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DISCLOSURES

- NONE
OBJECTIVES

- Identify the physiology of vasopressors and inotropes
- Discuss the deleterious side effects of these medications
- Discuss the management of septic shock
Adrenergic Receptor Physiology

- Alpha-1
- Beta-1
- Beta-2
- Dopamine
Alpha Adrenergic Receptors

- Located in vascular walls
  - Induces significant vasoconstriction

- Present in heart
  - Increase the duration of the contraction without increased chronotropy.
Beta Adrenergic Receptors

- Beta-1 adrenergic receptors are most common in the heart
  - Mediate increases in inotropy and chronotropy with minimal vasoconstriction.

- Beta-2 adrenergic receptors in blood vessels induce vasodilation.
Dopamine Receptors

- Present in the renal, splanchnic, coronary, and cerebral vascular beds.
- Stimulation of these receptors leads to vasodilation.
- Second subtype of dopamine receptors causes vasoconstriction by inducing norepinephrine release.
Principles Of Use Of Vasopressors and Inotropes

- Hypotension may result from:
  - Hypovolemia
  - Pump failure
  - Pathologic maldistribution of blood flow

- Vasopressors are indicated for:
  - Decrease of >30 mmHg from baseline SBP or
  - MAP <60 mmHg and
  - Evidence of end-organ dysfunction due to hypoperfusion

- Hypovolemia must be corrected first
Principles Of Use Of Vasopressors and Inotropes

- Use of vasopressors and inotropes is guided by three fundamental concepts:
  - One drug, many receptors
  - Dose-response curve
  - Direct versus reflex actions
Repletion of adequate intravascular volume, when time permits, is crucial prior to the initiation of vasopressors.

- Vasopressors will be ineffective or only partially effective in the setting of coexisting hypovolemia.

Fluids may be withheld in patients with significant pulmonary edema due to ARDS or CHF.
Selection and Titration

- Choice of an initial agent should be based upon the suspected underlying etiology of shock.
- Dose should be titrated up to achieve effective BP or end-organ perfusion.
- If maximal doses of a first agent are inadequate, then a second drug should be added to the first.
Tachyphylaxis

- Responsiveness to these drugs can decrease over time due to tachyphylaxis.
- Doses must be constantly titrated to adjust for this phenomenon and for changes in the patient's clinical condition.
Subcutaneous Drug Delivery

- Bioavailability of subcutaneous heparin or insulin can be reduced during treatment with vasopressors due to cutaneous vasoconstriction.
Phenylephrine (Neosynephrine)

- Purely alpha-adrenergic agonist activity
  - Vasoconstriction with minimal cardiac inotropy or chronotropy.

- Useful in settings of hypotension with SVR < 700 dynes x sec/cm<sup>5</sup>
  - Hyperdynamic sepsis, neurologic disorders, anesthesia induced hypotension.

- Contraindicated if SVR > 1200 dynes x sec/cm<sup>5</sup>
Norepinephrine (Levophed)

- Acts on both alpha-1 and beta-1 receptors
  - Potent vasoconstriction as well as a less pronounced increase in cardiac output
- Reflex bradycardia usually occurs in response to the increased MAP
  - Mild chronotropic effect is cancelled out and the HR remains unchanged or decreases slightly.
- Used most commonly to treat septic shock.
Epinephrine (Adrenalin)

- Potent beta-1 receptor activity and moderate beta-2 and alpha-1 receptor effects.
- Result is an increased CO, with decreased SVR and variable effects on the MAP.
- Beta-1 receptor stimulation may provoke dysrhythmias.
- Greater degree of splanchnic vasoconstriction.
- Most often used in treatment of anaphylaxis, as a second line agent in septic shock and for management of hypotension following CABG.
Dopamine (Intropin)

- At low doses, dopamine acts predominately on dopamine-1 receptors in the renal mesenteric, cerebral, and coronary beds, resulting in selective vasodilation.

- At moderate doses, dopamine also stimulates Beta-1 receptors and increases CO, predominately by increasing SV with variable effects on HR.
  - Can result in dose-limiting dysrhythmias

- At higher doses, dopamine stimulates alpha receptors and produces vasoconstriction with an increased SVR.
Dopamine (Intropin)

- The dose-dependent effects of dopamine mean that increasing the dose of the drug is akin to switching vasopressors.
- Most often used in hypotension due to sepsis or cardiac failure
Dobutamine (Dobutrex)

- Not a vasopressor but rather an inotrope that causes vasodilation.
- Predominant beta-1 receptor effect increases inotropy and chronotropy and reduces LV filling pressures.
- Minimal alpha and beta-2 receptor effects result in overall vasodilation, complemented by reflex vasodilation to the increased CO.
- Net effect is increased CO, with decreased SVR with or without a small reduction in BP.
Dobutamine (Dobutrex)

- Frequently used in severe, medically refractory heart failure and cardiogenic shock.
- Should not be routinely used in sepsis because of the risk of hypotension.
- Does not selectively vasodilate the renal vascular bed.
Phosphodiesterase Inhibitors

- Amrinone and Milrinone
- Nonadrenergic drugs with inotropic and vasodilatory actions.
- Effects are similar to dobutamine but with a lower incidence of dysrhythmias.
- Used to treat patients with impaired cardiac function and medically refractory HF.
- Vasodilatory properties limit their use in hypotensive patients.
Vasopressin

- Usually used in the setting of DI or esophageal variceal bleeding.
- May be useful in the treatment of refractory septic shock, particularly as a second pressor agent.
- Studies showed that the addition of vasopressin to norepinephrine was more effective in reversing late vasodilatory shock than norepinephrine alone.
- Complications include coronary and mesenteric ischemia, hyponatremia, pulmonary vasoconstriction, and skin necrosis from peripheral infusion.
Complications
Hypoperfusion

- Commonly occurs in the setting of inadequate cardiac output or inadequate volume resuscitation.
- Dusky skin changes at the tips of the fingers and toes, renal insufficiency and oliguria, and possible limb ischemia.
- Increase the risk of gastritis, shock liver, intestinal ischemia, or translocation of gut flora with resultant bacteremia.
Complications

Dysrhythmias

- Stimulation of beta-1 receptors.
- Increases the risk of sinus tachycardia, atrial fibrillation, AVnRT, or ventricular tachyarrhythmias.
- Limit the maximal dose and necessitate switching to another agent with less prominent beta-1 effects.
Complications

Myocardial ischemia

- Beta receptor stimulation can increase myocardial oxygen consumption.
- Excessive tachycardia should be avoided because of impaired diastolic filling of the coronary arteries.
Complications
Local effects

- Peripheral extravasation of vasopressors into the surrounding connective tissue can lead to excessive local vasoconstriction with subsequent skin necrosis.

- Vasopressors should be administered via a central line.

- Local treatment with phentolamine (5 – 10mg) sub-Q can minimize local vasoconstriction.
Complications

Hyperglycemia

- May occur due to inhibition of insulin secretion.
- Magnitude of hyperglycemia generally is mild.
- More pronounced with norepinephrine and epinephrine than dopamine.
Drug interactions/Contraindications

- Patients with pheochromocytoma are at risk of excessive autonomic stimulation from pressors.
- Dobutamine is contraindicated in the setting of IHSS.
- Patients receiving monoamine oxidase inhibitors are extremely sensitive to pressors, and require much lower doses.
“Renal-dose” Dopamine

- Dopamine selectively increases renal blood flow when administered at 1-3 mcg/kg/min
- Currently, there is no data to support the routine use of low dose dopamine to prevent or treat acute renal failure or mesenteric ischemia.
Vasopressor Use in Septic Shock

- Patients with hyperdynamic septic shock (hypotension, low SVR, and high CI) tend to have warm extremities due to inappropriate hyperperfusion of the skin and soft tissues.
  - Norepinephrine and phenylephrine appear more potent in hyperdynamic sepsis.

- Patients with hypodynamic septic shock (hypotension, low SVR, and low CI) manifest hypoperfusion of the extremities.
  - Dopamine may be preferable in patients with hypodynamic sepsis.
Management of Septic Shock
Introduction

- Over 750,000 cases of sepsis occur in the U.S. each year
- Approximately 200,000 fatalities
- Unfortunately, even with optimal treatment, the mortality rate from severe sepsis or septic shock is approximately 40%.
Therapeutic Priorities

- First priority is to employ supportive measures that counter physiologic abnormalities such as hypoxemia, hypotension, and impaired tissue oxygenation.
- Early efforts must determine if SIRS is due to a noninfectious cause or is the result of an infection.
- Identifying that infection is the cause of SIRS and finding the source are critical early priorities.
- Patient must be assessed for adequate tissue perfusion.
Initial Management

- Resuscitation
- Supportive care
- Monitoring
- Targeted antimicrobial therapy
- Drainage for infection
Resuscitation

- The first step in the management of the patient with septic shock is to assess the ABC’s.
- Supplemental oxygen should be supplied to all patients with sepsis.
- The next priority is to assist ventilation and augment oxygenation.
- Then, measures are taken to restore the BP to levels that perfuse vital organs.
Monitoring of Tissue Perfusion

- Circulatory failure is present by definition in patients with septic shock.
- The sphygmomanometer may be unreliable in hypotensive patients.
- An arterial catheter may be inserted if blood pressure is labile or if restoration of arterial perfusion pressures is expected to be a lengthy process.
Monitoring of Tissue Perfusion

- Signs of impaired organ perfusion that occur in shock include:
  - Cool, vasoconstricted skin
  - Obtundation or restlessness
  - Oliguria/anuria
  - Lactic Acidosis
  - Gastric intramucosal acidosis

- Clinical findings of shock may be modified by preexisting disease.
Restoration of Tissue Perfusion

- Hypotension is sepsis results from:
  - A loss of plasma volume into the interstitial space.
  - Decreases in vascular tone.
  - Myocardial depression.

- IV fluids, pRBC’s, and pressors are often required, depending upon the patient’s volume status, cardiac status, and the severity of shock.
Intravenous Fluids

- Rapid, large volume infusions of IVF are usually indicated as initial therapy in patients with septic shock.
- Fluid therapy should be administered in well-defined, rapidly infused boluses.
  - Careful monitoring is essential in this approach because patients with sepsis can develop pulmonary edema at wedge pressures <18
Vasopressors

- Second line agents in the treatment of severe sepsis and septic shock
  - IVF are preferred so long as they increase CO and/or BP without seriously impairing gas exchange.
- Large trials comparing outcomes with different vasopressors have not been performed, and therefore there is no definitive evidence of the superiority of one pressor over another.
Identification of the Septic Focus

- A careful history and physical may yield clues to the source of sepsis and help guide subsequent microbiologic evaluation.

- Gram stain of suspicious fluids may give early clues to the etiology of infection while cultures are incubating.
Eradication of Infection

- Essential to the successful treatment of septic shock.
- Source control should be undertaken when possible because undrained foci of infection may not respond to antibiotics alone.
- An empiric regimen of broad spectrum antibiotics should also be instituted as early as possible after appropriate cultures have been collected.
Eradication of Infection

- Choice of antibiotics should be based upon clinical and Gram stain data and local resistance patterns, and then should be adjusted as culture results become available.

- Potential gram negative pathogens are generally covered with two effective agents from different antibiotic classes.

- Regardless of the antibiotic regimen, patients should be observed closely for toxicity, evidence of response, and for the development of superinfection.
Corticosteroids

- Many patients with septic shock have a relative adrenal insufficiency.
- Physiologic stress dose steroids were associated with a shorter duration of pressor dependence, as well as an improvement in 28-day mortality.
- Therapy was not associated with an increased incidence of adverse events.
- Monitor for hyperglycemia in this setting.
Nutrition

- Adequate nutritional support is essential for optimal immune function, and appears beneficial in both the prevention and the treatment of sepsis.
  - Improves wound healing and decreases susceptibility to infection.
  - Enteral nutrition may offer more benefit than parenteral nutrition.
  - Nutritional support results in higher lymphocyte counts and higher serum albumin levels.
  - Hyperglycemia and insulin resistance are common in critically ill patients. Evidence suggests that aggressive glucose control may improve outcome in these patients.
THANK YOU
QUESTION #1

Which is the most correct answer

1) Phenylephrine may cause tachycardia
2) Epinephrine can be safely used through a peripheral IV
3) Norepinephrine only works on β1 receptors
4) Dobutamine causes vasodilation
Echocardiography: The Stethoscope of the 21st Century

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DISCLOSURES

- NONE
Objectives

- Indications for ultrasonography
- Traditional evaluation of hemodynamic instability
  - Preload
  - Cardiac
    - Right Ventricle
    - Left Ventricle
- TTE Hemodynamic Assessment
  - Preload
  - Cardiac
    - Right Ventricle
    - Left Ventricle
- Feasibility of training
## Indications for Ultrasound

<table>
<thead>
<tr>
<th>Indication</th>
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</thead>
<tbody>
<tr>
<td>Hemodynamic instability</td>
</tr>
<tr>
<td>Infective endocarditis</td>
</tr>
<tr>
<td>Aortic dissection</td>
</tr>
<tr>
<td>Unexplained hypoxemia</td>
</tr>
<tr>
<td>Intracardiac thrombus</td>
</tr>
<tr>
<td>Perioperative management of hemodynamics</td>
</tr>
<tr>
<td>Procedural guidance</td>
</tr>
<tr>
<td>Evaluation for PTX or pleural effusion</td>
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<tr>
<td>Evaluation of ICP</td>
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<tr>
<td>Evaluation of trauma patient</td>
</tr>
<tr>
<td>Airway mgmt</td>
</tr>
</tbody>
</table>

Crit Care Med May 2007 Suppl.
Table 1. Core emergency ultrasound applications.

- Trauma
- Intrauterine Pregnancy
- AAA
- Cardiac
- Biliary
- Urinary Tract
- DVT
- Soft-tissue/musculoskeletal
- Thoracic
- Ocular
- Procedural Guidance
<table>
<thead>
<tr>
<th>Advanced Echo</th>
<th>Transesophageal Echo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel (including intussusception, appendicitis, pyloric stenosis, diverticulitis, SBO)</td>
<td></td>
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<tr>
<td>Adnexal Pathology</td>
<td></td>
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<tr>
<td>Testicular</td>
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<tr>
<td>Transcranial Doppler</td>
<td></td>
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<tr>
<td>Contrast Studies</td>
<td></td>
</tr>
</tbody>
</table>
Shock Management

- **Preload**
  - Crystalloid or Colloid

- **Cardiac function**
  - Right Ventricle – Milrinone, Niseritide, Nitric Oxide
  - Left Ventricle – Dobutamine, Isoprel

- **Afterload**
  - Norepinephrine, Dopamine, Epinephrine, Vasopressin
Preload Evaluation

- CVP
- PAOP
- RVEDVI
Cardiac Function

- Central Venous Catheter – IJ, SC
- Pulmonary Artery Catheter
- Esophageal Doppler
- Arterial Wave Form Analysis
“PE is inaccurate and often cannot be trusted in the critically ill”

“CVP assessment was inaccurate and highly variable”
Controversy
- Highly invasive
- Associated morbidity and risks
- Diagnostic utility
- Correlation of pressure and volume indices
- Physician competence

Connors AF et al. JAMA 1996;276:889
Shure D. NEJM 2006;354:2273
Iberti et al. JAMA 1990;264:2928
Randomized trial of ARDS management

- Hemodynamic protocol guided by
  - Blood pressure
  - Urinary output
  - Physical exam

PLUS

PAC or CVP data
Multicenter

Inclusion
- Ventilation
- PaO2:FIO2 <300
- Bilateral infiltrates
- No left ventricular failure

Measured values
- PAOP, CI
- CVP

Non-measure values
- Lactate, SvO2, mixed venous
1001 randomized
501 PAC vs 480 CVC
Results – NO DIFFERENCE
- Death in first 60 days
- Ventilator free days
- ICU free days
- Shock resolution
- Organ function – lung, kidney
What is the value of PAOP?

Predicting fluid responsiveness

Clinical exam and static cardiac filling pressures are correct about 50% of the time

Feissel et al. Int Care Med 2004;30:1834
Preload by US
Predicting fluid responsiveness: TTE and IVC respiratory variation

- Feissel et al. *Int Care Med* 2004;30:1834
- Septic, ventilated patients
- TTE, Subxiphoidal long axis view
- Volume responsive = >15% increase in CO
- Respiratory change in IVC diameter >12% had a 93% PPV and 92% NPV
Preload – Subxiphoid
Preload – Subxiphoid
Non invasive evaluation of central venous pressure using echocardiography in the intensive care


16 bed medical/surgical ICU

560 pt w/ 477 IVC evaluations

APACHE II – 24 SAPS II – 56

ICU LOS - 12 days +/- 19 days

RESULTS

- IVC index < 25% and CVP > 13
- IVC index > 51 % and CVP < 7
- IVC > 20 mm and CVP > 13
Cardiac Function – Left Ventricle

Apical four chamber view

Short axis view

RV

LV

Anterior wall

Interior wall

Tricuspid valve

Mitral valve

RA

LA

PPM

APM

LV

LV

RV
Parasternal Long Axis
Cardiac Function – Left Ventricle

A

5.26 cm

B

2.99 cm
Parasternal Short Axis
Cardiac Function – Left Ventricle
Flow = Cross sectional area (CSA) \times \text{Average velocity}
- Average velocity not usually measured directly

VTI = velocity-time integral
- Area under the velocity curve for a single beat
  - Represents ‘stroke distance’

SV = VTI \times CSA
Cardiac Output – Left Ventricle
Cardiac Output – Left Ventricle

\[ \text{CSA} = \pi \cdot r^2 = 0.785 \cdot D^2 \]

\[ \text{SV} = \text{CSA} \cdot \text{VTI} \]

\[ \text{CO} = \text{SV} \cdot \text{HR} \]

\[ CI = \frac{\text{CO}}{\text{BSA}} \]
Cardiac Output – Left Ventricle

- Accurate measurement of CSA
  - Weakest link in the calculation
  - VTI very good for assessing change in cardiac output with therapy, by following changes in VTI, since CSA is largely invariant in an individual
- Measures forward flow only
  - Regurgitant fraction not considered
  - May over-estimate systemic cardiac output
- Echocardiographic window in mechanically ventilated patients may be poor
Cardiac Function – Right Ventricle
Cardiac Function – Right Ventricle
Pulmonary artery (RV) systolic pressure

\[ P_{ASP} = 4 \cdot V_{max TV}^2 + RAP \]
Global Cardiac Function
Global Cardiac Function

LA
Pericardial Effusion
RA
Shindler

Prospective study in Medical/Surgical ICU

Inclusion:
- SBP < 90 or MAP < 60 and nonresponsive to fluid challenge over 30 minutes

Goals:
- Exclude significant cardiac dysfunction (Tamponade)
- Evaluate global cardiac function (EF, CI)
- Evaluate IVC (preload)
Transthoracic Echocardiography for Evaluation of Hypotensive Critically Ill Patient

- 198/208 enrolled (4.5% unable to be examined)
- APACHE II – 30 SAPS II – 69
- Mortality 51%
- Mechanical Ventilation 82%
- Diseases
  - Cardiac 44% with severe 14% (28/87)
    - AS
    - Endocarditis
    - Dilated cardiomyopathy
    - Tamponade
- Results
  - CI and IVC Index correlated with mortality
  - Significant rate of unexpected cardiac abnormalities

- 10 one hour training sessions
- Limited TTE
  - LV fxn, RWMA, pericard. effusion
- Correctly interpreted 84%
- 94% completed studies
- Study time 10.5 +/- 4.2 min

*Limited TTE changed mgmt in 37% of patients*
FAST: A Curriculum Paradigm

- Established credentialing process and literature to support its use

- Documented success with current methods of training
  - 15-20 scans = 90% sen., 99% spec. and 99% accurate
  - 50 scans = 96% sen. and 100% accuracy
Table 3. ACEP recommended training and proficiency numerical goals per emergency ultrasound application.

<table>
<thead>
<tr>
<th>Primary Application</th>
<th>Minimum</th>
<th>Range of Documented and Outcome Reviewed Ultrasound Needed for Proficiency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trauma</td>
<td>25</td>
<td>25-50</td>
</tr>
<tr>
<td>IUP</td>
<td>25</td>
<td>25-50</td>
</tr>
<tr>
<td>Emergency cardiac</td>
<td>25</td>
<td>25-50&lt;br&gt;25 Endovaginal (if only doing EV)&lt;br&gt;25 Transabdominal (if only doing TA)</td>
</tr>
<tr>
<td>AAA</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Biliary</td>
<td>25</td>
<td>25-50</td>
</tr>
<tr>
<td>Renal</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td></td>
<td>Basic</td>
<td>Advanced</td>
</tr>
<tr>
<td>-------------------------</td>
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<td>-------------------------------</td>
</tr>
<tr>
<td>Minimum number of exams</td>
<td>150</td>
<td>300</td>
</tr>
<tr>
<td>Minimum number</td>
<td>150</td>
<td>300</td>
</tr>
<tr>
<td>personally performed</td>
<td>50</td>
<td>150</td>
</tr>
<tr>
<td>Program director</td>
<td>advanced perioperative echocardiography training</td>
<td>advanced perioperative echocardiography training, plus at least 150 additional perioperative TEE examinations</td>
</tr>
<tr>
<td>qualifications</td>
<td>wide variety of perioperative applications of echocardiography</td>
<td>full spectrum of perioperative applications of echocardiography</td>
</tr>
</tbody>
</table>

Abbreviations same as in Table 7.

Total = 150-200
Initial Training Goals

- LV function?
- RV function?
- Pericardial effusion present? Tamponade?
- Volume status?
  - Dynamic IVC assessment
**SPECIAL ANNOUNCEMENT FROM
THE NATIONAL BOARD OF ECHOCARDIOGRAPHY**

Registration is **NOW OPEN** for the inaugural Examination of Special Competence in Critical Care Echocardiography (CCEexAM).

Experts in the field have articulated the need for a critical care echocardiography examination. The NBE responded by developing a special competency examination with the help of nine societies.

We are thrilled to offer the exam and are confident experts in the field will be equally enthusiastic.

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**DELAYED OPERATIONS NOTICE**

Due to an unexpected fire at NBE headquarters, correspondence could be delayed. We appreciate your patience as we work to restore full operations. Email is the best form of communication at this time. NBE staff will be monitoring communications daily and strive to respond in a timely manner.

If you need to speak with NBE staff please call 1-833-270-1444 or 336-376-6300 to leave a message.

For **examination related questions** please email [Krista Russell, Examination Coordinator](mailto:Krussell@echoboards.org) at [Krussell@echoboards.org](mailto:Krussell@echoboards.org).
QUESTION #1

Physical exam is sensitive and specific for evaluating shock in the critically ill patient?

1) True
2) False
The FACTT Trial demonstrated that a PA catheter when compared to a CVP monitor improved

1) Mortality
2) Ventilator free days
3) Shock resolution
4) None of the above
Which of the below is most correct.

When predicting volume responsiveness during hypotension

1) Physical exam is superior to static cardiac pressure measurements
2) Static cardiac pressure measurements are superior to physical exam
3) Both static cardiac pressure measurements and physical exam are sensitive and specific for volume resuscitation
4) Neither static cardiac pressure measurements or physical exam are sensitive or specific for volume resuscitation
Which is the most correct

1) RV:LV ratio > 1 reflects the need for more volume
2) IVC index > 50% is consistent with a CVP > 13
3) A flattened septum noted on a parasternal short axis demonstrates a RV pressure overload state
4) VTI is a poor measurement to follow cardiac response to volume resuscitation