Neurological and humoral control of blood pressure

Nick Ashton

Abstract

Blood must be maintained under pressure to overcome the resistance offered by blood vessels, and thus ensure an adequate rate of flow to metabolizing tissues. If pressure is too low, the flow of blood cannot deliver sufficient oxygen; if it is too high, damage occurs to the blood vessels and organs. Hence, blood pressure is regulated around a 'set point'. Pressure in the arterial system is regulated on a minute-to-minute basis by the autonomic nervous system and in the long term by a number of hormones that act on the kidney. High-pressure sensors (baroreceptors) are located in the carotid sinus and aortic arch, which monitor pressure generated by the beating heart. Afferent fibres of the ninth and tenth cranial nerves (glossopharyngeal and vagus, respectively) project into the cardiovascular control centre in the medulla oblongata. Parasympathetic vagal tone acts to slow heart rate and thus cardiac output, whereas sympathetic tone increases both force and rate of contraction, as well as stimulating vasoconstriction of blood vessels to increase resistance. Long-term regulation of blood pressure depends on the maintenance of blood volume. This is achieved by the combined actions of the renin–angiotensin system, aldosterone and vasopressin (antidiuretic hormone), which act on the kidney to promote retention of sodium and water. Blood volume is reduced by atrial natriuretic peptide, which causes diuresis and natriuresis. Together, the nervous and endocrine systems act to correct fluctuations in blood pressure and ensure that it is maintained at an appropriate level.

Keywords angiotensin II; baroreceptor; parasympathetic fibres; sympathetic fibres; vasopressin

One of the principal functions of blood is the transport of gases and nutrients to metabolizing tissues. To achieve this, an adequate supply of blood must flow through the capillary network. Blood flow is determined by pressure, generated by contraction of the heart, and resistance, which is a function of blood vessel diameter and length. Coordinated control of cardiac output and arteriole diameter ensures that blood flow in the capillaries is maintained. The relationship between flow (F), pressure (P) and resistance (R) can be derived from Darcy's law. Originally based on experiments describing the flow of water through sand, Darcy established that flow rate is equal to the product of the permeability of the medium, the cross-sectional area to flow and the pressure drop, divided by the viscosity and the distance over which the pressure drop occurs. When simplified and applied to the flow of blood through a blood vessel, we get the equation: F is proportional to $\Delta P/R$. The pressure gradient (ΔP) along the vessel is more important than absolute pressure (P). However, there is a minimal pressure requirement to overcome the resistance to flow. If pressure is too low (hypotension), the pressure drop is too great and capillaries are not perfused adequately. If pressure is too high (hypertension) blood vessels and organs are damaged, leading to cardiovascular disease.

'Blood pressure' is usually understood as arterial pressure, specifically systemic arterial pressure. This is the pressure that is normally measured in the clinic, and is the pressure that is managed therapeutically to reduce the risk of cardiovascular disease. The pressure drops across the systemic arterial system from approximately 100 mm Hg at the aorta to 35 mm Hg at the start of a capillary network. Capillary hydrostatic pressure is a measure of the blood pressure within the capillaries. Typically, pressure falls from 35 mm Hg to 18 mm Hg across a capillary bed. Pressure in the venous circulation is much lower than that in the arterial branch, ranging from 18 mm Hg in the venules to 2–3 mm Hg at the right atrium.

What is normal blood pressure?

Textbooks usually quote blood pressure at 120 mm Hg systolic and 80 mm Hg diastolic (written as 120/80 mm Hg). However, arterial pressure is dynamic, changing according to the state of arousal. Blood pressure usually decreases at night during sleep and increases during stressful situations (the fight-or-flight response). Furthermore, resting pressure is influenced by a number of factors, including age (pressure increases with age), gender (pressure tends to be higher in men) and race (Afro-Caribbeans tend to have higher blood pressure than Caucasians). A range of environmental factors also affect blood pressure, including socioeconomic status, nutrition (obesity and salt intake), alcohol consumption, physical inactivity and exposure to environmental stressors. Consequently, the British Hypertension Society define normal blood pressure as 130/85 mm Hg, with 'high normal' pressure up to 140/90 mm Hg (Table 1).

Regulation of blood pressure can be divided into short-term mechanisms, which correct changes in pressure on a minute-to-minute basis, and long-term mechanisms, which manage pressure for days and weeks. Generally, short-term adaptations are regulated by neural reflexes; however, hormones can also play a part in rapid changes in blood pressure. Long-term regulation of blood pressure is achieved through the combined actions of a number of hormones, which influence the kidney and the regulation of extracellular fluid volume (ECFV).

Neurological regulation of blood pressure

The autonomic nervous system monitors and regulates arterial pressure on a minute-to-minute basis. This is achieved through groups of receptors that monitor blood pressure (baroreceptors), pH and the partial pressures of carbon dioxide and oxygen (chemoreceptors). These receptors send information to a central cardiovascular control centre, which then adjusts cardiac output (and thus 'flow') and vascular tone (and thus 'resistance'), and so corrects any change in arterial pressure away from the set point

Nick Ashton, ***PhD,*** *is lecturer in Physiology at the University of Manchester, Faculty of Life Sciences. He qualified from the universities of Manchester and Sheffield. His research interests include the hormonal regulation of renal function and blood pressure.*

British Hypertension Society classification of blood pressure

Category	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)
Optimal blood pressure	< 120	< 80
Normal blood pressure	< 130	< 85
'High normal' blood pressure	130–139	85–89
Grade 1 hypertension (mild)	140–159	90–99
Grade 2 hypertension (moderate)	160–179	100–109
Grade 3 hypertension (severe)	≥ 180	≥ 110
Isolated systolic hypertension (Grade 1)	140–159	< 90
Isolated systolic hypertension (Grade 2)	≥ 160	< 90

This classification equates with those of the European Society of Hypertension and the World Health Organization–International Society of Hypertension, and is based on clinic blood pressure (not values for ambulatory blood pressure measurement). Threshold blood pressures for the diagnosis of hypertension with self/home-monitoring are greater than 135/85 mm Hg. For ambulatory monitoring, 24-hour values are greater than 125/80 mm Hg. If systolic blood pressure and diastolic blood pressure fall into different categories, the higher value should be taken for classification. Reproduced with permission from B Williams, Poulter NR, Brown MJ. Guidelines for management of hypertension: report of the fourth working party of the British Hypertension Society, 2004—BHS IV. *J Hum Hypertens* 2004; **18:** 139–85

Table 1

(see below). This ensures that an appropriate blood pressure is maintained to meet the metabolic demands of respiring tissues.

Afferent input: the high-pressure sensors are located in the internal carotid arteries and the aortic arch, where they are in a position to detect maximal pressure generated by contraction of the heart. The carotid baroreceptors are located in the carotid sinus, a dilatation in the internal carotid artery where it joins the external carotid artery. Lamella-like receptors are found in the adventitia of the blood vessel, aligned parallel to the long axis of the vessel. These receptors are innervated by a branch of the glossopharyngeal nerve (ninth cranial nerve), which projects into the nucleus tractus solitarius in the medulla oblongata. Receptors in the aortic arch are innervated by the vagal nerve (tenth cranial nerve). The frequency of firing of both nerves increases when blood pressure rises, and decreases when blood pressure falls. Individual fibres vary, but the average threshold at which firing begins is normally not less than 50 mm Hg; maximal output occurs at about 170 mm Hg. The carotid and aortic baroreceptors are equally sensitive to pulsatile pressure; however, the carotid sinus baroreceptors are much more sensitive to non-pulsatile changes in arterial pressure. The chemical composition of the blood is monitored by receptors in the carotid bodies and aortic bodies adjacent to the baroreceptors, which are innervated by branches of the ninth and tenth cranial nerves, respectively. Although primarily involved in the regulation of respiration, changes in blood gas composition (low partial pressure of oxygen (PO_2) and high partial pressure of carbon dioxide (PCO_2)) can also lead to vasoconstriction. Low-pressure mechano- and chemoreceptors are found on the venous side of the circuit at the junction of the venae cavae and pulmonary veins with the atria; receptors are also located in the lungs, the atria and ventricles.

Efferent output: the heart receives both sympathetic and parasympathetic (vagal) fibres, which control the force and rate of contraction. Cholinergic parasympathetic tone predominates at rest, acting to slow depolarization of both the sinoatrial (SA) and atrioventricular (AV) nodes. Hence vagal tone slows heart rate. The adrenergic sympathetic fibres innervate the myocardium as well as the SA and AV nodes, hence they can increase both the rate and the force of contraction. The predominant adrenoceptors in the heart are β-receptors.

Blood vessels are innervated predominantly by sympathetic fibres; there is a limited parasympathetic supply to cerebral vessels, the tongue, salivary glands and external genitalia. While all vessels, with the exception of true capillaries, receive sympathetic fibres, neural influence on the large blood vessels is of far less importance than that on small arteries and arterioles. These are the 'resistance vessels' whose diameter has the most pronounced effect on total peripheral resistance and hence blood pressure. The resistance vessels possess both α- and β-adrenoceptors, whereas the capacitance vessels (veins) have only α-adrenoceptors. Norepinephrine (noradrenaline) released by sympathetic fibres causes vasoconstriction in all vascular beds via α-adrenoceptors. Epinephrine (adrenaline), which is secreted by the adrenal medulla along with norepinephrine, dilates resistance vessels at low concentrations, via β-adrenoceptors, and at high concentrations produces vasoconstriction, via the α-adrenoceptors. However, under normal physiological conditions, noradrenaline release from sympathetic fibres predominates.

Central integration and regulation: signals from the sensory afferent fibres are integrated and modulated centrally (Figure 1). The complex control processes are not fully understood, but it is apparent that cardiovascular control is much more complicated than a series of simple reflex arcs. There is good evidence to suggest that afferent signals are modulated at several levels in the brain, and that efferent output may also interact en route from the cortex to the spinal cord. A number of regions of the central nervous system play a role in circulatory control, including the spinal cord, medulla oblongata, hypothalamus, cerebellum and cerebral cortex. Of these, the medulla is probably the most important: section of the brainstem above the medulla does not affect blood pressure. This suggests that, while upper brain levels can modify medulla activity, they do not dominate its actions. Within the medulla a functional, if not anatomical, cardiovascular control centre regulates blood pressure. Stimulation of the dorsal lateral medulla causes vasoconstriction, cardiac acceleration and increased myocardial contractility, suggesting that this area acts as a pressor region. Caudal and ventromedial to the pressor region is an area that lowers blood pressure. This depressor region inhibits spinal sympathetic activity and inhibits the medullary pressor region.