LESSON ASSIGNMENT

SUBCOURSE MD0806 Therapeutics III.

LESSON 7 Antihypertensive Agents.

LESSON ASSIGNMENT Paragraphs 7-1--7-12.

LESSON OBJECTIVES After completing this lesson you will be able to:

7-1. From a group of statements, select the statement which best defines the term essential hypertension.

7-2. Given the name of a type of essential hypertension and a group of statements, select the statement that best describes that type.

7-3. Given a group of statements, select the statement that best describes why diuretics are used to treat hypertension.

7-4. Given a group of trade and/or generic names of antihypertensive agents match each trade name with its corresponding generic name.

7-5. Given the trade and/or generic name of an antihypertensive agent and a group of indications, side effects, or patient warnings; select the indication(s), side effect(s), or patient warning(s) associated with that agent.

SUGGESTION After studying the assignment, complete the exercises at the end of this lesson. These exercises will help you to achieve the lesson objectives.
LESSON 7

ANTIHYPERTENSIVE AGENTS

Section I.  INTRODUCTION TO HYPERTENSION

7-1.  INTRODUCTION

a. It is estimated that 23 million people in the United States suffer from hypertension. Of this number, it is thought that 11.5 million people have been diagnosed as having the condition and that 5.75 million of those people are being treated for it. Unfortunately, it is estimated that only 2.875 million of those persons treated for hypertension are being treated properly. Therefore, it is obvious that hypertension is a major medical problem which should be a concern of all medical personnel.

b. Hypertension (high blood pressure) is prevalent in both men and women. It frequently contributes to the death of many persons. The cause of most cases of hypertension is unknown. This type of hypertension is referred to as primary or essential hypertension. Hypertension that has a known cause (kidney disease, hyperthyroidism) is called secondary hypertension. Blood pressure is the force that the blood exerts on the vessel wall while the heart is contracting and at rest. The force against the vessel wall during contraction or systole is the systolic pressure and the force during rest or diastole is the diastolic pressure. The blood pressure is expressed in terms of millimeters of mercury (Hg). Normal blood pressure is less than 135 mm Hg (systolic) and less than 85 mm Hg (diastolic) = 135/85 mm Hg.

7-2.  TREATMENT OF HYPERTENSION

There is no cure for hypertension. Most patients who have a bacterial infection are accustomed to taking a 10-day treatment regimen of an antibiotic in order to rid themselves of the infection. The same is not true with hypertension. Once a person begins taking an antihypertensive agent, it is likely that he will continue taking some type of antihypertensive agent for the rest of his life.

7-3.  DEFINITION OF ESSENTIAL (PRIMARY) HYPERTENSION

Essential (primary) hypertension can be defined as a disorder of unknown origin characterized mainly by an elevated systolic or diastolic blood pressure associated with generalized arteriolar vasoconstriction (see Lesson 3). Essential hypertension may be divided into three classes according to the severity of the condition. Labile hypertension is a condition of elevated blood pressure with intervening periods of normal blood pressure.
7-4. CLASSES OF ESSENTIAL HYPERTENSION

a. Stage I Hypertension. Stage I hypertension is characterized by sustained, documented systolic pressure 140 to 159 mm Hg and/or diastolic pressure measurements 90 to 99 mm Hg. Signs of this type include increased heart rate (tachycardia) and increased cardiac output with normal total peripheral vascular resistance; however, the majority of patients cannot tell that they have hypertension.

b. Stage II Hypertension. Stage II hypertension is characterized by sustained, systolic elevation (160 to 179 mm Hg) and/or diastolic pressure (100 to 109 mm Hg). Symptoms are the same as noted in Stage I. Patients with Stage I or II DO NOT show signs of target end organ damage. The organs of most concern are the heart, kidneys, and eyes. Stage I and II hypertension may be treated nonpharmacologically with diet and exercise or pharmacologically with anti-hypertensive medications.

c. Stage III Hypertension. Stage III hypertension is characterized by a persistent elevation (systolic greater than 180 mm Hg; diastolic greater than 110 mm Hg) with target end organ damage. Damage to the heart may include strain or enlargement of the left ventricle. Kidney damage may appear as abnormal laboratory values that indicate inefficiency. Damage to the eyes may appear as small hemorrhages due to the sustained blood pressure in these small vessels. This stage is often treated immediately with anti-hypertensive medications.

d. Hypertensive Urgency/Crisis.

(1) Hypertensive urgency is a condition of persistent elevation in blood pressure without target end organ damage. However, the pressure is high enough that the patient presents for treatment because of symptoms of dizziness, chest pain, or confusion. The goal in treatment of this condition is to normalize the blood pressure as quickly as possible (usually over 1 to 3 days).

(2) Hypertensive crisis is a similar condition. However, the patient has symptoms of target end organ damage. This may be a life-threatening condition. The goal of therapy is to normalize the blood pressure in 12 to 24 hours. Both conditions are usually treated with intravenous (IV) anti-hypertensives.

7-5. REVIEW OF IMPORTANT FACTORS RELATING TO HYPERTENSION

Essential hypertension is a process of variable course and severity. Several options are open to the physician depending upon the severity of the drug therapy. Condition weight reduction and diet control may be adequate treatment; however, drug therapy is sometimes needed. When drug therapy is required, it usually begins with a diuretic followed by the addition of the other agents based on the patient’s response. However, certain classes of drugs may be more advantageous (less side effects) when patients have other diseases. It is not unreasonable to see patients treated by the same provider on different drugs.
7-6. DIURETICS IN THE TREATMENT OF HYPERTENSION

The effectiveness of diuretics in the treatment of essential hypertension arises from the fact that diuretic agents decrease tubular reabsorption of sodium, which caused a reduction in blood pressure. Some of the common diuretics include hydrochlorothiazide, spironolactone (Aldactone®), furosemide (Lasix®), and triamterene (Dyrenium®). These agents will be discussed in detail in Lesson 8 of this subcourse.

7-7. COMBINATION THERAPY IN THE TREATMENT OF HYPERTENSION

When diuretics alone are ineffective in controlling hypertension, it is necessary to combine the diuretic therapy with one or more additional agents. The physician may use many combinations of agents in order to control the patient's high blood pressure. The patient should be encouraged to discuss any questions he might have concerning the side effects (for example, drowsiness), which might be caused by an agent or agents.

Section II. DRUGS USED IN THE TREATMENT OF HYPERTENSION

NOTE: For this discussion commonly used antihypertensive agents will be classified into the following categories.

7-8. DRUGS WHICH ACT ON THE SYMPATHETIC NERVOUS SYSTEM

NOTE: For a review of the sympathetic nervous system, refer to Subcourse MD0805, Therapeutics II.

a. Methyldopa (Aldomet®). Methyldopa is one of the drugs of this type. It is believed to produce its effects by its being metabolized to a substance which is very similar to norepinephrine—but with considerably less vasoconstricting activity than is shown by epinephrine. Thus, methyldopa competes with norepinephrine and thereby depresses the activity of the sympathetic nervous system. This medication is rarely used, but is still one of the drugs of choice for pregnancy-induced hypertension. Side effects associated with this agent include bradycardia, swelling of the feet and lower legs (because sodium and water retention), drowsiness, and mental depression.

b. Clonidine (Catapres®, Catapres TTS®). Clonidine is an agent that is believed to act by decreasing sympathetic outflow from the brain and consequently inhibit vasoconstriction. It is used in mild to moderate hypertension. Side effects associated with this agent include swelling of the feet and lower legs (due to sodium and water retention) and mental depression. The patient taking this drug should be cautioned to check with his physician before suddenly discontinuing the medication because abrupt withdrawal from the drug may cause serious hypertension problems. Clonidine is also used in the treatment of symptoms associated with alcohol withdrawal.
7-9.  BETA ADRENERGIC BLOCKERS

Beta adrenergic blocking agents block the effect of the sympathetic neurotransmitters by competing for receptors.

   a.  **Propranolol (Inderal®).**  Propranolol is a drug used in the treatment of hypertension, angina pectoris, and cardiac arrhythmias.  Side effects associated with propranolol include dizziness, mental confusion, and mental depression.  It may also exacerbate congestive heart failure and mask the symptoms of hypoglycemia.

   b.  **Metaprolol (Lopressor®, Toprol XL®).**  Metaprolol is prescribed for the same conditions as propranolol and is also indicated used in the treatment of myocardial infarction and treatment of congestive heart failure.  Normal doses for hypertension are 25 – 100mg twice daily.  The dose for heart failure is 6.25 to12.5 mg twice daily and adjusted upward as tolerated by the patient.  This agent is available as an oral and injectable preparation.

   c.  **Other Beta Adrenergic Blockers.**  Other beta blockers used in the treatment of hypertension include betaxolol (Kerlone®), bisoprolol (Zebeta®), labetolol (Trandate®, Normodyne®), nadolol (Corgard®),  and carvedilol (Coreg®).  Carvedilol is also indicated for congestive heart failure.

7-10. SMOOTH MUSCLE RELAXANTS

Drugs in this category treat hypertension by acting directly on vascular smooth muscle by relaxing the blood vessels.  Consequently, they cause vasodilation and a decrease in peripheral resistance results in a lower blood pressure.

   a.  **Hydralazine (Apresoline®).**  Hydralazine is given orally or injected in the management of hypertension.  Preferably, it is used in conjunction with other antihypertensive agents.  Side effects associated with this agent include chest pain (angina pectoris), a general feeling of weakness, unexplained sore throat, joint pain, and headache.  The patient should to be told to avoid getting up suddenly from a lying or a sitting position.

   b.  **Alpha Adrenergic Blockers.**  Alpha adrenergic blockers block alpha receptors in peripheral vessels, therefore causing vasodilation.  Agents in the class include prazosin (Minipress®), doxazosin (Cardura®), and terazosin (Hytrin®).  Doxazosin and terazosin offer the advantage of once daily dosing and the added benefit of relieving the symptoms of benign prostatic hyperplasia (enlarged prostate gland).  Dizziness, drowsiness, and headache are common side effects associated with these agents, especially with the first dose.  Patients must be counseled on these side effects and instructed to take the first dose in the evening at home.  Some patients who have taken this drug have also experienced syncope (unconsciousness due to decreased oxygen supply to the brain).
c. **Calcium Channel Blockers.** Calcium channel blockers are potent peripheral vasodilators used in the treatment of hypertension. They are similar to beta blockers that can slow the heart rate. Calcium channel blockers are also used in the treatment of atrial fibrillation to control the heart rate. Many of the products are available in oral and injectable form and may be administered once daily. Side effects include dizziness, headache, heartburn, edema, and constipation. Agents include diltiazem (Cardizem®, Tiazac®, Dilacor®), verapamil (Calan®, Isoptin®, Covera®, Verelan®), amlodipine (Norvasc®), felodipine (Plendil®), and nifedipine (Procardia XL®, Adalat CC®).

d. **Angiotensin Converting Enzyme Inhibitors (ACE Inhibitors).** ACE inhibitors work by inhibiting the enzyme which converts angiotensin I to angiotensin II. Angiotensin II is one of the most potent vasoconstrictors known to man. By inhibiting the enzyme, these agents produce vasodilation and are used in the treatment of hypertension and congestive heart failure. Most products are administered one to two times daily. The most common side effects are rash, dry cough, and hyperkalemia. These agents are contraindicated in pregnancy. Selected agents include benazepril (Lotensin®), captopril (Capoten®), enalapril (Vasotec®), lisinopril (Prinivil®, Zestril®), and ramipril (Altace®). Enalapril is available in an injectable form.

e. **Angiotensin II Receptor Blockers (ARBs).** ARBs work by directly blocking the angiotensin II receptor to cause vasodilation and lower blood pressure. They appear to have less side effects than ACE inhibitors, especially the dry cough. Selected agents include irbesartan (Avapro®), losartan (Cozaar®), and valsartan (Diovan®).

### 7-11. Combination Products

It should be apparent that in order to control hypertension the patient may be required to take extremely large amounts of medication. In an attempt to develop a more convenient method of controlling hypertension, researchers have combined diuretic and antihypertensive agents in order to maximize the best attributes of each. These combination products are very convenient for the patient to use if the dosage of the product is exactly what the patient needs to control his hypertension. Since these combination products tend to be rather expensive, military pharmacies frequently have a limited selection of these items in stock. Two examples of combination products are listed below.

a. **Aldactazide® (Spironolactone and Hydrochlorothiazide).** Spironolactone and hydrochlorothiazide are both diuretics. This particular drug is used in the treatment of hypertension, congestive heart failure and cirrhosis of the liver. The patient taking this medication should be told to take the preparation with or after meals to minimize stomach upset.

b. **Dyazide® (Triamterene and Hydrochlorothiazide).** Triamterene and hydrochlorothiazide are both diuretics. This product is used as a diuretic and as an antihypertensive agent.
Patients presenting with extreme elevations of blood pressure and symptoms of impending stroke, pulmonary edema, kidney failure, or heart attack must be promptly. The following agents are used to treat hypertensive crisis:

a. **Diazoxide (Hyperstat® I.V.)** This agent is administered by rapid intravenous (I.V.) injection (150 to 300 milligrams immediately, repeated in 30 minutes and every four hours if needed). When administered, this agent produces a fall in blood pressure in from one to five minutes. Hyperglycemia and sodium retention are side effects associated with this agent.

b. **Nitroprusside (Nipride®)**. Nitroprusside is administered by continuous intravenous infusion at a rate of 0.5 to 0.8 micrograms per kilogram of patient weight per minute. The patient must be closely observed when he is receiving this drug since overdosage of nitroprusside results in cyanide poisoning. Nitroprusside is not intended for direct injection. Instead, the drug must be used as an infusion with sterile 5 percent dextrose in water. The intravenous infusion must be used within four hours once it is prepared. Furthermore, the prepared intravenous infusion must be protected from light (for example, the bottle wrapped with foil). Nausea, vomiting, and headache are side effects commonly associated with this agent.

Continue with Exercises

Return to Table of Contents
EXERCISES, LESSON 7

INSTRUCTIONS. The following exercises are to be answered by marking the lettered response that best answers the question or best completes the incomplete statement.

After you have completed all the exercises, turn to “Solutions to Exercises” at the end of the lesson and check your answers with the solutions. For each exercise answered incorrectly, reread the material referenced after the solution.

1. Match the drug name in Column A with its trade name listed in Column B.

<table>
<thead>
<tr>
<th>COLUMN A</th>
<th>COLUMN B</th>
</tr>
</thead>
<tbody>
<tr>
<td>_____ Lisinopril.</td>
<td>a. Cardura®</td>
</tr>
<tr>
<td>_____ Spironolactone and</td>
<td>b. Catapres®</td>
</tr>
<tr>
<td>hydrochlorothiazide combination.</td>
<td></td>
</tr>
<tr>
<td>_____ Doxazosin.</td>
<td>c. Adalat CC®</td>
</tr>
<tr>
<td>_____ Diltiazem.</td>
<td>d. Inderal®</td>
</tr>
<tr>
<td>_____ Metoprolol.</td>
<td>e. Calan®</td>
</tr>
<tr>
<td>_____ Propranolol.</td>
<td>f. Cardizem®</td>
</tr>
<tr>
<td>_____ Clonidine.</td>
<td>g. Zestril®</td>
</tr>
<tr>
<td>_____ Verapamil.</td>
<td>h. Lopressor®</td>
</tr>
<tr>
<td>_____ Nifedipine.</td>
<td>i. Aldactazide®</td>
</tr>
</tbody>
</table>

MD0806 7-8
2. Which of the following statements best defines the term essential hypertension?

a. A disorder of unknown origin characterized mainly by an elevated systolic or diastolic pressure associated with generalized arteriolar vasoconstriction.

b. A disorder caused by too many fats in the diet and by an excess of sodium in the intracellular fluid.

c. A disorder produced by unknown causes which results in a diastolic pressure which is higher than the systolic pressure.

d. A disorder of unknown origin that can be cured by a 10-day treatment regimen of diuretics and antihypertensives.

3. Which of the following statements best describes Stage I primary hypertension?

a. A type of essential hypertension characterized by documented pressure measurements greater than 159 mm Hg (systolic) and/or greater than 99 mm Hg (diastolic).

b. A type of essential hypertension characterized by a persistent elevation in diastolic pressure with minor target organ (heart and kidney damage).

c. A type of essential hypertension characterized by marked elevated blood pressure with definite target organ (heart and kidney) damage.

d. A type of essential hypertension characterized by a mild, but sustained, elevation in diastolic pressure without target organ (heart and kidney) damage.

4. Stage III primary hypertension is best described as a type of essential hypertension characterized by:

a. Persistent elevated diastolic pressure with minor damage to the heart and/or kidneys.

b. Documented diastolic pressure associated with generalized arteriolar vasoconstriction.

c. A mild, but sustained, elevation in diastolic pressure without damage to the heart and/or kidneys.

d. Marked elevated blood pressure with definite damage to the heart and/or kidneys.
5. Nitroprusside (Nipride®) is used in the treatment of:
   a. Essential hypertension.
   b. Hypertensive crisis.
   c. Labile primary hypertension.
   d. Moderate primary hypertension.

6. What side effect is associated with beta blockers?
   a. Swelling of the feet and lower legs.
   b. Tachycardia.
   c. Restlessness.
   d. Mask symptoms of hypoglycemia.

7. What should the patient taking terazosin be told?
   a. To be aware that many patients taking the drug experience impotence or decreased sexual interest.
   b. To take the medication one hour before meals in order to increase the absorption of the drug.
   c. To arise slowly from a lying or sitting position because of the possibility of orthostatic hypotension and syncope.
   d. To avoid taking the medication with fats because absorption of the drug is affected.
8. The patient taking nitroprusside should be closely monitored because:
   a. Hyperglycemia and sodium retention occur so abruptly with this agent that death can result if the drug is not withdrawn after their onset.
   b. Overdosage of nitroprusside results in cyanide poisoning.
   c. Abrupt withdrawal of this agent can result in an extreme hypertensive crisis.
   d. Too rapid administration of this product can result in a cerebrovascular accident.

9. Which of the following is a side effect associated with the use of enalapril?
   a. Hypokalemia (low potassium).
   b. Dry cough.
   c. Syncope.
   d. Chest pain.

10. What is an indication for Coreg®?
    a. Antihypertensive.
    b. Congestive heart failure.
    c. Antianginal agent (treatment of angina pectoris).
    d. a and b only.
    e. a, b, and c.

Check Your Answers on Next Page
SOLUTIONS TO EXERCISES, LESSON 7

1. ___G._ Lisinopril (para 7-10d).  
   a. Cardura®.  
   ___I._ Spironolactone and hydrochlorothiazide combination. (para 7-11a)  
   b. Catapres®  
   ___A__ Doxazosin (para 7-10b).  
   c. Adalat CC®  
   ___F__ Diltiazem (para 7-10c).  
   d. Inderal®  
   ___H__ Metoprolol (para 7-9b).  
   e. Calan®  
   ___D__ Propranolol (para 7-9a).  
   f. Cardizem®  
   ___B__ Clonidine (para 7-8b).  
   g. Zestril®  
   ___E__ Verapamil (para 7-10c).  
   h. Lopressor®  
   ___C__ Nifedipine (para 7-10c).  
   i. Aldactazide®  

2. a (para 7-3)  
3. a (para 7-4a)  
4. d (para 7-4c)  
5. b (para 7-12b)  
6. d (para 7-9a)  
7. c (para 7-10b)  
8. b (para 7-12b)  
9. b (para 7-10d)  
10. d (para 7-9c)  

Return to Table of Contents