CMC Certification Review Course:
   Handout

Session #: 4
Structural Abnormalities, Acute Inflammatory Disease,
Hypertensive Crisis, Pulmonary Edema,
Pulmonary Hypertension

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Myocardial Rupture: Etiology
- Most common cause is a recent MI
  - Typically occurs 3–5 days after infarction
- Cardiac trauma
- Endocarditis
- Cardiac tumors
- Infiltrative diseases of the heart
- Aortic dissection

Myocardial Rupture: Risk Factors
- Female gender
- Advancing age
- Low body mass index (BMI)
- LAD occlusion
- Delay in revascularization
  - > 2 hours

Myocardial Rupture: Classifications
- Type I
  - Abrupt slit-like tear that generally occurs within 24 hours of an acute MI
- Type II
  - Erosion of the infarcted myocardium, which is suggestive of a slow tear of the dead myocardium
  - Typically occurs more than 24 hours after the infarct has occurred
- Type III
  - Characterized by early aneurysm formation and subsequent rupture of the aneurysm
Myocardial Rupture: Anatomical Position
- Free wall of the left or right ventricles
  - Associated with immediate hemodynamic collapse and death secondary to acute pericardial tamponade
- Interventricular septum
  - Will cause a ventricular septal defect
- Papillary muscle
  - Will cause mitral regurgitation

Myocardial Rupture: Signs & Symptoms
- Recurrent or persistent
  - Chest pain
  - Syncope
  - Jugular venous distention

Myocardial Rupture: Diagnosis
- Physical exam
- Changes in vital signs
- Clinical suspicion
- Echocardiogram
Myocardial Rupture: Treatment

- Supportive
- Surgical correction of the rupture

Papillary Muscle Rupture: Overview

- Uncommon but often fatal complication of acute MI
- Responsible for approximately 5% of deaths following MI
- Mortality can be as high as 80% during the first week post MI

- Posteromedial has a single blood supply from the posterior descending branch for a dominant RCA
  - Associated with inferior wall MI (75%)
- Anterolateral muscle is less common (25%)
- Has dual blood supplies
  - From first obtuse marginal, originating from the left circumflex artery
  - From first diagonal branch originating from the LAD
Papillary Muscle Rupture: Symptoms

- Shortness of breath
- Diaphoresis
- Signs of CHF or cardiogenic shock
- Crescendo-decrescendo systolic murmur

Papillary Muscle Rupture: Treatment

- Medical Therapy
  - Aggressive afterload reduction
  - Nitrates
  - Nitroprusside
  - Diuretics
  - IABP
  - Inotropes
  - Dobutamine
  - Dopamine
  - Surgical Therapy
  - Valve Repair
  - Valve Replacement

Ventricular Aneurysm: Overview

- Arise from a patch of weakened tissue in a ventricle
- Can be fatal
- Usually nonrupturing, because they are lined by scar tissue
- LV aneurysm can be associated with ST elevation
Ventricular Aneurysm: Overview
- Seen in 10%–20% of patients after MI
- Usually occurs following an anterior or lateral wall infarction
- Untreated aneurysm can lead to:
  - Dysrhythmias: VT
  - Systemic embolization
  - Heart failure

Ventricular Aneurysm: Signs & Symptoms
- Dysrhythmias
  - PVCs
  - VT
- Palpitations
- Visible or palpable systolic precordial bulge
- Cardiac dysfunction
  - Weakness on exertion
  - Fatigue
  - Angina
- Pulmonary edema
- Systemic embolization

Ventricular Aneurysm: Treatment
- Close medical follow-up
- Limit patient activity
- Treat heart failure
  - Vasodilators
  - Diuretics
  - Digoxin
- Antidysrhythmics
- Anticoagulants
- Surgery
  - Persistent LV failure
  - Dysrhythmia occurs
  - Aneurysm is large
# Practice Exam Questions

## Structural Abnormalities

**Question #1 - Answer**

A risk factor for myocardial rupture is:

A. Female gender. Risk factors for myocardial rupture are female gender, LAD occlusion, advancing age, low BMI, and delay in revascularization > 2 hours.

B. RCA occlusion

C. 30–50 years of age

D. All of the above

## Structural Abnormalities

**Question #2 - Answer**

Upon auscultation you note a new crescendo-decrescendo systolic murmur, which indicates:

A. Myocardial rupture

B. Papillary muscle rupture. A crescendo-decrescendo systolic murmur is heard with a papillary muscle rupture.

C. Ventricular aneurysm

D. Ventricular septal defect
The dysrhythmia associated with a ventricular aneurysm is:

A. Complete heart block
B. Atrial fibrillation
C. VT. It is commonly seen before and after treatment and is the most common reason for sudden cardiac death in this patient population.
D. Paroxysmal supraventricular tachycardia

Question #3 - Answer

Acute Inflammatory Disease

Endocarditis

- Two types
  - Acute
  - Subacute
Endocarditis: Risk Factors

- IV drug use
- Prosthetic cardiac valves
- Previous bacterial endocarditis
- Congenital malformations
- Rheumatic heart disease
- Mitral valve prolapse
- Indwelling IV devices
- Dental or surgical procedures

Endocarditis: Clinical Presentation

- Fever, chills, and fatigue (25%–80%)
- Embolic phenomenon (50%)
- Skin
  - Petechiae
  - Osler nodes
  - Splinter hemorrhage
  - Janeway lesions
  - Splenomegaly

Osler Node

[Image of Osler Node]
Splinter Hemorrhage

Endocarditis: Management
- Culture and sensitivity
- Antimicrobials
  - Vancomycin + rifampin + gentamicin
  - Nafcillin or oxacillin + gentamicin
  - Penicillin + gentamicin

Pericarditis: Definition
- Inflammation of the pericardium
- Variety of etiologies
Pericarditis: Etiology
- Renal disease (uremia)
- Neoplasms
- Rheumatic heart disease
- Other
  - Anticoagulants
  - Idiopathic thrombocytopenic purpura (ITP)

Pericarditis: Clinical Presentation
- Severe constant pain
  - Pain intensifies with inspiration
  - Pain relieved by sitting up and leaning forward
  - Pericardial friction rub

Pericarditis: Diagnostics
- CBC with differential
- BUN, creatinine, cardiac enzymes
- ECG
- Chest x-ray
Pericarditis: Management

- Limit activity
- Patient education regarding complications
- Anti-inflammatory agents
  - Nonsteroidal anti-inflammatory drugs (NSAIDs)
  - Corticosteroids
- Ventricular rate control

Pericarditis: Complications

- Pericardial effusion
- Chronic constrictive pericarditis
- Cardiac tamponade
Myocarditis: Overview
- Inflammation of the myocardium
- If it becomes severe the pumping action of the heart weakens
- Clots can form in ventricles leading to:
  - Stroke
  - Myocardial infarction

Myocarditis: Symptoms
- Chest pain
- Dysrhythmia
- Shortness of breath
- Fluid retention
- Fatigue
- Heart failure
- Signs and symptoms of a viral infection
  - Headache
  - Body aches
  - Joint pain
  - Fever
  - Sore throat
  - Diarrhea

Myocarditis: Causes
- Viral
  - Coxsackie virus B
  - Adenovirus
  - Parvovirus B19
  - Echoviruses
  - Epstein-Barr
  - Rubella
  - Human immunodeficiency virus (HIV)
- Bacterial
  - Staphylococcus
  - Streptococcus
  - Bacteria that cause diphtheria
  - Tick-borne bacterium responsible for Lyme disease
Myocarditis: Causes

- Fungi
  - Candida
  - Aspergillus
  - Histoplasma
- Medications that may cause an allergic or toxic reaction
  - Antibiotics
  - Penicillin
  - Sulfonamides
  - Antiseizure medication
  - Cocaine

Myocarditis: Complications

- Heart failure
- Blood clots
- Heart attack
- Stroke
- Dysrhythmias
- Sudden death

Myocarditis: Diagnosis

- Magnetic resonance imaging (MRI)
  - Shows signs of inflammation of the heart muscle
  - Confirms a diagnosis of myocarditis
- Echocardiogram
  - Detects enlargement of the heart
  - Poor pumping function
  - Valve problems
  - Fluid around the heart
Myocarditis: Treatment

- Mild Cases
  - Rest
  - Antibiotics
  - Corticosteroids
  - Medications
    - ACE inhibitor
      - Relaxes blood vessels and increases blood flow
    - Beta-blockers
      - Regulate fast and irregular rhythms
    - Remodeling

- Severe Disease
  - IV medications
    - Dobutamine
    - Milrinone
  - IABP
  - Ventricular-assist device (VAD)
  - Extracorporeal membrane oxygenation (ECMO)

Myocarditis: Prevention

- Avoid people who have a viral or flu-like illness until they recover
- Follow good hygiene
- Avoid risky behaviors
- Minimize exposure to ticks
- Get immunizations
Practice Exam Questions

Acute Inflammatory Disease

Question #1 - Answer
The most common symptom seen in bacterial endocarditis is:

A. Fever. Fever, chills, and fatigue occur in 25%–80% of patients with endocarditis. Embolic events occur in 50%. Other less common symptoms include Osler nodes, Janeway lesions, splinter hemorrhages, and splenomegaly.
B. Osler nodes
C. Splenomegaly
D. Splinter hemorrhages

Question #2 - Answer
The treatment of choice for the management of endocarditis is:

A. Anticoagulants
B. Antibiotics. The most important treatment for the management is antibiotics. The patient usually requires 4–8 weeks of therapy. Anticoagulants and beta-blockers may be necessary if the patient has atrial fibrillation. Calcium channel blockers have no clinical benefit in the treatment of endocarditis.
C. Beta-blockers
D. Calcium channel blockers
The clinical presentation most consistent with acute pericarditis is:

A. Moderate, intermittent pain
B. Pain relieved best with a narcotic
C. Pain decreasing with inspiration
D. Pain relieved by sitting up and leaning forward. The pain associated with pericarditis is severe and constant, and relieved best with NSAIDs. The pain increases on inspiration and decreases by sitting up and leaning forward.

Which ECG change is seen in pericarditis during the first 24 hours?

A. Left bundle branch block pattern in V1
B. Right axis deviation in the frontal leads
C. Diffuse ST-segment elevation. The ECG change seen in pericarditis during the first 24 hours is diffuse ST-segment elevation. ST-segments stabilize within 48 hours without treatment.
D. Nonspecific ST-T wave changes over the lateral leads

Myocarditis is inflammation of the myocardium leading to a wide variety of symptoms. Treatment for a mild form of the disease would include:

A. ACE inhibitors
B. Corticosteroids. Management for mild myocarditis includes rest, corticosteroids, and antibiotics. ACE inhibitors would relax vessels and increase blood flow. Beta blockers would reduce the heart rate and assist in remodeling. Inotropes would increase contractility, which is needed in patients with severe myocarditis.
C. Beta-blockers
D. Inotropes
Hypertensive Crisis

**Introduction**

- Blood Pressure Parameters
  - SBP > 180 mm Hg
  - DBP > 120 mm Hg

- Hypertensive Emergency
  - Severe HTN with acute impairment of an organ system
  - CNS, CV, and renal impairment → irreversible organ damage
  - BP should be substantially lowered over minutes to hours with an antihypertensive agent

**Malignant Hypertension: Definition**

- Potentially life threatening
- Grade IV retinopathy
- CV and renal dysfunction
- Encephalopathy
Hypertensive Crisis

- Hypertensive Emergency
  - Acute end-organ damage
  - Requires rapid treatment
  - Within 1 hour

- Hypertensive Urgencies
  - No acute end-organ damage
  - Requires control of BP within 24 hours of presentation

Etiology

- Withdrawal of antihypertensive agent
- Pheochromocytoma
- Renovascular HTN
- Monoamine oxidase inhibitor (MAOI)
- Autonomic dysreflexia
- Collagen vascular diseases
- Cocaine/amphetamine use
- Head trauma
- Preeclampsia/eclampsia

Clinical Presentation

- Cerebral infarction – 24.5%
- Pulmonary edema – 22.5%
- Hypertensive encephalopathy – 16.3%
- Congestive heart failure – 12%
- Less common presentations include:
  - Intracranial hemorrhage
  - Aortic dissection
  - Eclampsia
Clinical Presentation

- **Neurologic Effects**
  - Encephalopathy
  - Stroke
  - Progressive headache
  - Stupor
  - Seizures

- **Renal Effects**
  - Vasoconstriction
  - Elevated BUN
  - Proteinuria
  - Decreased blood flow

- **CV Effects**
  - LV failure
  - Acute MI
  - Heart failure

Management

- **Antihypertensive agents depend on:**
  - Cause for the crisis
  - Severity of the elevated BP
  - Patient’s usual BP prior to the hypertensive crisis

Management Goals

- 10%–15% reduction in DBP within first 30–60 minutes
- If aortic dissection reduces SBP < 120 mm Hg or MAP < 80 mm Hg within 5–10 minutes
- If acute ischemic stroke reduces MAP by 15%–25% within first 24 hours
Interventions
- IV nitroprusside
- Gradually reduce BP
- Less urgent cases, oral agents may be used
  - Captopril
  - Clonidine
  - Labetalol

Goals
- Initial goal in hypertensive emergencies is to reduce the blood pressure by no more than 25%
  - Within minutes to 1–2 hours
- Continue toward a level of 160/100 mm Hg within 2–6 hours

Management Summary
Management Summary

<table>
<thead>
<tr>
<th>Condition</th>
<th>Recommended Agents</th>
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<tbody>
<tr>
<td>Hypertensive crisis, drug overdose</td>
<td>Diltiazem</td>
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<tr>
<td></td>
<td>Phentolamine</td>
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<td>Nicardipine + benzodiazepine</td>
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<td>Hypertensive encephalopathy</td>
<td>Labetalol</td>
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<tr>
<td></td>
<td>Nicardipine</td>
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<tr>
<td>Acute pulmonary edema, diastolic failure</td>
<td>Metoprolol</td>
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<td></td>
<td>Esmolol</td>
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<tr>
<td></td>
<td>Labetalol</td>
</tr>
<tr>
<td>Acute pulmonary edema, systolic failure</td>
<td>Nitroglycerin</td>
</tr>
<tr>
<td></td>
<td>Nitroprusside</td>
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<tr>
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<td>Nitroglycerin + loop diuretic</td>
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</table>

Practice Exam Questions

Management goals consistent with hypertensive crisis include:

- A. 10%–15% reduction in DBP within first 30–60 minutes for most patients
- B. Reduce SBP < 120 mm Hg or MAP < 80 mm Hg within 5–10 minutes for patients with an aortic dissection
- C. 15%–25% reduction in MAP within first 24 hours for patients with acute ischemic stroke
- D. All of the above

Question #1 - Answer

Management goals consistent with hypertensive crisis include:

- A. 10%–15% reduction in DBP within first 30–60 minutes for most patients
- B. Reduce SBP < 120 mm Hg or MAP < 80 mm Hg within 5–10 minutes for patients with an aortic dissection
- C. 15%–25% reduction in MAP within first 24 hours for patients with acute ischemic stroke
- D. All of the above
The antihypertensive medication with an onset of action within seconds is:

A. Esmolol (Brevibloc)
B. Nitroglycerin (Tridil)
C. Nitroprusside (Nipride) The onset of action is seconds. The onset of action for esmolol is 1–2 minutes; for nitroglycerin, 2–5 minutes; and for phentolamine, 1–2 minutes.
D. Phentolamine (Regitine)

The drug of choice in the management of elevated BP in a patient with an acute ischemic stroke is:

A. Labetalol (Normodyne) The onset of action is 5–10 minutes and may be given as a continuous IV infusion to maintain a coronary perfusion pressure of 70 mm Hg. Nitroprusside can increase intracranial pressure. Clonidine is longer acting and causes sedation. Diazoxide can cause cerebral edema.
B. Nitroprusside (Nipride)
C. Clonidine (Catapres)
D. Diazoxide (Hyperstat)
Definition

- Cardiogenic pulmonary edema
- Life-threatening condition
- Severe LV decompensation

Etiology

- Acute MI
- Exacerbation of CHF
- Valvular regurgitation
- Ventricular septal defect (VSD)
- Mitral stenosis
- Cardiac tamponade
- Endocarditis
- Myocarditis
- Dysrhythmias
- Cardiomyopathy
- Hypertensive crisis

Clinical Presentation

- Dyspnea
- Diaphoresis
- Cyanosis
- Pink, frothy sputum
- Moist, bilateral crackles
- S3
- Distended neck veins
**Diagnostics**
- ABGs
- Chest x-ray
- Echocardiogram
- Right heart catheterization

**Management**
- Sit patient up and dangle legs from side of bed
- 100% O₂
- Furosemide (Lasix): 40–100 mg IV
- Vasodilator therapy
- Inotropic drugs
- Afterload reduction
- Theophylline

**Complication**
- 60%–80% mortality
Practice Exam Questions

Pulmonary Edema

Question #1 - Answer

The most common etiology of acute pulmonary edema is:

A. Anterior MI. The most common cause is an acute MI. VSD, mitral stenosis, and coarctation of the aorta can be etiologies of acute pulmonary edema but not the most common cause.
B. VSD
C. Mitral stenosis
D. Coarctation of the aorta

Question #2 - Answer

Vasoactive drugs are ordered to manage the patient’s acute pulmonary edema. Which of the following hemodynamic profiles would be optimal?

A. PAOP 26 mm Hg, CI 1.2 L/min/m², BP 80/50 mm Hg, urine output 10 mL/hr
B. PAOP 9 mm Hg, CI 1.9 L/min/m², BP 95/60 mm Hg, urine output 15 mL/hr
C. PAOP 20 mm Hg, CI 2.5 L/min/m², BP 100/70 mm Hg, urine output 30 mL/hr. The goal is PAOP 15–18 mm Hg, CI > 2.2 L/min/m², SBP > 90 mm Hg; urine output > 1 mL/kg/hr
D. PAOP 18 mm Hg, CI 2.1 L/min/m², BP 110/65 mm Hg, urine output 20 mL/hr
The hemodynamic profile of the patient is PAOP 26 mm Hg, BP 80/55 mm Hg, and CI 2.0 L/min/m². The most appropriate treatment would be to:

A. Administer a beta-blocker
B. Begin an IV infusion of an inotropic agent. The safest drug to begin with would be dobutamine or milrinone. BP is too low to safely administer a beta-blocker, diuretic, or nitrate.
C. Administer an IV diuretic
D. Administer a nitrate

Pulmonary Hypertension

Definition

- Elevated PAS pressures
  - > 25 mm Hg at rest
  - > 30 mm Hg with exercise
  - Normal PAOP 15 mm Hg or less
Classifications
- Pulmonary arterial hypertension (PAH)
  - Collagen vascular disease
  - Portal hypertension
  - HIV
  - Drugs & toxins
  - Splenectomy
- Pulmonary venous hypertension (PVH)
  - Left-sided heart disease
  - Left-sided valvular disease

Classifications
- Pulmonary hypertension with hypoxemia
  - COPD
  - Alveolar hyperventilation disorders
  - Chronic exposure to high altitude
- Pulmonary hypertension due to chronic thrombotic and/or embolic disease
  - Proximal pulmonary arteries
  - Distal pulmonary arteries

Pathophysiology
- Vasculopathy
- Intimal, medial and adventitial proliferation
- Intimal ateramoas
- Plexiform lesions
Pathophysiology: Endothelin
- Potent vasoconstrictor
- Induces cell proliferation in vascular smooth muscle
- Promotes fibrosis
- Promotes inflammation

Endothelin ET<sub>A</sub> receptor
- Located on pulmonary vasculature smooth muscle cells
- Potent vasoconstriction by increasing intracellular calcium

Endothelin ET<sub>B</sub> receptor
- Pulmonary vascular endothelial cells and smooth muscle cells
- Vasodilation via increased production of prostacyclin and nitric oxide (NO) in normal pulmonary vasculature

Pathophysiology: Nitric Oxide
- Potent vasodilator produced in lung vascular endothelium by NO synthase from L-arginine
- Relaxes vascular smooth muscle by increasing production of cyclic guanosine monophosphate (cGMP)
- Decreased NO synthase in PAH
- PDE type-5 degrades cGMP and is abundant in the lung
- Inhalation of NO or PDE-5 inhibitors cause pulmonary vasodilation
Pathophysiology: Prostacyclin
- Vascular endothelium from arachidonic acid metabolism
- Vasodilator, antiproliferative and antiplatelet properties
- Low levels of prostacyclin and decreased expression of prostacyclin synthase are found in PAH
- Prostanoid analogs used for treatment

Pathophysiology
• Abnormally high BP in pulmonary arteries
• Increased pressure damages large and small pulmonary arteries
• Blood vessel walls thicken
• Unable to transfer oxygen and carbon dioxide normally
• Levels of oxygen in blood fall
• Constriction of pulmonary arteries
• Further increase in pressure in pulmonary circulation

Diagnosis
- Diagnosis of exclusion
- May be symptomatic for 2-3 years before the diagnosis is made
- Right sided heart failure
Signs and Symptoms
- RV lift
- Increased $P_2$ component of $S_2$
- Murmurs of tricuspid regurgitation and pulmonary insufficiency

Symptoms

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Percent of Patients with Symptom</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyspnea</td>
<td>60%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>19%</td>
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<tr>
<td>Near syncope/syncope</td>
<td>13%</td>
</tr>
<tr>
<td>Chest pain</td>
<td>7%</td>
</tr>
<tr>
<td>Palpitations</td>
<td>5%</td>
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</tbody>
</table>

Diagnosis
- Signs and symptoms of heart failure
  - Hepatomegaly
  - Peripheral edema
  - JVD
  - Ascites
Functional Classification

- **Class I**
  - No limitation of usual physical activity
  - Asymptomatic

- **Class II**
  - Slight limitation of physical activity
  - No discomfort at rest
  - Ordinary activity causes dyspnea, fatigue, chest pain or near syncope

- **Class III**
  - Marked limitation of usual activity
  - No discomfort at rest
  - Less than ordinary activity causes undue dyspnea, fatigue, chest pain or near syncope

- **Class IV**
  - Inability to perform any physical activity without symptoms
  - Signs and symptoms of right sided heart failure
  - Dyspnea and fatigue may be present at rest

Diagnostic Exams

- Transthoracic Echo
  - Measure RV systolic pressure
- Chest X-ray
- ECG
  - RV hypertrophy
  - Right axis deviation
- BNP elevated with RV failure
Laboratory Studies
- Autoimmune serologies
- Markers of liver function
- HIV serologies when dictated by history

Electrocardiogram
- Not sensitive enough to be a screen but can help guide diagnostic workup
  - RV hypertrophy
    - 87% of patients with pulmonary hypertension
  - Right axis deviation
    - 79% of patients with pulmonary hypertension
  - Right atrial enlargement
    - P wave > 2.5 mm in leads II, III and aVF

Chest X-Ray
- Not sensitive enough to screen
- Attenuated “moth eaten” peripheral pulmonary vasculature
- Enlarged pulmonary arteries – especially on the right
### Echocardiogram
- Order for screening when clinical suspicion exists
- Order for standard interval screening in selected groups
  - Family of those with idiopathic pulmonary arterial hypertension
  - Known bone morphogenetic protein receptor type II mutation
  - Scleroderma spectrum
  - Coronary heart disease patients
  - Pre-liver transplant

### Right Heart Catheterization
- Essential for firm diagnosis
  - Helps to rule out the diagnosis with patients who do not have it
- Vasoreactivity testing
  - NO, Flolan, Adenosine
    - Drop in mean PA pressure by 10 mm Hg to value < 40 mm Hg
  - Predicts calcium channel blocker response
- Evaluate for septal defects
- Shed light on the issue of diastolic dysfunction
- Interpret data in context of patient’s volume status

### General Measures
- Avoid pregnancy
  - Contraception imperative
- Maternal mortality 30%
- Immunizations for respiratory illnesses
  - Influenza and pneumonia vaccines
- Minimize valsalva maneuvers (Cough, constipation, heavy lifting, etc.)
  - Increases risk of syncope
Classes of Therapy

- Medical
  - Oxygen
  - Diuretics
  - Coumadin
  - Pulmonary hypertension specific therapy
- Surgical
  - Atrial septostomy
  - Lung transplantation

Oxygen

- Formal assessment of nocturnal and exertional oxygenation needs
- Minimize added insult of hypoxic vasoconstriction
- Keep \( O_2 \) saturation > 90%
  - May be impossible with large right to left shunt
- Exclude nocturnal desaturation
  - Overnight oximetry
- Rule out concomitant obstructive sleep apnea and hypoventilation syndromes

Diuretics

- Treat edema from right heart failure
- Ventricular interdependence
  - Ensure LV output is preserved
  - May need to combine classes
  - Thiazide and loop diuretics
  - Avoid too much preload reduction
  - Large doses are often required
**Coumadin**
- Improved survival in PAH
- Keep INR 2.0 – 2.5
- Lessens in-situ thrombosis

**Pulmonary Hypertension-Specific Therapies**
- Calcium channel blockers
- Endothelin receptor antagonists (ERAs)
  - Bosenten
  - Sitaxsentan
  - Ambrisentan
- Phosphodiesterase (5) inhibitors (PDE 5-I)
  - Sildenafil
- Prostanoids
  - Epoprostenol
  - Treprostinil
  - Iloprost

**Calcium Channel Blockers**
- Demonstrated vasoreactivity in right heart catheterization (about 10% or less of patients)
- Diltiazem or nifedipine preferred
- Titrate up to maximum tolerated dose
- Systemic hypotension may prohibit use
- Only 50% of patients maintain response to calcium channel blockers
- Not used in severe right heart failure
Endothelin Receptor Antagonists
- Targets relative excess of endothelin-1 by blocking receptors on endothelium and vascular smooth muscle
- Ambrisentan is ET-A selective
- Shows improvement in 6 minute walking test and time to clinical worsening
- Monthly transaminase monitoring required for both
- Annual cost about $40 000

Bosentan (Tracleer)
- Potential for serious liver injury
  - Hepatic cirrhosis with prolonged treatment
- Causes 3-fold increase in ALT and AST
  - May be accompanied by elevated bilirubin
- Teratogenic and lowers sperm count
- Significant drug interactions
  - Glyburide inhibits metabolism
  - Enhances metabolism of oral contraceptives, warfarin and statins
  - Increased metabolism of cyclosporin A, protease inhibitors, amiodarone, ketoconazole

Ambrisentan (Letairis)
- 5 or 10 mg once daily
- Much less risk of transaminase elevation (about 1%), but monthly monitoring still required
- No dose adjustment of coumadin needed
Drug interaction with nitrates
FDA approved dose is 20 mg three times per day
Adjusted per therapeutic effect
  • Higher doses sometimes needed
Side effects
  • Headaches
  • Epistaxis
  • Transient hypotension
  • Sudden hearing loss

Sildenafil (Revatio)

Prostacyclin analogues
  • Epoprostenol, treprostinil, iloprost
Benefits
  • Vasodilation
  • Platelet inhibition
  • Anti-proliferative effects
  • Inotropic effects

Epoprostenol (Flolan)
  • First pulmonary hypertension specific therapy available in the mid-1990s
  • Very short half life – 2 minutes
  • Delivered via continuous infusion
  • Cost about $100 000 per year
Epoprostenol (Flolan)
- Side effects
  - Headache
  - Jaw pain
  - Flushing
  - Diarrhea
  - Nausea and vomiting
  - Flu-like symptoms
  - Anxiety/nervousness
- Complex daily preparation
- Catheter complications
  - Dislodgement or malfunction
  - Catastrophic deterioration
  - Embolization
- Infection (3% deaths)

Treprostinil (Remodulin)
- Continuous subcutaneous infusion or IV infusion
- Longer ½ life than Epoprostenol – 4 hours
- Les risk of rapid fatal deterioration if infusion stops
- Significant site pain at infusion site limits use

Iloprost (Ventavis)
- Inhaled prostacyclin
- Administered 6 – 9 times daily via special nebulizer
- Reported risk of morning syncope
- Improvement in 6 minute walk test, functional class and hemodynamics observed
- Potential for increased hypotensive effect with antihypertensives
- Increased risk of bleeding, especially with co-administration of anticoagulants
- Increased liver enzymes
- Flushing, increased cough, headache, insomnia, nausea, vomiting, flu-like symptoms

Pulmonary Hypertension
PAH Treatment Algorithm

Monitoring Response to Therapy
- Six minute walk test
- Echocardiogram
- Right heart catheterization
- BNP
- Functional class

Practice Exam Questions
A. Nitric oxide
B. Endothelin. Elevated endothelin is responsible for vasoconstriction due to intracellular calcium influx. Elevated endothelin is seen in pulmonary hypertension. Decreased NO will lead to vasoconstriction by direct action. Prostacyclin is a vasodilator and is decreased in pulmonary hypertension. Thromboxane A2 is an arachidonic acid metabolite causing vasoconstriction.
C. Prostacyclin
D. Thromboxane A2

Question #2 - Answer
The most common symptom of pulmonary hypertension is:
A. Dyspnea. Dyspnea occurs in 60% of the patients with pulmonary hypertension. Fatigue is present in 19% of patients, syncope 13% and chest pain 7%.
B. Fatigue
C. Syncope
D. Chest pain

Question #3 - Answer
Which functional classification presents with slight limitation of physical activity, no discomfort at rest and ordinary activity causes dyspnea, fatigue, chest pain or near syncope?
A. Class I
B. Class II. Class II symptoms are slight limitation of physical activity, no discomfort at rest and ordinary activity causes dyspnea, fatigue, chest pain or near syncope.
C. Class III
D. Class IV
Question #4 - Answer

General treatment for pulmonary hypertension would include:

A. Prostacyclin analogue  
B. PDE-type V inhibitor  
C. Endothelin receptor antagonist  
D. Anticoagulant. Anticoagulants, diuretics and oxygen are the general treatments for pulmonary hypertension. Prostacyclin, PDE-type V inhibitors and endothelin receptor antagonists are pulmonary hypertension specific treatments.