Characteristics of special circulations

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Abstract

Blood flow through vascular beds is usually determined by the pressure gradient and the diameter of the precapillary resistance vessels. Special circulations have additional features of intrinsic blood flow control, allowing autoregulation. Coronary blood flow is linked to myocardial oxygen consumption by a metabolic mechanism, where increased metabolism releases vasodilator metabolites. Cerebral blood flow is primarily regulated by a myogenic mechanism whereby increases in transmural pressure stretch the vascular smooth muscle, which responds by contracting. Renal blood flow is regulated by myogenic mechanisms and tubuloglomerular feedback. Hepatic blood flow is delivered via the portal vein and hepatic artery, and flow varies in these vessels reciprocally to maintain constant total flow. The pulmonary circulation receives the entire cardiac output, and blood flow is regulated both passively and actively to allow increases in flow without significant increases in pressure.

Keywords Autonomic nervous system; autoregulation; blood flow; local control; vasoactive metabolites

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Learning objectives

After reading this article, you should be able to:

- describe the main factors which control blood flow through a vascular bed
- describe the special features of these factors as they relate to the coronary, cerebral, renal, hepatic and pulmonary circulations
- relate these special features to the particular role played by each circulation

In 'special circulations', additional factors govern the control of blood flow beyond the 'standard' mechanisms that prevail in other circulations. In this article, the 'special circulations' considered are the coronary, cerebral, renal, hepatic and pulmonary circulations.

Blood flow through the cardiovascular system is dependent on the force that drives the blood along the vessel (the pressure gradient) and is restricted by the resistance of the vessels. The resistance to blood flow is dependent on the radius and length of the blood vessel and the viscosity of the blood flowing through it. The relationship between these factors is described by the **Hagen-Poiseuille equation** (Figure 1).

This is an approximation for the cardiovascular system. Strictly, it applies only to Newtonian fluids (blood is non-Newtonian, as its viscosity changes with shear force) flowing through a straight, unbranched, non-distensible tube; clearly these conditions do not prevail in the cardiovascular system. However, the law provides a useful and practical approximation.

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The pressure is usually the difference between arterial and venous pressures; $\pi/8$ is a constant. The radius of the vessel is raised to the power of four; thus if the radius were to double, flow would increase 16-fold. The most important vessels regulating blood flow in this way are the small arteries and arterioles because they contain an abundance of vascular smooth muscle arranged circumferentially along the length of the vessel. Vessel tone is regulated by both extrinsic and intrinsic factors.[1]

Extrinsic control

This consists of:

1. **Neural control:** Occurs via the autonomic nervous system. The major vasomotor nerves are vasoconstrictor sympathetic fibres which have tonic activity, accounting for the basal tone in resistance vessels. The primary sympathetic neurotransmitter is noradrenaline, which acts on the α- and β-adrenoreceptors and in many vascular beds sympathetic activation causes α-adrenoreceptor- mediated vasoconstriction. Noradrenaline always acts as a vasoconstrictor, but adrenaline has differing effects on vessel diameter. In skeletal muscle, low concentrations act on the β-adrenoreceptors to induce vasodilation, whereas high concentrations act on the α-adrenoreceptors to induce vasoconstriction. Only a small proportion of the resistance vessels receive parasympathetic (vasodilator) input (e.g. the cerebral, meningeal and some splanchnic vessels).
2. **Humoural factors:** Vasoactive humoural agents include angiotensin II, bradykinin, vasopressin, free catecholamines, and natriuretic peptides. They act on receptors on vascular smooth muscle and endothelial cells.

Intrinsic control

Intrinsic control relates to local control within a vascular bed rather than a centrally mediated mechanism. It occurs in the absence of neural and humoural influences. **Autoregulation** is a manifestation of intrinsic control and is defined as 'the intrinsic ability of an organ to maintain a constant blood flow despite changes in perfusion pressure'. Different organs have pressure ranges between which autoregulation maintains flow at a near constant rate. Outside these ranges, flow becomes pressure dependent. In addition, many organs adjust blood flow to match metabolic activity. Intrinsic control can be divided into **direct effects on vascular smooth muscle** and **indirect effects via the vascular endothelium**.

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Hagen-Poiseuille equation

$$Q = \frac{\Delta P \, \pi \, r^4}{8 l \eta}$$

Where:

Q is the flow rate
ΔP is the pressure gradient
r is the radius of tubing
l is the length of tubing
η is the dynamic fluid viscosity

Figure 1

Vascular smooth muscle (Direct)

There are currently two main theories that explain autoregulation of blood flow via effects on vascular smooth muscle.

1. **Myogenic mechanism:** Increased blood flow increases tension in the blood vessel wall. One theory is that through stretching of the sarcolemma, calcium and sodium influx occurs through stretch sensitive ion channels. This leads to muscle cell depolarization and contraction. The increased resistance maintains steady pressure and hence flow. This is known as the Bayliss reflex and is a rapid process (less than 10 seconds response time). Decreased blood flow has the opposite effect.
2. **Metabolic mechanism:** In certain organs blood flow is closely coupled to tissue metabolic activity. As metabolic activity increases, there is an increase in blood flow (active hyperaemia). A decrease in blood supply or an increase in oxygen demand causes the tissue to release vasodilator metabolites such as potassium, hydrogen, phosphate, carbon dioxide, prostaglandins and adenosine. These metabolites act directly on local vascular smooth muscle, causing relaxation and thus an increase in blood flow. Hypoxia itself may also act directly, since inadequate oxygen delivery causes an inability to sustain smooth muscle contraction. When blood flow increases or metabolic demand decreases, the metabolites decrease and constriction occurs.

Endothelium (Indirect)

The vascular endothelium can also influence local blood flow. Endothelial cells produce and release both vasodilator and vasoconstrictor metabolites in response to stimuli such as shear stress and hypoxia. The three most important endothelial-derived substances are the vasodilators nitric oxide (NO) and prostacyclin (PGI_2), and the vasoconstrictor endothelin (ET-1). NO is perhaps the most important vasodilator and its release is thought to be due to an increase in shear stress (e.g. hypertension) rather than due to hypoxia. Damage to the vascular endothelium from inflammation or ischaemia alters the formation and release of endothelial factors. This is possibly due to loss of the endothelial glycocalyx, which mediates the mechanotransduction process. When endothelial damage occurs, the endothelium produces less nitric oxide and prostacyclin, which attenuates the dilatory response causing increased vascular tone.

Coronary circulation

The heart has the highest oxygen consumption (per tissue mass) of all organs and it also extracts more oxygen (70–80% versus approximately 25% for the rest of the body). The myocardium receives its entire nutritional blood supply from the left and right coronary arteries at about 5% of cardiac output (CO) (approximately 250 mls/min).

Control of myocardial blood flow

Coronary blood flow (CoBF) is determined by the coronary perfusion pressure (the difference between the aortic diastolic pressure and the left ventricular end diastolic pressure (LVEDP)), and the vasomotor tone of the coronary vessels.

The coronary vessels are compressed during systole. Thus, CoBF, in contrast to blood flow through other vascular beds, is highest during early diastole (when extravascular compression is minimal and aortic pressure is still high) and at its lowest during isovolumetric contraction (when extravascular compression can interrupt or even reverse flow in the left ventricular vessels) (Figure 2).

CoBF can be reduced by tachycardia (systolic time is relatively fixed, therefore with a tachycardia diastolic time shortens), elevation in LVEDP (e.g. congestive cardiac failure) and reduced arterial pressure (e.g. hypovolaemia). Compression of the coronaries is greatest near the endocardial surface and diminishes nearer the epicardial surface. Thus, the vessels in the left ventricular inner wall are most susceptible to ischaemic damage in coronary artery disease.

Autoregulation maintains the CoBF between a mean arterial pressure (MAP) of 60 and 140 mmHg through the myogenic response. However, a 'special' consideration in the coronary vascular bed is that the moment-to-moment CoBF is strongly influenced by mechanical activity of the heart. CoBF is tightly linked to myocardial oxygen consumption, the metabolic mechanism of intrinsic control. Due to the already high oxygen extraction ratio, the heart must increase its blood flow to meet increasing metabolic demand. The aforementioned metabolites cause vasodilatation, with adenosine playing a key role particularly under pathophysiological conditions. However, it may not be involved in coupling CoBF to myocardial metabolism under physiological conditions such as exercise.[2]

Cardiac nerve activity has minimal influence on CoBF. The coronary vessels have both α- and β-receptors and direct stimulation causes slight vasoconstriction. However, the indirect effect is much greater, as sympathetic stimulation causes increased metabolism and therefore coronary vasodilatation. There are a few parasympathetic receptors, meaning vagal stimulation causes a slight vasodilator effect.

Cerebral circulation

Blood flow to the brain is via the internal carotid and vertebral arteries which anastomose to form the circle of Willis at the base of the brain. The brain receives about 15% of CO (approximately 750 ml/min). The average cerebral blood flow (CeBF) is 50 mls/100 g of brain tissue/min. However, there is regional variation,

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