<td>Vasodilatation</td>
</tr>
<tr>
<td>Skeletal muscle</td>
<td>$\beta_2$</td>
<td>Vasodilatation</td>
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<tr>
<td><strong>Nonvascular</strong></td>
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<td></td>
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<tr>
<td>Renal tubule</td>
<td>DA</td>
<td>Diuresis</td>
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<tr>
<td>Bronchial tree</td>
<td>$\beta_2$</td>
<td>Bronchodilatation</td>
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</table>

DA, dopamine
Inotropes/Pressors: Sites of Action

Table 5.1. Inotropes and Vasodilators—Their Sites of Action and Hemodynamic Effects

<table>
<thead>
<tr>
<th>Drug</th>
<th>α</th>
<th>β₁</th>
<th>β₂</th>
<th>DA*</th>
<th>Na⁺/K⁺ ATPase</th>
<th>CO</th>
<th>Contr.</th>
<th>SVR</th>
<th>MAP</th>
<th>PCWP</th>
<th>HR</th>
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<tr>
<td>Epinephrine</td>
<td>+++</td>
<td>+++</td>
<td>+++</td>
<td></td>
<td>↑↑ ↑</td>
<td>↑↑</td>
<td>↓</td>
<td>↑←↓</td>
<td>↑←</td>
<td>↑←</td>
<td>↑←</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>+++</td>
<td>+</td>
<td></td>
<td></td>
<td>↑←↓ ↑</td>
<td>↑</td>
<td>↓</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
<td>↑↑↑</td>
</tr>
<tr>
<td>Dopamine</td>
<td>++</td>
<td>++</td>
<td>+</td>
<td>++*</td>
<td>↑↑ ↑</td>
<td>↑↑</td>
<td>↑←</td>
<td>↑←↓</td>
<td>↑←</td>
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<tr>
<td>Dobutamine</td>
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<td>+++</td>
<td>+</td>
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<td>↑↑ ↑</td>
<td>↑↑</td>
<td>↓</td>
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<tr>
<td>Isoproterenol</td>
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<tr>
<td>Amrinone</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td></td>
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<td>↑↑</td>
<td>↑←↓</td>
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<tr>
<td>Milrinone</td>
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<td></td>
<td>↑↑ ↑</td>
<td>↑↑</td>
<td>↑←</td>
<td>↓</td>
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<td>↓</td>
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<tr>
<td>Enoximone</td>
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<td>↑</td>
<td>↓</td>
<td></td>
<td>↑↑ ↑</td>
<td>↑↑</td>
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<td>↓</td>
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<tr>
<td>Nitroprusside</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td></td>
<td>↑↑ ↑</td>
<td>↑↑</td>
<td>↑←</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
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<tr>
<td>Nitroglycerin</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
<td></td>
<td>↑↑ ↑</td>
<td>↑↑</td>
<td>↑←</td>
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<td>↓</td>
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<tr>
<td>Captopril</td>
<td>↑</td>
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<td>↓</td>
<td></td>
<td>↑↑ ↑</td>
<td>↑↑</td>
<td>↑←</td>
<td>↓</td>
<td>↓</td>
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<tr>
<td>Digoxin</td>
<td>+++</td>
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<td></td>
<td></td>
<td>↑↑ ↑</td>
<td>↑↑</td>
<td>↑</td>
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</tr>
</tbody>
</table>

ATPase, adenosine triphosphatase; CO, cardiac output; Contr., contractility; DA, dopamine; HR, heart rate; MAP, mean arterial pressure; PCWP, pulmonary capillary wedge pressure; SVR, systemic vascular resistance

* Dopamine stimulates DA₁ and DA₂ receptors.
Physiologic effect of Pressors

- Increase force of contraction
  - β effect
- Increase heart rate
  - β effect
- Cause systemic vasoconstriction
  - α effect

*Increase myocardial oxygen consumption*
Pressors

- **Epinephrine** (α and β)
  - 0.02-0.1 mcg/kg/min
- **Dopamine** (α and β, DA)
  - 3-20 mcg/kg/min
- **Phenylephrine** (α)
  - 0.1-0.5 mcg/kg/min
- **Norepinephrine** (α, some β)
  - 0.05-1.0 mcg/kg/min
- **Vasopressin** (V1)
  - 0.0004-0.02 U/kg/min
Physiologic effect of Inotropes

- Increase force of contraction
- Increase HR (variable)
- May cause systemic vasodilatation or vasoconstriction...dependent on agent used.

*Increase myocardial oxygen consumption*
Inotropes

- Milrinone (PDE III inhibitor)
  - 0.25-0.75 mcg/kg/min
- Dobutamine ($\beta$, $\pm$ $\alpha$)
  - 2-20 mcg/kg/min
- Isoproterenol ($\beta$)
  - 0.05-2 mcg/kg/min
- Epinephrine ($\alpha$ and $\beta$)
- Dopamine ($\alpha$ and $\beta$)
- Digoxin (indirectly increase $[Ca]$)
- T3
Dilemma

- Can we improve cardiac output, but decrease myocardial oxygen consumption?
  - Afterload reduction (i.e. vasodilatation)
Afterload Reducers

- Nitroprusside
  - 0.3-10 mcg/kg/min (Keep thiocyanate < 12 mg/L)
- Milrinone
- Dobutamine
- ACE inhibitors (captopril, enalapril)
- Hydralazine
- Ca channel blockers
- AT receptor blockers
Choice of Vasoactive Agent

Hypotensive with poor perfusion

- **Physiology**: Low CO, ± high SVR
- **Clinical scenario**: “Pump dysfunction” (i.e. cardiomyopathy, post-CPB)
- **Goal of Rx**: Increase CO (pressor + inotrope)

Use combined α and β agent (dopa or epi), ± milrinone
Choice of Vasoactive Agent

- **Hypotensive with normal perfusion**
  - **Physiology:** Low SVR
  - **Clinical scenario:** Sepsis
  - **Goal of Rx:** Increase SVR (pressor)

*Use a agent* *(norepi, vasopressin)*

± *inotrope* *(epi or dopa)*
**Choice of Vasoactive Agent**

- **Normotensive with poor perfusion**
  - **Physiology**: High SVR, Low CO
  - **Clinical scenario**: Compensated cardiogenic shock (i.e. cardiomyopathy, myocarditis)
  - **Goal of Rx**: Decrease SVR, increase CO

*Use afterload reducer/inotropic agent (milrinone, dobutamine, nitroprusside)*
# Choice of Vasoactive Agent

<table>
<thead>
<tr>
<th>Shock type</th>
<th>Normal BP</th>
<th>Decreased BP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiogenic</td>
<td>Milrinone or dobutamine and nesiritide</td>
<td>Epinephrine or dopamine</td>
</tr>
<tr>
<td>Septic</td>
<td>None or dopamine</td>
<td>Norepinephrine</td>
</tr>
<tr>
<td>Anaphylactic</td>
<td>Epinephrine SC</td>
<td>Epinephrine IV</td>
</tr>
<tr>
<td>Hypovolaemic</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
Thank You