Discussion Points

• Drugs for heart disease
• Drugs for hypertension
• DVT
• Ulcer prophylaxis
Heart Disease

• Cardiac conduction
  • cardiac activity begins at the SA node, which is innervated by both sympathetic and parasympathetic nerves
  • sympathetic nerves release norepinephrine and cause adrenergic responses
  • parasympathetic nerves release acetylcholine and cause cholinergic (parasympathomimetic) responses
## Adrenergic and Cholinergic Effects

<table>
<thead>
<tr>
<th>Adrenergic</th>
<th>Cholinergic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• increased heart rate (positive chronotropy)</td>
<td>• decreased heart rate (negative chronotropy)</td>
</tr>
<tr>
<td>• increased force of contraction (positive inotropy)</td>
<td>• decreased force of contraction (negative inotropy)</td>
</tr>
<tr>
<td>• increased automaticity</td>
<td>• decreased automaticity</td>
</tr>
<tr>
<td>• increased AV conduction</td>
<td>• inhibition of AV conduction</td>
</tr>
</tbody>
</table>
Arrhythmias

- Deviation from the normal ECG
  - disorders of automaticity or conduction
  - impulse originates in someplace other than the SA node
  - impulse does not follow normal conduction pathway
  - nonautomatic cells become automatic, and therefore fire, creating the arrhythmia (i.e. PVCs)
- cardiac cells may also be excited by hypoxemia, ischemia, electrolyte imbalance
- may develop in atria or ventricles (atrial fib/flutter vs. ventricular tachy/fib)
Antiarrhythmic drugs

- **Therapeutic goals**
  - restore and maintain NSR
  - suppress excitable areas outside the normal conduction pathway (ectopic foci)
  - control ventricular rate and optimize cardiac output
- **Mechanism of action**
  - depress automatic properties of abnormal pacemaker cells
  - alter conduction characteristics within the heart by facilitating or depressing conduction
Classification of Antiarrhythmic Drugs

- Class I drugs block sodium channels (decrease contraction)
- Class II drugs are β adrenergic blockers – olol drugs (slow the heart)
- Class III drugs are calcium channel blockers (decrease contraction)
- Drugs in the same class don’t necessarily have the same medical indications to treat the same arrhythmias
- Unclassified drugs
  - digoxin: inhibits Na/K exchange, increases contractility (positive inotrope), slows ventricular rate; prolongs P-R interval, allowing more filling time
  - adenosine: used for SVT; slows conduction through the SA and AV nodes
Heart Failure

- Caused by increased afterload, right or left (HTN), myocardial damage (MI)
  - ventricles distend and are not able to pump sufficient blood to tissues
  - in response, kidneys retain fluid to increase vascular volume and edema ensues
- untreated, results in pulmonary edema
- may be right-sided or left-sided or both
Heart Failure

• Drugs to treat heart failure
  • remove sodium and water with diuretics (decreased preload)
  • increase contractility with positive inotropics (digitalis)
  • decrease afterload with vasodilators
Heart Failure Drug Classification and Action

- **Digoxin**
  - increases calcium availability for contraction (positive inotrope)
  - increases parasympathetic stimulation thereby decreasing AV firing (negative dromotripic)
  - allows improved ventricular filling
  - improves EF, CO and renal perfusion which decreases renal response to decreased CO
Heart Failure Drugs

- Angiotensin converting enzyme inhibitors (ACE inhibitors)
  - decrease levels of angiotensin II, a vasoconstrictor
  - angiotensin II also promotes sodium retention
  - decreases symptoms and prolongs life in HF
  - captopril, benazepril, elanapril

- Angiotensin II receptor blockers (ARB)
  - blocks angiotensin II
Heart Failure Drugs

- β antagonists (β blockers)
  - slow the heart to allow more ventricular filling
  - reduces myocardial oxygen demand and control blood pressure
  - -olol drugs
Heart Failure Drugs

Vasodilators: decrease afterload
- dilate arterial vessels
  - hydrazaline, Ca channel blockers
  - hydrazaline decreases PVR
- dilate venous vessels (nitrates)
  - dilates arterioles thereby decreasing afterload
  - decreases venous return thereby reducing preload
- ACE inhibitors allow vasodilation
- Ca channel blockers dilate arterial vessels, but do not effect preload
Heart Failure Drugs

- **Diuretics (furosemide)**
  - eliminates excess volume that increases work of the heart
  - automatically initiating K replacement is not always necessary
  - monitor by observing weight loss and changes in edema and breath sounds

- **Aldosterone antagonists**
  - aldosterone increases reabsorption of sodium and water in the kidneys
  - inhibitors include lisinopril that blocks ACE and decreases ADH secretion, spironolactone (a diuretic) and eplerenone
Heart Failure Drugs

• Dobutamine
  • β-1 agonist, prescribed for patients with acute heart failure after MI
  • increases CO and decreases LV filling pressure by improving contractility
• Other drugs for heart failure
  • dopamine: improves renal blood flow at low dose; positive inotrope at high dose
  • nitroprusside: arterial and venous vasodilator, used for acute HTN; may cause methemoglobinemia
  • nitroglycerine: IV for preload reduction, vasodilator
  • nesiritide: synthetic BNP, vasodilator
  • phosphodiesterase inhibitors: vascular smooth muscle relaxation and increased contractility, IV administration
Summary of Heart Failure

Drugs

• Positive inotropic drug
  • Digitalis

• Sympathetic blockade
  • B blockers

• Diuretics

• Vasodilators
  • Phosphodiesterase inhibitors
  • ACE inhibitors
  • Nitrates
  • Hydralazine
  • Ca channel blockers
Figure Legend:

Stages in the development of HF and recommended therapy by stage. ACEI indicates angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; ARB, angiotensin-receptor blocker; CAD, coronary artery disease; CRT, cardiac resynchronization therapy; DM, diabetes mellitus; EF, ejection fraction; GDMT, guideline-directed medical therapy; HF, heart failure; HFrEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; HRQOL, health-related quality of life; HTN, hypertension; ICD, implantable cardioverter-defibrillator; LV, left ventricular; LVH, left ventricular hypertrophy; MCS, mechanical circulatory support; and MI, myocardial infarction.
Angina

- Pathophysiology
  - symptom of myocardial ischemia
  - not enough blood to the coronary circulation/myocardium
  - drug therapy decreases myocardial oxygen consumption or increasing oxygen delivery
Angina

Pharmacologic therapy

• nitroglycerine for pain relief, preload and afterload reduction (arterial and venous dilation)

• β blockers: -olol drugs decrease myocardial oxygen consumption by decreasing heart rate, contractility, blood pressure and afterload; limit infarct size, and decrease incidence of arrhythmias; a selective β1 blocker should be used for patients with COPD or asthma, as the nonselective β1 blocker may cause bronchospasm.

• Ca channel blockers: vasodilate and decrease contractility, AV conductivity and automaticity
Acute Coronary Syndromes

• Rupture of an atherosclerotic plaque resulting in platelet adherence, activation, aggregation, and activation of the clotting cascade

• ST segment elevation ACS treatment is reperfusion therapy or administration of a fibrinolytic agent, oxygen, SL and IV nitro, IV β blocker, unfractionated heparin

• NSTEMI treatment is clopidogrel and/or glycoprotein IIb/IIIa receptor blocker
MI

- Save the myocardium, preserve LV function, reduce risk of complications
- Reperfusion, antithrombosis, and antiischemic therapy
- Follow-up with aspirin, β blocker, ACE inhibitor to prevent stroke, recurrent MI, death; statin to lower cholesterol

| Table 1. Antithrombotic and Fibrinolytic Agents Used for Acute Coronary Syndromes |
|---------------------------------|--------------------------------|
| Anticoagulants                  | Antiplatelet agents            | Fibrinolytic agents             |
| Unfractionated heparin          | Aspirin                        | Streptokinase                   |
| Low-molecular-weight heparins   | Adenosine diphosphate receptor | Recombinant tissue plasminogen |
| (eg, enoxaparin, dalteparin)    | blockers                       | activator (eg, alteplase, reteplase, tenecteplase) |
| Direct thrombin inhibitors      | Glycoprotein IIb/IIIa inhibitors|                               |
| (eg, argatroban, bivalirudin, hirudin) | (eg, abciximab, eptifibatide, tirofiban) |                               |
## Hypertension

### Table 1. Classification and management of blood pressure for adults

<table>
<thead>
<tr>
<th>BP Classification</th>
<th>SBP* MMHG</th>
<th>DBP* MMHG</th>
<th>LIFESTYLE MODIFICATION</th>
<th>WITHOUT COMPPELLING INDICATION</th>
<th>WITH COMPPELLING INDICATION (SEE TABLE 8)</th>
</tr>
</thead>
<tbody>
<tr>
<td>NORMAL</td>
<td>&lt;120</td>
<td>and &lt;80</td>
<td>Encourage</td>
<td>No antihypertensive drug indicated.</td>
<td>Drug(s) for compelling indications.‡</td>
</tr>
<tr>
<td>PREHYPERTENSION</td>
<td>120–139</td>
<td>or 80–89</td>
<td>Yes</td>
<td>Thiazide-type diuretics for most. May consider ACEI, ARB, BB, CCB, or combination.</td>
<td>Drug(s) for the compelling indications.‡ Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.</td>
</tr>
<tr>
<td>STAGE 1 HYPERTENSION</td>
<td>140–159</td>
<td>or 90–99</td>
<td>Yes</td>
<td>Two-drug combination for most† (usually thiazide-type diuretic and ACEI or ARB or BB or CCB).</td>
<td></td>
</tr>
<tr>
<td>STAGE 2 HYPERTENSION</td>
<td>≥160</td>
<td>or ≥100</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

DBP, diastolic blood pressure; SBP, systolic blood pressure.

Drug abbreviations: ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; BB, beta-blocker; CCB, calcium channel blocker.

* Treatment determined by highest BP category.
† Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.
‡ Treat patients with chronic kidney disease or diabetes to BP goal of <130/80 mmHg.
Drugs for Hypertension

• α2 agonists or central acting sympatholytics
  • when α2 receptors are stimulated, release of norepinephrine is blocked, resulting in vasodilation and decreased BP; for example clonidine an α2 specific drug decreases sympathetic outflow from the brain, resulting in decreased CO and PVR

• α1 blockers or peripheral acting symapthomimetics
  • stimulation of α1 receptors causes vasoconstriction
  • α1 blockers cause vasodilation
Drugs for Hypertension

- **β blockers**
  - inhibit sympathetic activity, decrease rate and force of contraction, lowering BP
  - nonspecific β blockers can cause bronchospasm in asthma and COPD

- **Diuretics**
  - reduce preload
  - do not allow sodium reabsorption, and water follows, increasing urine production
  - three categories:
    - thiazide, such as hydrochlorothiazide, increase excretion of sodium and water at the distal convoluted tubule;
    - loop diuretics (furosemide) increase sodium and water excretion at the proximal and distal tubules and the loop of Henle;
    - potassium sparing diuretics do not allow K to be excreted along with Na, avoiding hypokalemia (amiloride, spironolactone)
Drugs for Hypertension

• ACE inhibitors
  • angiotensin II causes the release of aldosterone, which increases Na and water reabsorption and is a vasoconstrictor; the increased blood volume along with vasoconstriction increases BP.
  • ACE inhibitors decrease levels of angiotensin II and aldosterone to decrease BP
  • 30% incidence of cough as a side-effect
• Angiotensin II receptor blockers (ARBs)
  • inhibit angiotensin II at receptor sites on blood vessels, as an alternative to ACE inhibitors; don’t cause cough
Drugs for Hypertension

• Ca channel blockers
  • produce arteriole relaxation by blocking Ca needed for contractility
  • may cause peripheral edema and dizziness
  • amlodipine, diltiazem, verapamil

• Vasodilators
  • relax smooth muscle in arteries > veins
  • last-line for nonacute hypertension due to reflex tachycardia and peripheral edema
Antihypertensives and Blood Pressure

- Blood pressure = CO X TPR

- B blockers decrease rate and force of contractions
- Decrease CO
- Central and peripheral sympatheticolics
- Vasodilators
- Ca channel blockers
- Diuretics
- ACE inhibitors/ARB
- Angiotensin II antagonists
  - Decrease TPR by vasodilation or volume reduction
ALGORITHM FOR TREATMENT OF HYPERTENSION

Not at Goal Blood Pressure (<140/90 mmHg)  
(<130/80 mmHg for those with diabetes or chronic kidney disease)

Initial Drug Choices

Without Compelling Indications

Stage 1 Hypertension  
(SBP 140–159 or DBP 90–99 mmHg)  
Thiazide-type diuretics for most.  
May consider ACEI, ARB, BB, CCB, or combination.

Stage 2 Hypertension  
(SBP ≥160 or DBP ≥100 mmHg)  
2-drug combination for most (usually thiazide-type diuretic and ACEI, or ARB, or BB, or CCB)

With Compelling Indications

Drug(s) for the compelling indications  
Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.

Optimize dosages or add additional drugs until goal blood pressure is achieved.  
Consider consultation with hypertension specialist.
## Classification and Management of BP for Adults

<table>
<thead>
<tr>
<th>BP classification</th>
<th>SBP* mmHg</th>
<th>DBP* mmHg</th>
<th>Lifestyle modification</th>
<th>Initial drug therapy</th>
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<tbody>
<tr>
<td>Normal</td>
<td>&lt;120</td>
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<td>120–139</td>
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<td>Yes</td>
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<tr>
<td>Stage 1 Hypertension</td>
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<td>or 90–99</td>
<td>Yes</td>
<td>Drug(s) for the compelling indications. ‡</td>
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<tr>
<td>Stage 2 Hypertension</td>
<td>&gt;160</td>
<td>or &gt;100</td>
<td>Yes</td>
<td>Other antihypertensive drugs (diuretics, ACEI, ARB, BB, CCB) as needed.</td>
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* Treatment determined by highest BP category.
‡ Initial combined therapy should be used cautiously in those at risk for orthostatic hypotension.
† Treat patients with chronic kidney disease or diabetes to BP goal of <130/80 mmHg.

**EVALUATION**

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<th>Classification of Blood Pressure (BP)*</th>
<th>SBP mmHg</th>
<th>DBP mmHg</th>
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<td>Hypertension, Stage 1</td>
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<td>90-99</td>
</tr>
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<td>Hypertension, Stage 2</td>
<td>≥160</td>
<td>≥100</td>
</tr>
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</table>

*See Blood Pressure Measurement Techniques (version 4.4)
Key: SBP = systolic blood pressure  DBP = diastolic blood pressure

**DIAGNOSTIC WORKUP OF HYPERTENSION**

- Assess risk factors and comorbidities.
- Reveal identifiable causes of hypertension.
- Assess presence of target organ damage.
- Conduct history and physical examination.
- Obtain laboratory tests: urinalysis, blood glucose, hematocrit and lipid panel, serum potassium, creatinine, and calcium. Optional: urinary albumin/creatinine ratio.
- Obtain electrocardiogram.

**ASSÉSS FOR MAJOR CARDIOVASCULAR DISEASE (CVD) RISK FACTORS**

- Hypertension
- Obesity
  (body mass index ≥30 kg/m²)
- Dyslipidemia
- Diabetes mellitus
- Cigarette smoking

**ASSÉSS FOR IDENTIFIABLE CAUSES OF HYPERTENSION**

- Sleep apnea
- Drug-induced/related
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Cushings syndrome or steroid therapy
- Phaeochromocytoma
- Contraindication of aorta
- Thyroid/parathyroid disease

**TREATMENT**

**PRINCIPLES OF HYPERTENSION TREATMENT**

- Treat to SBP <140/90 mmHg or SBP <130/80 mmHg in patients with diabetes or chronic kidney disease.
- Majority of patients will require two medications to reach goal.

**ALGORITHM FOR TREATMENT OF HYPERTENSION**

**LIFESTYLE MODIFICATIONS**

- Net at Goal Blood Pressure (<140/90 mmHg)
  (<130/80 mmHg for patients with diabetes or chronic kidney disease)
  See strategies for improving adherence to therapy

**INITIAL DRUG CHOICES**

- Without Compelling Indications
- With Compelling Indications

**STAGE 1 HYPERTENSION**

- Thiazide-type diuretics for most. May consider ACE inhibitor, ARB, or combination.

**STAGE 2 HYPERTENSION**

- Thiazide-type diuretics and ACE inhibitor, ARB, or combination.
- 2-drug combination for most (usually thiazide-type diuretic and ACE inhibitor, or ARB, or combination).

**NOT AT GOAL BLOOD PRESSURE**

- Optimized dosages or add additional drugs until goal blood pressure is achieved. Consider consultation with hypertension specialist.
  See strategies for improving adherence to therapy.
Hypertensive Emergencies

• Rapid rise in BP may precede a stroke or death
• Drugs include oral clonidine or captopril; diazoxide, a parenteral vasodilator; nitroprusside an arterial and veno-dilator (requires A-line)
Prophylaxis of Deep Venous Thrombosis

Anticoagulants

- Thrombin inhibitors: in the clotting cascade, fibrinogen in the presence of thrombin, forms fibrin, which causes clotting
- Indirect thrombin inhibitors
  - warfarin, unfractionated heparin, low molecular weight heparin
- Direct thrombin inhibitors
  - lepirudin, argatroban, bivalirudin
- Inhibit steps in the clotting cascade, but do not dissolve clots, prevent new clots from forming
- Prevent mostly venous thrombosis (DVT), postoperatively after vascular or heart procedures, and to prevent clotting after a stroke
Preventing DVT

• Heparin
  • standard unfractionated heparin binds with antithrombin III to inhibit conversion by thrombin of fibrinogen to fibrin.
  • PTT lab test is used to monitor heparin therapy, keep PTT 2-2.5 times normal
  • low molecular weight heparin is a modern replacement for heparin; fewer side-effects and less need for monitoring; Lovenox

• Warfarin
  • inhibits vitamin K in the clotting process
  • used to prevent clots in Afib, prosthetic valves and stroke
  • monitor monthly with INR which should be 2-3 times normal
Stress Ulcer Prophylaxis

• Prophylaxis against stress ulcers is frequently administered in most ICUs
• typically, histamine-2 antagonists are given.
• Currently available data suggest that high-risk patients, such as those with coagulopathy, shock, or respiratory failure requiring mechanical ventilation, benefit from such prophylactic treatment.
• pepcid, tagamet, zantac