Pharmacology

Pharmacology of Diuretics
Diuretics increase urinary sodium chloride (“saliuresis”). Diuretics are used for HTN and edematous states such as CHF, cirrhosis, nephrotic syndrome.

If salt input > output, you will retain water weight (see above) and begin to excrete more sodium. Therefore, steady state ECF depends on sodium intake. Similarly, incremental increases in ECF cause proportionate increases in sodium excretion (above).

Role of diuretics
Edema occurs if sodium is not properly excreted and ECF expands. This occurs in CHF, cirrhosis, and nephrotic syndrome. In addition to reduced excretion, the “threshold ECF” is elevated, so that sodium excretion doesn’t start until higher-than-normal ECF (see above).

Chronic Adaptation to Diuretics
Diuretics increase NaCl excretion, which lowers ECF. But body senses this natriuresis and hypovolemia, and adapts with renin-angiotensin-aldosterone system. This is the “diuretic braking effect.”

Loop Diuretics
Furosemide, Bumetanide, Ethacrynic acid. These block Na/K/Cl co-transporter in the TAL. These are “high ceiling” diuretics because of potency (25% of sodium is normally reabsorbed here). There is also a strong braking mechanism, because loop diuretics allow high Na⁺ at the distal tubule, where sodium re absorption is up regulated. This “rebound sodium retention” can be countered by concurrent use of a thiazide diuretic to block distal re absorption.

Other effects include increased calcium excretion, and increasing venous capacitance (pulls edema fluid into the ECV).

Side effects:
**hypokalemic metabolic alkalosis** due to lots of distal K⁺ and H⁺ wasting. Since there is volume contraction, renin and aldosterone increase, compounding this wasting.
--hyperuricemia due to reduced uric acid excretion may lead to gout.
--hypercalciuria
--Ethacrynic acid + aminoglycoside = ototoxicity!!!

Thiazide Diuretics
Hydrochlorothiazide (HCTZ), Chlorthalidone, Metolazone. These are “low ceiling” diuretics with no “rebound sodium retention” because they act at the DCT. Thiazides act by blocking the Na/Cl co-transporter.

Other effects include antihypertensive effect independent of diuretic effect. Also, decreased calcium excretion (opposite of loop diuretics) can help treat kidney stones and osteoporosis.

Side effects:
--hypokalemic metabolic alkalosis for the same reasons as loop diuretics.
--hyperuricemia due to reduced uric acid excretion may lead to gout.

**Potassium-sparing Diuretics**

Spironolactone: aldosterone antagonist, inhibits basolateral Na/K antiporter in the principal cell.
Amiloride, Triamterene: EnaC blockers.

These are low efficacy diuretics.

Other effects include:

- **Spironolactone reduces CHF mortality.** It has potent antihypertensive effects because myocardium also has aldosterone receptors.
- **Amiloride reduces kidney toxicity from lithium, which enters via the amiloride-sensitive EnaC channel.**

**Side effect:** Hyperkalemia – potentially fatal!

**Carbonic Anhydrase Inhibitors**

CA catalyzes the hydration of HCO3, which generates H+ for secretion into proximal tubule in exchange for Na+. CA inhibitors prevent this H+ generation, preventing Na+ and HCO3 reabsorption. Overall, the body wastes NaHCO3. This simulates RTA type 2.

Unlike other diuretics, the acidosis by CA inhibitors is accompanied by hypokalemia.

**Side effects:**
- Acidosis due to bicarbonate loss. Exactly like renal tubule acidosis (RTA) type 2.
- Hypokalemia.
- Teratogenic.

**Antianginal Drugs**

Although angina’s cardinal symptom is chest pain, the drugs used to treat angina aren’t typically analgesics.

Instead, antianginal drugs treat angina by reducing myocardial oxygen demand (reducing the amount of oxygen the heart needs to do its work), by increasing the supply of oxygen to the heart, or both.

The three classes of antianginal drugs discussed in this section include:

**Warning!**

**Adverse reactions to adenosine**

Common adverse reactions to adenosine include:
- facial flushing
- shortness of breath
- dyspnea
- chest discomfort.

**How antianginal drugs work**

Angina occurs when the coronary arteries (the heart’s primary source of oxygen) supply insufficient oxygen to the myocardium. This increases the heart’s workload, increasing heart rate, preload (blood volume in the ventricle at the end of diastole), afterload (pressure in the arteries leading from the ventricle), and force of myocardial contractility.

Antianginal drugs (nitrates, beta-adrenergic blockers, and calcium channel blockers) relieve angina by decreasing one or more of these four factors. This diagram summarizes how antianginal drugs affect the cardiovascular system.
Nitrates (for treating acute angina)
Beta-adrenergic blockers (for long-term prevention of angina)
Calcium channel blockers (used when other drugs fail to prevent angina).

**Antibiotics Introduction:**

Antibiotics are among the most frequently prescribed medications in modern medicine. Antibiotics cure disease by killing or injuring bacteria. The first antibiotic was penicillin, discovered accidentally from a mold culture. Today, over 100 different antibiotics are available to doctors to cure minor discomforts as well as life-threatening infections.

Although antibiotics are useful in a wide variety of infections, it is important to realize that antibiotics only treat **bacterial** infections. Antibiotics are useless against viral infections (for example, the common cold) and fungal infections (such as ringworm). Your doctor can best determine if an antibiotic is right for your condition.

**Types of Antibiotics**

Although there are well over 100 antibiotics, the majority come from only a few types of drugs. These are the main classes of antibiotics.

- Penicillins such as penicillin and amoxicillin
- Cephalosporins such as cephalexin (Keflex)
- Macrolides such as erythromycin (E-Mycin), clarithromycin (Biaxin), and azithromycin (Zithromax)
- Fluoroquinolones such as ciprofloxacin (Cipro), levofloxacin (Levaquin), and ofloxacin (Floxin)
- Sulfonamides such as co-trimoxazole (Bactrim) and trimethoprim (Proloprim)
- Tetracyclines such as tetracycline (Sumycin, Panmycin) and doxycycline (Vibramycin)
- Aminoglycosides such as gentamicin (Garamycin) and tobramycin (Tobrex)

Most antibiotics have 2 names, the trade or brand name, created by the drug company that manufactures the drug, and a generic name, based on the antibiotic's chemical structure or chemical class. Trade names such as Keflex and Zithromax are capitalized. Generics such as cephalexin and azithromycin are not capitalized.

Each antibiotic is effective only for certain types of infections, and your doctor is best able to compare your needs with the available medicines. Also, a person may have allergies that eliminate a class of antibiotic from consideration, such as a penicillin allergy preventing your doctor from prescribing amoxicillin.
In most cases of antibiotic use, a doctor must choose an antibiotic based on the most likely cause of the infection. For example, if you have an earache, the doctor knows what kinds of bacteria cause most ear infections. He or she will choose the antibiotic that best combats those kinds of bacteria. In another example, a few bacteria cause about 90% of pneumonias in previously healthy people. If you are diagnosed with pneumonia, the doctor will choose an antibiotic that will kill these bacteria.

Other factors may be considered when choosing an antibiotic. Medication cost, dosing schedule, and common side effects are often taken into account. Patterns of infection in your community may be considered also.

In some cases, laboratories may help a doctor make an antibiotic choice. Special techniques such as Gram stains may help narrow down which species of bacteria is causing your infection. Certain bacterial species will take a stain, and others will not. Cultures may also be obtained. In this technique, a bacterial sample from your infection is allowed to grow in a laboratory. The way bacteria grow or what they look like when they grow can help to identify the bacterial species. Cultures may also be tested to determine antibiotic sensitivities. A sensitivity list is the roster of antibiotics that kill a particular bacterial type. This list can be used to double check that you are taking the right antibiotic.

Only your doctor can choose the best class and the best antibiotic from that class for your individual needs.

**Taking Your Medicine**

It is important to learn how to take antibiotics correctly. Read the label to see how many pills to take and how often to take your medicine. Also, ask your pharmacist if there is anything you should know about the medication.

An important question to ask is how the medication should be taken. Some medications need to be taken with something in your stomach such as a glass of milk or a few crackers, and others only with water. Taking your antibiotics incorrectly may affect their absorption, reducing or eliminating their effectiveness.

It is also important to store your medication correctly. Many children's antibiotics need to be refrigerated (amoxicillin), while others are best left at room temperature (Biaxin).

Take your entire course of antibiotics. Even though you may feel better before your medicine is entirely gone, follow through and take the entire course. This is important for your healing. If an antibiotic is stopped in midcourse, the bacteria may be partially treated and not completely killed, causing the bacteria to be resistant to the antibiotic. This can cause a serious problem if those now-resistant bacteria grow enough to cause a reinfection.

**Side Effects**

- Antibiotics may have side effects. Some of the more common side effects may include:
  - Soft stools or diarrhea
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- Mild stomach upset

You should notify your doctor if you have any of the following side effects:

- Vomiting
- Severe watery diarrhea and abdominal cramps
- Allergic reaction (shortness of breath, hives, swelling of your lips, face, or tongue, fainting)
- Vaginal itching or discharge
- White patches on your tongue

**Allergy**
Some people are allergic to certain types of antibiotics, most commonly penicillin. If you have a question about a potential allergy, ask your doctor or pharmacist before taking the medicine.

Allergic reactions commonly have the following symptoms:

- Shortness of breath
- Hives
- Itching
- Swelling of your lips, face, or tongue
- Fainting

**Antihypertensive**

**Depending on mechanism of action, a given antihypertensive may:**

- Reduce preload
- Reduce afterload
- Decrease heart rate
- Reduce peripheral resistance
- Reduce contractility.

Many antihypertensive drugs have multiple effects.

**Side Effects**
Antihypertensive medications are prescribed to treat high blood pressure. According to the Mayo Clinic, angiotensin-converting enzyme (ACE) inhibitors calm blood vessels by halting certain hormone production. Beta blockers work by inhibiting nerve signals to the heart and blood vessels. Calcium channel blockers inhibit calcium from reaching heart and blood vessels cells so
the cells can relax and ease the patient's blood flow. Like all medications, antihypertensives have potential side effects.

Common Side Effects

- According to the U.S. Department of Health and Human Services, side effects of antihypertensives that are considered common but not serious include slight dizziness, fatigue, cough and headache. In mild cases, these side effects do not normally require medical treatment. In the event that the symptoms become more pronounced or difficult to tolerate, the patient should notify a physician.

Serious Side Effects

- Serious side effects of antihypertensives, as cited by the Mayo Clinic, include insomnia, decreased sex drive, shortness of breath and depressed mood. A patient experiencing these symptoms should consult with a physician before continuing doses of any antihypertensive medication.

Severe Side Effects

- Severe side effects associated with antihypertensives that require immediate emergency medical attention include chest pain, difficulty breathing, fainting, irregular heartbeat and rash. Swelling of the face, lips, tongue or extremities may be the sign of an allergic reaction to the medication. For these symptoms, treatment should not be delayed.

Existing Medical Conditions

- Before using an antihypertensive medication, a patient should advise her physician of existing medical conditions such as kidney disease, recent stroke, irregular heartbeat, systemic lupus or clinical depression. Beta blockers have the potential to trigger severe attacks in people suffering from chronic asthma, and thus asthmatic patients are advised to utilize a different form of antihypertensive. Some antihypertensive formulas may block signs of low blood sugar, including rapid heart beat, in patients living with diabetes, so blood sugar levels must be closely monitored on a consistent basis.

Types of Antihypertensive Medications

There are several types of medications that are available to treat high blood pressure. Hypertension, or elevated blood pressure, is one of the most common medical conditions. In most cases, it is a silent risk factor for other conditions, such as a heart attack or stroke. The medical community greatly emphasizes the importance of controlling blood pressure. Many drugs are available to control high blood pressure and work in many ways. The major classes of antihypertensive medications and their mechanisms of action are described as follows.

Diuretics

Diuretics are drugs that increase the amount of urine eliminated from the body. Normally, as blood flows through the kidneys, fluid, electrolytes, and small substances are filtered into the nephrons of the kidney but most of the filtrate is reabsorbed back into the bloodstream. Diuretics work by blocking the reabsorption process so that extra urine is produced. Depending on the site of action, diuretics are further classified into loop diuretics (e.g., furosemide) that act on the loop of Henle in the nephron, thiazide diuretics (e.g., hydrochlorothiazide) that block reabsorption at the distal tubule of the nephron, and potassium-sparing diuretics (e.g., spironolactone) that
ACE Inhibitors
Certain antihypertensive drugs may target the renin-angiotensin pathway, a set of chemical reactions that ultimately boosts blood pressure when it gets low. Though the process is complicated, the main steps involve the conversion of angiotensin I to angiotensin II by angiotensin-converting enzyme (ACE) in the lungs. ACE inhibitors (e.g., lisinopril), work by blocking ACE, thereby lowering blood pressure.

Angiotensin II Receptor Blockers
Instead of ACE inhibitors, antihypertensive drugs called angiotensin II receptor blockers (e.g., losartan) can lower blood pressure by blocking the receptors for angiotensin II. This class of drugs is considered when a patient is averse or allergic to ACE inhibitors.

Beta Blockers
Beta blockers (e.g., metoprolol) are drugs that decrease the heart's rate and contractility, which in turn lowers blood pressure. These medications are generally used when other conditions requiring beta blockers are present, such as congestive heart failure and myocardial infarction.

Calcium Channel Blockers
Calcium channel blockers (e.g., nifedipine) are medications that inhibit transport of calcium across cell membranes. They primarily act on the smooth muscle layer of arteries, causing relaxation of smooth muscle, increased arterial diameter, and lowered blood pressure. Certain drugs in this class, such as diltiazem, also reduce heart muscle contractility.

Heart Failure (Congestive Heart Failure) Medications

Definition of Heart Failure: The purpose of the heart is to pump blood, which contains oxygen and nutrients, to the rest of the body. Congestive Heart Failure (CHF) is simply the failure of the heart to perform this main function adequately. Of course, a lack of blood pumped to the body is only considered CHF if the heart actually receives a sufficient volume of blood from the incoming vessels in the first place (i.e., normal filling pressures). When there is not enough blood for the heart to pump out, the problem is not CHF. Congestive Heart Failure occurs when the flow of blood from the heart (cardiac output) decreases, or fluid backs-up behind the failing ventricle, or both.

Drugs associated with Heart Failure
The following drugs and medications are in some way related to, or used in the treatment of Heart Failure. This service should be used as a supplement to, and NOT a substitute for, the expertise, skill, knowledge and judgment of healthcare practitioners.

- **Accupril**: generic name: quinapril class: angiotensin converting enzyme inhibitors.

- **Aldactone**: generic name: spironolactone class: aldosterone receptor antagonists, potassium-sparing diuretics.
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- **Lasix**: generic name: furosemide class: loop diuretics.
- **Metoprolol Succinate ER**: generic name: metoprolol class: cardioselective beta blockers.
- **Norvasc**: generic name: amlodipine class: calcium channel blocking agents.
- **Lanoxin**: generic name: digoxin class: group V antiarrhythmics, inotropic agents.
- **Zestril**: generic name: lisinopril class: angiotensin converting enzyme inhibitors.

**Anticoagulants**

Anticoagulants are agents that prevent the formation of blood clots, by affecting blood coagulation factors. The mechanism of action of anticoagulation varies depending on the agent. They are used to treat thrombotic and thromboembolic disease such as stroke, myocardial infarction, deep vein thrombosis and pulmonary embolism.

**Drugs**

- **Coumadin**: generic name: warfarin.
- **Heparin Sodium**: generic name: heparin.
- **Lovenox**: generic name: enoxaparin.
- **Orgaran**: generic name: danaparoid.
- **Refludan**: generic name: lepirudin.
- **Angiomax**: generic name: bivalirudin.

**Antiarrhythmic Agents**

- **Lanoxin**: generic name: digoxin.
- **Adenocard**: generic name: adenosine.
- **Calan**: generic name: verapamil.
- **Calan SR**: generic name: verapamil.
- **Diltiazem Hydrochloride SR**: generic name: diltiazem.
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- **Diltzac**: generic name: diltiazem.
- **Pacerone**: generic name: amiodarone.
- **Tikosyn**: generic name: dofetilide.
- **Cordarone**: generic name: amiodarone.
- **Multaq**: generic name: dronedarone.
- **Sotalol Hydrochloride AF**: generic name: sotalol.
- **Corvert**: generic name: ibutilide.
- **Inderal**: generic name: propranolol.
- **Brevibloc**: generic name: esmolol.
- **Sectral**: generic name: acebutolol.
- **Ethmozine**: generic name: moricizine.
- **Norpace CR**: generic name: disopyramide.

**Tranquillizers**

**Anxiolytics, sedatives, and hypnotics**

- **Nembutal**: generic name: pentobarbital.
- **Mebaral**: generic name: mephobarbital.
- **Seconal**: generic name: secobarbital.
- **Restoril**: generic name: temazepam.
- **Valium**: generic name: diazepam.
- **Xanax**: generic name: alprazolam.
- **Ativan**: generic name: lorazepam.

**Shock Medications**
Definition of Shock: Shock is a life-threatening condition that occurs when the body is not getting enough blood flow. This can damage multiple organs. Shock requires IMMEDIATE medical treatment and can get worse very rapidly.

Drugs associated with Shock
The following drugs and medications are in some way related to, or used in the treatment of Shock. This service should be used as a supplement to, and NOT a substitute for, the expertise, skill, knowledge and judgment of healthcare practitioners.

- **Adrenalin**: generic name: epinephrine class: adrenergic bronchodilators, catecholamines, vasopressors.
- **Decadron**: generic name: dexamethasone class: glucocorticoids.
- **Dobutrex**: generic name: dobutamine class: cardiac stressing agents, catecholamines, inotropic agents, vasopressors.
- **Solu-Medrol**: generic name: methylprednisolone class: glucocorticoids.
- **Solu-Cortef**: generic name: hydrocortisone class: glucocorticoids.