Chapter B: Cardiovascular System

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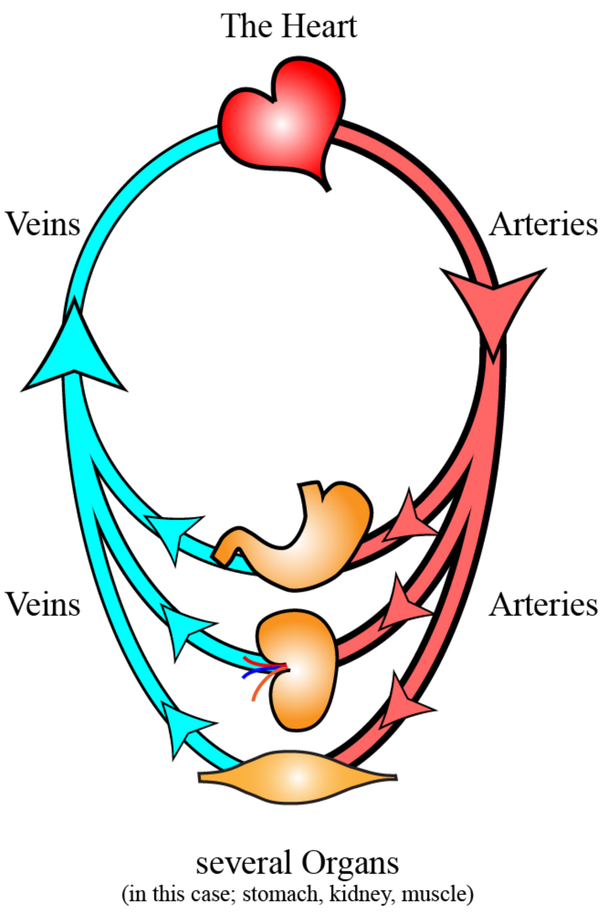
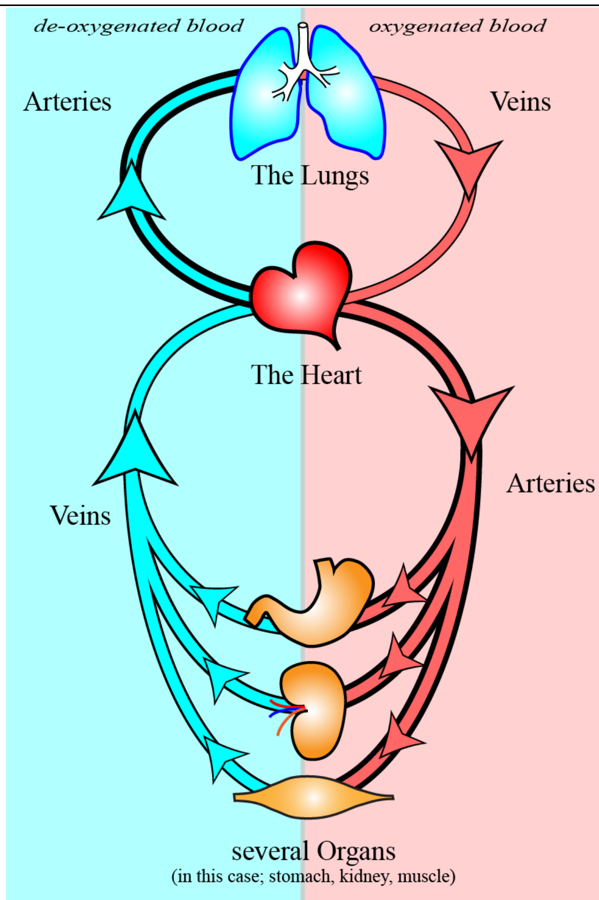
B.1. Introduction to the Cardiovascular System (= CVS).

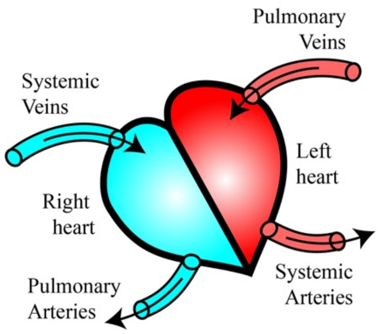
A. Function of the CVS:

<table>
<tr><td>1.
The purpose of the cardiovascular system (=CVS) is for the blood to flow through all the organs and tissues of the body.</td><td>2.
This blood flow is necessary to provide all the organs and tissues with oxygen and nutrients and to remove waste products from them.</td></tr>
<tr><td>3.
The CVS consists of the following major parts:
a. the heart (= cardio)
and the vessels (= vascular):
b. the arteries
c. the capillaries
d. the veins</td><td>4.
The heart is the pump that pushes the blood through the body. The heart does this by contracting regularly at about 70 beats/min. With every contraction, the heart ‘pushes’ or pumps the blood into the arteries.</td></tr>
<tr><td>5.
The arteries run from the heart to all the organs. These are really tubes that transports the blood to these organs and tissues. In other words, the blood flows though the arteries from the heart to the organs.</td><td rowspan="4">
</td></tr>
<tr><td>6.
The capillaries are located in all the organs and receive the blood from the arteries. Inside the capillaries, the blood exchanges the oxygen and nutrients with the fluid inside the organs and collects all the waste from these organs.</td></tr>
<tr><td>7.
The veins collect the blood from the capillaries in the organs and transport it back to the heart.</td></tr>
<tr><td>8.
In other words, the CVS system is one big circle with the heart (= the pump) at one end of the circle, and the organs (the receiving part), at the other side of the circle.</td></tr>
</table>

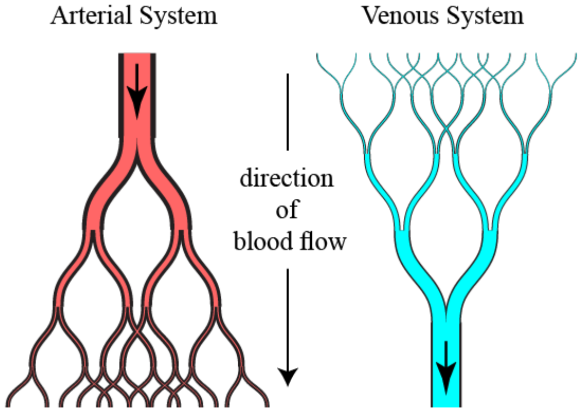
B. The systemic and the pulmonary circulation:

1. However, there are actually, **two** circulations in the body; the large (also called '**systemic**') circulation and a smaller circulation.	2. The smaller circulation transports the blood to the lungs (= *pulmones*). This is why this circulation is called 'the **pulmonary** circulation'.
3. The function of the **pulmonary** circulation is to transport de-oxygenated blood to the lungs where it is re-oxygenated ('filled with oxygen').	4. This oxygen rich blood flows back to the heart where it is then pumped into the **systemic** circulation.
5. In other words, there are actually **two hearts**; one heart that pumps the oxygenated blood into the systemic circulation and a second heart that pumps de-oxygenated blood to the lungs.	
6. Note that the blood vessels coming from the heart to the organs are called '**arteries**' and the vessels that go from the organs to the heart are called '**veins**'! This is **crucial** stuff!	
7. In the **systemic circulation**, the arteries transport oxygenated blood and the veins transport de-oxygenated blood back to the heart.	
8. In the **pulmonary circulation**, it is the other way around: the pulmonary arteries transport de-oxygenated blood to the lungs and the pulmonary veins transport oxygenated blood back to the heart.	

C. The Right and the Left Heart:

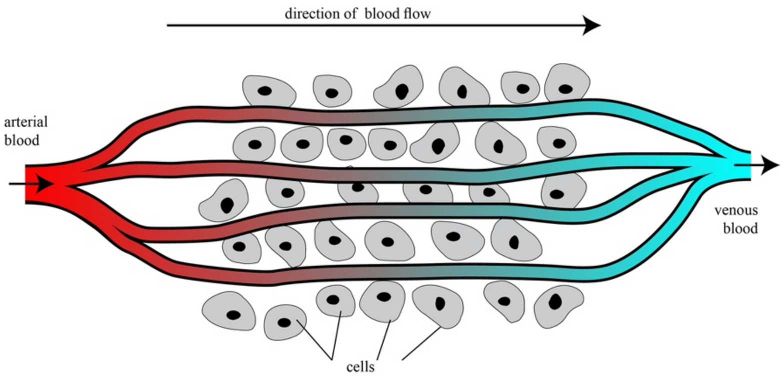
1. So, as you have seen above, there are actually two hearts, the **right** and the **left** heart.	2. The right heart collects the blood from the veins of the systemic circulation and pumps it to the lungs.
3. The left heart receives the oxygenated blood from the pulmonary veins and pumps it to the arteries of the systemic circulation.	
4. When the heart contracts (=pumps), this phase is called the **systole**. After each contraction (=systole), the heart then relaxes. This is called the **diastole**. *More information is available about the function of the heart on page B3. The Electrical Heart and B.4. The contracting Heart*	

D. The Arterial and the Venous 'trees':

1. Both the arterial and the venous vessels are built like a 'tree'.	2. This tree starts as a 'trunk'; which is a major artery or vein. This vessel then splits into smaller and small branches thereby developing into a tree.
3. The major difference between the arterial and the venous tree is that the arterial system splits up into smaller and smaller arteries while in the venous system, the reverse occurs. That is, smaller veins merge gradually into bigger ones.	
4. More information: *B5. The Vascular System*	

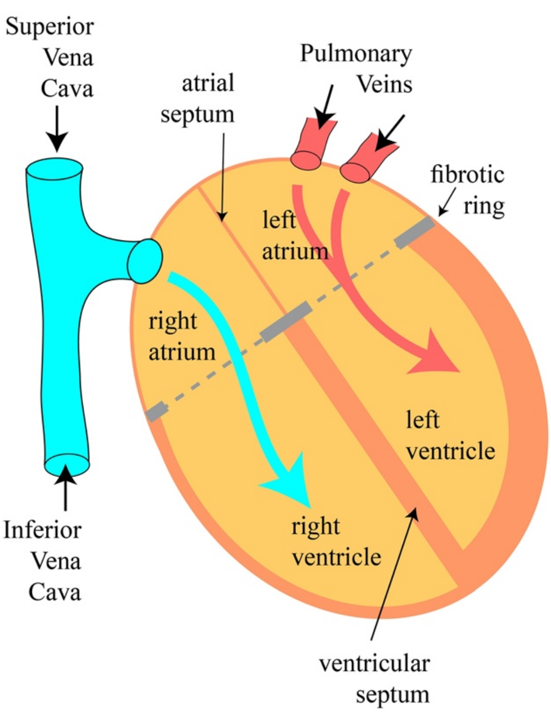
E. The Capillaries:

1. Finally, (!), the **capillaries**. These are vessels that are very small and very thin.	2. These vessels are so **thin** that fluid can easily leave the vessel and flow into the organ that they supply.
3. Because fluid, actually water, can easily flow into the tissue of an organ, it also carries the **oxygen** and other nutrients, which are dissolved in the water, into the organ.	4. At the same time, water can also flow back into the capillaries. This flow allows it to transport **waste** to the capillaries and back to the veins and, ultimately, to the heart



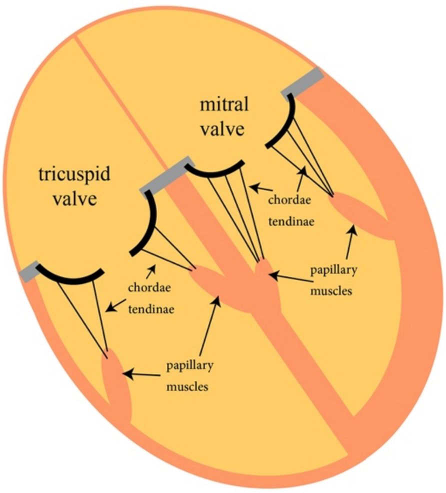
B.2. Structure of the Heart.

A. The heart is a muscle:

<table>
<tr>
<td>1.
The heart is a muscle; also called cardiac muscle (Remember that there are also two other types of muscles in the body; skeletal muscles and smooth muscles; see A.4.1. The Muscle Cell).</td>
<td>2.
The heart is actually a complicated muscle as it consists of two parts; the right heart and the left heart.</td>
</tr>
<tr>
<td>3.
Each heart (right and left) again consists of two parts:
- the atrium (plural; atria)
- the ventricle (plural; ventricles)</td>
<td>4.
The right heart consists of the right atrium and the right ventricle whereas the left heart consists of the left atrium and the left ventricle.</td>
</tr>
<tr>
<td>5.
Between the right heart and the left heart, there is a wall, a septum. In the atria, this is called the atrial septum. In the ventricles, this is the ventricular septum (which is much thicker).</td>
<td>6.
Between the atria and the ventricles, there is also a ‘wall’, which is called the fibrotic ring, AV fibrous tissue or Annulus Fibrosis. It is actually a rather thick fibrotic plate dividing the atria from the ventricles. It also contains several valves through which the blood can flow from one compartment to the next.</td>
</tr>
<tr>
<td>7.
In the right heart, the blood flows from the body (= systemic circulation), through the superior and inferior vena cava’s, into the right atrium. From there it flows to the right ventricle before it is pumped out into the pulmonary artery towards the lungs. This is the start of the pulmonary circulation.</td>
<td rowspan="3">


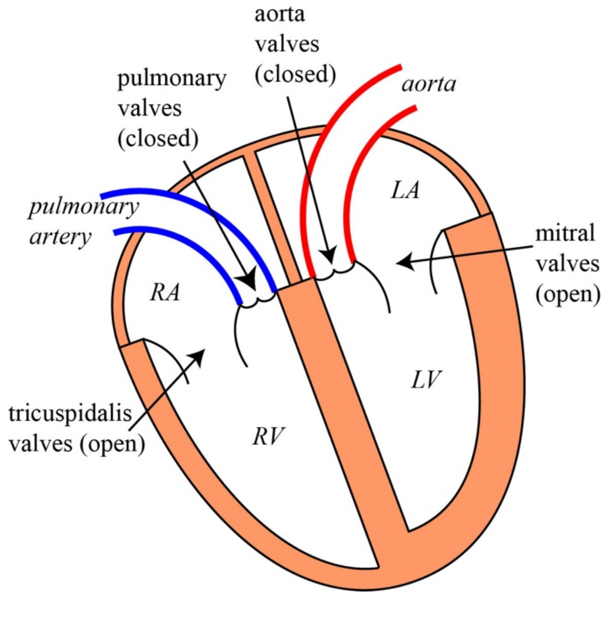
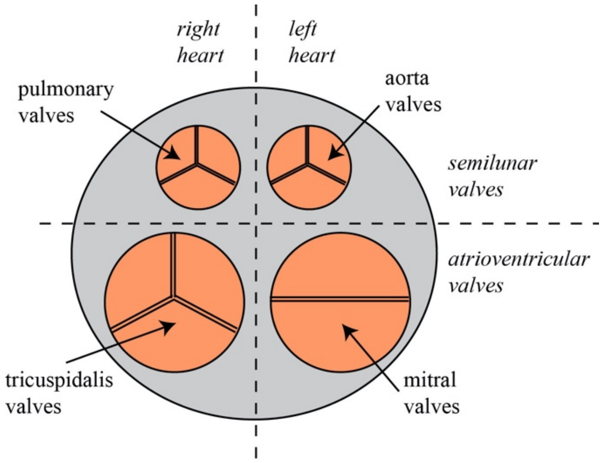
</td>
</tr>
<tr>
<td>8.
In the left heart, the blood flows from the lungs, through the pulmonary veins, into the left atrium. From there it flows into the left ventricle before it is pumped into a large artery, called the aorta. This is the start of the systemic circulation.</td>
</tr>
<tr>
<td>9.
Note, in the diagram, that the walls of the left ventricle are much thicker than that in the right ventricle or in the atria. This is because the left ventricle has to pump the blood at a much higher pressure than in the other compartments (see for more information: B.5.1. The Arteries).</td>
</tr>
</table>

B. The Cardiac Valves:

<table>
<tr>
<td>1.
To make sure that the blood flows in the correct direction, there are valves located between the atria and the ventricles. These are called the atrio-ventricular valves (= AV-valves).</td>
<td>2.
In addition, there are also valves located between the two ventricles and the arteries; the semilunar valves. There are two of them; the pulmonary valve (in the right heart) and the aorta valves (in the left heart).</td>
</tr>
<tr>
<td>3.
The valves consist of thin but strong cusps or valves. In all these valves except one, there are three slips or cusps.</td>
<td>4.
The exception is the AV-valve in the left heart. That particular valve only contains two cusps. We call this valve, the mitral valve (TT: mitral > miter > looks like the hat of a bishop; kind of a priest. See footnote!)</td>
</tr>
<tr>
<td rowspan="4">
</td>
<td>5.
The poor valve in the right heart then also likes to have a ‘name’! We call this valve, the tricuspid valve (as it contains three cusps).</td>
</tr>
<tr>
<td>6.
Note that there are several additional structures related to the AV-valves; the papillary muscles and the chordae tendinea.</td>
</tr>
<tr>
<td>7.
The papillary muscles are connected to the walls of the ventricles at one end, and to the collagen ‘wires’ at the other end, which are attached to the valves. These are actually tendons connecting the valves to the papillary muscle; hence the name ‘chordae tendinea’.</td>
</tr>
<tr>
<td>8.
As we shall see later, they take care of a proper functioning of the AV-valves. (xxxxx).</td>
</tr>
</table>

C. The Semilunar Valves:

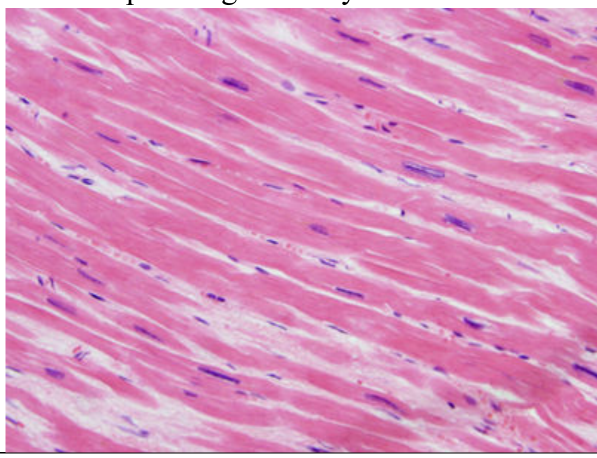
1. These valves, that prevent blood from flowing back from the arteries to the ventricles, are called the ‘semilunar’ valves. (*lunar = moon: because they have the shape of a half-moon!)*	

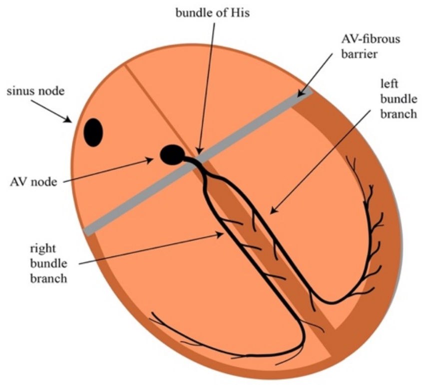
<table>
<tr>
<td>2.
There are two semilunar valves; one at the beginning of the pulmonary artery, the pulmonary valves, and one at the beginning of the aorta, the aortic valves.</td>
<td rowspan="2">
</td>
</tr>
<tr>
<td>3.
The semilunar valves don’t have strings (or chordae) attached to help them. They are by themselves strong enough!</td>
</tr>
<tr>
<td>4.
In the second figure, you see all the four valves together in one plane, all located in the Annulus Fibrosus. This is a very stiff fibrotic plane in which these four valves are located. It is so strong that it is sometimes called the ‘cardiac skeleton’ (although it is not built of bone cells).</td>
<td rowspan="2">
</td>
</tr>
<tr>
<td>5.
Did you notice, in the diagram, that the mitral valve only consists of two valves whereas all the other valves have three valves (or cusps)? This is the mitral valve!</td>
</tr>
</table>

Footnote: Mitral Valve = Miter = hat of a bishop:

B.3.1. The Cardiac Conduction System.

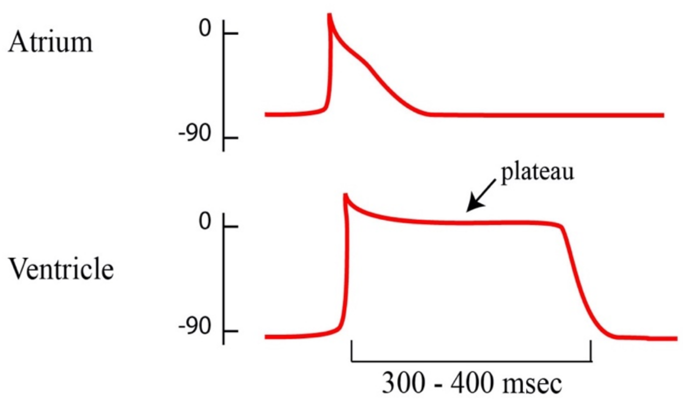
A. Components of the Cardiac Conduction System:

<table>
<tr><td>1.
The heart is special for many reasons but also because it has a unique propagation system in which the electrical impulse (= the action potential) propagates through this organ. This system of propagation is called the Cardiac Conduction System.</td><td>2.
This propagation occurs through special structures that are responsible for the initiation and the propagation of the electrical impulse (= the action potential).</td></tr>
<tr><td>3.
There are three types of structures/tissues involved in this Cardiac Conduction System:
a. the nodal tissue
b. the myocardium
c. the Purkinje tissue</td><td>4.
The nodal tissue is located in two areas:
a. the sinus node – located in the wall of the right atrium close to the inlet of the superior and inferior Vena Cava.
b. the atrio-ventricular node (= AV-node) located between the atria and the ventricles</td></tr>
<tr><td>5.
The myocardium – these are all the muscle cells in the wall of the atria and the ventricles. These cells are connected to each other through special channels called “gap junctions” (also called 'connexion'). Through these channels, an action potential can propagate from one cell to another, a similar mechanism as in the electrical synapse (see A.3.6. The Electrical Synapse).</td><td>Microscopic image of a myocardium:
</td></tr>
<tr><td>6.
The Purkinje tissue – cells that are specialized in fast propagation. Named after Dr. Purkinje who first discovered these special cells: en.wikipedia.org/wiki/Jan_Evangelista_Purkyně.</td><td rowspan="2"></td></tr>
<tr><td>7.
The Purkinje cells are arranged in several bundles and are only located in the ventricles – not in the atria!</td></tr>
</table>

8. The first Purkinje bundle is the **His-bundle** that starts at the bottom of the AV-node, and passes through the Annulus Fibrosus (= AV-fibrous barrier).	
9. In the ventricles, the Purkinje tissue runs along the ventricular septum in two separate bundles; the **right** and the **left** bundle branches.	

B. The shape of the Cardiac Action Potentials:

1. Unfortunately (for the students!), the **shape** of the cardiac action potential is not the same at different places in the heart but depends on the location in the heart. *(Remember what is an action potential? See: A.3.3. The Action Potential)*	2. In the **atria**, the action potential is triangular with a fast depolarization and a slower repolarization. In the **ventricles**, the potential between the depolarization and the repolarization is stable for some 100-300 msec and close to 0 mV. This is called the '**plateau**'. (*footnote: what is a plateau?)*



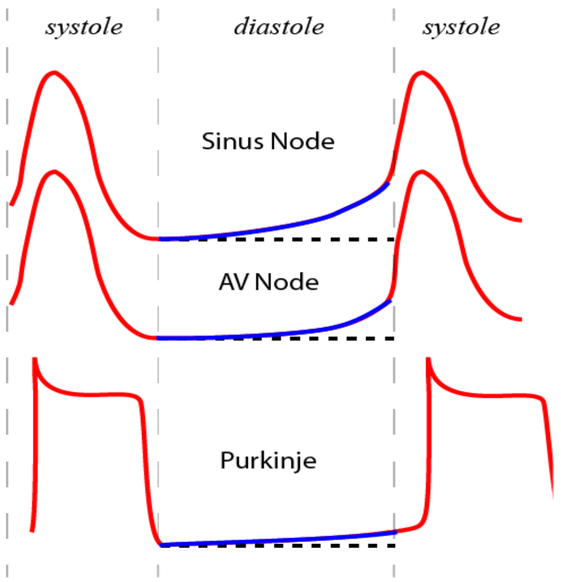
C. Diastolic Depolarization:

1. Please note that in both the atrial and in the ventricular **myocardium**, the potential between the action potential and the next, is **stable**, at about -90 mV.	2. However, in some cardiac tissues, the resting potential is **not** stable. This is the case in the **nodal** tissues (sinus node and AV-node) and in the **Purkinje** tissues.

3.
In those tissues, the resting potential, after the repolarization of the previous action potential, slowly **depolarizes** (blue in the diagram).

4.
Since this depolarization occurs between one action potential and the next, it occurs in the diastolic period and is therefore called the '**diastolic depolarization**'.

5.
This gradual depolarization, at a certain moment, reaches threshold and then initiates a **new** action potential. Therefore, this is the basis of the **pacemakers** in the heart.



C1. Advanced – The many shapes of the cardiac action potentials:

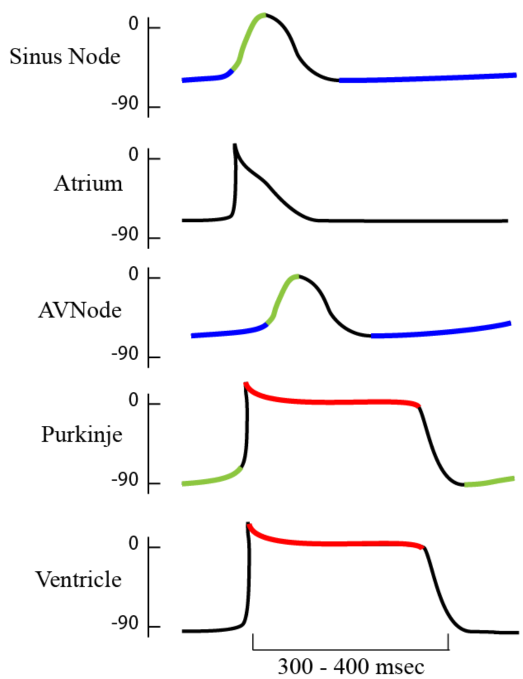
1.
So, in summary, action potentials in the heart have different shapes. The most important elements are:

- a diastolic depolarization
- a plateau
- a fast or slow depolarization

2.
Diastolic potentials from the nodal tissue (sinus and AV-node) and from the Purkinje fibers show a **slow depolarization** (green in the diagram).

3.
Action potentials from nodal tissue and Purkinje tissue show a **diastolic depolarization** (blue in the diagram).

4.
The action potentials from the ventricles (myocardium and Purkinje tissue) show a **plateau**, located between the depolarization and the repolarization (red in the diagram).

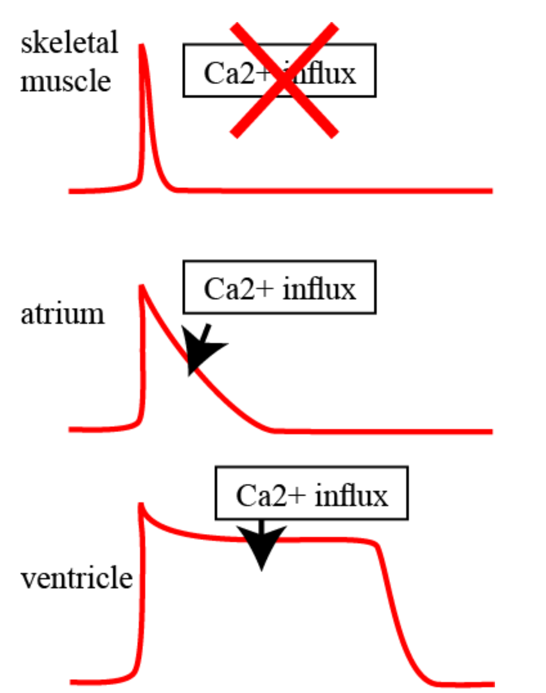


C2. Advanced – Calcium influx during the action potential:

1.
You may remember that calcium ion plays an important role in inducing contraction. (*A.4.3. The Sarcomere*)

2.
In the skeletal muscles, calcium ions are stored inside the cells, in the sarcoplasmic reticulum, from where they are released to flow to the sarcomere to induce contraction.

3.
In the heart, calcium ions are **not** stored inside the cells, but flow from outside into the cell. The trigger for calcium ions to flow into the cells is the action potential! Specifically, between the depolarization and the repolarization; in fact, during the plateau!

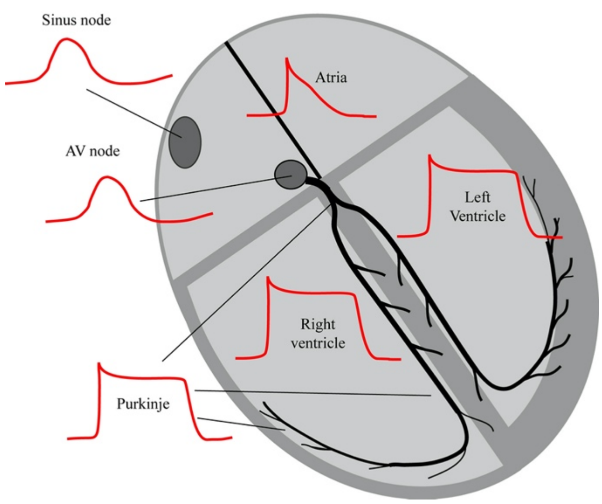


D. Topography of the Cardiac Action Potential:

1.
To understand the cardiac conduction system and how the heart behaves electrically, it is important to understand the location (= the **topography**) of the different type of action potentials in the heart.

2.
This diagram therefore summarizes the different shapes of the cardiac action potentials and their distribution in the heart.

3.
Note that the action potentials in the ventricles (myocardium and Purkinje) all have a **plateau** whereas the action potentials in the atria, both myocardium and nodal tissues, don't have a plateau!

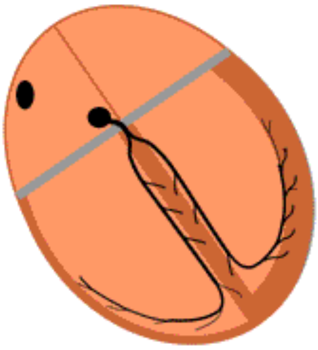
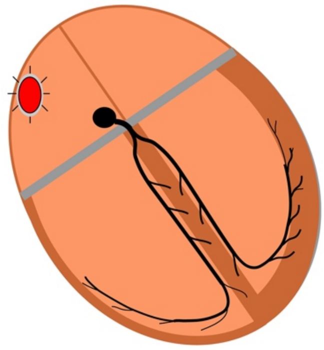
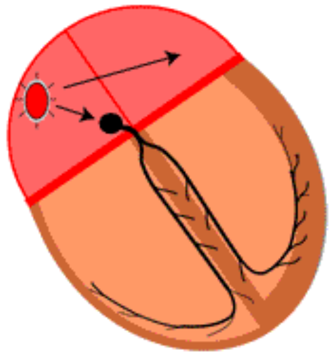
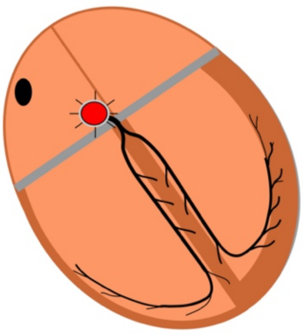
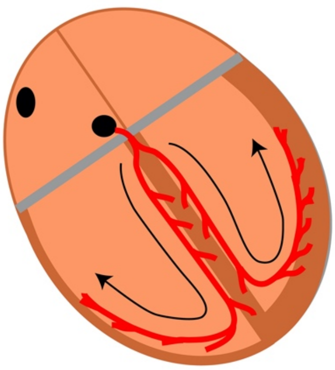
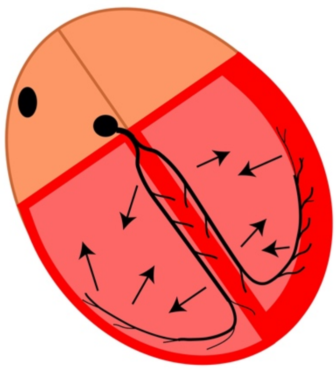


Footnote:
What is a plateau? In the mountains, at the top, there is sometimes not a peak but a flat piece of land. Such a flat land, high on top of a hill or a mountain, is called a plateau (from the French, meaning a 'plate').

B.3.2. Cardiac Excitation

Purpose: The heart has to be activated (=excited), through its conduction system, in a specific sequence so that it will contract (i.e. pump) in an orderly manner.

A. How does the Conducting System excite the heart?

 **Diastole:** During this phase of the cardiac cycle, the heart is **at rest**. There are no impulses propagating anywhere in the heart. The heart is electrically ‘silent’.	 **1. Sinus Node:** The impulse (= action potential) **starts** in the sinus node. This is normally always the case and that is why the sinus node is called the **pacemaker** of the heart.	 **2. Atria:** From the sinus node, the impulse propagates into the atria; first in the **right** atrium and, a little later, into the **left** atrium.
 **3. The AV-node:** At the bottom of the right atrium, the impulse propagates into the AV-node (the nodal tissue located between the atria and the ventricles). This is an important step, because the propagation of the action potential in the AV-node is **very slow**.	 **4. The Purkinje system:** As the impulse, after a long delay, propagates out of the AV-node, it propagates into the **bundle of His** and then through the two **bundle branches** (right and left). This propagation is, in contrast to the propagation in the AV-node, **very fast**.	 **5. Ventricles:** Finally, the impulse arrives in the ventricular cells, the ventricular **myocytes** (cardiac muscle cells), also called the ventricular **myocardium**.

B. Important Notes:

B1. The pacemaker:

1. The SA-Pacemaker:	2. Most rapid rhythm:	3. Abnormal pacemaker site:
The pacemaker is normally located in the sinus node. We call this therefore the sinus pacemaker (or the SinoAtrial-pacemaker). The rhythm induced by this pacemaker is called the **sinus rhythm.**	The pacemaker is normally located in the sinus node because these cells create new action potentials and they do that **faster** than other potential pacemakers in the heart.	If the sinus node cells did not make action potentials (because of a disease), then the other nodal cells, in the AV-node, would make action potentials. In that case, there would be an AV-nodal pacemaker.

B2. The AV-node:

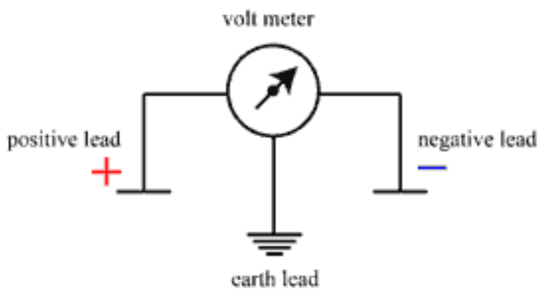
1. The role of the AV-node:	2. AV-nodal delay:	3. Blood flow:
The major function of the AV-node is to delay the propagation of the impulse from the atria to the ventricles.	This AV-nodal delay is important to make sure that the ventricles contract much later and well after the atrial contraction	This delay allows the blood to flow from the contracting atria into the ventricles. If there were no delay, then the ventricles would contract too early and before there was enough blood in the ventricles.

B3. The Purkinje System:

1. The role of the Purkinje system:	2. Synchronization:	3. No synchronization:
In contrast to the propagation of the impulse through the AV-node (which is very slow), the propagation through the Purkinje system is **very fast**!	This is necessary so that the different parts of the ventricles, which are big, are excited as quickly as possible (=**synchronized**) and will therefore contract more or less simultaneously.	If there were no Purkinje system (or if one branch is blocked), then there would be slow or little propagation in the ventricles. This would lead to some parts **contracting early** while other parts would contract much **later**; this would result in poor pumping of the heart.

B.3.3. Basic Stuff about the ECG.

C. What is an ECG and how do we record it?

1. The Electrocardiogram (**E**lectro**C**ardio**G**ram) is the electrical signal from the heart that can be recorded on the surface of the skin.	2. It is also possible to record other signals from the skin such as the **EEG** (ElectroEncefaloGram = electrical signals from the brain) and the **EMG** (ElectroMyoGram = electrical signals from the skeletal muscles).
3. It is also possible to record electrical signals from the heart with electrodes located **inside** the body (such as with a catheter for example) but this is then not called an ECG but simply an **electrogram** (electro = electrical ; gram = a graph).	4. To record an ECG, you need the following: a. **Three electrodes** (two recording electrodes, one positive, one negative, and a third electrode that is connected to earth) b. A **voltmeter** to record, magnify and graph the electrical signal. The recording electrodes are connected to the voltmeter.
5. **Earth electrode?** The earth electrode is necessary to discharge the body of any potential electrical charge, often static electricity. (Footnote: *what is static electricity*?)	
6: **Two recording electrodes:** Most often, an ECG is recorded with one electrode located on the right arm (the wrist is often used for this) and the other electrode is located on the left arm or wrist.	
7. The earth electrode could be located anywhere on the skin and is generally placed on the **right** leg or foot.	

D. How is an electrical signal generated?

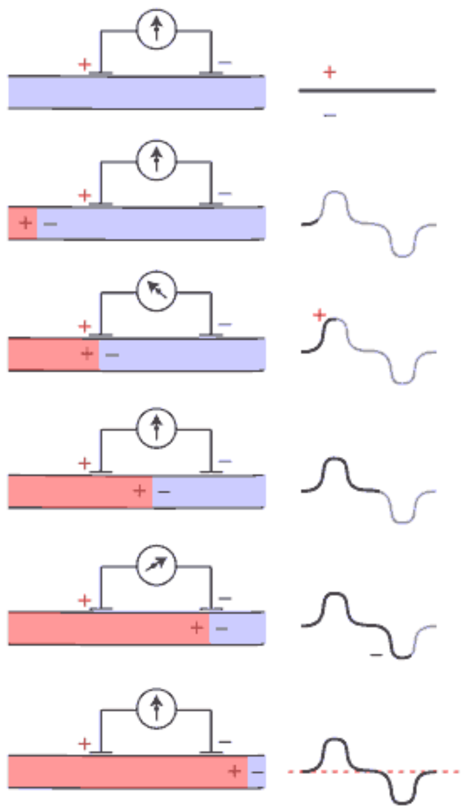
1.
The voltmeter records the potential from two electrodes; one is **positive** and the other is **negative**.

2.
When the tissue is resting (= no action potential), there will be no difference between the positive and the negative potential and the voltmeter will record 0 mV (m = milli Volt; 1/1000 of a volt).

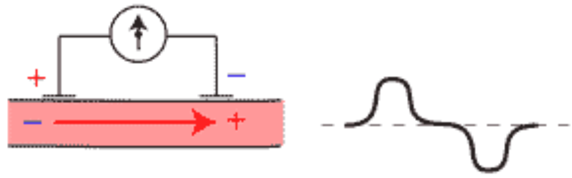
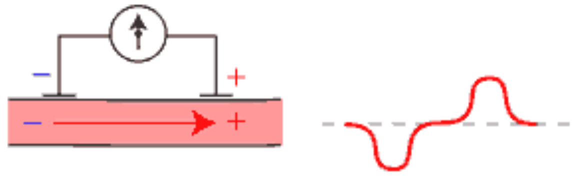
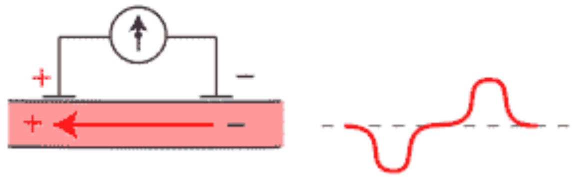
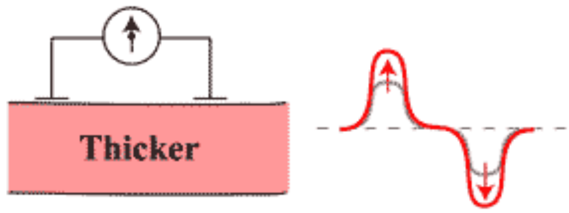
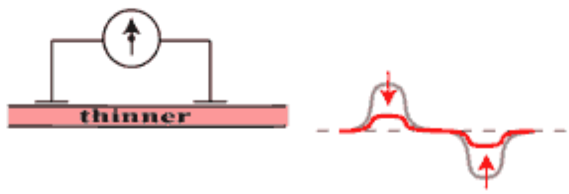
3.
When the tissue is activated (=excited), an action potential will **propagate** through the tissue. When the depolarization reaches the positive pole, a positive deflection (=change in signal amplitude) will be detected. (In the graph; positive is **up** and negative is **down**).

4.
When the depolarization is located **between** the two electrodes, no potential will be recorded (0 mV). This is called = **isoelectric** (iso = same or equal).

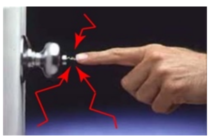
5.
A little bit later, when the depolarization reaches the negative pole, a second deflection will be recorded. This deflection is the **opposite** of the first deflection because this electrode is recording negatively.



E. Some basic ECG Rules:

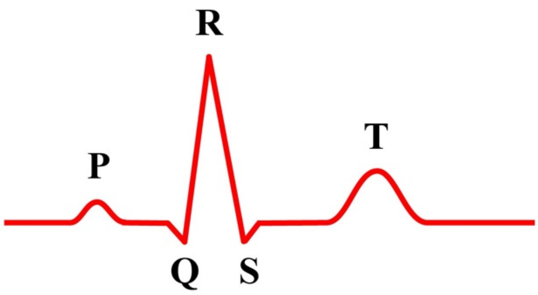
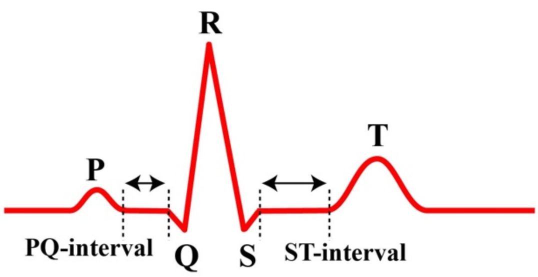
1. Suppose that this is an electrogram recorded from this excited tissue:	
2. If the polarity of the electrodes is changed (positive becomes negative and negative becomes positive) then the signal also changes its polarity (**first** negative and **then** positive). Thus, the ECG depends on the **polarity** of the electrodes!	
3. If the **direction** of depolarization is changed; from right to left, instead of left to right, then the polarity is also changed (=**reversed**). Thus, the shape of the ECG also depends on the **direction** of propagation of the action potential!	
4. If the amount of tissue that is excited is **large** (such as a thick muscle wall), then the ECG signal will also be **large**! Thus, the ECG can detect hearts that have an abnormal thick muscle (=**hypertrophy**).	
5. If the amount of tissue that is excited is **small**, reduced or thin (such as a thin muscle wall), then the ECG signal will be smaller then normal! Thus, the ECG can detect hearts that have an abnormal thin muscle (atrophy).	
6. This is not very common. Much more common is when a part of the muscle is no longer excitable, such as in a **heart infarct**. Thus, the ECG can detect infarcted tissue!	

TT: What is static electricity?
The body often contains (small) electrical charges, due to rubbing of clothes etc. These charges could seriously disturb the recording of an ECG so it is better to get rid of them during an actual recording. This is done with an earth electrode.



B.3.4. The ECG.

A. The components of the ECG:

1. In order to understand the ECG, you need to know and remember the normal conduction of the impulse in the heart: SA-node -> Atria -> AV-node -> Bundle of His -> Purkinje tissues -> Ventricles. (*see: B.3.2. Cardiac Excitation*)	
2. A typical ECG consists of a sequence of waves. The normal waves are labelled the P wave, the QRS wave and the T wave.	3. a. The **P-wave** is a reflection (= represents) the depolarization of the atria. b. The **QRS-complex** represents the depolarization of the ventricles. c. The **T-wave** represents the repolarization of the ventricles.
4. Because the atria are depolarized before the ventricles, the P-wave will occur **before** the QRS-complex.	5. Remember that the impulse was **delayed** in the AV-node (between the atria and the ventricles). This is visible as a delay in the ECG; there is therefore some time between the **end** of the P-wave and the **beginning** of the QRS complex; the **PQ-interval**.
6. There is a second **isoelectric** segment in the ECG; between the **end** of the S and the **beginning** of the T-wave. During this period, all the cells in the ventricles are depolarized. (*isoelectric = same or equal potential at both recording electrodes*).	

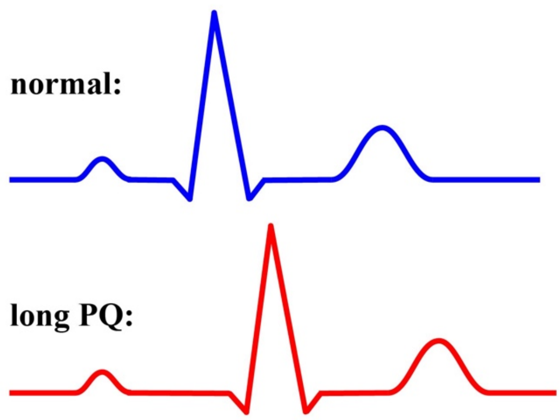
B. Difficult Stuff!!

1. **Where is the atrial repolarization on the ECG?**	2. **Weak signals are not visible on the ECG:**
It is not there! There is no visible atrial repolarization on the ECG. This is because the amplitude of the ECG signal depends on the speed and the strength of the electrical signal in the heart. Something that is very fast and excites a lot of tissue will show a strong signal on the ECG. A good example of this is the QRS-complex because it represents fast depolarization of the thick ventricular wall.	A very weak signal is not visible on the ECG. For example, the action potentials propagating in the Sinus Node (which occurs before the P-wave) and in the AV-node (which occurs between the P-wave and the QRS-complex) are too slow and too weak to be visible on the ECG.
3. Speed of excitation in the atria: In the atrium, the depolarization of the atrium is quite fast, and this creates the P-wave. But the repolarization of the atria is much slower (TT), and hence is too weak to be seen on the ECG. *(Remember the slow triangular shape of the repolarization in the atria?)*	**4**: **Speed of excitation in the ventricles:** Something similar also happens in the ventricles. There, the depolarization is very fast (one of the fastest in the heart) but the repolarization is slower (although not as slow as in the atrium). That is the reason why the T-wave is weaker and more spread out than the QRS-complex.
5. The T-wave is usually bigger than the P-wave. This is because much more tissue is being **repolarized** (in the ventricles) then **depolarized** (in the atria).	6. By the way, we call the QRS a "**complex"** and not a wave because it actually consists of three separate waves: "Q" "R" and "S".

C. Some Pathophysiology:

1.
The reason why the ECG is so popular is because it tells so well what is going on in the sick heart.

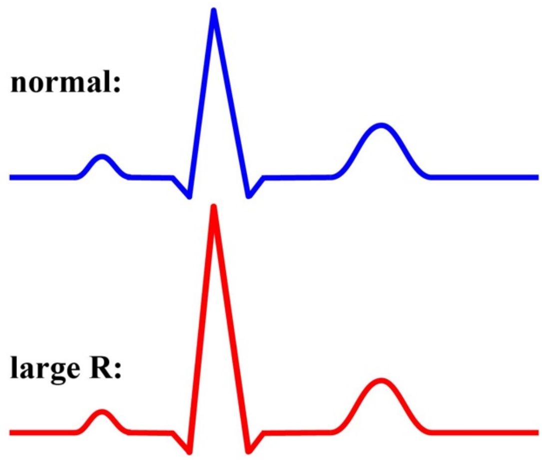
2.
For example, you may have noticed that the AV-node is quite a weak link between the atria and the ventricles. What would happen if the impulse took longer than normal to propagate through the AV-node and reach the ventricles?
Answer: the **PQ-interval** would be longer than normal. And that is exactly what a cardiologist does when analyzing an ECG; the analysis consists of measuring intervals such as this one.



3.

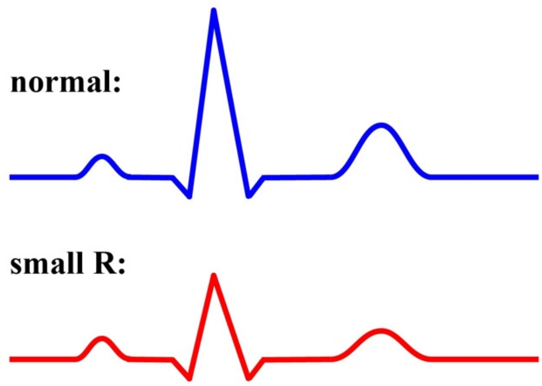
In some diseases, the left ventricle is thicker than normal (**left ventricular hypertrophy**). This would cause a stronger depolarization and therefore a **higher** QRS amplitude.

By the way, there is a mistake in this tracing! Can you spot it?
(link: mistaken T-wave)



4.
In other diseases, the opposite happens and the ventricles, or part of it, die (such as during a myocardial infarction). This will lead to a weaker QRS complex and a lower amplitude.

(Notice that the T-wave is now also smaller).



5.
Another reason why the ECG is so popular is because it also describes very well the rhythm and the rhythm disorders in the heart. When the heart beats too fast (= tachycardia) or too slow (= bradycardia), this is easily visible in the ECG. Especially the tachycardias are very important because these can degenerate into arrhythmias (= rhythm disturbances), which may cause **sudden death.**

B.3.5. The 12-leads ECG.

A. From where can you record an ECG?

<table>
<tr><td>1.
In fact, to record an ECG, you can place the recording electrodes anywhere you like as long as it is on the skin, such as on your chest, on your belly, on your foot and even on top of your head!</td><td>2.
It is possible to record the ECG anywhere on the skin because the current generated in the heart flows throughout the whole body. This current can flow because the body consists for a large part of fluid (water) and ions (electrolytes).</td></tr>
<tr><td>3.
A mistake that is often made is the belief that the ECG current flows with the blood. That is nonsense. The current flows through all fluids; blood, interstitial fluid and intracellular fluids.</td><td>4.
You can record the ECG everywhere but they will all look different.</td></tr>
<tr><td>5.
That is because if the electrodes are for example on the chest, they will mainly record the current originating from the front of the heart.</td><td>6.
If the electrodes are located at the back of the body, or at the side, then the electrodes will collect the current especially from the back or from the side of the heart.</td></tr>
<tr><td colspan="2">7.
To be able to compare ECGs between different people or at different times it is therefore necessary to standardize the locations from where you record the ECG.</td></tr>
</table>

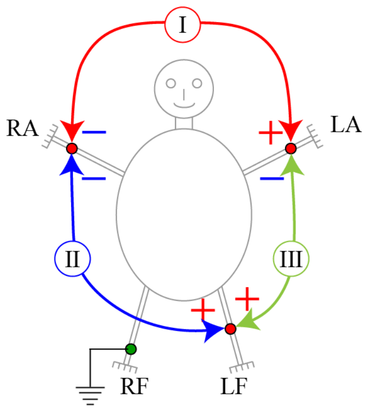
B. The Einthoven leads:

1. **The three Einthoven leads**:

The first standard locations were determined by Einthoven (in 1903) and are:

a. **lead I**: between right arm (RA) and left arm (LA)
b. **lead II**: between right arm (RA) and left foot (LF)
c. **lead III**: between left arm (LA) and left foot (LF).

*Note: these leads are always named 'I', 'II' and 'III' (Roman letters) and **NOT** '1', '2' or '3'!!*

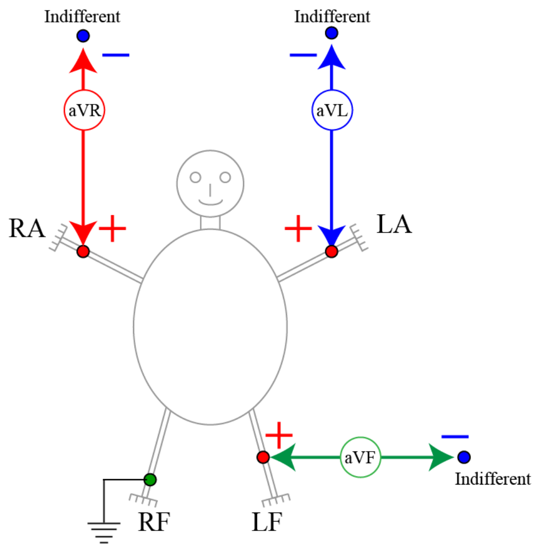


C. The Augmented leads:

<table>
<tr><td>1. Bipolar leads:

The Einthoven leads are essentially bipolar leads; that is, they record from two electrodes simultaneously, one positive and one negative and the signal is a composite of the current picked up at both sites. These leads are therefore called bipolar leads.</td><td>2. Unipolar leads:

Someone else, later, modified the connections by recording from a single location and connect that to the voltmeter.</td></tr>
<tr><td>3. Indifferent electrode:

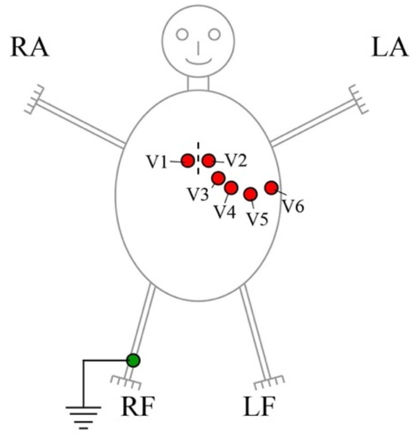
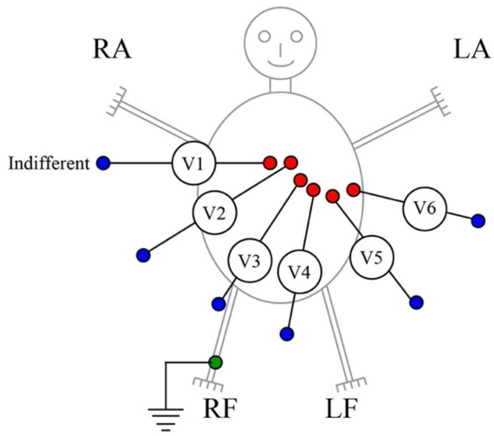
But a voltmeter needs two inputs': one positive and one negative.
The solution is to connect the negative pole to an indifferent electrode. This is like an imaginary or a virtual or a reference electrode. It is actually connected to all limbs together.</td><td rowspan="2">
</td></tr>
<tr><td>4. Augmented leads:

Again, later, someone else developed an even more clever connection scheme, which augments (=increases) the amplitude of the signals. That is why these leads are now called unipolar and augmented. There are three of these leads: aVR, aVL and aVF.
(The 'a' in front of VR, VL and VF means 'augmented'!)</td></tr>
<tr><td>5. Six limb leads:

We now have six leads: I, II, III (from Einthoven), and aVR, aVL and aVF (the augmented leads). These are all "limb" leads because they are connected to the arms and to the left leg.</td><td>6.

Three of these are bipolar leads (I, II, III) and three are unipolar leads (aVR, aVL, aVF).</td></tr>
</table>

D. The Pre-cordial leads:

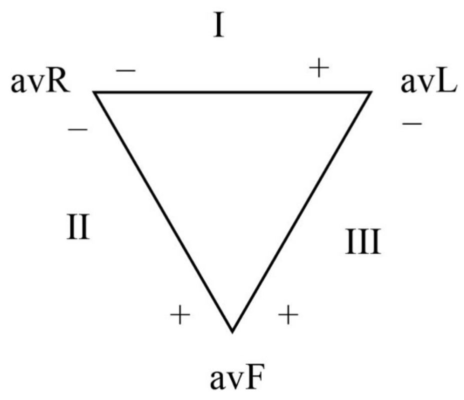
1. Another way to "look" at the heart is to place an electrode on the chest, as close as possible to the heart. These are therefore called precordial leads (pre = in front; cordis = heart). These are also unipolar leads (= the negative pole is connected to an indifferent electrode).	
2. The electrode locations on the chest are very **precise**: V1 -> 4th intercostal space, right of the sternum V2 -> 4th intercostal space, left of the sternum V3 -> halfway between V2 and V4 V4 -> 5th intercostal space in the mid-clavicular line V5 -> 5th intercostal space in the anterior axillary line V6 -> 5th intercostal space in the mid-axillary line	

E. The triangle of Einthoven:

1.
In summary, we now have 12 standard leads!

a. The Einthoven leads (I, II and III)
b. The Augmented leads (aVR, aVL, aVF)
c. The pre-cordial leads (V1-V6)

2.
The diagram to the right shows an easy way to remember the limb leads and their polarities. They are displayed in the so-called **triangle of Einthoven**.



3.
Tips: to help remember all this:
- The polarities at the right arm are always negative.
- The polarities at the (left) leg are always positive.
- The polarities at the left arm follow those at the right arm and the left leg.

F. So, what is a "lead"?

This is sometime confusing for students. A "**lead**" is really the wire and the electrode to connect the ECG recorder to the patient. But the word "lead" also means **which** connection is made; for example, Lead I (=Einthoven I; between right arm and left arm), or lead aVR, or chest lead V1. Note that some leads are **bipolar** and others are **unipolar**. Likewise, some leads are **limb** leads while others are **chest** leads (V1 to V6).

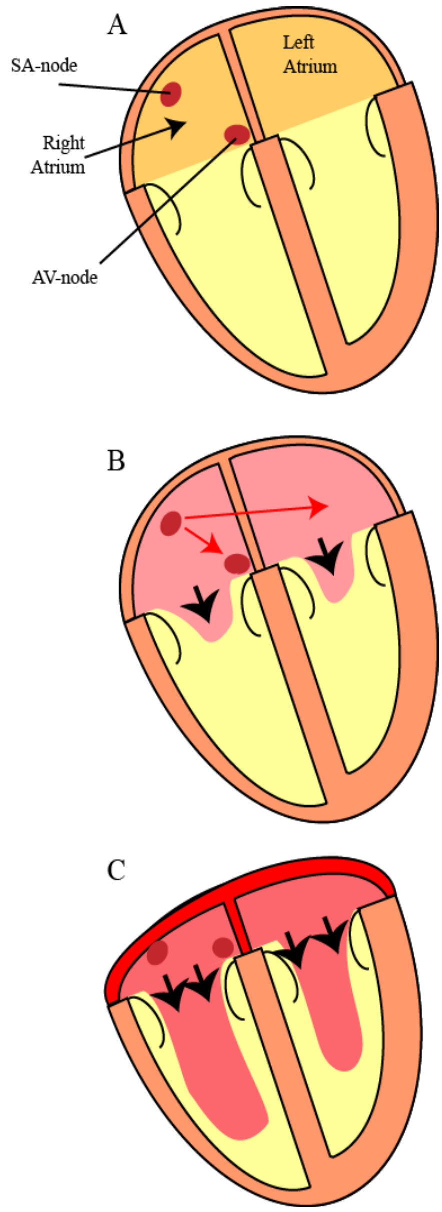
B.4.1. The Contracting Heart

Purpose: The heart contracts to pump blood into the arteries. Simple!

A. Diastole and Systole:

1. When the heart contracts, this is called the “**systole**” (old Greek for “squeeze”). This is the heartbeat.	2. In the period between the systoles, the heart relaxes and this is called the “**diastole**” (from a Greek word that means “dilate”).
3. The cardiac **systole** really consists of two parts: 1. The **atrial** systole 2. The **ventricular** systole	4. The **atrial** systole is the first to occur, as the atria are the **first** to be excited by the sinus node (which is located in the right atrium).
5. Soon after the atrial systole, as the impulse propagates through the AV-node into the Purkinje system, the **ventricles** is excited and this is the beginning of the ventricular systole (= contraction).	6. After the atrial and the ventricular systole, the cardiac muscle relaxes, dilates (= diastole) which allows blood from the body to **flow** into the heart, in preparation for the next systole. This period of relaxation is the **diastole**.

B. Atrial Systole

1. As in every cardiac cell, the excitation is followed by its contraction. So, the cells that are first activated will be the first to contract.	2. Although the sinus node is the first to be excited (i.e. the pacemaker), it is very small and thus hardly contracts. Therefore, this node does not play a significant role in the contraction of the atrium.
3. The important structures that contract are the right and the left atria.	
4. This is useful, as this will push the blood that has accumulated in the atria (from the veins) into the ventricles.	
5. Note that the impulse starts in the upper right atrium (close to the sinus node) and propagates towards the AV-ring (=annulus fibrosus).	
6. Therefore, the contraction will follow this pattern and start contracting in the right atrium (diagram B). This will push the blood towards the AV-valves and into the ventricles.	
7. Also note that both atria contract nearly simultaneously. The right atria will contract a little bit earlier than the left atrium (because the sinus node is located in the right atrium) but this difference is very small and negligible.	
8. As the atria contracts, the blood pressure increases in the atria and blood is pushed from the atria into the ventricles.	

C. Ventricular Systole

1.

The ventricular contraction starts as the impulse arrives at the ventricular myocardial cells.

2.

As in the atrial nodal cells, the bundle of His and the Purkinje cells are too small to help in the contraction (their function is only to distribute as quickly as possible the action potential throughout the ventricles).

3.

It is only when the ventricular myocardium is finally excited that the ventricular systole has started.

4.

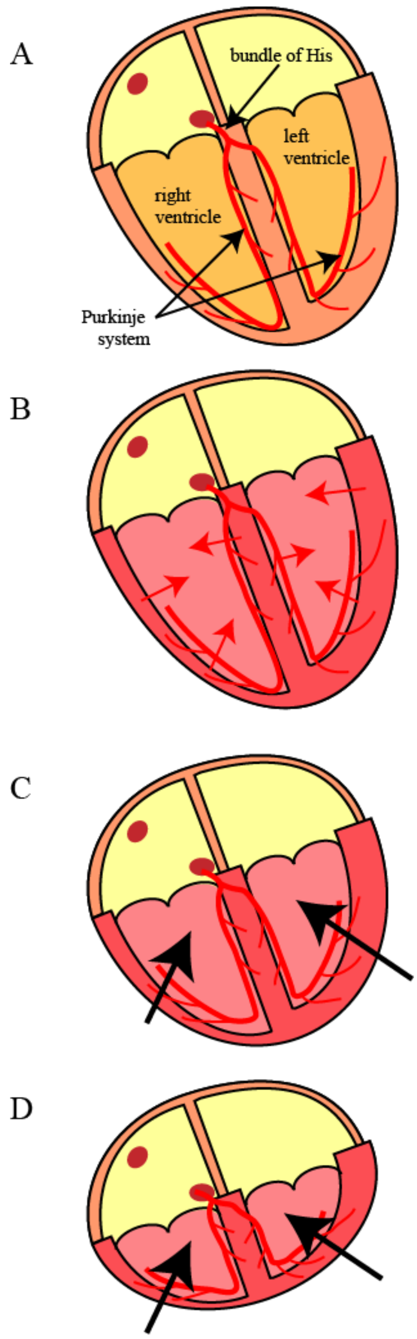
Again, as both the right and the left ventricle are activated, through the right and the left bundle branches, more or less simultaneously, both ventricles will also contract at the same time.

5.

As both ventricles contract, their length will decrease towards the fibrotic ring and the valves.

6.

With the decrease in length and size, the volume inside the ventricles will also decrease. This will push (= pump) the blood out of the ventricles into the major arteries (see next section: The haemodynamic heart).



B.4.2. The Cardiac Systole

Aim: How does the heart pump the blood into the arteries?

A. Role of the Cardiac Valves:

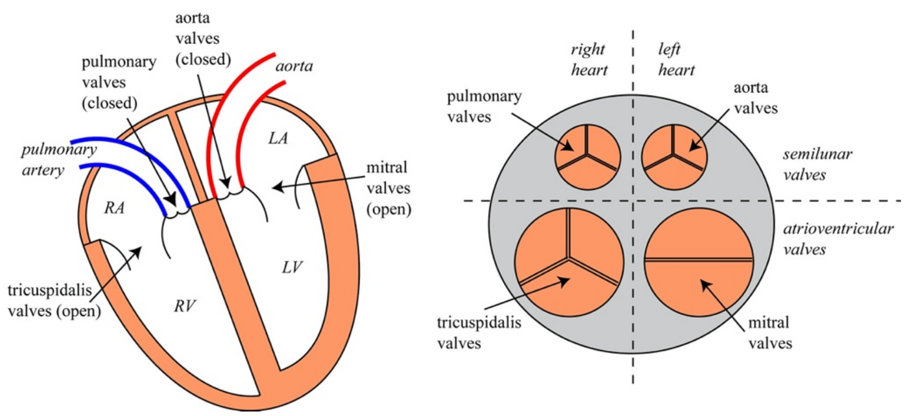
<table>
<tr>
<td>1.
Remember the structure and location of the cardiac valves?

The cardiac valves play a crucial role in the function of the heart. They make sure that the blood flows in the right direction.

The valves are located between the atria and the ventricles (= the atrio-ventricular valves) and between the ventricles and the arteries (= the semi-lunar valves).

(Semi-lunar = half moon shaped)

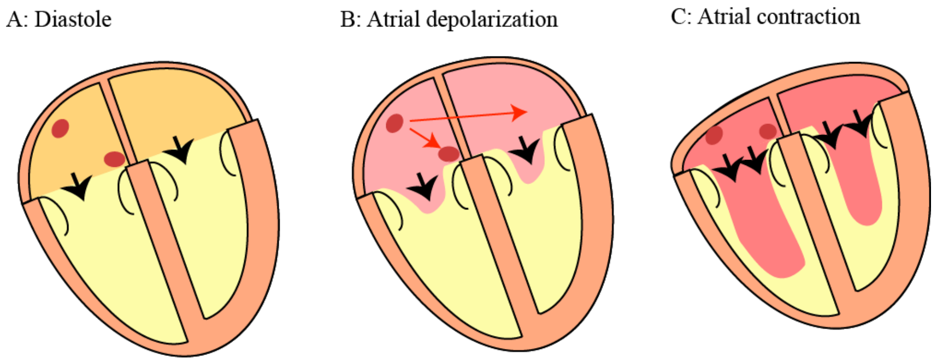
(RA = right atrium; LA = left atrium; RV = right ventricle; LV = left ventricle)</td>
<td>2.
There are, as we have seen, four different valves:

1. the tricuspid valves: located between right atrium and right ventricle,
2. the mitral valves: located between left atrium and left ventricle,
3. the pulmonary valves: located between right ventricle and the pulmonary artery,
4. the aorta valves; located between left ventricle and the aorta.</td>
</tr>
<tr>
<td colspan="2">
</td>
</tr>
<tr>
<td>3.
There is no machinery that makes the valves open and close. Instead, it is the blood pressure alone that determines whether the valves are open or closed.</td>
<td>4.
If the blood pressure in the atria is higher than in the ventricles then the AV-valves are open. But, if the pressure in the ventricles is higher than in the atria, then the valves close.</td>
</tr>
</table>

B. Atrial Systole:

<table>
<tr><td>1.

During diastole, the AV-valves are open and the semilunar (SL) valves are closed.</td><td>2.

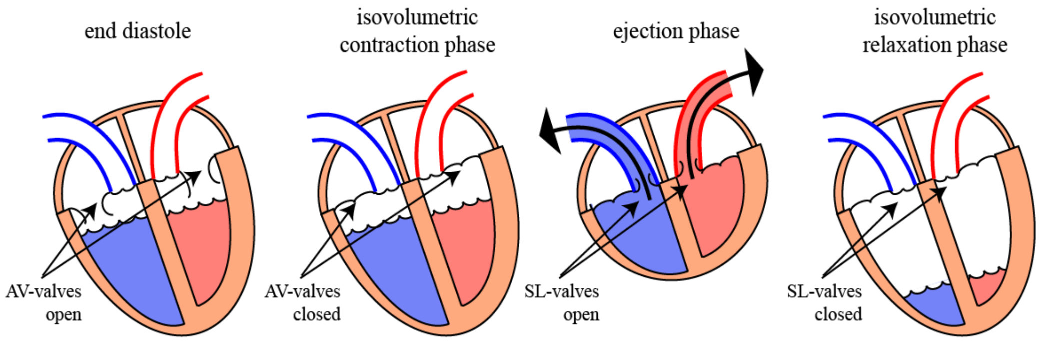
During this phase, the AV-valves are open because blood flows from the atria (higher pressure) into the ventricles (lower pressure). The SL-valves are closed because the pressure in the arteries is (much) higher than in the ventricles.</td></tr>
<tr><td colspan="2">
</td></tr>
<tr><td>3.

As we have seen before, the sinus node will initiate an action potential that propagates throughout the right and the left atria.</td><td>4.

This depolarization will initiate a contraction of both atria that will ‘push’ even more blood into the ventricles. This is the start of the cardiac systole.</td></tr>
</table>

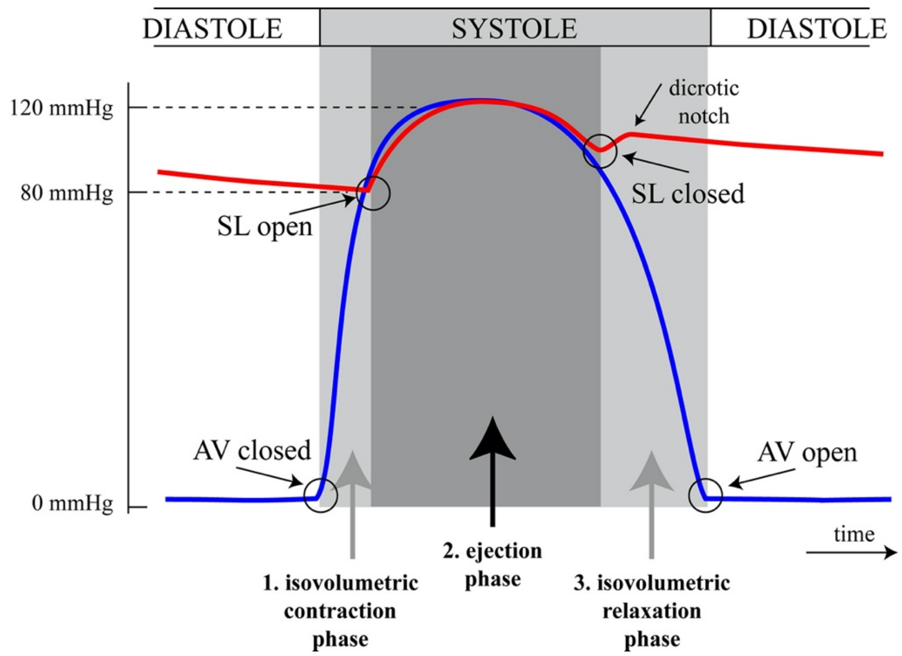
C. Ventricular Systole

1. At the beginning of the ventricular systole, the ventricles are activated and start to contract. This will make the volume inside the ventricular space smaller and this will then increase the pressure.	2. As the ventricles start to contract, the increasing pressure inside the ventricles will push the blood back to the atria. This will immediately close the AV-valves.



3. Now, at this stage, the AV-valves are closed and the SL-valves are still closed. In short, all the four cardiac valves are now closed! The ventricles behave now like a closed box.	4. Therefore, no blood can come into the ventricles and no blood can go out! In other words, the volume is (temporarily) constant; this is called isovolumetric and this phase of the contraction is therefore called the Isovolumetric Contraction Phase.
5. This isovolumetric phase only lasts a short time and until the pressure in the ventricles becomes higher than in the arteries.	6. As soon as the ventricular pressure is higher than the pressure in the arteries, the SL-valves will open and blood will be pushed (= ejected) into the arteries. Therefore, this phase is called the ejection phase.
7. After some time, the contraction has stopped and the pressure in the ventricles will start to drop. This will cause the blood in the arteries to start flowing back towards the ventricles and this backflow, in turn, will immediately close the SL-valves.	8. Again, we now have a situation in which all the valves are closed (= iso-volumetric). But now, the ventricles are relaxing and therefore this final phase of the contraction is called the isovolumetric relaxation phase.
9. During this phase, the pressure in the ventricles rapidly decreases to low values. As soon as the pressure in the ventricles is lower than in the atria, the AV-valves open again.	10. The opening of the AV-valves marks the end of the ventricular systole.

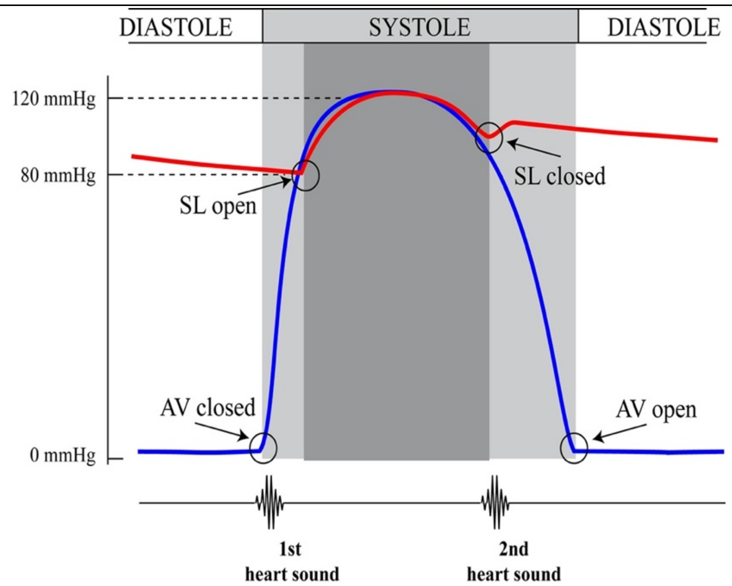
D. Ventricular Pressures:



1. Another important way to study the events during the ventricular systole is to look at the changes in blood pressure during the systole. The diagram above shows these pressures in the left heart (left ventricle in blue and aorta in red).	2. As shown in the diagram above, during diastole, the pressure in the ventricles (blue) is close to 0 mmHg. The pressure in the aorta (red) is much higher, somewhere between 80 and 120 mmHg. Therefore, the aorta valves (=SL valves) are closed.
3. At the beginning of systole, the pressure in the ventricles increases and this immediately closes the AV-valves. Remember that the SL-valves are still closed (the pressure in the arteries is still higher than in the ventricles).	4. The first phase, the isovolumetric contraction phase, has now started (light grey area). In this phase, the ventricular pressure increases rapidly, until the pressure becomes higher than in the aorta. When the ventricular pressure gets higher than in the aorta, then the SL-valves will now open.
5. As soon as the SL-valves open, the blood is ejected (= pumped) into the aorta; this is the ejection phase.	6. As the blood is being pumped out, the amount of blood in the ventricles will diminish, and the high pressure in the ventricles will eventually decrease. By

	then, the contraction has also stopped. Therefore, the blood will start to flow back and this will close the SL-valves. This is the end of the ejection phase.
7. The end of the ejection phase is the beginning of the isovolumetric relaxation phase (all valves are again closed). The ventricles relax, and the pressure inside the ventricle drops quickly.	8. As the ventricular pressure drops, the pressure eventually will become lower than in the atria and this will open the AV-valves. This marks the end of the isovolumetric relaxation phase and also the end of the systole!

E. Heart Sounds:



1. The behaviour of the cardiac valves also explains the heart sounds.	2. The closing of the valves creates strong vibrations in the cusps and this will cause turbulence in the blood. Together, these create a heart sound.
3. As the AV-valves close, at the beginning of the systole, this creates a sound and that is called the 1st heart sound.	4. A little bit later, at the end of the ejection phase, when the SL-valves close, this also creates a sound; this is the 2nd heart sound.

5. Note that opening of the valves do NOT cause a sound.	6. It is like when you open a door (no sound) and slam the door shut (loud noise)! Capitto?

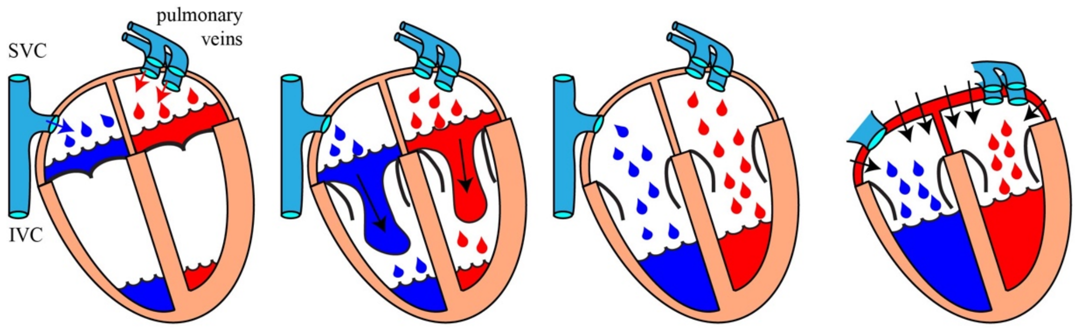
B.4.3. The Cardiac Diastole

Content: What happens in the heart during diastole?

A. Blood flow during the diastole

<table>
<tr><td>1.

The diastole is the period during which the ventricles relax and gets filled again with blood for the next systole.</td><td>2.

As with the systole, we can divide this period into three phases:
a. the rapid filling phase
b. the passive filling phase
c. the active filling phase</td></tr>
<tr><td colspan="2">

end of systole rapid filling phase passive filling phase active filling phase</td></tr>
<tr><td>3.

Remember that during the systole, the AV-valves are closed. Blood that has meanwhile flown from the veins (VCS = vena cava superior, VCI = vena cava inferior and from the pulmonary veins) into the atria have accumulated in that space.</td><td>4.

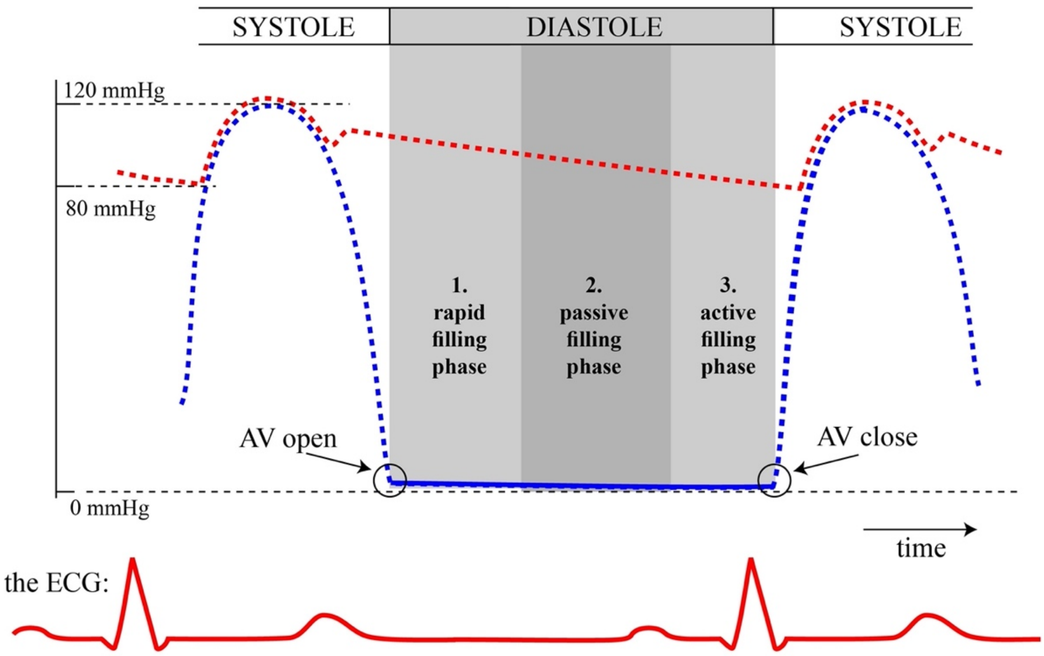
At the beginning of the diastole, when the AV-valves open, this accumulated blood will suddenly and rapidly flow into the ventricles; this the rapid filling phase.</td></tr>
<tr><td>5.

Once this accumulated blood has flown into the ventricles, blood keeps streaming in from the veins into the atria. This blood can immediately flow further into the ventricles: passive filling phase.</td><td>6.

At the end of the ventricular diastole, the sinus node will become excited again and the atrial systole will start (remember that the atrial systole starts before the ventricular systole). This atrial excitation will induce atrial contraction and this will squeeze the last remaining blood into the ventricles; active filling phase.</td></tr>
</table>

B. Blood pressure during the diastole:

1.	2.
As I said before, the diastole begins when the AV-valves open and ends when the AV-valves close (at the next systole).	During diastole, the pressure in the ventricles is very low, close to zero mmHg. This is important as it must be lower than the low pressures in the atria, or else, blood would not flow into the ventricles.



3.

Therefore, as shown in the diagram, there is not much change in the ventricular pressure during diastole, in contrast to the big change during systole.

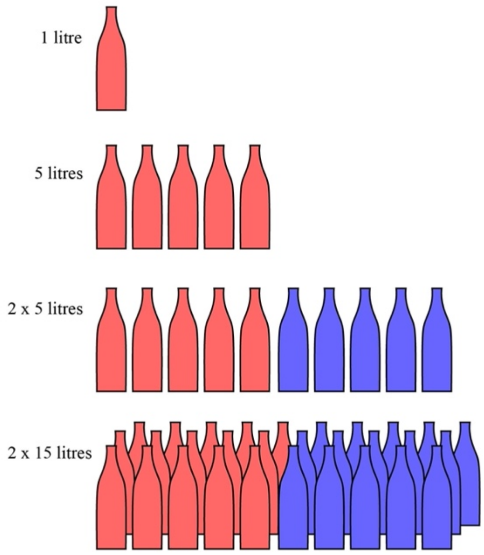
C. Additional notes:

1.	2.
Note that the blood flow from the veins into the atria is constant and continuous and is never interrupted during systole and diastole.	But, because of the pumping of the heart, the blood that flows out of the heart, into the arteries is not continuous but **pulsatile** (in “spurts”).

3. While the ventricles contract, the AV-valves are closed but there must be space available where meanwhile the venous blood can be collected or "pooled".	4. This pooling of blood is done in the atria. This is the major function of the atria.
5. Note that the atrial contraction only plays a minor role in the blood flow from the atria into the ventricles; estimated at about 25% of the total blood flow.	6. But, if the ventricles don't contract, then of course there will be **NO** blood flow into the arteries at all! This is simply incompatible with life.

B.4.4. Cardiac Output

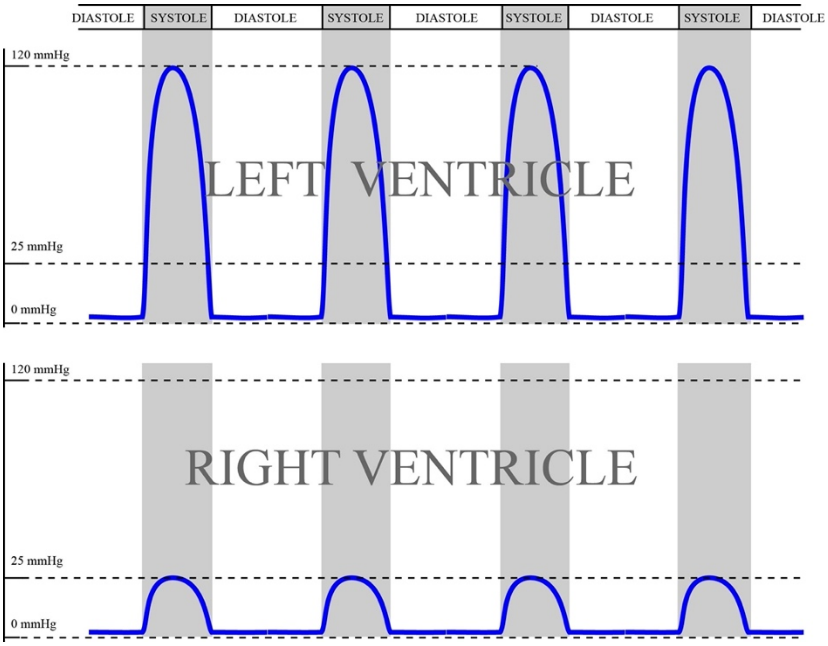
A. Cardiac Output:

1. The function of the heart is to pump blood out of the ventricle. This amount of blood is called the **cardiac output**.	2. Cardiac output is defined as the amount of blood that is pumped out of the left (or the right) ventricle in one minute.
3. This **cardiac output** (=CO) can be easily calculated by multiplying two values; the frequency of the heart (=F) and the stroke volume (=SV): Frequency*Stroke Volume = Cardiac Output.	4. The **frequency of the heart** is the number of times the heart beats every minute. At rest, when the body is not exercising, it is about 60-80 beats/minute.
5. The **stroke volume** is the amount of blood that is pumped out of a ventricle with every beat. This is, again at rest, about 70 ml.	6. Suppose that the heart beats at 70 beats/min and that the stroke volume is 70 ml; then the cardiac output is: 70 b/min * 70 ml = 4900 ml (or approximately 5 liters/min).
7. Eh! Wait a minute! **FIVE LITRES per MINUTE??** Yes, this is absolutely true; at rest, a normal heart in a normal size adult beats about 5 liters/min.	
8. **Just think about it**; here is a 1-litre bottle of water. Multiply this with 5, then, this is the amount of blood that **one** ventricle pumps every minute. And then, there is a second ventricle, which also pumps the same amount of blood, so, the two hearts together pump **10 LITERS** every minute!!!	

9. And this was at rest. When the body exercises, it will need more blood and the heart provides for this. Then, the heart has to beat faster (the **frequency** increases) and the force of contraction increases (to be discussed later). Increase in contraction force will increase the **stroke volume**.	
10. Therefore, as both the frequency and the stroke volume increase (in both ventricles!), this will easily increase the cardiac output (in each ventricle) to, for example, 15 litres/min.	11. Just to give you an idea of how much all this really is; go to kitchen and open the tap wide open. Try to fill a bucket (typically 10 litre) in one minute!

B. Major difference between the right heart and the left heart:

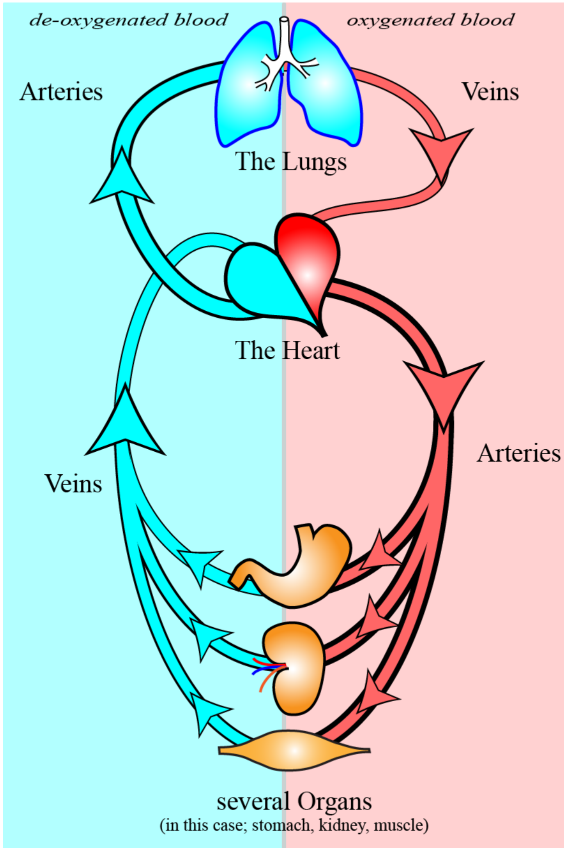
1. The behavior of the heart and the flow of blood during systole and diastole is very similar in the **right** and the **left** heart.	2. The valves work near simultaneously in closing and opening; both AV-valves close and open simultaneously and so do the SL-valves.
3. The amount of blood that is pumped out (= the stroke volume, i.e., SV) is also very similar in each ventricle.	4. The big difference between the right heart and the left heart is the blood **pressure** in the two ventricles.



5. As shown in the diagram, during systole, the pressure in the left ventricle increases from 0 to 120 mmHg.	6. But in the right ventricle, the increase is much less, and reaches a maximum of "only" 25 mmHg.
7. This difference is caused by the fact that the wall of the left ventricle is **much thicker** than that of the right ventricle.	8. Therefore, the left ventricular contraction is **much stronger** and the pressure achieved **much higher**; i.e., 120 mmHg instead of 25 mmHg.

C. Why is the blood pressure in the left ventricle so much higher than in the right ventricle?

<table>
<tr><td>1.

Remember the two circulations in our body? The pulmonary and the systemic circulation?</td><td rowspan="4">
</td></tr>
<tr><td>2.

So, the right heart collects (de-oxygenated) blood from all the organs in the body and pumps it to the lungs for oxygenation. And the lungs are literally next-door to the heart, both inside the chest. Small difference in height.</td></tr>
<tr><td>3.

But the left heart collects the oxygenated blood from the lungs and pumps it to ALL the organs in the body.</td></tr>
<tr><td>4.

All the organs, from the brain in your head all the way to the muscles in your legs and muscles.</td></tr>
<tr><td>5.

So, much bigger distances and, when you stand up on your feet, much bigger difference in height, and thus in pressure.</td><td>6.

That’s why the blood pressure in the systemic circulation has to be much higher than in the pulmonary circulation, approx. 120/80 mmHg.</td></tr>
</table>

B.4.5. Cardiac Sounds and Murmurs

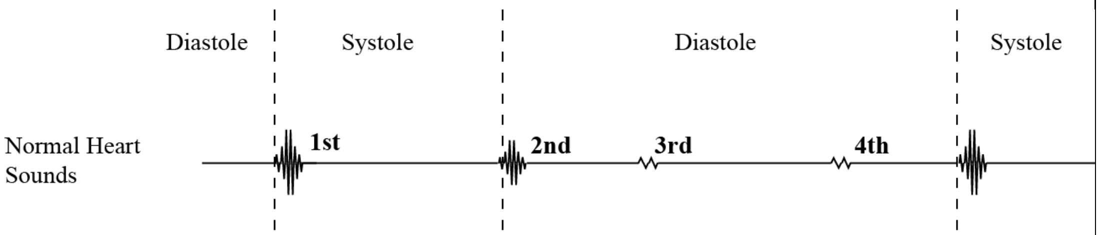
A. Heart (Cardiac) Sounds:

<table>
<tr>
<td>1.

The heart sounds are the sounds (=noise) that the heart makes while it is beating. They can best be heard using a stethoscope with the diaphragm located on the skin of the chest in ‘front’ of the heart.</td>
<td>
</td>
</tr>
<tr>
<td>2.

The first two sounds from the heart are the loudest: the closing of the valves causes these sounds.</td>
<td>3.

The first heart sound is caused by the closure of the AV-valves (at the beginning of the systole).

The second heart sound is caused by the closure of the SL-valves (at the end of the systole).</td>
</tr>
<tr>
<td colspan="2">

Listen: https://depts.washington.edu/physdx/audio/normal.mp3</td>
</tr>
<tr>
<td>4.
If you listen carefully, you may also detect two more sounds: the 3rd and the 4th heart sound.</td>
<td>5.

The third heart sound is caused by the flow of blood during the rapid filling phase.

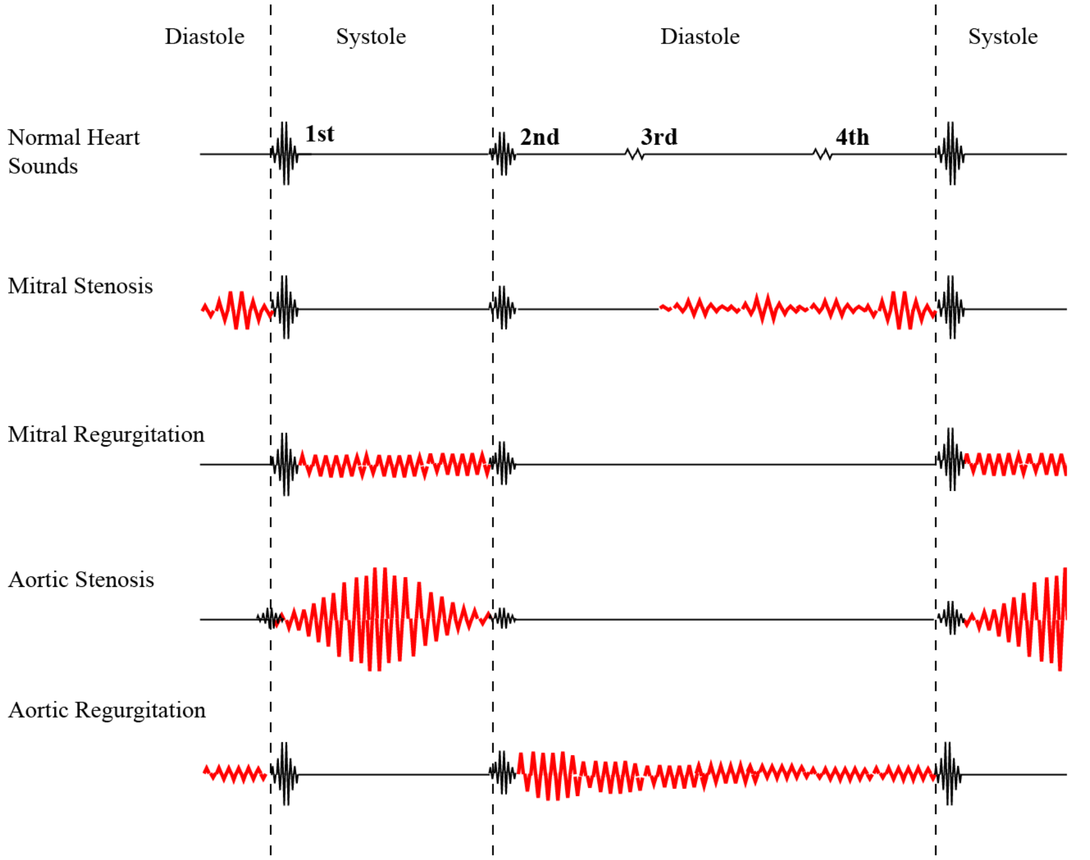
The fourth heart sound is caused by the flow of the blood during the active filling phase.

Both these two sounds are much softer that the first two sounds.</td>
</tr>
</table>

B. Cardiac Murmurs:

1. Murmurs are abnormal sounds, in this case originating from the heart (i.e. cardiac), and are often (but not always) caused by valve deficiencies.	2. There are two possible deficiencies of the valves: a. valvular **stenosis** b. valvular **regurgitation** Valvular regurgitation is often also called valvular **incompetence**.
3. In the case of a valvular stenosis, the valves do not **open** properly. In that case, the opening is smaller, and the blood rushing through the valves will cause more noise (= murmur).	4. In the case of a valvular regurgitation (or incompetence), the valves do not **close** properly. Therefore, when these valves should be closed, blood will leak (= regurgitate) through the valves, which also creates a murmur.
5. Depending upon a) the valve and b) the type of defect, a systolic or a diastolic murmur can occur.	6. For example; a mitral valve incompetence, will cause regurgitation when it should be closed, which is during cardiac systole and therefore will cause a **systolic** murmur.
7. A mitral valve stenosis on the other hand, which means it does not open properly, which should be the case during diastole, will then cause a **diastolic** murmur.	8. An aorta stenosis (does not open properly) will cause a murmur when blood should flow through it, which is during the ejection phase, and is therefore a **systolic** murmur.
9. Note, by the way, the diamond shape of this systolic murmur in the diagram, which is caused by the initial increase, followed by the subsequent decrease in the left ventricular pressure.	10. An aortic regurgitation occurs when the valves don’t close properly. This occurs of course during the diastole. This murmur indicates that blood is flowing from the aorta back into the left ventricle!

11.	12.
By the way, why are we only discussing the valves in the left heart and not those in the right heart?	*Because the pressure differences in the right heart are much lower than in the left heart. Therefore, although these valves could also develop stenosis or incompetence, the blood flow is much lower, the murmur is much softer and often can not be detected with a stethoscope.*



C. Some Additional Points:

1.	2.
So, when thinking of these cardiac murmurs, it is crucial to think of the phases of the heart.	So, if there is a mitral stenosis -> then not good opening during diastole -> so murmur during diastole

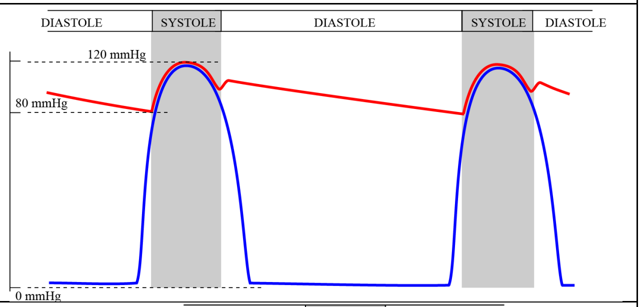
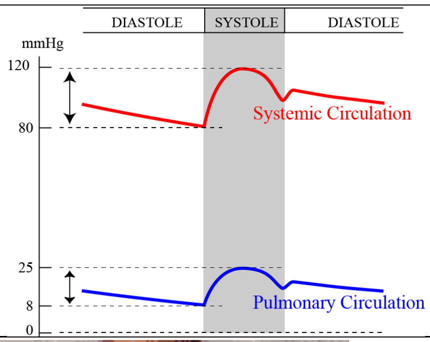
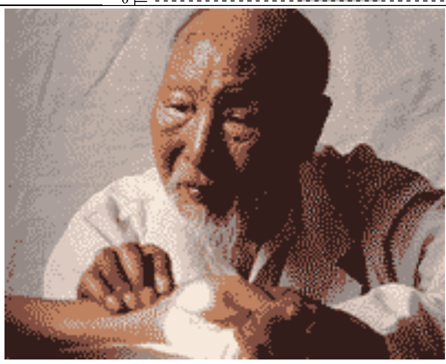
3. But if there is mitral incompetence -> poor closure of the mitral valve -> so then a murmur during systole.	4. You can apply the same reasoning for the aorta valves (with opposite results!).
5. By the way, these are not the only murmurs that can be detected, with a stethoscope, from the heart. The heart can also produce other types of murmurs but these will be discussed in another chapter (*coming …*).	6. By the way, it is understandable that the SL-valves, when they close, produce a heart sound (the 2nd sound). But the AV-valves are very weak and soft tissue; how come they make such a sound when they close?
7. Looking and listening to a parachute gives the answer! When somebody jumps from a flying plane with a parachute, after a few seconds, he (or she) will open his or her parachute.	8. As the air flows into the parachute, as you may know, suddenly, the 'skin' is filled with air and expands with a bang! (*link*)
9. The same thing is happening with the AV-valves.	10. As the AV-valves start to close, blood will flow into the cusps of the valves and pushes the valves with a bang against each other. This is the first heart sound!

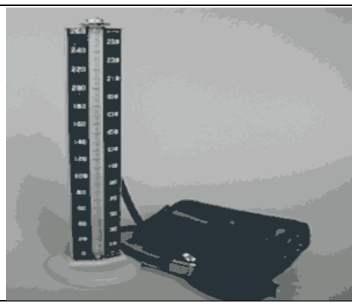
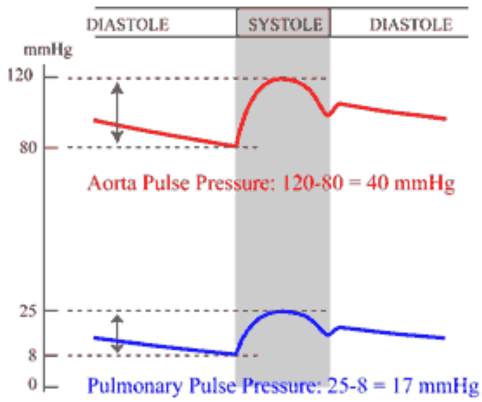
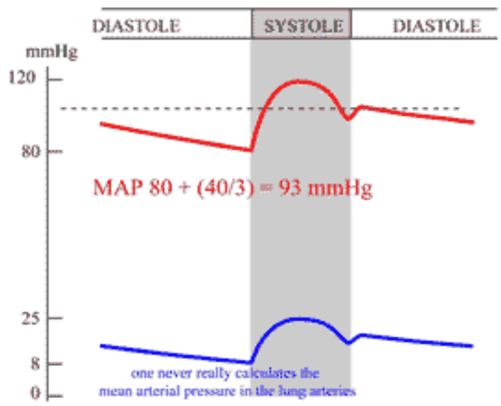
Link: https://freesound.org/people/Huggy13ear/sounds/138976/

B.5.1. The Arteries

Purpose: The arterial system consists of all the blood vessels that transport blood from the heart to the tissues. These vessels are located in a) the systemic circulation and b) in the pulmonary circulation.

A. Transportation of Blood

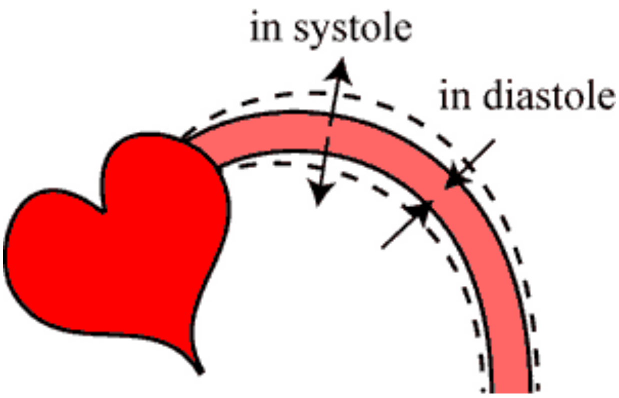
1. The task of the arterial system is actually very simple; transport blood from the heart to the tissues. Because the heart ejects blood at a high pressure, from the ventricles into the main arteries (aorta and pulmonary artery), and because the pressure in the tissue is low, blood flows easily from high to low pressure	2. The blood flow in the major arteries is **pulsatile**; that is, the blood flow and its pressure increase with every heartbeat. Between the beats, the pressure decreases.
3. The highest value is the **systolic** pressure and the lowest value is the **diastolic** pressure. Typical values are 120 mmHg for the systolic pressure and 80 mmHg for the diastolic pressure (in the aorta). This is written as 120/80 mmHg.	
4. You can feel this pulsatile action of the arteries when you feel the pulse, for example in the wrist. This has been used for centuries!	
5. Remember that in the pulmonary system, the blood pressures are much lower than in the (large) systemic circulation. In the pulmonary system, the blood pressures are typically 25/8 mmHg.	

6. When one talks about the blood pressure, one really talks about the blood pressures in the systemic circulation, not in the pulmonary system.	7. By the way, the systolic and the diastolic values, which together are known as the “blood pressure”, are two of the most important **vital signs.**
8. What are actually the “**Vital Signs**”? 1. consciousness 2. body temperature 3. blood pressure 4. heart rate 5. respiration rate	9. How do you measure the blood pressure? The blood pressure can be measured directly (but this is difficult, messy and bloody as you have to stick a needle inside an artery) or **indirectly**.
10. Indirectly, you can measure the blood pressure with a **sphygmomanometer** (awful word!) and a stethoscope (sphygmo = pulse and manometer = pressure recording).	
11. Another important value is the **Pulse Pressure**: this is the difference between the systolic pressure and the diastolic pressure. Example: if the systolic pressure is 120 mmHg and the diastolic pressure 80 mmHg, then the **pulse pressure** is 120-80 = 40 mmHg.	
12. Sometimes (not often), instead of the systolic and diastolic blood pressure, an average pressure is used. This is the Mean Arterial Pressure (=MAP) and is equal to the Diastolic Pressure + the Pulse Pressure divided by 3. Example: Systolic P = 120 mm Hg and Diastolic P = 80 mmHg, then the MAP = 80 + (120-80)/3 = 80 + 13 = 93 mmHg.	

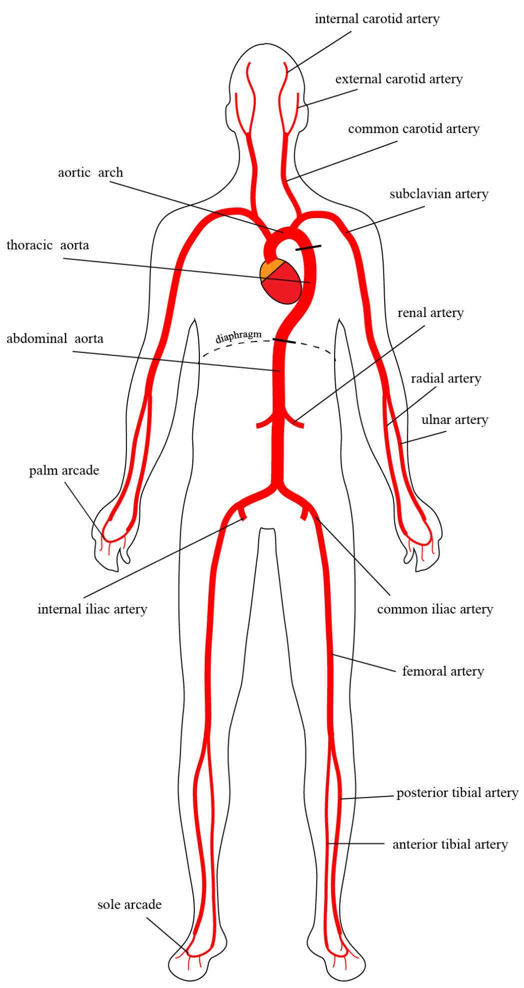
B. Some common mistakes and problems:

1. The blood pressure is always given as systolic/diastolic. Example: 120/80 mmHg. Never the other way around! (i.e., 80/120 mmHg). That would be extremely confusing.	2. Students often think that a blood pressure is always stable and fixed at 120 mmHg systolic and 80 mmHg diastolic pressure. This is not the case at all. The blood pressure varies considerably between every person and from moment to moment, from beat to beat!
3. Students often think that the blood pressure declines a lot from the aorta to the arteries that are far away such as the arteries in the foot. This is not true. The decrease in blood pressure along the arteries is actually very small, only a few mm Hg. A significant decrease in blood pressure occurs at smaller vessel sizes and especially in the arterioles (see next page).	**4. Accuracy:** Manual measurements of the blood pressure (with the sphygmomanometer) are not very accurate. Therefore, values are often rounded to the nearest 2-5 mmHg. So, a reading of 124.5/76.3 mmHg is nonsense. More realistic in this case would be: 125/75 mmHg.

C. A Detail: Windkessel.

Some teachers like to talk about the windkessel function of the aorta. The word “windkessel” is from German and means "air-chamber". The windkessel function relates to the fact that when the blood is ejected from the left ventricle into the aorta, there is then such an increase in blood pressure that the walls of the aorta will expand. After ejection, during diastole, when the aortic valves have closed, the walls of the aorta, because they are elastic, will constrict and thereby push the blood further down the arteries. This action works like a second ‘pump’ but its magnitude is often exaggerated. This is not really an important factor.	

D. The arteries in the (large) Systemic Circulation:

<table>
<tr><td>1.
Although strictly not physiological, but rather anatomical, I have plotted for your convenience the major arteries in the human body in this diagram.</td><td rowspan="4">The Systemic Arteries

</td></tr>
<tr><td>2.
The first artery is the aorta, the largest, biggest and longest artery in the body. It carries blood from the heart (the left ventricle), first along an arch (the aortic arch), then onwards through the thoracic aorta, perforating the diaphragm, into the abdominal cavity where it is called the abdominal aorta.</td></tr>
<tr><td>3.
From the aorta, numerous arteries emerge. From the arch, the common carotid arteries (to the brain), the subclavian arteries (to the shoulders and the two arms). And in the abdominal aorta, numerous arteries branch out to all the abdominal organs including the kidneys (renal arteries).</td></tr>
<tr><td>4.
Finally, low in the abdomen, the aorta splits into two iliac arteries, which, in the upper leg form the femoral artery, which, in the lower legs, splits into the anterior and posterior tibial arteries.</td></tr>
<tr><td>5.
Note that both in the hands and in the feet, the vessels develop into an arterial arcade to perfuse the muscles of the palms, soles, fingers and toes.</td><td>6.
Of course, this is only a very rough overview. There are many, many, more vessels coming out of these vessels. This is only an overview of the major arteries!</td></tr>
</table>

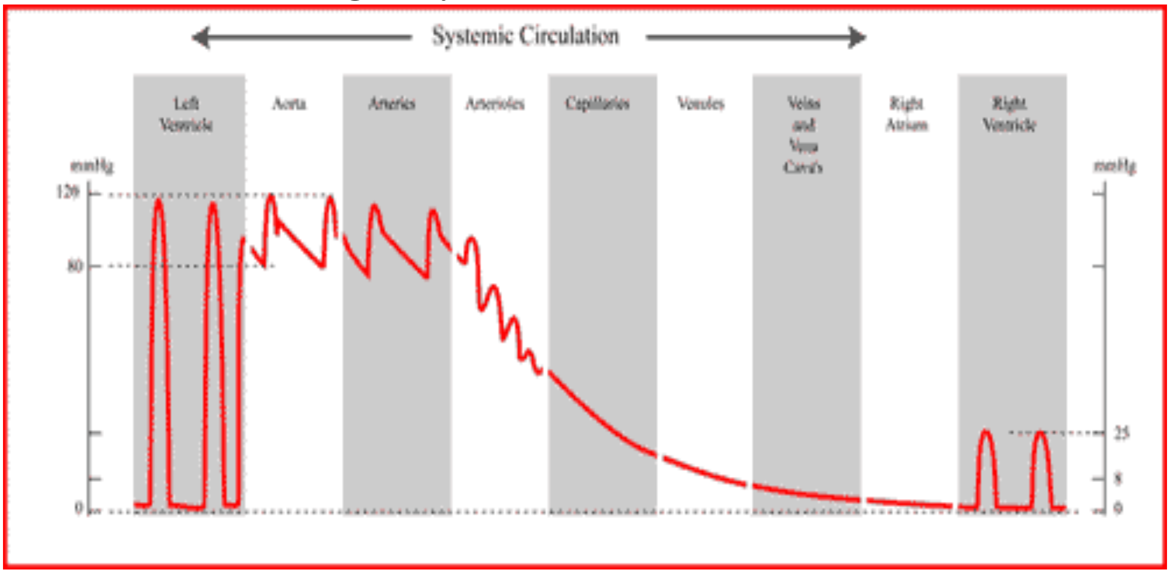
B.5.2. The Arterioles

Purpose: The arterioles are the small arteries that connect the large arteries to the capillaries and that play an important role in distributing the blood from the heart (= the cardiac output) to the organs.

A. Introduction:

1. All arteries (large and small) have a thick muscular coat with which the vessel can dilate or constrict. This is called **vasodilatation** and **vasoconstriction** (vaso = vessel).	2. As the blood flows through the arterial system to the tissues, the blood pressure will decrease. But the decrease is not uniform.
3. Throughout the large arteries, the blood pressure hardly decreases at all (only a few mmHg).	4. When the blood flows through the smaller vessels (arterioles), then the resistance increases and the pressure drops a lot.
5. **Arterioles** are the most important vasoconstrictor and vasodilators in the arterial system.	6. After the arterioles, the blood pressure has dropped to approximately 30-35 mmHg and is no longer pulsatile (= no more systolic / diastolic oscillations).

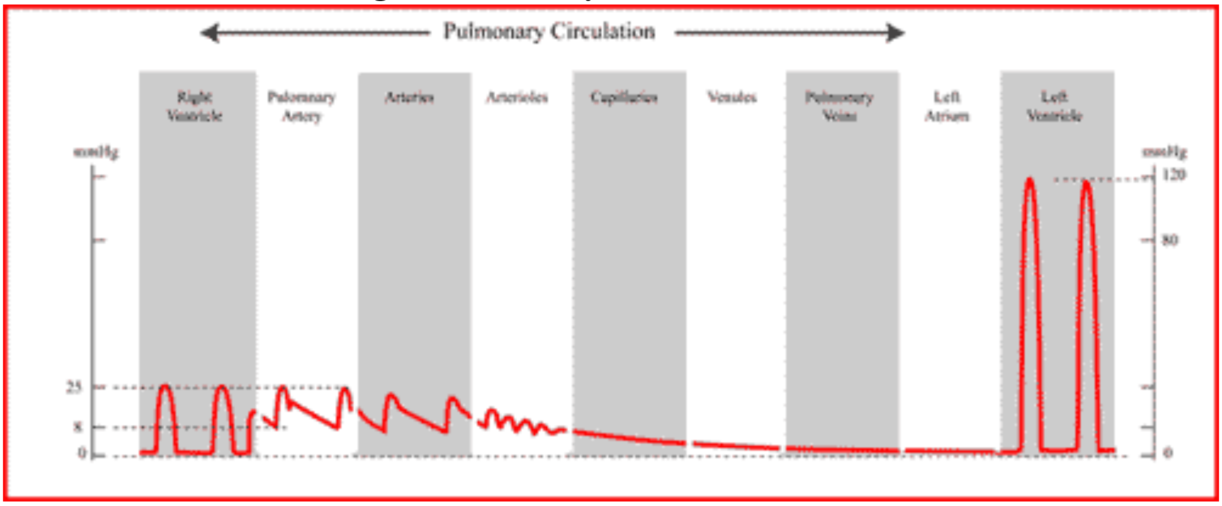
B. Blood Pressure along the Systemic Circulation:



1. This diagram shows the blood pressure from the left ventricle all the way to the right atrium.	2. In the **left ventricle**, the blood pressure varies between about 0 mmHg (diastole) and 120 mmHg (systole).

3. In the **aorta**, the blood pressure varies between about 120 mmHg (systole) and 80 mmHg (diastole). This variation in pressure is called pulsatile.	4. In the **large arteries**, the blood pressure also varies between about 120 mmHg (systole) and 80 mmHg (diastole). Not much different from the aorta; only slightly lower.
5. In the **arterioles**, the blood pressure drops a lot, to about 20-30 mmHg, because the vessels are relatively narrow. In addition, the pulsatile flow gradually disappears and the blood flow becomes non-pulsatile.	6. In the **venules, veins, large veins**, vena cava superior and inferior, the blood pressure continues to drop. The lowest pressure in the systemic circulation is found when the blood enters the right atrium (close to 0 mmHg).

C. Blood Pressure along the Pulmonary Circulation:



1. This diagram shows the blood pressure in the pulmonary system, from the right ventricle all the way to the left atrium.	2. In the **right ventricle**, the blood pressure varies between 25 and 0 mmHg (much lower pressures then in the left ventricle).
3. In the **pulmonary artery**, the blood pressure is pulsatile between 25 and 8 mmHg.	4. The blood pressure decreases a lot in the **pulmonary arterioles,** just like in the systemic circulation, and becomes non-pulsatile.
5. The pressure continues to decrease gradually along the **pulmonary venules and veins**.	6. The lowest pressure in the pulmonary circulation (about 0 mmHg) is found in the **left atrium**.

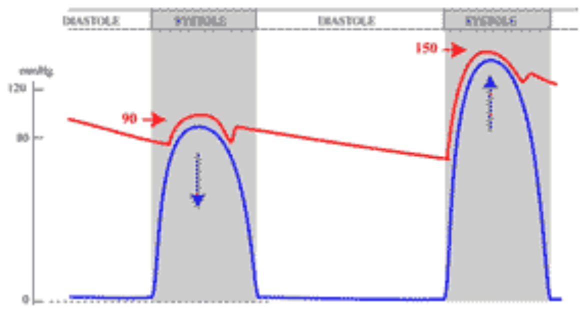
D. Cardiac Distribution:

1. The most important function of the arterial system is to distribute the blood through the body. This is called the **cardiac distribution** and the big question is always how much blood goes to which tissues.	2. Some organs need more blood than others; major users are the **kidney** (25%) and the **brain** (15%) for example. (% of the cardiac output; which is, at rest, about 5L/min).
3. Some organs or tissues need a lot of blood when they are **active** but not a lot when they are quiet. Examples are the **gut** (needs a lot of blood after a meal) and the skeletal **muscles** (during exercise).	4. The amount of blood that flows to an organ is determined by the **activity** of that organ. If the organ works hard, then the arterioles feeding that organ will dilate and more blood will flow to it. If the organ works less, then the arterioles will vasoconstrict and less blood will flow to it.
5. So, the distribution of blood is determined by **constricting** vessels (=arterioles) to some tissues and **relaxing** (dilating) vessels leading to other tissues, as determined by their respective needs.	6. So, for example, after a **meal**, more blood is needed in the intestines and therefore the intestinal arterioles will dilate, diverting more blood towards the intestines. The same would apply with **exercise**; then the skeletal arterioles will dilate.
7. But this could lead to a **conflict**. If one exercises after a meal then both gut and muscles need blood. There might then **not be enough** for all the organs in the body; like for the brain. This is one cause of **fainting**.	8. That is why your **mother** did not allow you to swim after lunch; the gut would need more blood, the muscles will need more blood and there might be not enough for your brain; you might then faint which, in a swimming pool, is quite dangerous!

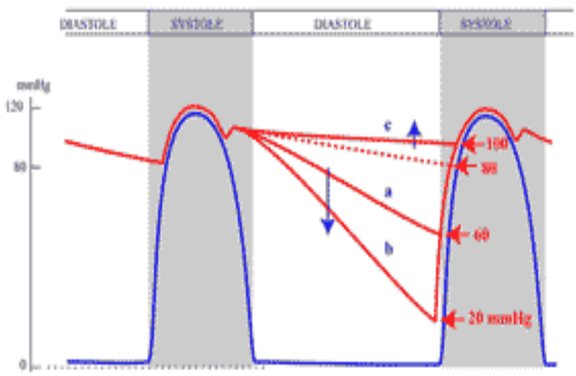
E. What determines the Blood Pressure?

1.
What determines the height of the **systolic** blood pressure?

Mainly the **contraction force** of the heart. If the ventricle contracts weakly then the contraction strength will be lower, the ejection will be less and the maximum pressure achieved will decrease. If, however the contraction is very strong, then the opposite will occur and the systolic pressure will increase (this occurs for example during exercise).

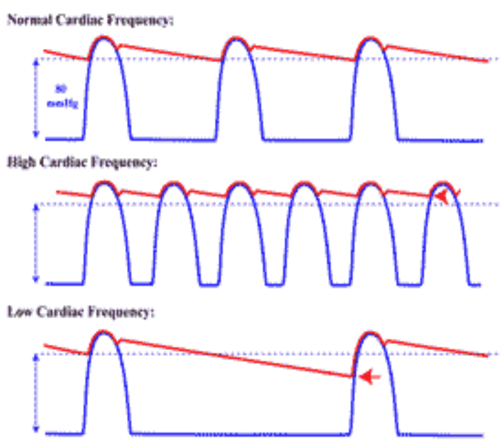


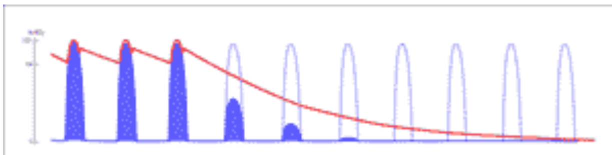
2.
What determines the height of the **diastolic** pressure?
This is, mainly, determined by the flow of blood into all the organs. As you saw previously, this is determined by the **arterioles** in the body. All these arterioles **resist** to various degrees the flow of blood. Together, this is called the peripheral resistance (*What is Peripheral Resistance? See section F*).



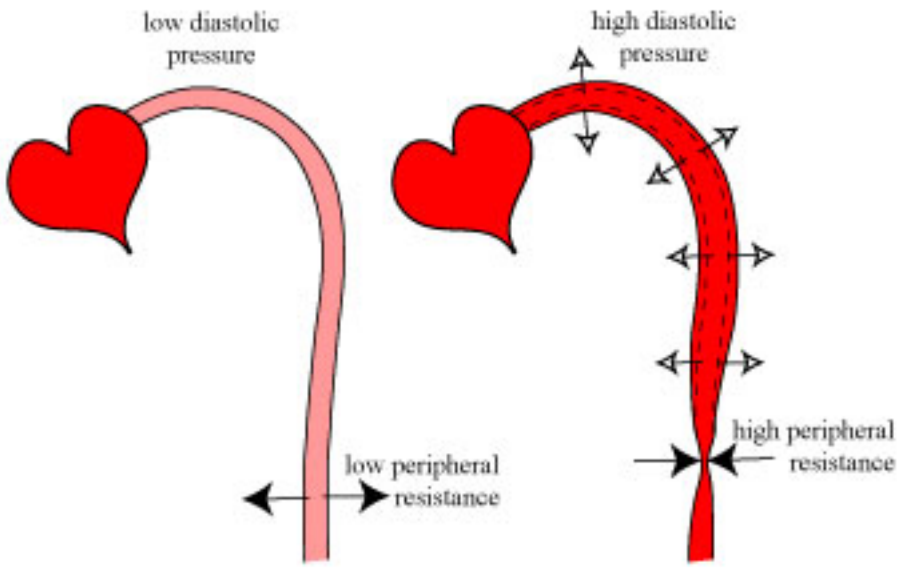
3.
In the diagram, if the resistance is very high (c), the pressure decrease will be very slow during diastole and the diastolic pressure will be high. If, however, the peripheral resistance is very low (a or b), the decrease in blood pressure will be very high and the diastolic pressure very low.

4.
Interestingly, the frequency of the heart has also an influence on the **diastolic pressure**. This is because the frequency of the heart determines the amount of time the blood is allowed to flow away in the periphery during the diastole.



5. If the heart frequency is high, then there is less time before the next systole and therefore the diastolic pressure will be higher.	6. If, however the heart rate is low, then there will be more time for the pressure to drop (before the next heart beat) and therefore the diastolic pressure will be lower (see red arrow).
7. **Why don't we die all the time?** This leads us to my favorite subject! Why don't we die all the time? Better said, what would happen if the heart (suddenly) stopped contracting? As shown in the diagram, the blood pressure will continue to decrease and reach **zero** quite quickly (within a few minutes). Why don't we die? Because the heart will save us every time from this fatal decrease in blood pressure. We are in danger of dying all the time but we are **saved** every time that the heart beats!	

F. What is "Peripheral Resistance"?



1. Some students have difficulty in understanding the concept or the idea of the "peripheral resistance".	2. We all know that as the blood flows through the blood vessels, it is "resisted" by the vessel wall, especially in the arterioles. If the vessel is narrow, the resistance is high; if the diameter is very large, the resistance is very low.

3. All the arterioles together could be considered as one giant “resistance”. If they all (vaso) constrict, the peripheral resistance will be high, and the blood pressure before the resistance will increase.	4. If, however, all the arterioles vasodilate, then the resistance will be very low and the blood pressure (especially the diastolic pressure) will decrease.
5. So, why is this resistance called “peripheral”?	6. Because it is “peripheral” (away) from the heart (which is considered “central”). That’s all!

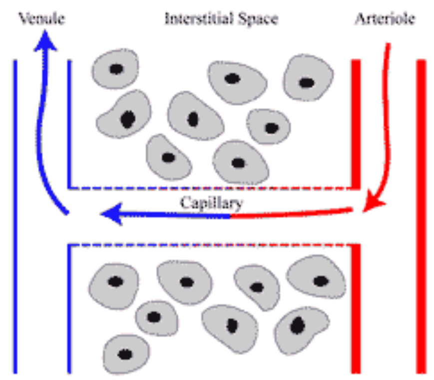
B.5.3. The Capillaries

Purpose: The function of the capillaries is to transport nutrients and oxygen from the blood to all the tissues in the body and to collect waste from these tissues back into the blood.

A. Hydrostatic Pressure in the capillaries:

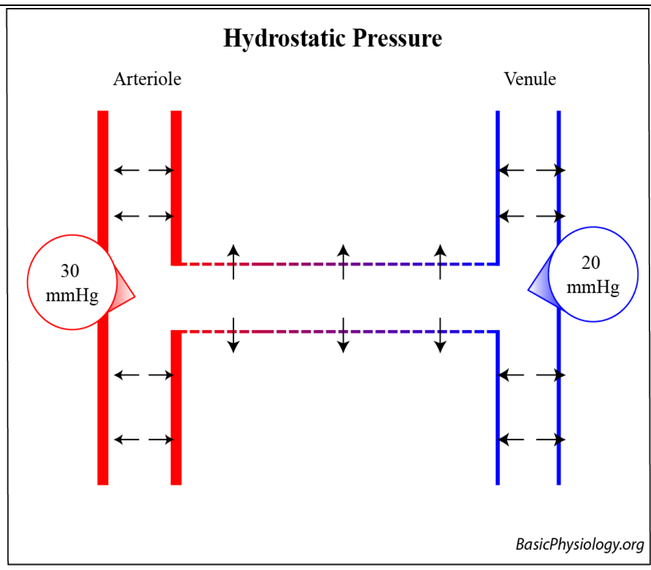
1.
The capillaries do not have a muscular wall. In fact, they only have a single layer of cells. These are called **endothelial** cells.

2.
Because of this thin wall, water and small molecules can easily filtrate (=seep) through this porous layer of cells. But the capillary membrane works as a filter; large molecules and cells **cannot** pass through the membrane.



3.
The blood pressure in the arterioles, at the start of the capillaries, is typically 30 mmHg. Remember that the blood pressure has decreased along the arterial system from about 120/80 to 30 mmHg (because of the arterioles). Furthermore, the blood flow is no longer pulsatile. This pressure is called the **hydrostatic pressure**.

4.
At the beginning of the capillary therefore, the hydrostatic pressure is 30 mmHg. But at the end of the capillary, this hydrostatic pressure has decreased to about 20 mmHg.



5.
Why? Because of the resistance of the capillary wall to the blood flow, just like in the arterioles.

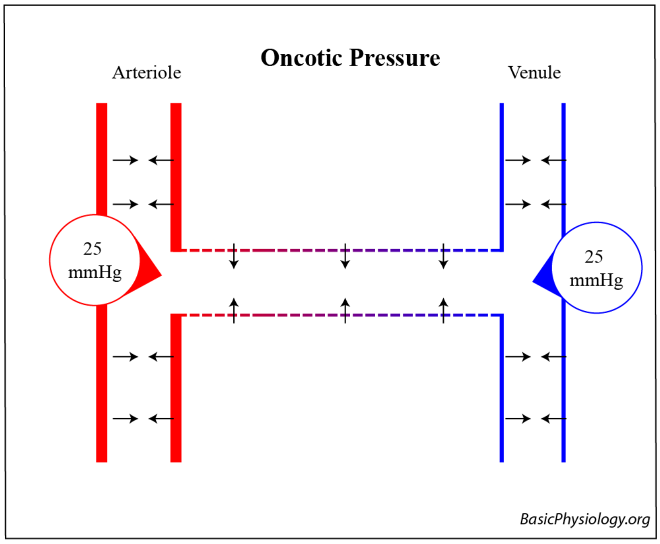
6.
At the same time, **outside** the capillaries, in the interstitial space, the pressure is much lower; about 0 mmHg.

7.
Therefore, the pressure difference (=**gradient**) between inside and outside the capillary would be 20-30 mmHg. This is quite a lot.

8.
In fact, if there were nothing else, we would quickly loose all our water (5 litres blood) into the larger interstitial space (typically 10-15 litres); we would then develop massive **oedema** and die of cardiovascular shock.

9.
Obviously, this does not happen and this is due to the **oncotic** pressure and the **capillary exchange system**.

B. Oncotic Pressure in the capillaries:

1. The **oncotic** pressure is an **osmotic** pressure. This is because the capillaries allow the filtration of water and small molecules but not of large molecules (such as **albumin**). If particles cannot pass a wall but water can, then water is transported and this is **osmosis**. *(Remember osmosis? A.2.3. Passive Transport Systems)* 2. The height of the **oncotic pressure** is determined by the number of particles that cannot filtrate through the membrane. In general, this is typically about 25 mmHg.	
3. Furthermore, in contrast to the hydrostatic pressure, the oncotic pressure is **constant** throughout the length of the capillaries.	4. Now, we are going to 'play' these two pressures against each other!
5. Remember that the **hydrostatic pressure** is a pressure from inside the capillary to the outside; it '**pushes'** the water to go out of the capillary.	6. The **oncotic pressure** works in the **opposite** direction; it is a '**sucking'** pressure. It absorbs water from outside to inside the capillary.

C. The Capillary Exchange System: (also called the Starling-exchange system):

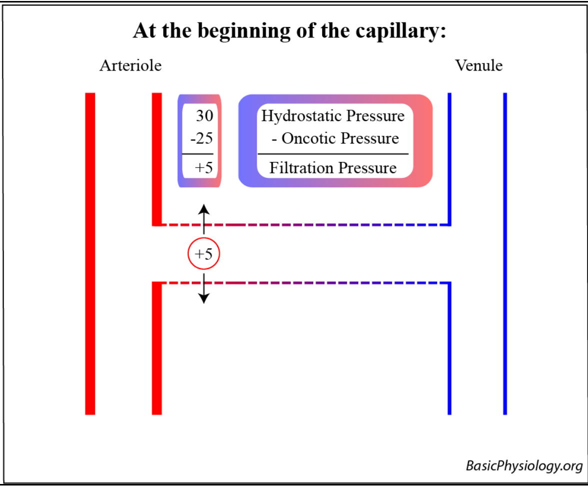
1. Now it gets interesting!	2. There are two pressures influencing the flow of fluid inside the capillaries.
3. The hydrostatic pressure pushes the blood fluid out of the capillaries.	4. And the oncotic pressure 'sucks' the fluid from outside back to the capillaries!
5. You can now calculate the pressure difference between the two pressures: Hydrostatic Pressure – Oncotic Pressure = **Filtration pressure**.	6. So, at the beginning of the capillary, the filtration pressure is: 30-25 = 5 mmHg.

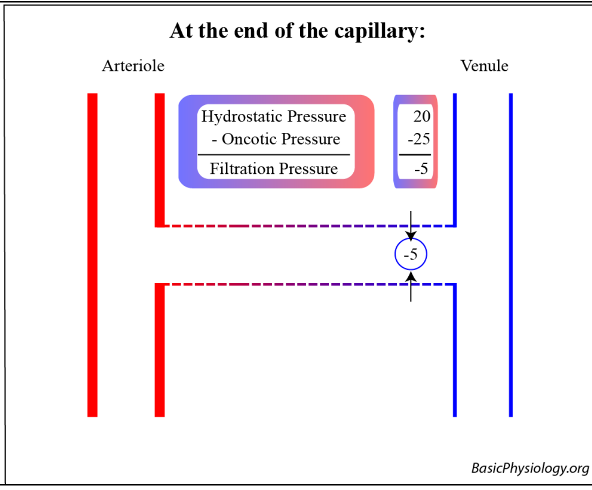
7.
This means, that some water will flow from the inside of the capillary to outside in the interstitial space.

However, this is at the beginning of the capillary.

8.
At the **end** of the capillary, things have changed. The hydrostatic pressure has **decreased** (because of the capillary resistance).

Now, at the end of the capillary, the hydrostatic pressure has decreased to about 20 mmHg.



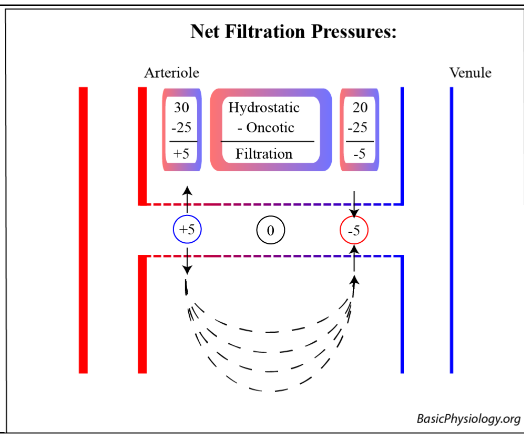


9.
But the oncotic pressure has **not changed** at the end of the capillary. This is because the number of particles that are unable to cross the capillary membrane has not decreased (they could not get out; remember?).

10.
So, at the end of the capillary, the hydrostatic pressure (20 mmHg) is **less** than the oncotic pressure (25 mmHg).

11.
The net filtration pressure is now negative (20-25 = - 5 mmHg) which means water is **reabsorbed** ('sucked') into the capillary.

12.
In conclusion, the water that leaves the capillaries at the beginning (close to the arterioles) is now reabsorbed at the end of the capillaries.



13.
Because the water that goes out contains (small) nutrients and dissolved oxygen, this will 'automatically' flow to the cells. At the same time, water from the cells that contain waste and CO2, will automatically flow back into the capillaries. The water at the beginning is **exchanged** with water at the end; hence the **name** of the system (exchange system!).

D. Some technical details:

1. The oncotic pressure is determined by the size of the dissolved particles that cannot pass the capillary membrane. This is approximately 50,000-60,000 molecular weights. This means that all the large proteins and all the blood cells cannot pass the membrane. The most common protein that cannot pass the membrane is **albumin** (molecular weight 69,000).	2. In the description above, we assumed that the **interstitial pressure** was 0 mmHg. Likewise, we also assumed that the **oncotic pressure** in the interstitial space is also 0 mmHg. But both these assumptions are not always true. For example, in the gut, after a meal, there are many food particles in the gut interstitial space.
3. If the interstitial hydrostatic and/or oncotic pressure are not zero, then one should first calculate the **real hydrostatic pressure gradient** (= the difference between the blood pressure and the interstitial pressure) and the **real oncotic gradient** (= the difference between the blood oncotic pressure and the interstitial oncotic pressure) before calculating the filtration pressure. (See example ->).	Example: *Hydrostatic pressure gradient:* Blood hydrostatic pressure = 32 mmHg - Interstitial hydrostatic pressure = 3 mmHg Real hydrostatic pressure gradient = 29 mmHg *Oncotic pressure gradient:* Blood oncotic pressure = 25 mmHg - Interstitial oncotic pressure = 5 mmHg Real oncotic pressure gradient = 20 mmHg ***So***: the net filtration pressure is 29-20 mmHg = ***9 mmHg***
4. The hydrostatic pressure is not always the same in all parts of the body. It is about the same, everywhere, when a person is lying flat. However, when a person is standing, the blood pressure in the legs is higher because of the weight of the blood column (an additional 5-10 mmHg).	5. The permeability of most capillaries works in the way described above. However, there are also capillaries in the body that are either much more permeable (such as the **fenestrated** capillaries in the gut and the kidneys and the **sinusoidal** capillaries in liver and bone marrow) or are much less permeable (such as the **blood brain barrier** in the brain).

E. Pathology: Oedema (the Americans say "Edema")

1. The capillary exchange system is not only important in normal daily life to keep our cells alive. The system also explains when something goes wrong and **oedema** (= tissue swelling, also spelled Edema) develops.	2. There are essentially three situations when something goes wrong in this system and oedema develops: • when the Oncotic Pressure becomes too **low** • when the Hydrostatic Pressure becomes too **high** • when the capillary membrane becomes too **leaky**.
3. **Oncotic Pressure** is too low. This is the situation when the amount of particles in the blood, that cannot pass the capillary wall, becomes too low. This is usually the case with albumen. **Albumen** is the most common protein in our blood. In the case of malnutrition (=chronic lack of food), the blood albumen is used for energy. This will decrease the albumen blood concentration, and hence the oncotic pressure.	4. Therefore, instead of a value of 25 mmHg, the oncotic pressure could drop to, say, 20 mmHg. That means that more fluid will leave the capillary and less will be reabsorbed, leading to accumulation of fluid in the tissue; **oedema**! This is seen in cases of malnutrition as often seen in poor, underdeveloped, countries. Remember the small children on TV with a big belly but thin arms??? The bellies are big because they are filled with fluid (oedema in the peritoneal space (=belly), which is called **ascites**). These children are severely malnourished.
5. **Hydrostatic Pressure** is too high. When the hydrostatic pressure is too high, then again, more fluid will leave the capillary into the interstitial space. This can be caused either by a too high arterial pressure or a too high pressure in the veins. This condition often occurs when the heart is not working properly (swelling in the **ankles** for example).	6. A problem with the **capillary membrane**. If the capillary does not function properly and becomes too leaky, then the oncotic pressure will be lower (because this is determined by the amount of particles that do not cross the capillary wall). This can happen for example during an **infection**. A typical example is the sting of a bee. The bee injects a toxic substance that makes the capillary leak. This will cause a swelling at that location.

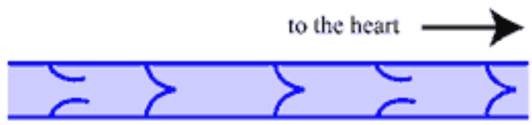
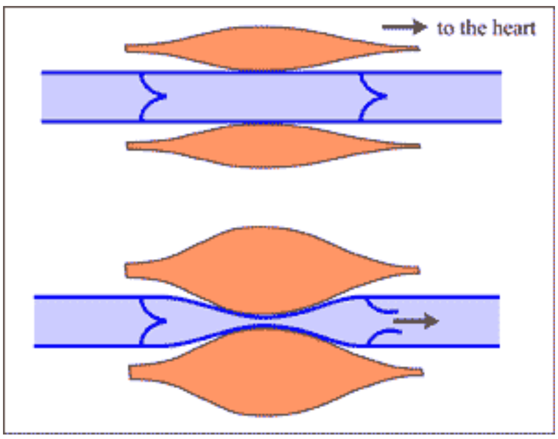
B.5.4. The Veins

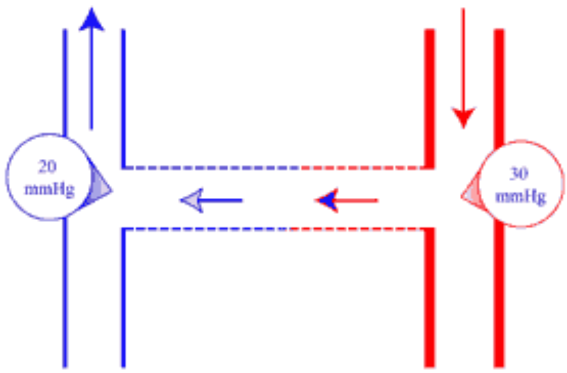
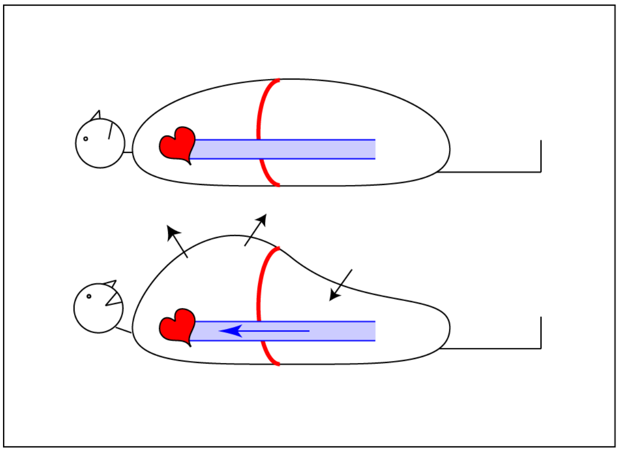
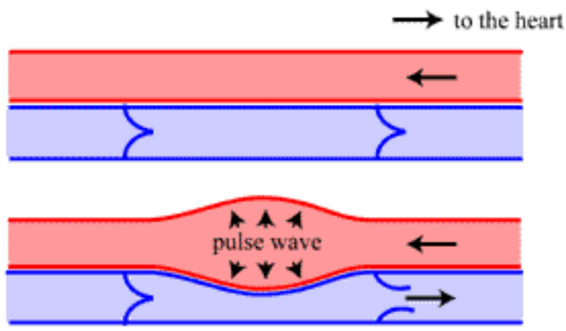
Purpose: The function of the veins is to transport blood from the capillaries back to the heart. This is the case for both the systemic (large) circulation as for the pulmonary circulation.

A. There is a problem here!

1. **The Problem:** In the arterial system there is a pump (the heart) that pumps the blood through all the arteries to the capillaries. However, there is no "venous pump" in the venous system to pump the blood back to the heart.	2. So, the problem is; how does the venous blood return to the heart? There are several factors that help in this and together they take care of what we call the **Venous Return**.
3. These are the **6** factors that help/promote the blood to flow back to the heart: 1. Valves 2. Muscle Pump 3. Capillary Pressure 4. Respiratory Pump 5. Arterial Pump 6. Cardiac Pump	4. Not all factors have the same importance. The first is the most important, no. 5 and 6 are the least important.

B. Factors that promote the Venous Return:

1. **Valves**: In contrast to the arteries, the veins have **valves**. These valves make sure that blood can flow in only one direction; towards the heart. That helps a lot!	
2. **Muscle Pump:** Probably the most important factor. When a skeletal muscle contract (which is often), the veins inside and between the muscles will be **squeezed**. This will increase the blood pressure inside the veins and make the blood flow away from the high pressure. Because of the valves, the blood will only flow in **one direction**, towards the heart. Since skeletal muscles mostly contract rhythmically (such as walking, running,	

cycling), this will induce a rhythmic blood pressure in the veins and therefore a rhythmic flow of venous blood towards the heart.	
3. **Capillary Pressure:** Another factor in the venous return is the capillary pressure. At the end of the capillaries, the hydrostatic (= blood) pressure is not zero but approximately 20 mm Hg. As the pressure in the big veins is much lower, close to 0 mmHg, there is therefore a pressure gradient from capillaries to veins which will cause blood flow through the veins to the heart. That helps!	
4. **Respiratory pump** (=breathing): When a person inhales, the pressure inside the chest gets lower (becomes more negative). At that moment, the pressure in the chest is lower than in the abdomen. This will induce a flow of blood in the large abdominal vein (vena cava inferior) towards the chest. And, when a person exhales, the pressure in the chest is higher than in the abdomen, and that will stop the blood flow (note that the blood will not flow back because it is blocked by the valves in the femoral veins).	
5. **Arterial Pump**: In the body, the arteries and veins often run parallel to each other. Therefore, when an arterial pulse propagates down the artery, this will cause a local expansion (bulging) and this swelling will push against the veins. This will increase the local pressure in the veins. This pressure increase will push the venous blood towards the heart.	

6. **Cardiac Suction**: This is a very small effect that is caused by the movement of the heart during its contraction. When the heart contracts, it ejects blood into the aorta and into the pulmonary heart. This ejection is quite a force that will cause the ventricles to move away from these major arteries (action = reaction; here blood ejection is the action and the movement away is the reaction). Anatomically however, the atria are located between the root of the major vessels and the ventricles. The major vessels are fixed in the chest (actually in the mediastinum), so, as the ventricles move away during ejection, the atria will be stretched. This will cause a lower pressure in the atria and will help venous blood flow, from the vena cava's and the pulmonary veins, into the atria.

C. Some additional notes:

1. As stated before, not all factors are equally important and the order of importance is pretty much the order discussed above. The **valves** and the **muscle pump** are the most important factor whereas the arterial pulse and the cardiac suction are the least important.	2. If the valves are deficient, venous return will become more difficult. If the valves become deficient in a particular area, then that area will have a problem in its venous return (swelling, oedema etc). This is for example the case with **varicosities**. This tends to occur in those people who, by profession, have to stand a long time (shopkeepers, teachers). Over the years, the valves will slowly deteriorate, expand, and blood will pool in those areas. These are visible as ugly swellings under the skin: **varicosities.**
3. We often use our muscle pump, especially when standing, because then the blood has to flow back from the legs all the way to the heart. During normal standing, we often use muscles without noticing it, to keep our muscle pump working. This can be done by walking (teachers in front of the class), or by shaking legs etc.	4. In some situations, people are told to stand absolute **immobile**. Soldiers for example in a parade. It is then not uncommon for a soldier to **faint** (this often happens during the summer, then you see pictures of such a poor fellow lying flat on the parade grounds). The reason why this person fainted is because he has to stand absolute motionless, he is not allowed to move a single muscle, his venous return became too low, which in turn decreased his cardiac output, therefore not enough blood flowed to his brain, hence he fainted!

5. The reason why this occurs more often during the summer is that the soldier, because of the high temperature outside, develops a high body temperature (especially if they have to wear thick ceremonial clothing or wear battle gear). To get the body temperature back to normal, the circulation in the skin must open (see *Special Circulations*). But this compromises even further the cardiac distribution, leaving less blood to flow to the brain. The result is fainting.	6. The nice thing about fainting and collapsing on the floor is that this behavior often solves the problem. Before collapsing, the venous return was too much reduced because it had to pump upwards to the heart. This is about 1 meter higher than the legs. If one is collapsed and lying flat on the ground, then the legs are at the same level as the heart and it is much easier for the blood to flow back to the heart and to the brain. You can actually help by lifting the legs when the fainted person is on the floor to increase blood flow from the legs to the heart.

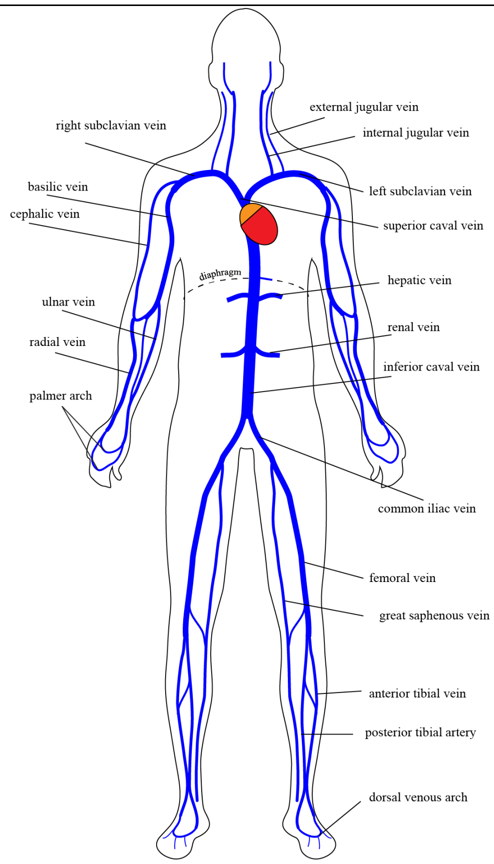
D. The Systemic Venous Tree:

1.
As with the arterial system, I will also give you here a sketch of the venous “tree”.

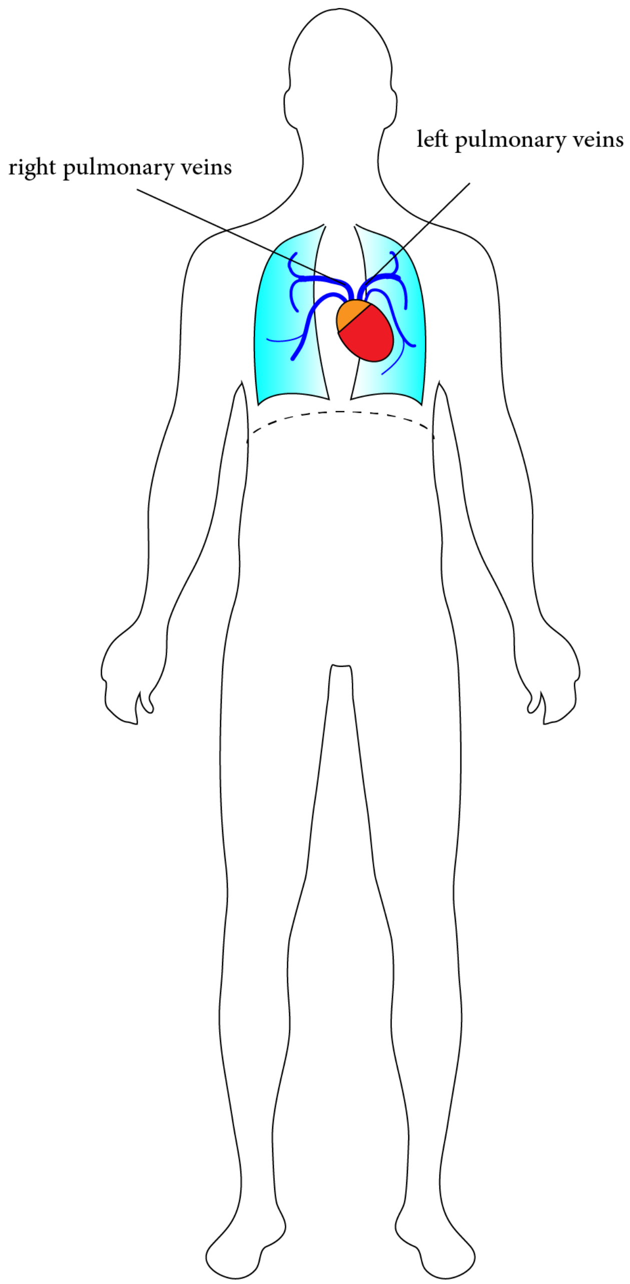
2.
The important thing here is that the venous tree is not an exact (reverse) copy of the arterial system. There are actually more vessels to help flow the blood back to the brain.

3.
In the arms and the legs, the veins are very similar to the arteries although there are, again, a few more vessels.

4.
What is really important are the major veins in the body. The superior and inferior caval veins (= vena cava superior and inferior). These are the major thoroughfares for the blood to flow back.



E. The Pulmonary Venous Tree:

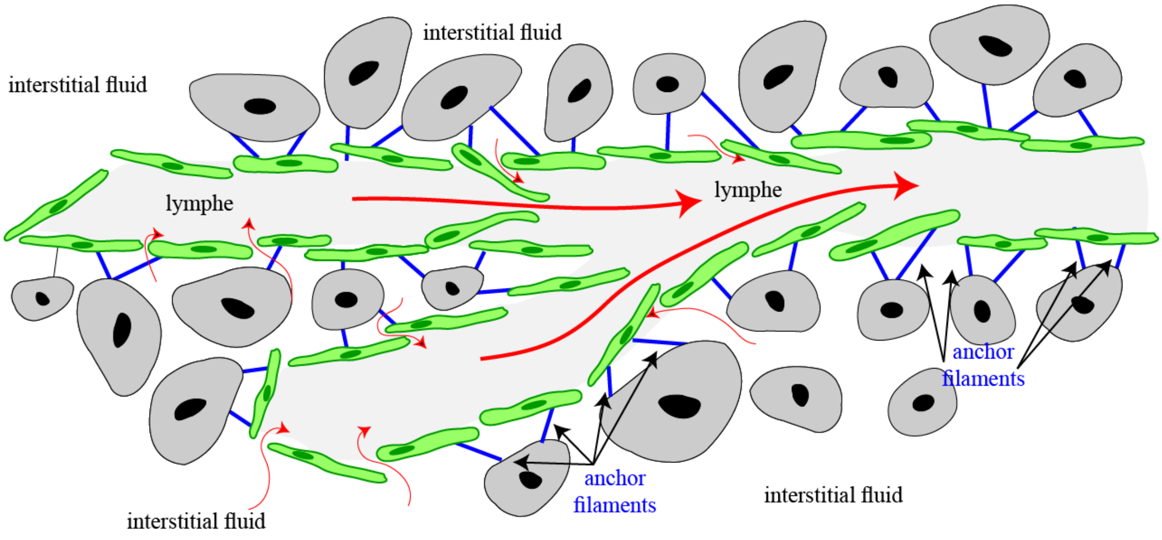
1. And this is my sketch of the veins in the pulmonary system.	
2. Again, there are more veins than arteries, just like in the systemic circulation.	
3. Noteworthy here is that, usually, two large veins run from each lung to the heart, to the right atrium.	
4. However, there are some anatomical variations between individuals. For example, in some people, the two veins from the right lung for example, merge into a single vessel before entering the right atrium.	
5. And, as with the arterial system, don't forget that these vessels, together, allow 5 litres/min blood to flow back to the atrium. And this is at rest!	

B.5.5. The Lymph Circulation

D. Why do we need a lymphatic system (= circulation)?

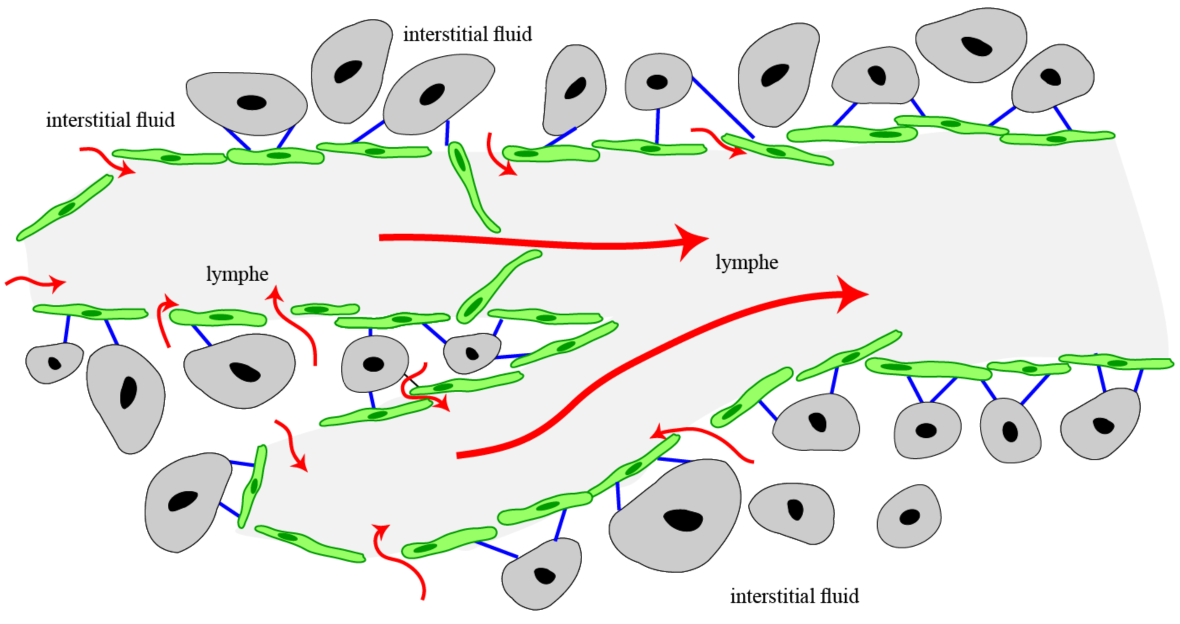
1. In the Starling-exchange system, I have said that all the fluid that leaves the capillary at the beginning of the capillary is reabsorbed again at the end of the capillaries.	2. This is not completely true. The vast majority of the interstitial fluid, approx. 95%, is indeed reabsorbed by the capillaries. However, a small amount (5%) is **NOT** reabsorbed and is left behind in the interstitial space.
3. This amount will gradually increase in time and cause swelling (=oedema!).	4. This fluid therefore has to find another way to go back to the circulation. This other way is the **lymph circulation**.
5. We also need the lymphatic system to defend ourselves against bacteria and viruses. This is done by specialized cells, such as **lymphocytes** and **macrophages**, who attack and phagocyte (=eat) these intruders.	6. That defence function of the lymph system is the discipline of the microbiologist and the immunologist and will not be further discussed here. We will (only) talk about the drainage of the lymph.

E. Micro structure of the lymphatic system:

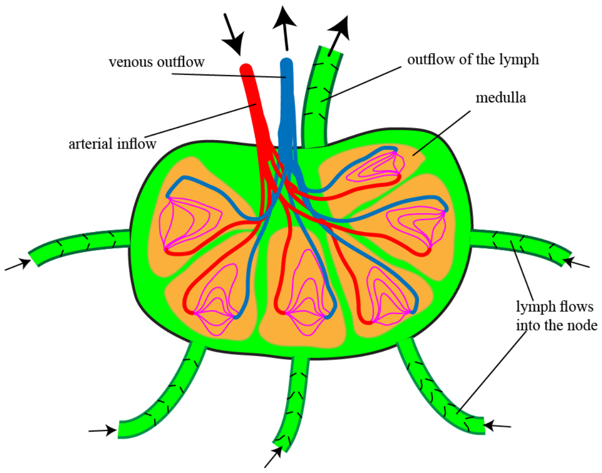


1. Lymph vessels look and behave very much like venules (=small veins) and veins.	2. They start in the tissues, as blind-ended vessels.

3. As shown in this diagram, there is a lot of space between the vessel's cells so that the interstitial fluid can easily flow, drift, into the lymph vessels.	4. These spaces and large holes are important because large molecules (proteins, fat) and even fragments of cells (in the case of an inflammation) can easily flow into those lymph vessels.
5. Remember that these large particles cannot pass the capillary wall into the blood circulation. The **only** way that they can be transported is through the lymph system.	6. The cells of the lymph vessels are arranged in such a way that they **overlap**. These overlaps work as **valves** that will allow fluid to go into the lymph but hinder the fluid to go out again.
7. There are also, as in the veins, **valves** inside the lymph vessels so that the fluid can only flow in one direction, away from the tissue towards the heart.	8. In fact, in lymph vessels, they are many more valves, large and small.
9. Finally, there are numerous **anchoring filaments** that attach the lymph wall to neighbouring cells.	10. These filaments (collagen) keep the lymph vessels open in case of an increase in interstitial fluid.
11. In fact, as the interstitial fluid increases, this increased amount of fluid will push the cells away from each other and this will pull the lymph vessels even more open! And this in turn will push more interstitial fluid into the lymph vessels.	

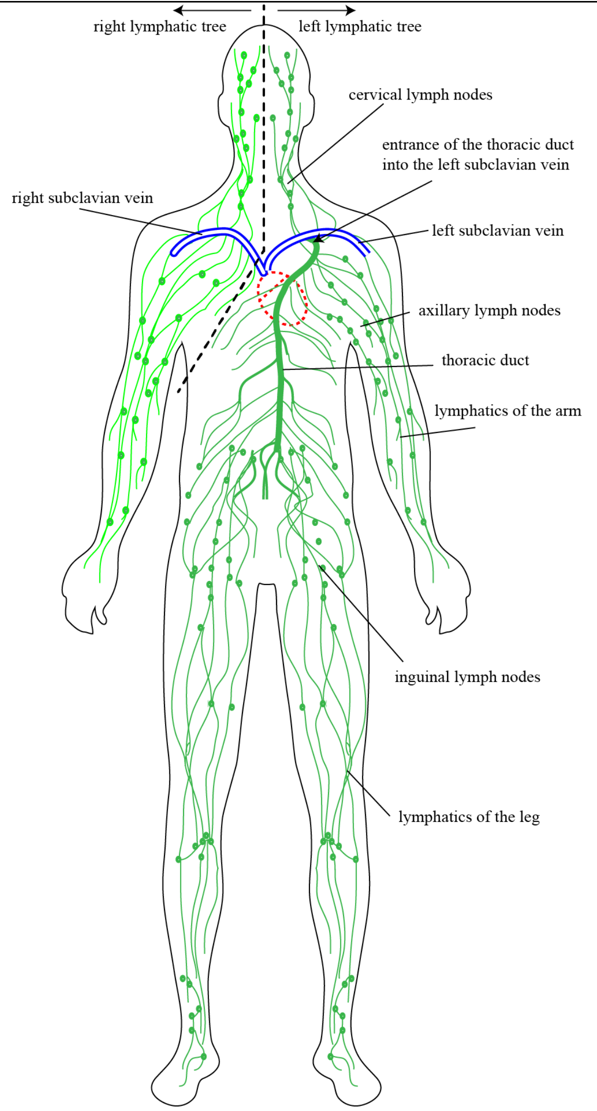


C. The lymph nodes:

1. The lymph nodes are small kidney-shaped structures into which the lymph flows from peripheral tissues. As explained above, this lymph is filled with extracellular fluid, large molecules, cell fragments and possibly bacteria and viruses.	
2. Inside the medulla of the lymph node, nodules filter the lymph. These nodules contain numerous lymphocytes and macrophages. These can 'eat' and destroy large molecules, bacteria, etc.	
3. Inside the medulla, there is also an elaborate capillary supply of blood, which also absorbs a lot of the lymph fluid and streams it back in to the venous system.	4. As stated before, approx. 50% of the lymph flows back into the venous system in all the lymph nodes together.

D. The lymph tree (both right and left!):

1. The lymph vessels, running away from the tissues, gradually merge together and form **larger** vessels.	
2. The lymph vessels collect in the lymph nodes where potential bacteria and viruses are attacked and removed. About 50% of the lymph is also absorbed back into the venous circulation in these nodes.	
3. From these nodes larger (lymph) vessels course through the body. They are actually very similar to the veins (with valves etc).	

4. In several areas, nodes congregate into clusters where they drain from large parts of the body. For example, the axillary lymph nodes drain and filter the lymph from the arms. The inguinal does do the same for the legs.	
5. The lower limbs, the abdomen, left arm and left chest and the left side of the head collect their lymph in the **thoracic duct** that runs through the abdomen and chest. The thoracic duct drains into the **left** subclavian vein.	
6. The right arm and the right side of head and chest drain into the **right** subclavian vein. I don't know why this is asymmetrical but this has undoubtedly something to do with the **embryology** of the system.	

E. Finally: How does the lymph flow?

1. The problem is how does the lymph **flow** to the lymph nodes and ultimately to the subclavian veins and back into the circulation? After all, there is no lymph 'pump' such as a heart.	2. The problem is very similar to the flow of blood in the **veins** (which also does not have a pump of its own).
3. The solution is also similar. Many of the same mechanisms that work for the veins also work for the lymph system. For starter, they also have **valves**, just like the veins.	4. The most important mechanism is the **muscle pump**. As skeletal muscles pump, they push blood (in the veins) and lymph (in the lymph vessels) towards the heart.

5. Other systems that helped the venous return, such as the respiratory pump, and the arterial pump, also work in the same manner for the lymph system.	6. It is important to realize that the total amount of lymph pumped is **very low**: about 2-4 litres per day. (Compare this with the cardiac output of 5 liters per minute!).
7. It is also important to realize that the lymph from different parts of the body may vary a lot. The lymph from skeletal muscles for example is very different from the lymph that comes from the gut (especially after a meal!).	8. The role of the lymph flow becomes very visible when nodes in a particular region are removed. This is the case for example in the case of a breast cancer.
9. In that disease, the tumour in the breast is removed and, often, also the lymph nodes in that region (to prevent metastasis).	10. These nodes are located in the axillaries and they drain the lymph from the arm.
11. If these nodes are removed surgically, then the lymph can no longer drain away from the arm.	12. This lymph stays in the arm and causes swelling (=oedema) of that arm.

B.5.6. Special Circulations.

Introduction: In several organs or tissues, local conditions may strongly modify or influence the behaviour of the blood circulation

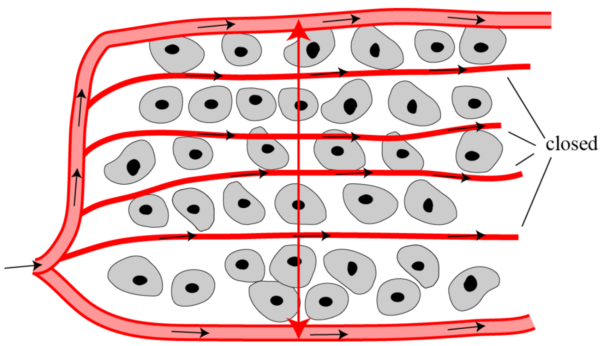
A. Circulation in the Skeletal Muscles:

1. What is the problem?

At rest, a skeletal muscle requires very little energy but during exercise the muscle requires much more energy to contract. Therefore, the blood flow, which is very small at rest, has to increase 5-20 times to accommodate this demand for oxygen.

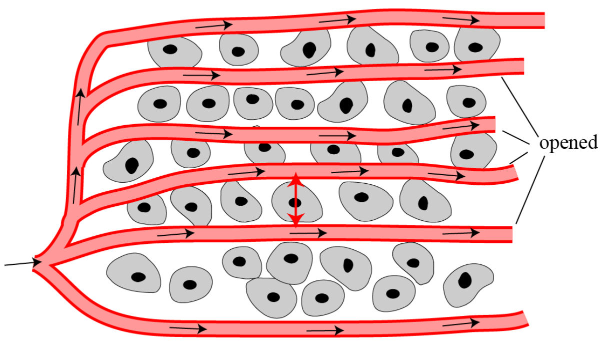
2. **Solution**

Opening more capillaries inside the muscle essentially solves this problem. At rest, most capillaries are closed (i.e., are not necessary) and only 10-20% are open. But with exercise, the number of capillaries opens up to 100%.



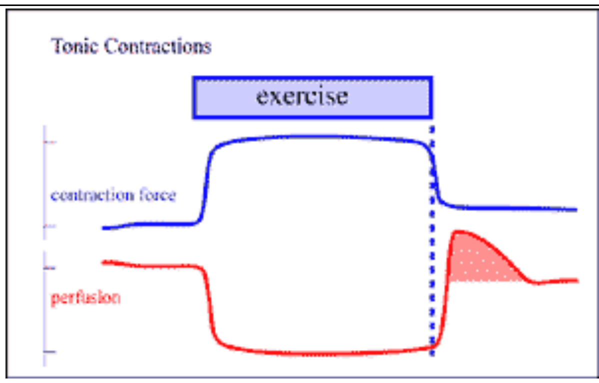
3. **Diffusion distance**

This, as such, will increase the blood flow to the muscle but it will also have another additional benefit; the average distance of a muscle cell to the nearest opened capillary will decrease (see diagram). And, as you may remember, a **decrease** in diffusion distance will **increase** diffusion! (*link*)



4. **But now there is a new problem!**

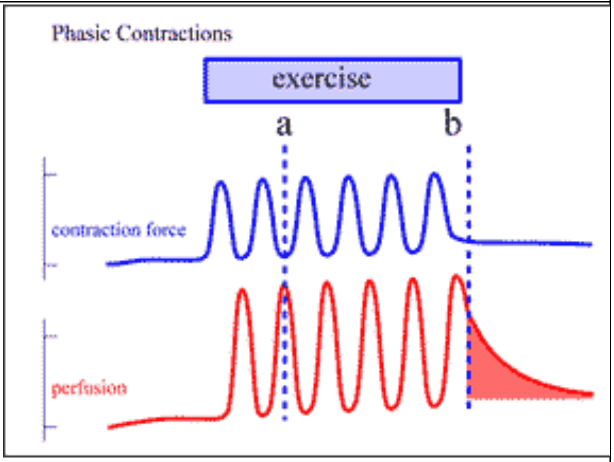
Contractions are quite strong and the pressure inside the muscle will increase during the contraction. If this pressure is higher then the blood pressure, then the blood flow will **stop**! This means that no oxygen will arrive to the cells and no waste is removed from the cells. Essentially, the metabolism of the cell is stopped and this will limit the duration of the contraction.



5. As you can see in this diagram, during the contraction (blue line), the blood flow (=perfusion) has virtually stopped. This means that no oxygen and no nutrients are reaching the muscle cells. However, when the contraction has stopped (dashed line), perfusion is immediately restored. In fact, for some time, it is even stronger than normal, in order to replenish the oxygen shortage in the cells and to get rid of the accumulated waste. This is called 'reactive hyperaemia' (*reactive = reaction to the contraction; aemia = blood and hyper = more*).

6. Tonic and Phasic Contractions:

In the previous diagram, the contraction was tonic (long lasting). Some contractions however are phasic and that is very good. Because in that situation, when there is contraction, the blood flow will stop, but when the contraction relaxes (see dotted blue line "a"), the blood will flow again! In other words, during phasic contractions blood is able to reach the cells. That is why it is possible to perform phasic contractions much longer than tonic contractions.



B. Circulation in the Cardiac Muscle:

1. What is the problem?

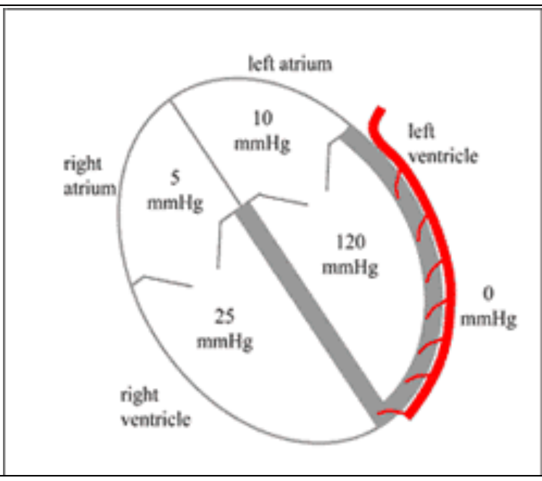
The situation here is similar to that in the skeletal muscle. During contraction, the vessels are closed due to the high pressure caused by the contraction.

2. **Systolic and diastolic perfusion**.

This is not as bad as it sounds, as the cardiac contractions are phasic. In other words, perfusion through the coronary vessels takes place during diastole and less or not at all during systole. Actually, this is the **only organ** that is not perfused during systole but during diastole; all other organs have a stronger blood flow during systole (= the pulse).

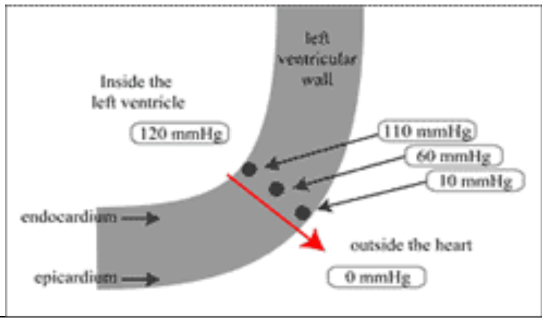
3. **Really?**

Ah!! The previous statements were somewhat **exaggerated**. In fact, in the atria, contraction pressures are very low; maybe 5-10 mmHg. Blood pressure in the perfusing arterioles and capillaries are much higher. So, in the atria, even during systole, perfusion (= blood flow) does not actually stop.



4. **What about the ventricles?**

Also in the right ventricle, maximum pressure achieved is 25 mmHg (remember the systolic pressure in the pulmonary arteries?). Therefore, the coronaries in the right ventricle are **hardly influenced** by the contraction.



5. **Left Ventricle:**

But the situation is very different in the left ventricle. The maximum pressure achieved during systole is much higher than anywhere else; normally 120 mmHg. This is more than enough to **stop perfusion** in the left ventricular wall.

6.

This story explains why practically all heart infarcts occur in the left ventricle. This muscle has to work the **hardest** but is most **impeded** in its perfusion.

7. **Pressure Gradient:**

In fact, there is a **pressure gradient** across the left ventricular wall during systole. The pressure inside the left ventricle is, during systole, 120 mmHg but outside, in the chest, it is 0 mmHg.

8.
So, the pressure in the muscle close to the endocardium (=inside) is close to 120 mmHg while the pressure in the muscle fibers close to the epicardium is close to 0 mmHg. Therefore, during systole, the **endocardium** will get less blood than the **epicardium**. That is why many infarcts occur along the endocardium and less along the epicardium.

C. Circulation in the Brain:

1. What is the problem?

The brain is protected from its environment by the **skull**. This is a hard and bony structure, which cannot expand.
Normally that is good because it offers a protection against accidental bumps.

2. **Cerebral Oedema**

But in a situation when **oedema** occurs (cerebral oedema), then tissue swelling may occur.
In any other tissue or organs, this would not really be a problem. Only maybe inconvenience or maybe even some pain because of the swelling.

3. **Intra-cranial pressure**

But in the brain, if there is a swelling of the brain tissue inside the skull, the **pressure** inside the skull may increase.
If this pressure becomes too high, then this may start to **stop blood perfusion**.

4. **Vicious** Circle:

This could easily lead to a **vicious circle**: increased swelling -> increased pressure -> reduced blood flow -> more ischemia (=lack of blood) -> more damage to the tissue and the blood capillaries -> more swelling -> etc -> etc

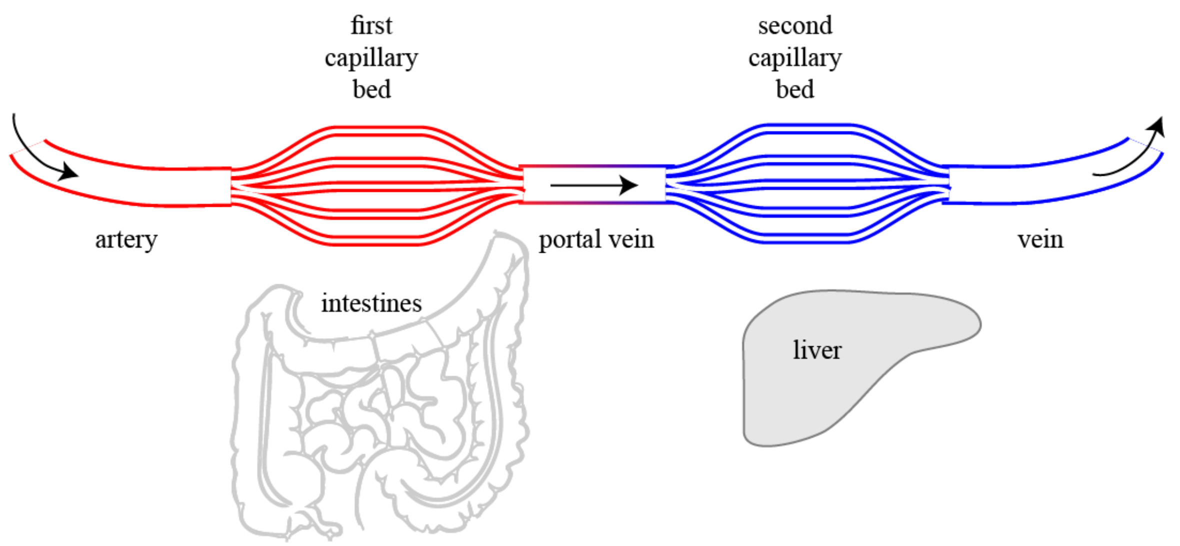
5. **Solution?**	6. **Medical solution:**
The body will try to solve this problem by increasing the arterial blood pressure (through a reflex).	But if this does not help, then the patient will gradually develop symptoms of brain dysfunction, become unconscious, and needs to be admitted urgently into the hospital. The solution then is to drill a hole through the skull to relieve the intra-cranial pressure!

D. Circulation in the Skin:

1. Cutaneous circulation:	2. **Regulation:**
Circulation in the skin (=**cutaneous**) is in some respects very different from that of other circulations.	The difference is that in this circulation, **local control** of the blood flow is not very relevant. Instead, the nervous regulation of the circulation is very important. This is mainly the task of the **sympathetic** autonomic nervous system.
3. **Why?** Why is the control of the circulation of the skin regulated by the brain? Because one of the functions of the skin is controlling the **body temperature**.	4. By increasing or decreasing the perfusion of the skin, the body can allow more or less heat to disappear, thereby keeping the temperature inside the body constant at 36°C. (98 °F).

E. The Portal Venous Circulation:

1. Sometimes, between the arteries and the veins there is not one but two capillary beds. This is the case in the hypophysis (a gland in the brain), in the kidneys and, most famously, in the **liver**. This has to do with the function of the intestines.	2. As you know, the intestine is where the food is ingested, broken down into many molecules and absorbed in the blood capillaries. These capillaries then drain into the intestinal veins. These veins do not go directly to the veins and to the heart. They first go to the liver!



3. Why? Why does the blood, from the intestines, first flow to the liver? This is because the liver is the major metabolic organ in our body. Therefore, our food first gets processed in the liver.	4. The liver is also important to detoxify possible toxins that have been ingested with your food. So, in a sense, it also offers additional protection.

B.5.7. Blood Flow

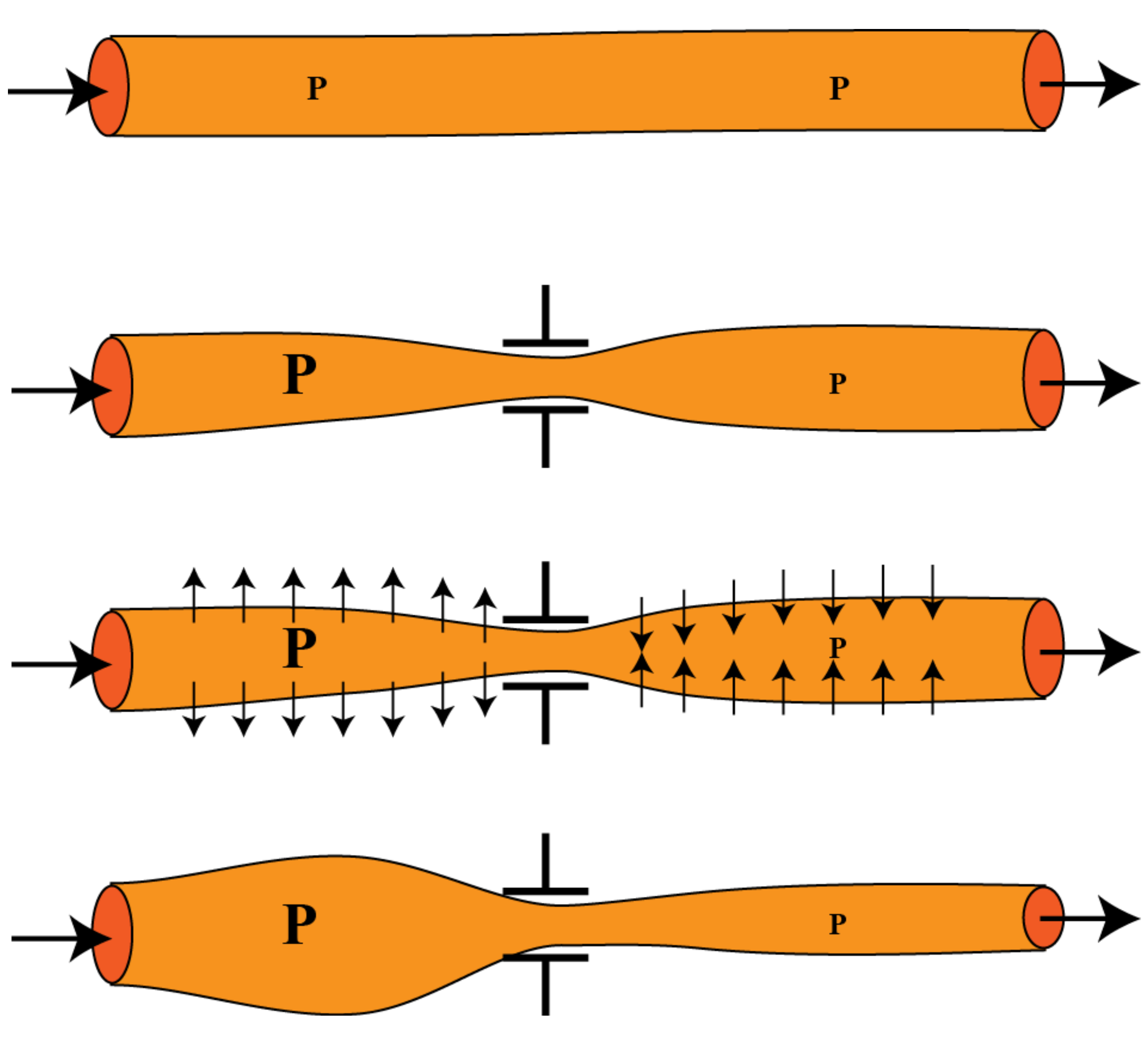
A. Introduction

1. **What is blood flow**? This is the amount of blood flowing through an organ or an organ system, expressed as ml or l (=litres) per minute. If you take the whole systemic circulation, then the blood flow is the same as the cardiac output: 5 L/min.	2. Blood flows from an area with a high pressure to an area with a lower pressure. If there were no difference in pressures, then there would be NO blood flow.
3. **Pressure gradient**. The difference in pressure is called the pressure gradient. The higher the pressure gradient, the higher the blood flow.	4. **Resistance**. But there is also a resistance to the flow of blood in the vessels. The higher the resistance, the lower the blood flow.
5. There are three important components to the **resistance**: • Blood viscosity • Vessel length • Vessel diameter	6. **Blood Viscosity**: This is the thickness or the "stickiness" or the "sluggishness" of the blood. Blood is much more viscous than water because it contains many cells, proteins etc.
7. **Vessel Length**: This is easy to understand: the longer the vessel, the higher the resistance. Think of the long water hose in the garden. This factor is also important in medicine; for example, fat (=obese) people tend to have longer vessels > more resistance > more difficulties with their hearts	8. **Vessel Diameter**: This is also easy to understand; if a vessel is narrower, the resistance will increase. If the vessel is wider, the resistance will be lower. This is very important in physiology and is the basis for regulating the blood flow distribution by vasoconstriction and vasodilatation.
9. **Summary**: Blood flow is directly proportional to the difference in pressure and inversely proportional to the resistance. In fact, this can be stated in a formula:	10. **Law!** Some of you may know this as a law (**Poiseuille's Law**). The important thing here is that the flow is related to the fourth power of the radius of the vessel!! This is very strong; a very small change in diameter (vasoconstriction or vasodilatation) will have a strong influence on blood flow!

$$\text{Flow} = \frac{\text{pi}(\pi) * \text{pressure difference} * r^4}{8 * \text{viscosity} * \text{length}}$$

B. A few words about (local) vasoconstriction:

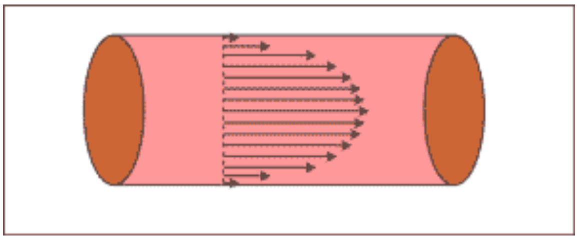
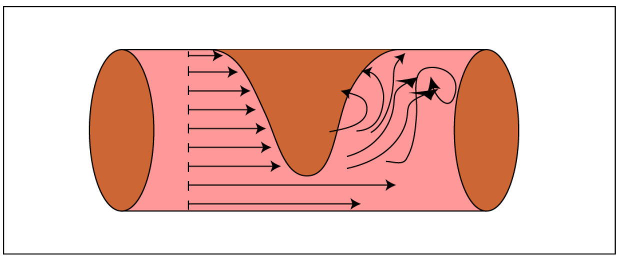
1.	2.
What really happens when there is a local vasoconstriction?	This is often a problem for students. They often think that the pressure changes under the constriction and not before or after the constriction.



3.	4.
In this drawing, at the top, there is a normal blood vessel with a normal pressure. The blood is flowing from left to right.	In the middle of the vessel, we squeeze the blood vessel. Therefore, the diameter at that point will decrease, the resistance increase and the blood flow will therefore decrease.

5. Therefore, blood is **accumulating** before the constriction (upstream of the narrowing). This accumulation will increase the pressure **there**!	6. After the constriction, downstream, the flow will decrease and the pressure will therefore also decrease.
7. The pressure increase will expand the blood vessel before the constriction.	8. While, downstream, the blood vessel will become narrower, due to the lower pressure. That's it!

C. Flow Types (laminar and turbulent flow):

1. **Laminar Flow:** In a normal vessel, blood flows straight through the tube. In fact, blood flows faster in the centre and more slowly along the wall of the vessels. This is of course due to the resistance of the blood against the walls of the vessel.	
2. You can then imagine a stack of thin layers of blood flowing at different velocities alongside each other; fast in the centre and much slower along the wall. This is called "**laminar**" flow.	
3. **Turbulent flow:** But sometimes, when the vessel is narrower, or if there is an obstruction, then this laminar flow is disrupted. Blood will flow in different directions, loops and become irregular. This is called "turbulent".	
4. Turbulent flow is important in medicine because turbulent flow makes a **noise**. Therefore, one can hear it with a stethoscope. If you hear such a sound in a patient, you can with this method detect a local obstruction in his or her blood vessels.	

D. Local Blood Flow Regulation:

1. Why is local blood flow important? Every tissue and every organ need blood for its function and for its survival. It needs oxygen and other nutrients and has to get rid of CO_2 and other waste products.	2. How much is needed? It turns out that the amount of blood delivered to a tissue or an organ is pretty well the amount that the tissue requires; not more, not less. If it needs more, it will get more. If it needs less, it will get less!! But how is this regulated?
3. **Not** the nervous system: It is not possible for the nervous system to regulate this (because this would require an enormous number of nerves to innervate all these arterioles).	4. Local regulators (= autoregulation): It is the **local** factors that determine how much blood is needed at a particular moment.
5. **Oxygen**: Local oxygen is probably the most important factor. If there is a shortage of oxygen, then the local arterioles will dilate, thereby increasing blood flow and increase in the oxygen. This is called the "**oxygen-demand**" theory: the oxygen **demands** more blood.	6. Other local factors: But there are many other factors that can also play a role; potassium, hydrogen ions, lactic acid, adenosine, several prostaglandins, and inflammatory signals (histamine)
7. **Active Hyperaemia**: Sometimes, the term "**active hyperaemia**" (= more blood in the tissue) is used to describe this condition. (*i.e., the tissue itself is active to get more blood*)	8. **Reactive Hyperaemia**: When an organ or a tissue, for some reason, like a temporary obstruction, has not received enough blood for some time, it will, after the obstruction has been removed, receive more blood than usual. The organ therefore "reacts" to a temporary lack of blood (see also Special Circulation).

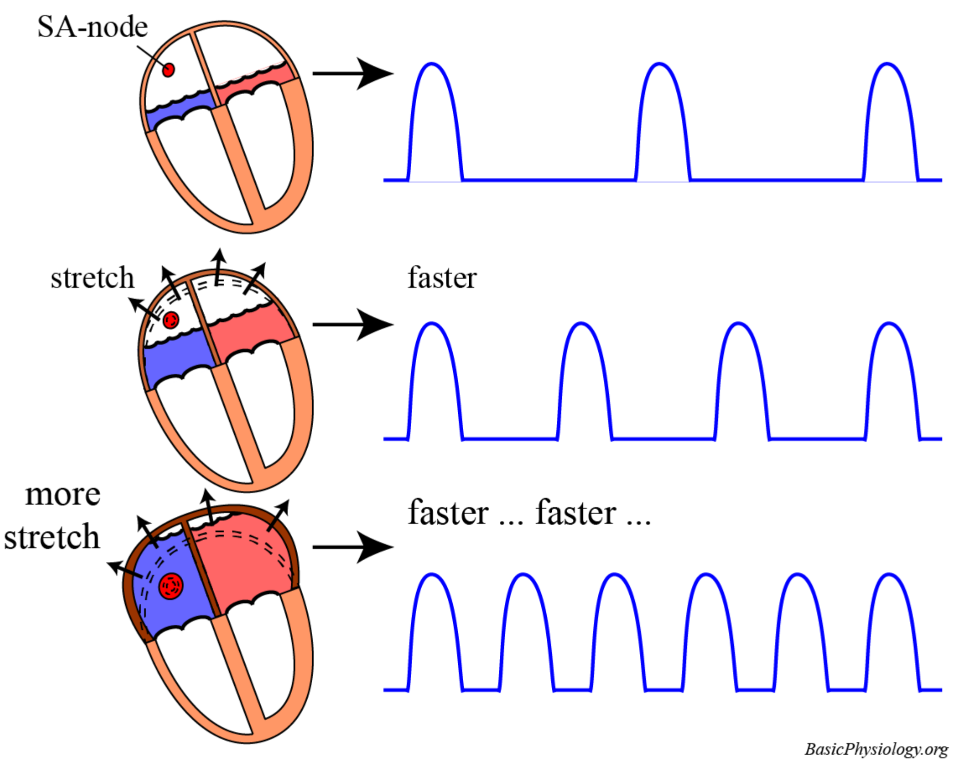
B.6.1. Regulation of the Heart.

Introduction:

1. The heart needs a lot of control mechanisms to allow it to perform its task of pumping blood reliably and adequately.	2. These control mechanisms can be classified into two groups: 1) **Intrinsic** regulation mechanisms (=from inside the heart) 2) **Extrinsic** regulation mechanisms (=from outside the heart)

A. Intrinsic regulation: Sinus Node Stretch

1. The sinus node is very sensitive to stretch. So, if the wall of the right atrium is stretched (by the presence of more blood), then the sinus node will also be stretched.	2. When the sinus node is stretched, it will respond by initiating more action potentials.

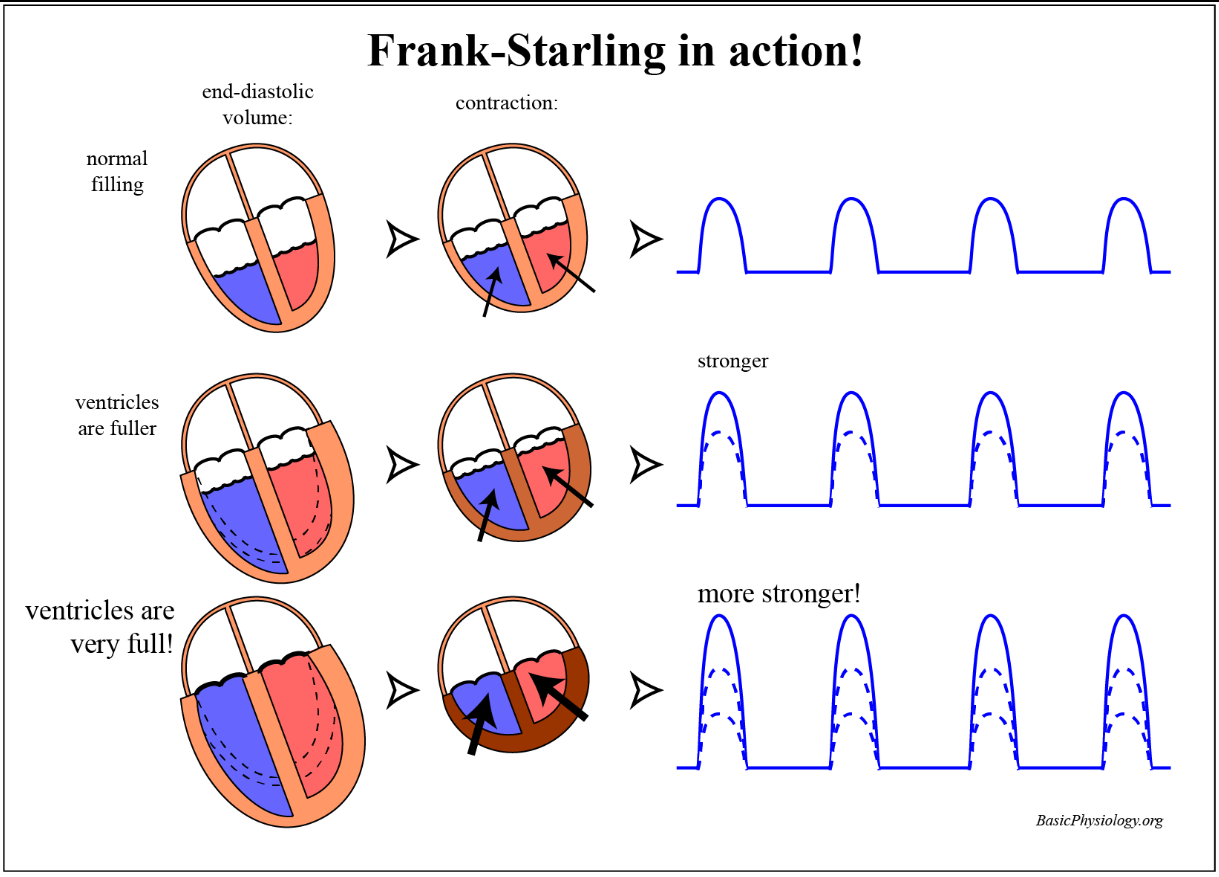


3. More action potentials will induce more excitations of the heart, and therefore more contractions.	4. In other words, if the right atrium is more stretched because it is filled with more blood (from the veins), then the heart will beat faster.

5. This is useful, as more blood will then be pumped out of the heart.	6. This rapid pumping will, in turn, reduce atrial filling and the heart rate will then return to normal.

B. Intrinsic regulation: The Frank-Starling system

1. This mechanism is located in the heart muscle itself (intrinsic = belonging to the organ itself). It is a very important system!	2. This system is named after the two people who first described this regulatory system (yes, you guessed it … Mr Frank and Mr Starling).
3. Do you remember that, in skeletal muscles, when you stretched the muscle before the contraction, that this would increase the force of contraction? (*link*)	4. The same mechanism applies to the heart. The more the cardiac wall is stretched, the stronger the next contraction will be.
5. But, in the heart, the stretching of the cardiac wall is done by the blood that is accumulating in the chambers. The more blood in a chamber (atria or ventricle), the more the stretch.	6. So, during diastole, blood flows into the ventricles, stretching the walls. The volume that is reached just before the contraction starts is called the **end-diastolic volume**.
7. This system is very nice! If, for some reason, more blood flows into the heart, then the end-diastolic volume is increased, and this will (automatically!) induce a stronger contraction that will pump this extra amount of blood into the arteries.	8. A stronger contraction means that more blood will be pumped into the arteries; i.e., the stroke volume will increase. Therefore, with this mechanism, the cardiac output (CO = SV*HF) has increased.
9. The reverse is also true. If less blood flows into the heart, then stretch and contraction force will decrease and the cardiac output will be less.	10. In summary, the heart, by itself (= intrinsic) adjusts itself to the amount of blood it receives to pump: if there is more, it will pump out more, if there is less, it will pump out less …



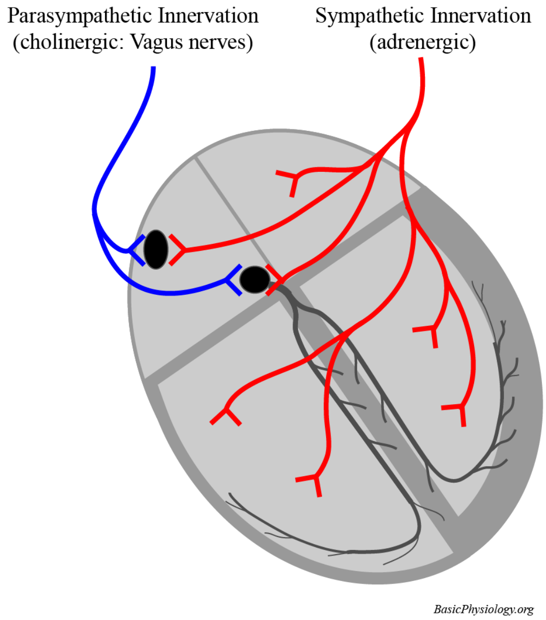
C. A few additional notes:

1. The sinus node stretch influences the **frequency** of the heart. The Frank-Starling system affects the **contraction** force.	2. Since the frequency is the **same** for both hearts, the cardiac output of the right and the left heart are both influenced by stretching the sinus node (it is not possible for the right heart to pump at a different frequency than the left heart!).
3. But in the Frank-Starling system, the end-diastolic volume stretches each ventricle and thus the contraction of the right ventricle could be higher or lower than that of the left ventricle.	4. In conclusion, the Frank-Starling system, amongst others, keeps the **balance** between the right and the left heart.

D. Extrinsic Regulations:

<table>
<tr>
<td>1.
Because a correct function of the heart is so critical, there are also several extrinsic regulatory systems.</td>
<td>2.
The major systems are:
a. The autonomic nervous system
b. The hormones (local and at a distance). These will be discussed later.</td>
</tr>
</table>

E. The Autonomic Nervous System

<table>
<tr>
<td>1.
As indicated in the diagram, there are two nervous systems innervating the heart; the parasympathetic and the sympathetic nervous system.</td>
<td rowspan="3">
</td>
</tr>
<tr>
<td>2.
The parasympathetic system (the vagus nerve) only innervates the sinus node and the AV-node. It inhibits the firing rate of the sinus node (longer P-P) and delays the propagation though the AV-node (longer P-Q).</td>
</tr>
<tr>
<td>3.
The sympathetic system also innervates both nodes, but also the myocardium itself, both in the atria and in the ventricles.</td>
</tr>
<tr>
<td colspan="2">4.
An increase in sympathetic activity will:
1. Increase the heart rate
2. Increase the propagation velocity in the AV-node
3. Increase the contraction force in the cardiac muscle (atria and ventricles).</td>
</tr>
</table>

F. The Bainbridge reflex

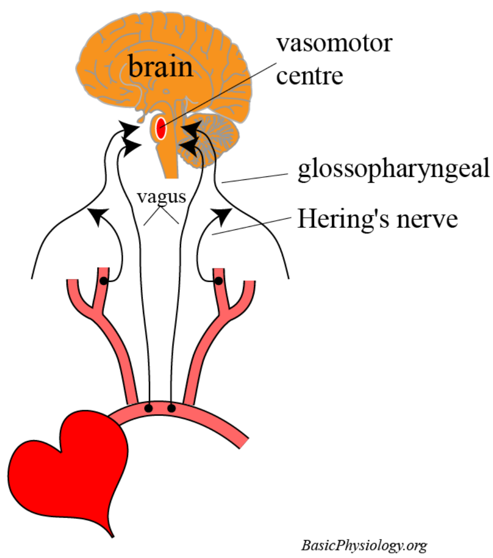
As an example of how the autonomic nervous system work on the heart, consider this very nice reflex: the Bainbridge reflex, also called the Respiratory Sinus Arrhythmia.	
1. The reflex is very simple: when the pressure in the right atrium increases, the heart beats faster. If the pressure decreases, the heart rate goes down.	2. As the pressure increases in the right atrium, possibly due to an increase venous return, the atrial stretch receptors are activated which send their signals to the medullary centre in the brain. This in turn activates the sympathetic system.
3. An increase in heart rate is then useful, as it makes the heart pump more blood, which will decrease the pressure in the atrium.	4. You see this reflex very well during forceful in- and expiration.
5. As you inhale, the pressure in the thorax decreases, which induces an increase in venous return and an increase in blood flow to the right atrium. This increases the atrial pressure -> increase heart rate.	6. After inhalation follows expiration, the thoracic pressure increases, the venous return decreases, less blood flows into the atria, the pressure decreases and the heart rate decreases.

B.6.2. Short-term Regulation

Introduction:

1. Short-term regulation of the blood pressure includes those regulators that work very fast, from seconds to minutes. There are also long-term regulators but these take days to weeks to work (see next page).	2. There are several short-term regulators: 3) Baro-reflex 4) Chemo-reflex 5) Vascular fluid shift

A. Baro-reflex:

1. This is a real nerve reflex. This means it has a **reflex arc**. In general, reflex arcs consists of: 1. a sensor 2. afferent nerves 3. a center in the Central Nervous System (= CNS) 4. efferent nerves 5. an effector.	2. In the case of the baro-reflex, these components are as follows: **Sensors**: the baro-receptors, which are located in the internal carotid arteries (located in the carotid sinus) and along the aortic arch. These are **stretch sensors**. When they are stretched (because of higher blood pressure), they will send more action potentials to the CNS. If the blood pressure is decreased, then the firing frequency is decreased. Therefore, they 'sense' the blood pressure.
3. **Afferent nerves**; the nerves from the aortic receptors "run" through the vagus nerve. The nerves from the carotid sinus go through Hering's nerve to the glossopharyngeal nerve. 4. Both nerves end in the **cardiovascular centre** (= vasomotor centre) in the medulla of the brain. 5. The **efferent nerves** are: a) the vagus (the para-sympathetic system) and b) the sympathetic system. 6. The **effectors** are: a) the heart b) the arteries c) the veins	The efferent nerves of the Baro-reflex: 

B. How does the Baro-reflex work?

Step 1:
Suppose the blood pressure decreases suddenly.

Step 2:
The baro-receptors will sense this and respond by producing less action potentials

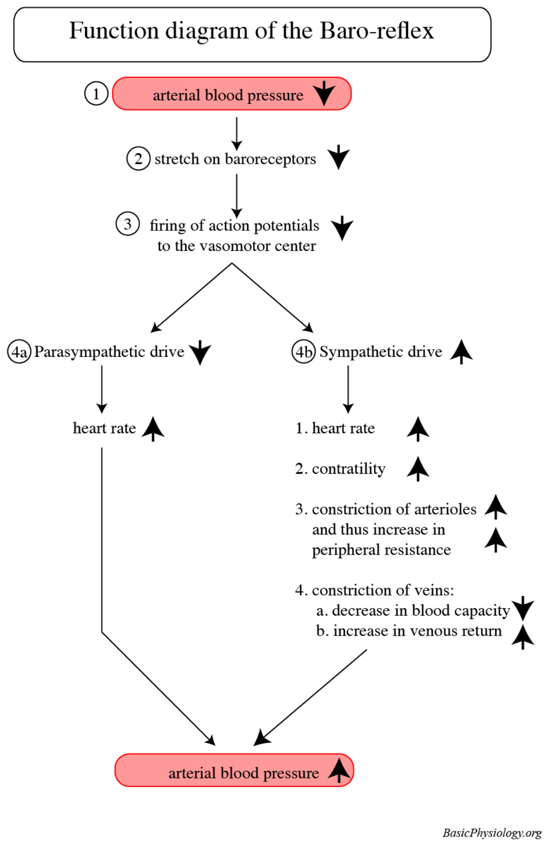
Step 3:
The Vasomotor center will respond by influencing **two** systems:

- the Parasympathetic system
- the Sympathetic system

Step 4A:
The parasympathetic system is then **inhibited**: this will **increase** the heart rate (by increasing the frequency of the cardiac sinus node).

Step 4B:
The sympathetic system is stimulated. This has multiple effects:

1) increase in heart rate (= chronotropy)
2) increase in contraction force of the heart (= inotropy)
3) vasoconstriction of the arterioles (this leads to an increase in the peripheral resistance).
4) vasoconstriction of the veins: this has **two** effects:
    a) decreasing the capacity of the veins
    b) increasing the venous return

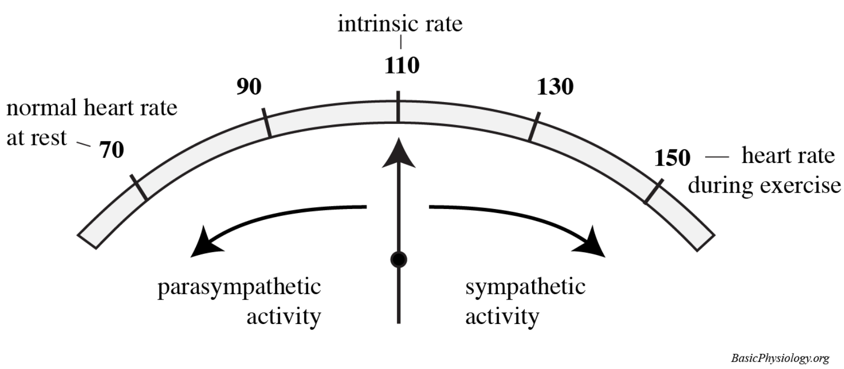


4a)
The **capacity** of the veins is decreased (remember that the veins are also being used as a buffer, a capacity or reserve). If these large veins constrict more, more blood will be pushed into the circulation, effectively increasing the circulating blood volume.

4b)
Increase in the **venous return**. This will make the heart beat:

a. faster (sinus node stretch).
b. stronger (Frank-Starling effect).

C. Wait! There is something strange here!

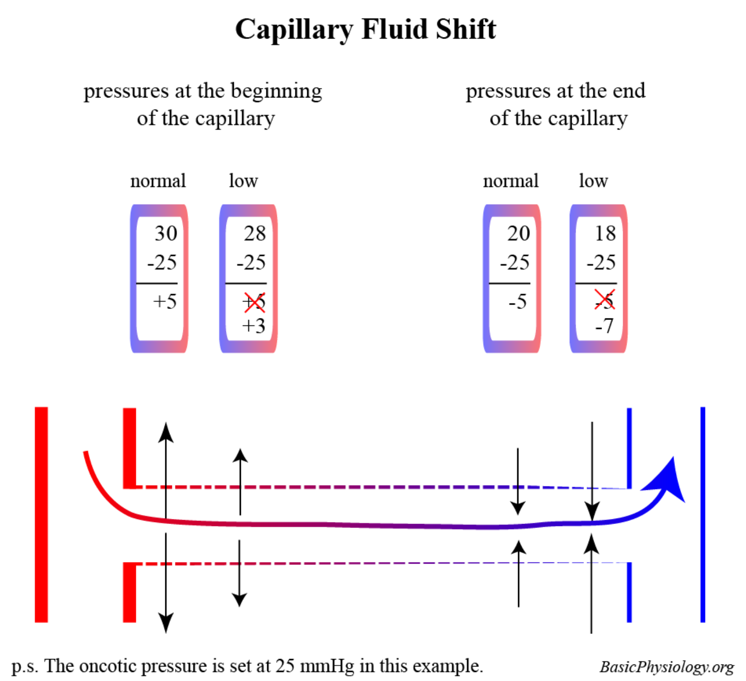
<table>
<tr><td>1.
In the above diagram, I said that the parasympathetic system is inhibited and that this will increase the heart rate??</td><td>2.
Till now, every time we have stimulated nerves (in muscles, heart etc.), we got more activity, not less. So, how is inhibiting a nerve going to increase the firing rate in the heart??</td></tr>
<tr><td>3. Good!
This is an important point, which I will now try to explain.</td><td>4.
First of all, you must know that the heart, by itself, without any interference of nerves, hormones or whatever, would beat automatically and at a higher rate than we are used to; typically, at about 110 beats/min. This is called the intrinsic rate.</td></tr>
<tr><td>5.
But in the body, at rest, the heart rate is much lower, at about 60-70 beats/min. Why is this?</td><td>6.
Because, at rest, the parasympathetic nerves (i.e., the vagus) is active and is inhibiting the sinus node. This will decrease the normal heart rate.</td></tr>
<tr><td colspan="2">
</td></tr>
<tr><td>7.
And, if necessary, for example during exercise, inhibition of the parasympathetic system, will ‘release’ the brake on the sinus node that will, by itself, then produce more action potentials.</td><td>8.
In my class, I always compared this with the behavior of a sports car in front of a red light! You may have seen something like this: you see the car shaking because the driver is at the same time pushing on the gas pedal and on the brake (and smoke coming out of the exhaust!).</td></tr>
<tr><td>9.
When the light turns green, the driver releases the brake and his car (it is always a ‘he’!) suddenly roars ahead of all the other cars.</td><td>10.
The same happens in the heart. Normally, the active parasympathetic system ‘brakes’ the heart. When the brake (=inhibition) is released, the heart jumps quickly to a higher rate. That’s the trick!</td></tr>
</table>

D. Chemo reflex:

1. The chemo reflex is very similar to the baro reflex. The only difference is that the sensors are not sensitive to stretch but sensitive to blood concentrations of **oxygen**, **carbon dioxide** and **pH**.	2. These chemoreceptors are also located in the aortic bodies and the carotid bodies, close to the corresponding stretch receptors.
3. Because the receptors are a **bit slower** than the stretch receptors, this reflex works slower.	4. Because they measure blood gasses, their function is much more important in the regulation of the **respiration**.

E. Vascular Fluid Shift:

1. Another way to regulate, in the short term, the blood pressure is not by influencing the heart but influencing, at the other end of the circulation, the capillary system!	
2. As you may remember, in the capillary, some of the fluid in the blood filtrates out of the capillary thereby carrying oxygen and nutrients to the cells. At the end of the capillaries, most of this fluid is reabsorbed back into the circulation.	3. But this system, to some extent, is sensitive to the arterial blood pressure. And this system tends to minimize the increase or decrease in blood pressures. This can be seen in the following example:



4. In the normal situation, the hydrostatic (=blood) pressure at the beginning of the capillaries is typically 30 mmHg and at the end of the capillaries 20 mmHg.	5. Suppose that the blood pressure has **decreased** a little. Therefore, the pressure at the beginning of the capillary will also, slightly, decrease to, let's say, 28 mmHg.
6. The oncotic pressure has not changed of course as the blood still has the same amount of albumin.	7. Therefore, the net filtration pressure at the beginning decreases from +5 to +3 mmHg. This means that **less** fluid will leave the capillary.
8. At the end of the capillary, the hydrostatic pressure will also have decreased, from 20 to 18 mmHg leading to a net filtration pressure of -7 mmHg. This means that **more** fluid will be reabsorbed into the blood.	9. This therefore causes a **shift of fluid**, from the interstitial space to the vascular space. This increase in blood **volume** will then increase the blood **pressure**.
10. The opposite of course happens when the blood pressure increases. Then, more fluid will go out of the capillary and this will reduce the blood pressure.	11. The amount of fluid shift is actually very little, about 5-10% of the plasma volume. Remember that the plasma volume is about 50% of the total blood volume. Therefore, these shifts typically only use 100 to 200 ml plasma.

F. The stupid Physiologist!

1. There was once a physiologist who thought he had a clever idea.	2. This idea, he thought, was so good he would become famous, win the Nobel prize and earn a lot of money.
3. As you know, **hypertension** is a big problem and difficult to treat.	4. Our soon-to-become world-famous physiologist, with the help of the Baro reflex, invented a clever way to treat hypertension.
5. His idea was to stimulate the Hering's nerve with an artificial (implanted) pacemaker!	6. In this manner, the vasomotor centre would think that the blood pressure was too high and would react by **exciting the parasympathetic** system and **inhibiting the sympathetic** system to decrease the blood pressure.

7. In his first group of hypertensive patients, his plan worked!! Indeed, the blood pressure decreased as soon as the pacemaker was switched on!	8. But after a few weeks, the blood pressure started to **creep back** to hypertensive levels, even while the pacemaker was switched on. In fact, when the pacemaker was switched off, the blood pressure became even **higher** than before the implantation of the pacemaker!
9. The poor physiologist, instead of treating his patients, was actually making things worse. Gone were his dreams of the Nobel prize, richness and fame.	10. Why had he failed? Why did his idea not work? Because stimulating through Hering's nerve is a **short-term** solution and **NOT** a **long-term** solution. Hypertension is a problem with the long-term regulation of the blood pressure (see next page).
Additional note: In recent years however, new technologies are being developed to treat hypertension by influencing the baro reflex! However, the point of this new potential treatment is not to influence the short-term regulation of the baro reflex but, instead, by stimulating the vagus nerve, thereby influencing the set point in the vaso-motor center in the brain. This could then reduce the blood pressure in patients. To be followed …!	

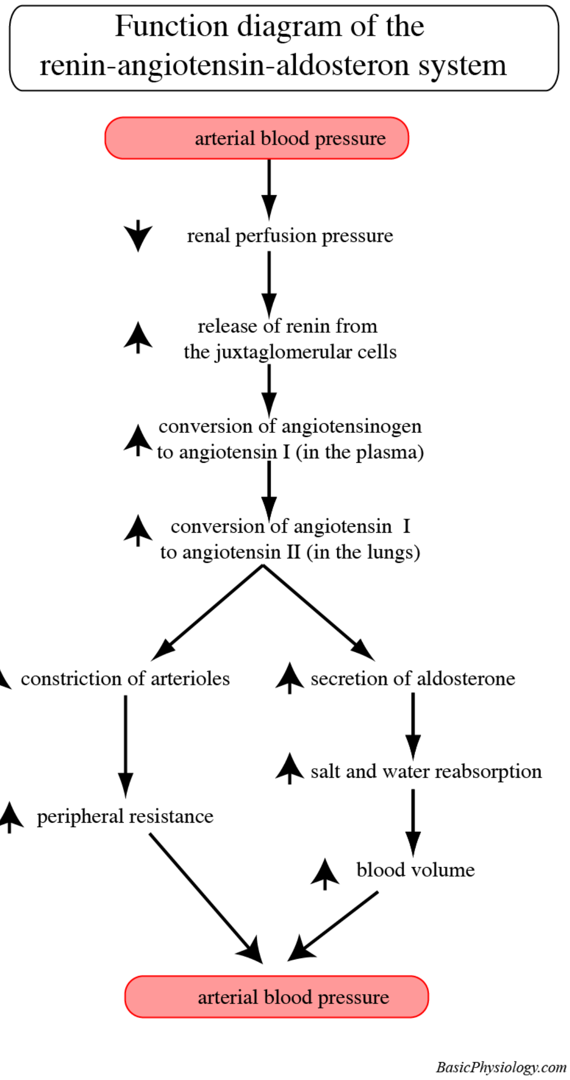
B.6.3. Long-term Regulation

Introduction

1. Long-term regulation of the blood pressure are those regulators that work very slow and usually takes weeks to months before their effects are visible.	2. However, these regulators are much **stronger** than the short-term regulators.

A. The Renin-Angiotensin-Aldosterone system:

1. This system is an interplay of several hormones from several organs.	
2. When the blood pressure is decreased, then the perfusion in the **kidney** (=renal) will decrease.	
3. This will induce the juxtaglomerular cells in the kidney to release the hormone **renin** in the blood.	
4. This renin will convert the precursor **angiotensinogen** into **angiotensin I**. The angiotensinogen is already present in the plasma. The conversion also takes place in the **plasma**.	
5. The angiotensin I will be converted into **angiotensin II**. This conversion requires an enzyme that is located in the **lungs**. This enzyme is called Angiotensin Converting Enzyme (=**ACE**).	
6. This Angiotensin II has a direct and an indirect effect. The **direct** effect is related to constriction of the arterioles. This will lead to an increase in the peripheral resistance. This, in turn, will increase the blood pressure.	



B. Indirect effects of Angiotensin II:

1. Angiotensin II will (also) stimulate the cortex of the adrenal glands to secrete **aldosterone**.	2. Aldosterone is a mineral-corticoid that regulates the sodium (=salt) concentration.
3. An increase in aldosterone will increase the reabsorption of sodium (= back to the plasma) by the kidney.	4. This increase in sodium will lead to an increased reabsorption of water, also by the kidney.
5. This increase in water will increase the blood volume.	6. A higher blood volume leads to an increase in blood pressure.

C. Another long-term system: Atrial Natriuretic Peptide (ANP):

1. Atrial natriuretic peptide is a hormone that is secreted by the heart! Eh! What a surprise; the heart is also a **gland**!	2. When there is an increase in blood pressure, more ANP is released into the circulation.
3. This ANP inhibits the function of the Renin-Angiotensin system by **releasing** more sodium by the kidney into the urine.	4. This release of sodium ions will be followed by a **loss of water** (in the kidney; water follows the sodium ion).
5. Therefore, the **blood volume** will decrease and the blood pressure decreases.	6. You could say that ANP is an **antagonist** of the Renin-Angiotensin-Aldosterone system.

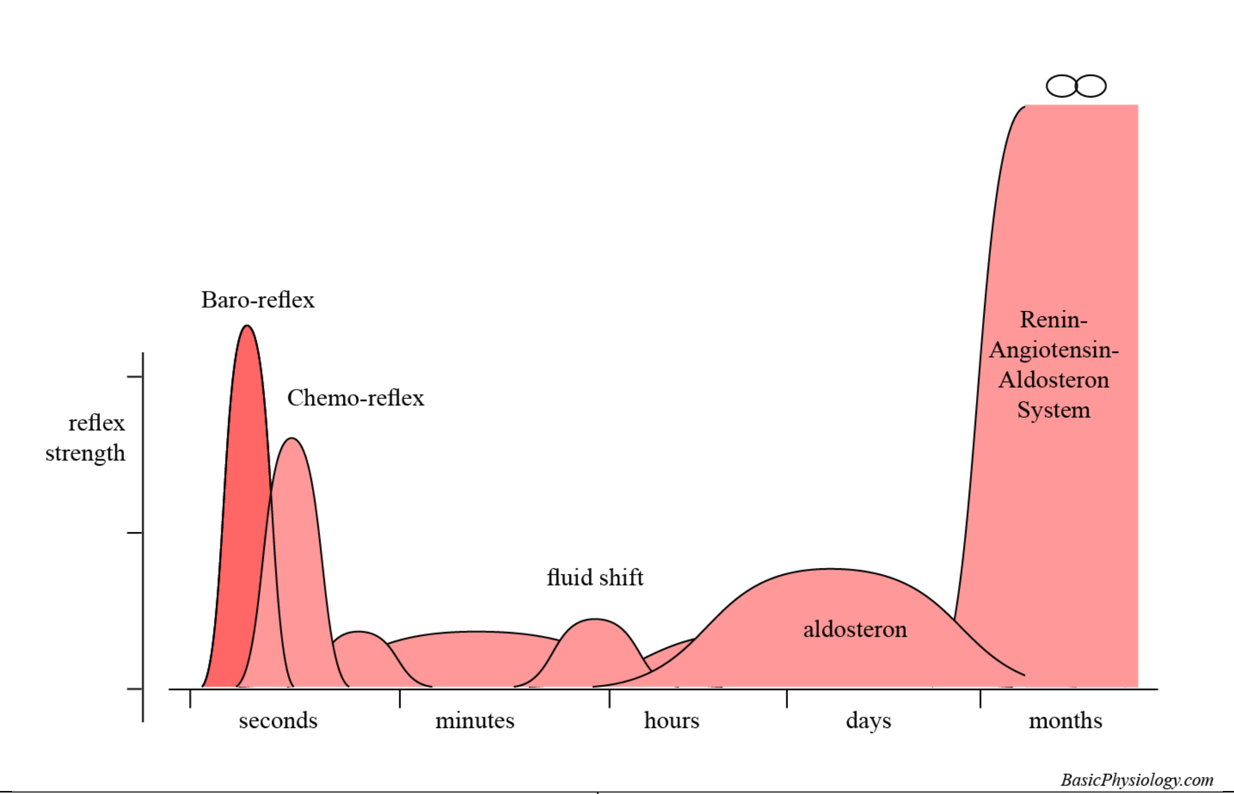
D. Other Short- or Long-term systems:

1a. **Adrenal Medulla hormones**: During stress -> Norepinephrine and Epinephrine are released in the blood.	1b. **Norepinephrine** induces vasoconstriction. **Epinephrine** increases cardiac output and also vasoconstriction.

2a. **AntiDiuretic Hormone** (=ADH):	2b. This hormone, secreted by the hypothalamus in the brain, keeps blood pressure by keeping water inside the body (anti = against; diuretic = urine release).

3a. **Nitric Oxide** (NO):	3b. NO is produced by the endothelial cells (= inner lining of all blood vessels) and provides for a strong but brief vasodilatation.

E. ALL TOGETHER now:



1. This diagram shows the most important blood pressure regulators.	2. On the Y-axis, the **strength** of the reflex is plotted. On the X-axis the **time** or the speed of reaction of the reflex is plotted.
3. The **baro reflex** is one of the strongest and reacts very fast; within seconds.	4. The **chemo reflex** is also quite strong but not as fast as the baro-reflex.
5. Some reflexes are not so strong and take longer to work such as the **fluid shift** and the **aldosterone** system.	6. The **renin-angiotensin-aldosterone** system reacts quite slowly; days to months. But it is the strongest; there is no limit to its strength!! (Check the symbol for 'infinity').

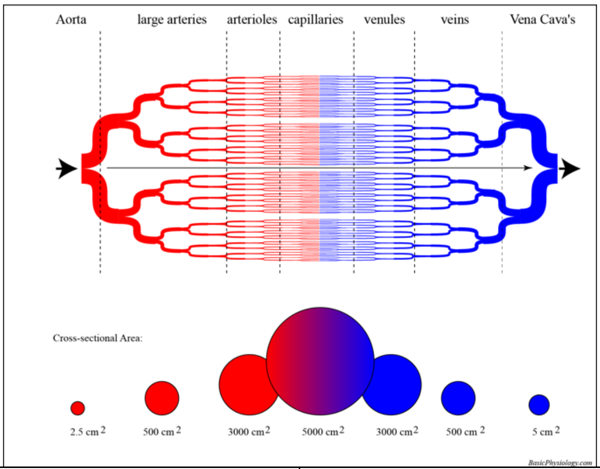
F. The Stupid Physiologist (continued …)

1. So, with all this new knowledge, how stupid was our physiologist?	2. His (*it was of course a him!*) mistake was to confuse short-term with long-term. In the short term he was successful; in the long term he failed.
3. He failed because we now know that hypertension is a problem in a long-term system.	4. Salt (sodium) is an important component that determines the blood pressure level.
5. In many cases, hypertension can be treated with a **good diet** and **exercise**. In that context it is important to realize that eating junk food will cause hypertension (and many other diseases!). The first thing you have to do in treating hypertension is to stop eating junk!	6. If a medical treatment is required, a decrease in blood volume can be obtained with **diuretics** (= produces more urine in the kidney). This will reduce the blood volume and therefore the blood pressure.
7. Another approach is to use drugs that reduce the **inotropy** (= contraction force) of the heart. This can be done by inhibiting the **sympathetic system**. The drugs are **blockers** of the receptors on the heart (= beta-receptors).	8. A more recent approach is to inhibit the conversion of angiotensin I to angiotensin II. This conversion is done by ACE (=angiotensin converting enzyme). The drugs are therefore called **ACE-inhibitors**.
9. There are more possibilities, such as using vasodilators etc. but these need more (careful) medication.	10. But the main thing is to treat the hypertension because, in time, it will affect badly the heart and the vessels. The problem with hypertension is that patients have no symptoms. That is why it is called the “silent killer”!

B.7.1. Cardiac Shock

Definition: Cardiovascular shock (= cardiac shock) is an acute failure to perfuse adequately the organs and the tissues in the body.

A. Background of Shock:



1. This diagram shows the cross section through the vascular system. At the beginning, in the aorta, its cross-section is very small (2.5 cm^2). As one moves forward towards the capillaries, then the vessels do become narrower, but the number of vessels increases much more. Therefore, the cross-sections of all these vessels (the "sum") increase a lot.	2. The cross section of all the capillaries together is a total of 5000 cm^2, compared to only 2.5 cm^2 for the aorta (2000x!).
3. Therefore, because there are so many, many, smaller vessels and capillaries in the body, this may cause a problem.	4. If they were all wide open, their total cross section would be much more than the cross section of the aorta.
5. In fact, if all the blood vessels were all wide open at the same time, then the blood volume (approx. 5 liters) would easily fit in the small vessels and the blood pressure would drop to zero!	6. In order to avoid that, the arterial and venous vessels must **always** show some degree of vasoconstriction.
7. **Shock** is the condition when the blood pressure is too low.	8. To be precise: this is called **cardiovascular shock**, to distinguish this from other types of shock such as psychological shock.

B. Types of Shock:

1) Problems with the heart: **cardiogenic** shock
2) Problems with the blood volume: **hypovolemic** shock
3) Problems with the vessel wall tension: **anaphylactic** shock and **septic** shock.

B1. Cardiogenic Shock (the Heart):

The heart can no longer pump properly due to:

a) Myocardial infarction: a (large) part of the left ventricle is no longer working (= dead)
b) Myocarditis: inflammation/infection of the heart makes the muscle weaker
c) Arrhythmias (disturbance in the rhythm): then there is not enough time during diastole for filling the ventricles.
d) Other cardiac causes (valvular, tamponade, etc)

B2. Hypovolemic Shock (Blood Volume):

1. External Fluid Loss: a) Hemorrhage (bleeding) b) Diarrhea (cholera) c) Vomiting (babies) d) Dehydration (sunstroke) e) Burns (> 20% of the body surface)	**2. Internal** Fluid Loss: a) Crushing injuries b) Pancreatitis c) Internal bleeding (ruptured spleen for example)

B3. Anaphylactic Shock and Septic Shock (Blood Vessels):

1. **Anaphylactic** Shock: Extreme vasodilation due to an intense allergic reaction (insect bite, allergic to medicine such as penicillin, etc.).	2. **Septic** Shock: Extreme vasodilation due to bacterial infections and the entry of bacteria and their toxic products (=endotoxins) inside the blood.

C1. Compensated Phase: Immediate Response

1. Nervous system: Decrease in parasympathetic and increase in sympathetic activity.	2. Hormones: Increases in Angiotensin II, adrenaline and vasopressin (=ADH)
3. Cardiac response: - Increased chronotropy (tachycardia) - Increased inotropy (contraction force)	4. Vascular Response: Vasoconstriction in muscles, gut, skin and kidney -> increase in the Peripheral Resistance.

5. **BUT**: Reduced perfusion in these organs also leads to acidosis, weakness, oliguria (=decreased urine output) and pallor.	6. Skin: The skin becomes wet, cold and pale due to the increased sympathetic stimulation.

C2. Compensated Phase: Intermediate Response

1. Vascular Fluid Shift: Up to 500 ml can be transfused back into the vascular system.	2. **BUT**: This will produce a temporary anaemia (= less oxygen transported, which is bad) but also reduce viscosity (=less work for the heart, which is good!)

C3. Compensated Phase: Long Term Response

1. Kidney: Reduction in renal excretion and increase in fluid intake (thirst)	2. Liver: Increase in liver glycolysis (induced by adrenal and sympathetic stimulation) -> more blood proteins -> increase in oncotic pressure
3. Bone Marrow: Increased production in red blood cells.	

D. Physical Signs of impending Shock:

It may be interesting to know (and understand) the physical signs of an impending cardiovascular shock:

1) Skin is pale, cold and sweaty
2) Pulse is rapid and weak
3) Breathing is rapid and shallow
4) Urine output is decreased or even stopped
5) General muscle weakness
6) Reduced mental awareness or confusion
7) Mean arterial pressure may be normal or reduced (last sign to be affected)

E. Ultimately: Decompensated Phase (= irreversible)

1. If the blood loss is too high and /or fluid replacement is started too late: then **irreversible** damage will occur to several organs or systems.	2. The most at risk are: 1) Myocardium 2) Tubular necrosis (kidneys) 3) Cardiac failure 4) Multi-organ failure Ultimately: **Death**

B.7.2. Hypertension

Definition: A too high pressure in the arteries of the systemic circulation.

A. What is hypertension?

1. Hypertension is, unfortunately, a very **common** disease. In industrialized countries (= western style), about 20% of the population suffer from this disease.	2. By definition, hypertension is present when the systolic pressure is higher than 160 mmHg and/or the diastolic pressure higher than 100 mmHg.
3. The start of hypertension is insidious (= silent / secret / stealthy) as it initially causes no symptoms.	4. But in the long run, it is very dangerous as it causes wear and tear of many organs such as heart, blood vessels, kidneys, brains etc.

B. What causes hypertension?

1. Remember that the blood pressure is determined by a) the heart and b) the peripheral resistance.	2. If the heart pumps too much, either by increasing the frequency or increasing the stroke volume (or both), then the blood pressure will increase. This is called **hyperdynamic hypertension**.
3. Or, the peripheral resistance (which is caused by the resistance of all the blood vessels together) can be too high, for example by vasoconstriction of the blood vessels. This is called **resistance hypertension**.	4. It is important to note that a **brief** increase in blood pressure is NOT hypertension. For example, during exercise, it is necessary to increase the blood pressure to get more blood to the exercising muscles.
5. But if the blood pressure is too high all the time (chronically), then this is hypertension.	6. Therefore, when making a diagnosis of hypertension, it is important to measure the blood pressure **several times**, on different days, to be sure that a patient suffers from hypertension.

C. Hyperdynamic Hypertension:

1. This can be caused by an increase in: a) the heart rate b) the extracellular volume c) the sympathetic nervous system d) responsiveness to catecholamines	2. An increase in **heart rate** will increase cardiac output and this will increase the blood pressure.

3. An increase in **extracellular volume** will increase venous blood, which increases the venous return to the heart, which increases the diastolic filling, stretching of the ventricles (Frank-Starling mechanism), and increase the cardiac output.	4. Increase in **sympathetic activity** will increase heart rate, stroke volume, vasoconstriction of the vessels (arteries & veins), and thus increase blood pressure.
5. Increase **sensitivity to catecholamine's** can be caused by an increase in cortisol (from the adrenal cortex) and/or an increase in the thyroid hormones (T3, T4) in the case of hyperthyroidism.	

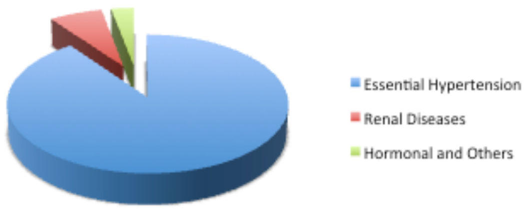
D. Resistance Hypertension:

1. Resistance hypertension is mainly caused by: a) vasoconstriction of the peripheral blood vessels b) an increase in blood viscosity	2. **Vasoconstriction** can be due to: a) increased sympathetic activity (either induced by increased nervous activity or by an increased adrenal medullary activity), b) increased sensitivity to catecholamine's (cortisol or thyroid hormones) or c) an increase in Angiotensin II (renin-angiotensin-aldosterone system)

E. Additional auto-regulatory damage:

1. An important point in hypertension is the damage that is caused by the **chronic** exposure to high blood pressure.	2. For example, because the heart is pumping more and against a higher pressure (after-load!), **hypertrophy** of the left ventricle will occur.
3. If this condition last too long, then the left ventricle will suffer (coronary arteries), possibly leading to **cardiac failure**.	4. Or, the pressure in the left atrium may increase, and then that of the pulmonary veins -> damage to the pulmonary system.
5. Furthermore, several organs, such as the kidneys, will "protect" themselves from this continuous high pressure by vaso-constricting the blood vessels to those organs.	6. As this is a chronic situation, **hypertrophy** of the muscles in the blood vessels will occur which will "fixate" the high peripheral resistance.

F. Mechanisms of Hypertension:

1. In contrast to all this knowledge, the reason why somebody develops hypertension are less well known.	2. In fact, in 90% of the patients, there is no detectable cause for their hypertension. This type is called **Primary** or **Essential Hypertension**.
 	3. There are of course many theories why these patients develop hypertension.
	4. Genetics? Indeed, women are slightly more affected than males.
5. Stress? Managers, pilots, personality ("frustrated fighter type"), salt-sensitive patient, sensitivity to catecholamine's are all possibilities but not yet proven or clarified.	6. In 10% of the patients, those that suffer from **Secondary Hypertension**, the cause of hypertension is due a definite disease (which makes it potentially treatable): a) 7% renal diseases b) 3% hormonal and other causes
7. **Renal diseases:** Many diseases of the kidney may induce renal ischemia, which in turn induces the release of **renin** into the blood stream. This in turn will activate angiotensinogen into angiotensin I which leads to an increase in angiotensin II (in the lungs by ACE). This will constrict the blood vessels and increase the blood pressure.	**8. Hormonal diseases:** a) **Adrenogenital syndrome**: the formation of cortisol in the adrenal cortex is blocked, leading to an increase in ACTH (=adrenocorticotrophic hormone) which leads to an increase in mineral corticoid precursors, leading to retention of Na+, decrease in diuresis, increase in extracellular volume and hence hypertension.
8 b) Primary hyperaldosteronism: A tumor in the adrenal cortex releases unregulated amounts of aldosterone, leading to Na+ retention and increase in extracellular volume.	**8 c) Cushing's syndrome:** Inadequate ACTH release (neurogenic or tumor in the hypophyses) or a tumor in the adrenal cortex increase glucocorticoid in the plasma. This increases the catecholamine effect (increased cardiac output) and mineral corticoid effect (increased Na+ retention).

8 d) Pheochromocytoma: A tumor in the adrenal medulla produces uncontrolled catecholamine's, which increases epinephrine and norepinephrine, thereby inducing both **hyperdynamic** and **resistance** hypertension.	**9. Neurogenic Hypertension:** Overstimulation of the sympathetic system due to a disease in the brain such as a hemorrhage, brain tumor, cerebral oedema, encephalitis etc.

G. Other factors involved in Hypertension:

1. **Environmental factors:** a) obesity b) alcohol c) salt intake d) stress e) drugs (oral contraceptives etc)	2. **Fetal factors.** A low birth weight is often correlated with hypertension later in life.
3. **Diabetes**. Insulin resistance > metabolic syndrome > Hypertension	4. **Pregnancy**. Normally, cardiac output (CO) increases while peripheral resistance (PR) decreases, so blood pressure stays normal
5. But sometimes, hypertension develops with possibility of developing pre-eclampsia.	6. **Pre-eclampsia** is hypertension during pregnancy with proteinuria (loss of proteins in the urine). This can lead to **eclampsia**: convulsions, cerebral oedema, clotting abnormalities, foetal death, maternal death.

H. Long term complications of Hypertension:

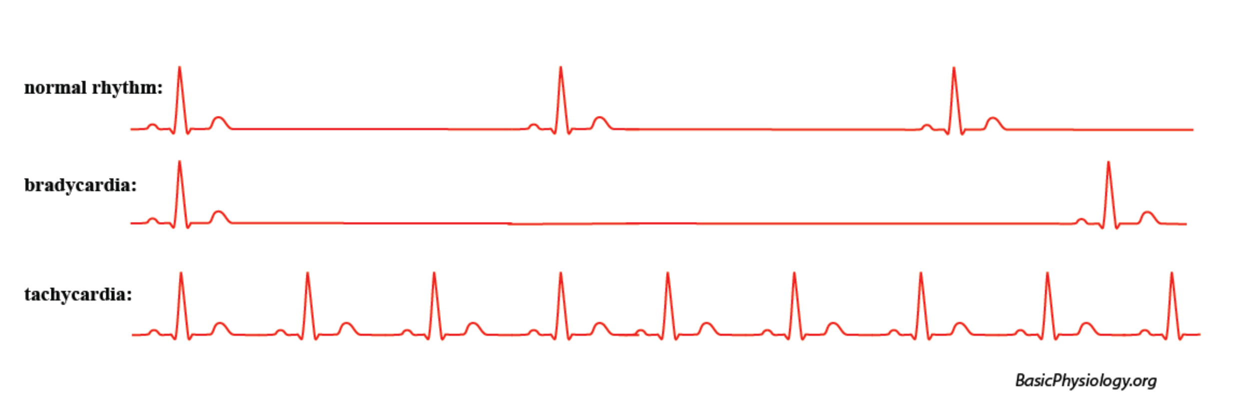
Many! And serious complications:

a) peripheral vascular diseases (check the eye!-> blood vessels in the retina)
b) renal failure
c) stroke
d) cardiac death due to coronary events and/or cardiac failure.

B.7.3. Cardiac Arrhythmias

Definition of a cardiac arrhythmia: Abnormal heart rhythm (simple!).

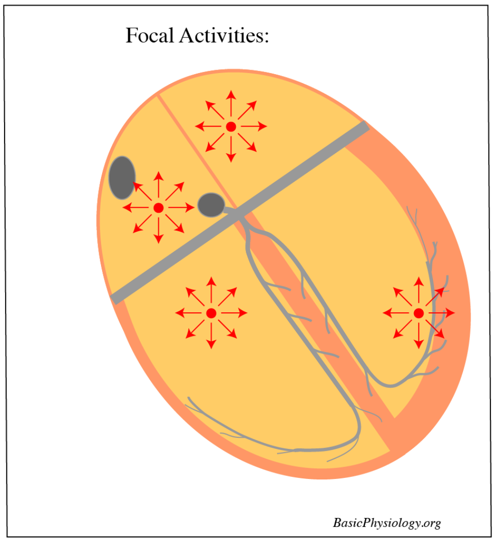
There are two types of arrhythmias; either the heart beats **too fast** or the heart beats **too slow**.

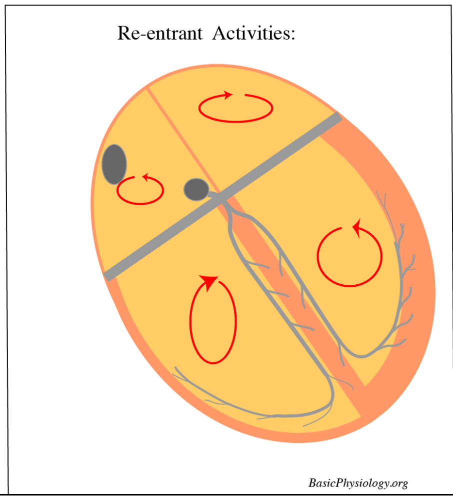


A. Bradycardia (also called Bradyarrhythmia): the heart beats too slow.

1. Sick Sinus Syndrome. In this disease, the sinus node is not functioning properly and action potentials are either not initiated or they have difficulty propagating into the right atrium.	2. The major problem is fibrosis of the sinus node area, mainly due to old age.
3. The ECG looks normal (normal P, QRS, T waves and normal PQ and ST intervals). The heart just beats too slowly.	4. Therapy: implantation of an **artificial pacemaker** that will stimulate the heart if the sinus node quits.

B. Tachycardia (also called Tachyarrhythmia): the heart beats too fast.

1. There are two major mechanisms for inducing tachycardia's: a. **focal** activity b. **re-entrant** activity	
2. Focal activity means that an abnormal site is generating impulses. This site is often called "**ectopic**", which really means outside the normal location (i.e., the sinus node).	
3. The site of ectopic activity can be located anywhere in the heart, in the right or left atria, in the right or left ventricle, in the AV-node etc.	

4. A second mechanism is called **re-entry**.	
5. In re-entry, the impulse turns around in a loop or a circuit. This is also called a **circus movement** arrhythmia. These circuits can occur in the atria or in the ventricles.	

C. Mechanisms of Focal Arrhythmias:

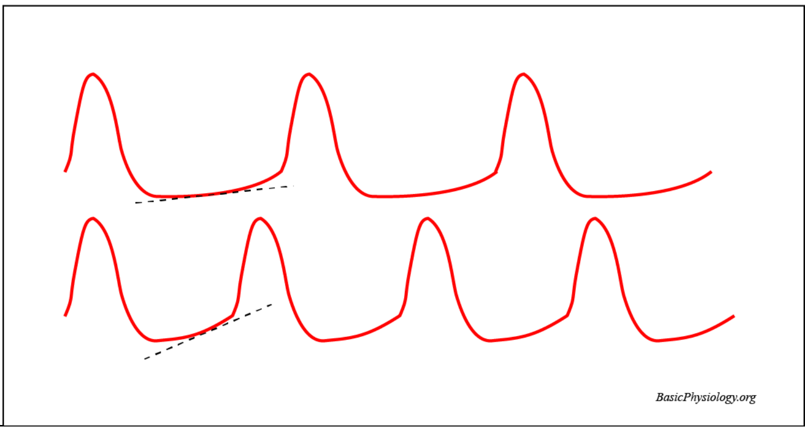
1.
There are several mechanisms that may induce focal arrhythmias:

a. Enhanced Diastolic Depolarization

b. Triggered Activity:
- early after depolarization
- delayed after depolarization

2.
Enhanced Diastolic Depolarization:

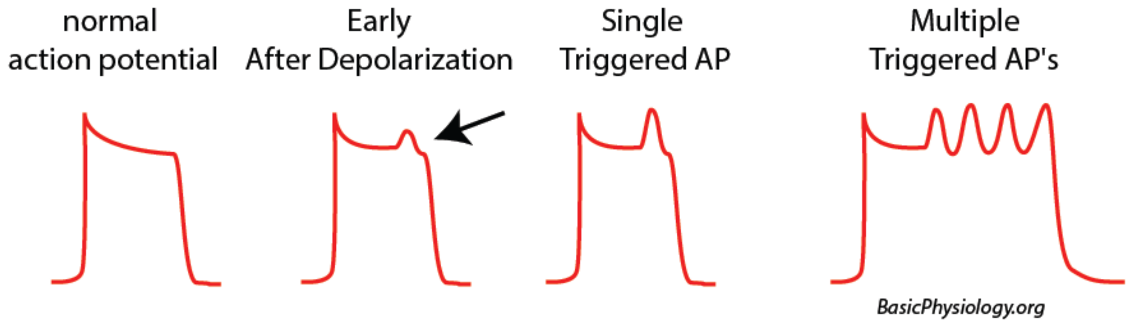
This occurs in the SA-node, usually by excessive sympathetic activity. Because the depolarization is **faster**, the potential will reach **threshold** quicker and produce action potentials at a **faster** rate. An example of this mechanism is **sinus tachycardia**.



3.

Triggered activity: Early After Depolarization:

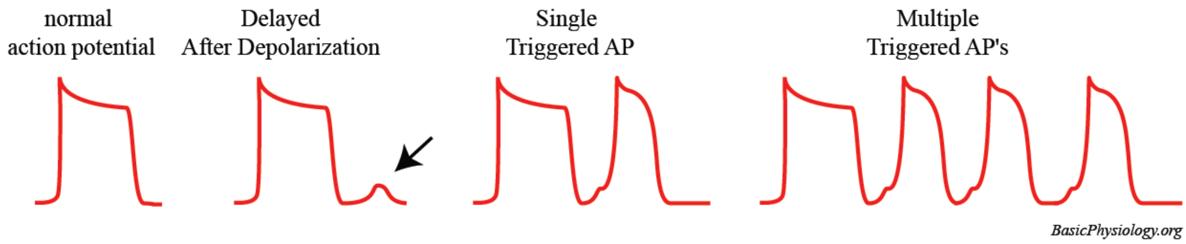
Sometimes, during the plateau phase of the action potential, a spontaneous depolarization may occur. This is often the case when there is too much calcium in the cell. These depolarisations may reach threshold and induce, too soon, a **new** action potential:



4.

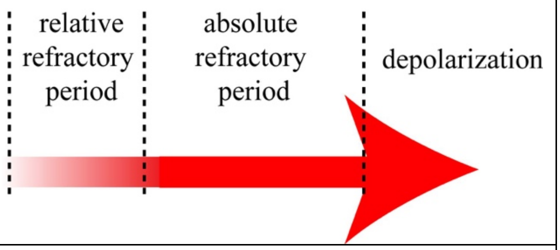
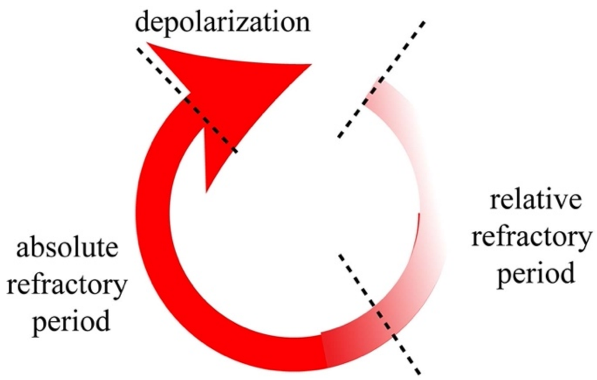
Triggered activity: Delayed After Depolarization:

This is similar to the early after depolarisations but this type of activity occur after full repolarisation has taken place, hence their name, delayed (or **late)** after depolarisations:

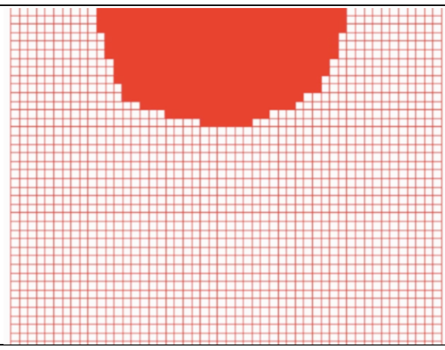


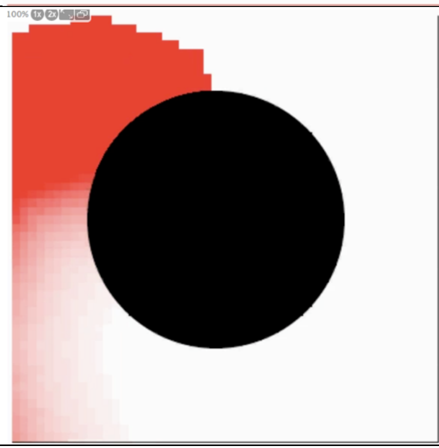
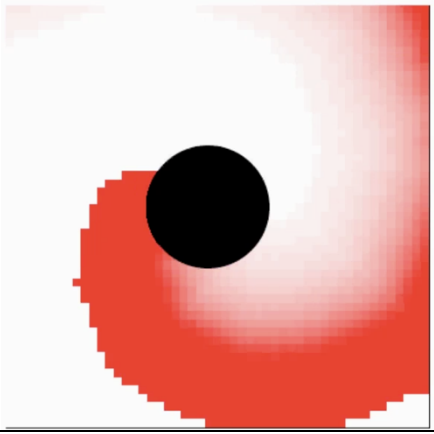
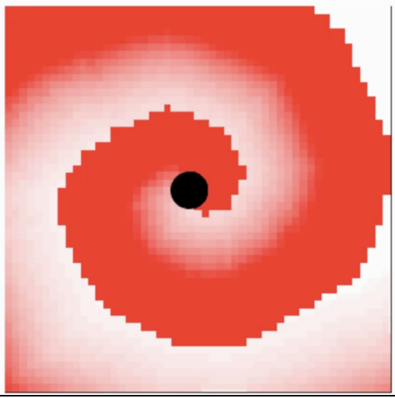
D. Mechanisms of Re-entrant Arrhythmias:

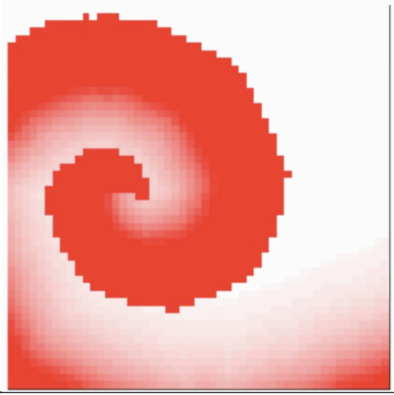
1. Re-entry literally means ‘to re-enter’ or ‘to come back’. In this case, it means that the action potential in the heart ‘comes back’ or re-excites itself. It can only do that if it turns around and ‘bite in its own tail’, just like the fox in Firefox.		

<table>
<tr><td>2.
Because the path of the impulse is no longer straight but propagates in a circle, this type of re-entry is often also called ‘circus movement’ arrhythmia.</td><td>3.
Note that if the impulse runs in a circle, it can only re-excite the cells in front of the advancing wave if those cells have recovered from the previous excitation. In other words, the refractory period of the cells now becomes very important.</td></tr>
<tr><td>4.
If you remember your cellular electrophysiology, the refractory period consists of two parts:
- the absolute refractory period
- the relative refractory period</td><td>
</td></tr>
<tr><td>5.
If the impulse propagates in a straight line, the absolute refractory period follows immediately after the depolarization. The relative refractory period occurs after the absolute refractory period.</td><td rowspan="2">
</td></tr>
<tr><td>6.
But in a circle, the depolarization may bite in its own tail, which may consist of relative refractory tissue. In fact, the circle cannot become ‘smaller’ than the (total) refractory period!</td></tr>
</table>

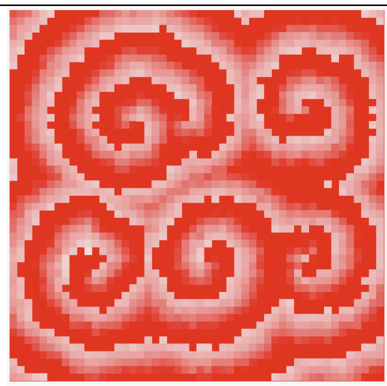
E. Types of Re-entrant Arrhythmias:

<table>
<tr><td>1.
In general, there are two types of re-entrant arrhythmias:
- anatomical re-entry
- functional re-entry</td><td>2.
The anatomical re-entry occurs around an obstacle, such as dead tissue, for example caused by an old infarct.</td></tr>
<tr><td>3.
In the following movie, I have simulated the initiation of such an anatomical re-entry. I will first start with a normal focal activity:</td><td></td></tr>
</table>

4. In the next movie, I have introduced a 'hole'. In this situation, two impulses will propagate around the block, collide against each other and thereby stop this strange (= '**aberrant'**) propagation.	
5. But, suppose that one of the two impulses was blocked at an early stage? Then the other impulse can continue to propagate around this hole. In fact, it will continue forever! This is an arrhythmia! Because the impulse is running around an obstacle, this is called an **anatomical re-entry** or an **anatomical circus movement**.	
6. Now let's, in our simulation, make the central hole smaller. You can still initiate an **anatomical circus movement re-entry**!	
7. And if the hole is very small? Still!	

8. And if there is no hole at all? Yes, you can still induce re-entry. But there is now no hole around which the impulse propagates. It now actually propagates around its own refractory tail! This is called '**functional re-entry**'.	

F. Fibrillation

1. In the previous examples, there was only one circuit revolving either around a 'hole' (= **anatomical** re-entry) or around its own refractory tail (= **functional** re-entry).	2. But what happens if there is **more** than one impulse revolving around in the heart?
3. This is shown in the next simulation where 5-6 circus movements are simultaneously taking place.	
4. Obviously, in this situation, there is no longer any rhythm in the heart. Normal rhythm has now been replaced by chaos. This chaos is called 'fibrillation'	

G. Therapies?

1. There has been a huge increase in therapies for treating cardiac arrhythmias; from all kind of drugs to electronic equipment.	2. It is now also possible to treat patients and their arrhythmias by inducing blocks (dead tissue) or 'destroying' abnormal pacemaker's area at specific locations in the heart muscles.
3. Especially in the field of electronics, many types of pacemakers have been developed which, on demand, can intervene to stop a specific arrhythmia and restore sinus rhythm.	4. But the ultimate device is of course the defibrillator! This device has new become available throughout society, as AED (=automatic external defibrillator) in multiple locations such as shopping centres etc.

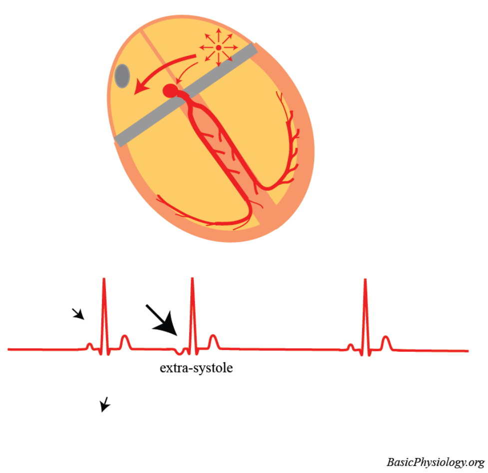
B.7.4. Supraventricular Arrhythmias

Introduction

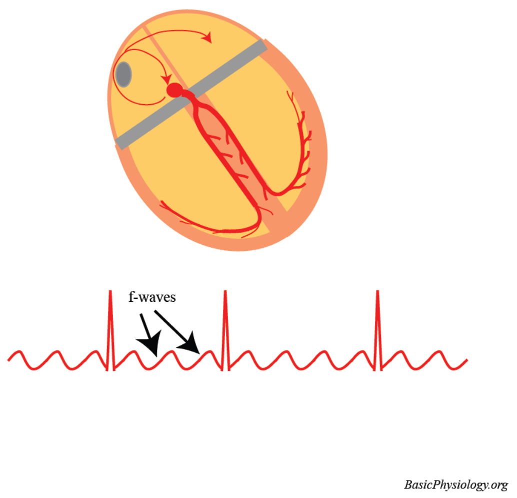
1. Arrhythmias are usually divided into those that occur in the ventricles and those that occur in the atrium, above the ventricles, also called “supra-ventricular”.	2. The major **supra-ventricular** arrhythmias are: 1. Atrial extra-systole 2. Atrial flutter 3. Atrial tachycardia 4. AV-nodal tachycardia 5. Atrial fibrillation
3. The major **ventricular** arrhythmias are: a. Ventricular extra-systole b. Ventricular tachycardia c. Ventricular fibrillation. *(see next page)*	4. There are a few arrhythmias that do not fit into one of these two groups. The most famous one is the WPW syndrome (=Wolf-Parkinson-White*; see next page*).
5. Also, the **duration** of the arrhythmia is important.	6. There are three types: - **Paroxysmal**: lasts for seconds to a few hours - **Persistent**: lasts for days to weeks - **Chronic**: lasts months to years.

Supra-ventricular Arrhythmias

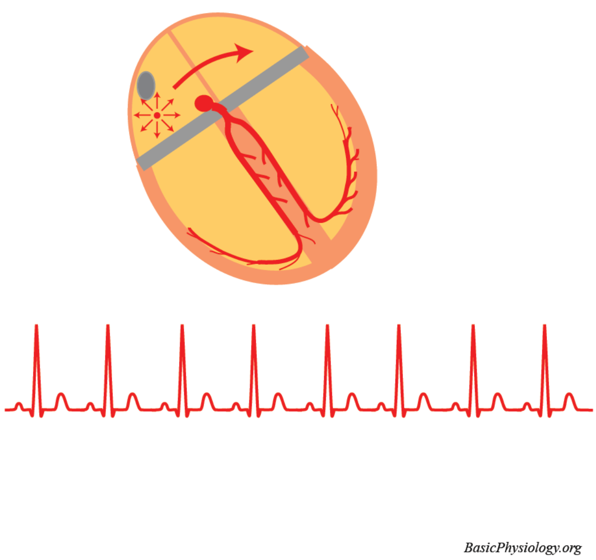
A. Atrial Extra systole

1. Atrial extra systole is when an “extra” beat occurs. In other words, an extra beat is “inserted” between the regular beats.	2. Because the origin of this extra-systole could occur anywhere in the atria, right or left, the P wave and the PQ-interval may be different from the normal P wave.
3. In this example, the focus was located in the left atrium. Therefore, the major direction of propagation is now opposite from the normal direction; hence the P-wave becomes opposite to the normal polarity (i.e., negative).	
4. Note that the QRS and T waves are normal. This is because the extra impulse, after entering the AV-node, will propagate through the major Purkinje pathways in the same manner as the normal impulses.	

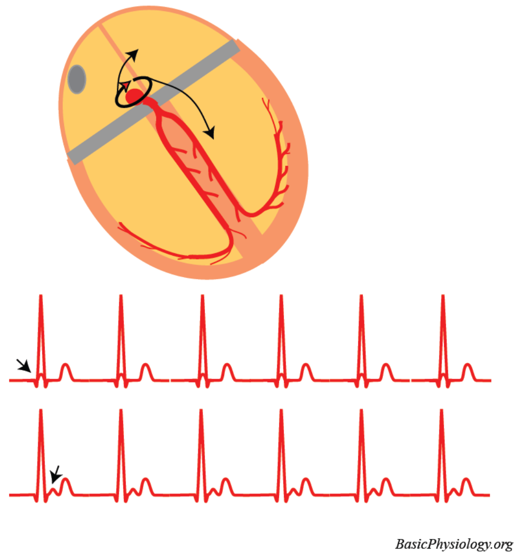
B. Atrial Flutter

1. In atrial flutter, there is a large re-entrant circuit, usually in the right atrium. This circuit revolves much faster than the normal sinus rhythm; hence it forms a tachycardia.	2. From the revolving circuit, impulses regularly propagate to the left atrium. These waves are visible as undulating F-waves on the ECG (F=flutter).
3. The circuit rotates too quickly for the AV-node (which has a long refractory period) so not all impulses propagate through the AV-node but are blocked.	
4. Now and then, when the AV-node has sufficiently recovered, an impulse propagates through the Purkinje system to the ventricles.	
5. Therefore, the QRS complex has a normal shape. The T-wave is often hidden by the flutter f-waves as in this example.	

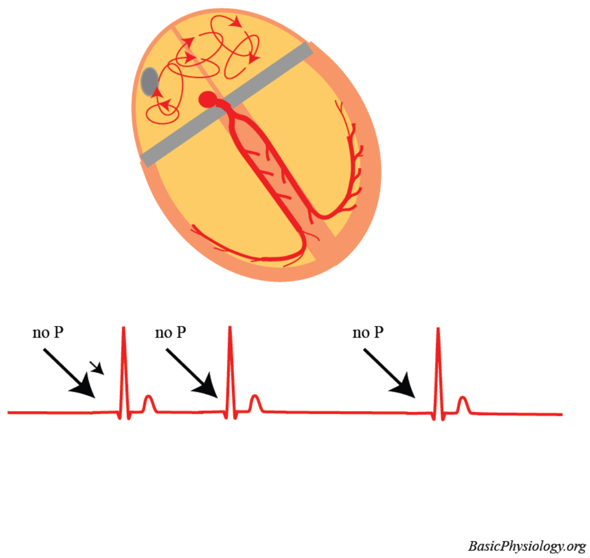
C. Atrial Tachycardia

1. An atrial tachycardia is caused by an ectopic focus that induces impulses at a rapid rate.	2. This repetitive focus can be located anywhere in the right or left atrium.
3. The polarity of the P wave and the PQ-interval therefore depends on the location of the focus.	
4. Often, the rate of the atrial tachycardia is lower than that of atrial flutter and every impulse does propagate through the AV-node and excite the ventricles, as in this case (diagram).	
5. Since the impulse propagates normally through the conducting system of the ventricles, the shape and polarity of the QRS and T-wave are normal.	

D. AV-nodal Tachycardia

<table>
<tr><td>1.
In this type of atrial tachycardia, a re-entrant circuit is located in and around the AV-node!</td><td>2.
These circuits can be quite small, mainly due to the very slow propagation in the AV-node (which produced the delay between the atria and the ventricles; remember?)</td></tr>
<tr><td>3.
As in other re-entries, impulses will propagate from the circuit to surrounding areas, in this case both the atria and the ventricles.</td><td rowspan="3"></td></tr>
<tr><td>4.
If the circuit is located high in the AV-node, then the PQ-time will be very short or the P-wave may even be hidden in the QRS complex (top ECG in the figure).</td></tr>
<tr><td>5.
If, however, the circuit is located low in the AV-node and close to the bundle of His, then propagation back to the atria will take a long time and the P-wave will occur after the QRS complex (bottom ECG in the figure).</td></tr>
</table>

E. Atrial Fibrillation

<table>
<tr><td>1.
In atrial fibrillation, there are multiple re-entrant propagations simultaneously present, in the right and in the left atrium.</td><td>2.
Therefore, some parts of the atria are constantly excited while others are recovering. All these excited and recovering areas shift all the time throughout the muscle.</td></tr>
<tr><td>3.
As there is no longer one single propagating impulse, but many impulses, there is no longer a significant signal on the ECG and therefore no P wave, not even an ‘F’ wave.</td><td rowspan="3"></td></tr>
<tr><td>4.
Occasionally, dictated by the long refractory period of the AV-node, an impulse will manage to propagate through the AV-node and excite the ventricles.</td></tr>
<tr><td>5.
Because these impulses propagate normally through the Purkinje system, the shape and polarity of the QRS and T-wave are normal.</td></tr>
</table>

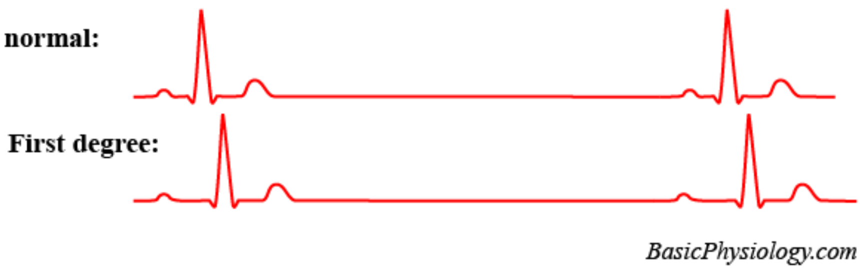
B.7.5. Ventricular Arrhythmias

Introduction *(repeat of previous page)*

1. Arrhythmias are usually divided into those that occur in the ventricles and those that occur in the atrium, above the ventricles, also called "supra-ventricular".	2. The major **supra-ventricular** arrhythmias are: 6. Atrial extra-systole 7. Atrial flutter 8. Atrial tachycardia 9. AV-nodal tachycardia 10. Atrial fibrillation *(see previous page)*
3. The major **ventricular** arrhythmias are: d. Ventricular extra-systole e. Ventricular tachycardia f. Ventricular fibrillation.	4. There are a few arrhythmias that do not fit into one of these two groups. The most famous one is the WPW syndrome (=Wolf-Parkinson-White).
5. Also, the **duration** of the arrhythmia is important.	6. There are three types: - **Paroxysmal**: lasts for seconds to a few hours - **Persistent**: lasts for days to weeks - **Chronic**: lasts months to years.

Ventricular Arrhythmias

A. Atrio-ventricular block

<table>
<tr><td>1.
In this disease, the impulse has difficulty in propagating from the atria, through the AV-node, into the ventricles.</td><td>2.
Based on the behavior of the heart, there are three types of AV-blocks:</td></tr>
<tr><td colspan="2">3. First degree AV-block:
This is not really a block but the impulse takes longer than normal to propagate through the AV-node. This is visible on the ECG by a longer PQ-interval.

</td></tr>
</table>

4. **Second degree AV-block:**
In this situation, some impulses propagate through the AV-node and some do not. The ratio between those that pass and those that do not pass can be expressed; for example, 1:3 second degree AV-block (as in this case).

5. **Third degree AV-block:**
In this case, there is **total** block between the atrium and the ventricles. The atrium will continue to function as before, visible by the P waves.

6.
The ventricles will also produce impulses (from the Purkinje system) but at a lower rate than the atrium. Furthermore, there is no relationship any more between the atrial activity (and contraction) and that of the ventricles.

B. Ventricular Extra systole

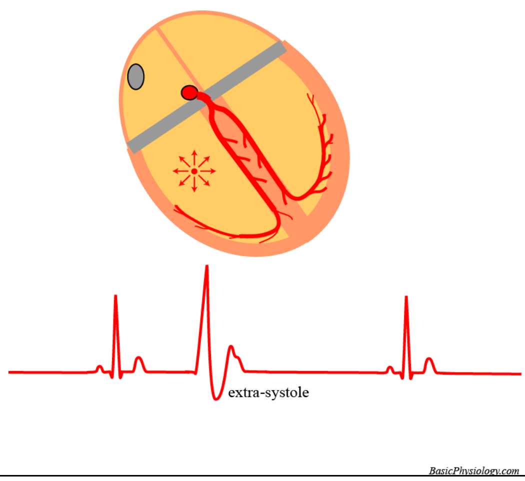
1.
As with the atrial extra systole, the ventricular extra systole is an “extra” beat.

2.
But this time, the extra beat starts somewhere in the ventricles and not in the atria.

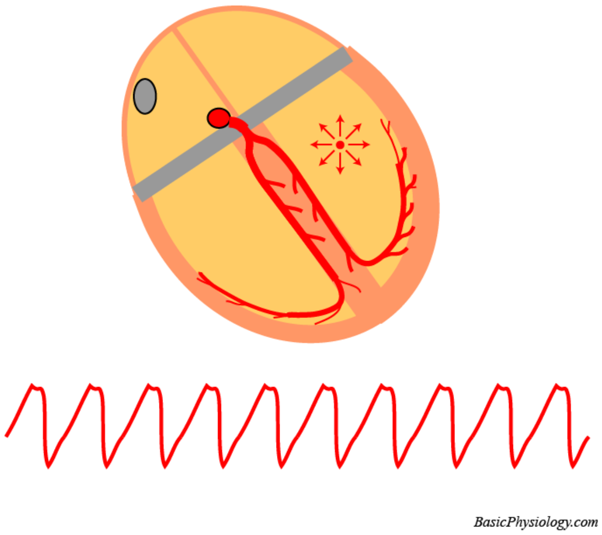
3.
There is therefore no relationship between the P wave and the QRS complex.

4.
In addition, and most importantly, the **shape** of the QRS has changed. This is because the propagation in the ventricles is different from the normal propagation.

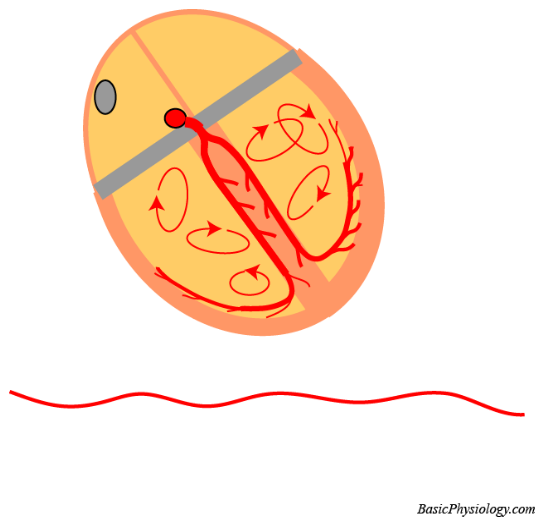
5.
Therefore, the shape of this strange QRS can be very weird and unpredictable.



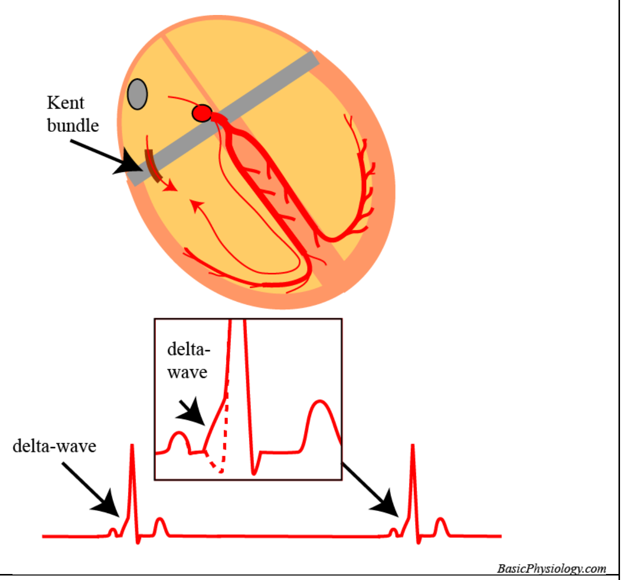
C. Ventricular Tachycardia

1. A ventricular tachycardia is usually caused by an ectopic focus that induces many impulses at a rapid rate.	2. This repetitive focus can be located anywhere in the right or left ventricle.
3. The shape and the polarity of the QRS complex depend on the location of the focus and the sequence of the propagation. The signals are often large.	
4. The P wave is hidden by these large waves and the repolarization (T-wave) can often no longer be distinguished.	
5. The problem with ventricular tachycardia is that the ventricles contract too often, leaving little time for the refill of the ventricles.	

D. Ventricular Fibrillation

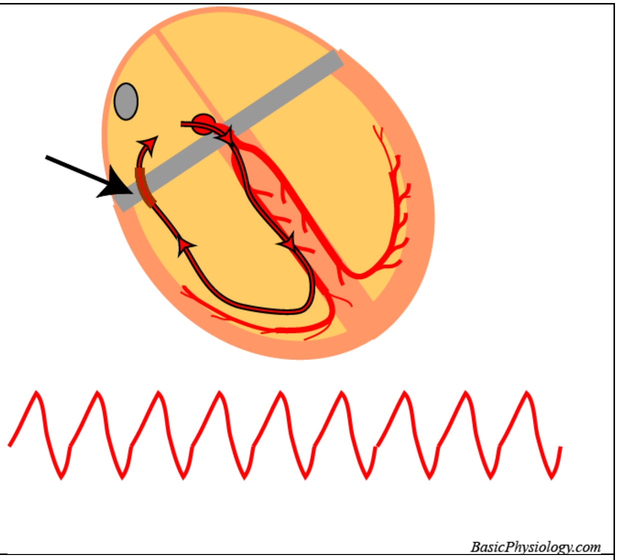
1. In ventricular fibrillation, there are multiple re-entrant propagations simultaneously present, in the right and in the left ventricles.	2. Therefore, some parts of the ventricles are constantly excited while others are recovering. All these excited and recovering areas shift all the time throughout the muscle.
3. As there is no longer one single propagating impulse, there is no longer a significant signal on the ECG and therefore no QRS and T waves.	
4. Because the heart is no longer contracting, it is not pumping any blood, and the whole heart will become very quickly **hypoxic** and **ischemic**.	
5. This will also affect the right atrium and the sinus node and the P wave will also disappear. This is the **final** arrhythmia!	

E. Wolf-Parkinson-White syndrome (=WPW)

<table>
<tr><td>1.
In the Wolf-Parkinson-White syndrome, the AV-bundle is not the only connection between the atria and the ventricles.</td><td rowspan="3">
</td></tr>
<tr><td>2.
In this disease, there are other muscle fibres that connect the atria to the ventricles. These fibres are often named as the bundle of Kent (after the first discoverer).</td></tr>
<tr><td>3.
When the heart beats normally, this bundle of Kent will be visible on the ECG as a “delta-wave”.</td></tr>
<tr><td>4.
The delta wave is caused by the fact that the atrial impulse does not only activate the ventricles through the normal AV-node but now also through the bundle of Kent.</td><td>5.
Because the Kent bundle does not delay the impulse (as the AV-node does), the ventricles will be activated a bit earlier than normal. Therefore, the PQ-time will be shorter than normal.</td></tr>
<tr><td>6.
In addition, because this earlier activation is propagating more slowly through the ventricle than through the Purkinje system, the delta wave is a slow wave on the ECG.</td><td>7.
However, the impulse also propagates through the AV-node and, after this delay, is conducted rapidly through the Purkinje system. This conduction is much faster than the impulse through the Kent bundle. Therefore, the major and second part of the QRS shows a normal configuration.</td></tr>
</table>

F. WPW reciprocating rhythm

<table>
<tr><td>1.
Patients who suffer from the presence of such an abnormal AV-bundle often complain of sudden (paroxysmal) palpitations.</td><td>2.
In that situation, the heart is beating much faster than normal. This is therefore a tachycardia.</td></tr>
<tr><td>3.
What is happening is shown in the diagram. An impulse is now propagating from the right atrium, through the AV-node and Purkinje system to the ventricles and conducting back into the right atrium through the bundle of Kent.</td><td></td></tr>
</table>

4. Therefore, this impulse is continuously propagating in a large re-entrant loop: from atria to ventricles to atria to ventricles etc etc.	
5. This abnormal rhythm is often called a “reciprocating rhythm” because the impulse is continuously “reciprocating” or propagating between the atria and the ventricles.	6. For the ECG, it looks very much like a ventricular tachycardia.
7. This rhythm is uncomfortable for the patient but does not kill. However, there is now another situation possible that will certainly **kill** the patient.	8. If for some reason the **atria** fibrillate then the situation becomes very dangerous. Then, all the impulses can propagate through the bundle of Kent to the ventricles. All these impulses will then make the **ventricles** fibrillate, which will immediately kill the patient. This is a typical example of “**sudden death**”.
9. Note that this does not happen in a normal heart. There, if the atria fibrillate, most impulses from the fibrillating atria will not reach the ventricles as they are delayed and blocked by the AV-node.	10. Therefore, in the normal heart, the AV-node protects the ventricles. But in WPW patients, their ventricles are **not protected** due to the presence of the abnormal Kent-bundles.

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