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The Down-Low (DL) on High Blood Pressure

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Introduction

I am a firm believer that knowledge is power. I believe that students of inner city schools are often not challenged in their educational experiences by the rigor of deep knowledge. If we, as an educational community, continue to teach students at a superficial level, we will propagate a culture of superficial people. While I am unaware of studies that prove my hypothesis, I do see its truth in my everyday teaching experiences. My students are consistently surrounded by medical information. These kids want to know how their body works. Unfortunately, their body is sometimes the only thing they have to call their own. It is my practice to present challenging, detailed topics whenever possible. For example, during cardiology, I teach students how to read electrocardiograms (EKGs). The students became so proficient in learning EKGs that they could analyze rhythms and describe their associated physiology. By the end of the unit, the students express confidence in learning a new skill. My hope is to have students learn this curriculum by this same holistic approach.

Rationale

After working for two years at an inner city high school, I've found the students have a strong desire for valid health knowledge. For their lifetime, their understanding of good health has come from television, parents, and friends. On a rare occasion, one of my students does recite something they learned while attending a primary care physician visit. Unfortunately, these visits are far too infrequent to make any impact on the students' lives. Fortunately, I have the opportunity to make a major impact on the health knowledge of my students. At my school, I am the only Anatomy and Physiology teacher. I am also an active Nationally Registered Paramedic. Likewise, I have the opportunity (and often the responsibility) of dispensing reliable health knowledge in such a way that is interesting, impacting, and memorable. While most of my students have a strong will to learn and be healthy, I have found three main components that prevent them from utilizing this knowledge. The first and biggest roadblock is a general lack of understanding. In general, my students have a lack of content knowledge that prevents their understanding of health. Many of them have an understanding that is based on incorrect information, and many of them are adamant when I refute their believed truths. Second, my students have a lack of drive when it comes to taking action in their own health. They don't know how to effectively motivate themselves. Lastly, a lack of quick results prevents further time spent and dedication to completing their goals. While these roadblocks can be said as the cause for most of America's health problems, I feel it is my responsibility, as an educator, to address these three inhibitors when I teach my students.

I teach approximately 110 students each year at Armstrong High School. During my time at Armstrong, my student population has been 99.4% African American. Out of the over 700 students in my school, 97% receive free and reduced lunch. Unfortunately, these two statistics correlate to a more serious statistic: my students are at a higher risk of developing high blood pressure (hypertension) [1] . My goal is to create a curriculum that focuses on the pathophysiology, diagnosis, treatment, and prevention of this disease. Furthermore, I intend to touch on the three inhibitors that I mentioned earlier. I believe hypertension can be taught and eventually prevented by breaking through the above three components that prevent true student learning.

Objective

The purpose of this curriculum is to give teachers the opportunity to present detailed medical information to their students. My wish is that more students will be stimulated by the opportunity to learn about their health, and the health of their family. Hypertension has a strong genetic component. Therefore, it will be common to have students mention family members (or themselves) that take the pharmaceuticals discussed. By the end of the unit, students should have a firm understanding of the sources and consequences of high blood pressure, as well as its possible pharmaceutical treatment, enabling them to make an informed decision on how this subject affects their own life. While this topic may encourage students to open up about their own health, the instructor needs to be mindful of the privacy of their students. It is also important to note that while the facts discussed in this curriculum are valid in the general population, medicine does not always follow strict rules in individuals. Medicine attempts to treat the "average" person. Likewise, this curriculum may not be applicable to specific cases. Lastly, while my intent is to provide detailed medical information, this curriculum (and its contents), is in no way a substitute for a physician's examination/opinion.

Background

Cardiovascular Physiology

In order to break down the different pharmacological treatments of hypertension (as well as primary prevention techniques), it is imperative to have a basic understanding of the pathophysiology of the cardiovascular system. As eluded in the name, the cardiovascular system has two main components, the heart (cardio), and vasculature (arteries, capillaries, veins, etc.). There are micro and macro ways of analyzing the cardiovascular system. To start, a micro view of the system focuses on the basic needs of the cells dispersed throughout the body. All cells of the body require the input of at least two things, oxygen and glucose, and the output of at least one thing, carbon dioxide. This is accomplished by a process known as perfusion. Without good perfusion in a tissue in the body, the cells within that tissue will soon die. Loss of perfusion can lead to a cascade of local cell death. When thinking of the cardiovascular system, its pathophysiology, and related pharmacology, it is easy to forget the fundamental biology that the cardiovascular system was created for. While humans are living breathing complex organisms, it is important not to forget that we are ultimately a formation of millions of cells that require transfer of oxygen, glucose, and carbon dioxide. Needless to say, the cardiovascular system has a big responsibility for maintaining the homeostasis, or balanced living, of all the body's cells.

This unit will briefly discuss the heart and its vessels; however, if more information on the entire cardiovascular system is desired, it is suggested to reference the units *Under Pressure! The Circulatory System and Hypertension* by Vanessa Vitug or *Building a Heart: The Function and Mechanics* by Eric Laurenson.

The heart is a pump that utilizes muscles to create pressure differences to move blood. Blood, as with any liquid, travels from areas of high pressure to low pressure. The pressure gradients created by the heart are determined by three factors: the amount of contractile force made by the heart (or how hard the heart muscle contracts when pumping blood), the amount of fluid the heart has to pump, and the amount of resistance in the vascular system. Once pressure is created in the heart (through contractions of heart tissue) blood is expelled into vessels called arteries. Arteries contain three layers: tunica intima, tunica media, and tunica adventitia. The intima, or inner layer (think of it as being intimate with the blood), contains only a single layer of endothelial cells. The media, or middle layer, is the thickest layer, and contains smooth muscle that allow for control of vessel radius. The adventitia, or outer layer, contains accessory tissue, and will not be discussed in this unit. [2] Throughout the duration of this unit when the word vessel is used it is referencing the arterial system. The venous system is not emphasized in this unit, as hypertension affects primarily the arterial tissues, and it is these vessels that are the targets for pharmacological agents to alter blood pressure.

For the remainder of this unit, the cardiovascular system will be discussed on a macro scale. When discussing the effectiveness of the cardiovascular system, it is important to be able to quantify its efficacy. Cardiac output, which is one way of measuring the efficacy of the heart, is measured by both the heart's ability to pump blood (cardio), and the vessels ability to distribute the blood (vasculature). The formula used to calculate the efficiency of the heart can be found in Figure One. Cardiac output (CO) (measured in milliliters per minute) equals the rate of heart contractions (also known as heart rate (HR), measured in beats per minute), multiplied by the amount of fluid that the heart expels on each beat (also known as the stroke volume (SV), measured in milliliters per beat). For example, a normal HR (70 bpm) multiplied by a normal SV (70 mL/min) gives a cardiac output of 4900 mL/min. In other words, the heart is able to pump approximately the equivalence of two and a half 2L sodas within a one minute time period! As one exercises, the body's cells require even more circulating blood. In many instances, exercise can increase CO sevenfold! That is comparable to 35L (or 17.5 2L soda bottles) pulsing through your body in one minute. On the other hand, if CO drops below what is necessary to maintain cellular homeostasis, problems can ensue, because at the micro level cells in the body will not receive the substrates that they need for their function. [3]

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Physiology of Blood Pressure

A major measurement of cardiovascular systems ability to transmit blood through the body is blood pressure (BP). Blood pressure, as many know, contains two numbers the "top" number, and "bottom" number. While many people know of these numbers, few seem to have a good grasp of their meaning. When the heart pumps/contracts, a physiological event called "systole" (sis'tole'ee), it creates a pressure inside the arteries of the body. This pressure wave, felt by the pulse in various locations of the body, pushes blood at a high velocity throughout the body. This initial wave of pressure through the body has to be high in order to propel blood throughout the entire body. Putting this altogether, the systole of the heart creates a high pressure in the major vessels just outside the heart, which is used to drive blood flow throughout the entire body. Likewise, the "systolic pressure" of blood pressure measurement is the higher number and represents the highest pressure achieved by the heart during contraction. Physicians consider 120 mmHg to be "normal" systolic pressure. That being said, normal can have deviations due to a multitude of reasons. After the heart beats, it takes a rest, and allows blood to flow throughout the body and return to the heart. This rest gives the heart muscle time to relax; in addition, the pause taken for rest gives the heart time to prime its pump and allow blood to re–collect inside itself. During this rest period, or "diastole" (die'as'tole'ee), the pressure is usually much lower. Likewise, the "diastolic pressure" is the lower number, and represents the amount of pressure of the system during the heart's resting period. Physicians define a normal diastolic pressure around 80 mmHg. [4] The measure mmHg, or millimeters of Mercury, is a standard measurement for pressure that can be usually explained by most physics teachers (if desired).

Just as CO is a measurement of the heart's average ability to pump blood, Mean Arterial Pressure (MAP) is a measure of an overall average blood pressure. Figure Two demonstrates the calculation of MAP. In general, MAP demonstrates the average pressure within the cardiovascular system. Since a greater proportion of the heart beat is spent in diastole than systole, the ? is applied to the equation to represent this difference. There are three things that can affect the average pressure of the cardiovascular system: Systemic Vascular Resistance (SVR), CO, and volume. Since MAP is an overall measurement for blood pressure, these three factors will be discussed for their implications in high blood pressure (HBP).[3]

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Systemic Vascular Resistance and Flow Etiology

Resistance within the arterial system has major implications for HBP. Resistance in an artery is a measurement of how easily fluid is able to flow. Resistance is inversely proportional to flow. Likewise, an increase in resistance correlates to a decrease in flow. As seen in Figure 3, resistance is also inversely related to vessel radius. The smaller the vessel, the more resistance to flow. To understand these implications, imagine yourself drinking red Gatorade through a straw out of a barrel. For this example, Gatorade will represent blood (hence the red color), while the straw, barrel, and your mouth will represent the cardiovascular system. First imagine drinking the Gatorade through a straw the size of a garden hose, with a radius of 2 millimeters, for 30 seconds. Your mouth would have to apply only a small amount of negative pressure (at a resistance of 1/16) to remove a large amount of Gatorade. Next, imagine drinking the Gatorade through a normal "McDonald's size" straw with a radius of 1 millimeter. In order to remove the same amount of Gatorade as was removed from the hose sized straw, you will need to apply more negative pressure (at a resistance of 1) to take out the same amount Gatorade in 30 seconds. Lastly, imagine drinking the Gatorade from a coffee straw with a radius of 0.5 millimeters. As you could guess, it would take an extreme amount of negative pressure (at a resistance of 16) to remove the same amount of Gatorade. In fact, it is doubtful you would be able to remove an amount even close to the normal or hose sized straws by utilizing a coffee straw.

The cardiovascular system works in the same way; however, instead of trying to EXTRACT Gatorade, it has to PUSH blood. The amount of flow through your Gatorade straws is inversely proportional to its resistance. Furthermore, the resistance of the straw is determined by the inverse of the radius to the fourth power, assuming the straws were of the same length. Therefore, a small decrease in radius causes a very large increase in resistance (and likewise inversely proportional decrease in flow). The same physics applies to the cardiovascular system. In the terms of the cardiovascular system there are many things that can cause changes in vessel radius. First, endogenous changes will be discussed (changes due to the body's control), followed by exogenous changes (changes due to external factors).

Figure 3

$$\text{Resistance} \propto \frac{1}{\text{radius}^4} \qquad \text{Flow} \propto \frac{1}{\text{resistance}}$$

Endogenous

There are many different ways the body can regulate peripheral resistance. For the purpose of this unit, only those that have direct pharmacological ties will be discussed. These endogenous systems will be divided by the system they impact. Be aware that many of these systems involve many complex steps. Having multiple steps enables the body to accurately/specifically alter its physiology. For example, instead of having one on/off switch for blood pressure there are many different, specific on/off switches. In terms of pharmacology, the presence of multiple control systems allows the body to alter physiology through a variety of mechanisms.

Renin-Angiotensin-Aldosterone System (RAAS)

The body uses the RAAS to regulate normal volume of the cardiovascular system. When blood volume is low, the kidneys realize this and release rennin, which is then secreted into the blood. Renin flows through the blood and converts angiotensinogen into angiotensin I. Angiotensin I is then converted into Angiotensin II by the action of the angiotensin converting enzyme (ACE). The Angiotensin II hormone is an important vasoconstrictor (meaning it decreases the radius of blood vessels). Angiotensin II can also stimulate the production of aldosterone. Aldosterone prevents the kidney from excreting water and sodium into the bladder (which is then released through urination). Likewise, aldosterone allows the body to hold onto its water (and sodium), which helps to maintain blood pressure. [5] In summary, the secretion of renin by the kidney leads to vasoconstriction (a decrease in arterial radius) and water retention (an increase in blood volume). Both of these things lead to an increase in blood pressure.

Adrenergic Receptor Systems

The nervous system contains two divisions: parasympathetic nervous system (PSNS) and sympathetic nervous system (SNS). For both of these systems, there are chemicals, enzymes, and hormones that can activate (called agonists) or block activation (called antagonists). These agonists and antagonists are called ligands.

Ligands work by interacting with receptors found on cell membranes. This interaction causes a response that is prescribed by each ligand/receptor. For example, the SNS agonist, epinephrine, would increase heart rate, while an antagonist drug, such as a beta–blocker, would slow heart rate. In general, the SNS is used for flight/fight responses. In other words, when a rabid grizzly bear starts running after you, your SNS increases your heart rate, dilates your blood vessels and allows you to either fight the bear (not advisable) or flee (run away). Your PSNS is the "chill" system. In terms of a human, the PSNS controls salivation, lacrimation (crying), urination, defecation, the gastrointestinal tract movement, and emesis (vomiting) (known collectively by the acronym SLUDGE).[3] These actions allow for normal bodily functions to occur (once you have dealt with the bear from the SNS example).

Overexposure to certain insecticides, herbicides, or nerve agents causes your body to over activate the PSNS. This causes a massive SLUDGE reaction. The antidote for this poisoning is the PSNS antagonist Atropine. Atropine works by blocking the PSNS receptors in an antagonistic fashion. Federal agencies often carry large quantities of Atropine in preparation for an attack that utilizes the aforementioned agents. [6]

The receptors that work specifically for the sympathetic nervous system, adrenergic receptors, are found throughout the body, and control a multitude of functions. The adrenergic receptor system is further complicated as it is broken into two divisions: alpha (α), and beta (β). To make things more perplexing, there are subsets of each division: there are α1 and α2, as well as β1, β2, and β3 receptors.[35] This complexity allows the body to have very specific control over its physiology: different tissues, expressing different combinations of receptors, can tailor their response to the same ligand (epinephrine).

For the purposes of this unit we will discuss α2, β1, and β2 adrenergic receptors. The α2 adrenergic receptors activate smooth muscle of the arteries. Smooth muscle is muscle that lines much of our internal organs and is used for general internal organ movement, including vessels of the cardiovascular system. Likewise, α2 receptors have implications for blood pressure regulation. The actions of β–adrenergic receptors can be easily remembered by remembering their number. β1 receptors affect our ONE heart, while β2 receptors affect our TWO lungs. The actions of the β1 adrenergic effects are broken down into three functions. Chronotropic refers to the how fast the heart beats (think chronology or time = chronotropic). Dromotropic refers to how well the electrical signal of the heart passes through the heart. When the electrical signal passes more easily through the heart, the HR is affected. Inotropic refers to the contractility of the heart. When the heart contracts more forcefully, this pushes more blood with each beat (i.e. increases SV).[3] These three functions are affected in different ways by different medications.

While the complexity of this system allows for specificity of its actions, cross activation of receptors can occur with certain pharmaceuticals. For example, if a patient is having an asthma attack, a paramedic may administer an albuterol nebulizer. One thing the paramedic must monitor during the administration is the patient's heart rate. While the albuterol is an β2 adrenergic agonist (i.e. it relaxes the smooth muscle in the lungs causing the patient to breath more easily), it can also affect β1 adrenergic receptors. Likewise, if β1 adrenergic receptors are activated, the patient's heart rate can increase. Generally, this is not a problem; however, if the patient is elderly, with chronic heart failure, and a history of heart attacks, elevating the heart rate may have detrimental effects. [6]

Calcium Channels

The contraction of cardiac muscle is dependent on the release of calcium throughout the cells of the myocardium (heart muscle tissue). Teaching the mechanisms of calcium channels, and action potential of muscle cells, is usually saved for advanced physiology classes. For the purposes of this unit, these mechanisms will not be discussed in detail. It is important to understand, however, that calcium is used for muscle contractions. For cardiac muscle, changing the permeability of calcium channels can affect the contractility of the heart muscle. This has implications for both inotropic and chronotropic changes in the heart. In endothelium smooth muscle (as found in arteries), changing the permeability of calcium channel affects its contraction; which in turn can cause changes in the vasodilation/vasoconstriction of these vessels.[3]

Endothelium–Derived Relaxing Factors (EDRF)

The endothelium of the cardiovascular system has its own regulatory system to control the constriction of its smooth muscle (hence the name). There are two factors that are endothelium–derived that control vasodilation/vasoconstriction: EDRF and Endothelin (ET). It is believed that Endothelin is consistently present in the blood stream, and regulates the vasoconstriction of the vessels. EDRF, on the other hand, is created to block ET's action, and likewise cause vasodilation. In general, EDRF–NO acts as a quick vasodilator that has a relatively short duration of action. [7]

Kidney Control

Up until now, this unit approached blood pressure as it directly affected by the cardiovascular system. Another important facet to blood pressure control is the amount of fluid in the cardiovascular system. To an extent, more fluid in the cardiovascular system (without change in vascular dilation/constriction) leads to increased blood pressure. Therefore, the work of the kidneys to maintain a balanced blood volume level is imperative for normal blood pressure. The study of the kidneys' ability to filter out water and electrolytes is a very complicated topic. For the purposes of this unit, a general understanding of the nephron is important for understanding pharmacological impacts. When blood enters the kidney it is split into pathways that flow through the approximately one million nephrons. The nephron is the basic structure in the kidney that is responsible for filtration. As blood enters the nephron it travels through a system of corresponding tubules that abut the blood vessel. Through changes in channel permeability in the nephron's structures, salt and water are able to enter/exit the kidneys' vessels. This exchange of salt and water leads to the production of urine, which eventually is excreted into the bladder where it is eliminated during urination. Water leaving the cardiovascular system (by accumulation in urine) causes a decrease in blood pressure due to a decrease in volume. The less volume in the system, the less pressure the system exerts. The body, as well as pharmaceuticals, work to change the amount of water that exits through urination.[3]

[Fun fact: ethyl alcohol [EtOH] (alcohol that is consumed in recreation), as well as caffeine, work to prevent the secretion of the antidiuretic hormone (ADH). Likewise, while consuming these substances, diuresis (i.e. excessive urination), can occur. This is potentially dangerous when large amounts of EtOH are consumed. Not only do these patients tend to become dehydrated, they also lose key electrolytes (that are usually excreted along with water).[6] In the hospital, these patients are administered "banana bags." Banana bags are large liter bags of a yellow fluid (hence the name banana) that helps to replenish lost water and electrolytes.]

Exogenous

There are many external factors that can affect the narrowing of blood vessels, and likewise affect blood flow. For the purposes of this unit, two main exogenous factors are most often concurrent with high blood pressure: tobacco use, and high cholesterol (or hypercholesterolemia). Nicotine, an active molecule in tobacco, can activate SNS receptors which causes vasoconstriction. While moving through the bloodstream, nicotine can also interrupt the normal functions of endothelium, and cause them to harden. Cholesterol is a main exogenous cause of increased SVR in hypertensive patients. The common types of circulating cholesterol (often heard in commercials, and physician offices) are high–density lipoprotein (HDL), and low–density lipoprotein (LDL). LDL, also known as "bad" cholesterol, in fact refers to the protein (specifically called a lipoprotein) that surrounds a cholesterol molecule. When LDL associates to a cholesterol molecule it is then called LDL–C. Circulating LDL–C has the potential to cause harm through the build up of plaque in arterial blood vessels. HDL, also known as "good" cholestesterol, is the protein that transports cholesterol molecules throughout the body. The "good" part of HDL is its interactions while holding onto a cholesterol molecules (thus becoming what is known as HDL–C). HDL–C travels through the bloodstream and is used it to clean up LDL.[2]

The buildup of cholesterol that causes hypertension does not occur within hours of eating a double quarter pounder (with or without cheese), but may take years to develop. Cholesterol starts as "fatty streaks." These one centimeter long yellow streaks occur on the tunica intima of arteries. Also known as foam cells, these streaks cause no disturbance of blood flow, and can regress over time. They are commonly found in individuals by age 20, and can act as precursors to further problems. Fibrous plaque forms off of fattty streaks. This plaque is usually larger, firmer, and is gray in color. While fibrous plaque can occur in many arteries of the body, they are commonly found in walls of the heart's blood supplying (also known as coronary arteries), locations along the aorta (the main artery of the body), carotid arteries (which supply blood to head), and the circle of Willis (a main collection of arteries within the brain). [2]

Many problems can incur from the presence of these plaques. The problem most related to this unit is the decrease of blood flow through areas of increased plaque build–up. Decrease of blood flow can occur for two reasons. The first reason is due to the decrease in radius of artery walls due to plaque build–up. Known as atherosclerosis, presence of plaque can cause turbulent blood flow, which can lead to a decrease in downstream perfusion. Arteriosclerosis, or the hardening of artery walls, occurs when fatty plaque builds up and prevents the body's endogenous control over vasoconstriction/vasodilation. Other complications that can arise from fatty plaque include the potential for a lethal thrombus. A thrombus is a piece of plaque that breaks off and causes blockages (called clots) downstream. This is especially dangerous when the clot forms in the lungs (pulmonary embolism). Even more critical is when a clot forms blockages within plaqued arteries and causes loss of perfusion directly downstream. This can occur in the vessels that deliver blood to heart muscle and cause a heart attack (myocardial infarction or MI), or in the brain, causing a stroke. An overall decrease in blood lipid levels, as well as stability of dangerous clot causing plaque can be achieved through drugs, such as statins; however, these will not be discussed in this unit.[2]

Non-Pharmacologic Treatment for Hypertension

While they are not often followed, non–pharmacological treatments for hypertension are well known. Even though these treatments may be the most difficult to integrate into a daily routine they can be just as effective (and sometimes more effective) than pharmacological treatment. The first, most common, but potentially most challenging treatment is modification of diet. Physicians often recommend a Dietary Approaches to Stop Hypertension (DASH) diet. [8] The diet contains some things that are obvious: eating more fruits, vegetables, and decreasing overall caloric intake. It is very important to monitor salt intake. Salt cause a general fluid accumulation in the body, which is anti–productive in hypertensive patients. More salt causes more fluid in the blood, which causes a higher blood pressure.

Another treatment, that can quickly lead to an increase in general health, is cessation of smoking. Smoking can decrease HDL–C in the blood, cause malfunction in the SNS, cause problems with normal endothelial regulation, and cause an increased chance of blood clots. While whatever method a patient needs to stop smoking is recommended, the key is to stop! Increasing physical activity is also imperative. While the exact amount of time required to achieve optimal health changes constantly, mostly all scientists/physicians recommend some type of increase. Exercise causes a reset of many negative pathologies that can occur due to hypertension. Adequate amounts of sleep, decrease in stress, and general feelings of happiness can also lead to a general increase in health. While studies still debate the exact minutes/hours, a general increase can sometimes be the key between a healthy and unhealthy individual. It is important, however, that a person consults a medical professional before starting a new (especially abruptly new) change in lifestyle. While going on a run for two hours may make a great impact on your health, it may also be extremely detrimental to some patients!

Pharmacological Treatments for Hypertension

Quick Introduction to Pharmacology

There are a couple important topics that need to be addressed prior to discussing pharmacology. First, most pharmaceuticals in the U.S. have two names. The first, and often most common, is the brand name. Brand names, such as Tylenol or Prozac, are patented and named by a specific company. Only that company is legally allowed to sell the chemical makeup that is contained in the medication. Once the patent period of a drug has expired (maximum of 20 years), other companies can legally produce and sell that drug in generic forms. The drug's non–proprietary name, or trade name, is then used by other companies. Trade names are written in lower case *italics*, while the brand name is Capitalized.[6] Examples of trade names are *acetaminophen* (Tylenol), or *fluoxetin*e (Prozac). It is often debated which drug performs better (trade vs. brand). The answer is usually based on the drug and/or the prescriber's opinion.

Renin–Angiotensin–Aldosterone System Drugs

Due to the complex nature of RAAS, there are different avenues for pharmacological interventions. A well–known RAAS agent is the Angiotensin Converting Enzyme (ACE) inhibitor. These drugs work by blocking the action of ACE, which likewise prevents the conversion of Angiotensin I into Angiotensin II. Without Angiotensin II (which is a strong vasoconstrictor), the body naturally cannot constrict its arteries. This, in turn, causes overall vasodilation. Common ACE inhibitor drug trade names end with the letters –pril (e.g. *lisinopril*). Common brand names include: Altrace, Accupril, Vasotec, and Capoten. Another way of preventing the effects of Angiotensin II are via Angiotensin receptor blockers (ARB). These work, as described in their title, by blocking Angiotensin II receptors in blood vessels. These are commonly prescribed to patients that cannot take ACE inhibitors. Examples of ARB drugs include Cozaar, Benicar, and Diovan. [4] [9]

Alpha and Beta Adrenergic Receptor Drugs

There are four main α2 adrenergic agonist drugs that work on hypertension. The oldest of this class, *methyldopa*, is currently only used for pregnancy induced hypertension. The other three, *guanabenz*, *guanfacine*, and *clonidine*, are still used today as primary treatments. There are many more options when it comes to β–adrenergic receptor drugs. Commonly called "Beta–blockers," beta adrenergic antagonist drugs have become a hallmark for hypertensive drug therapy. Beta–blockers antagonize the actions of β1 receptors. Trade names for these drugs usually end in the letters –olol. Common drugs include *atenolol* (Tenormin), *carvedilol* (Coreg), *metoprolol* (Lopressor or Toprol XL), and *propranolol* (Inderal). These drugs are also sometimes used with cardiovascular disease, and as antiarrhythmics (to prevent abnormal heart beating). Care must be taken with patients that also suffer from asthma, as the antagonistic features of β–blockers may cause bronchoconstriction (due to antagonism of β2 pathways). [4 6 9]

Calcium Channel Blockers (CCBs)

There are a variety of different CCBs on the market that can affect the cardiovascular system in a number of different ways. Four common CCBs on the market, that can be used for hypertension, include *nidefipine* (Procardia), *amlopdipine* (Norvasc), *diltiazem* (Cardizem), and *verapamil* (Isoptin). As with β–blockers, CCBs are commonly used for other purposes. Specifically, *diltiazem* is used in emergency situations to treat atrial–fibrillation.[4]

EDRF Agonists

EDRF Agonists are one of the only drugs that have a direct effect on blood pressure. All other drugs discussed in this unit work by activating/deactivating pathways that lead to a balance in blood pressure. EDRF works by directly interacting with vessel endothelium and causing vasodilation. The most common, and widely used, EDRF is nitroglycerine. While this chemical can be used in large quantities for explosives, it is commonly used in emergency medical to cause rapid vasodilation of occluded blood vessels. Patients that are at high risk for heart attacks are often prescribed nitroglycerin (or nitro). In the event they have chest pain (a common sign of heart attack), they are told to administer a nitroglycerin. This nitro acts to dilate coronary blood vessels, which allows much needed oxygenated blood to get to dying tissue. Nitro often gives the patient time to get to the hospital where doctors can administer treatments to clear out blocked blood vessels. [4 6 7]

Diuretics

This class of drugs was one of the first oral medications used for the treatment of hypertension.[5] Diuretics work on the volume of the cardiovascular system in order to correct elevated pressure. These drugs are normally known as "water pills," as they make the patient urinate frequently. There are three main types of diuretics: thiazide diuretics, loop diuretics, and potassium–sparing agents. A fourth type, central antiadrenergic agent, will not be discussed in this unit. Thiazide and Thiazide–like diuretics work on the distal renal tubules by increasing the amount of salt and water that leaves the kidneys and is excreted to the bladder. Examples include *chlorothiazed* (Diuril), and *hydrochlorothiazed* (better known as HCTZ). Loop diuretics work on the ascending section of the distal renal tubule, having a similar action to thiazide/thiazide–like drugs but do not last as long. Loop diuretics are usually used with patients that don't have optimal kidneys. Examples of these drugs include *bumetanide* (Bumex), and *furosemide* (Lasix). Both of these drug types result in less work on the heart (due to less fluid being pumped), and less SVR. [4 9]

One side effect seen in thiazide drugs is the excretion of potassium. Since the potassium atom likes to "follow" the sodium atom, patients can sometimes suffer from hypokalemia (low potassium levels in the blood) due to the kidney excretion of sodium. Hypokalemia can be a very serious problem. To prevent this, patients are often advised to eat a healthy diet including potassium rich foods (such as bananas). One way to prevent the loss of potassium is through potassium–sparing agents, which are usually given concurrently with thiazides. Examples of common potassium–sparing agents include *amiloride* (Midamor) and *triamterene* (Dyrenium). [4 9] .

Activities

Implementation Rationale

While this curriculum is created for high school anatomy and physiology students, I believe it can be adapted to health, biology, and chemistry classes. This specific unit is designed for three to four weeks, with students meeting for 90 minutes every other day. I believe it is imperative to have students "buy–in" with education. The more the students buy into a teacher's unit, the more they will be willing to put forth the effort to learn. I see this constantly with my students. If my students don't see the purpose to learning a subject, they shut down and create negative energy in the classroom. Likewise, this curriculum needs to be presented in such a way that is enticing to the students. To start, I will utilize statistics to peak interest in my students. Since I teach only African American students the epidemiology data for hypertension in that demographic speaks for itself. It is likely that at least one half to three quarters of my students will have family members being treated for hypertension. Another possible "hook" for students is in the presentation of the unit. I plan on creating a banner, calling the classroom "Armstrong Medical School." I want the students to feel like they have what it takes to learn the same material as medical students. To bring this a step further, teachers could contact local laboratories and request a class set of disposable lab coats. These coats, which cost between $1–5 dollars each online, are bought in bulk at many laboratory, university, and medical facilities. Likewise, these institutions may be willing to donate some for your students. If applicable, you may be able to have each student decorate their own lab coat, or if only a class set it available, have students create their own nametags. The key for this unit is to immediately draw the students' attention.

This unit's activities are broken down into "acute" and "chronic." As with medicine, an acute symptom is something that comes on quickly, and can usually be treated and/or resolved in a relatively short period of time. For example, acute myocardial infarction (AMI) is a heart attack. A heart attack comes on relatively quickly (usually within a couple minutes to an hour), and can be treated quickly if immediate medical care is enlisted. Chronic, on the other hand, is usually long lasting with often little to no resolution. For example, chronic angina is chest pain that intermittently causes discomfort. This pain, usually due to low oxygen supply to the heart, can last for years without resolution. Acute activities will occur during one to three class periods. Chronic activities, however, will last throughout the entire unit. When presenting this unit to students, the explanation of acute versus chronic will provide a great teachable moment.

Chronic Activity

The chronic activity should be presented during the introduction of the unit. This activity will take one half to one full class period to integrate. The focus of the initial integration is to get the students comfortable with the activity so that it becomes routine. During the unit, students will complete this activity as a warm up. In order to build excitement in the class, I would encourage students to wear their lab coats while obtaining vitals.

Vitals Activity

At the beginning of each period, students will be required to obtain a set of "vitals" on each other or themselves. The vitals that students will be obtaining are: blood pressure, pulse rate, breathing rate, and state of the pupils. Since this information is personal, it is suggested that teachers obtain permission from administrators and parents prior to this activity. If privacy becomes an issue, students may take their own vitals, or this activity may be removed from the unit. Students will be given a sheet to record their vitals (See Appendix A). If the teacher collects this sheet it is recommended that it be secured in a safe place that is only accessible to the teacher.

Detailed instructions for obtaining vital signs can be obtained through the following link: *https://www.dropbox.com/s/69lr8e00k3vwiky/Vital%20Signs.docx*. While there are many different techniques, the document's instructions are what I use both in the classroom and in the field as a paramedic.

Acute Activities

The following activities are designed to each last between one to two 90–minute class periods. There are a total of three acute activities that will last for approximately five to six class periods, or two weeks.

Gatorade Gulping: The Game of Resistance

Time: approximately one to one and a half 90–minute class period

Materials: red Gatorade (premixed in a large container; approximately 24oz needed per person), 5oz cups (one per person), coffee Straws (one per person), regular straws (two per person), Stopwatches (or utilize a projector and screen showing the online stopwatch at www.online–stopwatch.com), paper/pencil, calculator

Alternatives: If a student is allergic, or cannot drink Gatorade, water can be used as a substitute.

Introduction: The purpose of this experiment/demonstration is to show the decrease in flow in relation to the size of the straw. Mathematically, the students can be shown the relationship between flow, resistance, and vessel radius. For example, assume that the radius of the regular straw is one millimeter, and the coffee straw is 0.5 millimeters. Therefore, the double straw will represent two millimeters, the single straw one millimeter, and the coffee straw 0.5 millimeters. Utilizing the equations in Figure 3, the teacher should have the students calculate the resistance created with each straw set. The resulting calculations should show that the two millimeter straw set creates a resistance of 1/16, the one millimeter straw creates a resistance of one, and the

0.5 millimeter straw creates a resistance of 16. The concept of resistance may be difficult at first for some students as it will require them to conceptualize inverses. I believe the best way to overcome this is by practice. Have students do problems with different radii. As they are doing problems, integrate the concept of flow, as an inverse relationship of resistance. Slowly integrate the cardiovascular system into the problems as follows: Patient A has an artery radius of 0.25 millimeters, and Patient B has an artery radius of 0.33 millimeters. Which patient will have a better flow in their artery? I believe it is important for students to not only realize the inverse relationship of resistance and flow, but be able to explain their answer quantitatively. To apply more rigors you may pose the following questions:

- Whose heart has to pump harder to obtain homeostasis?
- What are some causes of decreased artery radius?
- Which straw set do you think contained the most pressure?
- How is flow related to blood pressure?
- In the patients above, who would most likely have a higher blood pressure?
- Challenge Question: If a drug could decrease Patient B's radius by 40%, how much of a change in flow would that cause?

Directions:

1. Divide the class into teams of two and distribute materials to each student
2. Students will take turns during each round. One student will do the experiment while the other will watch the clock.
3. Pour 4oz of Gatorade into each student's cup
4. The first round will involve using two regular sized straws. When the teacher says go, the one student will extract the Gatorade out of the cup using the two straws while the other student records the time.
5. The students will switch, and repeat step 3.
6. Refill 4oz of Gatorade into each student's cup
7. For the second round, students will only use one regular sized straw. When the teacher says go, the one student will extract the Gatorade out of the cup using the one straw while the other student records the time.
8. The students will switch, and repeat step 6.
9. Refill 4oz of Gatorade into each student's cup
10. For the final round, students will use a coffee straw. When the teacher says go, the one student will extract the Gatorade out of the cup using the coffee straw while the other student records the time.
11. The students will switch, and repeat step 9.
12. All data is then be collected by the teacher (or a selected teacher assistant), and the mean time for each step can be calculated. This step can be extrapolated to discuss statistical analysis of data.

Note: This example of flow and resistance is a gross oversimplification of vessel pathophysiology. More advanced students (especially those who have taken physics), may bring up the point of the resistance formula being incorrect. In order to more easily teach resistance and flow, I have made assumptions in the formulas. For example, I am assuming the viscosity of the liquid (blood) remains constant, the length of the vessel (the cardiovascular system) doesn't change, and the surface of the vessels (i.e. the amount of drag) doesn't change. Furthermore it should be emphasized that the experiment was a demonstration of negative pressure, while the arterial system works by positive pressure changes created from the heart.

Mapping Out Medicine

Time: approximately two 90–minute class period

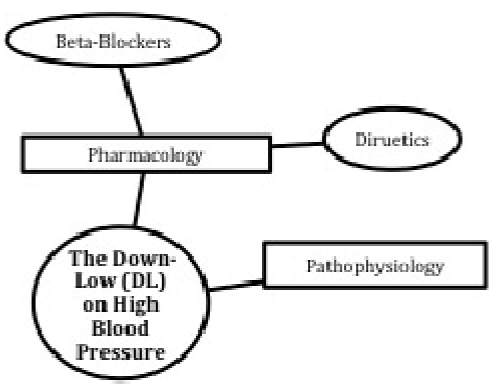
Materials: pencil, colored pencils and/or markers, large paper (8½" x 14") or larger construction paper, list of

Alternatives: This assignment can be completed as homework for more advanced students if desired by the teacher

Introduction: The mind works as a series of a millions connections inside your brain. Learning occurs in making and strengthening these neuronal connections. The purpose of this activity is to build connections to the topics discussed in this unit. Students will first need to be introduced to the concept of a mind web (if not already familiar). Once familiarized, students will be given a list of concepts that need to be linked together utilizing a mind web. When introducing this activity, I highly suggest presenting it as a puzzle that needs to be solved. Technically there is only one right answer; however, there are multiple ways of creating that answer. To add rigor to this activity, teachers will highlight certain pathways on students' mind maps (once completed) and require a written explanation.

Directions:

1. Using a pencil, start by creating a circle, in the middle of the page, with the title of the unit written inside: "The Down–Low (DL) on High Blood Pressure."
2. The students will then utilize the words from the list below to create a web that branches off the initial circle. For example:



1. Once students have created a web with all key words, have them add color and pictures. The students should be free to be as creative as possible. They should not be restricted to using only circles boxes, or connecting only two items. Their web can be graded not only on content, but also on the amount of effort put forth.
2. To add rigor to this assignment, once completed, the teacher can highlight (literally or figuratively) one pathway along the student's web. The student is then instructed to write, in paragraph form, what they know about this pathway. The teacher can direct the amount of writing that is required. For example:
3. >Highlight: DL on High Blood Pressure – Pharmacology – Beta Blockers
4. >Students Write: High blood pressure can often be controlled by pharmacological agents. One very common agent is beta–blockers. Beta–blockers work by blocking the beta–adrenergic receptors found on the tunica intima of blood vessels. Blocking these receptors causes vasodilation, which in turn can lower overall blood pressure.

While this list covers all topics discussed in the background information, I would recommend selecting words that you have covered in your class discussion.

Pathophysiology
Primary Prevention
Cells
Homeostasis
Heart
Pump
Tunica Intima
Tunica Media
Tunica Adventitia
Cardiac Output (CO)
Heart Rate (HR)
Stroke Volume (SV)
Mean Arterial Pressure (MAP)
Systole
Diastole
Flow
Resistance
Endogenous
Renin-Angiotensin-Aldosterone System (RAAS)
Adrenergic Receptor Systems
Parasympathetic Nervous System (PSNS)
Sympathetic Nervous System (SNS)
Agonist
Antagonist
Fight/Flight
SLUDGE
β1 adrenergic receptor
β2 adrenergic receptors
Lungs
Heart
Chronotropic
Dromotropic

Inotropic
Speed of Heart
Electrical signal transfer
Contractility
Calcium Channels
Endothelium-derived Relaxing Factors (EDRF)
Kidneys
Nephon
Salt
Water
Exogenous
High-Density Lipoprotein (HDL)
Low-Density Lipoprotein (LDL)
Good fat
Bad fat
Ateriosclerosis
Atherosclerosis
Hardening of arteries
Plaque buildup in arteries
Non-Pharmacologic Treatment for Hypertension
DASH
Smoking Cessation
Adequate amounts of sleep
Exercise
Lower salt intake
Pharmacology
Angiotensin Converting Enzyme (ACE) Inhibitors
Angiotensin Receptor Blockers (ARB)
α2 adrenergic agonist

drugs
β2-adrenergic receptor drugs
Calcium Channel Blockers (CCB)
EDRF Agonists
Diuretics
Thiazide like
Loop diuretics
Potassium-sparing agents
amiloride (Midamor)
triamterene (Dyrenium)
furosemide (Lasix)
bumetanide (Bumex)
hydrochlorothiazed
chlorothiazed (Diuril)
verapamil (Isoptin)
diltiazem (Cardizem)
amlopdipine (Norvasc)
nidefipine (Procardia)
propranolol (Inderal)
metoprolol (Lopressor)
carvedilol (Coreg)
atenolol (Tenormin)
methyldopa
guanabenz
guanfacine
clonidine
Diovan
Benicar
Cozaar
Altrace
Accupril
Vasotec
Capten
lisinopril

What's in YOUR Medicine Closet?

Time: approximately two 90–minute class period

Materials: computer with Internet access for each group/student, color printer, paper/pencil

Alternatives: Have students research a medication that someone in their family is currently taking for high blood pressure. The student should describe the medication via writing or drawing, and bring this writing/description into class on the day of this activity. This should not be mandatory, as not all students will have family members using hypertension medications.

Introduction: Although this activity requires some preparation on the part of the teacher, it can be a great culminating activity for the end of unit. During this activity students will utilize a website to identify medications from given pictures. When it comes time to have students research their medicines, I would recommend utilizing the website *http://pillbox.nlm.nih.gov/bin–release/PillBox.php.* This website, run by the National Library of Medicine (NLM), is very interactive and easy to maneuver. If, for some reason, that site doesn't run on an older computer, NLM has a more browser friendly site at *http://pillbox.nlm.nih.gov/pillimage/search.php.* After students have identified all the medications, they will then research a hypertension medication of their choosing. Teachers have the option of making this into a project, with PowerPoint, a written assignment, and/or boards. ,

Directions:

1. Using the list from the previous activity, and Google images, print out pictures of medications commonly used for treating hypertension. When printing these pictures, ensure their quality is decent enough to distinguish color, shape, and imprints on the pill (if applicable). Number each picture and create a key that can be used later for grading purposes. Create enough pictures so that there is at least one per student, with more being preferable.

2. Have students access the website *http://pillbox.nlm.nih.gov/bin–release/PillBox.ph*p, or alternatively *http://pillbox.nlm.nih.gov/pillimage/search.php.*

3. On a sheet of paper, list out the number of medications you have prepared. For example, if you have 20 medications, students should write one through twenty, one number per line.

4. Spread the pictures on a table, and have students pick out their own medication.

5. Have the students utilize the website to identify the pill.

6. Students should write the medication name, both trade and brand if applicable, on their paper.

7. Once students have finished identifying and recording the medication, they should return the medication photo and obtain another until all photos have been identified.

8. To add rigor to this activity, students could then select a specific hypertension medication. This selected hypertension medication can be one that a family member takes, one that they have previously seen on TV, or one at random. The student will then write a two–three paragraph summary of the drug. Information on the medication can be found on the NLM website. The paragraphs should focus on the following items:

a. Name (trade, brand, and chemical if applicable)

b. Manufacturer(s)

c. Description of the medication (color, shape, etc.)

i. There may be different descriptions for each dosage. Students should list all.

d. Mechanism of action

- i.How it works in the body?
- ii.What does it stimulate, antagonize, etc.

e. Why is it prescribed?

f. Who it is prescribed to?

g. What are the side effects?

h. What are the contraindications?

i.Contraindications are reasons the medication should not be prescribed. For example: Pregnancy is a contraindication for the medication Accutane. Those people who are pregnant should not be prescribed Accutane.

i. Are there are any other uses for the medication?

i.Some medications are used for multiple reasons, for example, **metformin** (Glucophage) can be used for both type two diabetes and women with polycystic ovary syndrome (PCOS).

j. How much does the medication cost?

i.This is what it would cost the consumer to buy without insurance. This is not a copay amount.

Final Discussion Questions

The following is a list of final discussion questions, broken down by Bloom's Taxonomy, which can be used at the discretion of the teacher. Lower performing students could work on these questions in small groups. Medium performing students could work on these questions individually. Higher performing students could be questioned in a Socratic format.

Remembering:

- Define hypertension.
- What is a normal blood pressure?
- What are some endogenous causes of hypertension?
- What are some exogenous causes of hypertension?

Understanding:

- Explain how each pharmaceutical class can decrease high blood pressure?
- Paraphrase the relationship among vessel radius, flow, and resistance.

Applying:

- If you could create a drug that treats hypertension, which pathway would you use and why?

- Choose a good pharmaceutical agent for the following patients and why:

- 80 year old male, obese, kidney failure
- 45 year old female, history of hypertension, stressful job
- Challenge: 75 year old male, complaining of chest pain

Analyzing:

- Compare and contrast exogenous and endogenous factors.
- Compare and contrast diuretics versus beta–blocking medication.

Evaluating:

- Defend the use of pharmaceutical agents in the reduction of high blood pressure versus natural means.
- Do you agree or disagree with the use of pharmaceuticals for ANY patient?

Creating:

- Pretend you are the marketing coordinator for a major pharmaceutical company. Create a one–minute pitch on one of the medications studied in this unit. Consider the following:

- The target audience
- Type of media used
- Selling points for your medication

Implementing District Standards

The following are the standards set forth by Richmond Public Schools for Human Anatomy and Physiology. This curriculum touches on the chemical, cellular, and body systems associated with hypertension. As shown in the progress of standards HA.3 through HA.5, starting from micro to macro is a very good pedagogical practice. This curriculum follows this practice throughout its background section. The activities used in this curriculum are inquiry based, and require student led investigation, analysis of data, observations, and creation of valid conclusions; thus aligning with standard HA.1, and many of the new National Science Teacher Association (NSTA) and National Science Foundation (NSF) recommendations.

table 12.05.03.03 is available in print form

Endnotes with Annotated Bibliography

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5. Kaplan, Norman M., and Joseph Flynn T. *Kaplan's Clinical Hypertension.* Philadelphia: Lippincott Williams & Wilkins, 2006. This book is written by clinicians for clinicians. Likewise, it contains acronyms and words that can be confusing to those not familiar with medical terminology.
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9. Krakoff, Lawrence R. 1995. *Management of the hypertensive patient*. New York: Churchill Livingstone. I found this resource extremely helpful for all topics related to hypertension. Krakoff made sure to include all facets of a hypertensive patient, including epidemiology and nutrition as well as pharmacology. This book is written at a upper college level.