

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.
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A. The Renin-Angiotensin-Aldosterone system:

1. This system is an interplay of several hormones from several organs.	Function diagram of the renin-angiotensin-aldosterone system <pre> graph TD ABP1[arterial blood pressure] --> RPP[renal perfusion pressure] RPP --> Renin[release of renin from the juxtaglomerular cells] Renin --> AngI[conversion of angiotensinogen to angiotensin I in the plasma] AngI --> AngII[conversion of angiotensin I to angiotensin II in the lungs] AngII --> AR[constriction of arterioles] AngII --> Ald[secretion of aldosterone] AR --> PR[peripheral resistance] Ald --> SWR[salt and water reabsorption] SWR --> BV[blood volume] PR --> ABP2[arterial blood pressure] BV --> ABP2[arterial blood pressure] </pre>
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.	

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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.

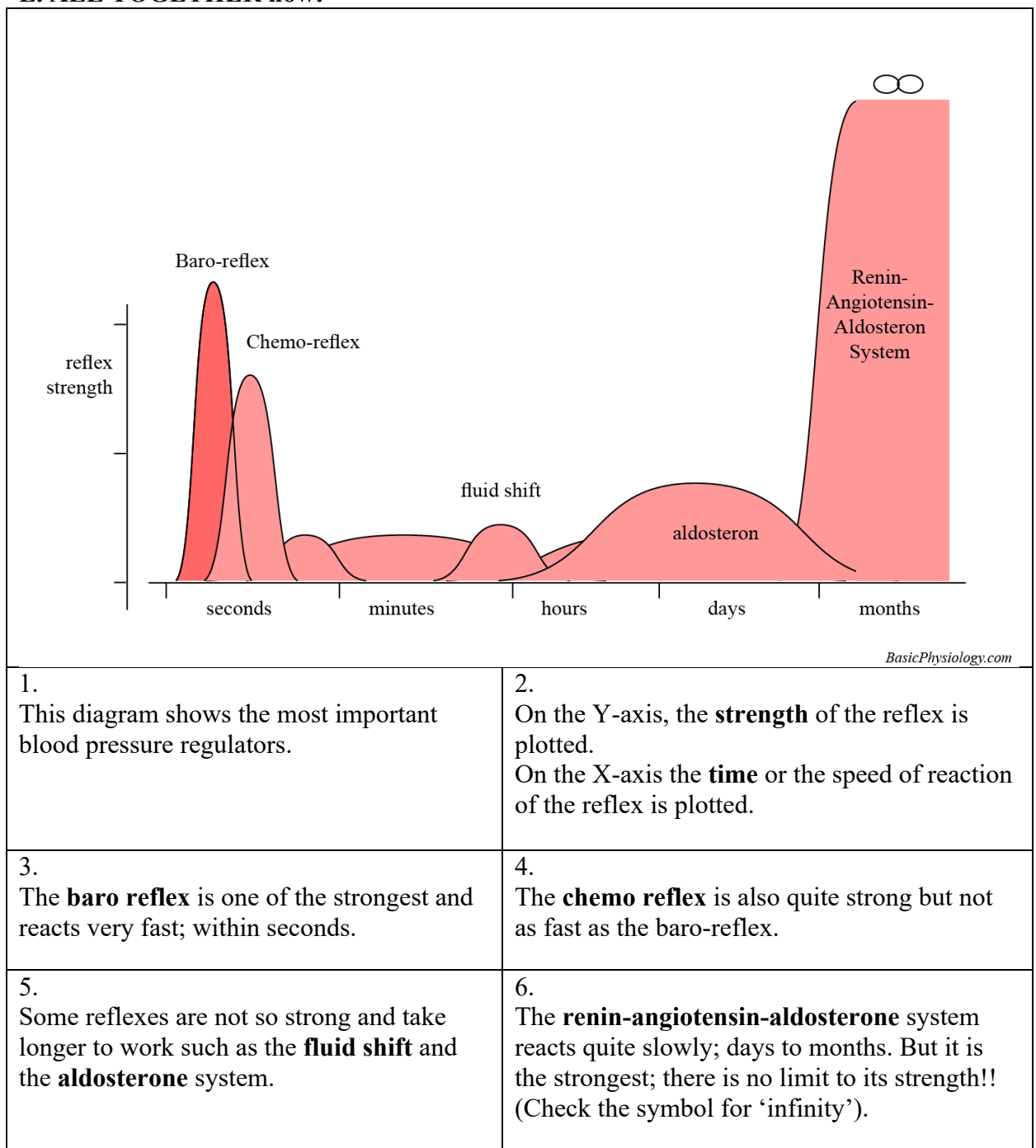
D. Other Short- or Long-term systems:

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 (<i>it was of course a him!</i>) 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”!