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# Intrinsic Regulation

*Intrinsic regulation:* In the early 1900's Otto Frank and Earnest Starling independently published findings showing that if you increase the end-diastolic volume, stroke volume increases, without any neural or endocrine input. In other words, if **venous return** increases (increased end-diastolic volume), cardiac output increases. They correctly observed that the more the cardiac muscle is stretched during diastole the more forcefully it contracts. This phenomenon is known as **Starling's Law of the Heart or the Frank-Starling Mechanism.** End-diastolic volume is a good indicator of stretch and hence, the degree of overlap of the thick and thin filaments in the sarcomeres. The degree of stretch at the end of diastole is often referred to as the **preload.** The degree of stretch is a property of the sarcomere. As in skeletal muscle, the initial length of the sarcomere affects the force of contraction due to optimal overlap of the thick and thin filaments. Maximum force is achieved when the starting position of the sarcomere is such that the thick filament is at the very end of the thin filament allowing the greatest range of movement and still allowing each myosin head to bind to actin. In heart muscle, the sarcomeres at rest are not quite optimal, thus more stretch means that the sarcomeres in the heart muscle are placed in their optimal alignment resulting in greater force. This principle is thought to contribute to the increased force of contraction and the accompanying increase in cardiac output observed when venous return increases, but it cannot account for the entire effect.

Other factors that may play a role include: 1) increased entry of extracellular calcium with more stretch because there may be an increased opening of stretch activated calcium channels in the sarcolemma, 2) increased calcium sensitivity in the muscle when it is stretched, and 3) stretch induced shortening of the distance between the thick and thin filaments, increasing the probability of the myosin heads binding to actin. Therefore, the end-diastolic volume or preload directly influences the force of contraction and cardiac output. Additionally, increasing the preload results in an increased heart rate, along with the increase in contraction strength. This is thought to be due to stretch of the SA node allowing more sodium to enter the cell thus increasing the slope of the pacemaker potential. The increased heart rate also contributes to the increased cardiac output.

The force that opposes the flow of blood out of the ventricles during systole is the **afterload.** Basically, afterload is the blood pressure in the large arteries that the heart has to pump against before the aortic semilunar valve can open. Under normal conditions, afterload does not have an impact on cardiac output. However, when aortic pressure exceeds 170 mmHg the afterload begins to decrease the stroke volume and reduce the cardiac output and the workload on the heart greatly increases.

**Preload** is also impacted by vein functions that pump blood back toward the heart. Veins are unique from arteries in that they contain one-way valves that open as blood flows toward the heart but will close as blood flows away from the heart, preventing loss. As the muscles in our limbs contract they squeeze the deep veins of the legs and arms and force the blood back to the heart. These are known as skeletal muscle pumps. As we stand, walk or run more blood is pumped back to the heart, increasing the preload. We also have a respiratory pump that functions as we breathe. When we breathe air in, the diaphragm pushes down, increasing abdominal pressure, which in turn increases the pressure on the vena cava and forces blood into the thoracic cavity and into the heart. As we breathe out, the pressure is released allowing the blood to refill the vena cava again. Through the utilization of these two vein pumps, it is easy to see how our body increases cardiac output by increasing preload when we are running or exercising.