
CARDIOVASCULAR PHYSIOLOGY

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INTRODUCTION

The cardiovascular system consists of the heart and two vascular systems, the systemic and pulmonary circulations. The heart pumps blood through two vascular systems - the low pressure pulmonary circulation in which gas exchange occurs, and then the systemic circulation, which delivers blood to individual organs, matching supply to metabolic demand. Blood pressure and flow is largely controlled by the autonomic nervous system (**The Autonomic Nervous System**, Update in Anaesthesia 1995;5:3-6), and is also influenced by surgery and anaesthetic drugs. A good working knowledge of cardiovascular physiology is necessary to practice safe anaesthesia.

THE HEART

The heart comprises four chambers, and is divided into a right and left side, each with an atrium and a ventricle. The

atria act as reservoirs for venous blood, with a small pumping action to assist ventricular filling. In contrast, the ventricles are the major pumping chambers for delivering blood to the pulmonary (right ventricle) and systemic (left ventricle) circulations. The left ventricle is conical in shape and has to generate greater pressures than the right ventricle, and so has a much thicker and more muscular wall. Four valves ensure that blood flows only one way, from atria to ventricle (tricuspid and mitral valves), and then to the arterial circulations (pulmonary and aortic valves). The myocardium consists of muscle cells which can contract spontaneously, also pacemaker and conducting cells, which have a specialised function.

ELECTROPHYSIOLOGY OF THE HEART

Myocardial contraction results from a change in voltage across the cell membrane (depolarisation), which leads to

an action potential. Although contraction may happen spontaneously, it is normally in response to an electrical impulse. This impulse starts in the sinoatrial (SA) node, a collection of pacemaker cells located at the junction of the right atrium and superior vena cava. These specialised cells depolarise spontaneously, and cause a wave of contraction to pass across the atria. Following atrial contraction, the impulse is delayed at the atrioventricular (AV) node, located in the septal wall of the right atrium. From here His-Purkinje fibres allow rapid conduction of the electrical impulse via right and left branches, causing almost simultaneous depolarisation of both ventricles, approximately 0.2 seconds after the initial impulse has arisen in the sinoatrial node. Depolarisation of the myocardial cell membrane causes a large increase in the concentration of calcium within the cell, which in turn causes contraction by a temporary binding between two proteins, actin and myosin. The cardiac action potential is much longer than that of skeletal muscle, and during this time the myocardial cell is unresponsive to further excitation.

The cardiac cycle

The relationship between electrical and mechanical events in the cardiac cycle is summarised in Figure 1. *Systole* refers to contraction, while *diastole* refers to relaxation.

Teaching point

The electrocardiogram (ECG) measures changes in skin electrical voltage/potential caused by electrical currents generated by the myocardium. The P wave reflects atrial depolarisation, the QRS complex ventricular depolarisation, and the T wave ventricular repolarisation (Figure 1). *Repolarisation* is a process that occurs in many cells where the electrical potential across the cell membrane returns from the value during the *action potential* to that of the resting state, the *resting potential*. Although the ECG shows heart rate and rhythm and can indicate myocardial damage, it gives no information on the adequacy of contraction. Normal electrical complexes can exist in the absence of cardiac output, a state known as *pulseless electrical activity* or *electromechanical dissociation*.

Both contraction and relaxation can be *isometric*, when changes in intraventricular pressure occur without a change in length of the muscle fibres. The cycle starts with depolarisation at the sinoatrial node leading to atrial contraction. Until this time blood flow into the ventricles has been passive, but the atrial contraction increases filling by 20-30%. Ventricular systole causes closure of the

atrioventricular valves (1st heart sound), and contraction is isometric until intraventricular pressures are sufficient to open the pulmonary and aortic valves, when the ejection phase begins. The volume of blood ejected is known as the stroke volume. At the end of this phase ventricular relaxation occurs, and the pulmonary and aortic valves close (2nd heart sound). After isometric relaxation ventricular pressures fall to less than atrial pressures. This leads to opening of the atrioventricular valves and the start of ventricular diastolic filling. The whole cycle then repeats following another impulse from the sinoatrial node.

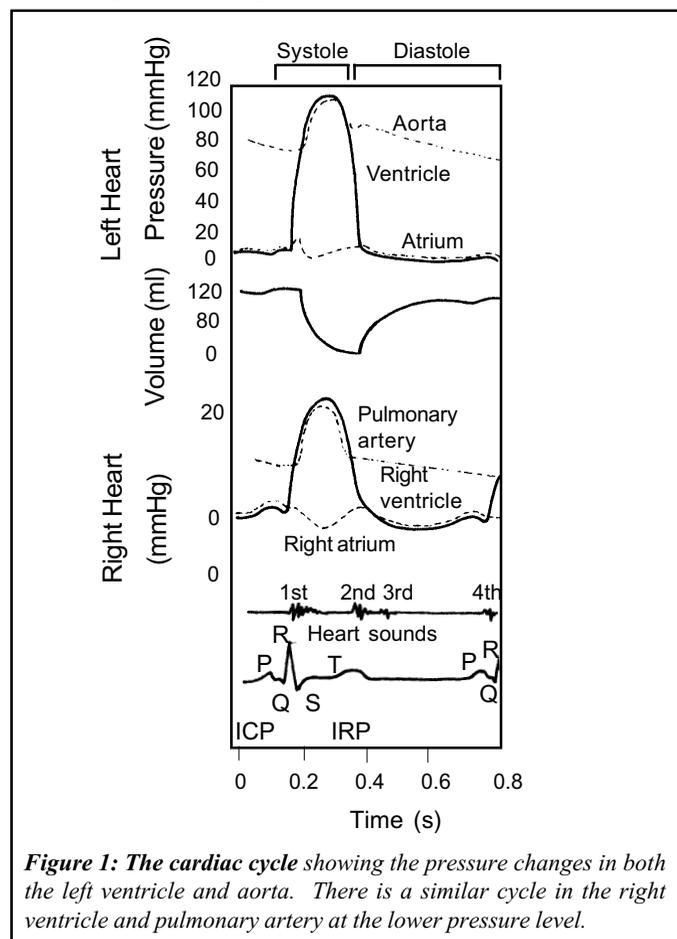


Figure 1: The cardiac cycle showing the pressure changes in both the left ventricle and aorta. There is a similar cycle in the right ventricle and pulmonary artery at the lower pressure level.

The coronary circulation

Myocardial blood supply is from the right and left coronary arteries, which run over the surface of the heart giving branches to the endocardium (the inner layer of the myocardium). Venous drainage is mostly via the coronary sinus into the right atrium, but a small proportion of blood flows directly into the ventricles through the Thebesian veins, delivering unoxygenated blood to the systemic circulation. Oxygen extraction by the tissues is dependent on consumption and delivery. Myocardial oxygen consumption is higher than in skeletal muscle (65% of arterial oxygen is extracted as compared to 25%). Therefore any increased myocardial metabolic demand must be matched by increased coronary blood flow. This

is a local response, mediated by changes in coronary arterial tone, with only a small input from the autonomic nervous system.

Teaching point

Coronary blood flow occurs mostly during diastole, because during systole the blood vessels within the myocardium are compressed. Increased heart rates, which reduce the time for diastolic filling, can reduce myocardial blood supply and cause ischaemia. In heart failure, the ventricle is less able to empty and therefore the intraventricular volume and pressure is higher than normal. During diastole, this pressure is transmitted to the ventricular wall and opposes and reduces coronary flow, especially in the endocardial vessels.

Cardiac Output

Cardiac output (CO) is the product of heart rate (HR) and stroke volume (SV): $CO = HR \times SV$

For a 70kg man normal values are HR=70/min and SV=70ml, giving a cardiac output of about 5litre/min. The cardiac index is the cardiac output per square metre of body surface area - normal values range from 2.5-4.0 litre/min/metre.square.

Heart rate is determined by the rate of spontaneous depolarisation at the sinoatrial node (see above), but can be modified by the autonomic nervous system. The vagus nerve acts on muscarinic receptors to slow the heart, whereas the cardiac sympathetic fibres stimulate beta-adrenergic receptors and increase heart rate.

Stroke volume is determined by three main factors: *preload*, *afterload* and *contractility*. These will be considered in turn:

Preload is the ventricular volume at the end of diastole. An increased preload leads to an increased stroke volume. Preload is mainly dependent on the return of venous blood from the body. Venous return is influenced by changes in position, intra-thoracic pressure, blood volume and the balance of constriction and dilatation (tone) in the venous system. The relationship between ventricular end-diastolic volume and stroke volume is known as **Starling's law of the heart**, which states that the energy of contraction of the muscle is related/proportional to the initial length of the muscle fibre. This is graphically illustrated in Figure 2 by a series of "Starling curves". As volume at the end of diastole (*end-diastolic volume*) increases and stretches

the muscle fibre, so the energy of contraction and stroke volume increase, until a point of over-stretching when stroke volume may actually decrease, as in the failing heart. Cardiac output will also increase or decrease in parallel with stroke volume **if there is no change in heart rate**. The curves show how the heart performs at different states of *contractility*, ranging from the normal heart to one in cardiogenic shock. This is a condition where the heart is so damaged by disease that cardiac output is unable to maintain tissue perfusion. Also shown are increasing levels of physical activity which require a corresponding increase in cardiac output.

Afterload is the resistance to ventricular ejection. This is caused by the resistance to flow in the systemic circulation and is the **systemic vascular resistance**. The resistance is determined by the diameter of the arterioles and pre-capillary sphincters; the narrower or more constricted, the higher the resistance. The level of systemic vascular resistance is controlled by the sympathetic system which, in turn, controls the tone of the muscle in the wall of the

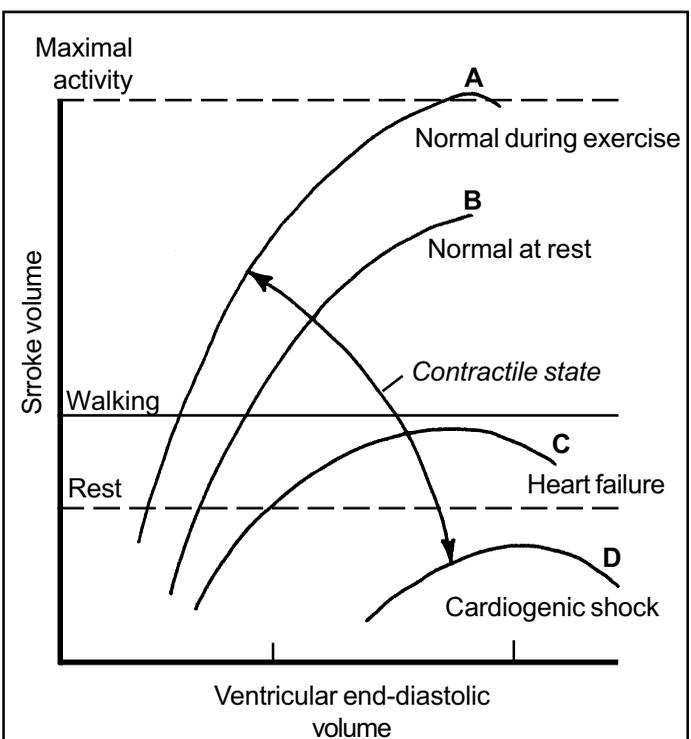


Figure 2. Starling's Law of the Heart - Curves A&B illustrate the rise in cardiac output with increases in ventricular end-diastolic volume (*pre-load*) in the normal heart. Note that with an increase in contractility there is a greater cardiac output for the same ventricular end-diastolic volume. In the diseased heart (C & D) cardiac output is less and falls if ventricular end diastolic volume rises to high levels, as in heart failure or overload.

arteriole, and hence the diameter. The resistance is measured in units of $\text{dyne}\cdot\text{sec}/\text{cm}^5$. A series of Starling curves with differing afterloads is shown in Figure 3, demonstrating a fall in stroke volume as afterload increases. The relationship between systemic vascular resistance and the control of arterial pressure is discussed below.

Contractility describes the ability of the myocardium to contract in the absence of any changes in preload or afterload. In other words, it is the “power” of the cardiac muscle. The most important influence on contractility is the sympathetic nervous system. Beta-adrenergic receptors are stimulated by noradrenaline released from nerve endings, and contractility increases. A similar effect is seen with circulating adrenaline and drugs such as ephedrine, digoxin and calcium. Contractility is reduced by acidosis, myocardial ischaemia, and the use of beta-blocking and anti-arrhythmic agents.

Cardiac output will change to match changing metabolic demands of the body. The outputs of both ventricles must be identical, and also equal the venous return of blood from the body. The balancing of cardiac output and venous return is illustrated during the response to exercise. Blood vessels dilate in exercising muscle groups because of increased metabolism, and blood flow increases. This

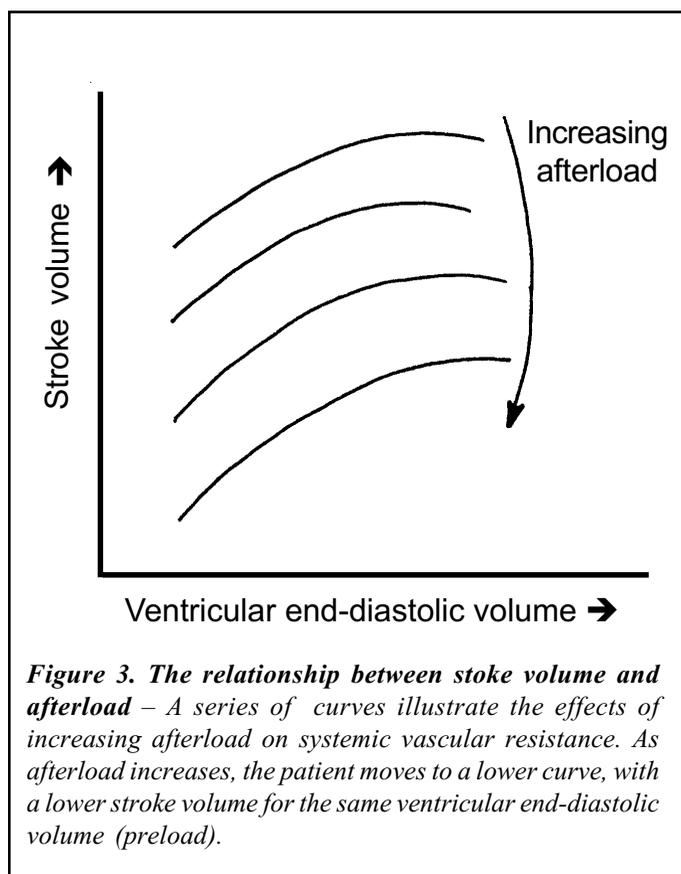


Figure 3. The relationship between stroke volume and afterload – A series of curves illustrate the effects of increasing afterload on systemic vascular resistance. As afterload increases, the patient moves to a lower curve, with a lower stroke volume for the same ventricular end-diastolic volume (preload).

increases venous return and right ventricular preload. Consequently more blood is delivered to the left ventricle and cardiac output increases. There will also be increased contractility and heart rate from the sympathetic activity associated with exercise, further increasing cardiac output to meet tissue requirements.

Teaching point

A pulmonary artery catheter can measure pressures in the right heart as it is *float*ed into position. The catheter includes a small balloon which is transiently inflated to *wedge* it into a small pulmonary artery, occluding pulmonary arterial flow. This will give a characteristic waveform, and it is assumed that the measured pressure equals that in the left atrium. The catheter can also be used to measure cardiac output. However, in the absence of such monitoring, clinical examination gives a good indication of cardiac function. Skin temperature, capillary refill*, pulse rate and volume, urine output and level of consciousness are reliable markers of cardiac output, and are easily assessed.

**Capillary refill*- when pressure is applied to skin or a finger nail, it goes white. When the pressure is released, the colour rapidly returns within 2-3 seconds. This is capillary refill, and is prolonged when the peripheral circulation is poor due to hypovolaemia or a poor cardiac output.

THE SYSTEMIC CIRCULATION

The systemic blood vessels are divided into arteries, arterioles, capillaries and veins. Arteries supply blood to the organs at high pressure, whereas arterioles are smaller vessels with muscular walls which allow direct control of flow through each capillary bed. Capillaries consist of a single layer of endothelial cells, and the thin walls allow exchange of nutrients between blood and tissue. Veins return blood from the capillary beds to the heart, and contain 70% of the circulating blood volume, in contrast to the 15% in the arterial system. Veins act a reservoir, and venous tone is important in maintaining the return of blood to the heart, for example in severe haemorrhage, when sympathetic stimulation causes venoconstriction.

Blood flow

The relationship between flow and driving pressure is given by the **Hagen-Poiseuille** formula. This states that flow rate in a tube is proportional to:

$$\frac{\text{Driving pressure} \times \text{Radius}^4}{\text{Length} \times \text{Viscosity}}$$

In blood vessels flow is pulsatile rather than continuous, and viscosity varies with flow rate, so the formula is not strictly applicable, but it illustrates an important point; small changes in radius result in large changes in flow rate. In both arterioles and capillaries changes in flow rate are brought about by changes in tone and therefore vessel radius.

Viscosity describes the tendency of a fluid to resist flow. At low flow rates the red blood cells stick together, increasing viscosity, and remain in the centre of the vessel. The blood closest to the vessel wall (which supplies side branches) therefore has a lower haematocrit. This process is known as *plasma skimming*. Viscosity is reduced in the presence of anaemia, and the resulting increased flow rate helps maintain oxygen delivery to the tissues.

Control of the systemic circulation

Arteriolar tone determines blood flow to the capillary beds. A number of factors influence arteriolar tone, including *autonomic control*, *circulating hormones*, *endothelium derived factors* and the local concentration of *metabolites*.

Autonomic control is largely by the sympathetic nervous system, which supplies all vessels except capillaries. Sympathetic fibres arise from the thoracic and lumbar segments of the spinal cord. These are under the control of the **vasomotor centre** in the medulla, which has distinct vasoconstrictor and vasodilator areas. Although there is a baseline sympathetic discharge to maintain vascular tone, increased stimulation affects some organs more than others (Figure 4). This tends to redistribute blood from skin, muscle and gut to brain, heart and kidney. Increased sympathetic discharge is one of the responses to hypovolaemia, for example in severe blood loss, with the effect of protecting blood supply to the vital organs. The predominant sympathetic influence is vasoconstriction via alpha-adrenergic receptors. However, the sympathetic system also causes vasodilation via beta adrenergic and cholinergic receptor stimulation, but only in skeletal muscle.

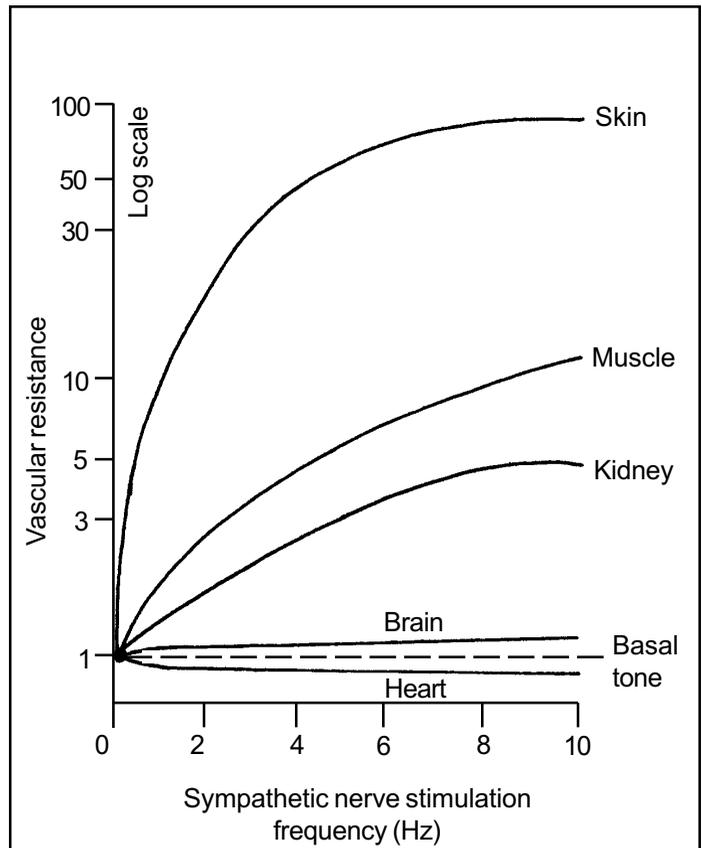


Figure 4. The effects of sympathetic nervous stimulation on vascular resistance in different organs – Note that for the same sympathetic stimulation, the resistance is higher in skin than in the kidney, thus helping to preserve the flow to the kidney.

This increased blood flow to muscle is an important part of the “fight or flight” reaction, when exercise is anticipated.

Circulating hormones such as adrenaline and angiotensin II are potent vasoconstrictors, but they probably have little effect on acute cardiovascular control. In contrast, *endothelium derived factors* play an important role in controlling local blood flow. These substances are either produced or modified in the vascular endothelium, and include prostacyclin and nitric oxide, both potent vasodilators. An accumulation of *metabolites* such as CO₂, K⁺, H⁺, adenosine and lactate causes vasodilation. This response is probably an important mechanism of *autoregulation*, the process whereby blood flow through an organ is controlled locally, and remains constant over a wide range of perfusion pressure. Autoregulation is a particular feature of the cerebral and renal circulations.

Control of arterial pressure

Systemic arterial pressure is controlled closely in order to maintain tissue perfusion. The **mean arterial pressure (MAP)** takes account of pulsatile blood flow in the arteries,

and is the best measure of perfusion pressure to an organ. MAP is defined:

$$\text{MAP} = \text{Diastolic arterial pressure} + \frac{\text{pulse pressure}}{3}$$

where pulse pressure is the difference between systolic and diastolic arterial pressure.

MAP is the product of cardiac output (CO) and systemic vascular resistance (SVR):

$$\text{MAP} = \text{CO} \times \text{SVR}$$

If cardiac output falls, for example when venous return decreases in hypovolaemia, MAP will also fall unless there is a compensatory rise in SVR by vasoconstriction of the arterioles. This response is mediated by **baroreceptors**, which are specialised sensors of pressure located in the carotid sinus and aortic arch, and connected to the vasomotor centre. A fall in blood pressure causes reduced stimulation of the baroreceptors, and consequent reduced discharge from the baroreceptors to the vasomotor centre. This causes an increase in sympathetic discharge leading to vasoconstriction, increased heart rate and contractility, and secretion of adrenaline. Conversely, rises in blood pressure stimulate the baroreceptors, which leads to increased parasympathetic outflow to the heart via branches of the vagus nerve, causing slowing of the heart. There is also reduced sympathetic stimulation to the peripheral vessels causing vasodilation. Baroreceptor responses provide immediate control of blood pressure; if hypotension is prolonged, other mechanisms start to operate, such as the release of angiotensin II and aldosterone from the kidneys and adrenal glands, which leads to salt and water being retained in the circulation.

Cardiovascular responses to anaesthesia

All anaesthetic agents have a direct depressant effect on the myocardium. Therefore they reduce myocardial contractility, and many also reduce sympathetic stimulation of the vascular system. The result is a decreased cardiac output accompanied by vasodilation, causing hypotension. This fall in blood pressure can compromise perfusion of vital organs, especially at induction of anaesthesia in the hypovolaemic patient. In **contrast**, agents such as **ketamine** and **ether** increase sympathetic activity, which opposes the direct depressant

Teaching point

The *Valsalva manoeuvre* is a simple test of the baroreceptor reflex. The patient tries to breathe out forcefully against a closed larynx - "straining" - resulting in an increased intrathoracic pressure. This causes decreased venous return, cardiac output and a fall in blood pressure leading to reduced baroreceptor discharge to the vasomotor centre. This then causes peripheral vasoconstriction, and an increase in heart rate which is the normal response. This has the effect of maintaining *systolic* pressure, although the *pulse* pressure is reduced due to vasoconstriction.

effect. Thus cardiac output and blood pressure are maintained despite the direct myocardial depressant action.

Volatile anaesthetic agents reduce discharge from the sinoatrial node. This can lead to *junctional* rhythms, when the atrioventricular node takes over as pacemaker, associated with an absent P wave on the ECG. Local anaesthetic agents depress conduction of the cardiac impulse. This effect can be therapeutic, for example in the treatment of ventricular arrhythmias with lignocaine. However, at higher concentrations local anaesthetics can cause cardiac arrest - it is vital to avoid accidental intravenous injection when using these agents.

Controlled ventilation in a paralysed patient has many effects. Firstly it increases intrathoracic pressure which reduces venous return and preload, causing a fall in cardiac output. Secondly, changes in the partial pressure of carbon dioxide (PaCO₂) resulting from changes in ventilation will also have cardiovascular effects. A low PaCO₂, which commonly occurs during controlled ventilation, causes peripheral vasoconstriction by a direct effect. This increases systemic vascular resistance, increases afterload and can result in a fall in cardiac output. It also causes cerebral vasoconstriction, reducing cerebral blood volume (**Neurophysiology**, Update in Anaesthesia 1998). A high PaCO₂ usually occurs in the anaesthetised patient during spontaneous breathing, and causes vasodilation and increased sympathetic activity, leading to increased cardiac output. However, the heart will be more likely to develop arrhythmias, particularly when using volatile agents.

Spinal and epidural anaesthesia blocks sympathetic nerves as well as sensory and motor fibres. This can lead to marked hypotension due to arteriolar and venous dilation because the sympathetic nerves to the lower extremities are blocked. Cardiac sympathetic nerve fibres, which arise

from the high thoracic spinal cord, may also be blocked, allowing an unopposed vagal action on the heart. In this case there will not be an appropriate increase in cardiac output, and blood pressure will fall further with a bradycardia.

Teaching point

For patients with coronary artery disease, it is important to use an anaesthetic technique which does not cause further myocardial ischaemia. The important principle is to ensure that *myocardial oxygen supply* is greater than *myocardial oxygen demand*. The balance between these two variables is influenced by the following factors:

Myocardial oxygen supply

Heart rate

Diastolic time

Coronary perfusion pressure

Aortic diastolic blood pressure

Ventricular end-diastolic blood pressure

Arterial oxygen content

Arterial oxygen partial pressure

Haemoglobin concentration

Coronary artery diameter

Myocardial oxygen demand

Heart rate

Ventricular wall tension

Preload

Afterload

Contractility