Cardiovascular 1&2
Hypertension, Angina, Heart Failure and Arrhythmias

Understanding the Renin-Angiotensin-Aldosterone System (RAAS)

Make sure you can make a “key” to this diagram. Use your lecture notes! There is more detail in the notes.
Diuretics

Hydrochlorothiazide (*Esidrix*) is a thiazide diuretic used to treat a wide variety of types of edema. It does lead to hypokalemia, and increased blood levels of glucose, cholesterol and uric acid.

Furosemide (*Lasix*) is a loop diuretic. This is a very potent diuretic and the accompanying electrolyte imbalances are common and may be severe enough to cause cardiovascular collapse. If it is injected rapidly, hearing loss is likely. As with hydrochlorothiazide, furosemide causes hypokalemia and increased blood levels of glucose, cholesterol and uric acid.

Spironolactone (*Aldactone*) is a potassium-sparing diuretic. It is also an aldosterone receptor blocker, so may be used to treat HTN associated with primary aldosteronism. Because it is potassium-sparing, it cannot be given with other drugs that cause potassium retention (e.g., ACEI, ARBs) or with potassium supplements or potassium rich foods.

Osmotic diuretics are a common IV additive

Water-soluble, non-electrolytes that are freely filtered by the kidney and poorly reabsorbed, they are commonly used during trauma treatment or surgery.

- Mannitol
- Urea
- Glycerol

Diuretic resistance

Diuretic drugs usually improve edema when used judiciously. Some patients, however, become resistant to their effects. Diuretic resistance may result from dietary indiscretion, poor compliance, impaired bioavailability, impaired diuretic secretion into the lumen of the renal tubule, or because other drugs interfere with diuretic activity....

If diuretics don’t work to bring down BP…

Atenolol (**Tenormin**) and Metoprolol (**Lopressor, Toprol**) are β1 specific β-blocking agents whereas Propranolol (**Inderal**) is a mixed, or non-specific β1&2 blocker. Metoprolol is one of the best selling drugs in the world. The β blockers act directly to decrease heart rate and indirectly by reducing renin secretion. Because they reduce renin secretion, and thus angiotensin II levels, the β blockers are considered to be cardioprotective. The β blockers are used to treat HTN, angina, arrhythmias and other conditions.

Aliskiren (**Tekturna**) is a direct renin inhibitor. It is a new, and very popular drug. It is not available in the USA due to the risk of hyperkalemia. It is not available in the USA due to the risk of hyperkalemia. It is also not available in the USA due to the risk of hyperkalemia.

The selective α1 blockers such as Doxazosin (**Cardura**) are no longer recommended, but may still be used. They tend to cause severe orthostatic hypotension.

Labetalol (**Normodyne**) is a mixed α1 and β1&2 blocker we covered in the Adrenergics lecture.

The calcium channel blockers (CCBs) fall into one of three categories represented by the drugs Amlodipine (**Norvasc**), Diltiazem (**Cardizem or Tiazac**) and Verapamil (**Covera HS**). The CCBs are also cardioprotective. They are used to treat HTN, angina and arrhythmias.

Hydralazine (**Apresoline**) is a vasodilator, too. It may be used in pregnant women, but may cause a lupus-like syndrome.

Nitroprusside (**Nitropress**) is a very potent vasodilator that will cause a precipitous drop in blood pressure. Since it is metabolized to cyanide, it can only be used for short periods of time at a slow infusion rate.

All the vasodilators trigger reflex sympathetic stimulation due to activation of the baroreceptor circuit.

Angiotensin Converting Enzyme (ACE) inhibitors (ACEI) include Benazepril (**Lotensin**), Captopril (**Capoten**) and Enalapril (**Vasotec**). Benazepril and Enalapril are prodrugs. ACEI cause HYPERkalemia. They are fetotoxic.
Angiotensin Receptor Blockers (ARBs) include **Irbesartan (Avapro)**, **Losartan (Cozaar)** and **Valsartan (Diovan)**. These drugs cause significant hypotension and are also fetotoxic.

**Methyl dopa (Aldomet)** is an $\alpha_2$ agonist and an inhibitor of DOPA decarboxylase, an enzyme in the catecholamine synthetic pathway. Inhibiting DOPA decarboxylase results in the reduction of all the catecholamines. Aldomet may be used to treat pregnancy-induced hypertension.

**Clonidine (Catapres)** is also an $\alpha_2$ agonist. It has a discontinuation syndrome so patients need to be weaned off it.

**Fenoldopam (Corlopam)** is a peripherally active D1 agonist. The D1 receptors are located in the kidney, heart and mesentery. Once activated, they cause vasodilation.

A number of fixed dose combinations are available to treat HTN. **Indeneride** is hydrochlorothiazide and propranolol, **Hyzaar** is hydrochlorothiazide and losartan, and **Lotrel** is amlodipine with benazepril.

Captorpril was developed based upon work done in Brazil on the venom of the Brazilian Pit Viper, *Bothrops jararaca*. If you are interested, read this fascinating story:

**From viper's venom to drug design: treating hypertension.** Margie Patlak, *FASEB Journal* V18N3P421

**Common Meds in Ambulances**

- Adenosine
- Atropine
- Aspirin
- Albuterol
- Diphenhydramine
- Dopamine
- Epinephrine
- Furosemide
- Glucagon
- Lidocaine
- Midazolam
- Morphine
- Naloxone
- Nitroglycerine
- Sodium bicarbonate

*Beans beans, good for your heart, the more you eat beans, and a lot of other good foods, in moderation of course. For a better tomorrow, eat beans from the ground up! (*Addie L. Layard, 1926)*
Angina

The Beta-blockers and CCBs are commonly used to treat angina. See the links to their labels in the HTN section on page 3. Nitrate vasodilators are also used.

Trimetazidine (Vasterel) is a partial fatty acid oxidase (pFOX) inhibitor used extensively overseas. It is not yet FDA approved.

Ranolazine (Renexa) is also a pFOX inhibitor. It is in the top 200.

Heart Failure

Acute decompensated heart failure (ADHF) is treated with

- Analgesics (morphine or another opioid),
- Diuretics (usually furosemide),
- Vasodilators (like Nitroglycerin, “Nitrostat” or “Nitro-Bid,”) or Nitroprusside (Nitropress),
- An agent to make the heart beat more forcefully
  - A catecholamine such as Dobutamine, “Novaplus,” or Dopamine.
  - A 3-PDE inhibitor such as Milrinone (Primacor)
- Natriuretic peptide such as Nesiritide (Natrecor) – the use of which is now limited.

Chronic Heart Failure is much more complicated. Drugs to AVOID in CHF include NSAIDs, 3-PDE inhibitors and the DMT2 drug Pioglitazone (Actos).
Antiarrhythmic drugs

Class I = Sodium channel blockers
- 1a = Procainamide (*Pronestyl*)
- 1b = Lidocaine (*Xylocaine*) & Phenytoin (*Dilantin*)
- 1c = Flecainide (*Tambocor*)

Class II = Mainly beta blockers
- Propranolol (*Inderal*)

Class III = Potassium channel blockers
- Amiodarone (*Cordarone, Pacerone*)

Class IV = Calcium Channel Blockers (CCB)
- Diltiazem (*Cardizem, Tiazac*) & Verapamil (*Covera*)

Class V = Other
- Digitalis (*Lanoxin*) & Adenosine (*Adenocard*)

Homework and Exercises

1. Read the “START HERE” announcement in Laulima for updates and instructions.
2. Read about Hypertension in Chapters 34 and 37, *Drugs affecting RAAS, and Pharmacotherapy of Hypertension*. See also Chapters 33, 35, 36, 38, 39 and 40. Read as necessary to understand the drugs covered in these two lectures. Adams & Urban, PHARMACOLOGY Connections to Nursing Practice.
3. Review the Powerpoints and listen to the audio from the face-to-face lecture. You may opt to watch the appropriate videos for this lecture. Review any handouts available for this lecture in the Course Index.
4. Complete the SLO practice sets for CV1&2 in Tasks, Tests and Surveys.
5. Use “Chat,” “Discussions and Private Messages” or the lecture “Forum” to ask questions and find answers or to seek assistance.
6. Complete the online quiz in Laulima, Tasks, Tests and Surveys.

If you have any questions, email me at abeale@hawaii.edu