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Del I

Background

1 | Anatomy and Physiology

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1.1 Cardiovascular System

The main function of the cardiovascular system is the blood supply of the whole body and the transportation of metabolites. The propulsion of this is the heart. It generates through the sputum strength of the left ventricle the systolic blood pressure. The pressure difference between the heart and the periphery emerging there from, ensures the blood flow. The blood flows from regions with high pressure, like the aorta, to regions with low pressure, like the periphery.

The heart supplies the body through two circuits with blood. On this occasion the heart regulates the blood allocation with adjustment of stroke volume and heart frequency.

The oxygen-rich blood accumulates in the left ventricle. From there the blood is thrown out through the aortic valve into the aorta and via the arteries spread into the whole body. The venous system returns the meanwhile low in oxygen blood back to the heart into the right atrium. From there the blood flows into the right ventricle and is thrown out through the pulmonary valve into the lung arteries. In the lung happens the gas exchange of the blood. Subsequent the oxygen-rich blood flows via the pulmonary veins back to the left heart to supply the body.

As mentioned, there are two types of vessels, arteries and veins. The difference between those two types of vessels is on the one hand that arteries transport the blood away from the heart and veins solely transport blood to the heart. On the other hand, there are some differences in the structure of arteries and veins. Arteries consist of three different layers, tunica interna, tunica media and tunica externa. The tunica interna consists of vascular endothelium, the tunica media consists of smooth muscle cells and elastic fibres, the tunica externa consists of connective tissue and also elastic fibres.

Furthermore, there are two different types of arterial vessels. In arteries of the elastic type prevail the elastic fibres in the tunica media. This allows an abrupt extension of the vessel during the systole and ensuing constriction, due to this the blood is transported. This phenomena is called windkessel function. In arteries of the muscular type prevail the muscular fibres in the tunica media. This allows regulation of the lumen by constriction and dilatation, whereby the resistance and the blood flow in the organs is regulated.

Venous vessels are similarly structured like arterial vessels, however they are thinner and have also semilunar valves inside, to inhibit back flow inside the vessels. This system is supported by muscle pump.

The arterial and the venous vessel system are connected through the capillary system.

1.2 Microcirculatory system

In this section the hand will be used as an example point, to describe the microcirculatory system.

The heart and larger arteries and veins are what we usually associate with the cardiovascular system, but actually those are only mainly used for transport of blood. Instead it is the capillaries, that permeate most tissues, that is responsible for the perfusion of tissue. These are the only vessels that permit exchange between the vessel and the surrounding interstitial fluids. Capillaries are made not of single individual fluid conductors like veins and arteries, but instead formed capillary beds. Here they work as a interconnected network of vessels. As mentioned before the arterioles divide into dozen of capillaries which then merge into a venule, after the blood has been de-oxygenated. A capillary is divided into two segments, first the metarteriole and second the capillary. The blood flow between arterioles and venules can also be a direct connection, made by an arteriovenous anastomosis. This works as a bypass diverting blood flow around the capillary bed. An example of the structure of the capillary bed can be seen on fig 1.1.[martini2012]

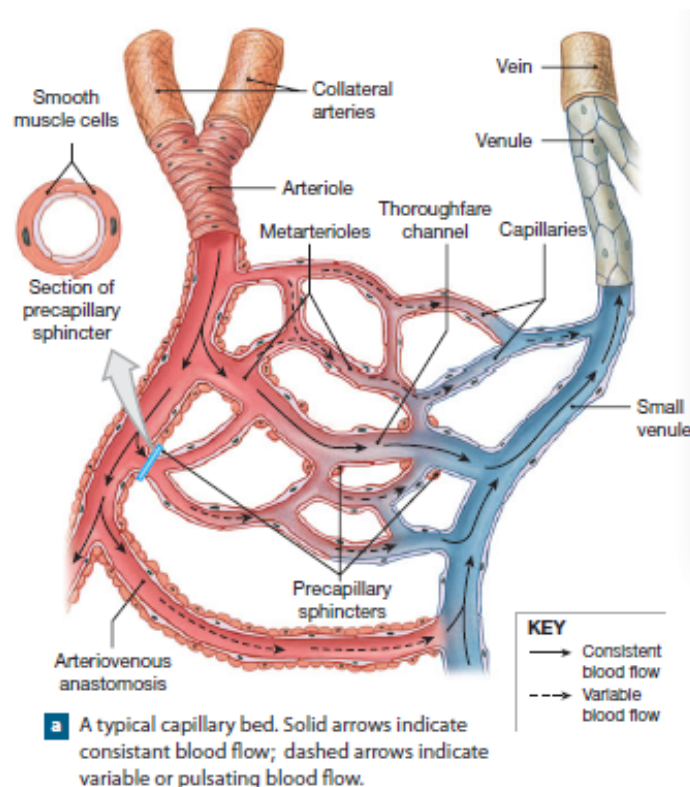


Figure 1.1: The basic structure of a capillary bed, with arteriole on the left side of the bed and a venule on the right.

Each capillary entrance is controlled by a precapillary sphincter, which is composed of smooth muscle cells, that are able to contract or relax and thereby limit access of blood flow to certain capillaries. The blood flows relatively slow within the capillaries giving time for the two way exchange of nutrients and wastes. [martini2012]

1.2.1 Vasmotion

The flow within the capillaries varies. This is due to the earlier mentioned precapillary sphincters contracts and relaxes. The opening and closing of sphincters is part of the autoregulation process performed at a local level, to control the blood flow. Local changes in concentration of chemicals and interstitial fluids eg. dissolved oxygen concentrations in tissue cause the sphincters to dilate permitting a greater flow of blood to the area. The cardiovascular system does not contain blood enough for every vessel a capillary beds to be filled with blood. Therefore only 25 percent of the vessels in a capillary bed contains blood, and vessels activity needs to be well coordinated.[martini2012]

Under normal circumstances cardiac output remains stable and the control of local blood flow happens through local peripheral resistance within local tissues. The regulation of cardiovascular activity is controlled by local homeostatic mechanism. These make sure that demands such as oxygen and nutrients are met and wastes are disposed. [martini2012]

Factors that promote dilation is called vasodilators and can be some of the following:

- Decreased oxygen level or increased CO₂ level
- Lactic acid or other acids generated from tissue cells
- Nitric oxide NO released from endothelial cells
- Rising concentrations of potassium ions or hydrogen ions in the interstitial fluid.
- Chemicals released during local inflammation
- Elevated local temperature

A vasodilation will result in increased oxygen, nutrients, buffers released to recreate homeostasis. Factors that stimulate constriction is called vasoconstrictors and can happen due to following:

- Damaged tissue
- Aggregating platelets

Factors that affect tissue perfusion is cardiac output, peripheral resistance and blood pressure[martini2012].

1.3 Sepsis

Sepsis is a condition, that develops on behalf of Systemic inflammatory response syndrome (SIRS) with presence of an infection or bacteria in the tissue, within the body which triggers an immune response. This response often overexposes the workload on the immune system to fight the inflammation or bacteria. The infection or bacteria can be anywhere in the body's tissue. Some of the normal macrohaemodynamics of sepsis are abnormal body temperature, abnormal heart rate, oxygen extraction and abnormal blood pressure [plunta2010, kanta2014]. Sepsis is often associated with three stages, sepsis, severe sepsis and septic shock. This is illustrated in figure 1.2.

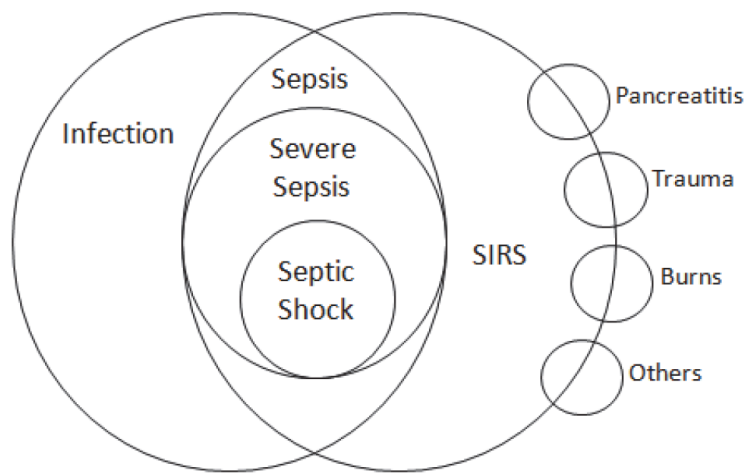


Figure 1.2: Relation between SIRS and infection. Showing the stages in sepsis and some of the causes of SIRS which include pancreatitis, trauma, burns etc.

sepsis

Under the condition of sepsis several things happen, mainly to the micro circulatory system at the capillary level, that leads to impaired homeostasis in the body. Infection or other bacteria that's responsible for causing some irregularity is present in the blood and in the tissues around the the vessels. Among the first thing's that happens when the body encounters an infection, white blood cells are recruited to release molecules that will fight the infection. Molecules that interact with the endothelia in the blood vessels, like nitric oxide (NO), are released. The interaction causes the vessels to dilate to increase the blood vessel diameter and permeability. The increased diameter slows down the blood flow, which causes a drop in blood pressure. Also the vessels permeability is increased. This reaction happens multiple places in the body where there is infected tissue present and will cause systemically vessel dilation. The characterization of sepsis is SIRS as a result of infection. [baudouin200, kanta2014]

Severe sepsis

When the permeability of the vessels is increased there will be more fluid in the tissue and the cells will get less oxygen because the oxygen has a harder time to get to the demanding tissue. Also the endothelia of the vessels will get damaged when the white blood cells try to destroy the pathogens. This triggers coagulation and clotting is formed in the damaged areas in the blood vessels. These clots can break off into the blood and cause further harm. At a point the damaged vessels leads to more leakage, because there will be a point where the coagulation can't follow up. Organs will start to dysfunction at this stage. The characterization of severe sepsis is presence of sepsis with organ dysfunction and hypoperfusion is often included in this state. [baudouin200, kanta2014].

Septic shock

Septic shock happens when the body has undergone sepsis for a greater duration of time. This stage is characterized by a condition with hypotension even after adequate fluid resuscitation is given. Because of lactic acidosis the cells are not getting a sufficient supply of oxygen and therefore the cells will begin to die. This can lead to a very dangerous state, where organs begin to fail because they get too damaged to function. When multiple organs get damaged the state in septic shock reaches multiple organ failure also called multiple organ dysfunction syndrome (MODS)[baudouin200, kanta2014]. The mortality for patients with septic shock are in the region of 50% [baudouin200].