Characteristics of special circulations

Marina Sawdon

Abstract

Blood flow through a vascular bed is usually determined by the pressure gradient across it and the diameter of the precapillary resistance vessels. Special circulations have additional specific features of blood flow control. Several organs control their blood supply by autoregulation. Coronary blood flow is linked to myocardial oxygen consumption, primarily by a metabolic mechanism. Increases in demand or decreases in supply of oxygen cause the release of vasodilator metabolites, which act on vascular smooth muscle to cause vessel relaxation and hence increase blood flow. 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 both extrinsic and intrinsic mechanisms; sympathetic vasoconstriction of the afferent arterioles reduces renal blood flow in response to a decrease in effective circulating volume, myogenic mechanisms and tubuloglomerular feedback, as well as the release of vasoactive metabolites from the vascular endothelium regulate renal blood flow intrinsically. Hepatic blood flow is delivered via the portal vein and hepatic artery, and the amount of flow varies in these vessels reciprocally to maintain constant total blood flow. The pulmonary circulation receives the entire cardiac output, and blood flow is regulated both passively and actively. Pulmonary vessels are highly distensible and can accommodate increases in blood flow without significant increases in pressure.

Keywords Autoregulation; blood flow; local control; vasoactive metabolites

Royal College of Anaesthetists CPD Matrix: 1A01

Learning objectives

After reading this article, you should be able to:

- describe the main factors that 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 most organ systems. In this article 'special' circumstances in coronary, cerebral, renal, hepatic and pulmonary circulations are considered.

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. In practice the radius of the arterioles has the greatest effect on blood flow. An approximate relation between vessel dimensions and blood viscosity is shown by the equation below (Poiseuille's law).

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Poiseuille's law is an approximation for the cardiovascular system. Strictly, it applies only to Newtonian fluids flowing through a straight unbranched, non-distensible tube (conditions that do not prevail in the cardiovascular system). However, the equation below does give a useful approximation of blood flow in the cardiovascular system.

$$Q = \frac{\pi(P_1 - P_2)r^4}{8\eta l}$$

where Q is the blood flow, P_1–P_2 is the pressure gradient (normally arterial minus venous), r is the radius of the vessel, η is the viscosity of blood, l is the length of the vessel, and $\pi/8$ is the constant of proportionality.

In Poiseuille's law, 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 in a circular manner along the length of the vessel, the tone of which is regulated by both extrinsic (neural and humoural) and intrinsic (myogenic and metabolic) factors.

Extrinsic control

The major vasomotor nerves are vasoconstrictor sympathetic fibres, which have tonic activity, accounting for the basal tone in resistance vessels. The primary neurotransmitter released from sympathetic nerve terminals is noradrenaline, which acts on the α-and β-adrenoreceptors. In many vascular beds the sympathetic system is associated with activation of α-adrenoreceptors to mediate a vasoconstriction. Only a small proportion of the resistance vessels in the body receives a parasympathetic (vasodilator) nerve supply (e.g. the cerebral and meningeal blood vessels, parts of the viscera, genitalia, large bowel and bladder, but not skeletal muscle or skin). The vasodilation of cutaneous blood vessels in association with sweating may be partly due to the production of a vasodilator polypeptide, bradykinin, within exocrine glands.

Adrenaline has many effects on vessel diameter and hence blood flow. In skeletal muscle, low concentrations of adrenaline act on the β-adrenoreceptors to induce vasodilation, whereas high concentrations act on the α-adrenoreceptors to induce vasoconstriction. However, noradrenaline always acts as a vasoconstrictor. Other vasoconstrictor hormones include angiotensin II and vasopressin.

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Intrinsic control

Intrinsic control relates to local control within a vascular bed rather than a centrally mediated reflex control. Local control of the circulation can be divided into direct effects on vascular smooth muscle and indirect effects via the vascular endothelium.

Properties of vascular smooth muscle

A number of vascular beds can maintain a constant blood flow despite variations in arterial blood pressure (within limits). This process is termed autoregulation. In addition, many organs adjust blood flow to match metabolic activity. This type of local regulation occurs independently of the endothelium and nervous input, and is the result of direct changes in vascular tone. There are currently two main theories that may explain autoregulation of blood flow.

Myogenic mechanism: increased tension in the blood vessel wall, due to increased blood flow, stretches the vascular sarcolemma. The vascular muscle responds by contracting, and increasing resistance to maintain pressure and hence blood flow.

Metabolic mechanism: in certain organs blood flow is regulated to match the metabolic activity of the tissue. A decrease in blood supply or an increase in demand of oxygen causes the tissue to release vasodilator metabolites such as:

- potassium ions
- hydrogen ions (lactic acid)
- phosphate ions
- carbon dioxide
- prostaglandins
- adenosine.

These metabolites act locally, acting directly on vascular smooth muscle, causing relaxation and an increase in blood flow. This process is called functional hyperaemia. A decrease in metabolic activity will decrease the formation of vasodilator metabolites, and hence lead to vasoconstriction. There is normally a background level of metabolites in the tissue and so this mechanism can also form the basis of autoregulation. An increase in blood pressure can increase blood flow (see equation above), which causes a 'wash-out' of vasodilator metabolites, leading to a loss of vasodilator influence and hence a vasoconstriction, reducing blood flow back to the original level.

Properties of the endothelium

The vascular endothelium can also influence local blood flow. Endothelial cells produce and release both vasodilator and vasoconstrictor metabolites in response to many stimuli such as shear stress due to increased blood flow, and hypoxia. Nitric oxide (NO) is perhaps the most important of the vasodilator substances.

Coronary circulation

The myocardium receives its entire nutritional blood supply from the coronary arteries. The right coronary artery mainly supplies the right atrium and ventricle, the left coronary artery divides into the anterior descending and circumflex branches, and mainly supplies the left atrium and ventricle.

Control of myocardial blood flow

The primary factor responsible for perfusion of the myocardium is aortic pressure. However, a 'special' consideration in the coronary vascular bed is that the moment-to-moment coronary blood flow (CBF) is strongly influenced by mechanical activity of the heart. The coronary blood vessels course through the myocardium and are compressed during systole. Thus, CBF, in contrast to blood flow through most other vascular beds in the body, is at its highest during early diastole (when extravascular compression is minimal and aortic pressure is still high) and at its lowest during isovolumic contraction (when extravascular compression can interrupt or even reverse blood flow in the left ventricular coronary vessels) (Figure 1). Tachycardia (reduced diastolic time), elevations in ventricular end-diastolic pressure, and reduced arterial pressure result in a reduction in CBF. Compression of the coronary arteries 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.

CBF is tightly linked to myocardial oxygen consumption, primarily by the metabolic mechanism described above. In contrast to most tissues, cardiac tissue extracts oxygen almost maximally even under normal conditions. The heart therefore adjusts its blood flow to meet its metabolic needs. Adenosine seems to play a significant role in metabolic vasodilation under pathophysiological conditions such as ischaemia, but may not be involved in matching CBF to myocardial metabolism under physiological conditions such as exercise.[1] Many other agents may be involved in functional hyperaemia (hypoxaemia, hypercarbia, potassium and hydrogen ions), but the full mechanism is yet to be determined.

Cardiac nerve activity has little influence on CBF. Activation of cardiac sympathetic nerve fibres initially constricts, and vagal nerve activity initially relaxes, the coronary resistance vessels slightly. However, the resulting changes in metabolic work have a far more potent effect on vascular tone.

Cerebral circulation

Blood flow to the brain is via the internal carotid and vertebral arteries, which anastomose to form the circle of Willis. The brain is particularly intolerant of periods of ischaemia. Indeed, interruption of cerebral blood flow for as little as 5 seconds results in loss of consciousness, and irreversible cell damage occurs within minutes. Cerebral blood flow is maintained at the expense of other organs in situations of reduced cardiac output such as haemorrhage.

The cerebral circulation lies within the cranium; a rigid structure, the contents of which are essentially incompressible (see *Anaesthesia and Intensive Care Medicine* 2013; **14**(9):395–400). After head injury, cerebral oedema often occurs, which may lead to intracranial hypertension. Under these conditions cerebral perfusion pressure is governed by the difference between arterial pressure and intracranial pressure (ICP) rather than the usual arteriovenous pressure difference. Increased ICP following head injury reduces cerebral blood flow and may lead to cerebral ischaemia. Recent studies suggest that resuscitation with hypertonic solutions may reduce ICP in these circumstances.

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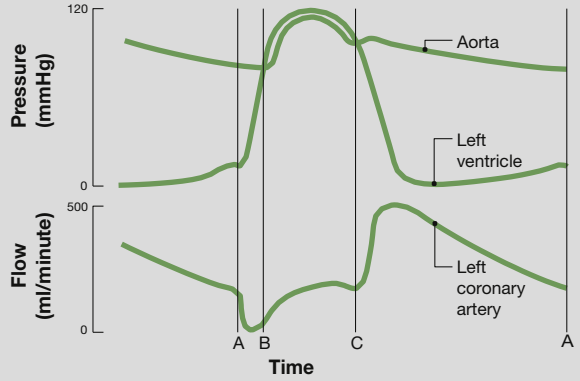
Pressures in the aorta and left ventricle, and flow in the left coronary artery during the cardiac cycle



Vertical lines A–B indicate the ventricular isovolumic contraction phase and C the onset of ventricular diastole. Note that coronary flow ceases abruptly during isovolumetric contraction and is greatest during diastole.

Figure 1

Control of cerebral blood flow

Total cerebral blood flow is maintained within tight limits to ensure an uninterrupted supply of oxygen to the brain, although local neuronal activity is associated with changes in regional cerebral blood flow via metabolic substances. Extrinsic control of total cerebral blood flow seems to be weak and mainly affects larger cerebral vessels, whereas the cerebral resistance vessels are regulated under a well-developed intrinsic mechanism. Autoregulation of total cerebral blood flow is apparent within the range of 60–180 mmHg arterial pressure, which may be due to a myogenic mechanism. However, this range may be right-shifted by sympathetic nerve activity or chronic systemic hypertension. Cerebral myogenic autoregulation can be overridden by changes in arterial carbon dioxide tension; even small degrees of hypercapnia cause vasodilation, and hypocapnia leads to vasoconstriction. Hypoxaemia also causes cerebral vasodilation at a threshold arterial oxygen tension that may be as high as 8.5 kPa. The vasodilatory effects of hypercapnia (but not hypoxaemia) seem to be mediated by NO from the endothelium.

Renal circulation

Blood flow to the kidneys occurs via the renal arteries, which eventually branch to form the afferent arterioles, glomerular capillaries and efferent arterioles. This arrangement aids tight regulation of renal blood flow (RBF) and, indirectly, the glomerular filtration rate (GFR).

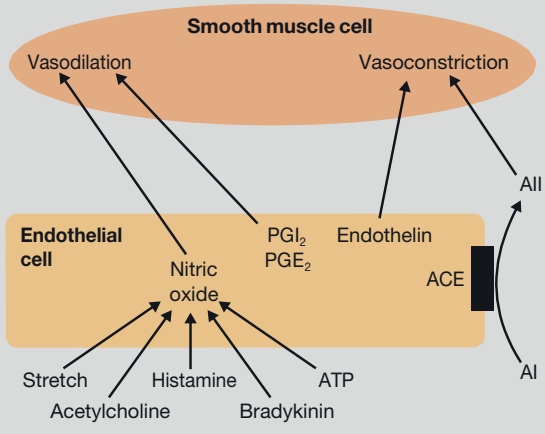
Control of renal blood flow

RBF is regulated by both extrinsic and intrinsic mechanisms. Autoregulation of RBF occurs in the range of arterial pressures 90–180 mmHg by three mechanisms: the myogenic mechanism (MM), tubuloglomerular feedback (TGF) and a third unknown mechanism.[2] Under normal resting conditions the relative contributions of these three mechanisms to overall RBF autoregulation are: MM, approximately 50%; TGF, 35–50%, and the third mechanism, less than 15%. These data have been derived from studies on rats and there may be variation between species. Unfortunately, detailed data for humans are currently unknown. In addition there is a dynamic interaction between these components of RBF autoregulation, resulting in alterations in the relative contributions under different circumstances. At very low blood pressures the third mechanism may assume greater importance. The relative rapidity with which the mechanisms operate also differs, with MM being the most rapid (requiring less than 10 seconds for completion) while both TGF and the third mechanism take 30–60 seconds to complete their response. In TGF, changes in tubular flow rate are detected by the cells of the macula densa, which in turn lead to changes in afferent arteriolar diameter, which alter the glomerular capillary hydrostatic pressure and hence control the GFR. The variable detected may be NaCl concentration of tubular fluid and the likely effector mediators are currently the subject of active research. Stimulation of renal sympathetic nerves causes an α-adrenoreceptor-mediated vasoconstriction of both afferent and efferent arterioles, but primarily affects afferent arterioles (e.g. sympathetic vasoconstriction of the afferent arterioles occurs in response to strong emotional stimuli and decreases in effective circulating volume, resulting in decreased RBF). Endothelial cells also play an important role in regulating RBF (Figure 2).

Hepatic circulation

The liver receives three-quarters of its blood supply from the portal vein (PV) (formed from the superior mesenteric and splenic vein) and one-quarter from the hepatic artery (HA) (a branch of the coeliac trunk). Because the blood in the PV has already passed through the spleen and gastrointestinal circulation, oxygen saturation is low. However, blood in the HA is fully

Role of endothelial cells in renal afferent and efferent arteriolar vascular tone



Endothelial cells produce several vasoactive hormones that act on the smooth muscle cells to regulate renal blood flow.
ACE, angiotensin-converting enzyme; AI, angiotensin I; AII, angiotensin II; PGI_2, prostaglandin I $_2$; PGE_2, prostaglandin E_2.
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Figure 2

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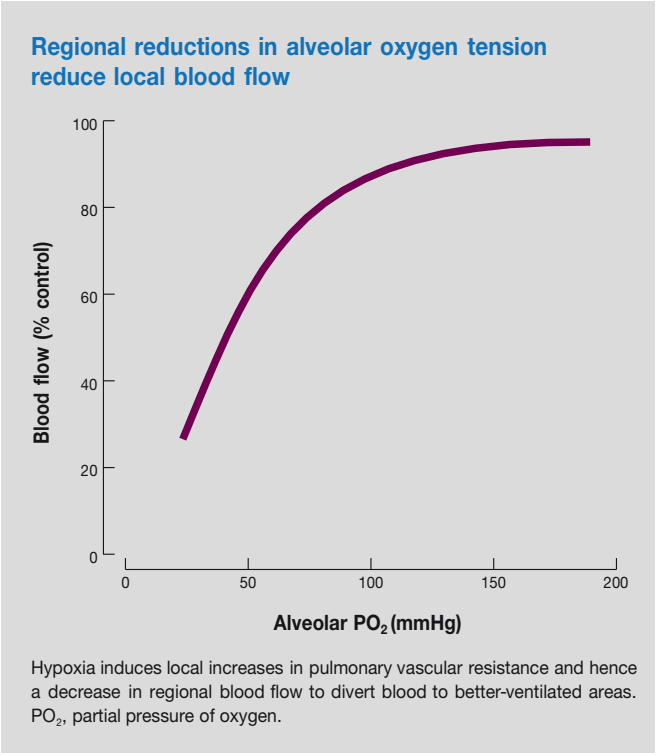

Figure 3

saturated. The PV and HA branch to form, respectively, the terminal portal venules and hepatic arterioles, both of which contain vascular smooth muscle, and drain into the sinusoids (capillary network) in the acinus.

Control of hepatic blood flow

Blood flow in the PV and HA varies reciprocally in an attempt to maintain hepatic blood flow. However, the increase in blood flow in one vessel does not fully compensate for reductions in the other. The hepatic arterial buffer response (HABR) normally maintains blood flow and hence constant oxygen delivery to the liver during reduced portal venous flow, and may be mediated by adenosine. Thus, under normal conditions, adenosine is constantly washed out by portal venous blood flow; however, under conditions of decreased portal venous flow adenosine accumulates and, because of the close proximity of the PV and HA, leads to dilation of the hepatic arterioles and increases in blood flow.

The PV and HA are innervated by noradrenergic sympathetic nerves. Activity of these nerves reduces blood flow during low-flow states such as hypovolaemia. However, stimulation of hepatic nerves has a more significant effect on capacitance vessels and can mobilize about half the hepatic blood volume following haemorrhage.

Pulmonary circulation

The pulmonary circulation is a low-resistance (one-tenth of systemic), low-pressure, high-flow network with a very high density of capillaries. Pulmonary arterioles have very little vascular smooth muscle and so do not have the same capacity for vasoconstriction as systemic arterioles. However, this structure matches its function in that it is required to accept the entire cardiac output at all times, while minimizing right ventricular work.

Passive regulation of pulmonary blood flow

Large increases in blood flow (e.g. during exercise) can be accommodated with only small increases in arterial pressure, thus resistance must fall further. This decrease in resistance is achieved by recruitment and distension of capillaries. Lung volume also has an effect on pulmonary vascular resistance (PVR): at low and high lung volumes resistance is high. PVR is at its lowest at functional residual capacity. The low pressures and high distensibility of the pulmonary vessels mean that gravity causes regional variations in blood flow within the lung, which is affected by posture and exercise. When an individual is upright, flow is at its highest at the bottom of the lung due to the hydrostatic pressure of the 'column' of blood above it. Flow at the apices is thus at its lowest and, in conditions of low pulmonary arterial pressure such as hypovolaemia or positive pressure ventilation, intravascular pressure may fall below extravascular (alveolar) pressure in this region, leading to cessation of blood flow and reduced gas exchange.

Active regulation of pulmonary blood flow

Pulmonary arterioles are innervated by the autonomic nervous system, and PVR may be altered by stimulation of the baro and chemoreceptor reflexes. However, the main influence on PVR is hypoxia. Regional reductions in alveolar oxygen tension constrict local arterioles (opposite to systemic effects) to divert blood to better ventilated areas and thus optimize the ventilation:perfusion ratio (Figure 3). However, if more than 20% of the lung is involved, the overall PVR may be increased, which may lead to pulmonary hypertension and pulmonary oedema. ◆

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FURTHER READING

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