3.5.5

Myogenic and Paracrine Regulation of Vasoconstriction and Vasodilation

An important characteristic of all tissues is the ability to “locally” control blood flow by regulating arteriolar resistance. Tissues utilize two methods of local control, **myogenic** and **paracrine** regulation. Myogenic regulation occurs because of the intrinsic property of smooth muscle cells to contract in response to stretch. This reflexive contraction to stretch occurs because of the presence of mechanically gated Ca2+ channels. Once Ca2+ enters the cell it induces the contraction cascade. This intrinsic property is effective at reducing blood flow via vasoconstriction in response to systemic increases in blood pressure. Although effective, the myogenic regulation is limited to specific circumstances and can only increase resistance. When the tissues require more precise regulation of blood flow they turn to local chemical regulation called paracrine signaling.

Endothelial cells can release paracrines such as nitric oxide in response to an increase in metabolic activity. Also, an increase in metabolic activity would decrease local O_2 levels while simultaneously increasing local CO_2 levels. Both of these conditions would result in vasodilation of associated arterioles, resulting in more blood flow which helps to eliminate CO_2 and replenish O_2. This process of increasing local blood flow in response to increased metabolic activity is called **active hyperemia**.

Sometimes O_2 levels decrease and CO_2 levels increase without a change in metabolic activity. This can happen when blood flow to a given tissue becomes occluded via a clot or injury. In addition to experiencing decreases in O_2 and increases in CO_2, the endothelial cells will also begin producing **nitric oxide** (NO) and **adenosine**, both potent vasodilators. If blood flow is suddenly restored to the occluded area, the tissue will have maximally dilated arterioles as the blood re-enters. This response is called **reactive hyperemia**.

Depending on the length of occlusion, paracrine metabolites can accumulate at higher than normal levels, resulting in a significant trigger of vasodilation when blood flow resumes. This rapid increase can cause an inflammatory response that results in more cellular damage. This is called a **reperfusion injury**. If the occlusion occurs in vessels supplying the brain, a reperfusion injury can worsen the initial effects of a stroke. It the occlusion occurs in vessels supplying the heart, a reperfusion injury can worsen the effects of a myocardial infarction.

Not all paracrine signals are associated with changes in local metabolism, instead some are associate with inflammation (**bradykinin** and **histamine**; vasodilators) and some with clotting cascades (**serotonin** and **ADP**; vasoconstrictors).