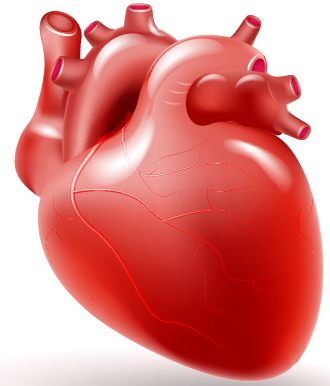


Mark's Failing Heart: Three Blood Volume Regulating Hormone Systems



by

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The heart is an integral organ of the cardiovascular system. It needs to remain healthy and strong to compensate for changes in blood volume and pressure during daily activities. The heart must maintain enough pressure throughout the cardiovascular system to meet the demands of the body (McKinley, O'Loughlin, and Biddle, 2018). The average blood pressure within the cardiovascular system is referred to as the mean arterial pressure (MAP). Blood volume along with cardiac output and peripheral resistance determines MAP. Maintenance of adequate mean arterial pressure is essential to prevent organ shutdown.

The heart pumps 50 to 70 ml of blood under high pressure to the aorta per contraction and 4 to 6 liters over a minute. This is known as cardiac output. Total peripheral resistance, the result of constriction or dilation of arteries, principally arterioles, either increases or restricts blood flow. The relationship between MAP and resistance is direct; if resistance increases, MAP will increase. Maintaining adequate MAP within a normal range through adjustments in cardiac output or peripheral resistance is vital for perfusion of tissues and essential for survival. Blood volume is the other component that maintains MAP.

This case study is intended to reinforce your understanding of the heart and three blood volume/pressure regulating hormone systems: renin-angiotensin-aldosterone-system (RAAS); antidiuretic hormone (ADH); and atrial natriuretic peptide (ANP) and brain (ventricular) natriuretic peptide (BNP). RAAS and ADH are activated during low blood volume or pressure and stimulate multiple pathways to increase volume/pressure. ANP is released from the atria and BNP is released from the ventricles when too much blood volume causes over stretching of the heart's chambers. The ANP/BNP system stimulates multiple pathways to decrease volume and pressure.

There are many causes and risk factors that can affect the health of the heart muscle, reducing its capacity as a pump and potentially leading to heart failure (see Causes and Risk Factors below). As a result a person can develop heart failure on either side. As a result of left ventricle heart failure, the left ventricle of the heart muscle has a reduced ability to pump; this causes MAP to decrease and trigger activation of the RAAS and release of ADH. The consequence of either a blood volume or blood pressure surge as compensation could have a detrimental effect on an already weak heart in a person with left ventricle failure.

Mark is a 65-year-old retired man playing baseball on a warm day with his family while attending a summer picnic. After hitting the baseball he runs to first base and feels shortness of breath, wheezing, fatigue, and has a hard time concentrating. His son takes him to the emergency room. There, the attending cardiologist obtains his history, physical exam and runs appropriate tests (see Hospital Chart below). The results indicate that Mark has acute left ventricle heart failure and a background of chronic heart failure.

Chronic heart failure is very common. Symptoms appear slowly over time and gradually get worse. Acute heart failure develops suddenly and symptoms are initially severe. Acute heart failure may follow a heart attack. It may also be caused by a sudden inability by the body to compensate for chronic heart failure (Heartfailurematters.org, *n.d.*). Heart failure can result in an alteration in ventricular structure (ventricular remodeling). The ventricle tends to become

enlarged, its general shape becomes more globular and less elliptical, the muscular wall of the ventricle often becomes thinner, and the volume of the chamber enlarges. These changes may be the result of myocyte hypertrophy, myocyte apoptosis, and interstitial fibrosis. This remodeling occurs due to myocardial injury and mechanical stress on the heart muscle (Konstam *et al.*, 2011).

Questions

Answer the questions below based on what you have just read and the following pages (Hospital Chart, etc.).

1. What is mean arterial pressure (MAP) and why is it important?
2. Identify three factors that maintain MAP.
3. What role does the heart play in regulating MAP?
4. What role does peripheral resistance play in maintaining MAP?
5. What effect would acute heart failure have on MAP?
6. What effect does angiotensin II of RAAS have on blood volume and pressure and how does it achieve this?
7. What is antidiuretic hormone (ADH)? What effect does it have on blood volume and pressure, and what stimulates its secretion and what are its actions?
8. What effect would the change in MAP due to heart failure have on RAAS and ADH? How and why?
9. What effect would activation of angiotensin II and ADH have on blood flow to the heart and pressure in the heart chambers?
10. There are many factors that can contribute to left ventricle heart failure. Based on what you have read above and after reviewing Mark's history, life style and physical examination, what risk factors do you think are contributing to Mark's heart failure and should be addressed as treatment?
11. The echocardiogram reveals a low ejection fraction and dilated left ventricle. What do the results of this test tell you about the efficiency of the heart?
12. The x-ray shows an enlarged heart and edema around the lungs. What is the cause of the edema of the lungs and throughout the body?
13. Why would a change in MAP and blood distribution due to heart failure cause body fatigue?
14. BNP is elevated in Mark's blood. What effect does BNP have on blood volume and pressure and how does it achieve this?

The cardiologist suggests that Mark start taking a drug called Entresto (sacubitril/valsartan). This drug received U.S. Food and Drug Administration approval in July 2015 for use in patients with chronic heart failure (see page listing medications used to treat heart failure). Entresto consists of two drugs, sacubitril and valsartan. Sacubitril inhibits the enzyme neprilysin, which is responsible for the degradation of BNP and ANP. Valsartan is an angiotensin II receptor antagonist (Fala, 2015).

15. Sacubitril is used to keep brain natriuretic peptide (BNP) levels in the blood elevated. What beneficial effect does sacubetril have on a person with left ventricle heart failure?
16. Valsartan is used to inhibit the release of angiotensin II. Why would you want to inhibit the production of angiotensin II by valsartan in a person with left ventricular heart failure?
17. What role do the kidneys play in the RAAS and BNP system?
18. Describe the homeostatic mechanism in this patient with acute heart failure.

Hospital Chart

Patient: Mark Doe **DOB:** 6/24/54 **Gender:** Male

Height: 5' 9"

Weight: 240 lbs. (*Normal 128 – 168 lbs.*)

Blood Pressure: 145/95 (*Normal systolic value <120 mmHg, normal diastolic value <80 mmHg*)

History: Mark is a 65 year-old retired man who is over-weight, smokes, and at times drinks to excess. He seldom goes to a physician. He states he is not very active and over the last two years has felt tiredness on exertion with hard time breathing.

Physical Exam: Mark has high blood pressure. Tachycardia (rapid heart beat). He has marked edema with abdominal and ankle swelling, distended jugular vein and has gained 5 pounds. He is fatigued and has shortness of breath. Auscultation of the lungs by stethoscope revealed crackles and rales at the base of the right and left lung (rattling, or crackling are noises made by the lungs during respiratory congestion).

BNP: 1200 pg/mL (*Normal male < 100 pg/mL*)

(Brain natriuretic peptide (BNP) is a hormone produced in the ventricles of the heart and released when the ventricles are stretched and working hard to pump blood. Although the hormone is produced by the ventricles it is called BNP because it was first discovered in the brain. BNP is followed rather than ANP, which is produced by the atria, because it is used to detect and evaluate the degree of left ventricular failure.)

Echocardiogram Measure of Ejection Fraction: 44%

(Echocardiogram measure of ejection fraction is the percent of blood leaving the heart each time it contracts. Normal is 50 to 70%. Watch the following short video on ejection fraction in patients with left ventricular failure: Ejection fraction measurement and heart failure. American Heart Association, 2017. Running time: 2:00 min. <<https://youtu.be/qS4jHMppRms>>.

Mark Doe's echocardiogram reveals a dilated left ventricle.

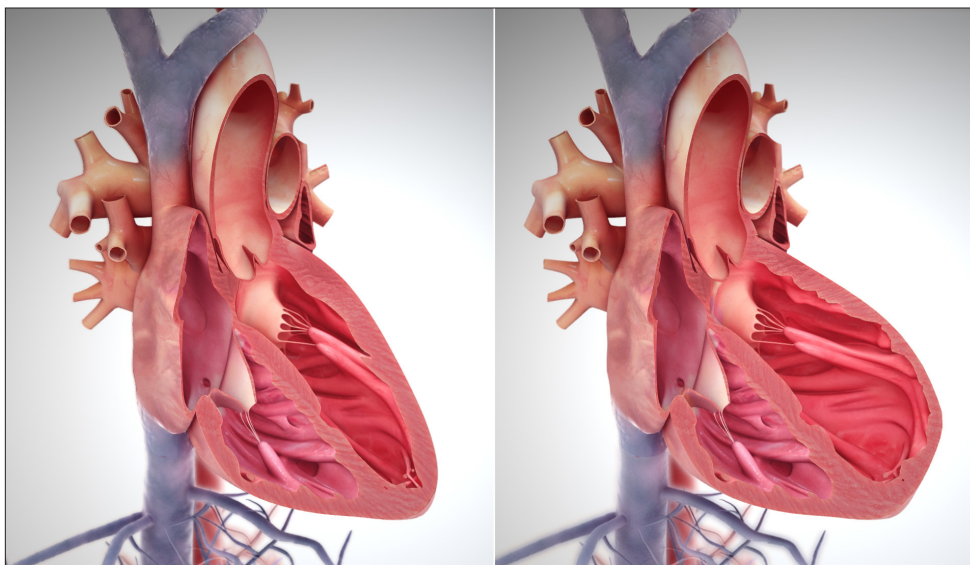


Figure 1. A comparison of healthy heart with contracted muscle (left) and a weakened heart with over-stretched muscle and dilated ventricle (right). Credit: Scientific Animations, CC BY-SA 4.0, <https://commons.wikimedia.org/wiki/File:Right_side_heart_failure.jpg>.

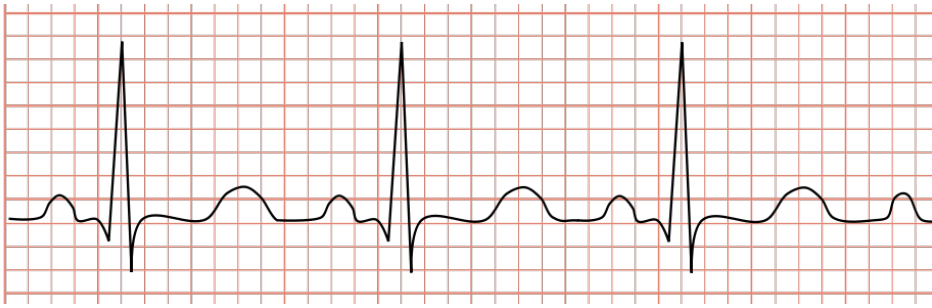


Figure 2. ECG reveals tachycardia (increased heart rate). *Credit:* Madhero88, CC BY-SA 3.0, <https://commons.wikimedia.org/wiki/File:Tachycardia_ECG_paper.svg>.



Figure 3. Comparison of normal chest x-ray (left) and x-ray showing congestive heart. *Credit:* Mikael Häggström, PD, <[https://commons.wikimedia.org/wiki/File:Normal_posteroanterior_\(PA\)_chest_radiograph_\(X-ray\).jpg](https://commons.wikimedia.org/wiki/File:Normal_posteroanterior_(PA)_chest_radiograph_(X-ray).jpg)>, <https://commons.wikimedia.org/wiki/File:Chest_radiograph_of_a_lung_with_Kerley_B_lines.jpg>.



Watch this video:

Osmosis. (Producer). *n.d.* Congestive heart failure. Running time: 14:27 min. <https://www.osmosis.org/learn/Congestive_heart_failure>.

Figure 4. A man with congestive heart failure and marked jugular venous distension. External jugular vein marked by an arrow. *Credit:* James Heilman, MD, CC BY-SA 3.0, <https://commons.wikimedia.org/wiki/File:Elevated_JVP.JPG>.

Heart Failure Causes and Risk Factors

Any of the following conditions can damage or weaken the heart and can cause heart failure (Mayo Clinic, 2017).

- *Coronary artery disease*, a common cause of heart failure, is due to an occlusion of arteries by fatty build-up, and this reduces perfusion of heart muscle.
- *High blood pressure (hypertension)* increases afterload causing the left ventricle to work harder to push blood to the aorta. This extra exertion by the left ventricle can make the heart muscle weak and ineffective.
- *Faulty heart valves* can also force the heart to work harder and make it weaker.
- *Heart muscle damage (cardiomyopathy)* can have many causes including genetics, diseases, infections, alcohol, and drugs.
- *Myocarditis*, an inflammation of the heart muscle, can lead to left-sided heart failure.
- *Congenital defects* of the heart or its valves put a strain on the healthy parts to compensate leading to heart failure.
- *Heart arrhythmias* such as an increased heart beat may create extra work for the heart. A slow heartbeat also may lead to heart failure.
- *Diseases* such as diabetes, HIV, hyperthyroidism, hypothyroidism, or a buildup of iron (hemochromatosis) or protein (amyloidosis) can also contribute to heart failure.
- *Certain medications* such as diabetes drugs rosiglitazone (Avandia) and pioglitazone (Actos) have been found to increase the risk of heart failure in some people. Another class of medications that may increase the risk of heart problems is nonsteroidal anti-inflammatory drugs (NSAIDs).
- *Sleep apnea* can deliver a lower than normal amount of oxygen to the heart, leading to weakening of the heart muscles.
- *Obesity, alcohol, and tobacco use* can also increase the risk of heart failure

Medications Used to Treat Heart Failure

The following list of medications used to treat heart failure is provided by the American Heart Association (2017). Patients may need multiple medications. Each medication treats a different symptom or contributing factor.

- *Angiotensin-converting enzyme (ACE) inhibitors* are used for the treatment of hypertension and congestive heart failure. They block the conversion of angiotensin I to angiotensin II. They lower peripheral resistance, increase venous capacity and decrease cardiac output.
- *Angiotensin II receptor blockers (ARBs)* block the action of angiotensin II by preventing angiotensin II from binding to receptors on the smooth muscles in the walls of blood vessels. As a result, blood vessels dilate and blood pressure is reduced.
- *Angiotensin-receptor neprilysin inhibitors (ARNIs)* combine a neprilysin inhibitor and an ARB, sacubitril/valsartan (the drugs in Entresto). Sacubitrilat inhibits the enzyme neprilysin that degrades natriuretic peptides. The natriuretic peptides cause blood vessel dilation and stimulate sodium excretion, which reduces extracellular fluid.
- *Beta blockers (beta-adrenergic blocking agents)* are medications that reduce blood pressure by reducing heart rate.
- *I_f channel blocker (inhibitor)* is a drug class that reduces the heart rate, similar to beta blockers. This is used for heart failure not fully managed by beta blockers.
- *Aldosterone receptor antagonists* block the effects of aldosterone, which can cause heart failure to get worse. They help lower blood pressure, reduce congestion and thus protect the heart.
- *Hydralazine and isosorbide dinitrate* is a drug treatment approved by the Food and Drug Administration (FDA) used to treat African Americans with congestive heart failure. It is a combination of hydralazine (an antihypertensive) and isosorbide dinitrate (a vasodilator).
- *Diuretics* cause the body to rid itself of excess fluids and sodium through the kidneys, which helps to relieve the heart's workload and decrease the buildup of fluid in the lungs and other parts of the body.

Other supporting medications that might be prescribed include:

- *Anticoagulants (blood thinners)* may be prescribed if a heart failure patient also has an increased risk of blood clot formation such as atrial fibrillation.
- *Cholesterol-lowering drugs (statins)* may be prescribed if a patient has high cholesterol or has had a heart attack.
- *Digoxin* is prescribed to some heart failure patients if necessary.

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