Physiology 1A

Intrinsic regulation of cardiac output and myocardial contractility

Tim Murphy
Wallace Wurth 316
tim.murphy@unsw.edu.au

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From this lecture you should:

- Know the factors altering cardiac output
- Understand Starling's Law of the Heart and the effects of preload and afterload on cardiac output
- Understand the concept of myocardial contractility, how it may be altered and it's effect on cardiac output
- Understand that heart rate is controlled by the autonomic nervous system and adrenaline

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- Reference: Standfield Principles of Human Physiology 5th Ed.: Ch. 13.6 (pp.382-390).

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Regulation of cardiac output

Cardiac output (CO) = Heart rate (HR) x Stroke volume (SV)

= 70 beats/min x 70 ml/beat

= about 5000 ml (5 L)/min

HR is controlled by neural, hormonal factors.

SV may be modulated by neural and hormonal factors plus 'intrinsic' mechanism, responding to forces on cardiac muscle.

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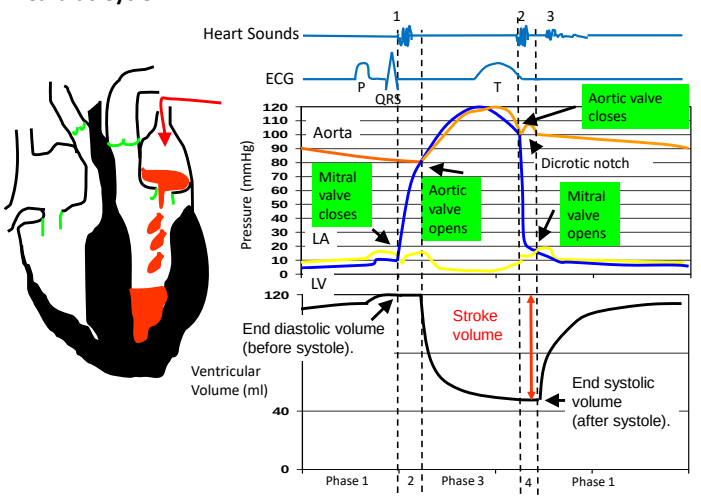
Cardiac Cycle



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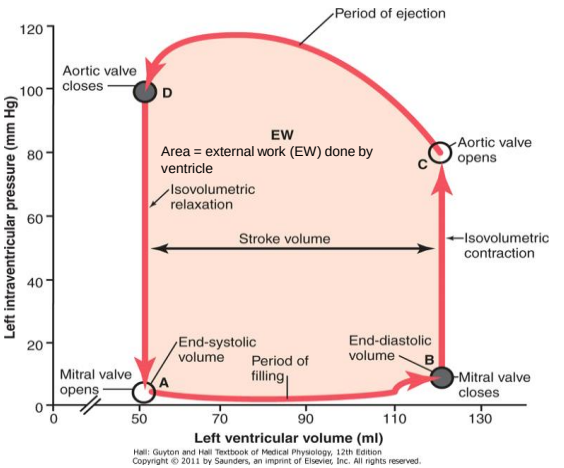
Left ventricular pressure-volume loop



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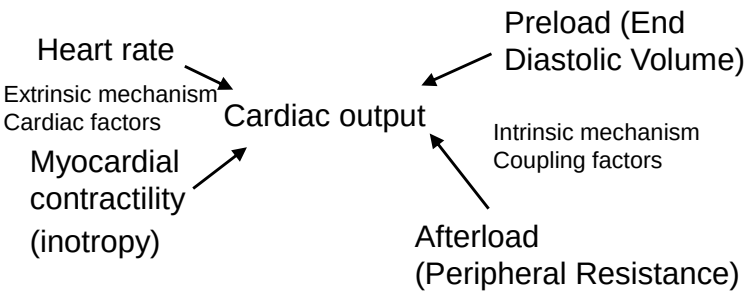
How to alter cardiac output?



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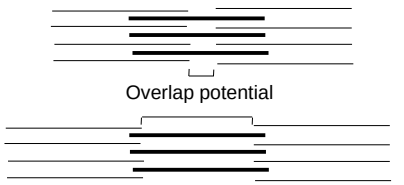
Intrinsic mechanism of stroke volume control
Striated muscle responds to increased tension with increased force of contraction.

Caused by overlap arrangement of myofilaments



Tension is generated by load on muscle.

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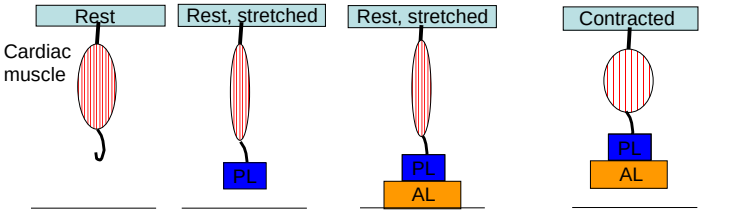

No load — Pre-AV valve opening

Pre-load — Ventricular filling

Pre-load and after-load — Pre-contraction with aortic valve closed

Lifting of loads — Ventricular ejection

In heart, pre-load is extent of ventricular filling.

After-load is the pressure required to open the aortic/pulmonary artery valve

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Pre-load or end diastolic volume (EDV)

Pre-load is pre-contraction tension or stress on the ventricular wall. It is primarily determined by extent of ventricular filling (end diastolic volume).

<u>Starling's Law of the Heart (also Frank-Starling Mechanism)</u>

"Energy of contraction of ventricle is a function of the initial length of fibres in its walls."

Ventricle automatically adjusts to increased volume of blood with increased force of contraction. (Blood in = blood out)

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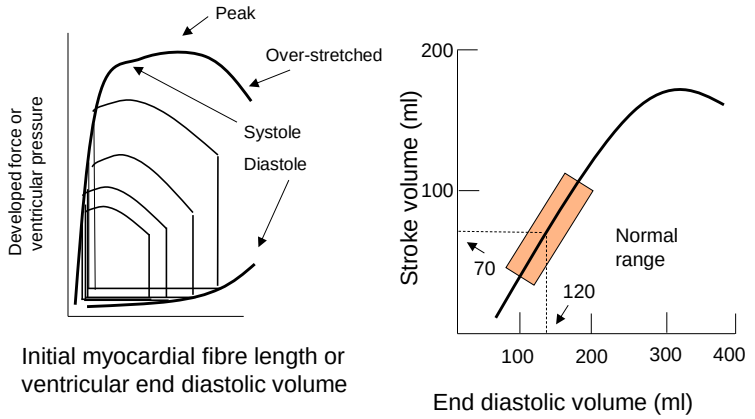

Starling's Law ensures output of both ventricles is the same.

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Stroke volume = End diastolic volume – End systolic volume

(SV = EDV - ESV). Eg. SV = 120 ml – 50 ml = 70 ml

Ratio stroke volume : end diastolic volume is called the <u>ejection fraction</u> (EF). EF = SV / EDV.

This example: EF = 70 / 120 = 0.58 (or 58%).

Starling's Law ensures EF is about the same over a wide range of EDV values.

A healthy heart should have an EF above 55%.

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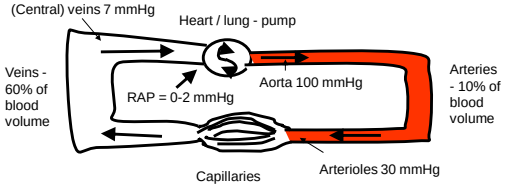
End-diastolic volume is determined primarily by <u>venous return</u>



Factors influencing venous return:

- pressure at end of capillaries
- (right) atrial pressure (RAP)
- blood volume
- venous tone
- muscle, respiratory and abdominal pumps

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Afterload

Afterload is the work the heart performs in ejecting blood . It is equivalent to the tension or stress on the ventricular wall during contraction.
A key physiological determinant is the pressure required to open the aortic or pulmonary artery valves.

Afterload increases if back-pressure on the valves increases, i.e. blood pressure in the aorta or pulmonary circulation

Increased afterload reduces stroke volume by increasing end-systolic volume (ESV). But <u>it is not the same as ESV</u>.

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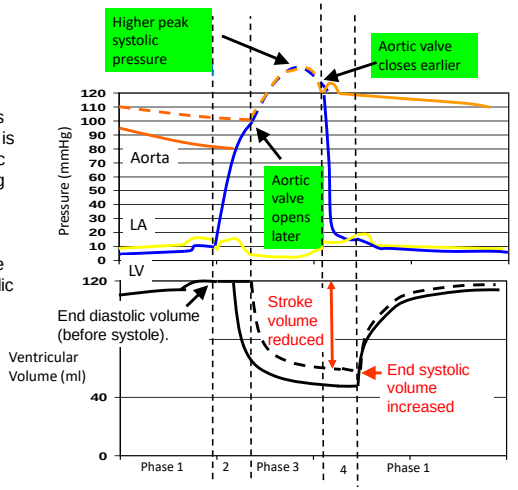
Effect of increased afterload on heart function.

Increased peripheral resistance (reflected by pressure in aorta) means more contraction energy is devoted to opening aortic valve and less to ejecting blood.

Increased afterload decreases stroke volume and increases end systolic volume.
Ejection fraction (EF) is reduced.



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Heart rate and myocardial contractility

Cardiac output may also be altered by changes in heart rate and myocardial contractility.

These factors are regulated by mechanisms extrinsic (external) to the heart, mainly nervous control and various hormones.

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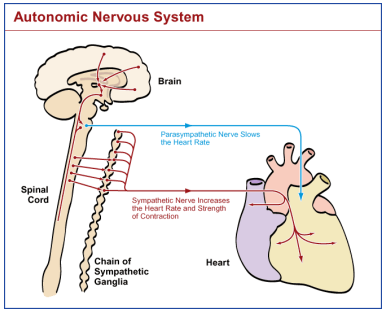
Control of heart rate

Nerves innervating the heart are part of the autonomic nervous system.

Parasympathetic nerves innervate the atria only. Their stimulation decreases heart rate (bradycardia). Main factor in controlling heart rate.



Sympathetic nerves innervate the atria and ventricles. Their stimulation increases both heart rate (tachycardia) and force of contraction (increased contractility).

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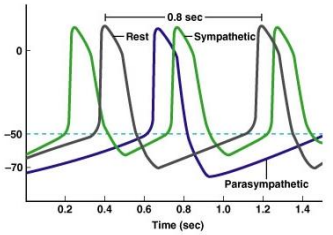
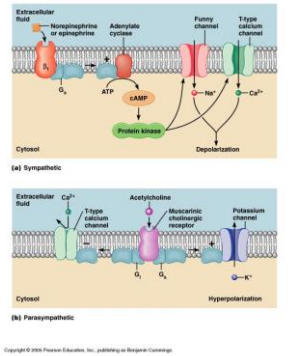
Heart rate is altered by increasing or decreasing the frequency of pacemaker action potentials in the SA node.

SA node action potentials





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Myocardial contractility

Myocardial contractility is a change in the force of cardiac muscle contraction, *independent* of end-diastolic volume / preload.

Also called <u>inotropy</u>. (Heart rate - chronotropy).

Increased myocardial contractility
– positive inotropy
Decreased myocardial contractility
– negative inotropy

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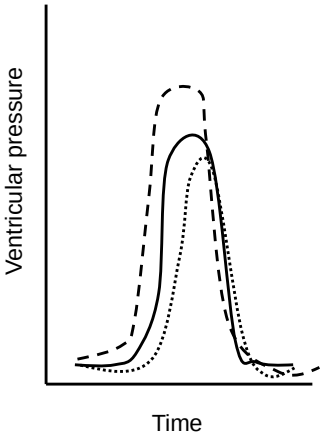
Inotropy reflects the velocity of contraction

Normal

Positive inotropy
Faster contraction
Greater pressure
Increased SV

Negative inotropy
Slower contraction
Lower pressure
Decreased SV



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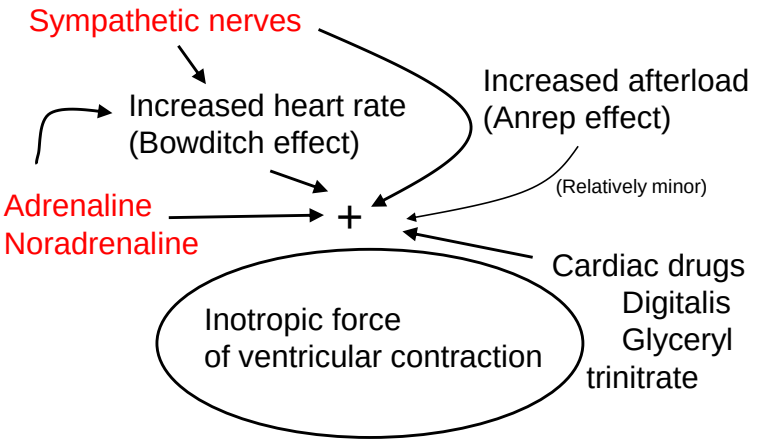
Positive inotropy



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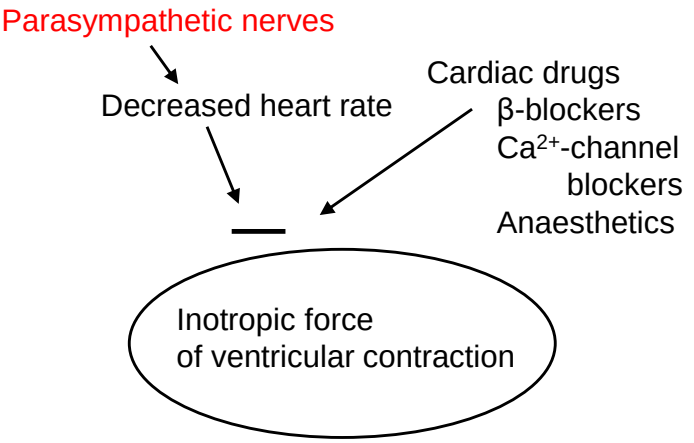
Negative inotropy – usually pathological



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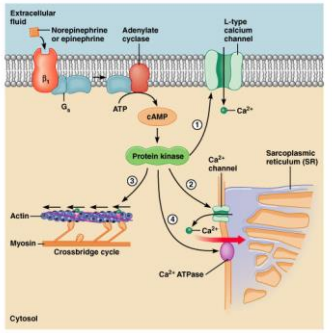
Noradrenaline and adrenaline increase myocardial contractility by:

1. Increasing Ca^{2+} influx into the cell during an action potential;
2. Increasing Ca^{2+} release from the sarcoplasmic reticulum (SR);
3. Increasing the ATPase activity of the myosin head thus increasing the speed of cross-bridge cycling;
4. Increasing activity of the Ca^{2+}-ATPase pump which refills the SR; cytosolic $[Ca^{2+}]$ is reduced faster and the cell relaxes more quickly.



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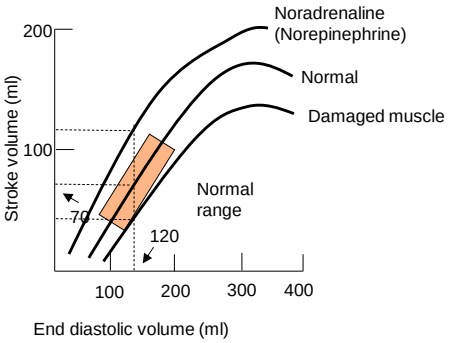
Myocardial contractility and Frank-Starling relationship

Increased contractility increases ejection fraction.

Decreased contractility decreases ejection fraction



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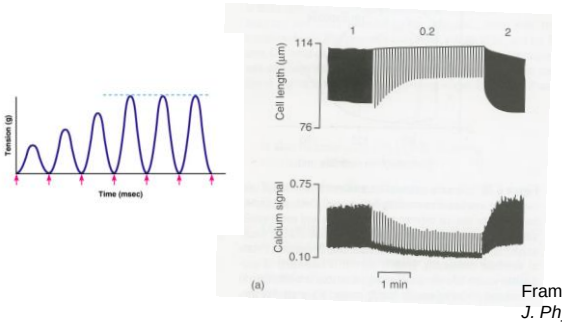
Bowditch effect (staircase / treppe)

Increase in inotropy caused by increased heart rate. Accumulation of intracellular Ca^{2+}



Frampton *et al*., 1991. *J. Physiol.* 437:351.

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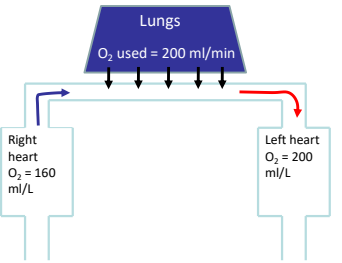
Measurement of CO: Fick Principle (also known as Fick Oxygen Method)

Rate of oxygen uptake into blood is a function of blood flow rate through lungs (= CO).

Need to measure:
Oxygen consumption from inspired air (VO_2).
Oxygen concentration in blood from pulmonary artery (mixed venous blood).
Oxygen concentration in arterial blood.



Cardiac Output (L /min) =

$\frac{O_2 \text{ absorbed per minute by lungs (ml/min)}}{\text{Arteriovenous } [O_2] \text{ difference (ml/L of blood)}}$

$= \frac{200}{200-160} = \frac{200}{40} = 5$ L /min

Considered most accurate method, but also highly invasive. Difficult to measure VO_2 accurately.

Non-invasive; Doppler ultrasound or electromagnetic probe. Accuracy?

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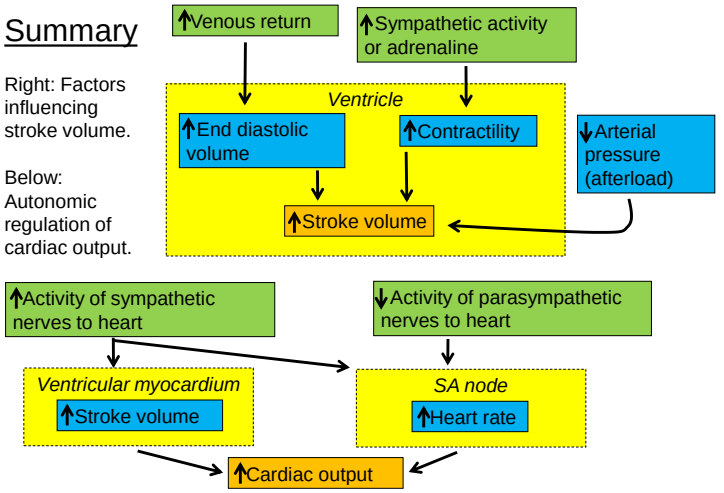
Summary

Right: Factors influencing stroke volume.

Below: Autonomic regulation of cardiac output.



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Summary

Cardiac output (CO) = heart rate x stroke volume

Intrinsic regulation of CO is expressed by Frank-Starling relationship: strength of ventricular contraction is a function of initial muscle fibre length (end diastolic volume, EDV). Determined by pre-load (venous return).

Myocardial contractility is altered independently of fibre-length: inotropy. Altered by nerves, drugs.

Heart rate is controlled primarily by the autonomic nervous system; sympathetic nerves increase rate, parasympathetic nerves reduce rate.

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