Keywords Arteries/Veins/Capillaries/Blood flow/Fluid movement

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In this article...

- Anatomy of the vascular system and structure of blood vessels
- The process of gas exchange and nutrient transfer between capillaries and tissues
- Physiological processes used by the body to regulate blood pressure

Vascular system 1: anatomy and physiology

Key points

The vasculature works with the heart to supply the body with oxygen and nutrients and to remove waste products

There are five classes of blood vessels: arteries, arterioles, veins, venules and capillaries

Capillaries allow the diffusion of gases and transfer of nutrients and waste products between blood and tissues

Blood flow and blood pressure are regulated by nervous, chemical and hormonal mechanisms

Some organs and tissues can automatically adjust their own blood flow

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Abstract The vasculature is a network of blood vessels connecting the heart with all other organs and tissues in the body. Arteries and arterioles bring oxygen-rich blood and nutrients from the heart to the organs and tissues, while venules and veins carry deoxygenated blood back to the heart. The exchange of gases and transfer of nutrients between blood and tissues take place in the capillaries. A solid understanding of how the vasculature works is key to understanding what can go wrong with it. This first article in a three-part series covers anatomy and physiology; parts 2 and 3 will discuss the pathophysiology of the vascular system.

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The body requires oxygen and nutrients and needs to eliminate waste products to maintain metabolic stability. The vascular system has a crucial role in bringing oxygen and nutrients to every organ and tissue, and removing waste products, via a series of blood vessels. In conjunction with the heart, which acts as a pump, it forms the cardiovascular system (Jarvis and Saman, 2018). Arteries leaving the heart with oxygenated blood provide oxygen, nutrients, hormones and other substances throughout the body. Veins leaving the organs and tissues return to the heart carrying metabolic waste.

Five classes of blood vessels

There are five classes of blood vessels: arteries and arterioles (the arterial system), veins and venules (the venous system), and capillaries (the smallest bloods vessels, linking arterioles and venules through networks within organs and tissues) (Fig 1). Arteries are described as 'branching' or 'bifurcating' vessels, as great arteries (such as the aorta) branch off into smaller arteries and arterioles. Veins are described as 'converging' or 'joining' vessels, as venules and veins join to return blood to the heart through the largest veins (such as the superior and inferior venae cavae) (Marieb and Hoehn, 2015). Capillaries are in intimate contact with the tissues, providing nutrients and removing waste products through their thin walls at a cellular level. Table 1 details the functions of the five blood vessel types.

Structure of blood vessels

Blood vessels, except the smallest ones, are made of three layers: the tunica interna, tunica media and tunica externa (or adventitia).

Tunica interna

The tunica interna (innermost layer) is a single layer of squamous (flat) epithelial cells called the endothelium; this smooth lining in direct contact with the blood offers little resistance to blood flow (Marieb and Hoehn, 2015). The endothelial cells can easily be damaged by hypertension, toxins such as cigarette smoke, or hyperglycaemia;

this damage can result in atherosclerosis. These delicate cells rest on a thin layer of connective tissue made of elastin and collagen (elastic and structural support fibres) that anchors the tunica interna to the tunica media. The endothelium regulates blood flow and prevents clotting; it produces chemicals such as nitric oxide that help regulate blood flow by relaxing the smooth muscle within blood vessels.

Tunica media

The tunica media (middle layer) takes up most of the arterial vessel wall and is composed of smooth muscle fibres and elastin. This is where an activated sympathetic nervous system can stimulate the smooth muscle fibres to contract, provoking blood vessel narrowing (vasoconstriction) and decreasing blood flow (Marieb and Hoehn, 2015). When the sympathetic nerves are inhibited, the muscle fibres of the tunica media relax, the blood vessels increase in diameter (vasodilation) and blood flow increases.

Tunica externa

The tunica externa (outer layer) consists mainly of connective tissue fibres that protect the blood vessels and attach them to any surrounding tissues. In larger blood vessels, additional small vessels – vasa vasorum – supply blood and nutrients to the tunica externa and tunica media.

Anatomy of the vasculature

Arterial system

Arteries supply the body with oxygenated blood – with the exception of the pulmonary arteries from the heart; these carry deoxygenated blood to the lungs, and the umbilical artery, which carries deoxygenated blood from the foetus to the placenta. Blood travels from the arteries to the arterioles and on to the capillaries, where gaseous exchange takes place.

The largest artery is the aorta, which extends from the left ventricle down the left side of the body. It divides into four major regions, the ascending aorta, aortic arch, thoracic aorta and abdominal aorta. Table 2 lists the major branches off the aorta.

Arteries can be divided into elastic arteries, muscular arteries and arterioles. The elastic arteries are the largest (1-2.5cm in diameter) and comprise large amounts of elastin as well as smooth muscle. They have a large lumen with low resistance to blood flow, and can expand and recoil to accommodate changes in blood volume.

Muscular arteries regulate local blood flow and deliver blood to individual organs. They measure 0.3mm-1cm in diameter and possess more smooth muscle but less elastin than elastic arteries.

The arterioles are the smallest arteries (0.01-0.3mm in diameter). In certain areas, they have all three vascular layers (tunica intima, media and externa). When they are close to the capillaries they comprise a single smooth muscle layer overlying endothelial cells. Blood flow into the capillaries is determined by the diameter of the arterioles and can be increased through vasodilation.

Venous system

The veins are thin, elastic vessels that act as a reservoir of blood. They do not need large amounts of elastin and smooth muscle, since they transport low-pressure blood back to the heart. They have a large lumen, as well as valves that ensure a one-way flow of blood to the heart.

Venules measure 8-100µ in diameter and the largest ones possess a thin tunica

Fig 1. **The five types of blood vessels**

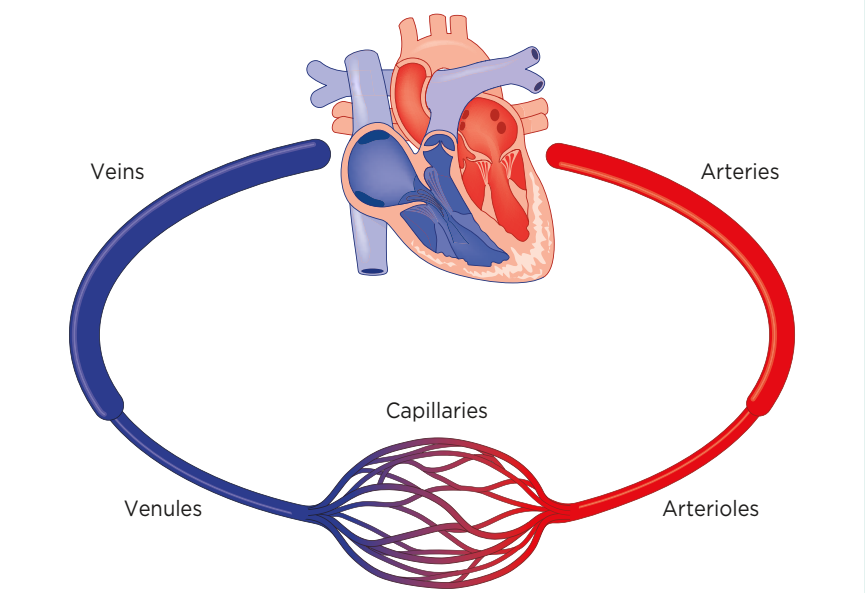

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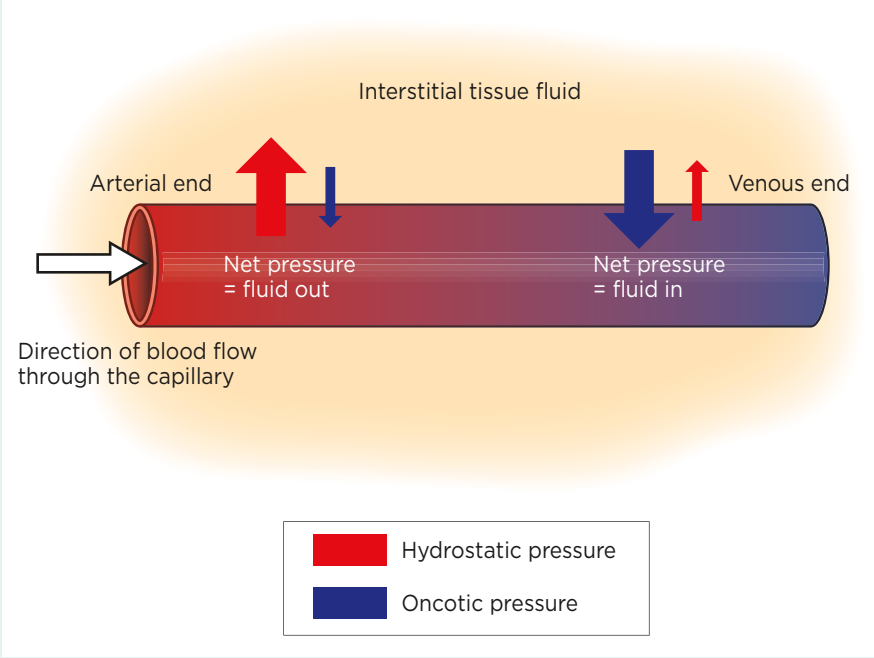
Table 1. **Five blood vessel types**

Vessel type	Function
Arteries	Transport high-pressure blood from the heart to smaller arteries and arterioles
Arterioles	Connect arteries and capillaries
Veins	Act as reservoir of blood and transport low-pressure blood from venules to heart
Venules	Connect capillaries and veins
Capillaries	Allow gas exchange, nutrient transfer and waste removal between blood and tissue fluid

Table 2. **Major branches off the aorta**

Area of the aorta	Arterial branches
Aortic arch	Brachiocephalic Left common carotid Left subclavian
Thoracic aorta	Bronchial Pericardial Oesophageal Mediastinal Posterior intercostal
Abdominal aorta	Coeliac Phrenic Superior and inferior mesenteric Suprarenal Renal Gonadal Lumbar Middle sacral Common iliac

Fig 2. **Fluid movement between capillary and tissue**



externa and a tunica media comprising two or three layers of smooth muscle cells. The venules join to form veins, in which the tunica externa, consisting of thick collagenous bundles, is the largest layer. The largest veins – the superior and inferior venae cavae – have a large tunica externa further thickened by smooth muscle bands (Marieb and Hoehn, 2015). The venous system is an irregular network that tends to follow the course of the arteries.

Capillaries

The capillaries can be compared to the smallest branches of a tree and connect arterioles to venules. The arteries divide into arterioles, which in turn divide into capillaries. These feed blood back into the venules, which connect to larger veins and ultimately to the superior or inferior vena cava. There are three main types of capillaries: continuous, fenestrated and sinusoidal. Table 3 lists their features and gives examples of where they are found in the body.

Capillaries act as a semipermeable membrane allowing the diffusion of gases and transfer of nutrients and waste products. The single layer of flattened endothelial cells of the capillaries facilitate the exchange of substances between capillaries and tissues. Gases, such as O_2 and CO_2, metabolic waste products, lactate, glucose and other nutrients are transferred across the walls of the capillaries through small slits in the endothelial cells known as pores or fenestrations. To prevent capillaries from losing vital substances such as plasma proteins, the slits in the endothelial cells are smaller than these proteins.

Fluid movement between capillaries and tissues

How do gas exchange and nutrient transfer happen between capillaries and tissues? According to the Starling principle (named after physiologist Ernest Starling who described it in 1896), fluid movement through the capillary walls is governed by hydrostatic pressure and oncotic pressure (Bit.ly/NottinghamUniStarling).

Like any fluid pushed through a confined space, blood in a capillary exerts pressure on the wall of the vessel because of the pressure exerted upstream by the blood coming from the arteriole. The blood pressure (BP) generates hydrostatic pressure, which expels fluid from the pores of the capillary into the interstitial compartment. The size of the pores in the capillary dictates whether particular nutrients are delivered to particular tissues. Hydrostatic pressure is highest at the arterial end, and lowest at the venous end, of the capillary.

The other influencing force is oncotic pressure, which is underpinned by the principle of osmosis; this is the passive movement of water through a semipermeable membrane from a region of low solute concentration to one of high solute concentration, with the aim of achieving equilibrium. In blood, plasma proteins – which cannot easily pass through the capillary walls – exert an osmotic pressure that tends to pull fluid from the surrounding tissue (which has a higher water concentration) into the capillary (which has a lower water concentration). This is referred to as oncotic pressure.

Fig 2 illustrates the interplay between hydrostatic and oncotic pressure. At the arterial end of the capillary, hydrostatic pressure exceeds oncotic pressure, so fluid moves out of the capillary into the interstitial compartment. At the venous end of the capillary, the two forces are reversed, so fluid moves back from the tissue into the capillary.

In recent years, the Starling principle has been contested. More work is required to fully understand the complex processes taking place in the capillaries (Levick and Michel, 2010).

Another important factor is the architecture of capillaries, which varies according to their site in the body and affects their permeability (Table 3). There are site-specific variations in fluid transfers between capillaries; for example, in the glomerulus (where capillaries supply and

Table 3. **Three types of capillaries**

Type	Features	Example of location
Continuous capillary	Uninterrupted lining of endothelial cells with tight junctions between cells, limiting passage of solutes	Skin Muscles
Fenestrated capillary	Similar to continuous capillary but some endothelial cells have pores (or fenestrations); usually found at filtration sites	Intestine Kidneys
Sinusoidal capillary	Modified, leaky capillaries with large fenestrations and less tight junctions, allowing large molecules and cells to pass	Liver Bone marrow Some endocrine tissues

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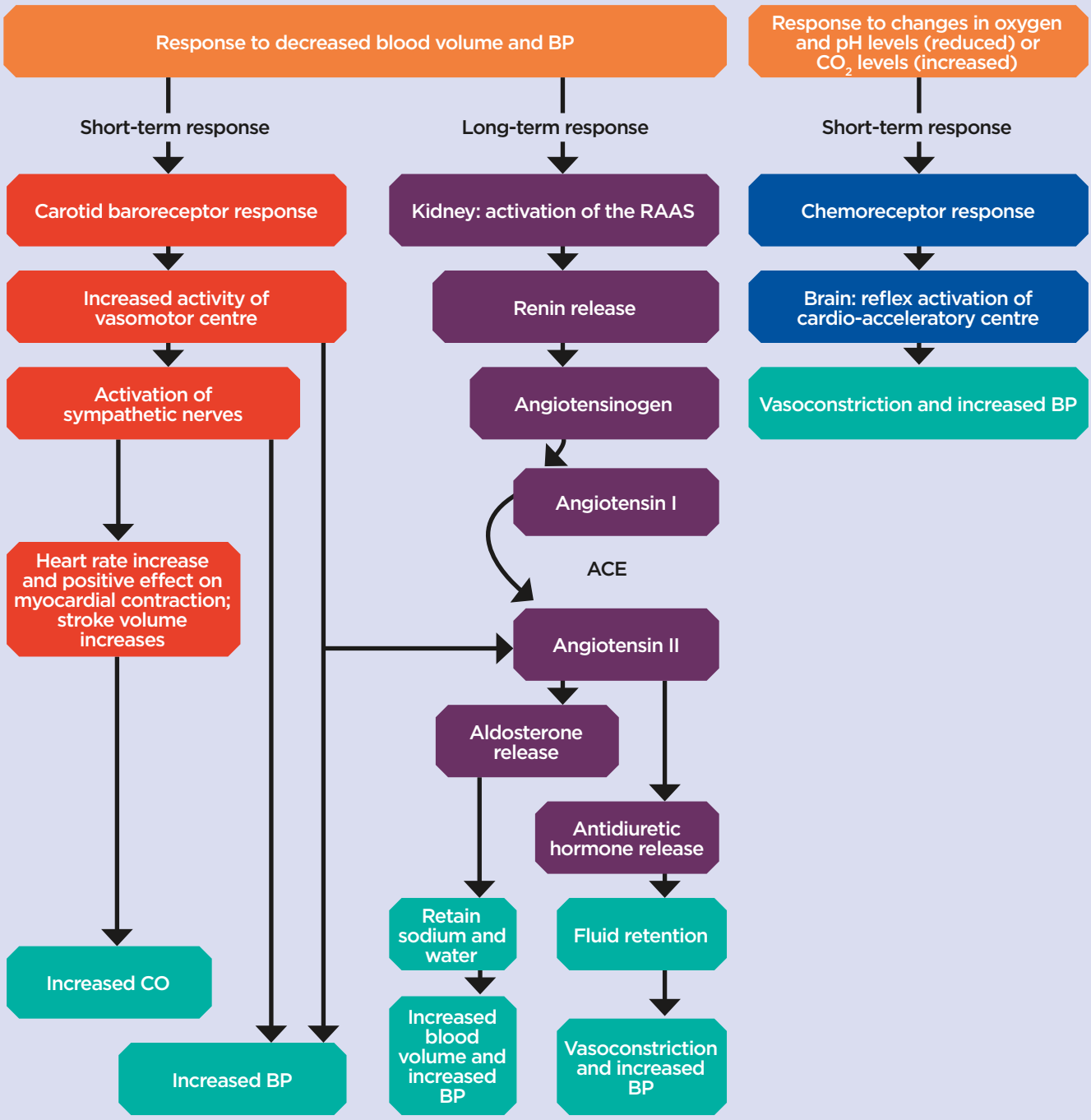
Fig 3. **Short- and long-term physiological regulation of blood pressure**



Key: ACE = angiotensin-converting enzyme; BP = blood pressure; CO = cardiac output; RAAS = renin-angiotensin-aldosterone system

drain the individual kidney units), the capillaries are porous and therefore highly permeable. Conversely, at the blood-brain barrier in the brain, the very tight architecture of capillaries reduces their permeability.

Physiological regulation of BP

BP, which is crucial to maintain the perfusion of organs, is influenced by:

- The total volume of blood in the body;
- Cardiac output – the amount of blood pumped out by the heart in one minute;
- Peripheral vascular resistance (PVR), resistance to the flow of blood in the arterial system, which is influenced by factors including vessel length, lumen diameter, and blood viscosity.

BP can be affected by a change in cardiac output or PVR. An important measure is the mean arterial pressure (MAP), which is the pressure that propels blood towards tissues with each cardiac cycle and generates perfusion pressure to the organs.

There are various short- and long-term physiological mechanisms that regulate BP, summarised in Fig 3 and outlined below.

Baroreceptor response

The vasomotor centre in the medulla oblongata of the brain, which hosts most

Table 4. **Mechanisms that trigger autoregulation of blood flow**		
Metabolic	**Myogenic**	**Endothelial**
Increase or decrease in metabolic products (for example, oxygen, carbon dioxide and hydrogen ions lactate) lead to increased or decreased blood flow	Changes in blood pressure directly stimulate vascular smooth muscle; increased intravascular pressure leads to increased vascular tone and vasoconstriction; reduced stretch leads to vasodilation and increased blood flow	Endothelial factors (including nitric oxide, endothelin and prostacyclin) directly affect vascular smooth muscle, altering blood flow

of the sympathetic neurons of the nervous system, has a key role in regulating vascular tone. It transmits signals along sympathetic nerve fibres to vascular smooth muscle, mostly at the level of the arterioles. This results in vasoconstriction or vasodilation, with corresponding effects on BP and blood flow to the tissues.

Alterations in BP are detected by mechanical pressure sensors (baroreceptors) found in the arterial wall of the carotid sinus (the site between the internal and the external carotid arteries) and the aortic arch. If BP suddenly rises, the walls of these vessels expand, which increases the frequency of nerve impulses sent to the vasomotor centre. The vasomotor centre is inhibited, causing reflex vasodilation (reduced vascular tone due to less sympathetic nerve activity) and a decrease in BP.

Conversely, if BP falls, the decreased stretch on the arterial walls causes a decrease in baroreceptor firing and culminates in reflex vasoconstriction and an increase in BP. This is the short-term baroreceptor response regulating BP.

Chemoreceptor response

A similar phenomenon occurs through a chemically induced reflex via chemoreceptors, which are found in specialised cells in the arteries of the neck (common carotid arteries) and in the aortic arch. These peripheral chemoreceptors predominantly detect changes in oxygen, carbon dioxide levels and pH (only carotid bodies). Along with the central chemoreceptors found in the brain they act to control respiration and maintain oxygen and acid-base status. However, they can also affect the cardiovascular function either directly by controlling the vasomotor centre in the brain or indirectly via the pulmonary stretch receptors (Klabunde, 2018).

Activation of the renin-angiotensin-aldosterone system

The kidneys and adrenal glands play a crucial role in the long-term regulation of BP, in which a hormonal system known as the renin-angiotensin-aldosterone system (RAAS) is involved. The RAAS activates the sympathetic nervous system and regulates plasma sodium and BP, and is targeted by many drugs designed to control BP and treat cardiac conditions, including the angiotensin-converting enzyme (ACE) inhibitor ramipril or the angiotensin II receptor blocker irbesartan.

The RAAS begins with the breakdown of angiotensinogen (a plasma protein produced by the liver) by renin (an enzyme produced by the kidneys). Specialised cells that make up the juxtaglomerular apparatus of the kidney can sense changes in BP. When it is low, renin is released, triggering a cascade of enzymatic reactions: angiotensinogen produces an inactive peptide called angiotensin I; ACE (an enzyme produced by the lungs) converts angiotensin I into angiotensin II, a potent vasoconstrictor, which triggers an increase in BP.

Angiotensin II can also trigger the adrenal gland to produce aldosterone, a mineralocorticoid hormone that sends signals via its receptor in the kidneys. This leads to sodium reabsorption and water regulation, increases blood volume and ultimately increases BP.

In addition, the hypothalamic-pituitary axis releases antidiuretic hormone, another hormone important for fluid balance, which stimulates the kidneys to conserve water. In severe conditions such as a haemorrhage, more antidiuretic hormone is produced. This can cause vasoconstriction and help restore a falling BP (Marieb and Hoehn, 2015).

Autoregulation of local blood flow

Some organs and tissues are able to automatically adjust their own blood flow by changing the diameter of the arterioles (Marieb and Hoehn, 2015). Without autoregulation, a decrease in perfusion pressure could lead to cell death, while a high perfusion pressure could damage delicate blood vessels. For some organs – particularly the kidneys, heart and brain, this autoregulation of local blood flow is crucial.

In an organ capable of autoregulation, when the perfusion pressure drops (which would lead to a fall in blood flow) the organ responds by reducing the vascular resistance via local vasodilation leading to an increase in blood flow. This response may be mediated through metabolic, myogenic or endothelial mechanisms (Table 4).

Not all organs or tissues are capable of autoregulation, and in a 'passive' vascular bed, a fall in perfusion pressure and ultimately blood flow is simply not corrected.

Conclusion

The blood vessels of the vasculature work together in a closed circuit with the heart to bring oxygen and nutrients to the body and eliminate waste products. The different anatomical and physiological features of the arteries, arterioles, veins, venules and capillaries allow each to perform their function correctly. BP and vital perfusion of organs are maintained via a series of mechanisms implicating the baroreceptors, chemoreceptors, RAAS and hypothalamic-pituitary axis. Understanding these physiological mechanisms helps understand how various diseases (for example, atherosclerosis) affect the vasculature and how they can be treated.

Parts 2 and 3 of this article series will cover the pathophysiology of the vascular system. **NT**

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